



MAYO CLINIC



MR Elastography: State of the Art In Practice and Clinical Trials

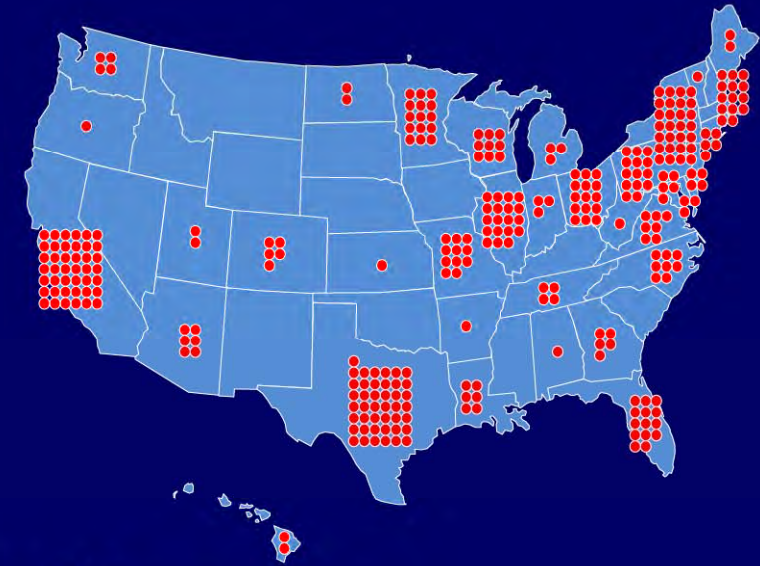
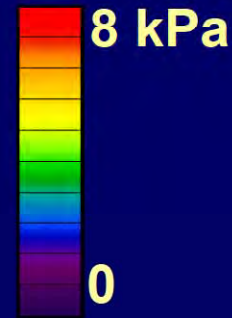
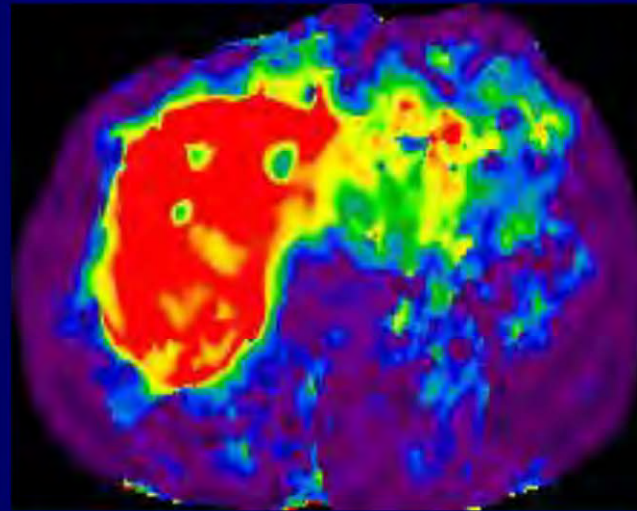
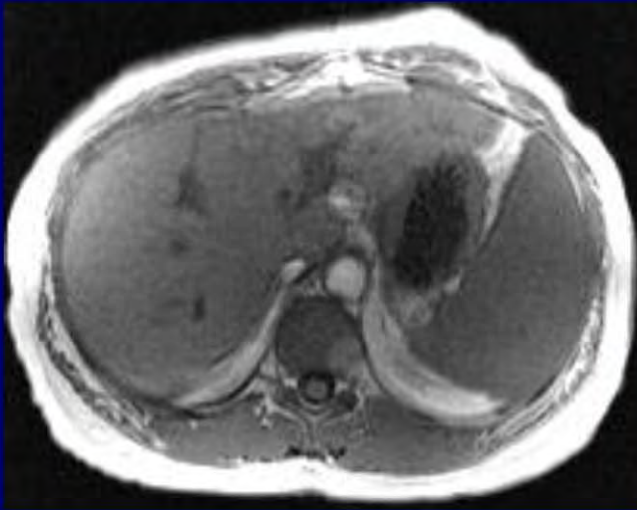
Richard L. Ehman, M.D.

Professor of Radiology

Blanche R. & Richard J. Erlanger Professor of Medical Research

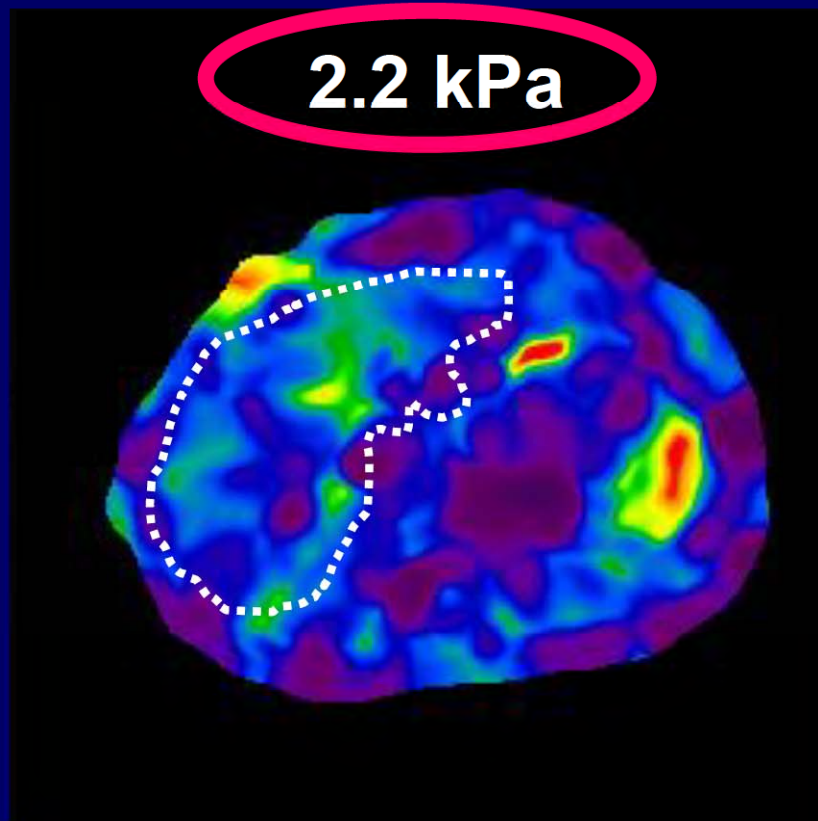
Mayo Clinic

Magnetic Resonance Elastography

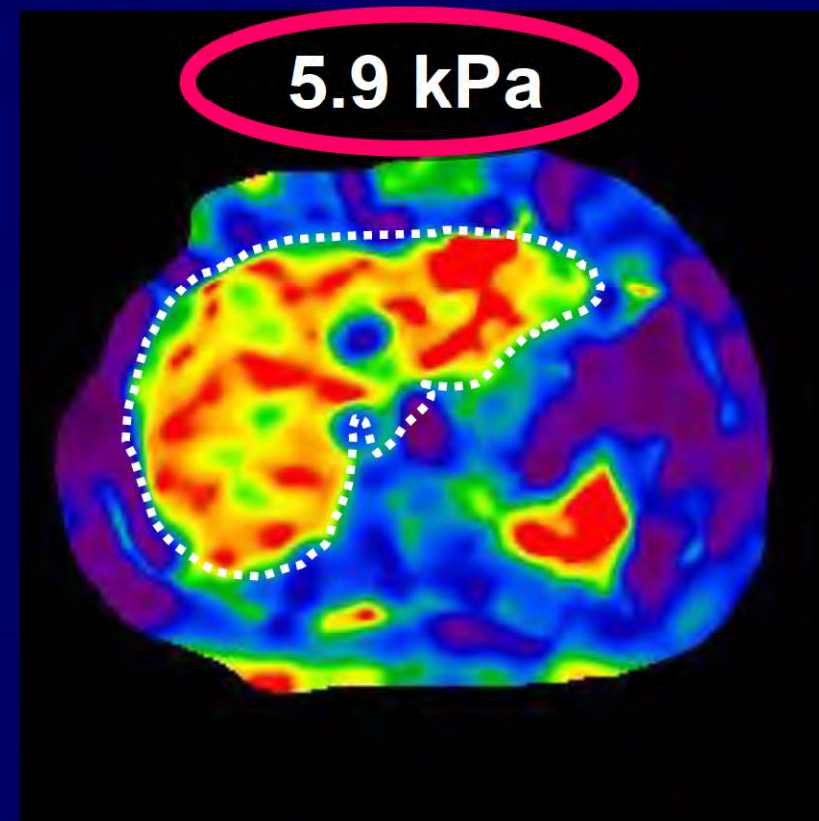


- **Main current application: Assessing liver fibrosis**
- **Acquisition time: ~ 1 minute**
- **FDA-cleared since 2009**
- **Installed clinical base ~ 1000 clinical systems (300+ in US)**
- **CPT code approved October 2017**

Two Patients with Chronic Liver Disease: Is Hepatic Fibrosis Present?

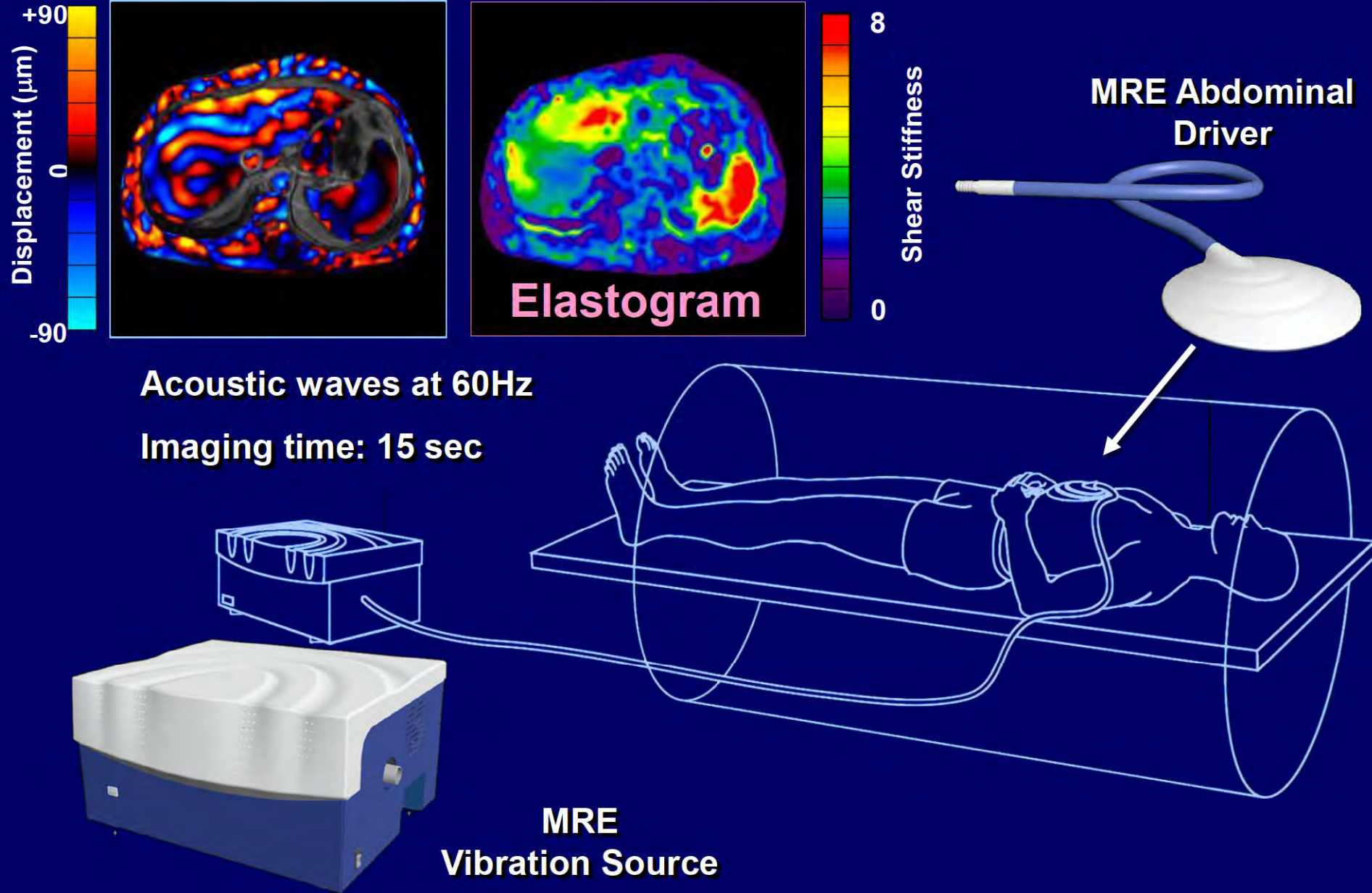


Shear Stiffness (kPa)



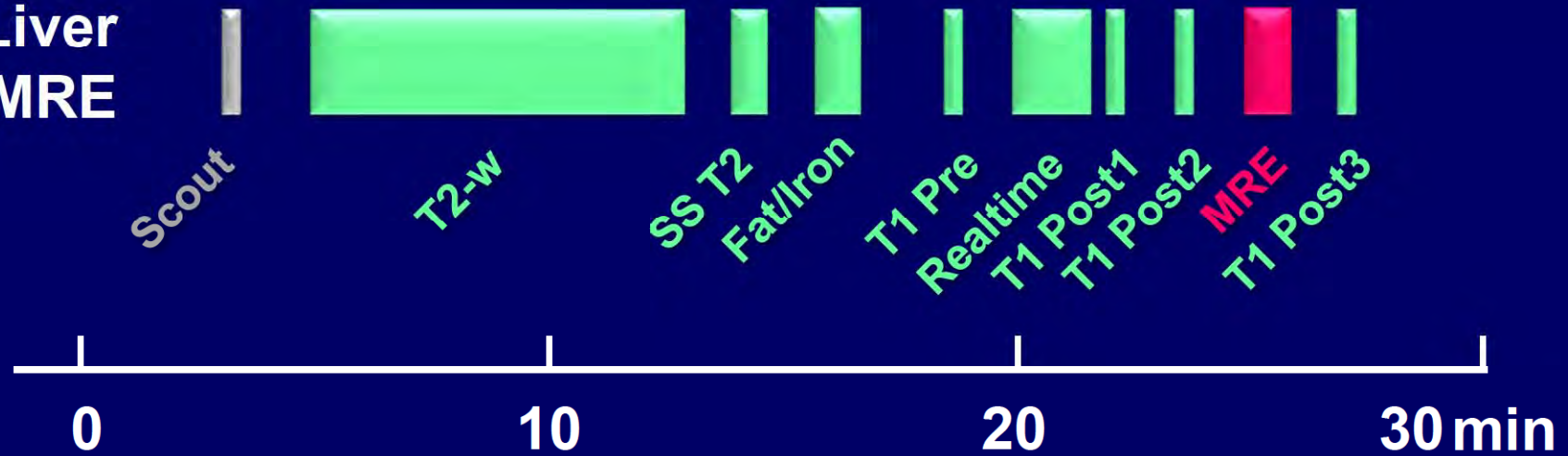
Shear Stiffness (kPa)

MR Elastography



Typical Liver MRI Protocol

MRI Liver
with MRE



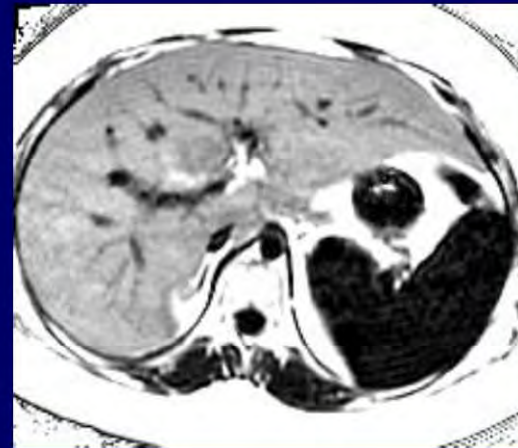
Rapid MR Hepatogram



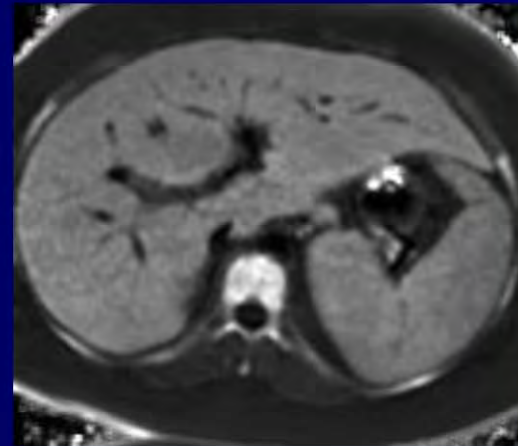
0 10 min

Target Charge in US:

