Magnetic Resonance Elastography for Liver Fibrosis

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Outline

• Introduction – Importance of Elasticity in Biological Tissues
• Liver Disease
• Ultrasound Elastography (UE)
• Basics of Magnetic Resonance Imaging (MRI)
• Magnetic Resonance Elastography (MRE)
• MRE vs. UE
• Future of MRE
Importance of Elastography in Biological Tissues

• Elasticity – physical property which indicates a tissue’s ability to change shape in response to a force and recover its original form

• Tissue property which changes the most as a result of disease
  – i.e. Tumours are stiffer, other diseases have fatty deposits which increase elasticity
Importance of Elastography in Biological Tissues

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The Liver

The liver is a very important organ.

It has many important tasks in the body including detoxification, protein synthesis and aiding in digestion.

Its hundreds of tasks are vital for human survival.
Tissue Properties of the Liver

The tissue in the liver is normally very soft.

Changing the tissue properties disrupts the normal functioning of the liver.

The elasticity of the liver drastically changes with the onset of liver disease.
### TABLE 1: Shear Stiffness Values in Liver Parenchyma and Liver Tumors

<table>
<thead>
<tr>
<th>Group</th>
<th>$n$</th>
<th>Shear Stiffness (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Malignant tumors</td>
<td>31</td>
<td>10.1 ± 3.6</td>
</tr>
<tr>
<td>Benign tumors</td>
<td>13</td>
<td>2.7 ± 0.4</td>
</tr>
<tr>
<td>Fibrotic liver</td>
<td>16</td>
<td>5.9 ± 2.5</td>
</tr>
<tr>
<td>Normal liver</td>
<td>13</td>
<td>2.3 ± 0.3</td>
</tr>
</tbody>
</table>
Liver Disease

When the body experiences a viral infection, heavy alcohol consumption, toxins or trauma, the liver cells die.

This stimulates the release of hepatic stellate cells, which causes build up of extracellular matrix (a connective tissue).

Liver cells are able to regenerate themselves and eventually the scar tissue is replaced with normal liver tissue.
Liver Fibrosis and Cirrhosis

However, in a diseased liver the break down of scar tissue is much slower than the build up.

Fibrosis occurs when an excessive amount of scar tissue builds up and disrupts the normal functioning of the liver. If the disease progresses it can lead to cirrhosis—where the liver is severely scarred and it must be replaced.

Liver Fibrosis is reversible. Once it reaches the point of cirrhosis, nothing can be done to salvage the liver.
Detecting Liver Fibrosis in the Past

Elasticity is a key property in diagnosing liver fibrosis and cirrhosis.

The only way to quantify liver stiffness was through a liver biopsy.

A piece of the liver is removed and examined to determine the extent of scarring that has occurred.

However, liver biopsies are invasive, usually inaccurate and make it difficult to monitor the liver over time.
Elastography

• Elastography – non-invasive measurement of tissue elasticity
  – Helps to diagnose diseases and monitor their development!

• How?
Wave Propagation Through Different Tissues

Waves propagate through tissue at varying rates, depending on the tissue elasticity.
Soft tissue = short wavelength which propagate slowly
Hard tissue = long wavelength which propagates more rapidly

Therefore, by measuring the length of a wave as it passes through a material, the elasticity can be calculated.

By finding the wavelengths in different regions, the distribution of elasticity can be determined and indicate if any stiff tissue exists.
Elastography

2 Main Types:

• Ultrasound Elastography (UE)
• Magnetic Resonance Elastography (MRE)
Basics of Ultrasound

- Transmit high frequency sound waves in the body (1-5 MHz)
- When waves hit tissue boundaries, some are reflected and some are transmitted
- Based on acquired reflected rays can obtain internal images
- Can calculate depth of tissue based on time for reflected ray to return and speed of sound in tissue
Ultrasound Elastography (UE)

- Technique formed during the 1990s at the University of Texas Medical School at Houston
- Mainly used in diagnosis of breast, thyroid and prostate cancer
  - Benign tumours compress more than malignant tumours
- Two main types:
  - Sonography-based elastography
  - Ultrasound-based transient elastography
Sonography-based Elastography

- Obtain regular ultrasound image
- Compress the tissue by pushing slightly and image again
  - Harder substances compress less
- Compare two images at each point to calculate tissue displacement during compression
- Map relative elasticity of tissue
Ultrasound-based Transient Elastography

- Special vibrator applies compressing, mechanical impulses at low frequency
- Doppler system measures propagation velocity of shear waves in the body
- Young’s modulus is proportional to square of shear wave velocity
- Map relative elasticity of tissue
Overview of MRE

MRE is the latest form of elastography to detect tissue elasticity, developed by Mayo Clinic in 1995.

