Outline

- Introduction
- Mechanical properties of tissue
- Approaches in elasticity imaging
- Elasticity imaging systems
- Applications
- Challenges, advantages and limitations
- Future developments

Elasticity Imaging – Goal

Remote

non-invasive (or adjunct to invasive) imaging (or sensing) of
mechanical properties of tissue for clinical applications

Notations

\( X = (x_1, x_2, x_3) \) – coordinate system

\( U = (u_1, u_2, u_3) \) – displacement vector

\( \epsilon_{ij} \) – strain tensor \( i = 1, 2, 3 \)

\( \sigma_{ij} \) – stress tensor \( j = 1, 2, 3 \)

\( \delta_{ij} \) – Kronecker delta

(1 for \( i = j \), 0 otherwise)

Einstein summation convention – summation is implied over the repeated index, for example:

\[ a_i = \sum a_{ij} \delta_{ij} \]

\[ a_{ij} = \sum a_{ijk} \delta_{ik} \]

ρ – density (kg/m³)

ν – Poisson’s ratio

E – Young’s modulus

\( \lambda, \mu \) – Lame coefficients

G – shear modulus

K – bulk modulus

\( \eta \) – shear viscosity

\( \xi \) – bulk viscosity

c₁ – shear wave speed

c₃ – longitudinal wave speed

\[ c_1 = \sqrt{\frac{\mu}{\rho}} \]

\[ c_3 = \sqrt{\frac{\lambda + 2\mu}{\rho}} \]
Elasticity Imaging – Glance at History

Hippocrates, circa 460-377 B.C.

Mechanical Properties of Tissue
(i.e., Why Bother)

Elasticity (e.g., bulk and shear moduli)

Viscosity (e.g., bulk and shear viscosities)

Nonlinearity (e.g., strain hardening)

Other (e.g., anisotropy, pseudoelasticity)

Elasticity

Changes in tissue elasticity are related to pathological changes

... Such swellings as are soft, free from pain, and yield to the finger; ... and are less dangerous than the others.
... then, as are painful, hard, and large, indicate danger of speedy death; but such as are soft, free of pain, and yield when pressed with the finger, are more chronic than these.

THE BOOK OF PROGNOSTICS, Hippocrates, 400 B.C.

Which Elastic Moduli?

Most soft tissues are incompressible, i.e., deformation produces no volume change

$$c_1 = \frac{G}{\rho} < c_1 = \sqrt{\frac{K + \frac{4}{3}G}{\rho}}$$

$$\frac{G}{K} \to 0 \quad \nu \to \frac{1}{2}$$
Elasticity

Relations between various elastic constants

<table>
<thead>
<tr>
<th>Constant</th>
<th>Common Pair</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\lambda, \mu)</td>
<td>(\frac{E}{(1+\nu)(1-2\nu)})</td>
</tr>
<tr>
<td>(\mu)</td>
<td>(\frac{\mu(3\lambda+2\mu)}{(\lambda+\mu)})</td>
</tr>
<tr>
<td>(E)</td>
<td>(\frac{\nu}{(3\lambda+2\mu)})</td>
</tr>
<tr>
<td>(\nu)</td>
<td>-</td>
</tr>
<tr>
<td>(K)</td>
<td>(\frac{\lambda+2\mu}{3(1-2\nu)})</td>
</tr>
<tr>
<td>(G)</td>
<td>(\frac{\mu}{(1+\nu)})</td>
</tr>
</tbody>
</table>

How to (Directly) Measure Tissue Elasticity

- Sample preparation
- Deformation method
  - Static
  - Oscillatory (low frequency)
- Preconditioning of the tissue
- Load – Displacement measurements
- Strain – Stress calculations
- Elastic modulus evaluation

Human sense of touch – what do we feel?

Incompressible material

\[ F_i = 3\mu_0 \]

Static deformation of (nearly) incompressible material is primarily determined by shear or Young’s modulus (!!!), and boundary conditions (!!!)

