A CARTILAGE GROWTH MIXTURE MODEL FOR INFINITESIMAL STRAINS: EQUILIBRIUM SOLUTIONS

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INTRODUCTION

Two of the molecular components of the solid matrix of articular cartilage, proteoglycan and collagen, appear to be predominantly responsible for the functional mechanical properties of the tissue. *In vitro* experiments have quantified the cellular metabolic response to mechanical stimuli that leads to distinct rates of material deposition for the proteoglycan and collagen constituents [1]. We have derived a cartilage growth mixture model that allows the solid matrix constituents to grow independently [2,3]. The model is capable of describing the evolution of tissue geometry, composition, residual stress field, and mechanical properties during growth and degeneration. In this paper, we linearize the cartilage growth mixture model for infinitesimal elastic and growth strains so that illustrative boundary-value problems can be solved analytically. Specifically, we use the linear cartilage growth mixture model to solve an equilibrium growth boundary-value problem for a cylindrical cartilage specimen.

METHODS

Theory

The linear model equations were derived from the general equations presented in [2,3] by assuming infinitesimal elastic and growth strains and infinitesimal changes in fluid density and pore pressure. Upon linearization, the infinitesimal strain tensors $\mathbf{e}^p$ and $\mathbf{e}^c$ for the proteoglycan and collagen constituents are

$$\mathbf{e}^p = \mathbf{e}^p_e + \mathbf{e}^p_g, \qquad \mathbf{e}^c = \mathbf{e}^c_e + \mathbf{e}^c_g, \tag{1}$$

where $\mathbf{e}^\alpha_e$ and $\mathbf{e}^\alpha_g$ are the constituent elastic and growth strain tensors (superscript α=p,c,f denotes the proteoglycan, collagen, or fluid constituent). The linearized continuity equations are

$$\phi^\alpha = \phi^p_0(1-\mathrm{tr}\mathbf{e}^p_e), \qquad \phi^c = \phi^c_0(1-\mathrm{tr}\mathbf{e}^c_e), \qquad \phi^f = \phi^f_0(1+n^f), \tag{2}$$

where ϕ^α is the constituent volume fraction (the subscript O denotes the reference configuration), tr(.) is the trace operator, and n^f is the infinitesimal fluid density change. The growth continuity equations are

$$\mathrm{tr}\mathbf{e}^p_g = \int c^p dt, \qquad \mathrm{tr}\mathbf{e}^c_g = \int c^c dt, \tag{3}$$

where c^α are mass growth functions (rate of mass deposition/current mass). Two constraints are used whose validity was discussed in [3]. First, the proteoglycan and collagen constituents are assumed to be bound to the extracellular matrix so that $\mathbf{e}^p$ and $\mathbf{e}^c$ are equal. Second, intrinsic incompressibility is assumed. These constraints are

$$\mathbf{e}^s = \mathbf{e}^p = \mathbf{e}^c, \qquad \eta^f\phi^f_0 = \phi^p_0\mathrm{tr}\mathbf{e}^p_e + \phi^c_0\mathrm{tr}\mathbf{e}^c_e, \tag{4}$$

where $\mathbf{e}^s$ is the solid matrix strain tensor. Due to these constraints, there are Lagrange multiplier terms in the constituent stresses and diffusive forces that reveal that the equations of equilibrium need to be satisfied only for the solid matrix $\mathbf{T}^s$ and the fluid stress $\mathbf{T}^f$:

$$\mathrm{div}\mathbf{T}^s = \mathbf{0}, \qquad \mathrm{div}\mathbf{T}^f = \mathbf{0}, \tag{5}$$

where div(.) is the divergence operator and $\mathbf{T}^s = \mathbf{T}^p + \mathbf{T}^c$.

