

12 - volume growth cardiac growth



12 - volume growth - cardiac growth

1

organ level - human heart and its characteristic microstructure

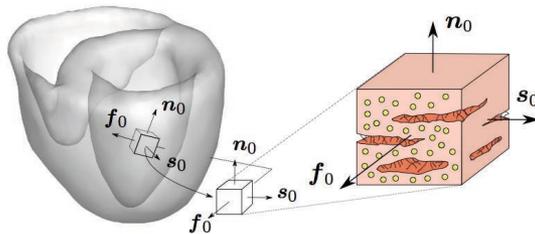


Figure 1. Normal healthy heart, courtesy of Chengpei Xu (left). Microstructural architecture of the heart (right). The orthogonal unit vectors f_0 and s_0 designate the muscle fiber direction and the sheet plane vector in the undeformed configuration. The orthogonal vector n_0 completes the local coordinate system, where the constitutive response of the heart is typically viewed as orthotropic.

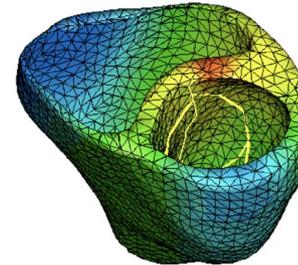
oktapa, abilez, kuhl [2010]

motivation - cardiac growth

3

heart disease

- primary cause of death in industrialized nations
- affects 80 mio americans
- damaged cardiac tissue does not self regenerate



forms of cardiac growth

- case I - athlete's heart
stress driven isotropic growth
- case II - cardiac dilation
strain driven eccentric growth
- case III - cardiac wall thickening
stress driven concentric growth

motivation - cardiac growth

2

cellular level - cardiomyocyte and its characteristic microstructure

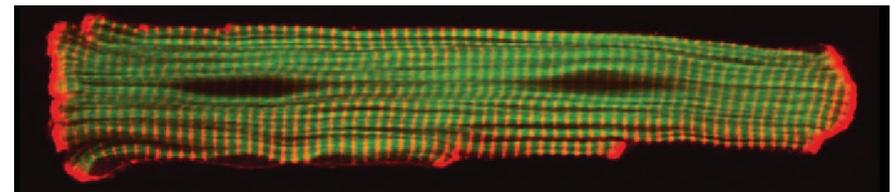


Figure 1. Adult ventricular cardiomyocyte. The sarcomeric actin is labeled in green and the periodically spaced t-tubule system is marked in red, giving the cell its characteristic striated appearance. Healthy cardiomyocytes have a cylindrical shape with a diameter of 10-25 μm and a length of 100 μm , consisting of approximately 50 sarcomere units in series making up a myofibril and 50-100 myofibrils in parallel. Cardiac disease can be attributed to structural changes in the cardiomyocyte, either through eccentric growth in dilated cardiomyopathy or through concentric growth in hypertrophic cardiomyopathy.

kevin.kit.parker, disease.biophysics.group.harvard

motivation - cardiac growth

4

molecular level - sarcomere and its characteristic microstructure

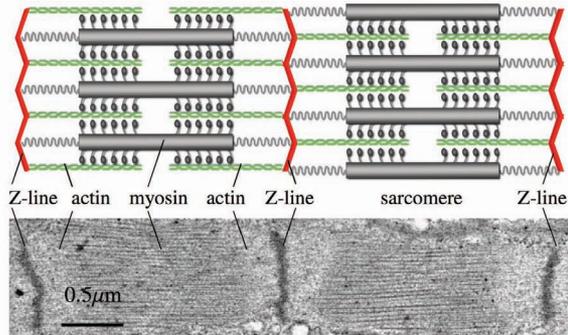


Figure 2. Sarcomere units of human embryonic stem cell-derived cardiomyocyte. Sarcomeres are defined as the segment between two neighboring Z-lines, shown in red, which appear as dark lines under the transmission electron microscope. Healthy sarcomeres are 1.9-2.1 μm long characterized through a parallel arrangement of thick filaments of myosin, displayed in grey, sliding along thin filaments of actin, labeled in green. Although cardiac cells are known to change length and thickness in response to mechanical loading, the individual sarcomeres maintain an optimal resting length.

oktepe, abilez, parker, kubl [2010]

motivation - cardiac growth

organ level - pathophysiology of maladaptive growth



Figure 2. Pathophysiology of maladaptive growth of the heart viewed in transverse heart sections, reprinted with permission from Robbins & Cotran. Compared with the normal heart (left), eccentric hypertrophy is associated with ventricular dilation in response to volume overload (center). Concentric hypertrophy is associated with ventricular wall thickening in response to pressure overload (right).

kumar, abbas, fausto [2005]

motivation - cardiac growth

cellular level - pathophysiology of maladaptive growth

healthy cardiomyocyte	eccentric hypertrophy	concentric hypertrophy
physiological loading	volume overload	pressure overload
p, λ	$\theta^{\parallel} (\lambda)$	$\theta^{\perp} (p)$
healthy heart	ventricular dilation	wall thickening

Figure 3. Eccentric and concentric growth on the cellular and organ levels. Compared with the normal heart (left), volume-overload induced eccentric hypertrophy is associated with cell lengthening through the serial deposition of sarcomere units and manifests itself in ventricular dilation in response to volume-overload (center). Pressure-overload induced concentric hypertrophy is associated with cell thickening through the parallel deposition of sarcomere units and manifests itself in ventricular wall thickening in response to pressure-overload (right).

oktepe, abilez, parker, kubl [2010]

motivation - cardiac growth

molecular level - pathophysiology of maladaptive growth

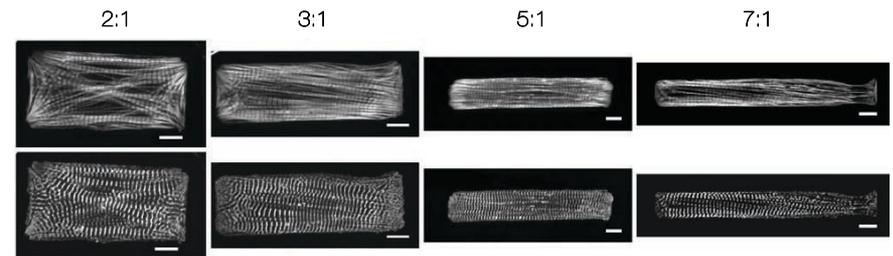


Figure 3. Controlled cardiomyocyte remodeling in vitro. Cardiomyocytes adapt their size, shape, and intracellular architecture when spatially confined in vitro through patterning on fibronactin islands at different aspect ratios (2:1, 3:1, 5:1, and 7:1). Isolated confocal slices display 2D morphology of myofibrils with respect to actin (top) and alpha-actinin (bottom). Although overall cardiomyocyte size changes, the individual sarcomere units remain at constant length.