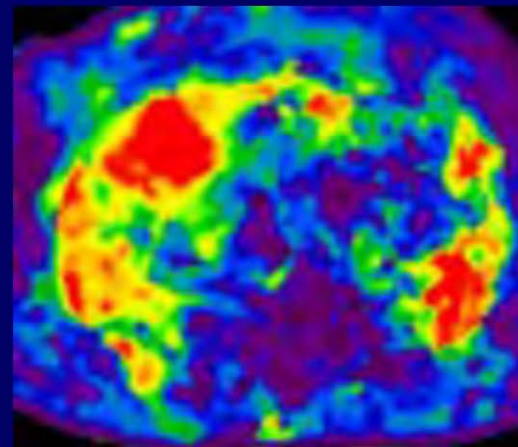
\$300-\$400



PDFFF:
Fat Fraction



T2*:
Iron



Stiffness:
Fibrosis/
Inflammation

Standardized Display Parameters

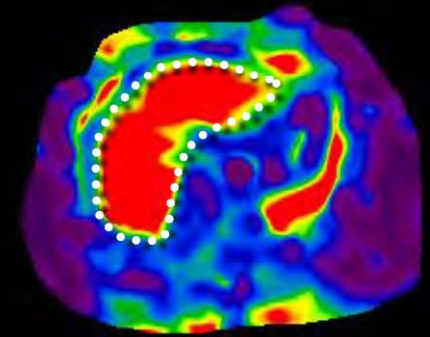
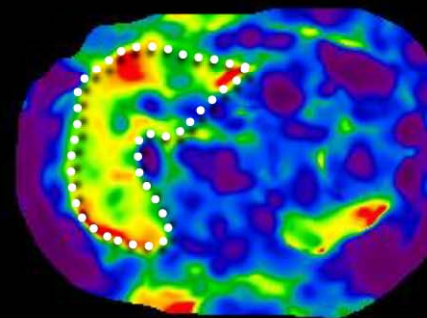
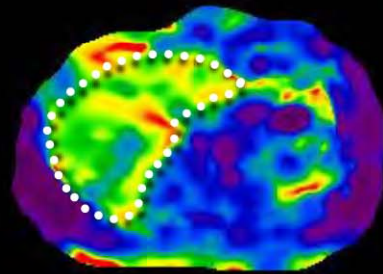
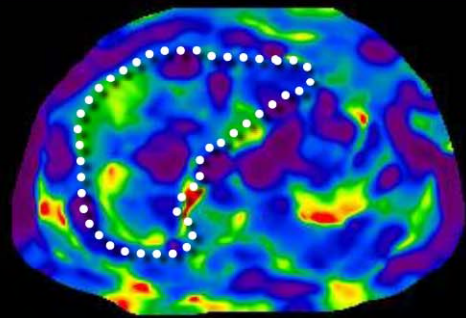
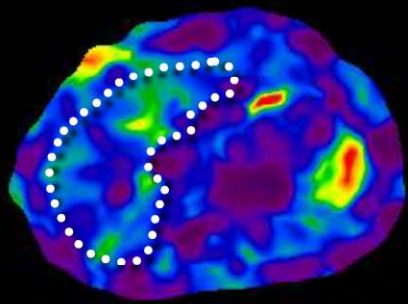
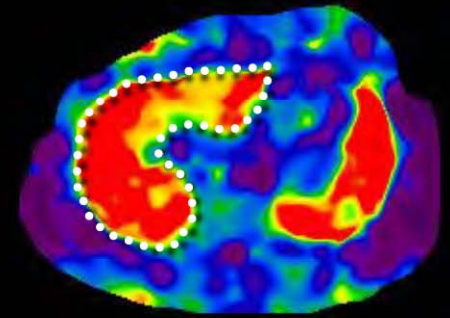
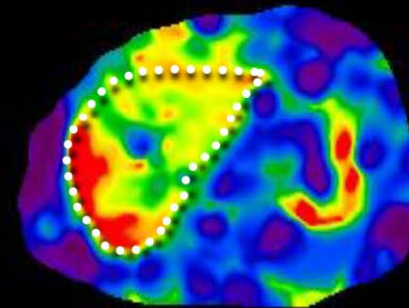
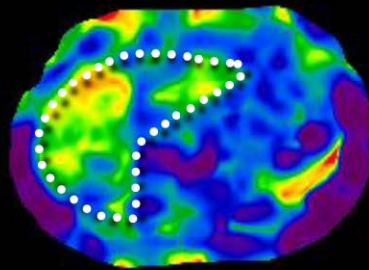
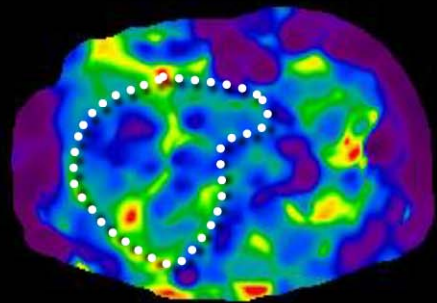
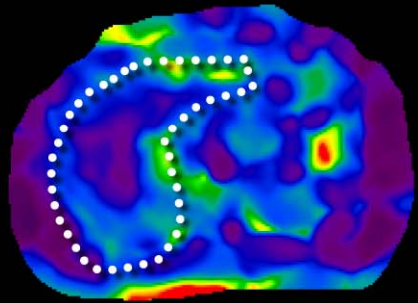
Normal

F1

F2

F3

F4

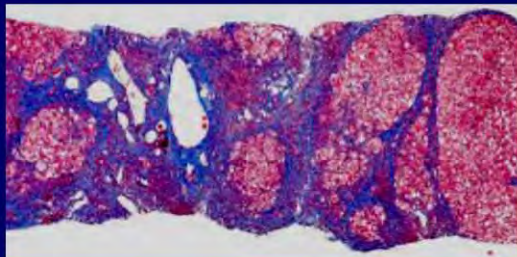


0

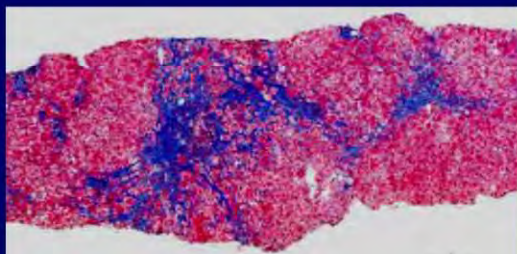
Shear Stiffness (kPa)