The Equilibrium Boundary-Value Problem

The boundary-value problem models the axisymmetric growth of an initially homogeneous cylindrical specimen (radius R, height H) with traction-free boundary conditions. For the boundary-value problems studied here, the fluid pore pressure vanishes throughout the tissue. Axisymmetric growth tensors for the proteoglycan and collagen constituents may be specified using cylindrical coordinates as

$$\mathbf{e}^\alpha_g = e^\alpha_{grr}\mathbf{e}_r\otimes\mathbf{e}_r + e^\alpha_{g\theta\theta}\mathbf{e}_\theta\otimes\mathbf{e}_\theta + e^\alpha_{gzz}\mathbf{e}_z\otimes\mathbf{e}_z, \tag{6}$$

where $(e^\alpha_{grr}, e^\alpha_{g\theta\theta}, e^\alpha_{gzz})$ are the radial, circumferential, and axial components, $(\mathbf{e}_r, \mathbf{e}_\theta, \mathbf{e}_z)$ are the basis vectors, and $\otimes$ is the dyadic product. Two types of growth symmetries were studied: isotropic $(e^\alpha_{grr} = e^\alpha_{g\theta\theta} = e^\alpha_{gzz})$ and planar $(e^\alpha_{grr} = e^\alpha_{g\theta\theta}, e^\alpha_{gzz} = 0)$. The stress constitutive equations were assumed to be

$$\mathbf{T}^c = \lambda^c(\mathrm{tr}\mathbf{e}^c_e)\mathbf{I} + 2\mu^c\mathbf{e}^c_e + \Gamma^c\mathbf{I}, \tag{7}$$

$$\mathbf{T}^p = \eta^p(\mathrm{tr}\mathbf{e}_e^p)\mathbf{I} + \eta^c(\mathrm{tr}\mathbf{e}_e^c)\mathbf{I} + \eta^f n^f \mathbf{I} + T_0^p\mathbf{I}, \quad (8)$$

where $(\lambda^c, \mu^c, \Gamma^c, \eta^p, \eta^c, \eta^f)$ are material constants and T_0^p is the initial proteoglycan stress ($T_0^p = -\Gamma^c$ in the reference configuration). The collagen material constants may change with time as remodeling occurs. The material constants were determined by generalizing a procedure previously used to determine proteoglycan and collagen materials constants using confined compression and tissue composition data for a typical bovine specimen [4].

Solution of the Boundary-Value Problem

Since *in vitro* experiments have shown that mechanical loading and growth factors may differentially regulate proteoglycan and collagen synthesis [1], two cases (A and B) were considered that allow for differential amounts of proteoglycan and collagen mass deposition. To investigate the effects of the growth and remodeling parameters, additional cases were studied:

A: Isotropic growth ($\mathrm{tr}\mathbf{e}_g^p > \mathrm{tr}\mathbf{e}_g^c$, $\mathrm{tr}\mathbf{e}_g^p = 0.30, \mathrm{tr}\mathbf{e}_g^c = 0.15$).

B: Isotropic growth ($\mathrm{tr}\mathbf{e}_g^p < \mathrm{tr}\mathbf{e}_g^c$, $\mathrm{tr}\mathbf{e}_g^p = 0.15, \mathrm{tr}\mathbf{e}_g^c = 0.30$).

C: Isotropic growth ($\mathrm{tr}\mathbf{e}_g^p > \mathrm{tr}\mathbf{e}_g^c$) and collagen remodeling.

D: Planar growth ($\mathrm{tr}\mathbf{e}_g^p > \mathrm{tr}\mathbf{e}_g^c$).

E: Non-uniform planar growth ($\mathrm{tr}\mathbf{e}_g^p > \mathrm{tr}\mathbf{e}_g^c$).

