



THE FORUM

For Collaborative ResearchSM

MRI:

Diagnostic Application of cT1 & Elastography Through the Lens of Regulatory Science

Session V: Diagnostic Context of Use

Friday April 22, 2022

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UC San Diego





Disclosures

Research grants from industry
(Money paid to institution)

Bayer, GE, Gilead, Pfizer, Philips, Siemens

Lab service agreements
(Money paid to institution)

Enanta, Gilead, ICON, Intercept, Nusirt, Shire, Synageva, Takeda

Institutional consulting
(Money paid to institution)

AMRA, BMS, Exact Sciences, IBM-Watson, Pfizer

Personal consulting
(Money paid to me)

Blade, Boehringer, Epigenomics

Position in company
(Own stock options)

Livivos (Chief Medical Officer, pending)

Member of advisory board
(Unpaid)

Quantix Bio

Royalties and educational
(Money paid to me)

Medscape, Wolters Kluwer

Outline



Diagnostic biomarkers
in NAFLD clinical trials

MultiScan: iron-corrected T1 (cT1)
as a diagnostic enrichment biomarker in NAFLD clinical trials

MR elastography: magnitude of complex modulus ($|G^*|$), “shear stiffness”
as a diagnostic biomarker in NAFLD clinical trials

MultiScan-cT1 and MRE-stiffness
friend or foe?