How to (Directly) Measure Tissue Elasticity

- Sample preparation
- Deformation method
  - Static
  - Oscillatory (low frequency)
- Preconditioning of the tissue
- Load – Displacement measurements
- Strain – Stress calculations
- Elastic modulus evaluation

Direct Elasticity Measurements

Load – Displacement Tests

\[ F = 8RW\mu \]

Semi-infinite elastic medium

\[ F = 3\mu \]

Semi-infinite elastic medium

Scale

Stress (kPa)

Strain (%)
Direct Elasticity Measurements

Breast Tissue Elasticity and Pathology

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Young's Modulus (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal gland</td>
<td>0.5 - 1.5</td>
</tr>
<tr>
<td>Infiltrative ductal cancer with fibrous tissue predominating</td>
<td>2.0 - 3.0</td>
</tr>
<tr>
<td>Infiltrative ductal cancer with fibrous tissue predominating</td>
<td>5.0 - 12.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Young's Modulus (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal fat</td>
<td>15 ± 7</td>
</tr>
<tr>
<td>Normal glandular tissue (n = 10)</td>
<td>28 ± 14</td>
</tr>
<tr>
<td>Fibrous tissue</td>
<td>96 ± 34</td>
</tr>
<tr>
<td>Infiltrative ductal cancer (n = 10)</td>
<td>27 ± 3</td>
</tr>
<tr>
<td>Invasive and infiltrating ductal cancer (n = 25)</td>
<td>906 ± 33</td>
</tr>
</tbody>
</table>

Breast Tissue Elasticity and Pathology

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Elastic Modulus at Strain 0.01</th>
<th>SD</th>
<th>Elastic Modulus at Strain 0.05</th>
<th>SD</th>
<th>Elastic Modulus at Strain 0.10</th>
<th>SD</th>
<th>Elastic Modulus at Strain 0.15</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fat</td>
<td>4.8 ± 2.5</td>
<td></td>
<td>6.6 ± 2.7</td>
<td></td>
<td>7.9 ± 3.0</td>
<td></td>
<td>17.4 ± 8.4</td>
<td></td>
</tr>
<tr>
<td>Gland</td>
<td>17.5 ± 8.6</td>
<td></td>
<td>13.0 ± 6.7</td>
<td></td>
<td>88.1 ± 66.7</td>
<td></td>
<td>271.8 ± 167.7</td>
<td></td>
</tr>
<tr>
<td>Phyllodes Tumor</td>
<td>56.0 ± 90.8</td>
<td></td>
<td>8.6 ± 163.4</td>
<td></td>
<td>164.3 ± 0.0</td>
<td></td>
<td>297.7 ± 0.0</td>
<td></td>
</tr>
<tr>
<td>Papilloma</td>
<td>22.2 ± 5.8</td>
<td></td>
<td>54.4 ± 19.7</td>
<td></td>
<td>169.7 ± 80.6</td>
<td></td>
<td>537.8 ± 209.1</td>
<td></td>
</tr>
<tr>
<td>Lobular Carcinoma</td>
<td>34.7 ± 7.9</td>
<td></td>
<td>78.9 ± 42.9</td>
<td></td>
<td>221.8 ± 0.0</td>
<td></td>
<td>628.4 ± 0.0</td>
<td></td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>45.5 ± 20.1</td>
<td></td>
<td>100.5 ± 39.6</td>
<td></td>
<td>288.4 ± 110.9</td>
<td></td>
<td>889.2 ± 205.9</td>
<td></td>
</tr>
<tr>
<td>Infiltrating Ductal Carcinoma</td>
<td>47.1 ± 19.8</td>
<td></td>
<td>115.7 ± 42.9</td>
<td></td>
<td>384.5 ± 126.9</td>
<td></td>
<td>1366.5 ± 348.2</td>
<td></td>
</tr>
<tr>
<td>Ductal Carcinoma in Situ</td>
<td>71.2 ± 18.7</td>
<td></td>
<td>188.7 ± 618.7</td>
<td></td>
<td>638.0 ± 206.2</td>
<td></td>
<td>2162.1 ± 0.0</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Adipose tissue</th>
<th>Fibroglanular tissue</th>
<th>High grade ductal carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>x (N m⁻²)</td>
<td>13.8</td>
<td>12.75</td>
<td>87.2</td>
</tr>
<tr>
<td>E (kPa)</td>
<td>1.9</td>
<td>1.8</td>
<td>12.0</td>
</tr>
</tbody>
</table>


Krouskop et al., 1998, Ultrasonic Imaging, 20:260-274.