8

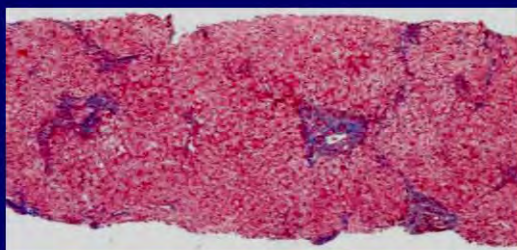
F4



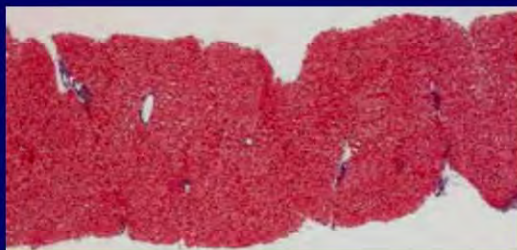
F3



F2



F0



Metavir Staging for Liver Fibrosis

kPa

Shear Stiffness in 697 Exams with Biopsy

10

5

0

0

1

2

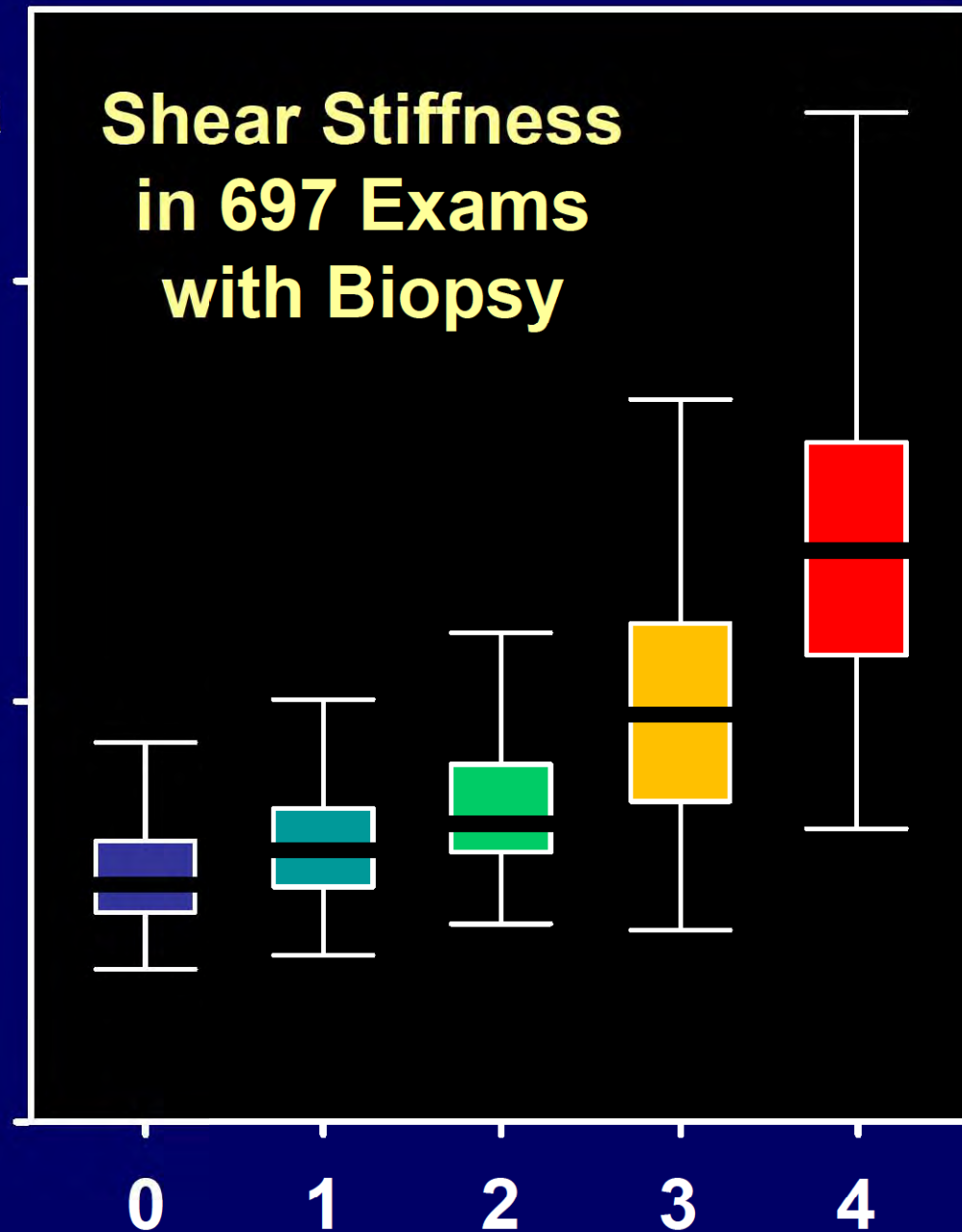
3

4

Fibrosis Stage

Singh, CGAH 2015; 13: 440-451

Over 150 publications on Liver MRE since 2006



Typical MRE Cut-off Values



Performance in Staging Hepatic Fibrosis

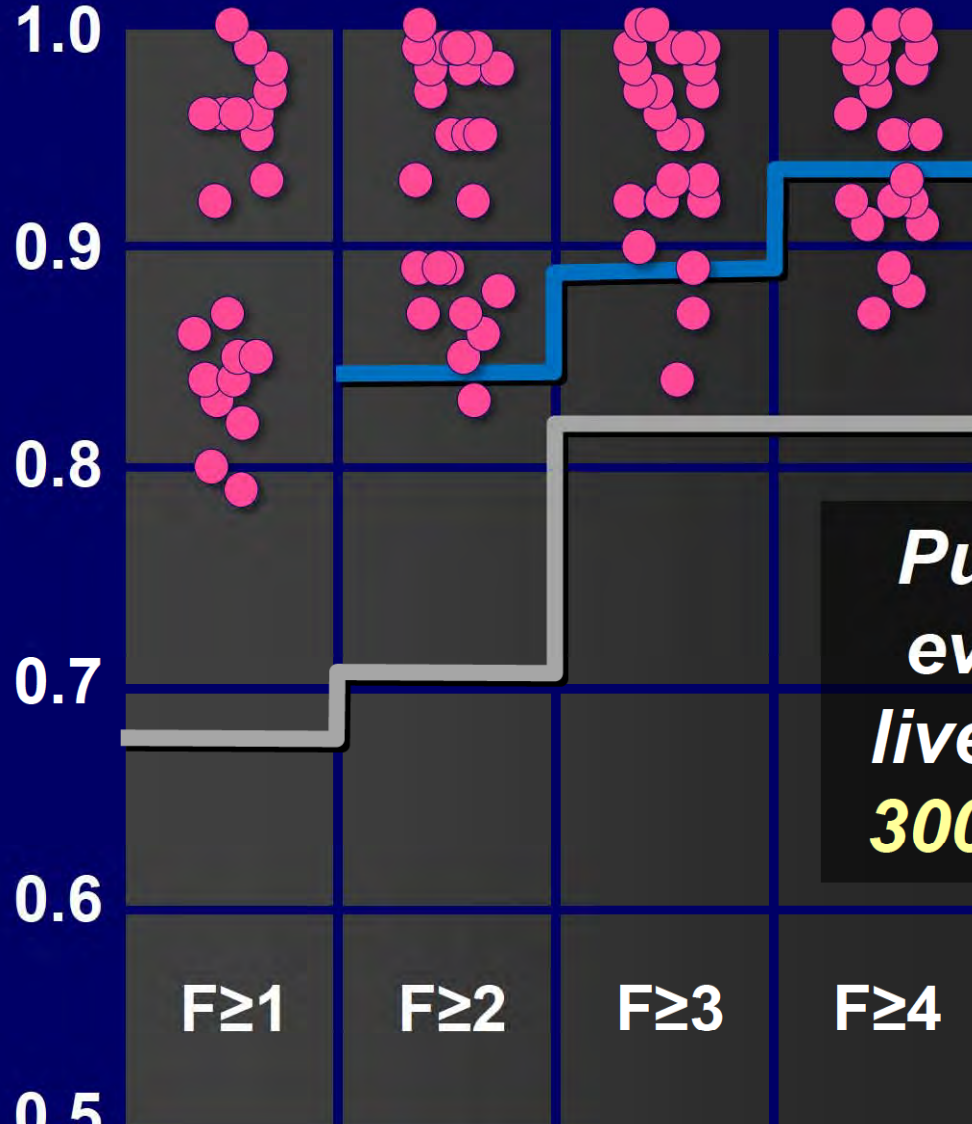
100% Correct → 1.0

MRE: 26 publications

FIBR

APRI*

Area under
ROC Curve

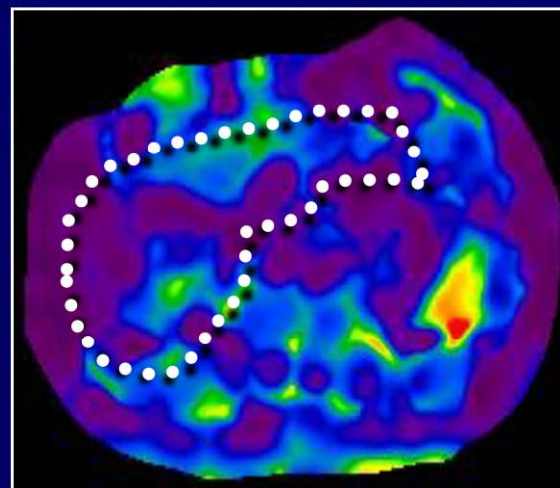
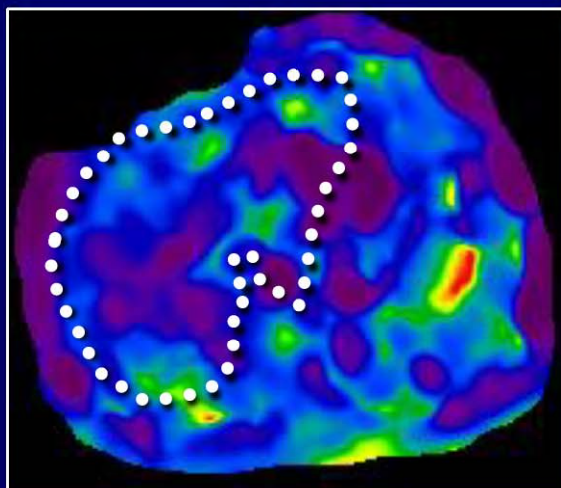
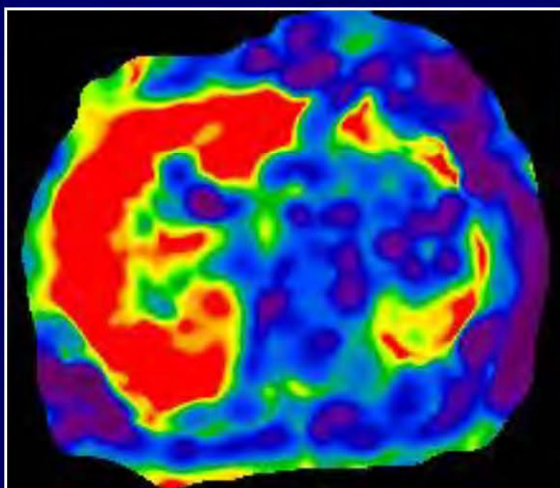
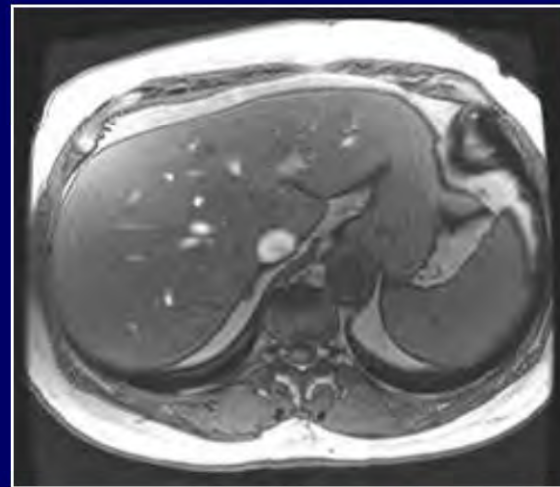
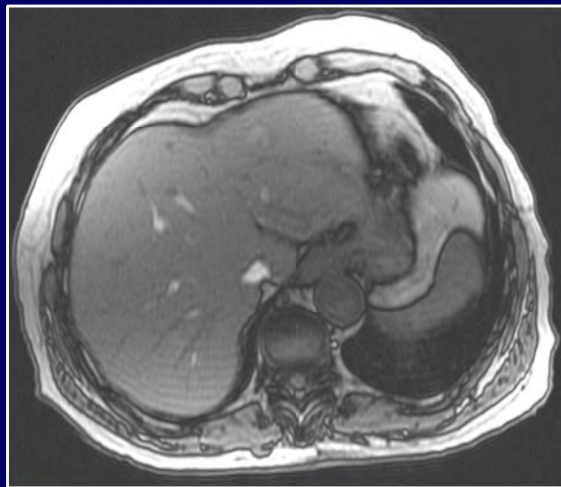
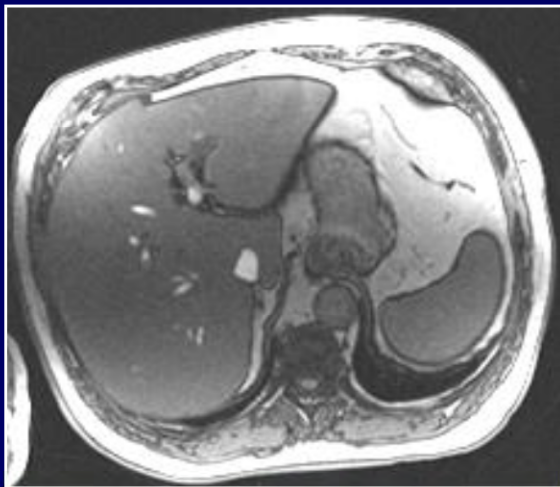


Published studies have evaluated MRE against liver biopsy in more than 3000 subjects since 2007

Worthless → 0.5

*AST to platelet ratio index

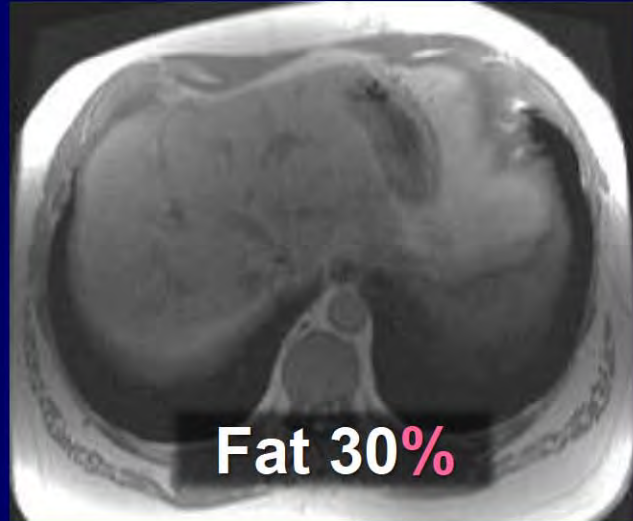
Three Patients with Fatty Liver Disease



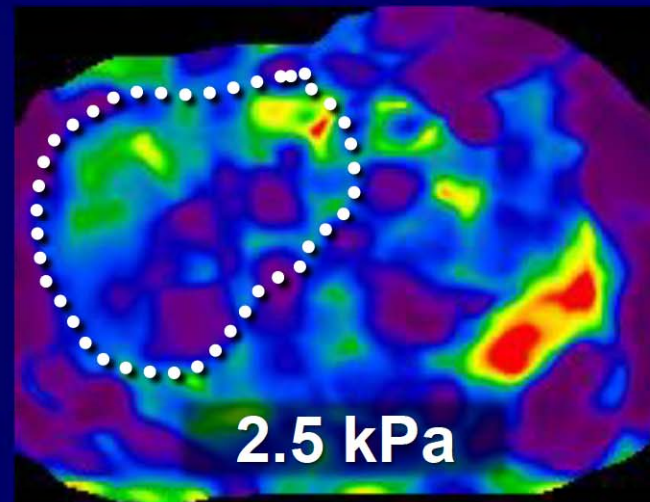
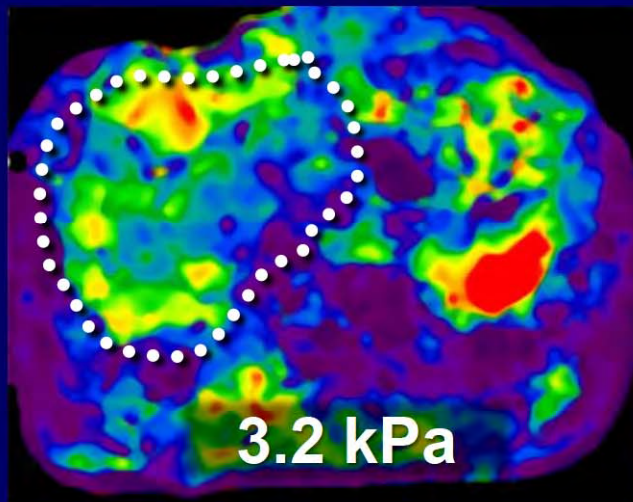
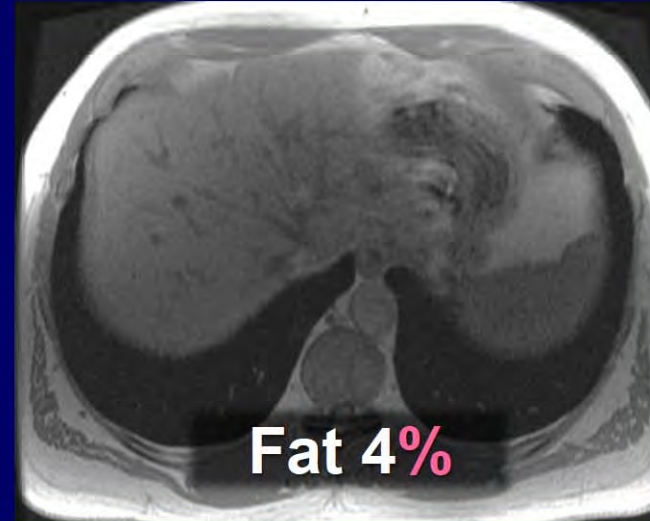
? Treatment response

51/M with NASH (liver Bx at Bariatric surgery)

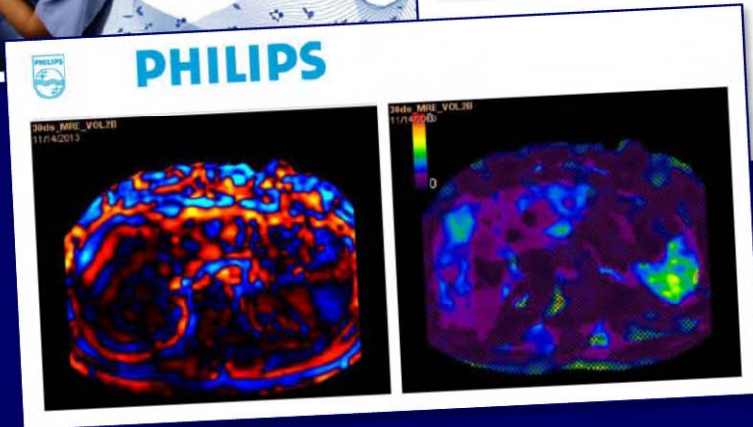
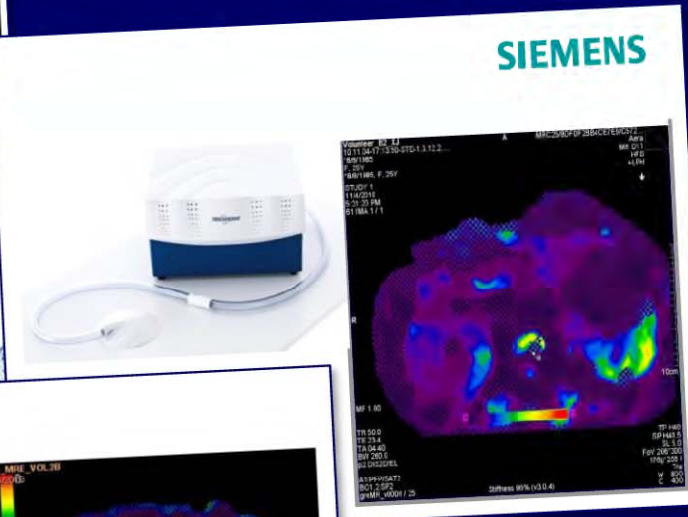
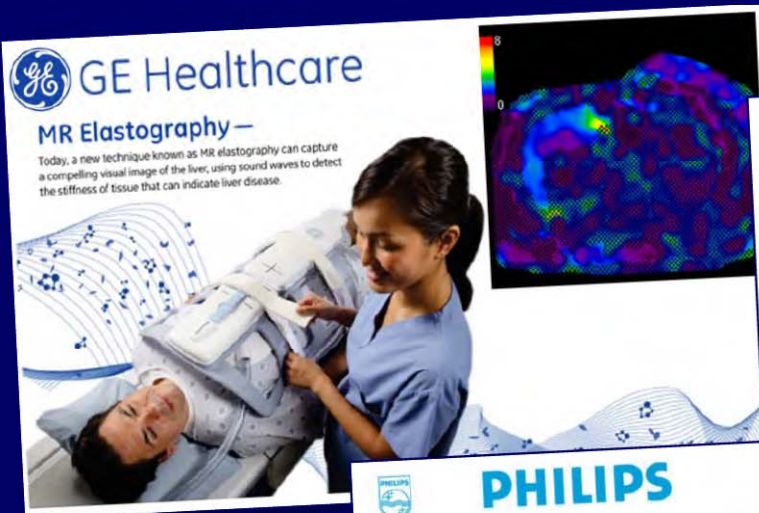
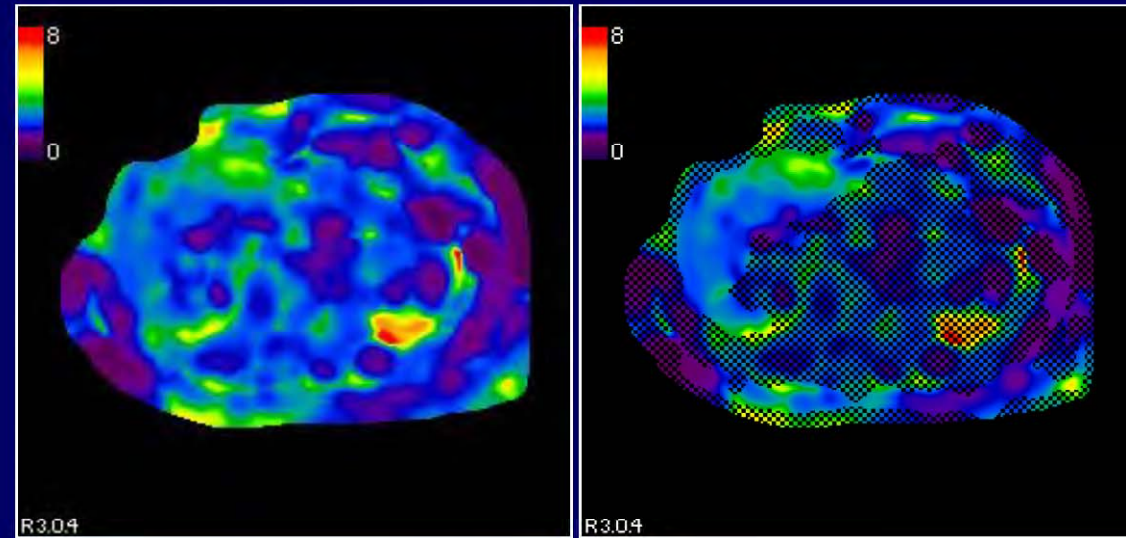
2010
Elevated AST



2011
Normal AST



Cross-Platform Commonality For MRE



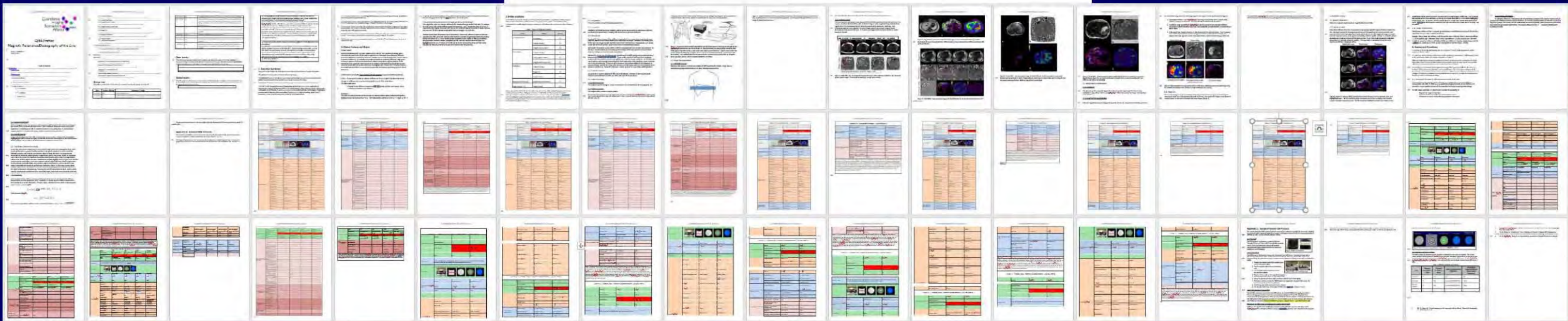
Common Features:

- MRE driver hardware
- 2D MMDI Algorithm*
- Reporting $|G^*|$
- Default 60 Hz, 0-8 kPa display
- Standard color scale
- Confidence map overlay
- *Published Cross-platform validation*