geisse, sheehy, parker [2009]

motivation - cardiac growth

linking growth across the scales - fiber orientation

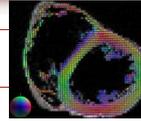
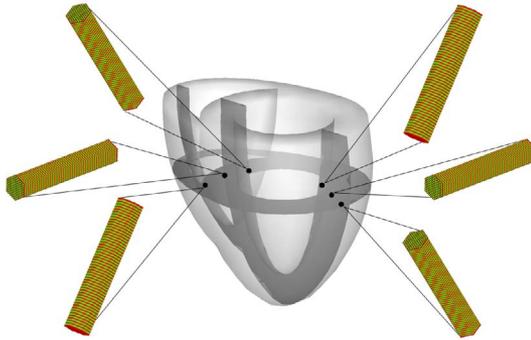


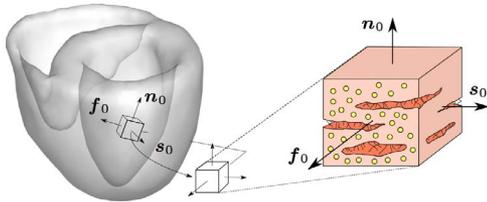
Figure 6. Generic biventricular heart model generated from two truncated ellipsoids, with heights of 70mm and 60mm, radii of 30mm and 51mm, and wall thicknesses of 12mm and 6mm, respectively. In the healthy heart, cardiomyocytes are assumed to be cylindrical, 100 μ m long with a diameter of 16.7 μ m. They consist of 50 serial sarcomere units in length and 91 parallel units per cross section, each of them 2 μ m long and 2 μ m in diameter. They are arranged helically around the long axis of the heart with a transmurally varying inclination of -55° in the epicardium, the outer wall, to $+55^\circ$ in the endocardium, the inner wall, measured with respect to the basal plane.

göktepe, abilez, parker, kuhl [2010], collaboration with dan ennis, dept. radiology, UCL A

motivation - cardiac growth

9

locally orthotropic material behavior



$$\psi = \kappa [J^e - \ln(J^e) - 1] + \frac{a}{2b} \exp(b|I_1^e - 3|) + \frac{a_s}{2b_s} [\exp(b_s|I_s^e - 1|^2) - 1] + \frac{a_f}{2b_f} [\exp(b_f|I_f^e - 1|^2) - 1] + \frac{a_{fs}}{2b_{fs}} [\exp(b_{fs} I_{fs}^{e2}) - 1]$$

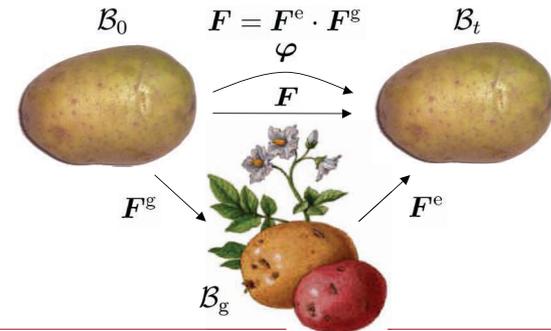
$$\tau = 2 \frac{\partial \psi}{\partial \mathbf{g}} = J^e p \mathbf{g}^{-1} + 2 \psi'_1 \mathbf{b}^e + 2 \psi'_f \mathbf{f}^e \otimes \mathbf{f}^e + 2 \psi'_{fs} [\mathbf{f}^e \otimes \mathbf{s}^e]^{\text{sym}} + 2 \psi'_s \mathbf{s}^e \otimes \mathbf{s}^e$$

dokos, small, young, le greece [2002], schmid, nash, young, hunter [2006], holzapfel, ogden [2009], göktepe, acharya, wong, kuhl [2010]

constitutive equations

11

kinematics of finite growth



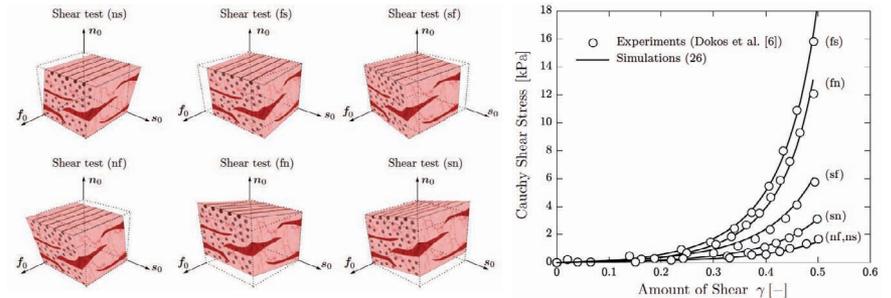
concept of incompatible growth configuration

lee [1969], rodriguez, hoger, mculloch [1994], taber [1995], epstein, maugin [2000], humphrey [2002], ambrosi, molica [2002], himpel, kuhl, menzel, steinmann [2005]

motivation - cardiac growth

10

locally orthotropic material behavior

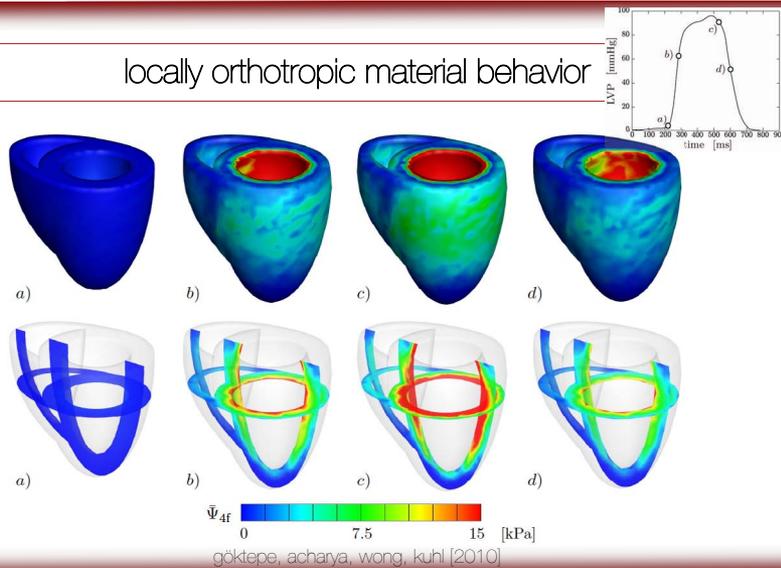


dokos, small, young, le greece [2002], schmid, nash, young, hunter [2006], holzapfel, ogden [2009], göktepe, acharya, wong, kuhl [2010]