Elastic Properties of Arteries


<table>
<thead>
<tr>
<th>Type of soft tissue</th>
<th>E, kPa</th>
<th>Comments</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Human, in vitro</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic aorta</td>
<td>300-940</td>
<td></td>
<td>McDonald, 1974</td>
</tr>
<tr>
<td>Abdominal aorta</td>
<td>180-1-400</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Iliac artery</td>
<td>1,000-3,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femoral artery</td>
<td>1,200-5,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascending aorta</td>
<td>183-582</td>
<td></td>
<td>Alessandro et al., 1995</td>
</tr>
<tr>
<td>Coronary artery</td>
<td>1,000-4,110</td>
<td></td>
<td>Gobba et al., 1998</td>
</tr>
<tr>
<td>Saphenous small arteries</td>
<td>100-1,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic wall</td>
<td>700-1,600</td>
<td></td>
<td>Equilibrium values for various ages (0-80 y.o.) and osteoarthritis conditions in right and left aortas.</td>
</tr>
<tr>
<td>Porcine, in vitro</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thoracic aorta</td>
<td>300-940</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intramural layer</td>
<td>100-1,500</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Media</td>
<td>700-1,600</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adventitia</td>
<td>342</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Descending aorta</td>
<td>348</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intramural layer</td>
<td>342</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

For normal physiological conditions of longitudinal tension and distending blood pressure, below 200 mm Hg.

Elastic Properties of Prostate Gland


Contrast in Elasticity Imaging

Sarvazyan et al., 1995

Elastic Properties of Prostate Gland


Strain hardening

- Most soft tissues exhibit strain hardening
- Tissues of organs with primary "mechanical" functions (muscle, skin, tendon, etc.)
- Other tissues (kidney, brain, blood clot, etc.)
- Strain hardening vs. strain softening (strain energy density function)
Strain hardening

This and other graphs as well as other literature data suggest that tissue strain hardening (or nonlinearity in stress-strain relations) can be used for tissue analysis including composition, differentiation, etc.

Anisotropy

- Arterial wall: orthotropic material – 9 constants
- Muscle: transversely isotropic – 5 constants
- Isotropic – 2 constants

Viscosity

- Shear viscosity: shear waves
- Bulk viscosity: longitudinal ultrasound waves
- Viscoelastic models:
  - Maxwell, Voigt, Kelvin, KVFD, etc.
- Is there a characteristic time?

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>Ratio to Fat at Strain = 0.01</th>
<th>Ratio to Fat at Strain = 0.05</th>
<th>Ratio to Fat at Strain = 0.10</th>
<th>Ratio to Fat at Strain = 0.14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gland</td>
<td>4</td>
<td>5</td>
<td>8</td>
<td>16</td>
</tr>
<tr>
<td>Phyllodian Tumor</td>
<td>12</td>
<td>14</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Papilloma</td>
<td>5</td>
<td>6</td>
<td>14</td>
<td>31</td>
</tr>
<tr>
<td>Lobular Carcinoma</td>
<td>7</td>
<td>12</td>
<td>21</td>
<td>36</td>
</tr>
<tr>
<td>Fibroadenoma</td>
<td>0</td>
<td>15</td>
<td>28</td>
<td>51</td>
</tr>
<tr>
<td>Intestining Ductal</td>
<td>10</td>
<td>18</td>
<td>37</td>
<td>59</td>
</tr>
<tr>
<td>Carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ductal Carcinoma in 5%</td>
<td>15</td>
<td>20</td>
<td>61</td>
<td>124</td>
</tr>
</tbody>
</table>

Table 4: The ratio of elastic modulus of each tissue type to fat at 4 different strain levels.

Witkowsky et al., 1999

Krouskop et al., 1998

Opitz et al., 2001
Viscosity

• Hysteresis loops: independent of the rate of loading (most soft tissues)
• Pseudoelastic material: elastic after preconditioning (with hysteresis)

![Graph showing stress-strain relationship with loading cycles](image)

Mechanical Properties of Tissue: References

• Fung YC. Biomechanics – mechanical properties of living tissues. Springer-Verlag; New York, 1981
• Other text books and archival publications

Phantoms for Elasticity Imaging

- Tissue-mimicking phantoms
  - Gelatin gels
  - Agar-agar and gelatin mixtures
  - Rubber (plastisol, silicone) materials
  - PVA (poly-vinyl alcohol)
  - Polyacrilamide gels

- Tissue-containing phantoms
  - Gelatin gels
  - Agar-agar and gelatin gels
  - Polyacrilamide gels

- Gelatin and Gelatin/Agar-agar
  - Easy to prepare
  - E ~ C^2, C – concentration, n=1-2
  - Short shelf life
  - Additives are possible