Outline

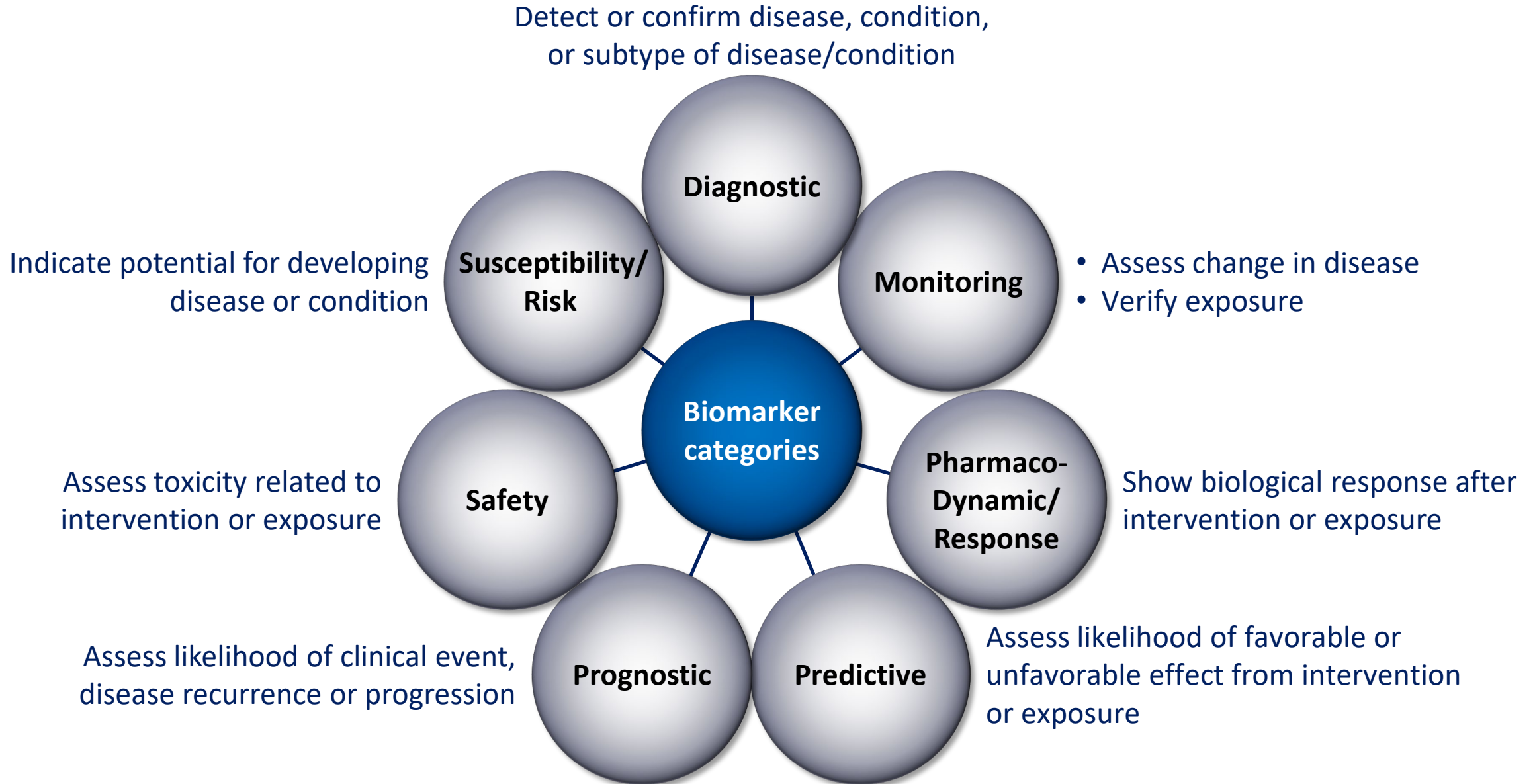
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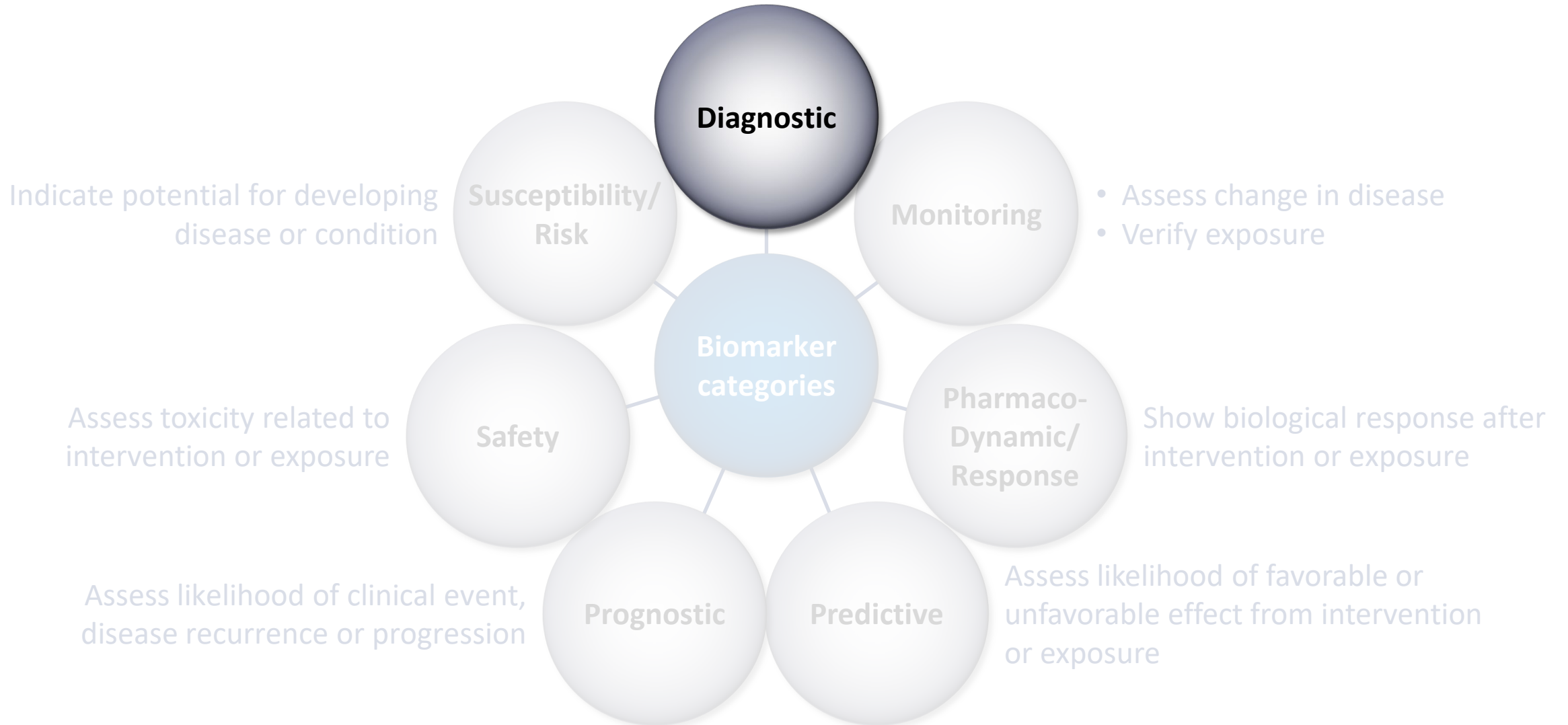
MR elastography: magnitude of complex modulus ($|G^*|$), “shear stiffness”
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friend or foe?