QIBA Profile: Magnetic Resonance Elastography of the Liver

Stage: A. Initial Draft
July 28, 2017



Ultrasound-based Shear Wave Elastography

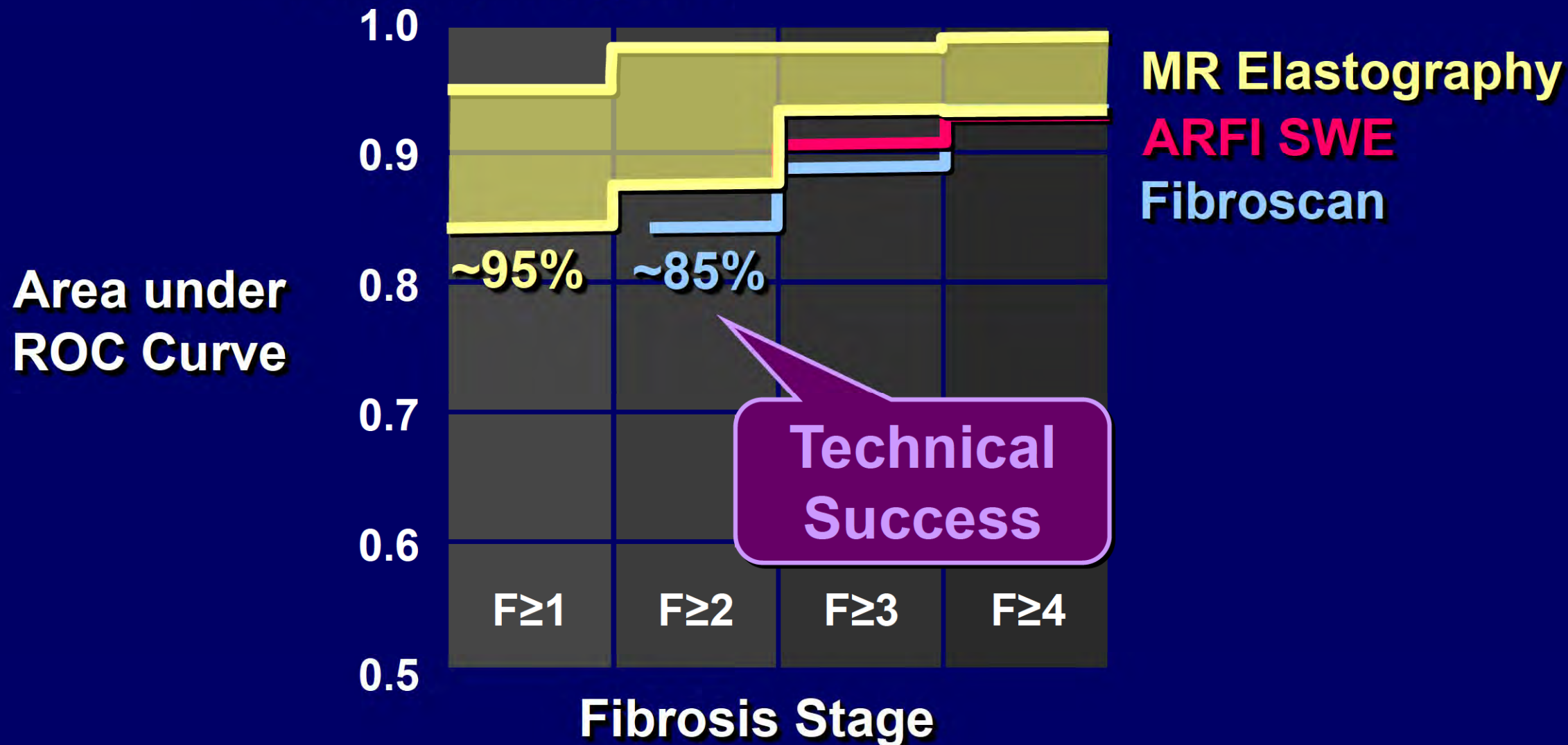


Diagnostic Performance Meta-Analyses

Friedrich-Rust, Gastroenterology 2008; 134: 960-974

Friedrich-Rust, J Viral Hepatitis 2012; 19: 212-219

Wang, Hepatology 2012;56 + Singh, Eur Rad 2012;26





American College of Radiology Appropriateness Criteria for Chronic Liver Disease

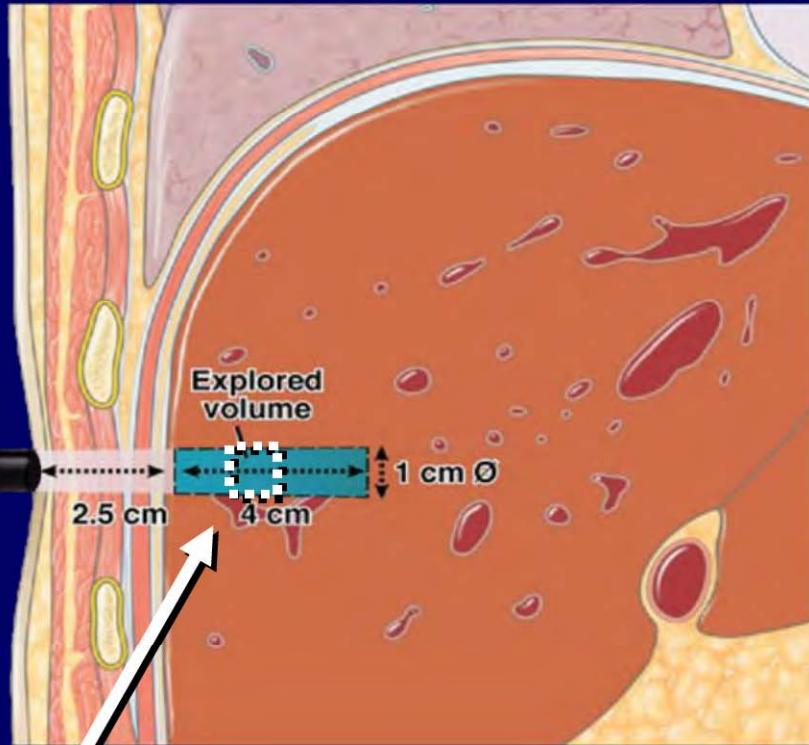
*Identifies MRE as the technology with the highest rating for
diagnosing liver fibrosis, ahead of ultrasound-based elastography
and MRI, ultrasonography, and CT.*



American Gastroenterological Association Institute Guideline on the Role of Elastography in the Evaluation of Liver Fibrosis

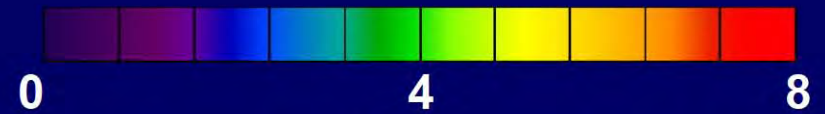
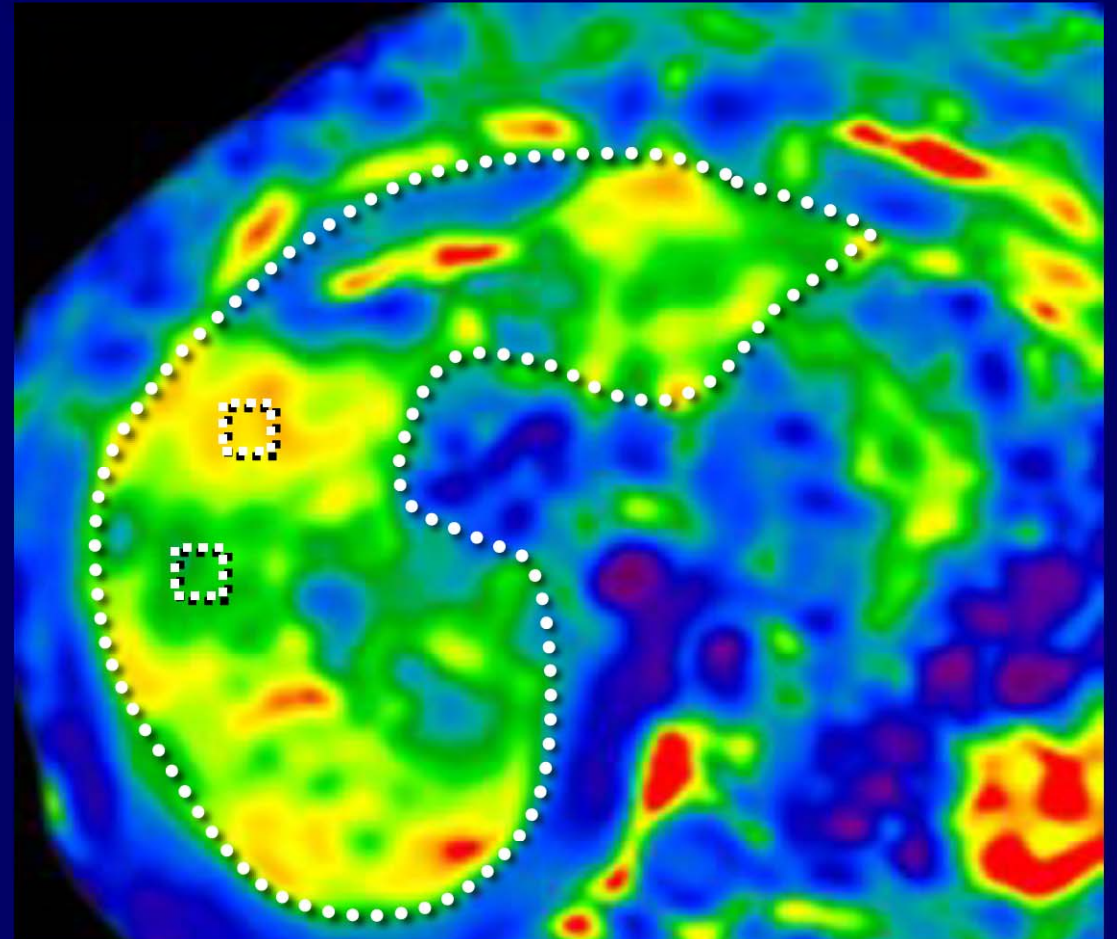
“In adults with NAFLD and a higher risk of cirrhosis, MRE is suggested, rather than VCTE, for detection of cirrhosis”

Fibroscan



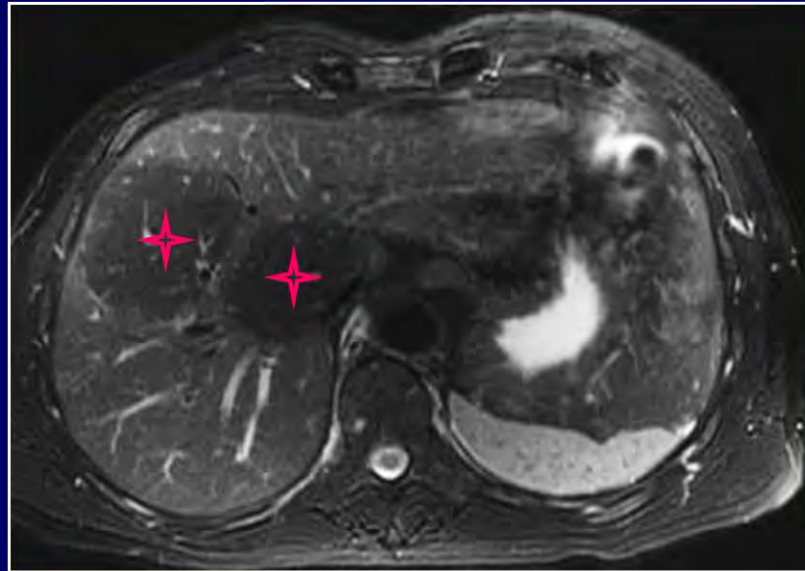
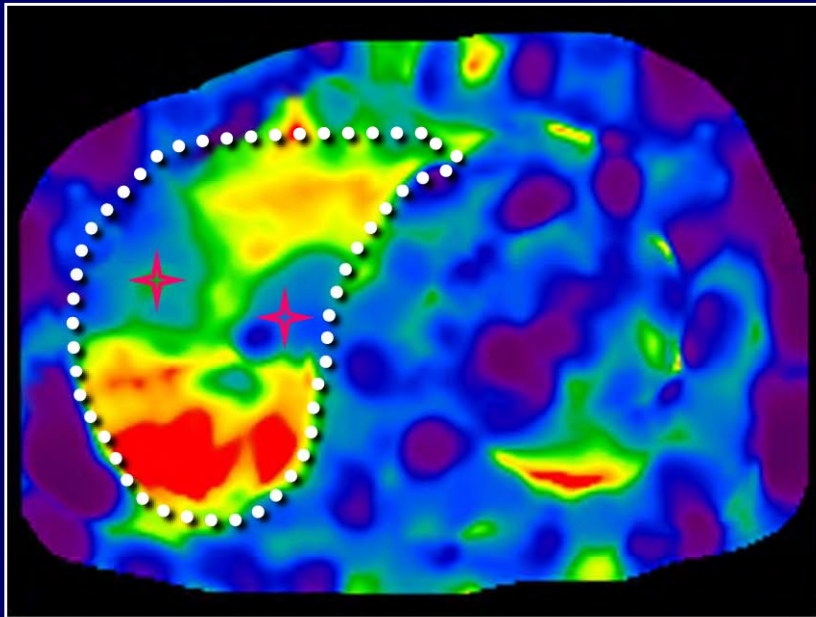
Shear Stiffness (kPa)

MRE



Shear Stiffness (kPa)

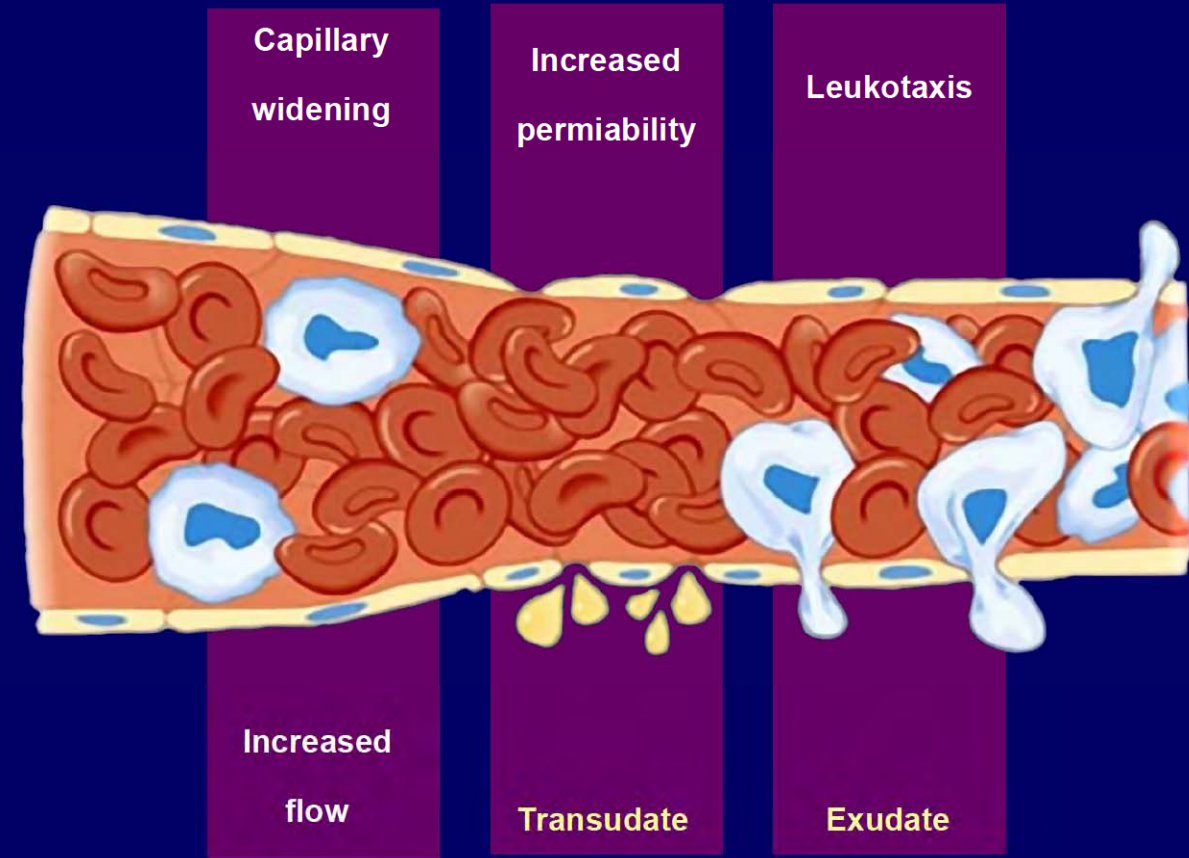
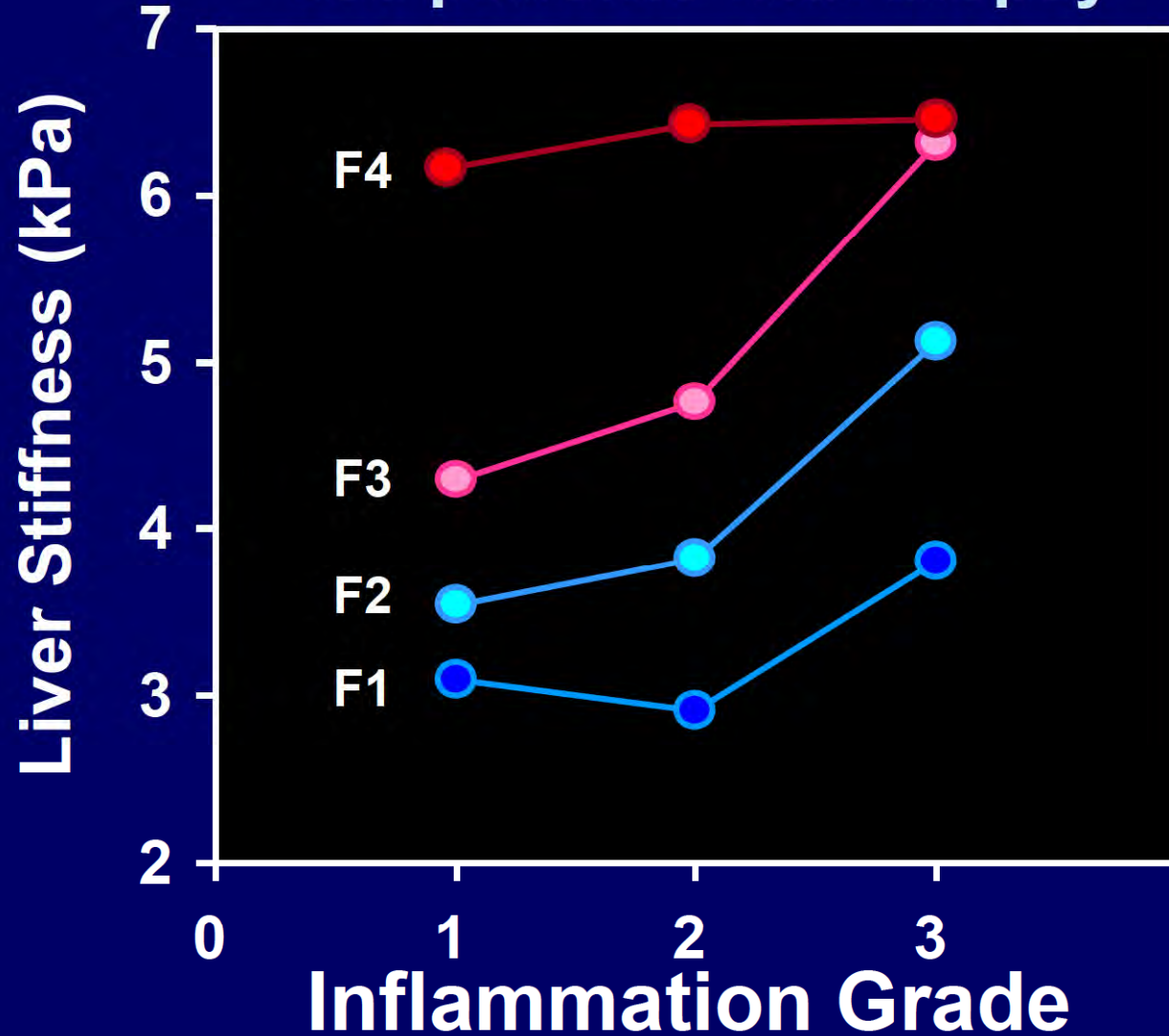
Spatial Patterns of Stiffness Change



