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STRESS-DEPENDENT FINITE GROWTH IN SOFT ELASTIC TISSUES

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Abstract—Growth and remodeling in tissues may be modulated by mechanical factors such as stress. For example, in cardiac hypertrophy, alterations in wall stress arising from changes in mechanical loading lead to cardiac growth and remodeling. A general continuum formulation for finite volumetric growth in soft elastic tissues is therefore proposed. The shape change of an unloaded tissue during growth is described by a mapping analogous to the deformation gradient tensor. This mapping is decomposed into a transformation of the local zero-stress reference state and an accompanying elastic deformation that ensures the compatibility of the total growth deformation. Residual stress arises from this elastic deformation. Hence, a complete kinematic formulation for growth in general requires a knowledge of the constitutive law for stress in the tissue. Since growth may in turn be affected by stress in the tissue, a general form for the stress-dependent growth law is proposed as a relation between the symmetric growth-rate tensor and the stress tensor. With a thick-walled hollow cylinder of incompressible, isotropic hyperelastic material as an example, the mechanics of left ventricular hypertrophy are investigated. The results show that transmurally uniform pure circumferential growth, which may be similar to eccentric ventricular hypertrophy, changes the state of residual stress in the heart wall. A model of axially loaded bone is used to test a simple stress-dependent growth law in which growth rate depends on the difference between the stress due to loading and a predetermined growth equilibrium stress.

INTRODUCTION

Growth and remodeling are fundamental mechanical processes both in the normal development of tissues and in various pathological conditions. Mechanical quantities such as the stress and strain in the tissue can modulate its growth. For example, cardiac and vascular hypertrophy are thought to be due, at least in part, to increased wall stress (Fung, 1990; Grossman, 1980). It is also well known that growth and remodeling in long bone are affected by the state of stress in the limb (Carter and Hayes, 1977; Cowin, 1983, 1986; Guo and Cowin, 1992). Indeed, considerable progress has been made in developing models of growth and remodeling in bone and cartilage. Cowin (1985) developed an analytical description of the microstructural evolution of fibrous tissues and bone in terms of a fabric tensor. They made theoretical predictions for diaphyseal surface remodeling and internal remodeling of bones (Cowin and Firoozbakhsh, 1981). More recently, Firoozbakhsh and Aleyaasin (1989) studied the effects of stress concentrations in internal bone remodeling, and Guo and Cowin (1992) studied surface growth under torsional loading. Hart (1990) developed a finite element analysis for adaptive elastic materials and studied the time course of strain-induced surface remodeling. Harrigan and Hamilton (1992) determined the conditions required for the stability of strain energy based laws for bone remodeling. In contrast to the extensive work on bones, very little has been done on modeling the relationship between stress, strain and growth in soft tissues, probably because they usually exhibit large elastic deformations under physiological loading and because soft tissues, unlike bones, may be residually stressed.

One of the first applications of continuum mechanics to the study of growth in deformable tissues was a model of homogeneous stress-dependent growth for linearly elastic materials developed by Hsu (1968). Later, a continuum description of finite growth kinematics was formulated by Skalak (1981) and Skalak *et al.* (1982). They examined volumetric growth, growth by accretion on surfaces and growth fields with discontinuities. Skalak (1981) pointed out that if the growth strain is incompatible, for example if the growth of the different cells comprising a body occurs in such a manner that the continuity of the body is compromised, continuity may be maintained by an elastic stress. Therefore, residual stress occurs as a result of the elastic deformation required to keep all cells continuous with each other without introducing gaps or superpositions. The fundamental importance of residual stress in intact tissues was demonstrated by Fung (1990) in blood vessels. The presence of a residual stress field can be identified if deformation occurs when cuts are made in the unloaded tissue. Using this experimental approach, Fung and coworkers have shown the existence of residual stress in arteries (Choung and Fung, 1986; Liu and Fung, 1988), veins (Xie *et al.*, 1991), ventricular myocardium (Omens and Fung, 1990) and trachea (Han and Fung, 1991). The deformation that returns the cut state of the tissue to

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the residually stressed, intact state defines the 'residual strain'. Fung (1990) suggests that changes in the residual strain reveal the effects of nonuniform growth and remodeling. He measured changes in residual strain in blood vessels by measuring the opening angles that resulted when rings dissected from blood vessels were cut across the wall relieving circumferential residual stress. Remodeling after infrarenal aortic banding in the rat correlated with significant changes in residual strain.

Stress in a tissue may not only be caused or altered by growth, but it may also affect the growth itself. Grossman (1980) proposed that cardiac hypertrophy and normal cardiac growth develop in response to increased hemodynamic loading and altered systolic and diastolic wall stresses. He suggested that the resulting patterns of hypertrophy reflect the nature of the stress changes. A variety of laws for growth as a function of stress, strain or strain energy have been proposed for bone (Cowin, 1983). For soft tissues, Fung (1990) proposed an equation for the mass rate of growth as a function of some suitable measure of the stress. In his formulation, growth or resorption occur so that the stress due to loading in the tissue returns to one of three equilibrium states. Around one of these equilibrium states, if loading stress is high, then growth occurs to reduce stress. If the stress is lower than the equilibrium state, then resorption takes place. However, if the stress is too high or too low, one of the other two equilibrium states governs growth. In this case, high stresses may lead to resorption as may occur, for example, around a stress concentration in bone. Similar ideas have also been proposed by Pauwels (1980) for bone. However, growth is a three-dimensional process whose rate is only fully described by a tensor measure and not a single scalar growth rate. Since the stress is also a tensor in the three-dimensional body, a general formulation for stress-dependent growth requires a tensorial constitutive relation. The form of this relation and the conditions restricting it have not been previously described.

A general continuum formulation for growth must therefore allow for the possibility of residual stress arising from growth, and should not rely on the existence of a global zero-stress state. Moreover, since the kinematics of growth cannot always be separated from the stress in the tissue, the constitutive law for stress in the tissue will generally be required. The purpose of this paper is to develop a general three-dimensional theory for the continuum mechanics of finite volumetric growth in soft elastic tissues. This theory may be useful for studying the relationship between stress and normal tissue growth or pathologic growth such as cardiac hypertrophy.

METHODS

In this section, the kinematics of finite growth are introduced using the notation of finite deformations. In general, the shape change that occurs during the growth of an unloaded body is due to two processes: (1) material may be added or removed, changing the local stress-free reference state of the tissue; (2) an elastic deformation may be required to accommodate this change in tissue configuration and volume in order to make the total growth deformation compatible (i.e. so that the material can undergo the growth without introducing discontinuities in the body). Residual stress arises from the elastic part of the total deformation. Therefore, in our description of growth kinematics, the total shape change during growth is decomposed into these two parts: the change in tissue stress-free reference state and the elastic deformation. The dependence of the growth rate tensor on the stress tensor is also examined in this section and a general constitutive law for stress-dependent growth is formulated. Finally, we give two examples of finite growth in three-dimensional elastic bodies with possible applications to ventricular hypertrophy and connective tissue.