constitutive equations

12

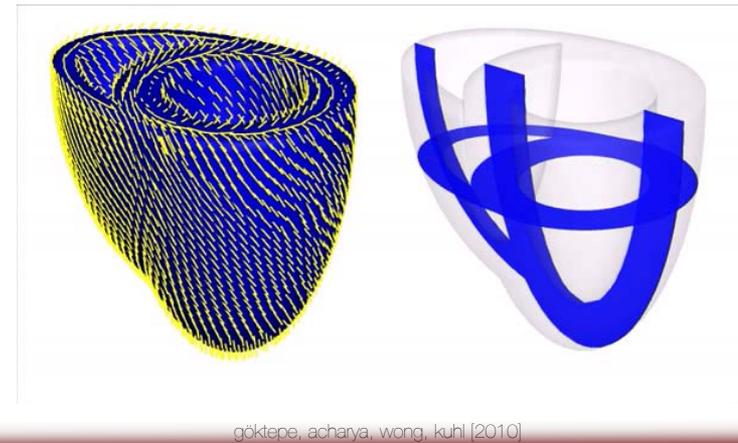
locally orthotropic material behavior



constitutive equations

13

locally orthotropic material behavior



constitutive equations

14

case I - athlete's heart syndrome



- growth due to **significant exercise**
- driven by **elevated pressure** and **increased filling**
- cardiac **output increases** from 6 l/min at rest to **40 l/min**
- cardiac **mass increases** up to **50%**
- cardiomyocyte number remains constant ~6 billion
- cardiomyocyte **size increases isotropically up to 40%**

eckblom, bermansen [1968], hunter, chien [1999], plum, zwinderman, van der laarse, van der wall [2000]

athlete's heart - isotropic growth

15

first reported case of heart failure in athletes



the word **marathon** originates from the **legend of phidippides**. phidippides was sent from the battlefield of marathon to athens to announce that the persians who had invaded greece had been defeated in the battle of marathon. the legend states that phidippides ran the entire **distance of 26 miles** without stopping and burst into the assembly, to announce greece's victory before he **collapsed and died on the spot**. [490bc]

athlete's heart - isotropic growth

16

physiology of athlete's heart

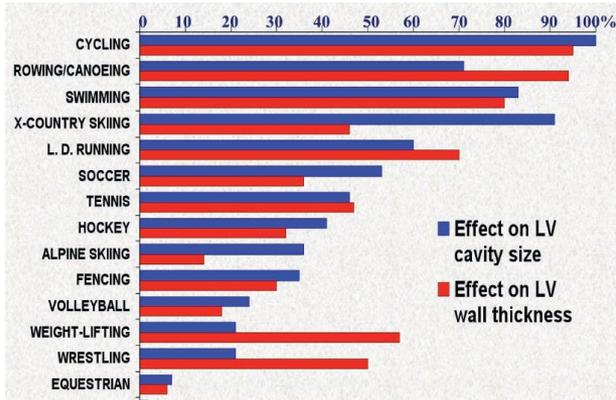
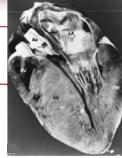
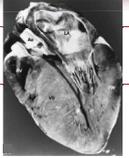


Table. Relative impact of different sports on left ventricular (LV) dimensions.
pellucida [1998]

athlete's heart - isotropic growth

17

governing equations



- multiplicative decomposition

$$\mathbf{F} = \mathbf{F}^e \cdot \mathbf{F}^g \quad \text{with } \mathbf{F} = \nabla_{\mathbf{x}} \varphi$$

- growth tensor

$$\mathbf{F}^g = \vartheta^g \mathbf{I}$$

- evolution of isotropic growth multiplier
cardiomyocyte volume increase rate

$$\dot{\vartheta}^g = k^g(\vartheta^g) \phi^g(\mathbf{M}^e) \quad \text{with } k^g(\vartheta^g) = \frac{1}{\tau} \left[\frac{\vartheta^{\max} - \vartheta^g}{\vartheta^{\max} - 1} \right]^\gamma$$

- growth criterion

$$\phi^g = \text{tr}(\mathbf{M}^e) - M^{e \text{ crit}}$$

maximum cardiomyocyte increase ϑ^{\max} , sarcomere deposition time τ , deposition nonlinearity γ , critical pressure level $M^{e \text{ crit}}$

athlete's heart - isotropic growth

18

four parameter growth model - sensitivity analysis

$$\phi^g = \text{tr}(\mathbf{M}^e) - M^{e \text{ crit}} \quad k^g(\vartheta^g) = \left[\frac{\vartheta^{\max} - \vartheta^g}{\vartheta^{\max} - 1} \right]^\gamma / \tau$$

maximum cardiomyocyte increase ϑ^{\max} sarcomere deposition time τ

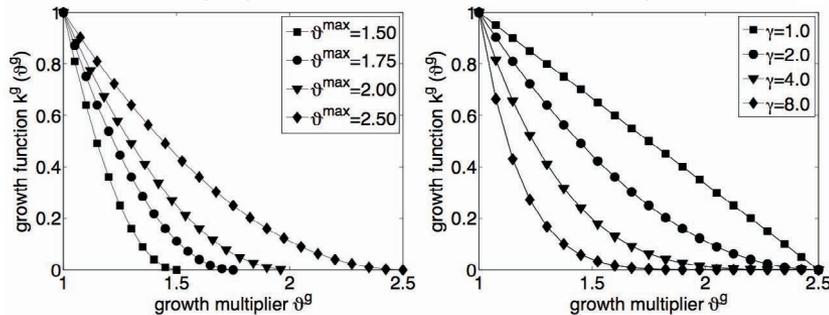


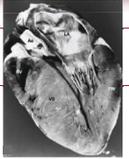
Figure 5. Three-parameter growth function. The growth rate decays smoothly until the growth multiplier ϑ has reached its maximum value ϑ^{\max} , here shown for $\gamma = 2.0$ and $\tau = 1.0$ (left). The nonlinearity of the growth process increases for increasing γ , here shown for $\gamma = 2.5$ and $\tau = 1.0$.

oaktopa, abilez, kuhl [2010]

athlete's heart - isotropic growth

19

algorithmic treatment



given \mathbf{F} and ϑ_n^g	
initialize $\vartheta^g \leftarrow \vartheta_n^g$	
local Newton iteration	
calculate elastic tensor $\mathbf{F}^e = \mathbf{F} / \vartheta^g$	(1)
calculate elastic right Cauchy Green tensor $\mathbf{C}^e = \mathbf{F}^{e \text{ t}} \cdot \mathbf{F}^e$	(2)
calculate second Piola Kirchhoff stress $\mathbf{S}^e = 2 \partial \psi / \partial \mathbf{C}^e$	(10)
check growth criterion $\phi^g = \text{tr}(\mathbf{C}^e \cdot \mathbf{S}^e) - M^{e \text{ crit}} \geq 0$?	(29)
calculate growth function $k^g = \left[\frac{\vartheta^{\max} - \vartheta^g}{\vartheta^{\max} - 1} \right]^\gamma / \tau$	(28)
calculate residual $\mathbf{R} = \vartheta^g - \vartheta_n^g - k^g \phi^g \Delta t$	(30)
calculate tangent $\mathbf{K} = \partial \mathbf{R} / \partial \vartheta^g$	(31)
update growth multiplier $\vartheta^g \leftarrow \vartheta^g - \mathbf{R} / \mathbf{K}$	
check convergence $\mathbf{R} \leq \text{tol}$?	
calculate second Piola Kirchhoff stress $\mathbf{S} = 1 / \vartheta^{g 2} \mathbf{S}^e$	(32)
calculate Lagrangian moduli \mathbf{L}	(35)
push forward to Kirchhoff stresses $\boldsymbol{\tau} = \mathbf{F} \cdot \mathbf{S} \cdot \mathbf{F}^{\text{t}}$	(36)
push forward to Eulerian moduli $\mathbf{e} = [\mathbf{F} \otimes \mathbf{F}] : \mathbf{L} : [\mathbf{F}^{\text{t}} \otimes \mathbf{F}^{\text{t}}]$	(37)