**Large
regenerative
nodules with
lesser degree of
fibrosis**

Effect of Inflammation

239 patients with biopsy

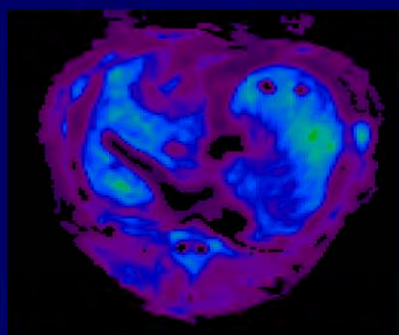
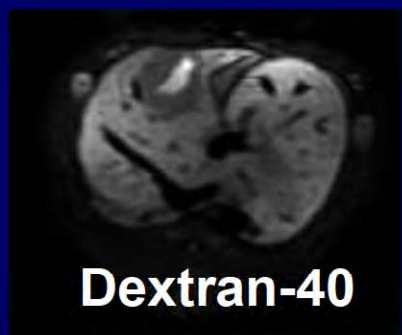
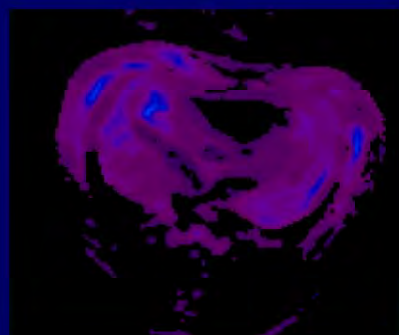
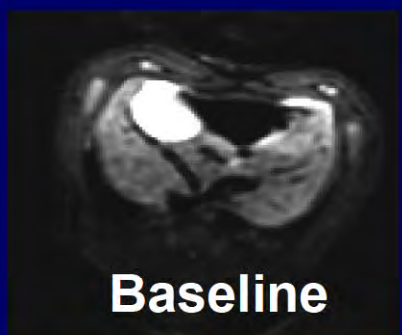


Yin M, et al.
Radiology.
2016;278:114-24.

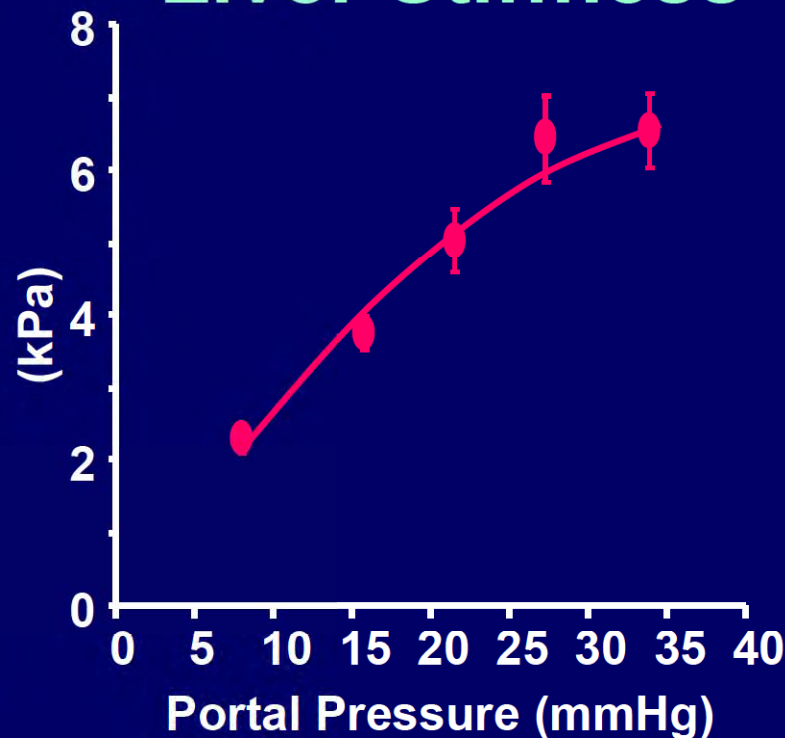
Portal Hemodynamic Effect

Yin M, et al. JMIR
2013;38:809-15.

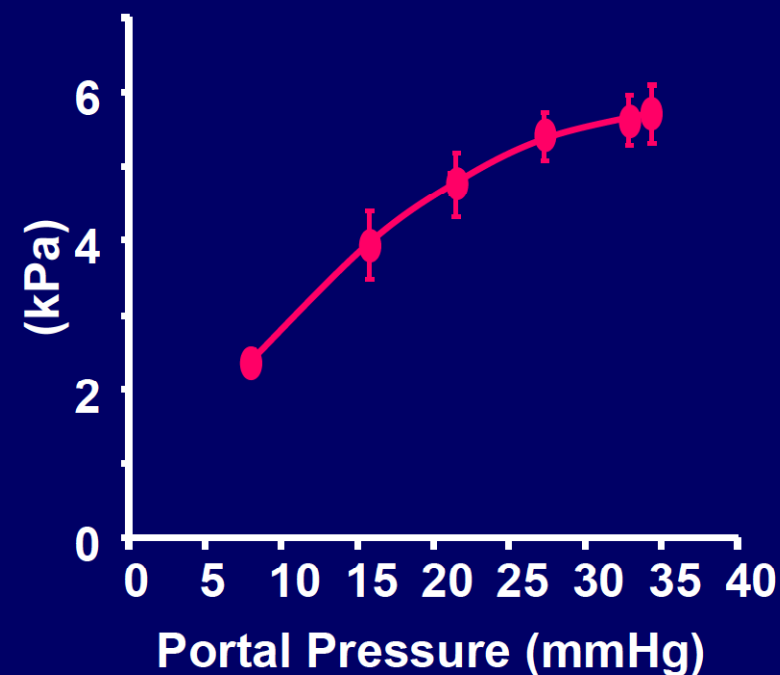
- Both liver and spleen stiffness have a dynamic component that correlates significantly with portal pressure.



Liver Stiffness



Spleen Stiffness



Portal Hypertension Increases Liver Stiffness

- Portal pressure rises after meals in patients with liver disease

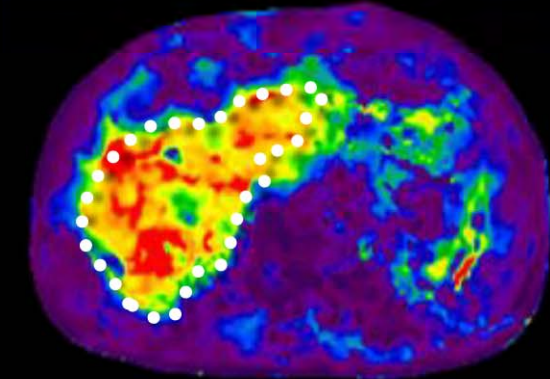
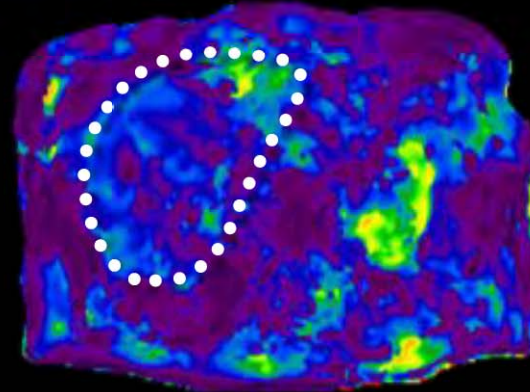
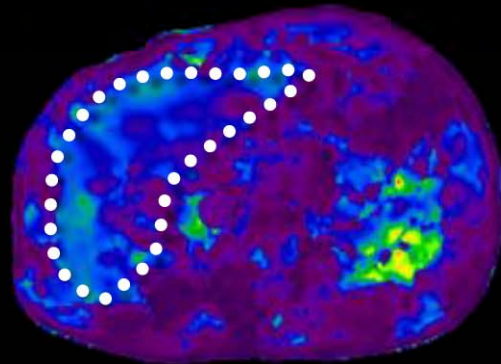
Yin M, et al. AJR.
2011;197:64-70.

Normal

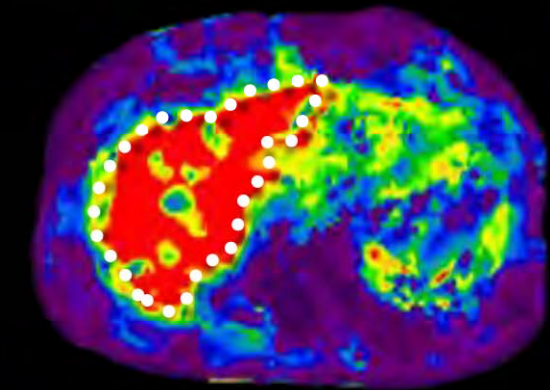
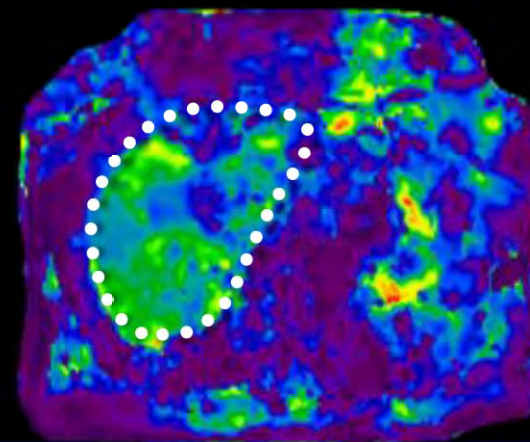
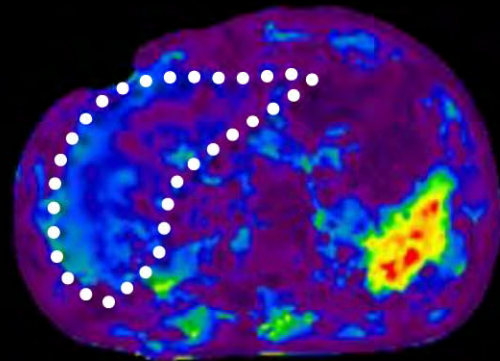
Patient with CLD
(F0)

Patient with CLD
(F4)

Before Meal
(Fasting)



After Meal
(30 min)



8
0
Shear Stiffness (kPa)

Inflammation

Fibrosis

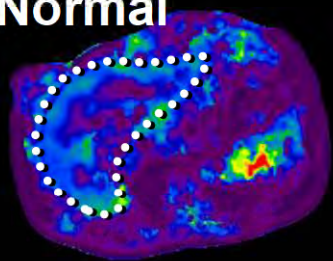
Congestion

Portal
Hypertension

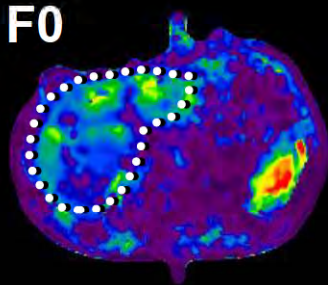
Liver Stiffness
&
Shear Modulus



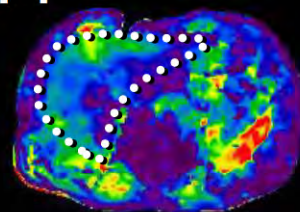
Normal



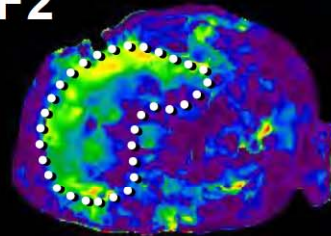
F0



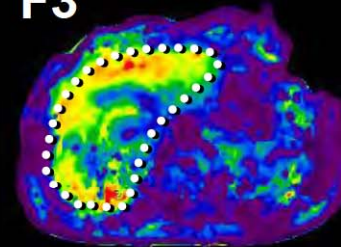
F1



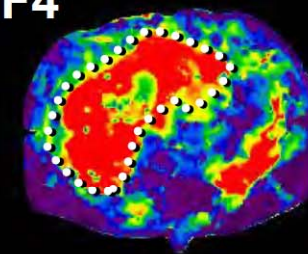
F2



F3

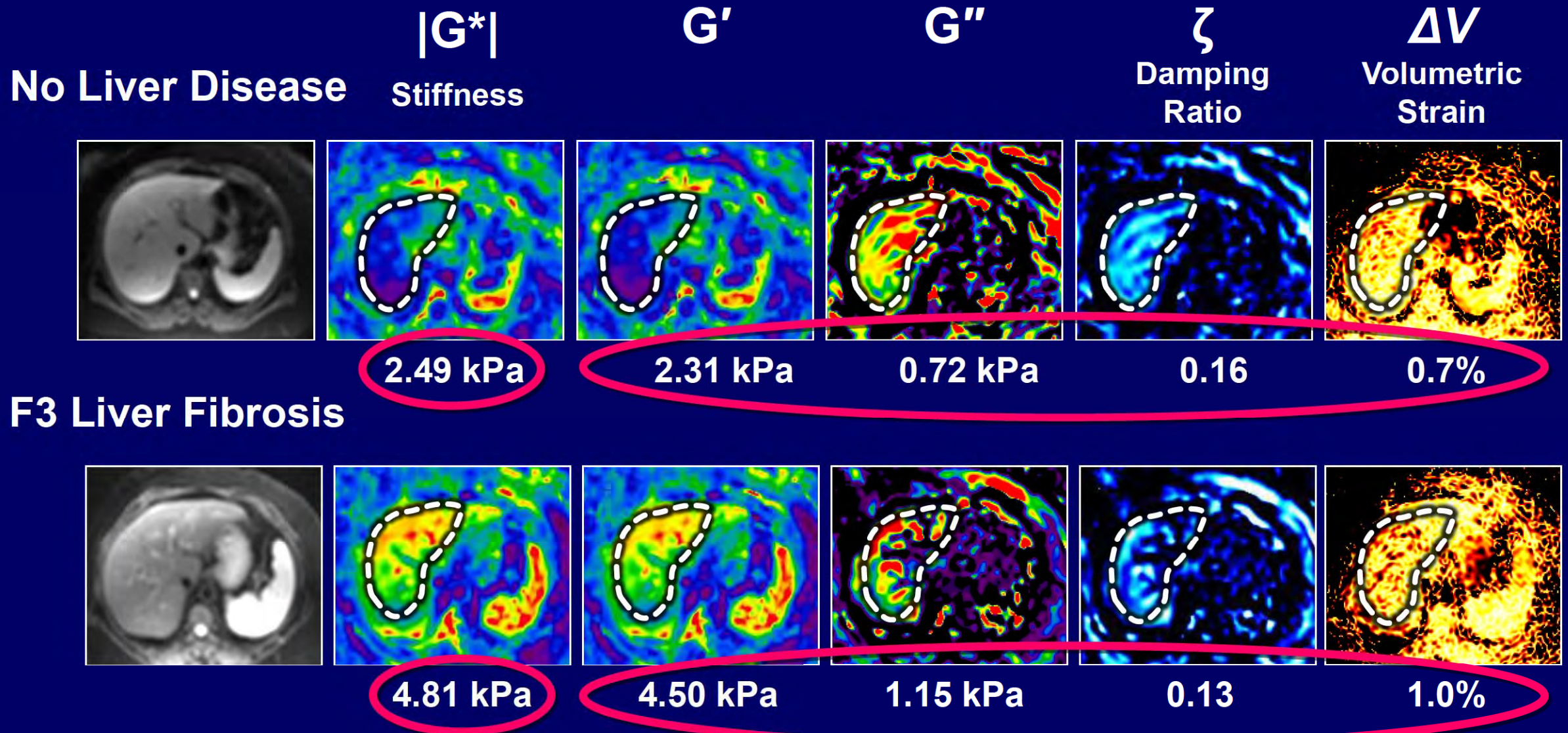


F4



Advanced Multiparametric MRE

(Imaging time: 1 minute)