To analyze the kinematics of growth, we define the volumetric growth of a soft elastic tissue as the change in the local zero-stress state of the body without requiring that there exists a corresponding global zero-stress state. Let $B(t_0)$ denote a stress-free body at time t_0. We will see later that the analysis generalizes directly for the case when $B(t_0)$ is not stress-free when it is unloaded. The body may change in shape, density and material properties with time as it grows and remodels in the absence of any external loads. Let it grow into a new stress-free state, $B(t_1)$. The mass rate of growth per unit tissue volume V at a point is defined by

$$\dot{m}=\frac{\mathrm{d}(\rho V)}{\mathrm{d}t}. \tag{1}$$

If ρ, the mass density, is constant with time then

$$\dot{m}=\rho\frac{\mathrm{d}V}{\mathrm{d}t}. \tag{2}$$

Conservation of mass (Spencer, 1980) requires that

$$\dot{m}=\frac{\partial\rho}{\partial t}+\mathrm{div}(\rho\,\mathbf{v}), \tag{3}$$

where $\mathbf{v}$ is the growth velocity vector (Skalak *et al.*, 1982), which represents the rate and direction of motion at each point in the tissue during growth. Skalak suggested that velocity fields are useful for describing growth because they embody the continuous growth rate rather than discrete changes. Cowin (1983), Cowin and Firoozbakhsh (1981) and Luo *et al.* (1991) used growth velocities to describe surface remodeling in bone as a function of strain. If density is constant with time and position then

$$\dot{m}=\rho\,\mathrm{div}\,\mathbf{v}. \tag{4}$$

Density is considered here to be constant in time and position because we assume that material properties

do not change with growth alone. This assumption was also adopted by Hsu (1968) and others (Cowin and Firoozbakhsh, 1981; Guo and Cowin, 1992; Mattheck and Huber-Betzer, 1991). We consider the growth to consist of the addition or removal of the same tissue material. Hence, from equations (1) and (4), the rate of unit tissue volume change is

$$\frac{dV}{dt} = \operatorname{div} \mathbf{v} = \operatorname{tr} \mathbf{D}_g, \tag{5}$$

where $\mathbf{D}_g$ is the rate of growth tensor, which is analogous to the rate of deformation tensor in continuum mechanics (Spencer, 1980); it is the symmetric part of the gradient of the growth velocity field. The trace of $\mathbf{D}_g$ is the rate of volumetric growth or dilation. The tensor $\mathbf{D}_g$ has the advantage that growth rate functions can be described without an initial reference configuration, which may be difficult to define experimentally. Alternatively, the growth rate may be described by an equivalent Lagrangian measure, the rate of growth stretch tensor $\dot{\mathbf{U}}_g$, which is referred to a defined reference state. The growth stretch tensor $\mathbf{U}_g$ can be obtained simply by integrating $\dot{\mathbf{U}}_g$ in time. The relation between the rate tensors $\mathbf{D}_g$ and $\dot{\mathbf{U}}_g$ is given in Appendix B.

The growth stretch tensor $\mathbf{U}_g$ is related to the growth deformation gradient tensor $\mathbf{F}_g$ by the right polar decomposition*

$$\mathbf{F}_g = \mathbf{R}_g \mathbf{U}_g, \tag{6}$$

where $\mathbf{R}_g$ is the rotation part of the growth deformation. The growth deformation gradient $\mathbf{F}_g$ is analogous to the deformation gradient tensor in continuum mechanics (Spencer, 1980). Its components are given in Appendix A. To formulate a problem, $\dot{\mathbf{U}}_g$ may be specified and integrated in time to obtain $\mathbf{U}_g$. It will be seen below that $\mathbf{R}_g$ may be chosen to equal the identity tensor so that $\mathbf{U}_g = \mathbf{F}_g$ without loss of generality.

Let the Cauchy stress tensor $\mathbf{T}$ in the original elastic body $B(t_0)$ be given by the function $\hat{\mathbf{T}}$:

$$\mathbf{T} = \hat{\mathbf{T}}(\mathbf{C}), \tag{7}$$

where $\mathbf{C} = \mathbf{F}^T \mathbf{F}$ is the right Cauchy–Green deformation tensor referred to material coordinates in the original body. Following volumetric growth with no change in the elastic response of the tissue, the stress in the grown body is given in terms of deformation components referred to the original material coordinates by

$$\mathbf{T} = \hat{\mathbf{T}}(\mathbf{F}_g^{-T} \mathbf{C} \mathbf{F}_g^{-1}). \tag{8}$$

The preceding description establishes the kinematics of the local change in the zero-stress reference state. We now consider how growth affects the state of stress in the body. Even in the absence of external loads, the state of stress in a grown body may be altered by the introduction of residual stress during growth. This arises because there is no requirement that the growth deformation gradient $\mathbf{F}_g$ corresponds to a compatible displacement field, i.e. the change in local zero-stress state during growth need not be continuous from point to point. For example, a cell may grow independently of its neighbors. Later we see that there are also smooth growth fields that are not compatible. Hence, if we require that the tissue remains intact and continuous as it grows, the *observed* growth deformation in the absence of external loads may not be the same as $\mathbf{F}_g$ defined above. As shown in Fig. 1, the deformation defined by $\mathbf{F}_g$ describes the growth from the original zero-stress reference state $B(t_0)$ to a new locally stress-free state $B(t_1)$, which may differ from the observed intact grown state $B'(t_1)$. The part of the total growth deformation that maps $B(t_1)$ to the unloaded state $B'(t_1)$ is an elastic deformation $\mathbf{F}_e$ that ensures the continuity of the body.

From the preceding discussion, the overall observed growth deformation $\mathbf{F}_{eg}$ that maps $B(t_0)$ to $B'(t_1)$ is then given by

$$\mathbf{F}_{eg} = \mathbf{F}_e \mathbf{F}_g. \tag{9}$$

It is now evident why $\mathbf{R}_g$ in equation (6) can be chosen to be the identity without loss of generality; any rotational part of $\mathbf{F}_g$ can be incorporated into the elastic part of the total growth deformation.

Since $B(t_1)$ is the new zero-stress reference configuration, the state of stress in $B'(t_1)$ must be

$$\mathbf{T} = \hat{\mathbf{T}}(\mathbf{F}_e^T \mathbf{F}_e). \tag{10}$$

If the body is in equilibrium in the absence of external loads, then the stress given by equation (10) is a residual stress $\overset{0}{\mathbf{T}}$. Therefore, incompatible growth fields

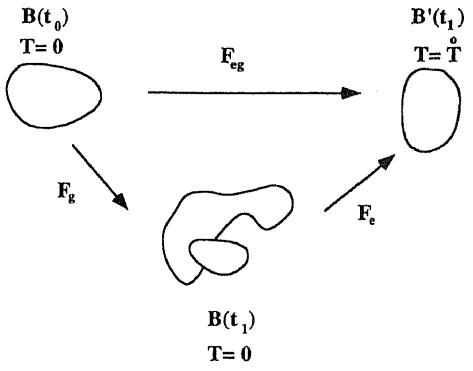

Fig. 1. Three states in finite growth of a stress-free tissue: (a) the original zero-stress reference state $B(t_0)$; (b) the grown zero-stress $B(t_1)$; (c) the observed intact and unloaded grown state $B'(t_1)$ with residual stress $\overset{0}{\mathbf{T}}$. The growth deformation gradient $\mathbf{F}_g$ maps $B(t_0)$ into $B(t_1)$. However, $\mathbf{F}_g$ may not be compatible so $B(t_1)$ is shown as a collection of discontinuous and superimposed material. So that the overall growth deformation is compatible, the elastic deformation $\mathbf{F}_e$ is required to map $B(t_1)$ into the intact grown state $B'(t_1)$. $\mathbf{F}_e$ gives rise to the residual stress $\overset{0}{\mathbf{T}}$ in $B'(t_1)$. The overall growth deformation is then the composition given by equation (9).

*Right as opposed to left because it leads naturally to the Lagrangian formulation.

lead to residual stress that arises as a direct result of the elastic deformations required to maintain continuity of the body. Clearly, the analysis of finite growth kinematics in an elastic tissue will, in general, require that the constitutive law for stress in the tissue be known. When growth occurs under conditions of external loading, $\mathbf{F}_e$ also includes the elastic deformation due to the load. When the original undeformed reference state is residually stressed, the above analysis generalizes directly provided that the mapping that describes the local stress-free state at each point in the reference body is known, even though that mapping will not be compatible. The problem then becomes the same as that of a subsequent growth deformation referred to a previously grown state. If this local stress-free configuration of the reference residually stressed body is not known, but the residual stress $\overset{0}{\mathbf{T}}$ is, then the analysis will require a form for the constitutive law that is valid for a residual stress field. For the case of finite elastic deformations, a valid general form is not presently known. However, Hoger (1993) has presented a constitutive law for residually stressed elastic bodies that undergo small strains and arbitrary rotations.

