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Post-Infarction Left Ventricular Remodeling and the Law of Laplace

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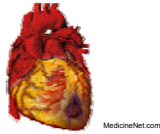


Abstract

The contractile function of the heart is determined by factors including cavity volume, wall thickness, internal pressure, intrinsic muscle property, and circumferential stress and strain. In this study, we used the Law of Laplace to investigate how left ventricular (LV) geometry and the heart's intrinsic properties impact chamber function during passive inflation. The geometric parameters were identified by means of image analysis of MRI scans of a healthy and failing mouse heart, while the end-diastolic pressure (EDP) and muscle property parameters were identified from literature. Changes in geometric configurations, pressure-volume relationships, and stress-strain relationships were studied across healthy and infarct geometries and three elastic modulus configurations. The results show that LV geometry and the muscle's intrinsic properties independently impact chamber function and together contribute to the changes in cardiac function.

Background

- Myocardial infarction is the death of heart muscle caused by the occlusion of a coronary artery.
- Myocardial infarction is a leading cause of morbidity and mortality in the United States, accounting for approximately 607,000 (1 of every 5) deaths in 2005¹.
- Consequences of myocardial infarction include diastolic dysfunction and post-infarction LV remodeling², which involves:
 - Infarct expansion
 - Ventricular dilatation
 - Hypertrophy
 - Wall thinning
 - Progressive fibrosis
 - Contractile function deterioration
 - Heart failure



Objective

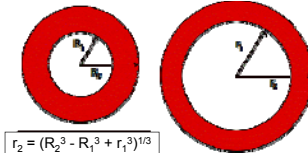
To identify the adaptive responses of the heart after myocardial infarction with regards to its changes in geometry and intrinsic muscle properties to better understand the mechanics underlying LV remodeling and heart failure.

Methods

- We used the a mathematical model of LV mechanics based on the Law of Laplace to represent the heart's geometry as a thin spherical shell.
- Muscle property and geometric parameters were identified from literature and image analysis of mouse heart MRI scans.
- The parameters were entered into a custom program modeling an inflating sphere to calculate internal pressure, cavity volume, wall volume, circumferential stress, and circumferential strain.
- Pressure-volume and stress-strain relationships were obtained and analyzed for various changes in geometric and elastic modulus configurations.

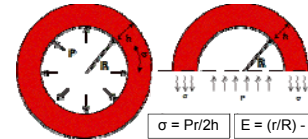
Modeling LV Inflation

Inflation of an incompressible sphere



$$r_2 = (R_2^3 - R_1^3 + r_1^3)^{1/3}$$

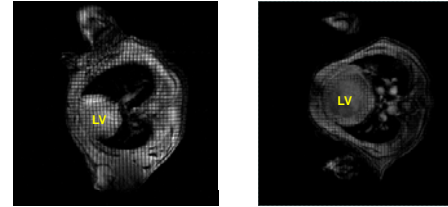
Law of Laplace for calculating wall stress



$$\sigma = Pr/2h \quad E = (r/R) - 1$$

We modeled the heart's geometry as a thin spherical shell using the Law of Laplace to derive formulas for deformed radius, LV cavity and wall volumes, wall stress (σ), and circumferential strain (E).

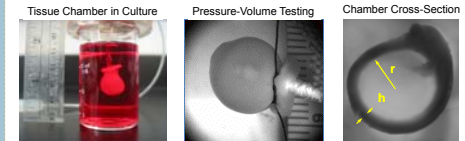
Mouse Heart MRI



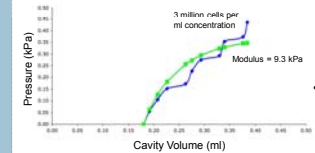
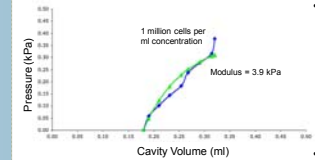
Healthy Diastole, Modulus = 18 kPa	Unloaded Model	Infarct Diastole, Modulus = 55 kPa	Unloaded Model
Image Analysis	Image Analysis	Image Analysis	Image Analysis
$R_1 = 1.25$ cm	$R_1 = 1.228$ cm	$R_1 = 2.30$ cm	$R_1 = 1.968$ cm
$R_2 = 2.60$ cm	$R_2 = 2.595$ cm	$R_2 = 3.20$ cm	$R_2 = 3.045$ cm
EDP = 0.4 kPa	$P = 0.0$ kPa	EDP = 2.0 kPa	$P = 0.0$ kPa