Hepatic
Inflammation

Hepatic
Fibrosis

Venous
Congestion

Portal
Hypertension

Shear Stiffness



Damping Ratio



Volumetric Strain



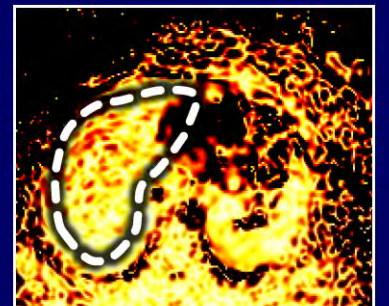
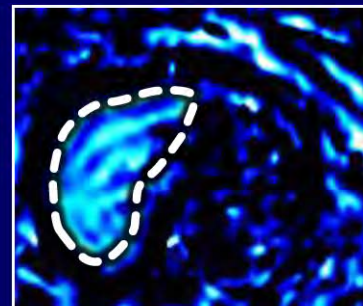
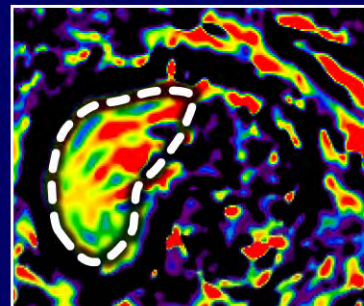
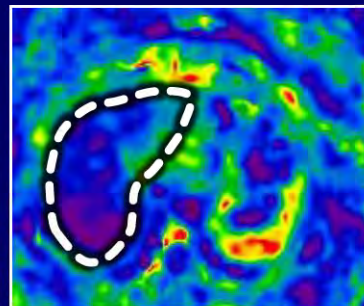
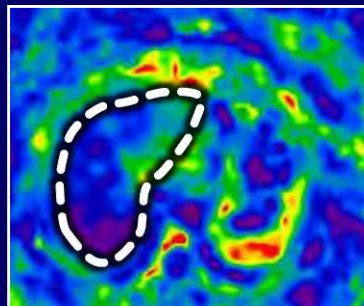
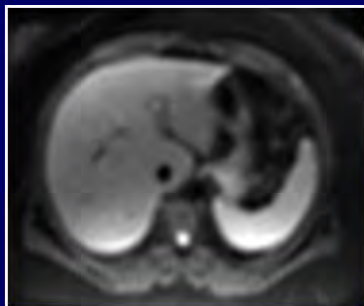
Shear
Stiffness

Storage
Modulus

Loss
Modulus

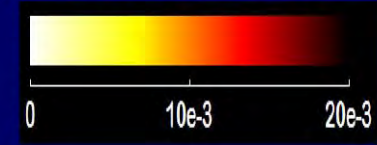
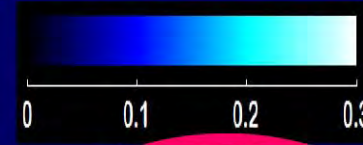
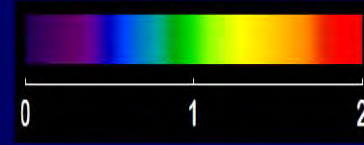
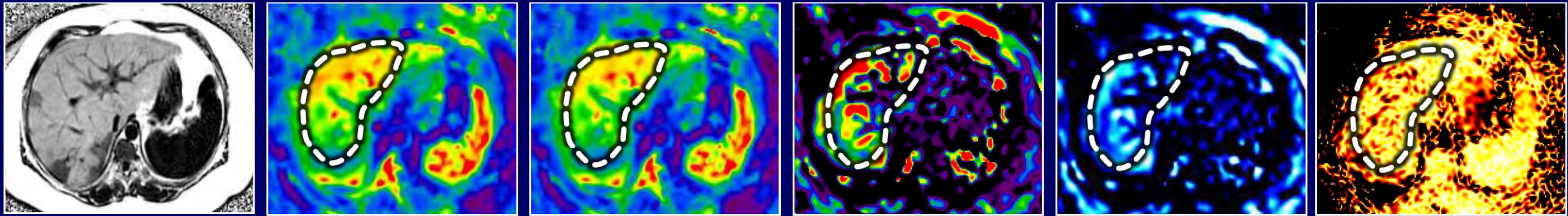
Damping
Ratio

Volumetric
Strain



Multiparametric *Rapid MR Hepatogram*

(Imaging time: 1-2 minutes)



PDFFF

Proton
Density Fat
Fraction

$|G^*|$

Stiffness

G'

Storage
Modulus

G''

Loss Modulus

ζ

Damping Ratio

ΔV

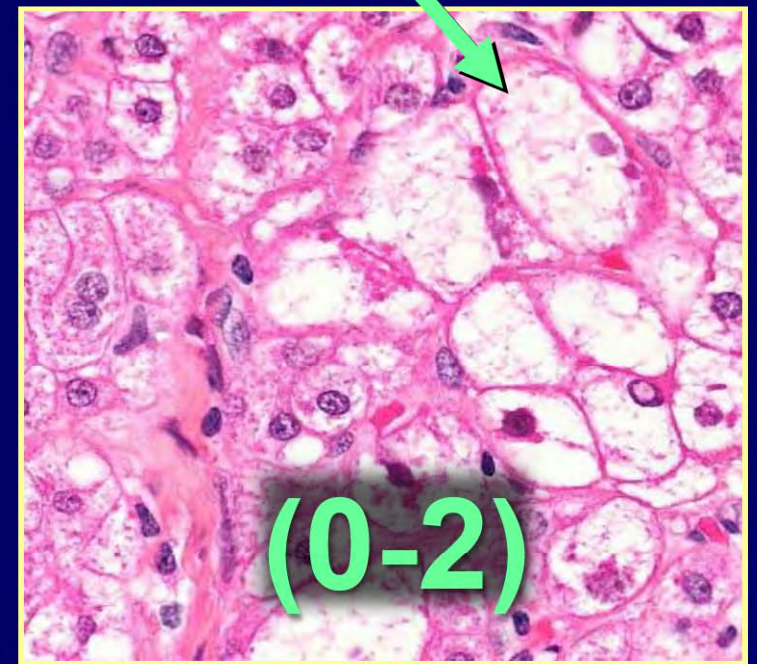
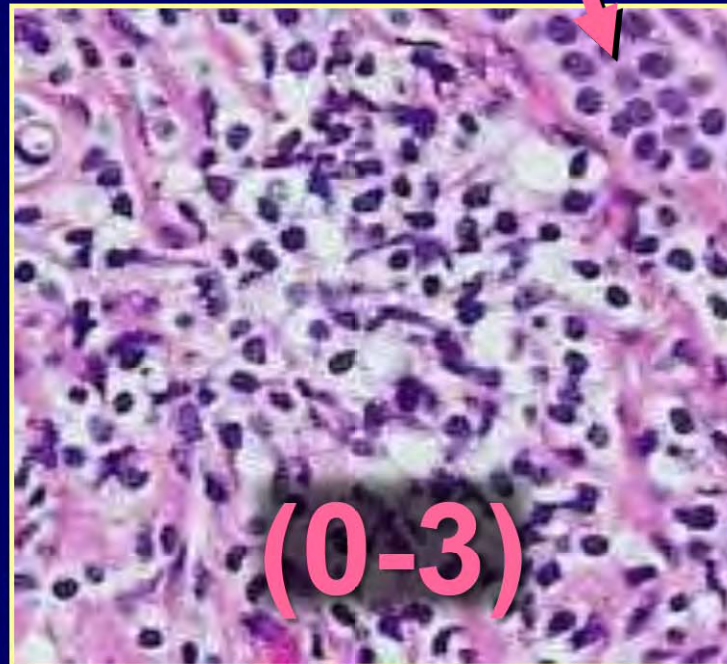
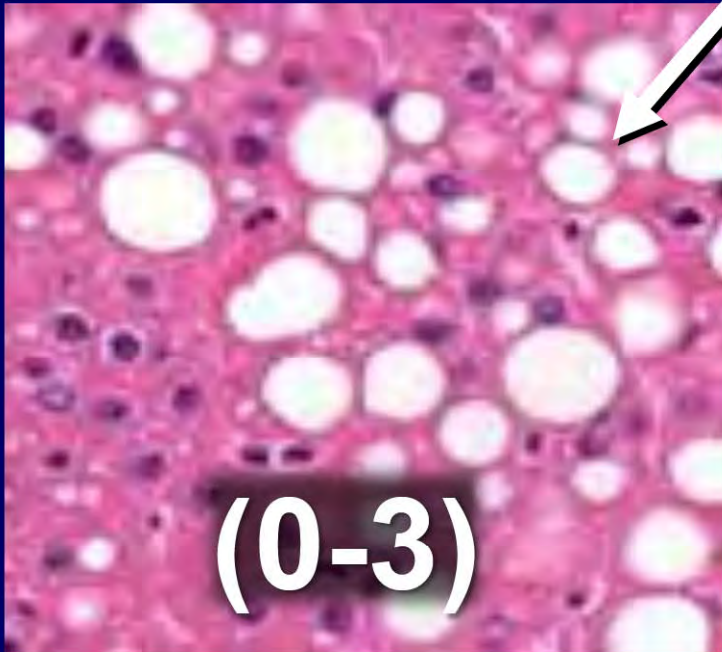
Volumetric
Strain

Can we train a machine learning algorithm to interpret these parameters and predict histologic staging?

NASH Activity Score

- Biopsy-based measure of NASH severity
- Validated against clinical outcome

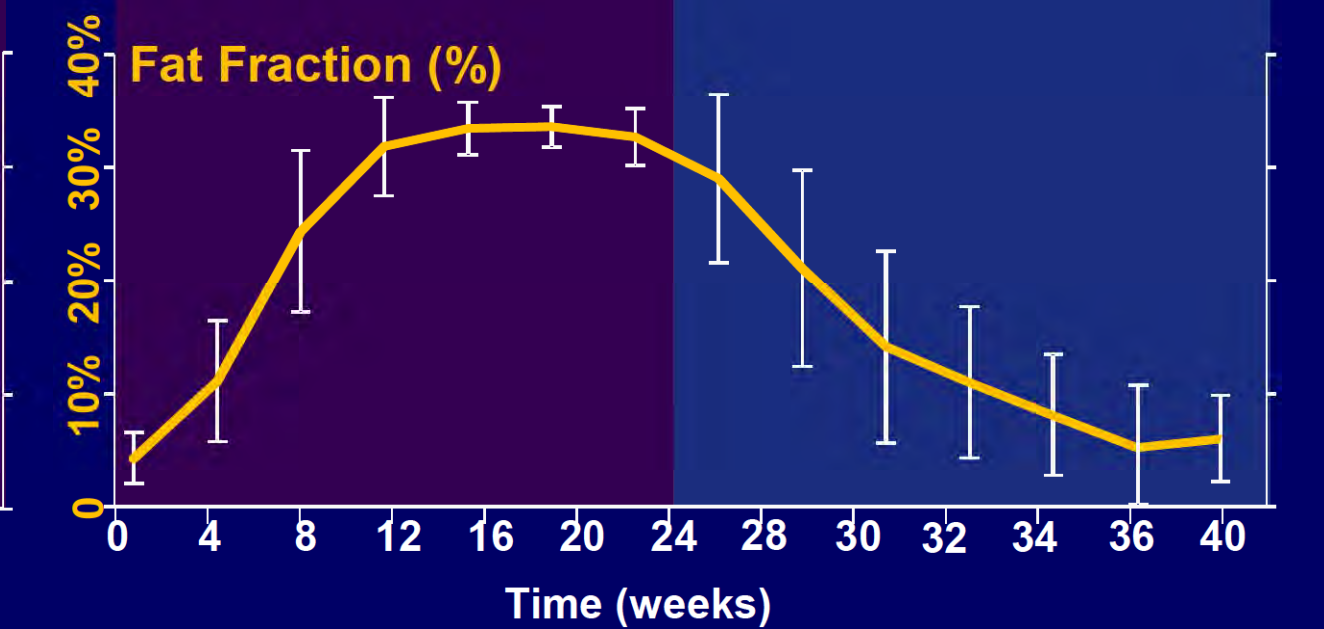
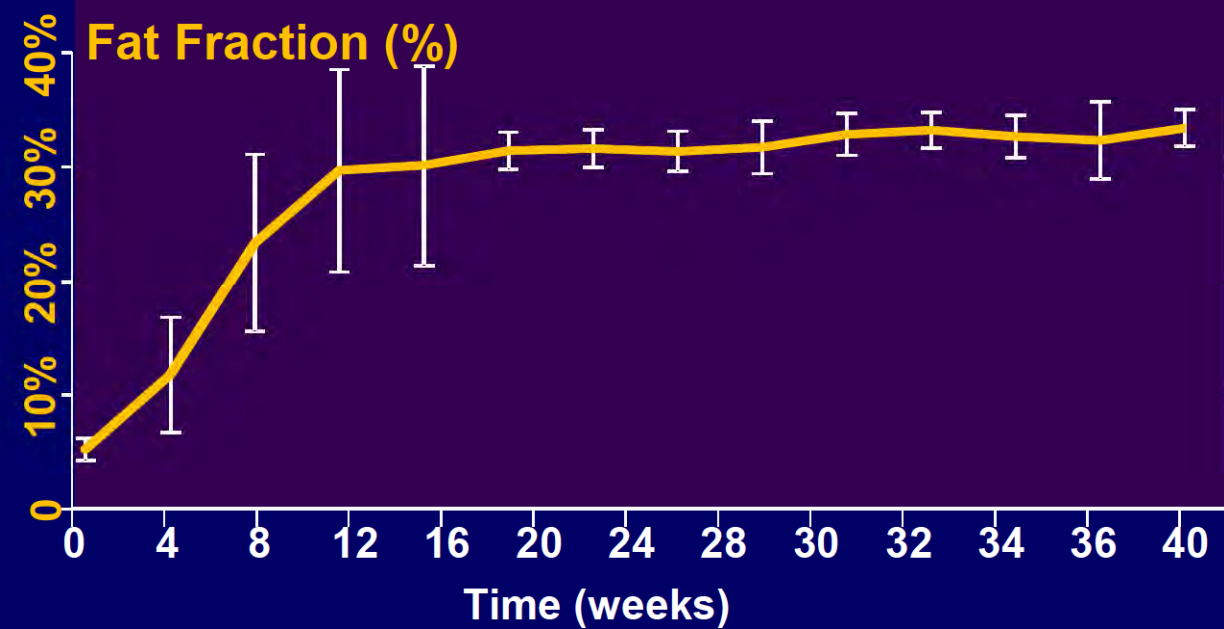
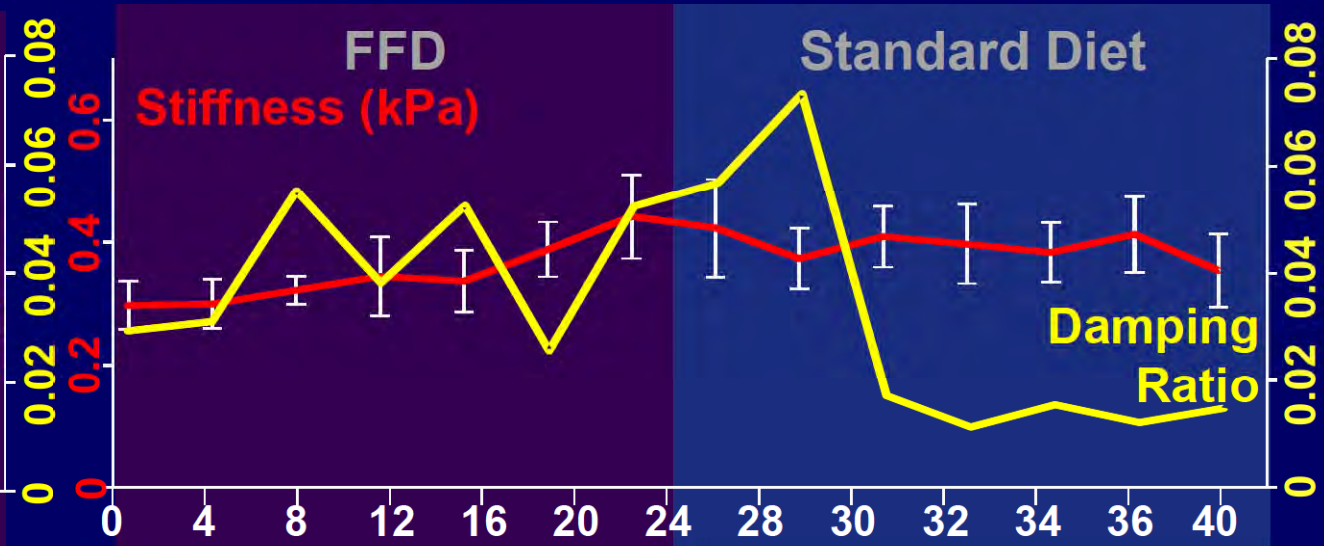
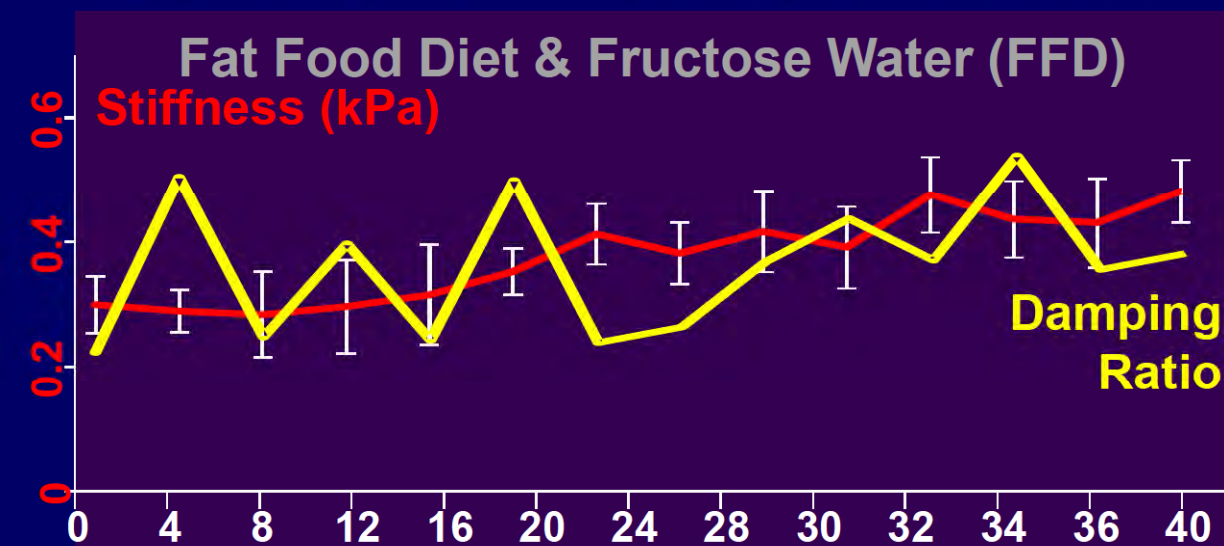
NAS Score = Steatosis + Inflamm + Necrosis



