Development and Introduction of New Medical Imaging Technology: Lessons Learned in the Trenches

FDA Workshop: Facilitating Innovation in Medical Device Development
June 24, 2010

Richard L. Ehman M.D.
The Mayo Clinic and RLE have intellectual property and a financial interest related to the technology discussed in this presentation.

Research conducted under oversight of the Mayo Clinic Conflict of Interest Review Board.
1980’s

Spatial Presaturation

Navigator-Based Motion Correction

United States Patent

Ehman


[45]

[54] METHOD FOR REDUCING ARTIFACTS IN NMR IMAGES

4,535,290 8/8

VIEW

TR

TR

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United States Patent

Ehman et al.


[45]

[54] ADAPTIVE METHOD FOR REDUCING MOTION AND FLOW ARTIFACTS IN NMR IMAGES

4,387-392,


“Instaart Images of Whole Body MR”, 1986, 149.


Cardiac Imaging, P. Lanzer et al., 1984.

Related U.S. Application Data


[45] Date

[74] [75] [73] [21] 365,632

Jun. 13, 1989
Palpation
Magnetic Resonance Elastography

An MRI-based technology that uses mechanical waves to quantitatively assess tissue stiffness
Two Patients with Fatty Liver Disease
(Now Affecting 1 in 3 Americans)
Two Patients with Fatty Liver Disease
(Now Affecting 1 in 3 Americans)
Diagnostic Performance: APRI, UTE, & MRE


100% Correct → 1.0

MRE

UTE

Area under ROC Curve

APRI

AST to platelet ratio index

Worthless → 0.5

Fibrosis Stage

F≥1  F≥2  F≥3  F≥4
Patient Impact

- 66/M - chronic Hepatitis C
- Needs biopsy to rule out fibrosis – but…
- Biopsy contraindicated - patient also has Hemophilia

- MRE: Positive for fibrosis
- Consistent with Stage 3
- Pt. started on antiviral Rx for Hepatitis C

Shear Stiffness (kPa)

5.2 kPa
MRE: Current Status

- Emerging as a useful non-invasive method for diagnosing hepatic fibrosis
- Safer, less expensive, and potentially more accurate than liver biopsy
- Many other potential applications await exploration

Our Overall Goal:
To determine whether this technology can provide reliable quantitative biomarkers for diagnosing disease, assessing treatment, and studying the natural history of disease
We Are Not There Yet ....Why Not?

MR Elastography Timeline

- Project started
- First Successful Experiment
- Publication in Science
- NIH Grants
- MRE patents
- Liver fibrosis application published
- Liver MRE in Clinical use at Mayo Clinic

We Are Not There Yet ....Why Not?
Can you identify the 3 Patients with Cirrhosis?

Shear Stiffness (kPa)
Why is it so Hard to Find Standard Tools for Presenting Quantitative Imaging Data?

Quantitative Metrics for the Tissue Properties Assessed with Palpation

- Shear modulus (based on wave speed)
- Young’s modulus (for most tissues equivalent to 3 x Shear modulus)
- Loss modulus (the real part of the complex shear modulus)
- etc…
Why we Need Standardization for Similar Biomarkers

Acoustic Driver System for MRE

Prerequisite: Multidisciplinary teams with strong clinical translational capabilities

Approach: Iterative technology development with bidirectional information transfer

MRE Vibration Source

MRE Abdominal Driver

Issue #3
Praesumptio Iuris Tantum

Rebuttable Presumption

“An assumption that is made that will stand unless someone comes forward to contest it and prove otherwise”

Protecting Subjects, Preserving Trust, Promoting Progress—

Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research

Task Force on Financial Conflicts of Interest in Clinical Research

December 2001
Rebuttable Presumption Against Financial Interests in Human Subjects Research means the institution will presume, in order to assure that all potentially problematic circumstances are reviewed, that a financially interested individual may not conduct the human subjects research.

This rule is not intended to be absolute... ...may rebut the presumption by demonstrating facts that, in the opinion of the COI committee, constitute compelling circumstances.
## Conflict of Interest Management

### Non-significant Risk HSR

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<th>Intermediate Clinical Studies</th>
<th>Validation &amp; Multi-Site Trials</th>
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Comparative Effectiveness Research

“Comparative Effectiveness of Advanced Diagnostic Imaging for Hepatic Fibrosis Fatty Liver Disease”

PI: Jayant Talwalkar, M.D.

RC1 EB010393
“Initiating qualification of an imaging biomarker will be contingent upon adequate standardization of the particular imaging process”

-Janet Woodcock MD (FDA)

• Mission: Improve value and practicality of quantitative imaging biomarkers by reducing variability across devices, patients, and time.
Standardizing Cross-Platform Technologies

Driver System and Inversion Algorithm Sequence

Normal Liver

Fibrotic Liver

Displacement (μm)

Shear Stiffness (kPa)
Medical Device Technology Development Would be Facilitated by:

1. Establishing accessible recommended tools for presentation of quantitative medical information
2. Creating incentives to standardize among similar biomarkers and suitable forums to accomplish this task
3. Instituting a more precise, pragmatic, and focused approach for recognizing and effectively managing conflicts of interest
4. Finding new ways to accomplish comparative effectiveness studies in a more efficient fashion
5. Creating incentives for vendors to standardize multiplatform technologies
-- Thank you! --