- Geometric parameters were identified by image analysis of MRI scans of a healthy and failing (2-weeks post-LAD occlusion) mouse heart, with typical EDP parameters used to model unloading.
- Intrinsic muscle parameters were assumed at 18 kPa for healthy and 55 kPa for a failing (fibrosis) mouse heart from literature³

Engineered Cardiac Chambers



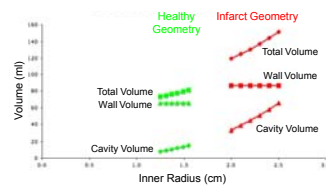
Internal Pressure vs. Cavity Volume



- The spherical model of the heart's geometry is consistent with the pressure-volume data from engineered cardiac tissue (ECT) chambers
- The spherical model is useful to separate the geometric and mechanical properties of ECT-related data
- Estimated mechanical properties consistent with cell composition

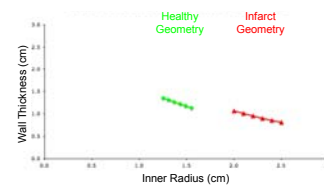
Results

Volume vs. Inner Radius



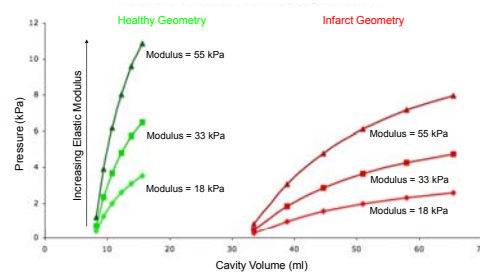
- Infarcted wall volume is increased (hypertrophy)
- For a given geometric configuration, wall volume stays constant, while the cavity and total volume increases at the same rate
- Infarcted geometry has a larger cavity volume at diastole that further expands with inflation (LV dilation)

Wall Thickness vs. Inner Radius



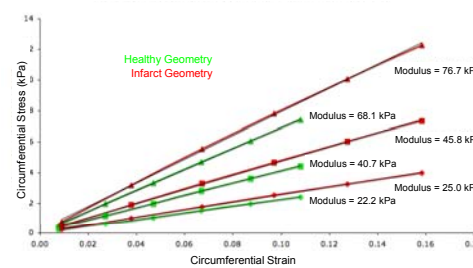
- Infarcted geometry has a thinner wall thickness at diastole (wall thinning)
- As inner radius increases with inflation, wall thickness decreases

Internal Pressure vs. Cavity Volume



- As cavity volume increases, the internal pressure increases nonlinearly
- Increasing elastic modulus causes the internal pressure to increase at a faster rate for the same change in cavity volume
- Infarct geometry has a higher cavity volume range and slower rate of changing pressure

Mid-Wall Circumferential Stress vs. Strain



- As circumferential strain increases, stress increases linearly
- Although two different geometries, stress/strain curves are similar
- The muscle's elastic modulus is independent of the geometry
- Increasing modulus increases pressure and workload on the heart (contractile function deterioration)

Summary

- Myocardial infarction results in ventricular remodeling which consists of changes in geometry and mechanical properties
- LV Geometry and the muscle's intrinsic contractile property can change independently, and together account for the difference in chamber function between a healthy and infarcted heart
- Only altering the muscle's elastic modulus affects:
 - Internal pressure-volume relationship
 - Circumferential stress-strain relationship
- Only altering geometric configurations affects:
 - Amount of changes in wall thickness as inner radius increases
 - Ratio of cavity volume to wall volume
 - Pressure-volume workload
- A combination of modeling based on the Law of Laplace and engineered cardiac tissue chambers can be a powerful tool for understanding LV remodeling and chamber function

References

- Lloyd-Jones D. *et al. Circulation* 119(3):e21-181, 2009.
- Sutton M, Sharpe N. *Circulation* 101:2981-2988, 2000.
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