In general, growth may depend on the state of stress in the tissue at each point. To describe stress-dependent growth, we require a constitutive law for the mathematical form of the growth tensor as a function of the stress tensor. Since the growth deformation $\mathbf{F}_g$ does not include a rotation, the growth law may be formulated by writing the growth stretch $\mathbf{U}_g$ as a function of the Cauchy stress $\mathbf{T}$:

$$\mathbf{U}_g = \hat{\mathbf{U}}_g(\mathbf{T}), \tag{11}$$

where $\hat{\mathbf{U}}_g$ is a tensor-valued function that maps symmetric tensors into symmetric tensors. In most cases $\det \mathbf{U}_g \neq 1$.

Another, perhaps more physiological, approach to the formulation of stress-dependent growth functions is to write the growth *rate* as a function of the stress. This would admit a growth law of the type described by Fung (1990). Recall that the rate of volume change at a point is given by the trace of the growth rate tensor $\mathbf{D}_g$ [equation (5)]. However, a complete description of the growth rate requires all the components of $\mathbf{D}_g$. Thus, the growth function may take the form

$$\mathbf{D}_g = \hat{\mathbf{D}}_g(\mathbf{T}), \tag{12a}$$

where $\hat{\mathbf{D}}_g$ is a symmetric function that maps symmetric tensors into symmetric tensors. Since $\dot{\mathbf{U}}_g$ and $\mathbf{D}_g$ are related by equations (B1) and (B2), equation (12a) can be written as

$$\dot{\mathbf{U}}_g = \hat{\mathbf{U}}_g(\mathbf{T}), \tag{12b}$$

where $\hat{\mathbf{U}}_g$ is also a symmetric valued function of symmetric tensors.

A formulation in terms of $\dot{\mathbf{U}}_g$ is easier to integrate than one in terms of $\mathbf{D}_g$ since integrating $\dot{\mathbf{U}}_g$ provides $\mathbf{U}_g$ ($=\mathbf{F}_g$). The growth stretch tensor $\mathbf{U}_g$ is invertible and positive-definite.

If, as suggested by Fung, there exists a stress state $\overset{*}{\mathbf{T}}$ corresponding to growth equilibrium, then it is well motivated to define the growth rate tensor to be zero when the stress is at the growth equilibrium state, i.e.

$$\mathbf{D}_g = \hat{\mathbf{D}}_g(\mathbf{T} - \mathbf{R}\overset{*}{\mathbf{T}}\mathbf{R}^T) \tag{13a}$$

and

$$\dot{\mathbf{U}}_g = \hat{\mathbf{U}}_g(\mathbf{T} - \mathbf{R}\overset{*}{\mathbf{T}}\mathbf{R}^T). \tag{13b}$$

In these equations, the rotation $\mathbf{R}$ is required to ensure that $\mathbf{T}$ and $\overset{*}{\mathbf{T}}$ are measured in the same frame of reference, as required by observer independence (Gurtin, 1981).

Two models were used to study independently how growth leads to residual stress and how stress may determine the growth pattern of a tissue. For the first case, a growth displacement field is specified in an unloaded cylindrical tube and the residual stress fields that result from different growth fields are examined. In the second example, a loaded specimen is used to study stress-dependent growth using a simple law. The basic equations of this boundary value problem are given in Appendix C.

Residual stress arising from growth

A hollow cylindrical tube model composed of an incompressible isotropic elastic material is used to illustrate how circumferential growth gives rise to a transmural distribution of residual stress that would cause the cylinder to change shape when cut. Circumferential growth serves as a first approximation for eccentric ventricular hypertrophy, a clinical term that describes ventricular enlargement in response to chronic volume overload (elevated filling pressure). The residual stress present in the cylinder after growth is calculated assuming that growth strains generate stresses similar to those of loading so that a constitutive equation for an isotropic material can be used. To obtain the growth deformation $\mathbf{F}_g$ we prescribe the following growth displacement field:

$$\rho = R, \qquad \varphi = K_\theta(R)\Theta, \qquad \zeta = Z. \tag{14}$$

A point P in the original stress-free configuration $B(t_0)$ has the coordinates (R, Θ, Z). $\mathbf{F}_g$ maps the original state $B(t_0)$ into the new locally stress-free state $B(t_1)$, in which P has coordinates (ρ, φ, ζ). The term $K_\theta(R)$ is a circumferential growth stretch ratio that depends on the radius, but for simplicity we use a constant which is sufficient to introduce a nonuniform residual stress. A value $K_\theta > 1.0$ simulates growth, and when $K_\theta < 1.0$ resorption occurs. This displacement field is incompatible since φ is not unique at $\Theta = 0, 2\pi$. The incompatibility can be seen in Fig. 2, where the locally stress-free state $B(t_1)$ is shown when $K_\theta = 0.9$ and $K_\theta = 1.1$. When $K_\theta = 0.9$ there is discontinuity in

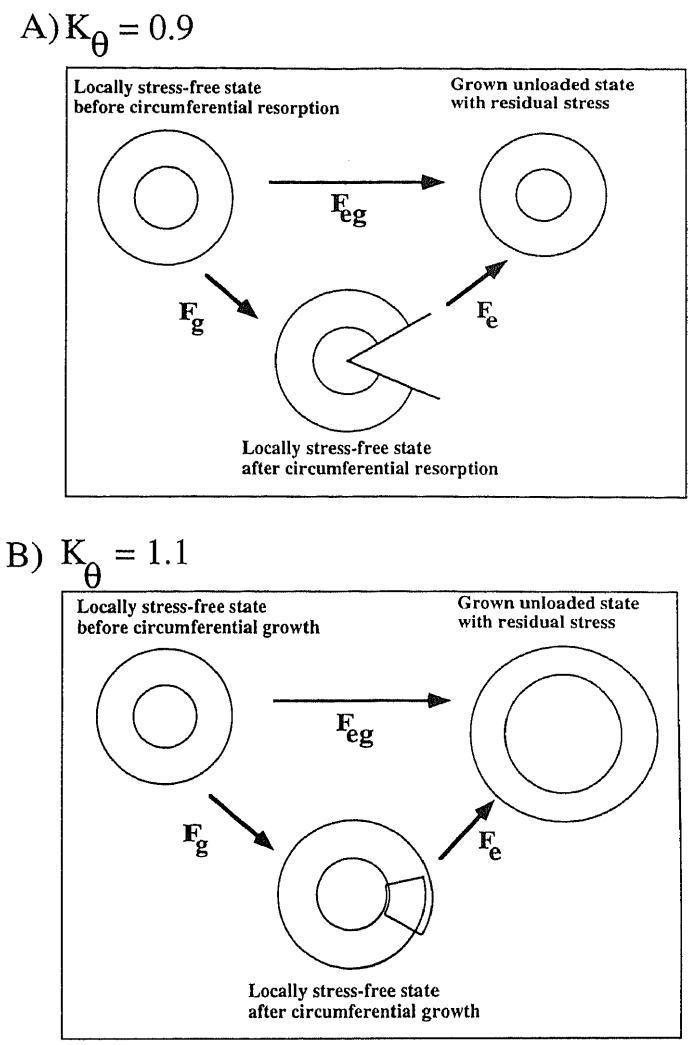

Fig. 2. Cylindrical models of the left ventricle in the zero-stress state after uniform circumferential growth: (A) resorption ($K_\theta = 0.9$); (B) growth ($K_\theta = 1.1$). The original zero-stress is a hollow cylinder ($B(t_0)$). Note that the grown state $B(t_1)$ is stress-free and discontinuous in both cases. In the case of resorption, to achieve an intact grown state, an elastic deformation that takes the grown open configuration into a closed cylinder is required. This elastic deformation, in turn, will give rise to residual stress. After uniform circumferential resorption the $B(t_1)$ state will appear as shown in panel B. This state is stress-free but it shows a superposition of material. To achieve an intact configuration, an elastic deformation that opens the cylinder to prevent any superposition is required. As before, this elastic deformation will also give rise to residual stress in the final grown state.

