RADIAL VARIATION IN RESIDUAL STRESS IN MOUSE LV IS LIKELY TO BE HIGHLY NONLINEAR

John C. Criscione (1), Jeffrey H. Omens (2), Andrew D. McCulloch (2)

(1) Department of Biomedical Engineering
Texas A&M University
College Station, TX

(2) Department of Bioengineering
University of California San Diego
La Jolla, CA

INTRODUCTION

Residual stress in organs has implications not only for stress gradients in the tissue, but also for growth and remodeling [1-3]. 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 [4,5]. 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 [6], and it could play a role in ventricular geometric remodeling [7,8].

Residual strain inherently does not satisfy compatibility, and 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 which may exist at the microscopic level. Yet, in the heart and arteries, it is generally assumed that a single radial cut across an axial section of tissue relieves all of the residual stress, and most theoretical and computational analyses have made this assumption [9,10]. 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 cut reveals significantly different, and possibly much more complex, distributions of residual stress and strain than those predicted from models with a single radial cut.

METHODS

Expermental

Protocols for arresting the mouse heart have been given previously [11], and were performed according to the NIH *Guide for the Care and Use of Laboratory Animals*. Animal protocols were approved the by the UCSD Animal Care Subjects Committee. Full methods for this analysis will be published shortly [12].

Briefly, Swiss mice were anesthetized, the heart was arrested and excised. Following procedures used previously to define the stress-free state of the left ventricle [9,11], rings of tissue were cut perpendicular to the long axis of the heart, approximately 1-2 mm thick. A radial cut (referred to hereafter as **cut 1**) was made opposite the center of the right ventricle, at the center of the LV free wall [9]. Next, the open rings were cut parallel to the epicardium along the circumference at the midwall (reffered to hereafter as **cut 2**) to produce 2 open arcs of tissue from each original ring. The epicardial and endocardial halves are referred to as the outer and inner arcs, respectively. The right ventricle was left intact on the epicardial side. All tissue sections were submerged in a small dish filled with BDM containing cardioplegic solution during imaging. In several hearts, time series images were taken after the initial cuts to determine if the geometry changed over time. Opening angles were measured in all slices using the center of the intact left ventricle as the vertex of the opening angle [9]. Angles were averaged for each location and mean comparisons made with a Student's t-test.

Computational

Briefly (see [12] for details), these excised heart rings were modeled as 100 concentric, cylindrical shells of arbitrary yet short length with plane stress assumed (i.e., z-component stresses are zero). Four separate (cases 1-4) profiles of residual hoop stress were chosen with each having an opening angel of 65 after cut 1 (see Figure 1). Qualitatively, these profiles are: 1) highly nonlinear near epi and endo, 2) highly nonlinear near endo, 3) highly nonlinear near epi, and 4) nearly constant near epi and endo. The material of each shell was incompressible and had the same shear modulus μ multipling the square of the magnitude of Green strain in W, the strain energy per unit reference volume. Strains were referred to the intact reference configuration. The deformation was constrained such that radial sections remain planar, or equivalently, so that the strain only depends on initial radius—no hoop or axial dependence. Although not valid near the edges of cut 1 (because of warping), this assumption is good in the region opposite the cut. Moreover, the curvature opposite cut 1 is the primary determinate of opening angle. By dividing the residual hoop stress by μ, the problem was non-dimensionalized for any thickness to radius ratio (2/3 was used herein).