- Plastisol
  - Time-stable phantoms
  - Requires excessive heating during preparation

- PVA
  - Freeze-thaw cycles to vary elasticity
  - Time-stable

Phantoms for Elasticity Imaging: Preparation

- PVA (poly-vinyl alcohol) tissue-mimicking phantom

- Background:
  - 8% PVA solution
  - 1% silica (40um diameter)
  - 1 freeze/thaw cycle

- Inclusion:
  - 10% PVA solution
  - 2% silica particles
  - 3 freeze/thaw cycles

- Imaging: SONIX RP imaging system
  - 5-7 MHz, 40 mm linear probe

- Deformations
  - Manual 0.3%

![Diagram showing phantom preparation](image)
Phantoms for Elasticity Imaging: References

- Other text books and archival publications
- Where to buy
  ATS Laboratories, Inc. (http://www.atslabs.com/)

Elasticity Imaging – Approaches

**Static (strain-based, or reconstructive)**
*imaging internal motion under static deformation*

**Dynamic (wave-based)**
*imaging shear wave propagation*

**Mechanical (stress-based, also reconstructive)**
*measuring tissue response at the surface*

Elasticity Imaging using ...?

**Computerized Tomography:**
*spatial distribution of the absorption (density)*

**MRI:**
*proton spin density and relaxation time constants*

**Ultrasound Imaging:**
*variation in acoustical impedance (bulk modulus and density)*

**Optical Imaging:**
*refraction index*

How … Static Elasticity Imaging?

![Diagram showing displacement, strain, and mechanical properties]

- Displacement
- Strain
- Range
- Soft
- Hard
How … Static Elasticity Imaging?

- Capture data during deformation
- Estimate displacements
- Compute strain tensor
- Reconstruct mechanical properties

Elasticity Imaging – Main Components

- Capture data during externally or internally applied tissue motion or deformation
- Evaluate tissue response (displacement, strain, stress)
- Reconstruct elastic modulus based on theory of elasticity

Theory of elasticity is common part in all approaches in Elasticity Imaging

Theory of Elasticity (Static Approach)

General (3-D) case

\[
\begin{align*}
\varepsilon_i &= \frac{1}{2} \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} + \frac{\partial u_j}{\partial x_i} \right) \\
\sigma_{ij} &= \lambda \varepsilon_i \delta_{ij} + 2 \mu \varepsilon_{ij} \\
\sum \frac{\partial \sigma_{ij}}{\partial x_j} + f_i &= 0
\end{align*}
\]

Equations of Equilibrium

Small deformations of linear, isotropic (i.e., Hookean) material

\[
\begin{align*}
\frac{\partial}{\partial x_1} \left( \frac{\partial \sigma_{11}}{\partial x_1} + \frac{\partial \sigma_{12}}{\partial x_2} + \frac{\partial \sigma_{13}}{\partial x_3} \right) + \frac{\partial}{\partial x_2} \left( \frac{\partial \sigma_{21}}{\partial x_1} + \frac{\partial \sigma_{22}}{\partial x_2} + \frac{\partial \sigma_{23}}{\partial x_3} \right) + \frac{\partial}{\partial x_3} \left( \frac{\partial \sigma_{31}}{\partial x_1} + \frac{\partial \sigma_{32}}{\partial x_2} + \frac{\partial \sigma_{33}}{\partial x_3} \right) + \frac{\partial}{\partial x_i} \left( \frac{\partial \sigma_{ij}}{\partial x_j} \right) + f_i &= 0
\end{align*}
\]

Examples (incompressible material)

\[F_1 = 3 \mu \varepsilon_{ij}\]
References

• Nowazki W. Dynamics of elastic systems. Wiley; New York, 1963
• Nowazki W. Thermoelasticity. Pergamon Press; New York, 1983
• Other text books and archival publications

Beware: most (soft) tissues are (nearly) incompressible

Displacements

• Speckle motion ↔ Tissue motion ↔ Speckle tracking
• Ultrasound Imaging (2-D → 3-D)
• Displacement vector: \( \mathbf{U} = (u_1, u_2, u_3) \)
  - \( u_1 \) – lateral component
  - \( u_2 \) – axial (along the ultrasound beam)
  - \( u_3 \) – elevational (out-of-plane) component
• Various speckle tracking techniques
• “Anisotropy” in displacement measurements

Image during Deformation

• Externally or internally induced deformation
• Continuous deformation while imaging
• Constrained or free-hand transducer
• Various imaging techniques
• Deformation, not translation