the cylinder which is not permissible if the total growth deformation is to be compatible. When $K_\theta = 1.1$ there is a superposition of material which should not occur in a compatible deformation. The displacement field of equation (14) defines the following growth deformation gradient:

$$\mathbf{F}_g = \begin{bmatrix} 1 & 0 & 0 \\ 0 & \frac{\rho}{R} K_\theta & 0 \\ 0 & 0 & 1 \end{bmatrix}. \tag{15}$$

In order that the overall growth deformation field is compatible, an additional elastic deformation is required that will be used in the constitutive equation for the material to determine the residual stress that must satisfy equilibrium and the zero traction boundary condition. A displacement of the form

$$r = r(\rho), \quad \theta = \eta_\theta(\rho)\varphi, \quad z = \varepsilon z, \tag{16}$$

which maps the state $B(t_1)$ to the final grown state of the intact body $B'(t_1)$ in which P has coordinates (r, θ, z), gives rise to the elastic deformation

$$\mathbf{F}_e = \begin{bmatrix} \frac{dr(\rho)}{d\rho} & 0 & 0 \\ 0 & \frac{r}{\rho}\eta_\theta & 0 \\ 0 & 0 & \varepsilon \end{bmatrix}. \tag{17}$$

An appropriate choice of $\eta_\theta(\rho)$ allows the overall growth deformation $\mathbf{F}_e\mathbf{F}_g$ to be compatible by restoring continuity of displacements at $\Theta=0,2\pi$. For the case when K_θ is a constant, the simplest choice is $\eta_\theta=1/K_\theta$. The elastic deformation also allows for some axial change in length via the parameter ε.

The incompressibility constraint is only applied to $\mathbf{F}_e$ so that the third principal invariant of $\mathbf{C}$ is unity, i.e.

$$I_3=\left(\frac{\partial r}{\partial\rho}\frac{r}{\rho}\varepsilon\eta_\theta\right)^2=1, \tag{18}$$

which can be integrated to obtain an expression for the net grown radius, r.

From equation (7) with $\mathbf{C}=\mathbf{F}_{eg}^{\mathrm{T}}\mathbf{F}_{eg}$, the stress becomes a function of $\mathbf{F}_e$. Lagrangian strain components referred to the coordinates in state $B(t_1)$ calculated from $\mathbf{E}=\frac{1}{2}(\mathbf{F}_e^{\mathrm{T}}\mathbf{F}_e-\mathbf{I})$ are given by

$$E_{\rho\rho}=\frac{1}{2}\left[\left(\frac{RK_\theta}{r\varepsilon}\right)^2-1\right],$$
$$E_{\varphi\varphi}=\frac{1}{2}\left[\left(\frac{r}{RK_\theta}\right)^2-1\right],$$
$$E_{\zeta\zeta}=\tfrac{1}{2}(\varepsilon^2-1). \tag{19}$$

For this example, we adopt the form for the stress–strain relationship used by Guccione *et al.* (1991) for resting passive ventricular myocardium. They used the strain energy function suggested by Choung and Fung (1986):

$$W=\frac{c}{2}(e^Q-1), \tag{20}$$

where c is a constant and Q is a function of the three principal strain components that defines the material symmetry of the tissue under consideration. For an isotropic material, Q is

$$Q=2\,b_1(E_{\rho\rho}+E_{\varphi\varphi}+E_{\zeta\zeta}), \tag{21}$$

where b_1 is a constant. The stress is then obtained from

$$T_{ij}=\tfrac{1}{2}F_{iS}F_{jT}\left(\frac{\partial W}{\partial E_{ST}}+\frac{\partial W}{\partial E_{TS}}\right)-p\delta_{ij}, \tag{22}$$

where p is the hydrostatic pressure that enters into the constitutive equation as a Lagrange multiplier.

The equilibrium equations are

$$\frac{\mathrm{d}T_{rr}}{\mathrm{d}r}+\frac{T_{rr}-T_{\theta\theta}}{r}=0, \tag{23}$$

$$\frac{\mathrm{d}T_{r\theta}}{\mathrm{d}r}+\frac{2\,T_{r\theta}}{r}=0, \tag{24}$$

$$\frac{\mathrm{d}T_{rz}}{\mathrm{d}r}+\frac{T_{rz}}{r}=0. \tag{25}$$

However, since the zero traction boundary condition at the inner and outer walls was used, only equation (23) has to be solved. Integrating this equation gives

$$T_{rr}=\int_{r_2}^{r}\frac{T_{\theta\theta}+T_{rr}}{r}\mathrm{d}r+T_{rr}|_{r=r_2}, \tag{26}$$

where T_{rr} at $r=r_2$ is the radial stress at the outer grown wall and was specified as zero. The internal pressure is equal to $-T_{rr}$ at $r=r_1$. The model is solved by specifying the grown inner radius r_1 and solving for the final value of inner radius that gives zero transmural pressure. Transmural residual stress distributions are then calculated for the grown state.

Stress-dependent growth

In this example, we analyze stress-dependent growth in the absence of residual stress by considering a simple homogeneous stress-field. Since reliable data on stress-dependent soft tissue growth are not available, we solve a rectangular model of bone tissue subjected to compressive stress and small strains but without assuming infinitesimal linear elasticity. The block grows in external dimensions as a linear function of the difference between the loading stress and a preestablished no-growth equilibrium state of stress.

We assume elastic properties for tissue from the diaphysial region of human femur with a Young's modulus along the long axis (z-axis) estimated to be 18.4 GPa (Cowin, 1983). The block is compressed along its long axis with the two other dimensions corresponding to the radial (x-axis) and circumferential (y-axis) directions (Fig. 3). Since the problem is homogeneous, there is no residual stress (Hoger, 1986; Hsu, 1968). The original specimen $B(t_0)$ was subjected to compressive loading that gave rise to the deformed state characterized by the elastic deformation gradient $\mathbf{F}_e$. If the corresponding axial stress is different from the growth equilibrium stress, then the tissue grows or resorbs along its x and y dimensions until equilibrium is restored.

The elastic deformation gradient that arises from compressive loading is given by

$$\mathbf{F}_e=\begin{bmatrix}\dfrac{1}{\sqrt{\lambda_3}} & 0 & 0\\ 0 & \dfrac{1}{\sqrt{\lambda_3}} & 0\\ 0 & 0 & \lambda_3\end{bmatrix}, \tag{27}$$

where λ_3 is the stretch ratio (<1) in the axial direction. Although the shortening specified was only 0.1% ($\lambda_3=0.999$), we developed this example using finite deformation theory for generality. Strains are computed from

$$\mathbf{E}=\tfrac{1}{2}(\mathbf{F}_e^{\mathrm{T}}\mathbf{F}_e-\mathbf{I}) \tag{28}$$

and the axial stress due to loading is computed from

$$\mathbf{T}=\mathbf{F}_e\left(\frac{\partial W}{\partial\mathbf{E}}\right)\mathbf{F}_e^{\mathrm{T}}, \tag{29}$$

with the strain energy W given by

$$W=c_1\,(E_{xx}^2+E_{yy}^2+E_{zz}^2) \tag{30}$$

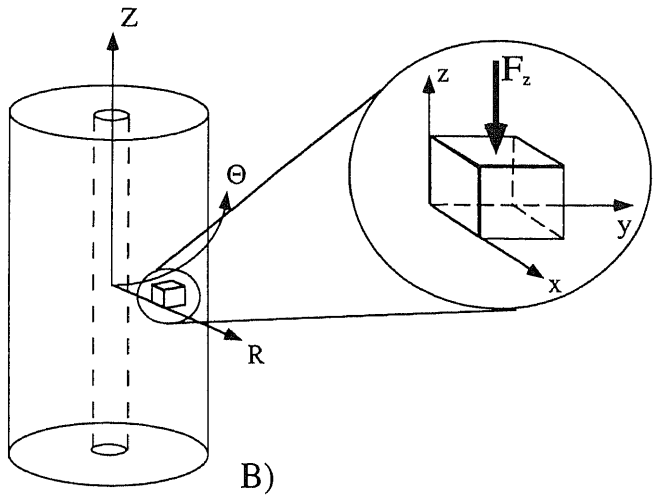

Fig. 3. A block of bone with material properties from the diaphysial region of human femur was subject to compression along its long axis (Young's modulus of 18.4 GPa along the z-axis). Upon compression, it grows along the radial (x-axis) and circumferential (y-axis) directions as a linear function of the difference between the applied stress and a predetermined no-growth equilibrium stress.