Table 1. Algorithmic treatment of stress-driven isotropic growth.

oaktopa, abilez, kuhl [2010]

athlete's heart - isotropic growth

20

physiology of athlete's heart syndrome

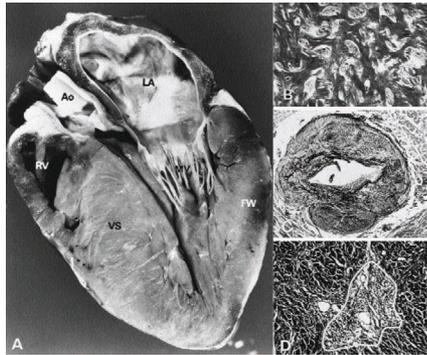


Figure. Morphological components of the disease process in hypertrophic cardiomyopathy (HCM), the most common cause of sudden death in young competitive athletes. A. Gross heart specimen sectioned in cross-sectional plane; left ventricular wall thickening shows an asymmetrical pattern and is confined primarily to the ventricular septum, which bulges prominently into the left ventricular outflow tract. The left ventricular cavity appears in reduced size. B-D Histological features characteristic of left ventricular myocardium in HCM.

maron [1997]

athlete's heart - isotropic growth

21

athlete's heart - stress-driven isotropic growth

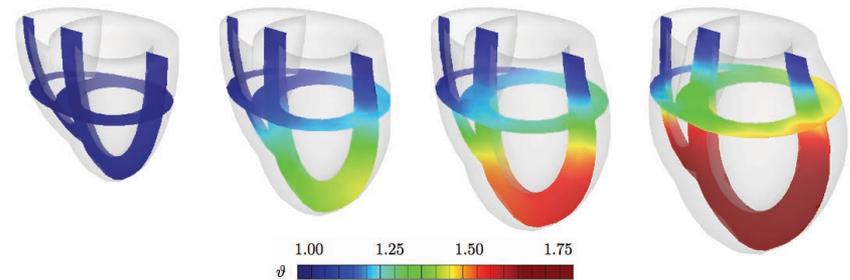


Figure 7. Athlete's heart, stress-driven isotropic eccentric and concentric growth, left ventricular dilation and wall thickening. The isotropic growth multiplier gradually increases from 1.00 to 1.75 as the individual cardiomyocytes grow both eccentrically and concentrically. On the macroscopic scale, the athlete's heart manifests itself in a progressive apical growth with a considerably increase in left ventricular cavity size to enable increased cardiac output during exercise. To withstand higher blood pressure levels during training, the heart muscle grows and the wall thickens.

oakley, abelez, kuhl [2010]

athlete's heart - isotropic growth

22

case II - cardiac dilation



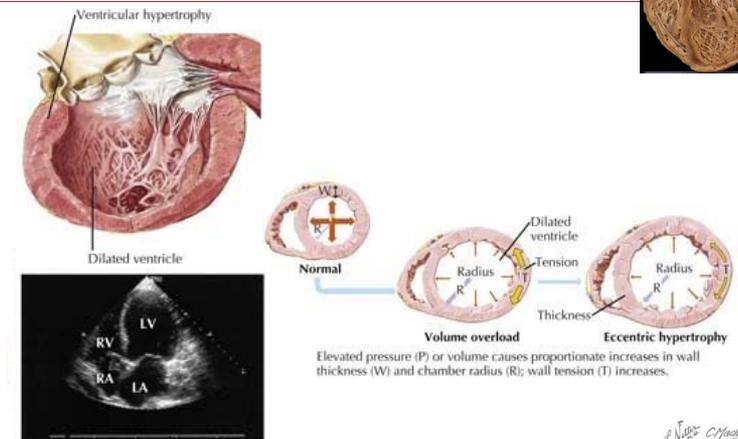
- chronic **enlargement** at constant wall thickness
- cardiac **mass increases 3x** to 1000 g
- cardiomyocyte number remains constant ~6 billion
- cardiomyocytes **lengthen 40%** at constant cell diameter
- sarcomere number increases **from ~50 to ~70** in series
- sarcomere length remains constant at 1.9-2.1 μm

eckblom, hermansen [1968], gerdes et al [1992], hunter, chion [1999], plum et al [2000], yoshida et al [2010]

cardiac dilation - eccentric growth

23

case II - cardiac dilation



Elevated pressure (P) or volume causes proportionate increases in wall thickness (W) and chamber radius (R); wall tension (T) increases.

netter's cardiology [2010]

A. Netter, M.D.

cardiac dilation - eccentric growth

24

constitutive equations



- multiplicative decomposition

$$\mathbf{F} = \mathbf{F}^e \cdot \mathbf{F}^g \quad \text{with } \mathbf{F} = \nabla_{\mathbf{x}} \varphi$$

- growth tensor

$$\mathbf{F}^g = \mathbf{I} + [\lambda^g - 1] \mathbf{f}_0 \otimes \mathbf{f}_0$$

- evolution of eccentric growth multiplier
serial sarcomere deposition rate

$$\dot{\lambda}^g = k^g(\lambda^g) \phi^g(\lambda^e) \quad \text{with } k^g = \frac{1}{\tau} \left[\frac{\lambda^{\max} - \lambda^g}{\lambda^{\max} - 1} \right]^\gamma$$

- growth criterion

$$\phi^g = \lambda^e - \lambda^{\text{crit}} = \frac{\lambda}{\lambda^g} - \lambda^{\text{crit}}$$

maximum serial sarcomere deposition λ^{\max} , sarcomere deposition time τ , deposition nonlinearity γ , critical sarcomere stretch λ^{crit}

cardiac dilation - eccentric growth

25

pathophysiology of cardiac dilation

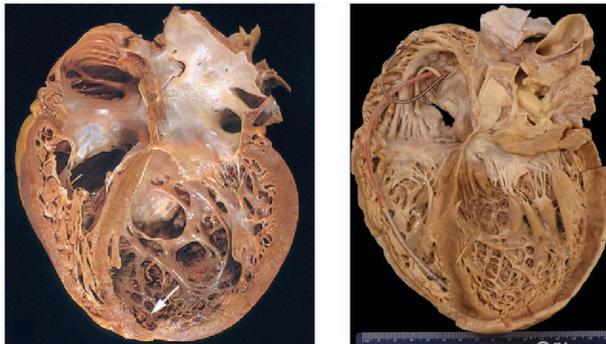
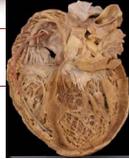


