Modeling the Mechanical Properties of Large Ovine Arteries using in-vivo and in-vitro data

Daniela Valdez-Jasso, MS

Department of Mathematics
Biomathematics
NC State University
Objective

- Develop elastic and viscoelastic models of the large ovine arteries using stress-strain laws that relate blood pressure and cross-sectional area.

- Use these models to quantify elastic and viscoelastic wall properties across vessels including vessel stiffness, unstressed radius, and viscoelastic relaxation times.

- Validate the models against in-vitro and in-vivo data measured in male Merino sheep.
Artery elastin & eosin

- Tunica intima
- Internal elastic lamina
- Tunica media
- Fine elastic fibres
- External elastic lamina
- Tunica adventitia
Arterial wall viscoelasticity

- Large arteries have more elastin fibers than the smaller arteries, which are mainly composed of collagen.
  - Large arteries (diameter $> 2$ mm) are viscoelastic.
  - Small arteries are almost rigid.

- Smooth muscle cells have an inner helix formation.

- Cardiovascular diseases change arterial viscoelasticity both locally and globally.
  - Aging (global).
  - Hypertension (global).
  - Atherosclerosis (local).
In-vitro data

- 11 male Merino sheep 25-35 kg, 2 years old

- Pressure, wall-thickness, and external vessel diameter were measured in seven segments
  - Ascending aorta (S1)
  - Central descending aorta (S2)
  - Medial descending aorta (S3)
  - Peripheral descending aorta (S4)
  - Femoral artery (S5)
  - Brachiocephalic trunk (S6)
  - Carotid artery (S7)
Diagram of in-vitro experiment

- Jarvik
- PP
- Chamber
- Reservoir
- Ultrasonic Crystals
- Pressure Microtransducer
- Sonomicrometer
- Amplifier Converter A/D
- Osilloscope
- PC
In-vivo data

- 7 male Merino sheep 25-35 kg, 2 years old.
- Pressure and external vessel diameter were measured in the proximal descending aorta of conscious with the heart beating at 6-9 frequencies from 60-200 BPM.
  - A pacemaker were sutured to the ventricle wall during open chest surgery.
- Sheep were allowed to return to pre-surgery status (7 days).
- Range of heart rates were obtained by stimulating the pacemaker electrically.
Experimental measurements

In Vitro Data

In Vivo Data
### In-vitro and in-vivo data

<table>
<thead>
<tr>
<th>Pressure</th>
<th>In-vitro</th>
<th>In-vivo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max [mmHg]</td>
<td>136.3-146.6</td>
<td>65.8-180.5</td>
</tr>
<tr>
<td>Min [mmHg]</td>
<td>54.5-65.3</td>
<td>50.3-82.2</td>
</tr>
<tr>
<td>Difference [mmHg]</td>
<td>71.5-87.7</td>
<td>12.8-98.3</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>22.5-28.3</td>
<td>3.8-15.71</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Diameter</th>
<th>In-vitro</th>
<th>In-vivo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max [mmHg]</td>
<td>2.03-2.1</td>
<td>1.8-2.25</td>
</tr>
<tr>
<td>Min [mmHg]</td>
<td>1.82-1.9</td>
<td>1.75-2.09</td>
</tr>
<tr>
<td>Difference [mmHg]</td>
<td>0.17-0.23</td>
<td>0.04-0.26</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>0.05-0.07</td>
<td>0.01-0.05</td>
</tr>
</tbody>
</table>
Stress-strain models relating pressure and vessel area

- Elastic model

- Viscoelastic models
  - Kelvin viscoelastic model
  - Generalized viscoelastic model
Elastic model

- Obtained from Hooke’s law for a thin walled tube

\[ s(t) = \frac{r_0}{Eh} p(t), \quad s(t) = 1 - \sqrt{\frac{A_0}{A(t)}} \]

- \( r_0 \) - zero pressure radius
- \( A_0 \) - area at zero pressure \( \left( \pi r_0^2 \right) \)
- \( E \) - Young's modulus
- \( h \) - wall thickness
- \( s \) - strain
- \( p \) - pressure
- \( A \) - area
Viscoelastic models

- Exhibit both elastic and viscous responses to deformation.

- Have three features: relaxation, creep, hysteresis.