so that

$$T_{zz}=2c_1 E_{zz} F_{zz} F_{zz}, \tag{31}$$

where $2c_1$ corresponds to the Young's modulus along the long axis.

The no-growth equilibrium state is defined by a growth equilibrium value for axial stress $\overset{*}{\mathbf{T}}_{zz}$. At any given time t, the components of the rate of growth tensor $\dot{\mathbf{U}}_g$ are given by

$$\dot{\lambda}_x(t)=K_x[\mathbf{T}_{zz}(t)-\overset{*}{\mathbf{T}}_{zz}], \tag{32a}$$

$$\dot{\lambda}_y(t)=K_y[\mathbf{T}_{zz}(t)-\overset{*}{\mathbf{T}}_{zz}], \tag{32b}$$

where K_x and K_y are constants. The no-growth equilibrium axial stress $\overset{*}{\mathbf{T}}_{zz}$ is -4.5 MPa (Firoozbakhsh and Aleyaasin, 1989). K_x and K_y have equal values for this example and were obtained from Luo *et al.* (1991), who used growth constants of -0.5 mm time^{-1} in their *strain*-dependent growth formulation. We divided this growth rate constant by the Young's modulus to obtain a constant for *stress*-dependent growth and then normalized it by a characteristic length of 1 mm to describe growth stretch rates per unit stress. Our growth rate constants (K_x and K_y) were -0.27 time^{-1} GPa^{-1}.

The growth stretch ratios with respect to the ungrown stress-free reference state at time 0 are then given by

$$\lambda_x(t+\mathrm{d}t)=\lambda_x(t)+\dot{\lambda}_x\,\mathrm{d}t, \tag{33a}$$

$$\lambda_y(t+\mathrm{d}t)=\lambda_y(t)+\dot{\lambda}_y\,\mathrm{d}t. \tag{33b}$$

Equations (32) can be used to write the rate of growth tensor $\dot{\mathbf{U}}_g$:

$$\dot{\mathbf{U}}_g(t)=\begin{bmatrix} K_x[\mathbf{T}_{zz}(t)-\overset{*}{\mathbf{T}}_{zz}] & 0 & 0 \\ 0 & K_y[\mathbf{T}_{zz}(t)-\overset{*}{\mathbf{T}}_{zz}] & 0 \\ 0 & 0 & 0 \end{bmatrix}. \tag{34}$$

The tensor $\dot{\mathbf{U}}_g$ can then be integrated in time to yield $\mathbf{U}_g$ ($=\mathbf{F}_g$ since $\mathbf{R}_g=$identity):

$$\mathbf{F}_g(t+\mathrm{d}t)=\begin{bmatrix} K_x[\mathbf{T}_{zz}(t)-\overset{*}{\mathbf{T}}_{zz}]\,\mathrm{d}t+\mathbf{F}_{g_{xx}}(t) & 0 & 0 \\ 0 & K_y[\mathbf{T}_{zz}(t)-\overset{*}{\mathbf{T}}_{zz}]\,\mathrm{d}t+\mathbf{F}_{g_{yy}}(t) & 0 \\ 0 & 0 & \mathbf{F}_{g_{zz}}(t) \end{bmatrix}, \tag{35}$$

where the time period $\mathrm{d}t$ corresponds to an arbitrary increment in time corresponding to one iteration and where $\mathbf{F}_g(t+\mathrm{d}t)$ is the growth deformation gradient referred to the original stress-free state of time 0.

In each iteration, the axial stress calculated from the prescribed compressive strain is computed and the tissue is allowed to grow accordingly. In successive time steps, the axial strain is adjusted so that the applied axial force remains constant. As the cross-sectional area grows, the elastic stress is reduced, the block shortens less, and the growth rate falls. To observe the progress of growth, the unloaded dimensions were plotted at each time step.

RESULTS

The hollow tube model illustrates how circumferential growth can give rise to a transmural distribution of residual stress that would cause the cylinder to change shape when cut. With $K_\theta = 0.9$ (resorption), $\varepsilon = 1.0$ and initial internal and external radii of 2.0 and 3.0 cm, the grown radii satisfying equilibrium were 1.76 and 2.76 cm, respectively. The transmural residual stresses in Fig. 4(A) show zero radial stress T_{rr} at the outer and inner walls since the cylinder was unloaded. Circumferential stress $T_{\theta\theta}$ increases nonlinearly from compression in the inner layers to tension in the epicardium. The neutral axis is closer to the inner boundary. This distribution is similar to the solution of the flexure problem when an open arc is closed into a circle. Indeed it is equivalent to the solution for an arc with an opening angle of $(1 - K_\theta)\, 2\pi$ (Guccione *et al.*, 1991).

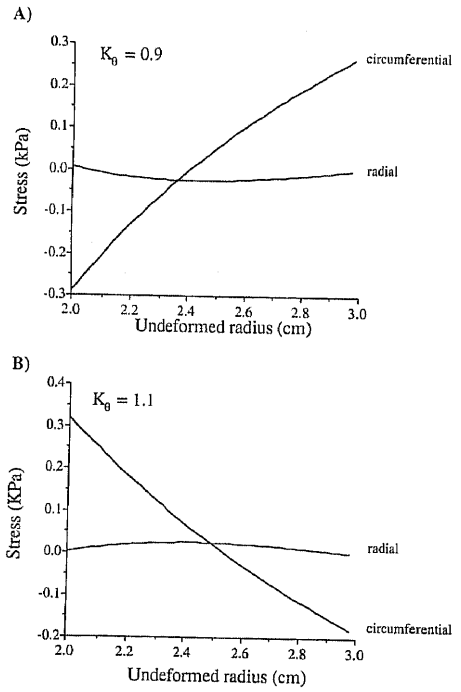

Fig. 4. Plots of residual stress vs undeformed radius for a hollow cylinder after uniform circumferential resorption (A) and uniform circumferential growth (B). In both cases radial stress is zero at both boundaries since the cylinder is unloaded. When the circumferential growth stretch ratio $K_\theta = 0.9$ (resorption), circumferential residual stress is compressive in the inner wall and tensile in the outer wall. Referring to Fig. 2(A) this is as expected, since this distribution can be interpreted as the result of an elastic deformation that 'bends' the open cylinder to form a closed residually stressed cylinder without any discontinuities. When $K_\theta = 1.1$ (growth) the circumferential residual stress is compressive in the outer wall and tensile in the inner half. This is also the expected distribution when the locally stress-free state is as diagrammed in Fig. 2(B).

With $K_\theta = 1.1$ (growth) and $\varepsilon = 1.0$, the grown inner and outer radii were 2.25 and 3.25 cm, respectively. In this case, the transmural stress gradients reversed from those from resorption [Fig. 4(B)]. The circumferential residual stress is compressive in the outer layers and tensile in the inner half of the wall. This distribution is such that it would give rise to a negative opening angle (closing) if circumferential residual stress were relieved.