Figure 8. Strain-driven eccentric growth, cardiac dilation, and increase in cavity size at constant wall thickness. The heart is usually enlarged, rounded, flabby, and heavy with a weight of up to three times its normal weight (left), reprinted with permission from Robbins and Cotran. Heart specimen from a patient with cardiac dilation who died in end-stage heart failure. The ventricles are significantly dilated while the wall thickness has remained unaltered, courtesy of Allen P. Burke.

cardiac dilation - eccentric growth

27

algorithmic treatment



given \mathbf{F} and λ_n^g	
initialize $\lambda^g \leftarrow \lambda_n^g$	
local Newton iteration	
check growth criterion $\phi^g = \lambda^e - \lambda^{\text{crit}} \geq 0$?	(46)
calculate growth function $k^g = [(\lambda^{\max} - \lambda^g)/(\lambda^{\max} - 1)]^\gamma / \tau$	(45)
calculate residual $R = \lambda^e - \lambda^g - k^g \phi^g \Delta t$	(47)
calculate tangent $K = \partial R / \partial \phi^g$	(48)
update growth stretch $\lambda^g \leftarrow \lambda^g - R / K$	
check convergence $R \leq \text{tol}$?	
calculate growth tensor $\mathbf{F}^g = \mathbf{I} + [\lambda^g - 1] \mathbf{f}_0 \otimes \mathbf{f}_0$	(41)
calculate elastic tensor $\mathbf{F}^e = \mathbf{F} \cdot \mathbf{F}^{g-1}$	(1)
calculate elastic right Cauchy Green tensor $\mathbf{C}^e = \mathbf{F}^{e\text{t}} \cdot \mathbf{F}^e$	(2)
calculate elastic second Piola Kirchhoff stress $\mathbf{S}^e = 2 \partial \psi / \partial \mathbf{C}^e$	(10)
calculate second Piola Kirchhoff stress $\mathbf{S} = \mathbf{F}^{g-1} \cdot \mathbf{S}^e \cdot \mathbf{F}^g$	(17)
calculate Lagrangian moduli \mathbf{L}	(18) with (19), (20), (43), (49)
push forward to Kirchhoff stress $\boldsymbol{\tau} = \mathbf{F} \cdot \mathbf{S} \cdot \mathbf{F}^t$	(21)
push forward to Eulerian moduli $\mathbf{e} = [\mathbf{F} \otimes \mathbf{F}] : \mathbf{L} : [\mathbf{F}^t \otimes \mathbf{F}^t]$	(22)

Table 2. Algorithmic treatment of strain-driven transversely isotropic growth.

oaktena.abilez.kubli [2010]

cardiac dilation - eccentric growth

26

cardiac dilation through strain-driven eccentric growth

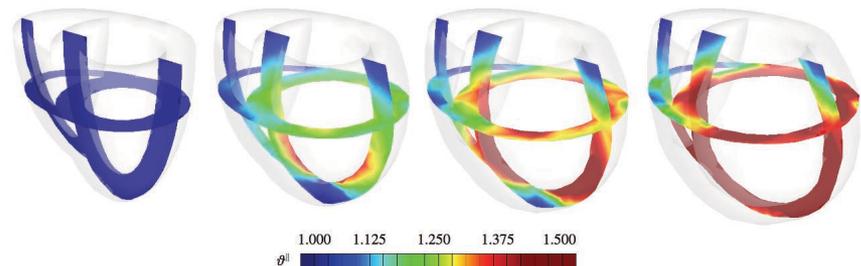


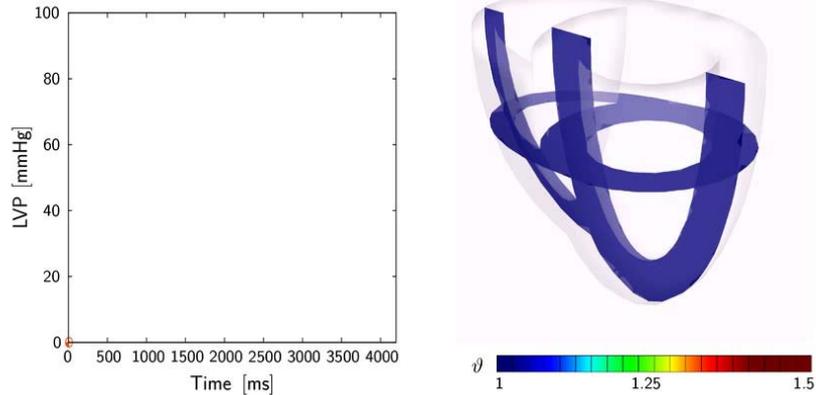
Figure 10. Strain-driven eccentric growth. The eccentric growth multiplier gradually increases from 1.00 to 1.50 as the individual cardiomyocytes grow eccentrically. On the structural level, eccentric growth manifests itself in a progressive dilation of the left ventricle accompanied by a significant increase in cardiac mass, while the thickness of the ventricular wall remains virtually unchanged.

oaktena.abilez.parker.kubli [2010]

cardiac dilation - eccentric growth

28

cardiac dilation through strain-driven eccentric growth



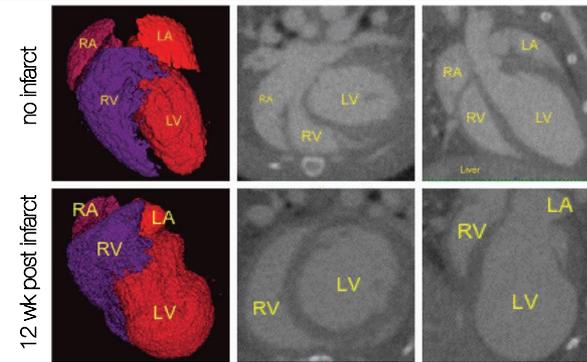
goktepe, abilez, parker, kuhl [2010]

cardiac dilation - eccentric growth

29



in vivo model of cardiac dilation



end-diastolic volume \uparrow from 37.12mm^3 to 133.16mm^3

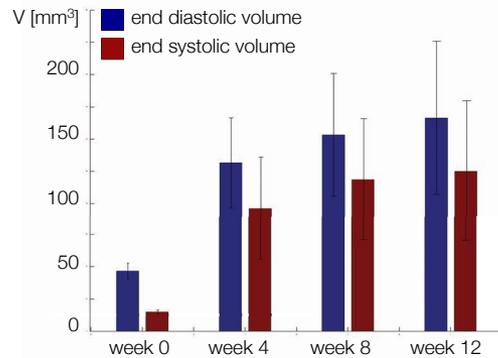
doyle, sheikh, sheikh, cao, yang, robbins, wu [2007]