**If the same liver specimen is evaluated independently by 2 different pathologists:
Will the interpretations agree?**

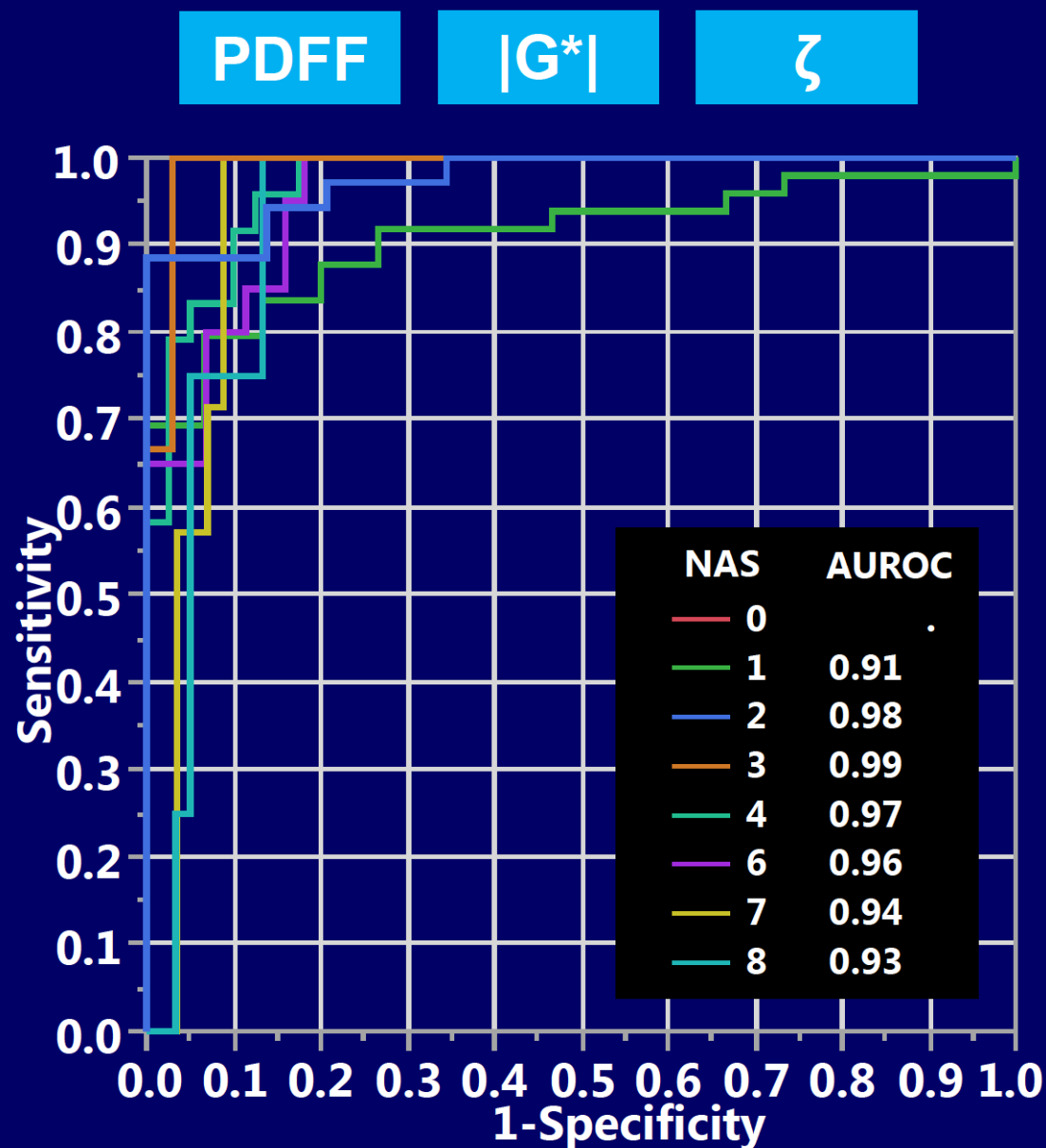
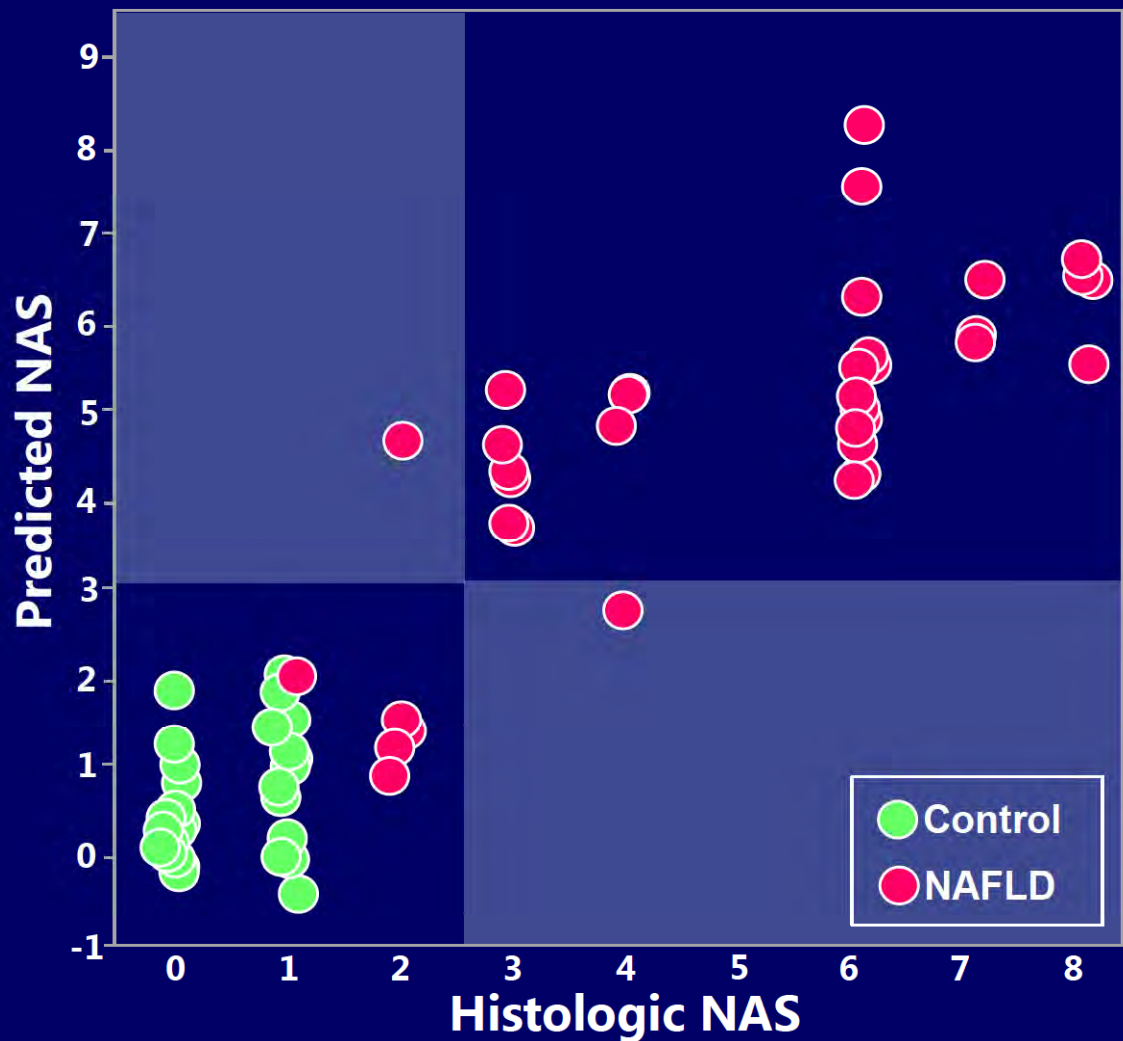
Feature	Kappa	Agreement
Fibrosis	0.84	Excellent
Steatosis Grade	0.79	Good to Excellent
Inflammation Grade	0.45	Fair
Ballooning	0.56	Fair
NASH vs Not NASH	0.61	Fair to Good

Independent Value of Damping Ratio as Biomarker



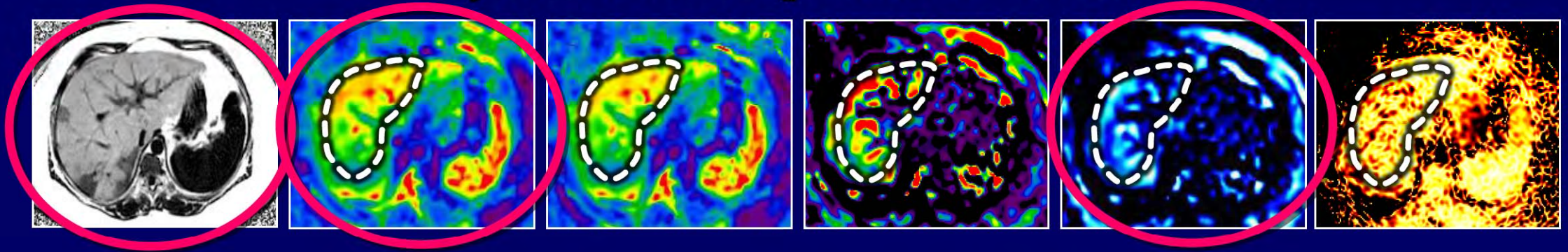
NAS Prediction in Preclinical NASH Model

Linear Regression (All data)



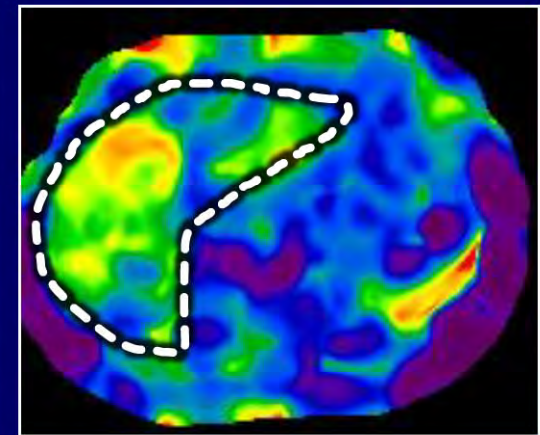
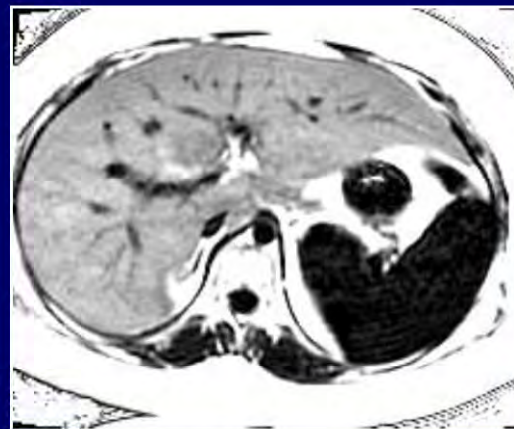
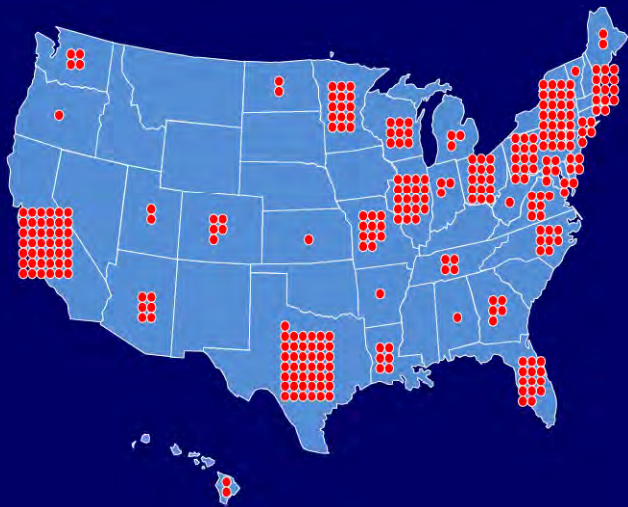
Advanced Multiparametric MRI/MRE