In both cases, the axial stress T_{zz} was also nonzero. The resultant of this stress determines whether the cylinder would stretch or shorten. The solution of this model with a fixed length is a simplifying approximation. In a fully three-dimensional solution, the axial residual strain that eliminates this stress would be nonhomogeneous precluding analytic solution. Nevertheless, the resulting axial force in this model, when no changes in length were allowed, was close to zero. The axial deformation that minimized the axial resultant was less than 1% of the length. This approximation does not affect the validity of our observations regarding the circumferential residual stress since the problem of interest is two-dimensional.

To demonstrate how stress-dependent growth can be incorporated into a model of tissue growth, the growth of a rectangular bone block subjected to stress was modeled. In this example, all stresses arose from loading and there was no residual stress involved. The initial compressive axial stress due to 0.1% shortening was about four times the growth equilibrium stress of −4.5 MPa and decreased with time as the specimen grew asymptotically reaching the equilibrium value [Fig. 5(a)]. Although a small deformation was imposed (0.1% shortening), the model parameters specified led to large growth deformations (100%) [Fig. 5(b)]. The time constants for both variables were also different. Whereas the axial stress took 201 time units to reach 50% of the asymptotic value, the growth of the x and y dimensions took 241 time units. In both cases, the rate of change of these values was highest immediately after the load was applied.

DISCUSSION

In this paper, we have presented a general continuum formulation for finite volumetric growth in soft elastic tissues in which residual stress arises naturally and growth may be dependent on the state of stress in the tissue. The shape change of an unloaded tissue during growth is described by a mapping analogous to the deformation gradient tensor. This mapping is decomposed into a transformation of the local

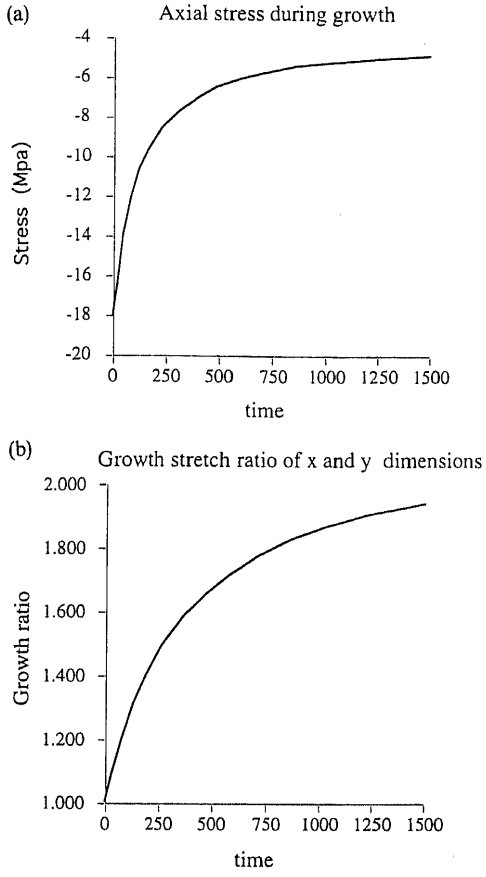

Fig. 5. Results from a stress-dependent growth simulation on an axially (z-axis) loaded bone block. A load leading to 0.5% shortening was imposed and growth occurred to reduce the state of stress to a predetermined equilibrium state. The top panel shows the time course of axial stress as it decreases asymptotically towards the no-growth equilibrium stress of 4.5 MPa. The lower panel shows the growth ratios for the x and y dimensions.

zero-stress reference state and an accompanying elastic deformation that ensures the compatibility of the total growth deformation. Residual stress arises from this elastic deformation. Intuitively, residual stress arises from the part of the total growth deformation that is responsible for accommodating the newly grown tissue to prevent discontinuities in the grown state of the body. This theory was used to develop a model that illustrates how uniform circumferential growth, as may occur in eccentric hypertrophy, may reduce the residual stress in the ventricular wall.

A second model was developed to illustrate stress-dependent growth. Since growth may be influenced by the state of stress and strain in the tissue, a complete continuum formulation of growth mechanics should include the relationship between the growth and stress or strain arising from loading. However, in soft tissues, strain-dependent growth laws like those used for bone (Cowin, 1983; Cowin and Firoozbakhsh, 1981) have the disadvantage that many reference states for the finite strain are possible. If the local stress-free state is chosen as the reference state for strain, then this reference state changes with growth. If some original reference state of the body is used, then the strain at growth equilibrium may change. For example, a hypertrophied state of the heart may be at growth equilibrium, yet it will be strained with respect to an original growth equilibrium reference state. Later, if increased loading causes further hypertrophy, a new growth equilibrium state may again be reached at a different strain. Therefore, since we define growth by the change in the zero-stress reference state, we have chosen a formulation in which growth is stress-dependent rather than strain-dependent. The stress dependence of growth *rate* was derived by defining both the Eulerian rate of growth tensor $\mathbf{D}_g$ and its Lagrangian equivalent, the rate of growth stretch $\dot{\mathbf{U}}_g$. A definition for stress-dependent growth rate in linearly elastic materials had been previously formulated by Hsu (1968) in terms of stress and stress rate.

The theory suggests several experimental approaches. One is to measure the total growth deformation $\mathbf{F}_{eg}$. For example, Omens and Covell (1991) used biplane radiography of metal markers to measure the transmural distribution of three-dimensional growth strains in the end-diastolic state of the left ventricle during volume overload hypertrophy. If $\mathbf{F}_{eg}$ is measured, then educated proposals for $\mathbf{F}_g$ may be formulated. The validity of the proposed growth field can then be tested by seeing if the elastic part of the total deformation satisfies equilibrium under the existing loading conditions. Alternatively, it is also possible to measure $\mathbf{F}_e$ if a locally stress-free state can be obtained in a practical way. In the case of the passive rat heart, a satisfactory approximation of the stress-free state was obtained by Omens and Fung (1990), who made a radial cut across the free wall of an equatorial slice of the left ventricle to relieve circumferential residual stress. The slice sprang open with a mean opening angle of about 45°. The 'residual strain' describing the deformation from the zero-stress state to the intact state was measured by analyzing the motion of small markers on the tissue surface and is equivalent to $\mathbf{F}_e$ in our model. More recently, Costa *et al.* (1993) successfully measured the three-dimensional residual strains that are relieved in the free wall of the canine left ventricle when a segment of the myocardium with implanted radiopaque markers was excised. Once the stress-free state is known, its evolution can be measured in specimens studied at different stages of growth so that a time-dependent form for $\mathbf{F}_g$ can be proposed. This has been done by Rodriguez *et al.* (1993) for the rat heart in a model of concentric hypertrophy arising from pressure overload hypertrophy induced by surgical banding of the ascending aorta. The changes in shape of the stress-free state were measured at 3, 7, 14 and 21 days after banding. Taber *et al.* (1993) measured residual strains in the ventricle of the Hamburger–Hamilton stage 16–24 (2.5–4.5 days of incubation) chick embryo. They

showed significant changes in residual stress with cardiac development during morphogenesis. A limitation of this experimental approach is that a unique global stress-free state may not exist. The cutting experiments in soft tissues reveal the presence of residual stress but, in general, the true stress-free state may not be obtainable by one or even many cuts or by a unique set of cuts. For example, Takamizawa and Hayashi (1987) examined the zero-stress state that would result in a thick-walled pressure vessel if the strain under load was assumed to be uniform across the wall. A unique global stress-free state could be found for a cylindrical geometry under the uniform strain hypothesis, but there was no such state for a sphere. This, however, is not a limitation of our theory, which does not rely on the existence of a global zero-stress state. Indeed, it may be possible to use our model to estimate how much of the residual stress arising from growth would be relieved by one or more cuts.