cardiac dilation - eccentric growth

30



in vivo model of cardiac dilation



ejection fraction \downarrow from 68.16% to 23.33%

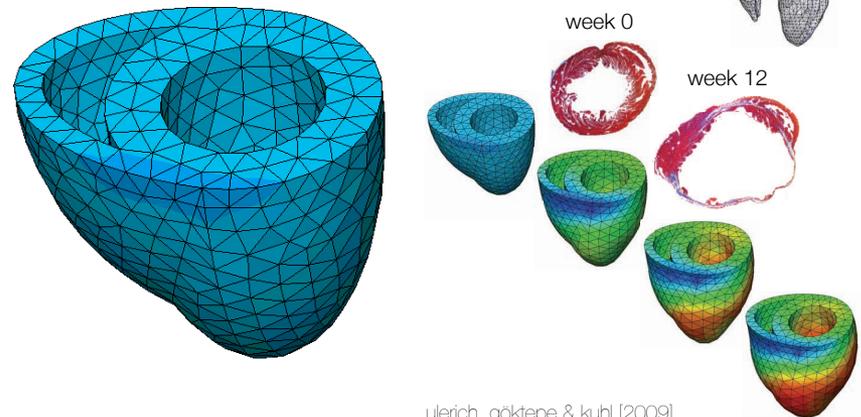
doyle, sheikh, sheikh, cao, yang, robbins, wu [2007]

cardiac dilation - eccentric growth

31



in silico prediction of cardiac dilation



ulerich, goktepe & kuhl [2009]

doyle, sheikh, sheikh, cao, yang, robbins, wu [2007]

cardiac dilation - eccentric growth

32

in vivo model of sarcomerogenesis

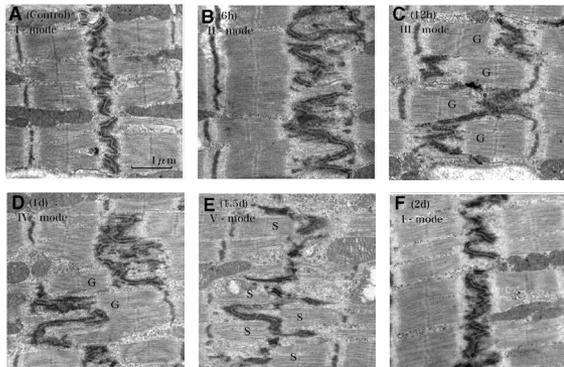
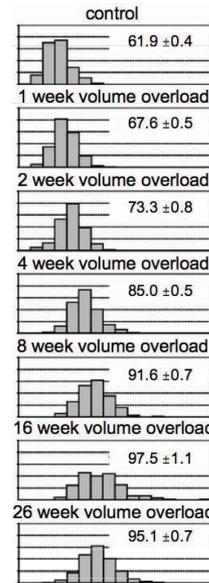


Figure 10. Ultrastructural changes of the intercalated disk after volume overload. A Control. After 6 hours of volume overload, the ICD becomes thick with one-sarcomere-long interdigitations. B After 12 hours, the ICD is folded to form one-sarcomere-deep grooves and contra-grooves with short interdigitations. C At 1 day, interdigitations elongate up to one-sarcomere long in the folded ICD, D, so that the ICD broadens to ~two sarcomere wide. Grooves and contra-grooves appear in this mode. At 1.5 days, the ICD is thin with mostly short interdigitations, but one-sarcomere-long interdigitations sporadically appear as spikes. E. There appear spaces surrounded by several spikes. At 2 days, the ICD is thin and flat with short interdigitations similar to those of controls, finishing one cycle of serial sarcomere addition.

yoshida, sho, nonjo, takahashi, kobayashi, kawamura, honma, komatsu, sugita, yamauchi, hosoi, ito, masuda [2010]

cardiac dilation - eccentric growth

33



strain-driven eccentric growth through sarcomerogenesis

Figure 7. Strain-driven eccentric growth. Overall, eccentric growth is clearly heterogeneous with a transmural variation in serial sarcomere deposition. Cardiomyocytes in the endocardium, the inner wall, reach their maximum length of 150µm through the serial deposition of 25 additional sarcomere units of 2µm each. Cardiomyocytes in the epicardium, the outer wall, reach a stable state at a length of 130µm through the serial deposition of 15 additional sarcomere units. Eccentric growth along the septum is almost identical to eccentric growth along the free wall initiating an overall shape change from elliptical to spherical.

ocktapa, abilez, parker, kubi [2010]

cardiac dilation - eccentric growth

35

in vivo model of sarcomerogenesis



- **14% dilation** due to volume overload
- dilation by **cardiomyocyte elongation**
- elongation by **serial sarcomere deposition**
- sarcomere **number increases linearly** from 62 to 85
- sarcomere deposition **rate is linear** in weeks 1 to 4 decays smoothly to **saturation** at week 26

yoshida, sho, nonjo, takahashi, kobayashi, kawamura, honma, komatsu, sugita, yamauchi, hosoi, ito, masuda [2010]

cardiac dilation - eccentric growth

34

case III - cardiac wall thickening



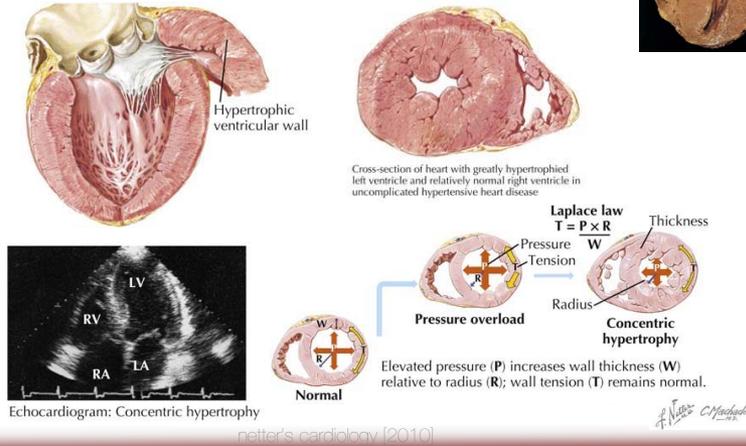
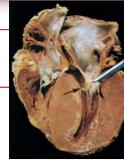
- chronic **wall thickening** at constant cardiac size
- wall thickness **increases from 1cm to 3cm**
- cardiomyocyte number remains constant ~6 billion
- cardiomyocyte diameter **increases from 15µm to 40µm**
- sarcomere number **increases in parallel**
- sarcomere length remains constant at 1.9-2.1µm

opie [2003], maron, mc kenna [2003], kumar, abbas, fausto [2005]

cardiac wall thickening - concentric growth

36

case III - cardiac wall thickening

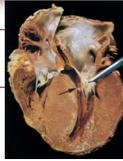


netter's cardiology [2010]

A. Netter, M.D.

cardiac wall thickening - concentric growth

constitutive equations



- multiplicative decomposition

$$\mathbf{F} = \mathbf{F}^e \cdot \mathbf{F}^g \quad \text{with } \mathbf{F} = \nabla_{\mathbf{x}} \varphi$$