- Beyond assessing fibrosis and steatosis



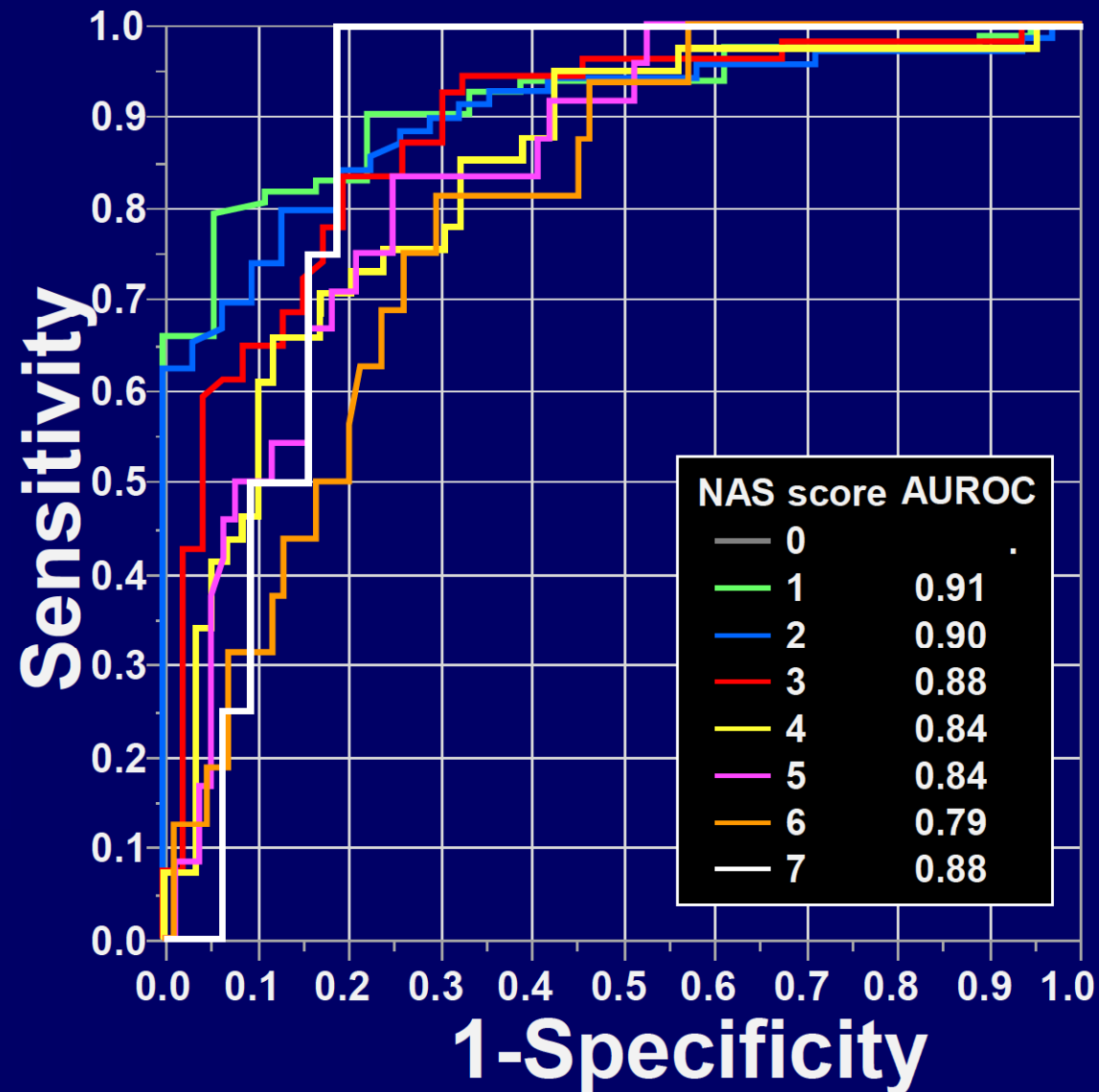
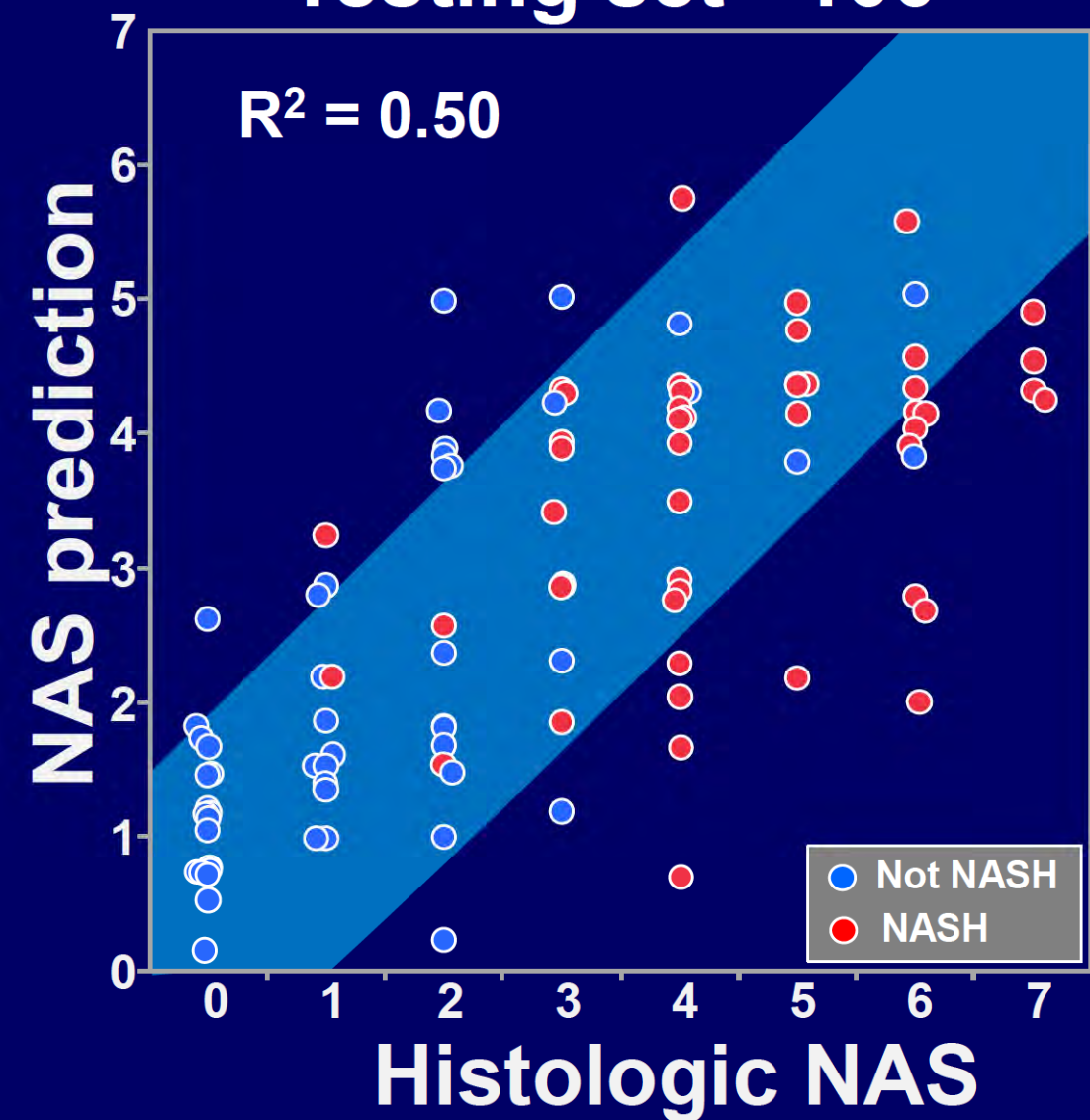
2D Multiparametric MRI/MRE

- Already available at more than 1000 locations worldwide
- Is there a role in NAFLD beyond assessing fibrosis and steatosis?



NAS Prediction: 2D MRI/MRE

Testing set= 100

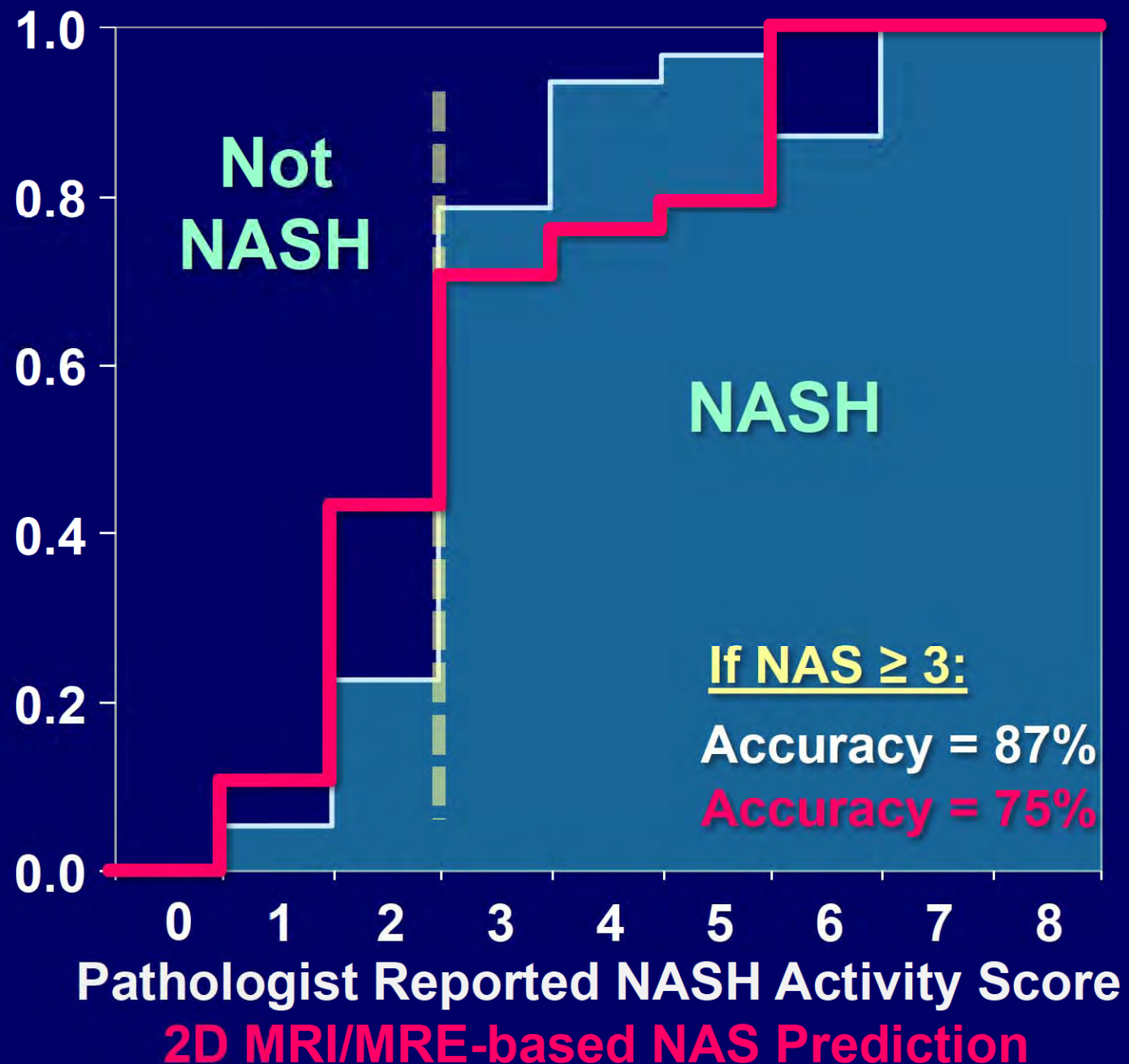
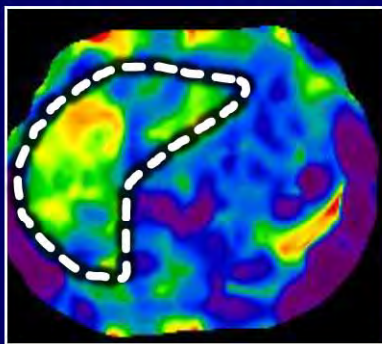


250 NAFLD Patients with Biopsies

Fraction Classified as NASH by Pathologist

PDFFF (%)

MRE (kPa)



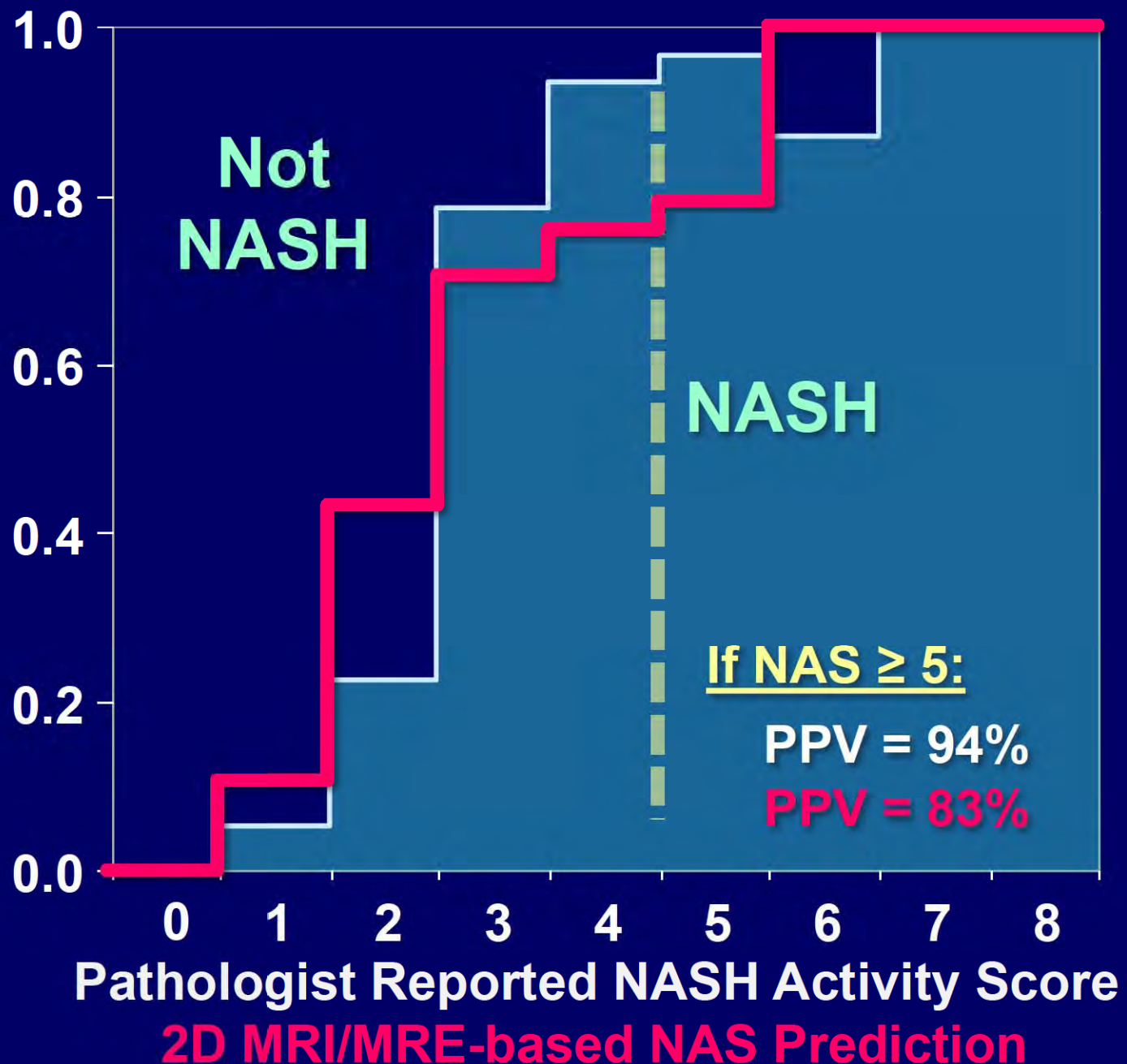
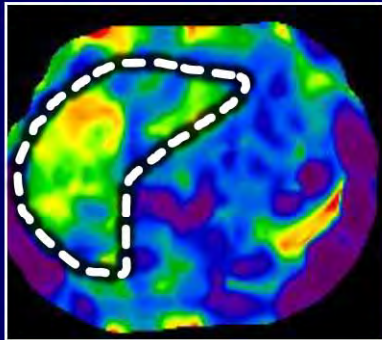
250 NAFLD Patients with Biopsies

Fraction Classified as NASH by Pathologist

Fraction Classified as NASH by Pathologist

PDFFF (%)

MRE (kPa)



MRI-Based Noninvasive Assessment of NAFLD

- MRE and MRI-PDFF technology is now widely available
- Reliably quantifies hepatic fibrosis and steatosis
- Hepatic stiffness also reflects inflammation, portal hypertension, and venous congestion
- Increasing evidence base for use of MRI/MRE in assessing clinical progression, regression, and treatment response in NAFLD/NASH
- Emerging *advanced multiparametric* MRE technology is adding new capabilities