A represents a 30% increase in proteoglycan mass and a 15% increase in collagen mass, whereas B represents a 15% increase in proteoglycan mass and a 30% increase in collagen mass. In C-E, the growth tensor components were specified so that the total mass deposited for each of the constituents was the same as in A. In C, the collagen material constants (μ^c, Γ^c) were each increased by 30% to represent a stiffening of the collagen network, possibly due to increased crosslink density. D may model a loading regimen that results in a preferential direction for mass deposition in the extracellular matrix. In E, the growth tensor components ($e_{grr}^{\alpha} = e_{g\theta\theta}^{\alpha}$) were specified to be linearly decreasing from r= 0 to r=R. This non-uniform case may more accurately model a real growth process, where the mechanical parameters that drive the growth process are nonhomogeneous.

To solve the boundary-value problem, the equilibrium equations $(5)_1$ subject to the traction-free boundary conditions were solved for the solid matrix strain tensor using (1), (4), and (6-8). Then, the constituent elastic strains were calculated from (1) and $(4)_1$, the constituent stresses were calculated from (7-8), and the constituent volume fractions were calculated from (2) and $(4)_2$. Finally, the solid matrix strain tensor was used to calculate the radial and axial displacements of the solid matrix to determine tissue geometry. Results are presented for an initially cylindrical specimen with radius R=1 mm and height H=1 mm.

RESULTS

For cases A-D, the solid matrix strain and, consequently, the constituent elastic strains, volume fractions, and stresses were all homogeneous (Table 1). Also, the constituent stresses were spherical tensors and the total solid matrix stress was zero. For E, the solid matrix strain components varied with radial position r. Consequently, the constituent volume fractions (Fig 1A), constituent stresses, and total solid matrix stress (Fig 1B) varied with radial position r (the solid matrix axial stress was zero everywhere). The final geometry of the specimen depended on the type of growth that occurred (Table 2). The final geometry was cylindrical except for case E, where the axial displacement of the solid matrix depended on radial position r.

CASE	ϕ^p(%)	ϕ^c(%)	ϕ^f(%)	T^p (MPa)	T^c (MPa)
reference	2.00	10.00	88.00	-0.051	0.051
A	2.13	9.13	88.74	-0.054	0.054
B	1.87	10.87	87.26	-0.048	0.048
C	2.41	10.56	87.02	-0.064	0.064
D	2.28	9.13	88.59	-0.054	0.054

Table 1. Constituent volume fractions and stress results.

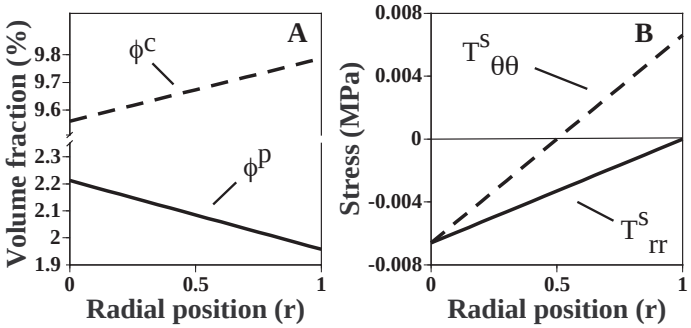

Figure 1. Results for non-uniform planar growth.

CASE	D(mm)	H(mm)	V(mm^3)
reference	2.00	1.00	3.14
A	2.16	1.08	3.95
B	2.14	1.07	3.86
C	2.06	1.03	3.45
D	2.21	1.03	3.94
E	2.07	1.02	3.42

Table 2. Diameter, height, and volume of each specimen.

DISCUSSION

The results quantify how the tissue composition, constituent stresses, and geometry of growing cartilage depend on the relative amounts of growth of the constituents (A vs. B), the amount of collagen remodeling (A vs. C), and the symmetry of the growth tensors (A vs. D). Also, the results predict that non-uniform growth leads to a nonhomogeneous specimen with a residually-stressed solid matrix (E), in agreement with previous studies. The results presented here and in [3] suggest that the cartilage growth model can be used to quantify the evolution of the nonhomogeneous material properties and tissue composition during a growth and remodeling process.

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