1-D, 2-D (3-D) Correlation Tracking

Normalized Correlation Coefficient

\[
\rho(t) = \frac{\int x_1(t) x_2(t+\tau)dt}{\sqrt{\int x_1^2(t)dt \int x_2^2(t+\tau)dt}}
\]

Kernel Size

Before Deformation

After Deformation

Correlation coefficient

1-D

2-D

Before Deformation

After Deformation

Lag
Strains

- Displacement vector → Strain tensor
- Displacement derivatives

\[ \varepsilon_i = \frac{1}{2} \left( \frac{\partial u_i}{\partial x} + \frac{\partial u_i}{\partial x} + \frac{\partial u_i}{\partial x} \right) \]
- Six (3-D) or three (2-D) independent components

\[ \begin{pmatrix} \varepsilon_{11} & \varepsilon_{12} & \varepsilon_{13} \\ \varepsilon_{21} & \varepsilon_{22} & \varepsilon_{23} \\ \varepsilon_{31} & \varepsilon_{32} & \varepsilon_{33} \end{pmatrix} \]
- Sources of error
- Improvement and Optimization
- Effect of strain hardening, anisotropy, etc.

Deflection: Challenges

Deformation vs. rotation and translation

- Translation – no information about tissue elasticity
- Rotation – no information about tissue elasticity and speckle tracking difficulties
- Deformation – consider “anisotropy” in displacement measurements (example 1)

Volumetric deformation vs. 1-D or 2-D US imaging

Deformation – control the deformation state (i.e., plane strain) if possible

Deformation vs. temporal and spatial sampling

Control deformation rate and/or frame rate and spatial sampling

Deformation vs. distribution and symmetries of elasticity

Spatial symmetries (if any) must be considered to assist
- Displacement estimation
- Imaging of strain and interpretation (example 1 and 2)
- Elasticity reconstruction (example 1 and 2)

Strain Imaging: Challenges

Sources of error in strain images

- Ultrasound imaging system (electronic SNR, etc.)
- Interpolation
- Strain-induced decorrelation
- Other sources (out-of-plane motion, peak hopping, etc.)

Optimal SNR and CNR in strain images

- Short-time correlation, companding, temporal stretching, strain filter, etc.
- Adaptive strain imaging for large deformations, multi-compression, etc.

Anisotropy in displacement measurements

- Incompressibility processing
- Other approaches (phase sensitive interpolation, grid slopes, etc.)

Effect of tissue strain hardening on strain images

- Utilize as independent parameter of tissue differentiation
A fundamental limit on delay estimation

\[ \sigma^2 \geq \frac{3}{2 f_0^2 \pi^2 T (B^3 + 12B)} \left( \frac{1}{\rho^2} \left[ 1 + \frac{1}{SNR^2} \right] - 1 \right) \]

- \( f_0 \) – center frequency
- \( T \) – the observation time
- \( B \) – fractional bandwidth
- \( SNR \) – root mean squared signal-to-noise ratio
- \( \rho \) – correlation coefficient
- \( \sigma^2 \) – root mean squared time delay estimate error

Walker and Trahey, 1995

Interpolation Error

Two-step approach
- Correlation peak position of complex baseband signal
- Phase zero-crossing of analytic signal correlation

Some other approaches are discussed in:
- Cespedes et al., 1995
- Cohn et al., 1997
- Pesavento et al., 1999
- Greiman et al., 2000

O’Donnell et al., 1992
Lubinski et al., 1999

Strain Decorrelation

Strain \( \rightarrow \) Decorrelation \( \rightarrow \) Displacement Error \( \rightarrow \) Strain Error

No strain
- Displacement error \( \sim 1 \) / Kernel Size
- (Kernel size \( \leftrightarrow \) Observation time \( \leftrightarrow \) Window size)

Strain decorrelation
- Reduce kernel size

Filter correlation functions
- Spatial resolution vs. error

Lubinski et al., 1999
Time Delay Estimation and Interpolation Techniques

Time Delay Estimation
- Doppler-based techniques
- Optical Flow
- Normalized Covariance
- Normalized Cross-correlation
- Hybrid-sign Correlation
- Polarity-coincidence Correlation
- Cross-correlation
- Sum of Squared Differences (SSD)
- Sum of Absolute Differences (SAD)
- Many, many other algorithms

Interpolation
- Parabolic
- Phase zero crossing
- Cosine
- Spline
- Grid slopes
- Autocorrelation

• Correlation window is longer than pulse length: the axial resolution of elasticity imaging is determined by the correlation window.
• Correlation window decreases to pulse length and below: spatial resolution is ultimately limited by the bandwidth of the ultrasonic imaging system.