If changes in the time course of growth deformation and tissue stress can be estimated, then a stress-dependent growth law for the intact tissue may be proposed in the form of equations (12) or (13). Another approach is to study morphological and cellular changes in cell or tissue culture preparations subjected to known mechanical loading (Sadoshima *et al.*, 1992; Terracio *et al.*, 1990). Nonconfluent cell culture preparation may be best for identifying the stress-dependent growth relations since, as the culture becomes confluent, residual stress may arise from the interaction between cells.

If any two combinations of the growth $\mathbf{F}_g$, the residual elastic deformation $\mathbf{F}_e$ or the total growth $\mathbf{F}_{eg}$ are known and are nonsingular, then the third quantity can be found from equation (9). One restriction is that $\mathbf{F}_g$ consists only of stretch so that any rotation in $\mathbf{F}_{eg}$ must reside in $\mathbf{F}_e$. However, if only $\mathbf{F}_{eg}$ is known, then many combinations of the growth and elastic deformations may be possible because a certain growth state may arise from more than one growth path.

For the growth deformation with gradient $\mathbf{F}_g$, the ratio, at a point, of material volumes after and before growth is the determinant. If the deformation is isochoric (i.e. volume preserving), then the determinant is unity. If material is added it is greater than one, and if it is being removed (due to resorption) it is less than one. A difficulty arises in the situation where resorption of existing material or creation of new material occurs at a point. For a given material volume element, resorption may reduce the volume to zero. In this case, $\det \mathbf{F}_g = 0$. Conversely, when new material particles appear, $\det \mathbf{F}_g$ may tend to infinity in local regions. These situations introduce singularities in the growth strain field. To overcome this we consider a region P of the body over which the average of $\det \mathbf{F}_g$ is larger than zero and less than infinity since not all particles in the region are disappearing or appearing at the same instant. An alternative approach may be to make use of the theory of distributed dislocations to describe growth. Kroner (1958) used dislocation theory to examine the problem of 'extra mass' in a single crystal in the form of a hollow ring. After an increase in internal mass due to heating or atomic diffusion the ring opened when cut. Furthermore, as proposed by Skalak (1981), using dislocation theory to study growth leads naturally to the concept of incompatibility. The relation between incompatibility and dislocation density has been well established in the literature (Gairola, 1979; Nabarro, 1987). The incompatibility of a growth field can be expressed in terms of an incompatibility tensor and dislocation density in terms of a dislocation density tensor (Gairola, 1979).

A common example of discontinuous growth is the case where volume is added by accretion or deposition onto a surface, such as occurs in bones, branches, shells and horns. In soft tissues, wound healing and scar formation may be similar in this respect. Skalak *et al.* (1982) treated the problem of describing the motion of points growing from a surface by introducing a second time variable. These points do not have an original position in the reference configuration and the additional time variable describes the time elapsed from the moment of their creation at the growth surface. For those points originally present in the reference configuration, the secondary time variable and the primary time variable are equivalent. Cowin (1983) formulated a theory of bone surface growth in terms of the growth velocity of the external surface of a bone.

In general, material added to an external surface may affect the state of stress in the newly grown material as well as the existing material. In fact, in different situations the state of stress is changed in different ways. For example, material added to the surface of a seashell may not give rise to residual stress in the existing material and the whole shell may remain stress-free after growth. On the other hand, a branch growing horizontally is affected by bending stresses. Finite element modeling studies by Mattheck and Huber-Betzer (1991) have shown that the distribution of stress on a branch can be optimized by specific patterns of surface growth. Tree branches grow by accretion to their outer surfaces. In soft tissues such as skin, surface scar formation may affect the stress in deeper layers.

We used two examples of our formulation to illustrate separately how residual stress arises from growth and how stress from loading may affect growth patterns. The first example was motivated by experimental work on residual stress in passive ventricular myocardium. The model showed that circumferential growth or resorption in a cylindrical tube leads to circumferential residual stress in the wall. Omens and Fung (1990) measured compressive residual strains at the inner wall of the rat left ventricle and tensile residual strain in the outer wall. A corresponding stress distribution is found if a stress-free arc is

closed by bending it into a circular tube (Guccione *et al.*, 1991). The residual stress distribution arising in the circumferential resorption problem showed precisely the same pattern. Although it is not clear from this analysis how the residual stress arises in the normal myocardium, it suggests that circumferential growth, which may occur in eccentric ventricular hypertrophy, may reduce the residual stress and opening angle of the left ventricular wall. This remains to be tested experimentally.

Our second example simulates a bone sample increasing in size by homogeneous growth in a manner analogous to interstitial growth. From a biological perspective, this is a limitation of the example since interstitial bone growth has been described mainly by changes in density and trabecular architecture. If incompatible interstitial growth occurred in bone, residual stress would arise according to our theory. The stresses could be significant due to the relative high elastic stiffness of bone. That volumetric bone growth occurs primarily by surface apposition may be because the same changes in shape cannot be achieved by interstitial growth without resulting in undesirable residual stresses.

The second example uses parameters based on experimental studies of bone remodeling and it is generalized for the case of finite elasticity. An example using bone was selected in the absence of sufficient experimental work on stress-dependent soft tissue growth. Finite deformation analysis was retained for generality. The example illustrates the application of a growth law in which growth is a linear function of the difference between the stress arising from loading and a preestablished no-growth equilibrium stress. Model parameters were based on the linear strain-dependent growth law used by Cowin (1983). To our knowledge, an external remodeling law of this form has not been previously used in the literature on bone remodeling. The rate of change of bone *density* (internal remodeling) has been expressed as a function of the difference of a loaded-state strain energy and an equilibrium strain energy (Harrigan and Hamilton, 1992). Changes in density have also been expressed as a function of the state of stress with respect to the stress existing at a specific reference density (Firoozbakhsh and Aleyaasin, 1989) but not in the form of a difference between the stress in the loaded state and the equilibrium state. External remodeling has been expressed by Cowin (Cowin, 1983; Cowin and Firoozbakhsh, 1981) by relating the growth velocity of an external surface to the difference in *strain* arising from loading and a preestablished equilibrium strain. The increase in size of the bone block in this example is of the same relative magnitude and qualitatively comparable to predictions by Cowin and coworkers, who modeled diaphyseal surface remodeling in long bone under compression (Cowin and Firoozbakhsh, 1981). This simple law may offer an alternative approach to the modeling of this phenomenon. The simple form of the presently applied law may also be a useful starting point for a model of soft tissue growth such as stress-induced hypertrophy. For example, Grossman (1980) has suggested that myocyte fiber diameter and ventricular wall thickness in ventricular pressure overload increase in response to increased systolic wall stress. Alternative forms may include different growth rates in different directions.

An example of how the analytical concepts presented so far may be helpful is the study of the mechanics of cardiac morphogenesis. In the developing embryo, the heart begins as an unfused cylinder that eventually closes to form the cardiac tube (Manasek, 1983). In this original state, the heart may possibly be stress-free. As cells multiply, they become confluent and form tissues; in the developing heart, the tube fuses into a cylinder and continues to grow. Existing tissue has to accommodate growing and multiplying cells and this introduces residual stress (Taber *et al.*, 1993). As the growing tissue develops, its development will be influenced by the load and pressures it has to support. Stalsberg (1970) showed that normal development of the cardiac tube is affected when external mechanical factors have been altered, and Manasek (1983) described how changes also occur when the internal support offered by the cardiac jelly is affected. This suggests that loads and internal pressure arising from the pumping activity are required for normal morphogenesis to take place. To study this, a general formulation of stress-dependent growth is now available.