- growth tensor

$$\mathbf{F}^g = \mathbf{I} + [\vartheta^g - 1] \mathbf{s}_0 \otimes \mathbf{s}_0$$

- evolution of concentric growth multiplier parallel sarcomere deposition rate

$$\dot{\vartheta}^g = k^g(\vartheta^g) \phi^g(M^e) \quad \text{with } k^g(\vartheta^g) = \frac{1}{\tau} \left[\frac{\vartheta^{\max} - \vartheta^g}{\vartheta^{\max} - 1} \right]^\gamma$$

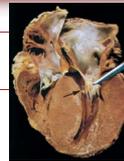
- growth criterion

$$\phi^g = \text{tr}(M^e) - M^{e \text{ crit}}$$

maximum parallel sarcomere deposition ϑ^{\max} , sarcomere deposition time τ , deposition nonlinearity γ , critical pressure level $M^{e \text{ crit}}$

cardiac wall thickening - concentric growth 38

algorithmic treatment



given \mathbf{F} and ϑ_n^g	
initialize $\vartheta^g \leftarrow \vartheta_n^g$	
local Newton iteration	
calculate growth tensor $\mathbf{F}^g = \mathbf{I} + [\vartheta^g - 1] \mathbf{s}_0 \otimes \mathbf{s}_0$	(51)
calculate elastic tensor $\mathbf{F}^e = \mathbf{F} \cdot \mathbf{F}^{g-1}$	(1)
calculate elastic right Cauchy Green tensor $\mathbf{C}^e = \mathbf{F}^{e \dagger} \cdot \mathbf{F}^e$	(2)
calculate second Piola Kirchhoff stress $\mathbf{S}^e = 2 \partial \psi / \partial \mathbf{C}^e$	(10)
check growth criterion $\phi^g = \text{tr}(\mathbf{C}^e \cdot \mathbf{S}^e) - M^{e \text{ crit}} \geq 0$?	(56)
calculate growth function $k^g = [(\vartheta^{\max} - \vartheta^g) / (\vartheta^{\max} - 1)]^\gamma / \tau$	(55)
calculate residual $\mathbf{R} = \dot{\vartheta}^g - \vartheta_n^g - k^g \phi^g \Delta t$	(58)
calculate tangent $\mathbf{K} = \partial \mathbf{R} / \partial \vartheta^g$	(59)
update growth multiplier $\vartheta^g \leftarrow \vartheta^g - \mathbf{R} / \mathbf{K}$	
check convergence $\mathbf{R} \leq \text{tol}$?	
calculate second Piola Kirchhoff stress $\mathbf{S} = \mathbf{F}^{g-1} \cdot \mathbf{S}^e \cdot \mathbf{F}^g$	(17)
calculate Lagrangian moduli \mathbf{L}	(18) with (19), (20), (53), (60)
push forward to Kirchhoff stress $\boldsymbol{\tau} = \mathbf{F} \cdot \mathbf{S} \cdot \mathbf{F}^t$	(21)
push forward to Eulerian moduli $\mathbf{e} = [\mathbf{F} \otimes \mathbf{F}] : \mathbf{L} : [\mathbf{F}^t \otimes \mathbf{F}^t]$	(22)

Table 3. Algorithmic treatment of stress-driven transversely isotropic growth.

optkara.abiliz.kubli [2010]

cardiac wall thickening - concentric growth 39

pathophysiology of cardiac wall thickening

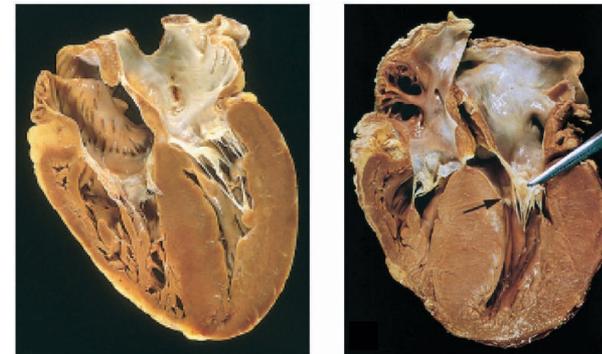


Figure 10. Stress-driven concentric growth, cardiac wall thickening, and transmural muscle thickening at constant cardiac size, reprinted with permission from Robbins & Cotran. Left ventricular outflow obstruction has caused pressure-overload hypertrophy associated with a significant wall thickening (left). A pronounced septal hypertrophy has caused the significantly thickened septal muscle to bulge into the left ventricular outflow tract (right).

optkara.abiliz.kubli [2010]

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cardiac wall thickening through stress-driven concentric growth

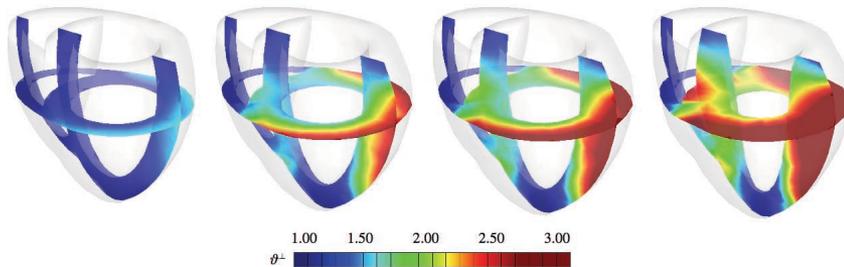
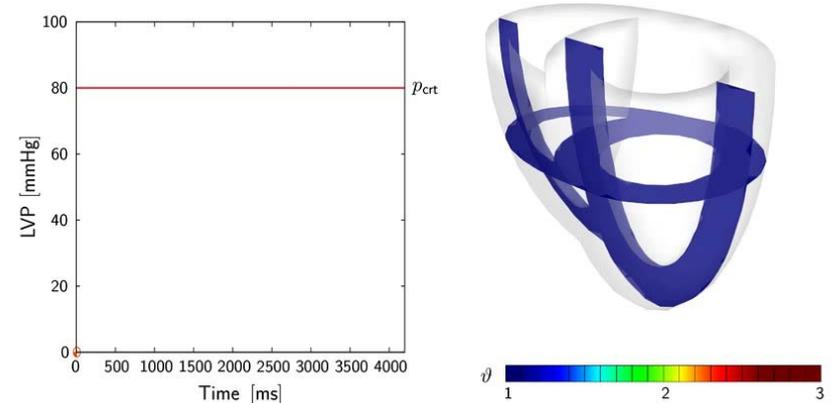


Figure 10. Stress-driven concentric growth. The concentric growth multiplier gradually increases from 1.00 to 3.00 as the individual cardiomyocytes grow concentrically. On the structural level, concentric growth manifests itself in a progressive transmural wall thickening to withstand higher blood pressure levels while the overall size of the heart remains virtually unaffected. Since the septal wall receives structural support through the pressure in the right ventricle, wall thickening is slightly more pronounced in the free wall where the wall stresses are higher.