Kernel size vs. resolution and SNR

Formula for optimal kernel size:
\[ T_{opt} \approx \frac{3B}{2s^2f_0} \]

Resolution

SNR

Liu et al., 2003

Varghese et al., 1998

Elasticity Imaging – Approaches

Static (strain-based, or reconstructive)  
imaging internal motion under static deformation

Dynamic (wave-based)  
imaging shear wave propagation

Mechanical (stress-based, also reconstructive)  
measuring tissue response at the surface

Theory of Elasticity  
(Dynamic Approach)

General (3-D) case

\[ \varepsilon_i = \frac{1}{2} \left( \frac{\partial u_i}{\partial x_j} + \frac{\partial u_j}{\partial x_i} - \frac{\partial u_j}{\partial x_i} \right) \]

\[ \begin{align*}
\varepsilon_{i1} & \quad \varepsilon_{i2} & \quad \varepsilon_{i3} \\
\varepsilon_{i2} & \quad \varepsilon_{i3} & \quad \varepsilon_{i1} \\
\varepsilon_{i3} & \quad \varepsilon_{i1} & \quad \varepsilon_{i2}
\end{align*} \]

\[ \begin{align*}
\sigma_{i1} & \quad \sigma_{i2} & \quad \sigma_{i3} \\
\sigma_{i2} & \quad \sigma_{i3} & \quad \sigma_{i1} \\
\sigma_{i3} & \quad \sigma_{i1} & \quad \sigma_{i2}
\end{align*} \]

\[ \begin{align*}
\sigma_{x} & = \lambda \varepsilon_x \delta_x + 2\mu \varepsilon_x + \zeta \frac{\partial \varepsilon_x}{\partial t} \delta_x + 2\eta \frac{\partial \varepsilon_x}{\partial t} \\
\sigma_{x} & \Rightarrow \frac{\partial \sigma_{x}}{\partial x_i} + f = \rho \frac{\partial^2 u_i}{\partial t^2}
\end{align*} \]
Example: plane waves

- Infinite homogeneous ($\lambda, \mu$=const) elastic medium (i.e., ignore bulk and shear viscosities), no body forces ($f=0$)
- Assume that $u_1(x_1,t), u_2(x_1,t),$ and $u_3(x_1,t)$

\[
\frac{\partial}{\partial t} (\lambda \frac{\partial u_1}{\partial x_1} + \mu (\frac{\partial u_1}{\partial x_1} + \frac{\partial u_2}{\partial x_2}) + (2\mu) \frac{\partial u_1}{\partial x_3}) + \frac{\partial}{\partial x_1} (\mu (\frac{\partial u_2}{\partial x_1} + \frac{\partial u_3}{\partial x_3})) = \rho \frac{\partial^2 u_1}{\partial t^2}
\]

\[
\frac{\partial}{\partial t} (\lambda \frac{\partial u_2}{\partial x_2} + \mu (\frac{\partial u_1}{\partial x_1} + \frac{\partial u_2}{\partial x_2}) + (2\mu) \frac{\partial u_2}{\partial x_3}) + \frac{\partial}{\partial x_2} (\mu (\frac{\partial u_2}{\partial x_1} + \frac{\partial u_3}{\partial x_3})) = \rho \frac{\partial^2 u_2}{\partial t^2}
\]

\[
\frac{\partial}{\partial t} (\lambda \frac{\partial u_3}{\partial x_3} + \mu (\frac{\partial u_1}{\partial x_1} + \frac{\partial u_2}{\partial x_2}) + (2\mu) \frac{\partial u_2}{\partial x_3}) + \frac{\partial}{\partial x_3} (\mu (\frac{\partial u_2}{\partial x_1} + \frac{\partial u_3}{\partial x_3})) = \rho \frac{\partial^2 u_3}{\partial t^2}
\]

\[
(\lambda + 2\mu) \frac{\partial^2 u_1}{\partial x_1^2} - \rho \frac{\partial^2 u_1}{\partial t^2} = 0 \rightarrow \frac{\partial^2 u_1}{\partial x_1^2} - c_l^2 \frac{\partial^2 u_1}{\partial t^2} = 0 \text{ where } c_l = \sqrt{\frac{\lambda + 2\mu}{\rho}} \text{ Longitudinal wave (ultrasound)}
\]

\[
\mu \frac{\partial^2 u_2}{\partial x_2^2} - \rho \frac{\partial^2 u_2}{\partial t^2} = 0 \rightarrow \frac{\partial^2 u_2}{\partial x_2^2} - c_s^2 \frac{\partial^2 u_2}{\partial t^2} = 0 \text{ where } c_s = \sqrt{\frac{\mu}{\rho}} \text{ Shear wave}
\]