- Models in study: Kelvin and Generalized.
Kelvin Viscoelastic model

\[ s + \tau_\sigma \frac{ds}{dt} = \frac{r_0}{Eh} \left( p + \tau_\varepsilon \frac{dp}{dt} \right), \quad s = 1 - \sqrt{\frac{A_0}{A(t)}} \]

\[ \tau_\varepsilon = \frac{\eta}{\mu_1}, \quad \tau_\sigma = \frac{\eta}{\mu_0} \left( 1 + \frac{\mu_0}{\mu_1} \right), \quad \mu_0 = \frac{Eh}{r_0} \]

\[ s(t) = s(0)e^{-t/\tau_\sigma} + \frac{r_0}{Eh\tau_\sigma} \left( \tau_\varepsilon p(t) - \tau_\varepsilon p(0)e^{-t/\tau_\sigma} + \frac{\tau_\sigma + \tau_\varepsilon}{\tau_\sigma} \int_0^t e^{-(t-\gamma)/\tau_\sigma} p(\gamma) \, d\gamma \right) \]

- \( \mu_0 \) - spring constant
- \( \mu_1 \) - spring constant
- \( \eta \) - dashpot constant
- \( s \) - strain
- \( p \) - pressure
- \( A \) - area
Extending the Kelvin model
Generalized model

\[ s_K(t) = \left[ s(0) - \frac{r_0}{Eh} p(0) \right] e^{-t/\tau_\sigma} + \frac{r_0}{Eh} p(0) + \frac{r_0}{Eh} \int_0^t \left( 1 - \frac{\tau_\sigma - \tau_\varepsilon}{\tau_\sigma} e^{-(t-\gamma)/\tau_\sigma} \right) \frac{dp(\gamma)}{d\gamma} d\gamma \]

\[ \theta_K = \{ r_0, Eh, \tau_\sigma, \tau_\varepsilon \} \]

\[ s_G(t) = \left[ s(0) - \frac{r_0}{Eh} p(0) \right] J(t) + \frac{r_0}{Eh} p(0) + \frac{r_0}{Eh} \int_0^t G(t-\gamma) \frac{dp(\gamma)}{d\gamma} d\gamma, \quad \text{where} \]

\[ J(t) = B_1 e^{-t/b_1} + (1 - B_1) e^{-t/b_2}, \]

\[ G(t) = 1 - A_1 e^{-t/b_1} - A_2 e^{-t/b_2} \]

\[ \theta_G = \{ \theta_K, A_2, b_1, B_1 \} \]
Model validation

- Blood pressure used as an input to compute strain.

- Nonlinear least squares optimization used to estimate model parameters that minimize the difference between computed and measured values of the cross-sectional area.

- Used fminsearch in matlab, an unconstrained nonlinear minimization algorithm based on the Nelder-Mead simplex (direct search) method.

\[ J(\theta) = \frac{1}{n - n_p} \sum_{j=1}^{n} \left| f_j(\theta) - a_j \right|^2 , \]

where \( n_p \) is the number of parameters used.
Elastic (red) and Kelvin (blue) model
Blood pressure and vessel area

In Vitro Data

In Vivo Data
Elastic and Kelvin model Hysteresis

In Vitro Data

In Vivo Data
In-vivo data [110-160 BPM] Kelvin model
Linear regression of parameters within a sheep in-vivo

- Optimized r0
  - \( y = 0.0002x + 0.8648 \)
  - \( R^2 = 0.8034 \)

- Optimized Tau Epsilon
  - \( y = 9E-05x + 0.0059 \)
  - \( R^2 = 0.1601 \)

- Optimized Eh
  - \( y = 1.2139x + 720.37 \)
  - \( R^2 = 0.2837 \)

- Optimized Tau Sigma
  - \( y = 6E-17x + 2E-14 \)
  - \( R^2 = 0.064 \)
Kelvin and Generalized model

In Vitro Data

In Vivo Data
Kelvin and Generalized model
Hysteresis

In Vitro Data

In Vivo Data
Multi-frequency Kelvin and Generalized models
Nonlinearity in data
Model dependency

Statistical model is assumed to be

$$\tilde{A}_j = f_j(\theta_0) + \epsilon_j, \quad j = 1, \ldots n$$

$\epsilon_j$ error i.i.d, random variables with $E[\epsilon_j] = 0$, and $\text{var}[\epsilon_j] = \sigma^2$. 
Conclusions

- Incorporating viscoelasticity in the vessel modeling significantly decreases the least squares error.

- Viscoelasticity describes hysteresis observed in the data, which is more pronounced in-vitro than in-vivo.

- In-vivo data are more noisy than the in-vitro data – probably due to experimental techniques and the fact that the sheep are conscious.

- Generalized viscoelastic model does not significantly improve model predictions.

- Data is itself nonlinear.
References

- D. Bia, Y. Zocalo, R. Armentano. “Regional Differences in viscosity, elasticity and wall buffering function in systemic arteries: pulse wave analysis of the arterial pressure-diameter relationship.”


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