The FDA defines **seven biomarker categories**



Detect or confirm disease, condition,
or subtype of disease/condition



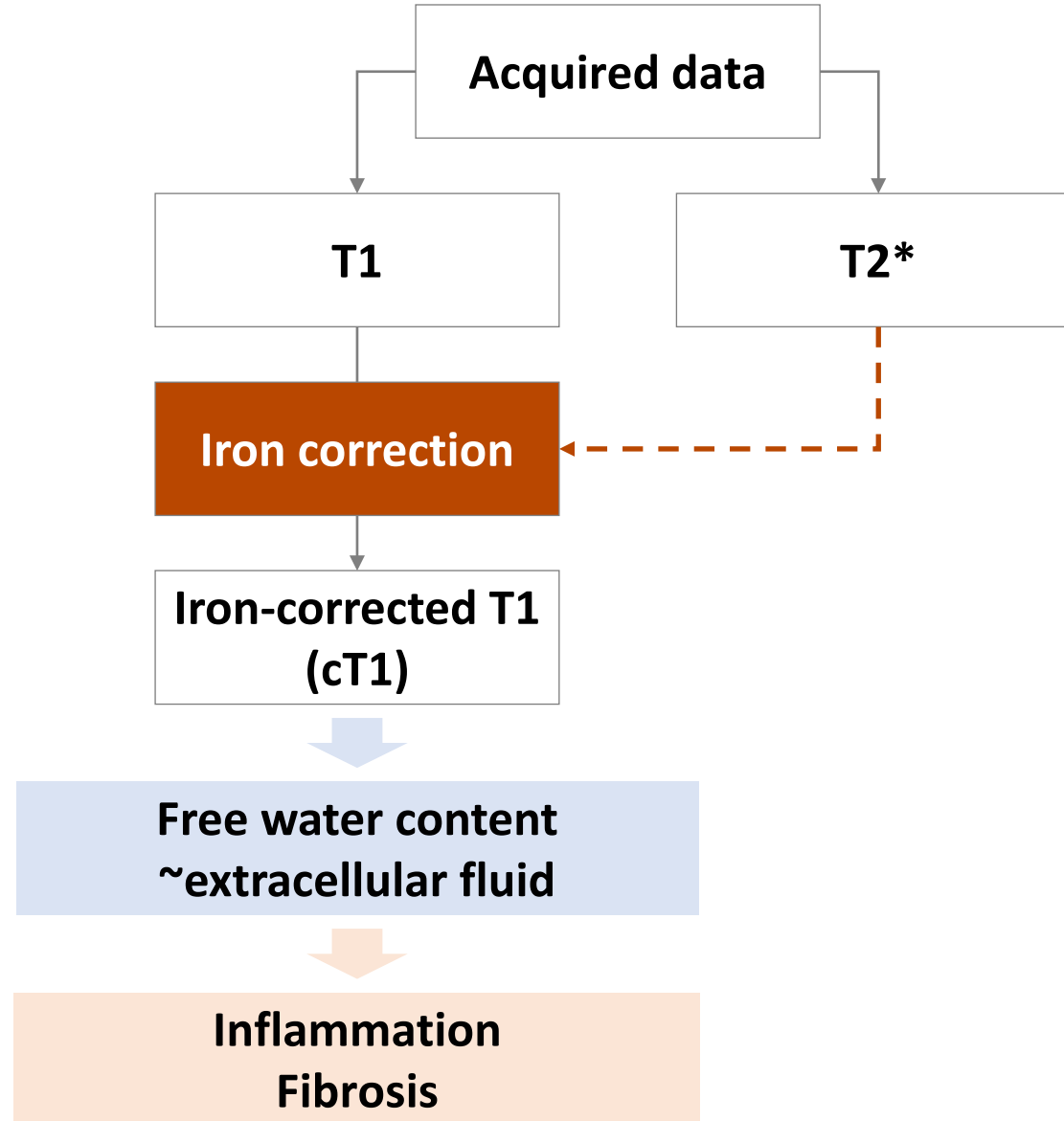