**Transient Elastography**

Image shear waves and measure its velocity using ultrafast imaging and motion tracking

**Conventional Imaging**

- Imaging with active elements

**Ultrafast Imaging**

- Imaging with transmit and receive elements

Time needed to acquire 1 frame:

\[
t_{\text{frame}} = \frac{2 \cdot 75 \text{ mm}}{1.5 \text{ mm/um}} \cdot 256 \approx 25 \text{ ms}
\]

\[
t_{\text{frame}} = \frac{2 \cdot 75 \text{ mm}}{1.5 \text{ mm/um}} = 100 \text{ ms}
\]

**Transient Elastography**

Evaluate shear modulus from shear wave velocity

Isotropic, homogeneous, elastic medium

\[
\rho \frac{\partial^2 u}{\partial t^2} = (\lambda + \mu) \nabla \left( \nabla \cdot \frac{\partial u}{\partial t} \right) + \mu \Delta \frac{\partial u}{\partial t}
\]

Shear wave propagation equation

\[
\rho \frac{\partial^2 u}{\partial t^2} = \mu \Delta \frac{\partial u}{\partial t}, \quad i = x, y, z
\]

Local inversion algorithm

\[
V_i(x, z) = \sqrt{ \frac{1}{N} \sum_{m=1}^{N} \frac{\partial^2 u_m(x, z, t)}{\partial t^2} \left( \frac{\partial^2 u_m(x, z, t)}{\partial x^2} \right)^2 + \left( \frac{\partial^2 u_m(x, z, t)}{\partial z^2} \right)^2 }
\]
Transient Elastography

Acoustic Radiation Force Imaging

1. Focused Acoustic Radiation Force generates localized, impulsive (<0.1 ms) tissue excitation
2. Track tissue response with the same ultrasonic transducer used for force generation
3. Repeat in multiple locations throughout 2D FOV
4. Generate images of relative tissue response within the region of excitation (displacement after force removal, recovery time, etc) to assess structural information about tissue

Shear Wave Imaging

Supersonic Shear Wave Imaging

Bercoff et al. 2003
Bercoff et al. 2004
Nightingale, Trainey et al. Duke University
Elasticity Imaging Systems
(Static / Dynamic)

- Siemens/Acuson Antares
- Hitachi Imaging System
- Sonic RP by Ultrasonix Medical, Inc.
- Volcano Therapeutics IVUS Imaging
- Winprobe Research Platform
- Other systems

Siemens Sonoline Elegra and Acuson Antares systems

eSiemens Touch elasticity imaging
- Provides additional qualitative information by demonstrating the typical internal characteristics pattern of three cysts.

Fibroadenoma: changing contrast equal lesion size ratio

IDC: constant contrast large lesion size ratio

Hall, Zhu et al, 2000
www.eng.wisc.edu/eng/faculty/hall_hanley.html
www.medphys.wisc.edu/medphys_docs/papers/hall.html
Lesion size comparison technique

Benign fibroadenoma

WR - size ratios for width
AR - size ratios for area
A, B, C, D, E – five observers

Invasive ductal carcinoma

WR - size ratios for width
AR - size ratios for area
A, B, C, D, E – five observers

Potential problems: for some lesions it is difficult to distinguish from the surrounding breast tissue on B-mode images.

Benign fat necrosis

WR - size ratios for width
AR - size ratios for area
A, B, C, D, E – five observers

Regner et al. 2006

Regner et al. 2006

Regner et al. 2006

Regner et al. 2006
Hitachi Hi Vision 8500/900 systems

Noncirrhotic type invasive ductal carcinoma in 29-year-old woman

Fibroadenoma with in 39-year-old woman

Itoh et al. 2006

Acoustic Radiation Force Imaging: Breast

ARFI image of an in vivo breast lesion (an infected lymph node) showing differences in displacement and recovery response of different tissues to radiation force excitation

In vivo Breast Lymph Node (Reactive, Benign)

Typical Lymph Node Histology
Reproduced from Wheaton’s Functional Histology, 4th Ed.