goktepe, abilez, parker, kuhl [2010]

cardiac wall thickening - concentric growth 41

cardiac wall thickening through stress-driven concentric growth



goktepe, abilez, parker, kuhl [2010]

cardiac wall thickening - concentric growth 42

stress-driven concentric growth through sarcomerogenesis

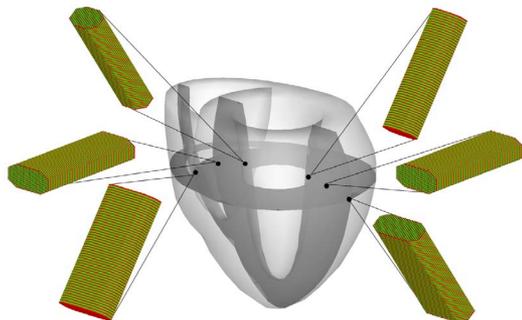


Figure 9. Stress-driven concentric growth. Concentric growth is clearly heterogeneous with a transmural variation in parallel sarcomere deposition. Cardiomyocytes in the endocardium, the inner wall, reach a stable state at a thickness of $31.4\mu\text{m}$ through the parallel deposition of 84 additional sarcomere units. Cardiomyocytes in the epicardium, the outer wall, reach their maximum thickness of $50\mu\text{m}$ through the parallel deposition of 182 sarcomere units. Concentric growth at the free wall is slightly more pronounced than at the septum.

goktepe, abilez, parker, kuhl [2010]

cardiac wall thickening - concentric growth 43

systemic vs pulmonary hypertension

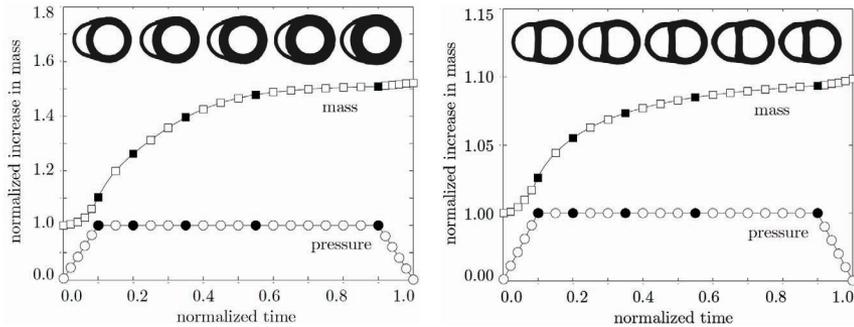


Figure. Stress-driven concentric growth, cardiac wall thickening, and transmural muscle thickening at constant cardiac size. Left ventricular wall thickening in response to systemic hypertension (left) from Kumar, Abbas, Fausto [2005]. Right ventricular wall thickening in response to pulmonary hypertension (right), from Padera.

rausch, dam, goktepe, abilez, kuhl [2010]

cardiac wall thickening - concentric growth 44

systemic vs pulmonary hypertension

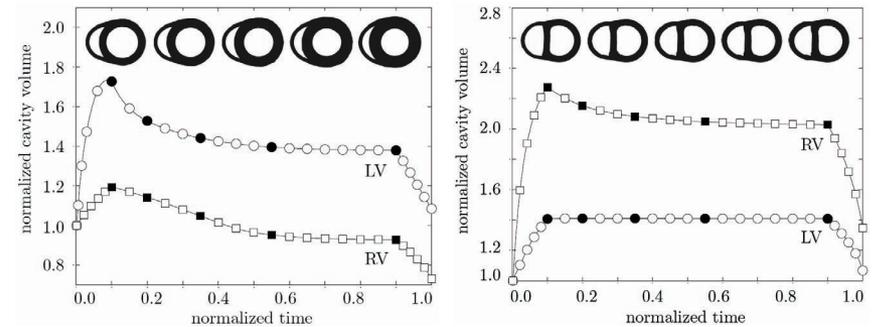


cardiac mass increases more
in systemic (+50%) than in pulmonary (+10%) hypertension

rausch, dam, goktepe, abilez, kuhl [2010]

cardiac wall thickening - concentric growth 45

systemic vs pulmonary hypertension

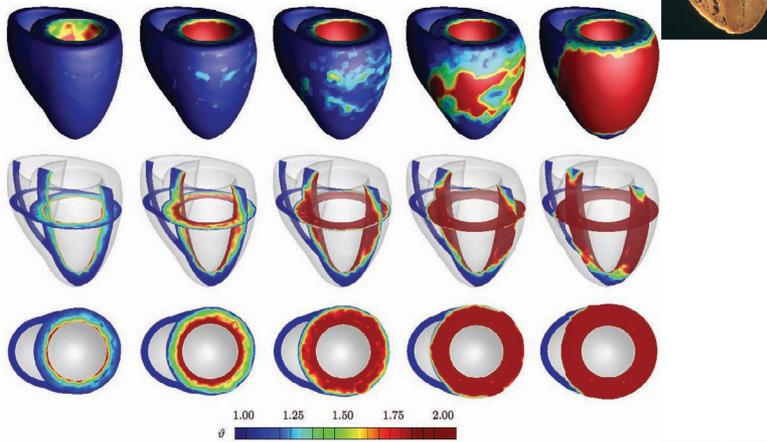


cavity volumes decrease significantly
in both systemic and pulmonary hypertension

rausch, dam, goktepe, abilez, kuhl [2010]

cardiac wall thickening - concentric growth 46

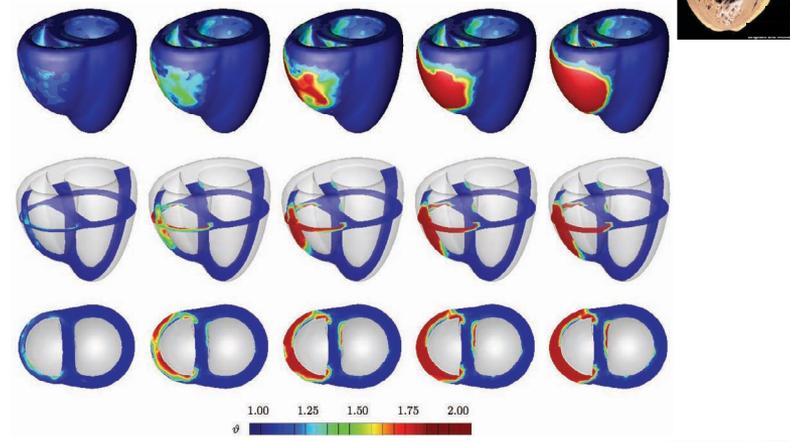
systemic hypertension - LV wall thickening



rausch, dam, goktepe, abilez, kuhl [2010]

cardiac wall thickening - concentric growth 47

pulmonary hypertension - RV wall thickening



rausch, dam, goktepe, abilez, kuhl [2010]

cardiac wall thickening - concentric growth 48