It provides an early warning in detecting hardening of the liver, and can detect liver fibrosis before it reaches cirrhosis.

It uses MRI imaging techniques combined with an external mechanical compression to obtain an image of propagating waves through an organ.

Using the wavelength, the elasticity is calculated for each part of the tissue.

The information is compiled into an image mapping the elasticity of each region.
Magnetic Resonance Imaging

MRI uses radio waves and magnetic fields to image the tissue in the body.

The patient is placed in a magnetic field and radio waves are sent in.

The protons of water and fat absorb the radio wave energy.

Then when the applied radio waves are turned off, the energy is released.

The energy is measured, and an image is constructed.
Applying the Magnetic Field

Protons spin continuously, like a top around an axis. The dipoles are randomly oriented in all directions, and the net magnetic field is zero.

During an MRI, the patient lies in a solenoid coil that carries DC current through it. This produces a magnetic field $B_0$, which is perpendicular to the coil (it’s along the Z axis).

Protons align with this magnetic field.

They are either:
- parallel to it (a lower energy state, which is preferred)
- or anti parallel to it (a higher energy state).
Protons align with the applied magnetic field – either with or against it.

Parallel and anti parallel pairs of protons cancel each others magnetic moment. Only a very few number of protons do not cancel to produce a net dipole moment in the direction of the applied magnetic field Bo.
Precessing Protons

The static magnetic field causes the protons to ‘wobble’ around the direction of the magnetic field. This ‘wobbling’ is called **precession**.

They precess at a fixed frequency called the **Larmor Frequency**.

This wobbling splits the net magnetic vector into two components:

- **Mz** – that is parallel to Bo
- **Mxy** – a transverse component perpendicular to Bo

The Mxy vectors point in all directions and cancel out. So the net transverse magnetism is zero.
RF Pulse

There is another set of coils, near the patient connected to an RF generator.

The RF generator sends out radio frequency energy at a frequency in the radio frequency range.

This short RF pulse is sent out at the same frequency as the Larmor Frequency.

This creates an RF current in the inner coils.
Excitation of Protons

When the RF pulse is sent through the coils, it produces a **rapidly alternating magnetic field** that is perpendicular to Bo. This has two effects:

- It causes some of the protons that are parallel to Bo to pick energy and tip toward the anti parallel direction. They become ‘excited.’ Depending on the length and strength of the RF pulse, this causes Mz to decrease, become zero, or reverse.
  - A $90^\circ$ pulse has enough energy to excite half the dipoles so that an equal number are parallel and anti parallel. Mz becomes zero. MRI sends in many 90 deg pulses at a repeated time interval (TR).

- It causes the protons to precess together in phase, and create a transverse magnetic field that rotates in the xy plane at the Larmor frequency.
Once the 90 degree RF pulse is over, the dipoles return back to their original states.

The transverse $M_{xy}$ component decreases (proton spins de-phase $\rightarrow$ T2 relaxation) and the longitudinal $M_z$ component re-establishes itself (T1 relaxation).

The protons return to their original states at different rates.
Protons become excited from the RF pulse, and then return back to their original state when it is over.
Obtaining The MRI Signal

M\textsubscript{xy} produces the MRI signal. So as it decays and M\textsubscript{z} grows, the MRI signal decreases.

As the spins of the protons go from high energy state back to a low energy state, the RF energy is released back into the surrounding lattice.

Coils can receive the signal in the transverse plane due to variations of transverse magnetization vector.

An RF amplifier picks up the signal and amplifies the resonant frequency (Larmor Frequency).
MRI Image

A **voxel** is a volume pixel, the smallest 3D box of an image or scan.

To produce an image, the signal released from each voxel is picked up and processed.

The amplitude and the phase of the signal is sampled and digitalized.

The raw data are written into a data matrix called **K-space**. K-space data are equivalent to a Fourier plane (in the frequency domain).

To go from the K-space to an image, each data point is processed using a 2D inverse Fourier Transform. This converts the amplitude to a particular pixel grey level on the MRI image (going from the frequency domain to the time domain).
The Fourier Plane

- Horizontal and vertical axis correspond to horizontal and vertical spatial frequencies
- Pixel intensity corresponds to the amplitude of frequency component
- Color corresponds to the phase of frequency component
Magnetic Resonance Elastography (MRE)

- Uses MRI combined with harmonic mechanical excitation to the tissue to determine how quickly a wave propagates through the organ.
How Does MRE Work?

3 Main Steps

– Mechanical excitation – send mechanical waves to the region of interest

– Use modified MRI imaging techniques to image the propagating mechanical waves throughout the organ (wave image)

– Process the wave image into an elastogram (mapping of local elasticity)
Mechanical Excitation

- MR compatible transducer drives an electromechanical actuator attached to the body surface over the region of interest
- Longitudinal, mechanical compression waves are produced and experience mode conversion at organ interface
Mechanical Excitation

- Shear waves (50 - 1000 Hz) propagate throughout the organ
  - Less attenuated than shear waves at higher frequencies
  - Wavelength produced in tissues is within useful range
  - Direct generation of shear waves from transverse-motion drivers lack penetration depth
Propagating Waves

• Applied waves travel differently in various materials
  – Velocity is fast through hard, stiff tissue
    • Long wavelength and minimal phase shift
  – Velocity is slow through soft, rubbery tissue
    • Shorter wavelength and larger phase shift
Motion Sensitizing Gradient (MSG)

- Use modified phase-contrast MRI sequence with a motion-sensitizing gradient (MSG) to measure phase shift and calculate displacement
  - MSG = series of oscillating polarity gradients in the read out direction which detects cyclic motion
- Synchronize switching of the MSG polarity with external oscillation (frequency of shear waves)

Figure 5. An example of MR elastography pulse sequence with gradient echo acquisition. MSG (motion sensitizing gradients) encodes the fine oscillation induced by acoustic strain waves into the phase of the acquired NMR signal.
Measuring Phase Shift

- Determine phase shift and displacement

\[ \Phi(\tau) = \frac{1}{2} \gamma N T G \cdot \xi \cos(k \cdot r + \alpha) \]

\(\gamma\) = gyromagnetic ratio for protons
\(N\) = number of cycles of oscillating field gradient
\(T\) = period of mechanical excitation and oscillating gradient
\(G\) = vector of the gradient amplitude
\(\xi\) = vector of the mechanical displacement amplitude
\(k\) = wave vector
\(r\) = vector of the central spin position
\(\alpha\) = phase difference between mechanical excitation and oscillating gradient

Figure 6. Motion sensitizing gradients (MSG) and the local oscillation. Since MSG is gated to oscillation, the direction of motion always agrees with polarity of gradients. The resulting phase shifts are amplified by MSG.
Obtaining the Wave Image

- Calculate displacement of the spin from the phase shift for each voxel to give wave image
- Repeat sequence for other two MSG directions to give 3D wave image
Obtaining the Elastogram

- Calculate the wavelength of the propagating wave
- Use inversion algorithm to calculate the local shear modulus values
- Map out distribution to obtain a 3-D elastogram model of an organ
Full MRE Process
Advantages of Elastography

Elastography is a far better method of sampling the elasticity of biological tissue over a biopsy.

Biopsies are invasive and tend to be inaccurate due to sampling errors.

MRE and UE are:
• Non-invasive
• Reproducible and
• Make it easier to detect liver fibrosis (before it reaches cirrhosis) and monitor the progress of the disease or treatment given.
**Comparing MRE and Ultrasound Elastography**

<table>
<thead>
<tr>
<th>MRE</th>
<th>Ultrasound</th>
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<tbody>
<tr>
<td><em>Looks at a 3D volume, which improves the ability to reconstruct the elasticity of tissue</em></td>
<td><em>Is a 1D method</em></td>
</tr>
<tr>
<td><em>Can analyze a larger volume. It represent more of the entire organ, which leads to fewer sampling errors. It is more reproducible.</em></td>
<td><em>Can only probe a small sample size, and can lead to sampling errors</em></td>
</tr>
<tr>
<td><em>Has better depth capability. The waves penetrate further into the body.</em></td>
<td><em>The waves do not penetrate into the body as far</em></td>
</tr>
<tr>
<td><em>Using a mechanical wave allows for quantitative estimates of elasticity.</em></td>
<td><em>Using static stress allows only for qualitative estimates of elasticity.</em></td>
</tr>
<tr>
<td><em>More expensive</em></td>
<td></td>
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<tr>
<td><em>Longer acquisition times</em></td>
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</table>
Future of MRE

Improvements

• Pulse sequence design with lower acquisition time
• Signal-to-noise limitations for all areas of the body
• Processing algorithms for more accurate and higher resolution images
Future of MRE

Other Potential Uses

• Detect cancer and malignancies in the breast, kidneys and prostate

• Detect brain disease or classify lesions
  – In development → inconsistencies in elasticity of grey and white matter

• Measure muscle activity to evaluate rehabilitation
  – Stronger the contraction, stiffer the muscle
Thank You!

Questions?
References


References