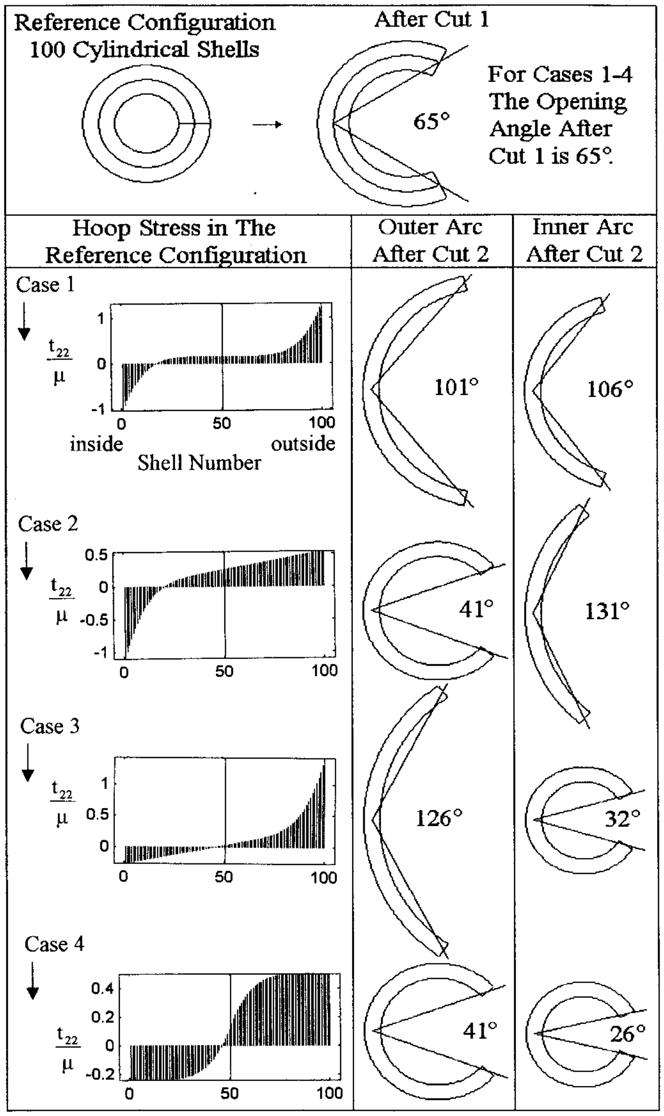

Figure 1. Top panel: reference configuration and opening angle after cut 1 for cases 1-4 of the computational model. Bottom panel: residual hoop stress and opening angle of outer and inner arc after cut 2 for the separate cases.

RESULTS

Experimental

In 8 mice, average body weight was 31.3±1.3 g, and heart weight was 0.158±0.018 g. Inner diameters for the basal and apical rings were 1.5±0.3 and 1.7±0.5 mm, and corresponding wall thicknesses were 1.8±0.2 and 1.7±0.2 mm. Previous studies have shown that opening angles increase with contracture [9]. There were small increases in the opening angles with time, indicating the effects of contracture were small. On average the opening angle increased by <10% in the first 2 minutes after cutting. The initial opening angle after the first radial cut was 64±17° (n=16) for all of the sections. There was no significant difference in initial opening angle between the apical and basal rings (65±18° vs. 63±17°). After the circumferential cut, all rings had larger opening angles, but the opening pattern was different in the apical and basal rings. At the apex the inner vs. outer arc angles were 226±47° vs. 89±28°, while at the base they were 160±30° vs. 123±35°.

Computational

Although each case has an initial opening angle of 65º, the motion after cut 2 is very different (Fig. 1). The initial opening angle depends primarily on the moment alone rather than on the distribution of the residual hoop stress. The angles after cut 2, however, are greatly dependent on the residual stress distribution. In general, if the compression-hoop-stress is concentrated toward the innermost part of the intact ring (cases 1 & 2), then the inner ring will open after cut 2. If the compression-hoop-stress is more uniformly distributed on the inner half (cases 3 & 4) then the inner ring will close. Likewise for the tension-hoop-stress, if it is concentrated toward the outer radii (cases 1 & 3), then the outer ring will open, and if it is uniformly distributed on the outer half (cases 2 & 4) then the outer ring will close.

DISCUSSION

A single radial cut can provide insight into the stress-free state of tubular tissue, but the current results indicate that this procedure may not give a complete description of residual stresses. Indeed, a second cut can be a more sensitive indicator of residual stress. Differences in the endo and epi strips in normal hearts indicate that the distribution of residual stress may not be linearly distributed wrt radius. The current mathematical model is limited in its application to the myocardium, but does give insight into the general issues. Based on the current analysis, the residual stress distribution appears to be more like case 2 of the theoretical analysis. In particular, our results suggest that there may be a much larger gradient of hoop stress near the endocardium—especially on the apical side of the equator of the left ventricle.

A mathematical analysis of this problem is also in [4]. Therein, a linear residual hoop stress is assumed, and a single radial cut does not release all stress because of material nonlinearity. Here we present the compliment—nonlinear residual hoop stress with linear material properties. In actually, nonlinearities in both the residual stress and material properties are present and likely significant.

REFERENCES

[1] Fung YC. 1991. What are the residual stresses doing in our blood vessels? Ann Biomed Eng 19: 237-249.
[2] Lin IE, Taber LA. 1995. A model for stress-induced growth in the developing heart. J Biomech Eng 117: 343-349.
[3] Taber LA, Humphrey JD. 2001. Stress-modulated growth, residual stress, and vascular heterogeneity J Biomech Eng 123: 528-535.
[4] Guccione JM, McCulloch AD, Waldman LK. 1991. Passive material propreties of intact ventricular myocardium determined from a cylindrical model. J Biomech Eng 113: 42-55.
[5] Taber LA. 1991. On a nonlinear theory for muscle shells: II. application to the active left ventricle. J Biomech Eng 113: 63-71.
[6] Weis SM, et al. 2000. Myocardial mechanics and collagen structure in the … (oim). Circ Res 87: 663-669.
[7] Omens JH. 1998. Stress and strain as regulators of myocardial growth. Progress Biophys. Mol. Bio. 69: 559-572.
[8] Kresh JY, Wechsler AS. 1998. Heart reduction surgery can reconstitute the residual stress-train state of the left ventricle. J Thorac Cardiovasc Surg 116: 1084-1086.
[9] Omens JH, Fung YC. 1990. Residual strain in rat left ventricle. Circ Res 66: 37-45.
[10] Chuong CJ, Fung YC. 1986. On residual stress in arteries. J Biomech Eng 108: 189-192.
[11] Omens JH, Rockman HA, Covell JW. 1994. Passive ventricular mechanics in tight-skin mice. Am J Physiol 266: H1169-H1176.
[12] Omens JH, McCulloch AD, Criscione JC. Complex distribution of residual stress and strain …, Accepted to Biomechanics and Modeling in Mechanobiology.