In cardiac hypertrophy, growth occurs in mature tissue with an existing distribution of residual stress. Growth is also different from that in morphogenesis, where hyperplasia as well as hypertrophy take place. Ventricular hypertrophy also includes remodeling, where the material characteristics of the added tissue may or may not be similar to those of the existing one. In cardiac morphogenesis, the material properties and symmetry may be changing as the heart grows. Cardiac hypertrophy may also be of different types and the stress dependence of growth is unlikely to be the same for volume overload as it is for pressure overload. Modeling studies in which different growth formulations are used will allow us to determine which formulation can most realistically predict the observed growth patterns in a heart undergoing hypertrophy.

Hsu (1968) recognized that homogeneous growth could not introduce residual stress without the interference of external factors and that only restricted forms of growth fields are permissible in a body without introducing residual stress. However, he did not identify this restriction as corresponding to compatibility of the growth deformation and limited his models to homogeneous isotropic growth in bodies of rectangular geometry and axial growth in a cylindrical bar, conditions under which no residual stress is induced. The compatibility problem, and how it gives rise to residual stress, was first summarized by Skalak (1981) as follows:

. . . 'the growth strain field is assumed to be compatible at any time and therefore stress-free. If instead a growth tensor is considered to be arbitrarily specified by the growth process, the first question to consider is whether or not any internal stresses will be generated. The answer is that no stresses will be necessary if the specified tensor growth strains are compatible. If they are not compatible, then internal stresses are required in the final state to maintain continuity of the body.'

This first insight into how residual stress arises has now been expanded into a general formulation; yet still to be developed is an explicit form for a constitutive relation for the finite deformation of an elastic body that incorporates the state of residual stress. Any constitutive relation defined for the stress in a body after growth must consider not only the deformation arising from the loads applied but also the residual stress in the grown state. The stress tensor for residually stressed elastic bodies under small deformations and arbitrary rotations that has been proposed by Hoger (1993) is an example of recent advances towards this direction.

Of all these issues to be considered in the improvement of our formulation, the highest priority is the requirement for experimental data to develop an appropriate form of a constitutive law for growth. This theory will be of most value to researchers and clinicians, so that they can study and predict growth patterns, once the morphology of growth can be described as a function of loading and specific growth laws established.

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APPENDIX A

Consider a body B with the three states of growth defined by $B(t_0)$, $B(t_1)$ and $B'(t_1)$. A point P in $B(t_0)$ has coordinates $\{X_R\}$, in $B(t_1)$ it has coordinates $\{\chi_\alpha\}$ and in $B'(t_1)$ it has coordinates $\{x_i\}$. We can now explicitly write the growth deformation gradients defined in the present formulation as

$$[\mathbf{F}_g]=\frac{\partial \chi_\alpha}{\partial X_R}=\mathbf{F}_{g_{\alpha R}}, \tag{A1}$$

$$[\mathbf{F}_e]=\frac{\partial x_i}{\partial \chi_\alpha}=\mathbf{F}_{e_{i\alpha}}, \tag{A2}$$

$$[\mathbf{F}_{eg}]=\frac{\partial x_i}{\partial X_R}=\mathbf{F}_{eg_{iR}}. \tag{A3}$$

Using indicial notation we can write the final composition of $\mathbf{F}_e$ and $\mathbf{F}_g$ given by equation (9) as

$$F_{eg_{iR}}=F_{e_{i\alpha}}F_{g_{\alpha R}}. \tag{A4}$$

The stress tensor of equation (10) can be written as

$$T_{ij}=\hat{T}_{ij}(C_{\alpha\beta})=\hat{T}_{ij}\left(\frac{\partial x_i}{\partial X_\alpha}\frac{\partial x_i}{\partial X_\beta}\right), \tag{A5}$$

$$T_{ij}=\hat{T}_{ij}\left(\frac{\partial X_R}{\partial \chi_\alpha}C_{RS}\frac{\partial X_S}{\partial \chi_\beta}\right)$$

$$=\hat{T}_{ij}\left(\frac{\partial X_R}{\partial \chi_\alpha}\frac{\partial x_i}{\partial X_R}\frac{\partial x_i}{\partial X_S}\frac{\partial X_S}{\partial \chi_\beta}\right). \tag{A6}$$

The growth rates given by equations (12a), (12b), (13a) and (13b) are, respectively, given in indicial notation by

$$D_{g_{\alpha R}}=\hat{D}_{g_{\alpha R}}(T_{ij}), \tag{A7}$$

$$\dot{U}_{g_{\alpha R}}=\hat{\dot{U}}_{g_{\alpha R}}(T_{ij}), \tag{A8}$$

$$D_{g_{\alpha R}}=\hat{D}_{g_{\alpha R}}(T_{ij}-R_{ik}\overset{*}{T}_{kl}R_{lj}), \tag{A9}$$

$$\dot{U}_{g_{\alpha R}}=\hat{\dot{U}}_{g_{\alpha R}}(T_{ij}-R_{ik}\overset{*}{T}_{kl}R_{lj}). \tag{A10}$$

APPENDIX B

RELATIONS BETWEEN THE RATE OF DEFORMATION TENSORS $\mathbf{D}_g$ AND $\dot{\mathbf{U}}_g$

The rate tensors $\mathbf{D}_g$ and $\dot{\mathbf{U}}_g$ are related by

$$\mathbf{D}_g=\tfrac{1}{2}(\dot{\mathbf{U}}_g\mathbf{U}_g^{-1}+\mathbf{U}_g^{-1}\dot{\mathbf{U}}_g). \tag{B1}$$

The inverse is given by Hoger and Carlson (1984):

$$\dot{\mathbf{U}}_g=\frac{1}{I_1I_2-I_3}\{-\mathbf{U}_g^2\mathbf{D}_g\mathbf{U}_g^2+I_1(\mathbf{U}_g^2\mathbf{D}_g\mathbf{U}_g+\mathbf{U}_g\mathbf{D}_g\mathbf{U}_g^2)$$
$$+(I_1^2+I_2)\mathbf{U}_g\mathbf{D}_g\mathbf{U}_g+2(\mathbf{U}_g^2\mathbf{D}_g+\mathbf{D}_g\mathbf{U}_g^2)$$
$$-I_3(\mathbf{D}_g\mathbf{U}_g-\mathbf{U}_g\mathbf{D}_g)+I_1I_2\mathbf{D}_g\}, \tag{B2}$$

where I_1, I_2 and I_3 are the principal invariants of $\mathbf{U}_g$.

APPENDIX C

FORMULATION OF A BOUNDARY VALUE PROBLEM

To use the present growth formulation in a boundary value problem, we assume that $B(t_0)$ is known and the material properties can be experimentally determined. A form for $\mathbf{F}_g$ can then be postulated, and it may be stress-dependent since stresses are believed to affect remodeling and growth in soft tissues. In this case $\mathbf{F}_g=\mathbf{F}_g(\mathbf{T})$ where the dependence on t_0 is implicit and the stress in this expression is related to the loading that the body experiences. The grown state $B'(t_1)$ and its residual stresses may not be known but may be obtainable by a solution of a boundary value problem for the residual stress $\overset{0}{\mathbf{T}}$. This boundary value problem takes the form

$$\operatorname{div}\overset{0}{\mathbf{T}}=0. \tag{C1}$$

Since from equation (10), $\overset{0}{\mathbf{T}}=\hat{\mathbf{T}}(\mathbf{F}_e^T\mathbf{F}_e)$, then from equation (9)

$$\overset{0}{\mathbf{T}}=\hat{\mathbf{T}}(\mathbf{F}_g^{-T}\mathbf{F}_{eg}^T\mathbf{F}_{eg}\mathbf{F}_g^{-1}) \tag{C2}$$

since

$$\mathbf{F}_e=\mathbf{F}_{eg}\mathbf{F}_g^{-1}. \tag{C3}$$

Here $\mathbf{T}=\overset{0}{\mathbf{T}}(t_0)$ is subject to the traction-free boundary condition

$$\overset{0}{\mathbf{T}}\mathbf{n}=0 \quad \text{on } \partial B'. \tag{C4}$$