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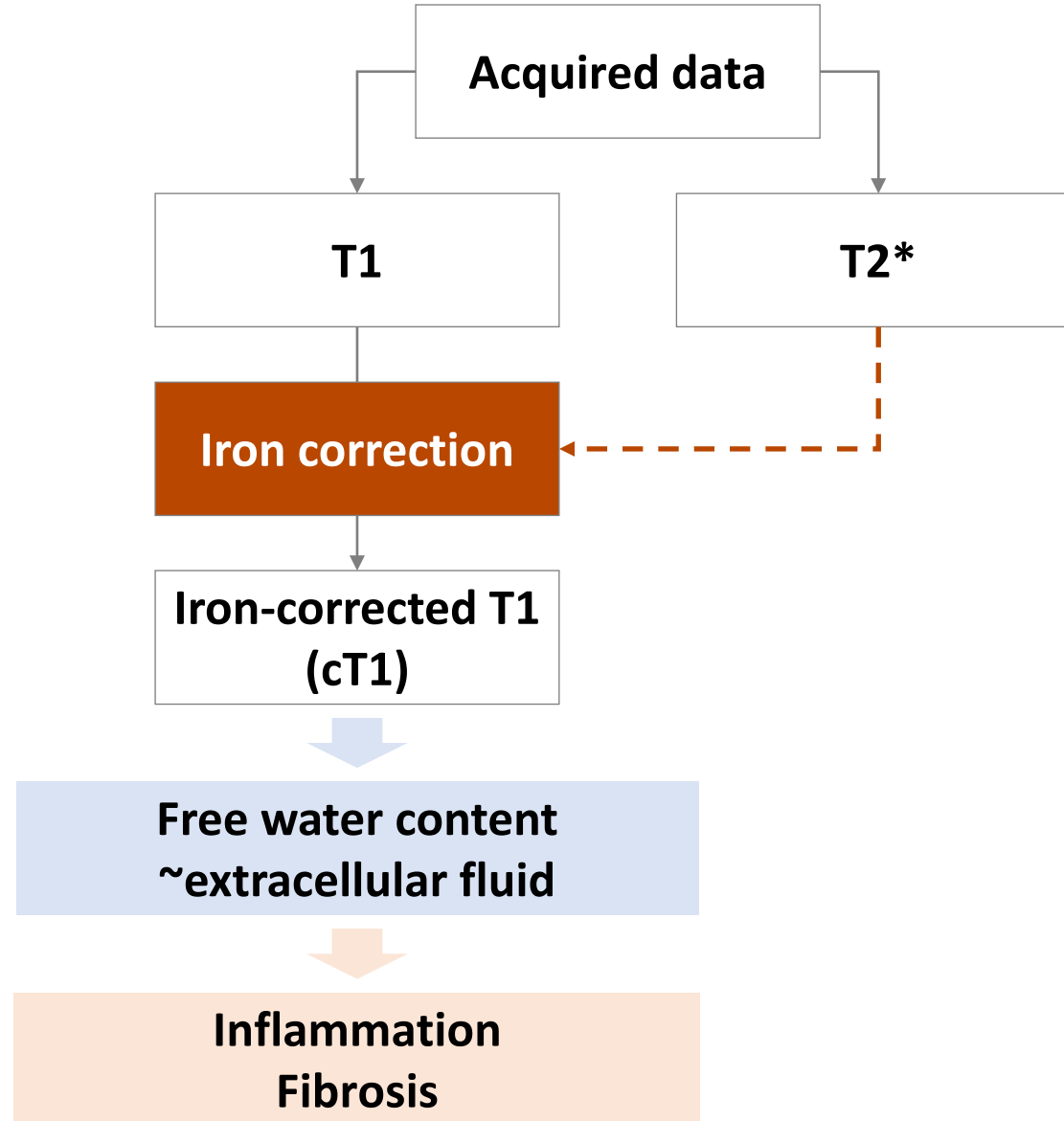


Standardized across

- Feld strength
- