MRI ELASTOGRAPHY:
PRIMER, QC AND ARTIFACTS

RAMSES HERRERA
Hunter Holmes McGuire VA Medical Center
1. Research collaboration with Philips Medical Systems (Koninklijke Philips NV).
1. RVAMC
2. Liver Disease
3. Elastography
   1. Stiffness
   2. Shear Waves
   3. Inversion problem
4. MRE Physics
   1. Pulse Sequence
   2. Phase contrast Imaging
   3. MRE
5. MRE Indication of Liver Disease
6. Artefacts & Pitfalls
7. Quality Control
8. Future & Challenges
Hunter Holmes McGuire VAMC

- Only VA MC with in-house Heart Transplants
- Home site of VALOR trial
  - Multi-Phase, National clinical trial
  - SBRT vs. Lung Lobectomy
- Primary VA MC for spinal cord injury
- Part of RSNA Quantitative Imaging Biomarker Alliance (QIBA)
  - First to implement new lung nodule screening criteria
  - First to certify CT Low Dose Lung nodule scans with QIBA phantom (CTLX1)
- Second Largest government facility in Virginia
  - Largest is the Pentagon
- Most MRE in the Eastern United States
  - Second in USA to Mayo Clinic
  - 4 - 6 MRE’s per week
Chronic Liver Disease

- MOST FORMS OF Chronic Liver Disease (CLD) lead to:
  - Fibrosis
  - Cirrhosis

- CAUSES ARE:
  - Alcoholism
  - Viral
  - Non-Alcoholic Fatty Liver Disease (NAFLD)
  - Autoimmune
  - Genetic
  - Metabolic (Diabetes Mellitus)
Chronic Liver Disease

CDC estimates are:

- 240 Million World Wide with Hepatitis B (1.4 M in USA)
- 160 Million World Wide with Hepatitis C (3.2 M in USA)
- NAFLD affects 27% - 34% of U. S. population
- >30 Million Americans have CLD, majority from NAFLD.
Liver Fibrosis

- It is vital to be able to accurately stage the degree of Fibrosis
  - Liver Fibrosis is an independent risk factor for Hepatocellular Carcinoma (HCC)
  - Prognosis and Management depend on Staging
  - Outcome of surgical resection of HCC depend on Fibrosis staging.

- Available diagnostics:
  - Blood Test (Platelet, PT, albumin, total bili, aminotransferase, hyaluronic acid, α2-Macroglobulin)
    - Pro: Inexpensive & easily available
    - Cons: Low Specificity (‘positives not overlooked’) & Limited ability to quantify Fibrosis.
  - Panel of these tests
    - Pro: Considered superior to stand-alone test.
    - Cons: at <0.2, NPV = 98%, >0.8, PPV = 62% (Exclude or confirm disease, cannot stage)
Liver Fibrosis (Diagnostics Cont’)

- **Cross-sectional Imaging**
  - CT, MRI, US
  - Can give some idea of disease state
    - Anatomic signs/distortion, change in density (attenuation), echotexture
    - Ratio > 0.65 of Caudate lobe width to right lobe width = 100% Cirrhosis.
    - Insensitive for Early Fibrosis - only useful at full cirrhosis.

- **Biopsy**
  - Pros: Gold Standard (5-11 portal tracts sampled)
  - Cons:
    - Invasive (1.7% risk Morbidity, 0.01%-1.0% risk Mortality)
    - Excellent establishing disease, but less reliable for staging
    - Large inter/intra observer variability in staging
    - 20% Error rate in staging among expert pathologists
    - Requires yearly repetition
    - SAMPLING ERROR (not enough of the Liver is sampled)
Elastography: Elasticity & Shear waves

- **Elasticity:** Tendency to return to normal state after a force is exerted.

- **Strain:** Relative amount of deformation
  - Young’s Modulus – tendency to deform along the axis of stress
  - Shear Modulus – change in shape w/o change in volume

- Generally assume that tissue is linearly elastic & isotropic
  - Follows Hooke’s Law: \( \vec{F} = k \times \Delta x \)
  - Young’s Modulus (E) is related to Shear Modulus (\( \mu \))
    - \( E = 3\mu \)

- The shear modulus of linear, isotropic tissue is:
  - \( \mu = \rho v_s^2 \) - \( \rho \) is mass density & \( v_s \) is velocity of propagation

- **Shear Waves:** Transverse waves in elastic medium due to shear
  - Shear – Change in shape w/o change in volume.
Elastography

- Palpation, to feel difference in mechanical properties of tissues
  - Abnormal tissue
  - Normal tissue

Mechanical properties of tissue vary at different physiological and pathological states. i.e., Breast cancer palpation

- Manual palpation depends on:
  - Organ proximity to surface
  - Subjective to touch/sensitivity of practitioner

- Conventional imaging modalities are not capable of assessing properties of palpation
  - ELASTIC MODULUS
Elastography: Types

**Static Stimulus:**
- Manual Palpation
- Strain elastography (internal motion... cardiac/breath, mild compression)
- Superficial tissues

**Dynamic Stimulus:**
- Induce vibrations in 50 – 500 Hz
- Image the propagation of waves from excitation
- US & MR
Elastography: Types

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Elastography: Static

**Static Stimulus:**
- Mainly used in Ultrasound
- Qualitative interpretation
- Gauge for pressure applied
- Cannot accurately stage Fibrosis
Elastography: Shear Wave

- **Dynamic Stimulus:**
  - Ultrasound
    - Uses shear waves
    - Semi Quantitative
    - Disease specific staging criteria
    - Sampling error like biopsy
MRI Elastography (MRE)

- Uses external, pneumatic driver to create shear waves
  - ‘shake’ the liver
  - GE uses 60 Hz
  - Relative Amplitude - 70
  - Breath-hold (expiration)
  - 12 hour Nips per Os

- Usually 3 to 4 slices of liver acquired

- Motion Encoding gradients used
  - Same type as in phase contrast angiography (MRA)
  - Motion encoding in direction of propagation
  - Wave displacement maps created with four (4) phase-offs
  - Acquisition - 14 seconds per slice (56 sec)
MRI Phase Contrast

- A quickie!!

- Waves have two three fundamental properties:
  - Amplitude (A)
  - Frequency (F)
  - Phase ($\phi$)

- When spatial gradients are applied ($G_z$) phase is 'remembered' after gradient off.

- Changes in phase accumulation can be converted to displacement.
  - HOW: $G_z$ changes proton frequency as function of distance in a very precise way.
  - Tissue that does not move has no 'net-phase accumulation'
    - Can be cancelled out from an initial reference image.
MRI Phase Contrast

- Movement-related dephasing:
  - Moving tissue
  - Static tissue
  - Uni-polar gradient - $G_z$

- Phase of static tissues also grows

- We want static phase to be zero.

$$G_z = 1, \ 0 < t < T$$

$$\Phi_2 - \text{moving tissue}$$

$$\Phi_1 - \text{static tissue}$$

$$\Phi_2 - \text{position}$$

$$\Phi_1 - \text{position}$$

$$G_z \ \text{gradient}$$

$$\vec{w} = \gamma (|\vec{B}_0| + \vec{g}_z \cdot \Delta z)$$

$$\Phi = \int_0^T \vec{w} \ dt'$$
MRI Phase Contrast

- Movement-related dephasing:
  - Moving tissue
  - Static tissue
  - Bi-polar gradient - $G_z$

- Phase of static tissues also grows

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\[
\tilde{w} = \gamma \left( |B_0| + \hat{G}_z \cdot \Delta z \right)
\]

\[
\phi = \int_0^{T/2} \tilde{w} dt' - \int_{T/2}^T \tilde{w} dt'
\]
MRI Elastography (MRE)

Purpose
Measure shear modulus (stiffness) of liver
Capable of detecting fibrosis (staging possible)

Method
Use mechanical waves to “shake” liver tissue at 60Hz (GE) and set up traveling shear waves
Use concurrent oscillating gradients to map periodic displacement into a periodic MR phase map

How
Keep track of the accumulated phase...

\[ \phi(\vec{r}, \theta) = \frac{2\gamma NT (G_0 \cdot \xi_0)}{\pi} \cos(k \cdot \vec{r} + \theta) \]
Physics Fundamentals: Pulse Sequence

\[ z_0 = 0 \]
Physics Fundamentals: Pulse Sequence

\[ z_0 = 0 \]

\[ \phi \]
Physics Fundamentals: Pulse Sequence

\[ z_0 = 0 \]
 PHYSICS FUNDAMENTALS: Traveling Waves

\[ z = A \cos(Ky - Wt) \equiv A \cos \left( K \left[ y - \frac{W}{K} t \right] \right) \]

\[ W = 2\pi F \equiv \frac{2\pi}{T} \quad K = \frac{2\pi}{\lambda} \]

Stay on crest of wave (travel with the wave):

\[ y - \frac{W}{K} t = 0 \text{ (at crest)} \rightarrow \frac{y}{t} = v = F\lambda \equiv \frac{W}{K} \]

This is the wave velocity
MRI Elastography (MRE)

- **Phase Accumulation:**

  Lamour Frequency: \( \bar{\omega} = \gamma |B_0| \)

  Gradient applied in \( \hat{z} \): \( w = \gamma (|B_0| + \vec{G}_z \cdot \Delta z) \)  ...In rotating frame of reference

  \[
  \phi = \int_{0}^{T} w \, dt \quad \& \quad z = A \cos(Ky - Wt + \theta)
  \]

  \[
  G_z = \begin{cases} 
  1, & 0 < t < \frac{T}{2} \\
  -1, & \frac{T}{2} < t < T
  \end{cases}
  \]

  Bi-polar Gradient
MRI Elastography (MRE)

- Phase accumulation:

\[ \phi = \gamma G_0 \left\{ \int_0^{T/2} \left[ z_0 + A \cos(Ky - wt + \theta) \right] dt - \int_{T/2}^{T} \left[ z_0 + A \cos(Ky - wt + \theta) \right] dt \right\} \]

\[ \phi = \gamma G_0 \left\{ z_0 \left( \frac{T}{2} - 0 \right) - \frac{A}{w} \left[ \sin \left( Ky - w \frac{T}{2} + \theta \right) - \sin(Ky + \theta) \right] \right\} - \left\{ z_0 \left( T - \frac{T}{2} \right) - \frac{A}{w} \left[ \sin(Ky - wT + \theta) - \sin \left( Ky - w \frac{T}{2} + \theta \right) \right] \right\} \]
MRI Elastography (MRE)

\[ \Phi_2 = \gamma G_0 A \sin K y - \frac{\pi}{2} + \theta - \sin K y + \theta - \sin K y - \pi + \theta + \sin K y - \pi + \theta \]

\[ G_z \]

\[ \phi = -\frac{4\gamma G_0 A}{\omega} \sin (Ky + \theta)_{|\omega=2\pi/T} \]

\[ \phi_n = -\frac{2\gamma n G_0 A T}{\pi} \sin (Ky + \theta) \]

\[ \phi(\vec{r}, \theta) = \frac{2\gamma NT(\vec{G}_0 \cdot \vec{\xi}_0)}{\pi} \cos (\vec{K} \cdot \vec{r} + \theta) \]
MRI Elastography (MRE)

- We’ve tracked the phase evolution
  - Phase $\rightarrow$ velocity

- But we want stiffness...

\[
\phi(x, y) \rightarrow \lambda(x, y) \rightarrow \mu(x, y)
\]

\[
\nu = \sqrt{\frac{\mu}{\rho}} \quad \rightarrow \quad \nu = F\lambda
\]

\[
\mu(x, y) = \rho \cdot [\nu(x, y)]^2 \quad \rightarrow \quad \rho F^2 [\lambda(x, y)]^2
\]

...Et voilà!

\begin{align*}
\lambda &= \text{wavelength} \\
\mu &= \text{Shear modulus (kPa)} \\
F &= \text{frequency} \\
\rho &= \text{mass density}
\end{align*}
MRI Elastography (MRE)

Data Analysis

$$\mu(x, y) = \rho[\nu(x, y)]^2 = \rho F^2 [\lambda(x, y)]^2$$

Need to get $$\lambda(x, y)$$ from $$\Phi(x, y)$$:

$$\Phi = \frac{2\gamma G_0 A n T}{\pi} \sin\left(\frac{2\pi y}{\lambda} + \theta\right)$$

"Stiffness" $$\mu(y)$$
MRE: Indications of Liver Disease

- So what do we end up with?

Anatomical Image  Wave Propagation Image  Elastogram Image
MRE: Indications of Liver Disease

<table>
<thead>
<tr>
<th>Stiffness (kPa)</th>
<th>Fibrosis Staging</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2.5</td>
<td>None (F 0)</td>
</tr>
<tr>
<td>2.5 – 3.0</td>
<td>Normal + Inflammation</td>
</tr>
<tr>
<td>3.0 – 3.5</td>
<td>F(1) – F(2)</td>
</tr>
<tr>
<td>3.5 – 4.0</td>
<td>F(2) – F(3)</td>
</tr>
<tr>
<td>4.0 – 5.0</td>
<td>F(3) – F(4)</td>
</tr>
<tr>
<td>&gt;5</td>
<td>F(4)</td>
</tr>
</tbody>
</table>
MRE: Accuracy

- Systemic review & Meta analysis (Sing et al.):
  - 12 studies
  - 697 patients
  - <1 year between MRE & biopsy

- ROC analysis – area under curve at 95% C.I.:
  - 0.84 (0.76 – 0.92) for F(1)
  - 0.88 (0.84 – 0.91) for F(2)
  - 0.93 (0.90 – 0.95) for F(3)
  - 0.92 (0.90 – 0.94) for F(4)

- Failure rate <4.3%
MRE: Accuracy

- Systemic review & Meta analysis (Su et al.s,)
  - 13 studies
  - 989 patients

- Pooled Sensitivities and Specificities
  - 87% (95%ci: 84%-89%) and 92% (95%ci: 87%-96%) for f ≥ 1,
  - 87% (95%ci: 84%-90%) and 92% (95%ci: 89%-95%) for f ≥ 2
  - 88% (95%ci: 85%-91%) and 91% (95%ci: 88%-93%) for f ≥ 3
  - 91% (95%ci: 87%-94%) and 92% (95%ci: 89%-94%) for f4

- The pooled area under the roc curve was 0.95 for f ≥ 1, 0.97 for f ≥ 2, 0.97 for f ≥ 3, and 0.98 for f4.
Case 1: 33 yo, NAFLD (3.4kPa – F(1-2))
Case 1: 65 yo, (M) NASH (11.5kPa – F(4)
Artifacts & Pitfalls

Excessive Noise:
• driver pneumatic tube
• disconnected
  No wave signal

Susceptibility Artifact
• Seen on Magnitude Image
• Lack of wave propagation
• Interposed colon (anatomy)
Artifacts & Pitfalls

Hot Spot:
• Artefactual "hot spot" under driver
• Avoid

Partial Volume:
• ROI exclude 1 cm inside liver
• ROI exclude ½ wavelength
• Exclude Fossa, Fissures
Artifacts & Pitfalls

1. Vessels > 3 mm do not reflect parenchymal stiffness
2. Waves can interfere
   a. Standing wave – Highest stiffness
   b. Pseudo standing wave – High stiffness
   c. Destructive interference – Low stiffness

- Major vessels in liver cause major interference
- Complex boundary conditions for wave propagation
Quality Control

- Currently not aware of:
  - QC recommendation by AAPM, ACR or similar
  - No phantoms available
  - Must rely on manufacturer calibration

- In talks to develop MRE specific phantom
  - Targets with different stiffness values
  - Semi-anthropomorphic
  - Simulate major blood vessels

- Major cause of artefacts
  - Magnet homogeneity
  - Gradient linearity
  - Eddy current correction
  - Ghosting

  - Best with dual echo GRE (phase subtraction). Detailed in ACR doc. Alternative: Engineer
  - Can accurately check with ACR phantom
  - Degrades speed/efficiency of gradient switching – Check the .LSVM files + engineer
Quality Control

- Richmond VAMC: Currently testing a prototype phantom

- In talks to develop comprehensive MRE phantom
  - Several stiffness targets
  - Semi-anthropomorphic
  - Simulate blood vessels
Richmond VAMC

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Quality Control
Future & Challenges

- MRE - Kidneys
- MRE - Breast (MQSA 2.0 ???)
Future & Challenges

- MRE – Lower Extremities
- MRE – Brain
- MRE – Cardiac
REFERENCES

1. Michael Carl, Ph.D., GE Healthcare, Private Correspondence.
QUESTIONS

"My insurance won’t pay for an MRI!"