In Vivo Breast Lesions

IDAC
Fibroadenoma

Fat Necrosis
Supersonic Imagine: Elasticity Imaging of Breast

Elasticity Imaging of Prostate cancer

Real-time (30 fps) Strain Imaging of Prostate: Digital System, 7.5 MHz

Elastography of Thermal Lesions in the Liver after RF Ablation
Monitoring liver stiffness after RF ablation

Canine liver tissue *in vitro*

![Image of liver tissue before and after RF ablation]

Ex Vivo RF Liver Ablation

Before RF Ablation  
After RF Ablation

Staging of Liver Fibrosis with Radiation Force

Key clinical question is degree to which liver fibrosis has occurred  
Biopsy? Imaging?  
Quantitative measure of liver stiffness is needed  
SWEI: new shear wave speed estimation approach  
eliminates 2nd order differentiation

![Image of Fibroscan device and user interface]

Fibroscan

http://www.echosens.com
Non-invasive staging of liver fibrosis

SuperSonic Imagine: ShearWave Elastography

In vivo assessment of Young's modulus in a healthy volunteer

Ultrasonix Sonix RP Imaging System

Winprobe Elasticity Imaging System (FPGA-based solution)
Characterizing lesions - Palpograms

In vivo acquisition scheme

3 Dimensional Elastography: feasibility in a human coronary

Vascular Strain Imaging using Arterial Pressure Equalization
Vascular Strain Imaging using Arterial Pressure Equalization

Cardiac Strain and Strain Rate Imaging

- Cross-correlation method
  - high sensitivity
  - high accuracy
  - 2-D or 2.5-D
  - computationally intensive

- Gradient velocity method
  - fast
  - 1-D (axial)
  - aliasing

- Real-time implementation is required

Clinical Data: 5 healthy, 5 diseased arteries
Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE)

Can elasticity imaging age DVT?

First Set of Experiments (learning set, 10 rats)

Second Set of Experiments (4 rats)

Elasticity Imaging to Age DVT

- Sprague-Dawley rats (300 g)
- Surgically induced clots in IVC
- Imaging studies clots at 2-day (acute)
  6-day (sub-acute)
  9-day (chronic)
- Siemens Sonoline Elegra
  9-13 MHz center frequency
- 2-D correlation and strain imaging

Fitting of data from the first set of experiments

\[ \varepsilon = e(aD + b) \]

\( \varepsilon \) = normalized strain

D = age of the clot (day)

Can first data set predict the age of the clot in the second set of experiments?

Estimation error:

\[ \pm 0.5 \text{ day} \]

-20 %

-60 %

Acute DVT

Chronic DVT

Strain magnitude

Ultrasound backscatter

Normalized Strain

Normalized Strain

Age (day)

Age (day)
3-D Strain Imaging

- Deformation → 3-D motion
- Ultrasound imaging: 2-D
- 3-D tracking is needed
- Results:
  - 2-D linear array
  - Siemens Antares
  - 5:1 contrast
  - 1.5% deformation

Non-linearity in stress-strain relations

![Graph showing non-linearity in stress-strain relations](image)

\[ \frac{\partial \mu}{\partial \varepsilon} = \begin{cases} 13 & \text{at } 40 \text{ kPa} \\ 3 & \text{at } 20 \text{ kPa} \end{cases} \]

Imaging of Tissue Non-linearity

![Imaging of Tissue Non-linearity](image)

- Emelianov et al., 1998
- Erkamp et al., 1998, 1999

Elastic Modulus (kPa)
- 40 kPa
- 20 kPa

Strain (%)
- 0
- 5
- 10
- 15
Viscoelasticity Imaging

Strain $\leftrightarrow$ Elasticity
Creep $\leftrightarrow$ Viscosity

Retardance Time Imaging, $T_1$

$\varepsilon(x, k \Delta t) = \varepsilon'_i(x) + \varepsilon'_e(x) \times (1 - \exp(-k \Delta t / T_1(x)))$

Two patients with 1-cm, non-palpable lesions detected mammographically. With the retardance time image, malignant and benign lesions can be differentiated because of differences in the collagen ultrastructure between the two lesion types.

$T_1$:

- Fibroadenoma
- IDC

In Vivo Patient Studies
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