Complex distributions of residual stress and strain in the mouse left ventricle: experimental and theoretical models

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Abstract Most soft biological tissues, including ventricular myocardium, are not stress free when all external loads are removed. Residual stress has implications for mechanical performance of the heart, and may be an indicator of patterns of regional growth and remodeling. Cross-sectional rings of arrested ventricles opened up when a radial cut was made (initial mean opening angles were $64 \pm 17^\circ$), but further circumferential cuts revealed the presence of additional residual stresses in the tissue with further opening of the rings. In normal mouse hearts, the inner half of a short-axis ring opened more than the outer half, and this change was dependent on apex–base location. At the apex the inner section vs. outer section opening angles were $226 \pm 47^\circ$ vs. $89 \pm 28^\circ$, while at the base the same two angles were $160 \pm 30^\circ$ vs. $123 \pm 35^\circ$. A simple theoretical cylindrical shell model with incompressible hyperelastic material properties was used to model the experimental deformations based on the cutting experiments. The model predicts different residual stress fields depending on the nature of the opening after the circumferential cut (which is done after the conventional radial cut). The observed opening angles were consistent with steep stress gradients near the endocardium compared with those predicted if the first cut was assumed to relieve all residual stresses. These results imply a more complex distribution of residual stress and strain in ventricular myocardium than previously thought.

Introduction Residual stress in organs has implications not only for stress gradients in the tissue, but also for growth and remodeling (Fung 1991; Lin and Taber 1995; Rodriguez et al. 1994; Taber and Humphrey 2001). In the heart, it has been proposed that residual stresses are one mechanism by which the normal left ventricle maintains optimal function in terms of fiber stress (Guccione et al. 1991; Taber 1991). Residual stress can also play a role in remodeling during disease. For example, altered residual stress in the heart may be a beneficial adaptation to the mechanical alterations seen in the osteogenesis imperfecta murine model of type I collagen deficiency (Weis et al. 2000), and it could play a role in ventricular geometric remodeling (Kresh and Wechsler 1998; Omens et al. 1998).

It is thought that a biological material can only be truly "stress free" if a large number of cuts are made to relieve all of the residual stress that may exist at the microscopic level (Fung 1990). In the heart and arteries, it is generally assumed that a single radial cut across an axial section of tissue relieves most of the residual stress, and most theoretical and computational analyses have made this assumption (Chuong and Fung 1986; Omens and Fung 1990). Although the material near the cut edge...
will have no residual circumferential stress, we show that significant residual stress still exists in much of the ring after a radial cut is made in the mouse myocardium used in the present study. Indeed, further stress is relieved by making a circumferential cut after the radial cut. A modeling analysis shows that these secondary cuts reveal significantly different, and possibly much more complex, distributions of residual stress and strain than those predicted from models with a single radial cut.

Methods

Measuring the stress-free state of the tissue

Protocols for arresting the mouse heart have been given previously (Omens et al. 1994), and were performed according to the National Institutes of Health “Guide for the Care and Use of Laboratory Animals”. Animal protocols were approved by the UCSD Animal Care Subjects Committee. Swiss mice were anesthetized with 8 mg/kg xylazine, 100 mg/kg ketamine IP. The chest was opened, the ascending aorta clamped, and the heart was arrested by injecting up to 0.3 ml of a hypothermic, hyperkalemic cardioplegic solution through the apex into the left ventricle. The arresting solution contained in g/l, NaCl 4.0, KCl 2.2, NaHCO$_3$ 1.0, glucose 2.0, 2,3 butaneidine monoxide 3.0, plus heparin (10,000 U/l). The arrested heart was excised and rinsed in arresting solution and weighed.

Following procedures used previously to define the stress-free state of the left ventricle (Omens and Fung 1990; Omens et al. 1994), rings of tissue were cut perpendicular to the long axis of the heart, approximately 1–2 mm thick. Two rings were taken from each heart, one immediately above the equator (largest diameter) and one below, termed the basal and apical rings, respectively. These intact rings were imaged with a digital camera (Nikon Coolpix 950, 3 M Pixel) and saved on a PC computer for later analysis. Each ring was then cut radially and imaged. The radial cut was made opposite the center of the right ventricle, at the center of the LV free wall (Omens and Fung 1990). Finally, the open rings were cut parallel to the epicardium along the circumference at the midwall to produce 2 open arcs of tissue from each original ring. These are referred to as the epicardial and endocardial rings. The right ventricle was left intact on the epicardial ring. All tissue sections were submerged in a small dish filled with cardioplegic solution during imaging. In several hearts, time series images were taken after the initial cuts to determine if the geometry of the slices changed over time.

From the digital images in the intact slices, measurements were made of left ventricular wall thickness and left ventricular chamber radius. As in previous publications, the opening angles were measured in all slices using the center of the intact left ventricle as the vertex of the opening angle (Omens and Fung 1990). This same definition was used for slices with an opening angle greater than 180° – the vertex of the opening angle was always on the “endocardial” side of the slice, taken to be where the center of the left ventricle would have been. Angles were averaged for each location and mean comparisons made with a Student’s $t$-test.

Modeling the experiment

To analytically calculate the residual stress from our opening angle data, we would need to know the precise material properties of myocardium as well as any strain components that are out of the plane of our slice. These quantities are presently unattainable. In lieu of such, we use a simple model that provides insight into how certain residual-stress fields could give rise to the behavior that we observe. Our model (Fig. 1) consists of 100 concentric cylindrical shells (shell number 1 and 100 are innermost and outermost, respectively) with the same thickness $H$ and length $Z$, but with different radii ($R_i$ is the average radius of shell $i$). Let $R_c$ be the central radius, $H_{tot}$ be the total thickness of the ring, and $\alpha$ be thickness-to-radius ratio (i.e., $H_{tot}/R_c$) (we do not consider rings without a central hole (i.e., $\alpha = 2$) and hence $\alpha < 2$ herein). Consequently,

$$R_i = R_c \left(1 + \frac{2i - 101}{200} \alpha\right), \quad H = \frac{\alpha R_c}{100}$$

We use a value of $\alpha = 2/3$ based on intact mouse heart geometry (Omens et al. 2002), and we keep the equations in terms of $\alpha$. We consider $Z$ to be small enough that a plane stress assumption in the plane of the ring is valid. In so doing, it is not necessary to choose a particular value for $Z$. In this theoretical analysis, cut 1 is the radial cut and cut 2 is the circumferential cut.

The reference configuration is one with an intact ring, and all strains are referred to this intact reference. A Cartesian coordinate system is defined as follows (and depicted in Fig. 1): coordinate directions $e_1$ and $e_2$ are in the plane of the ring with $e_1$ parallel to cut 1 and $e_2$ perpendicular to it; direction $e_3$ is axial or out of the plane of the ring. The assumed deformation is constrained so that there is no warping of radial segments (i.e., a radial segment in the reference configuration is a straight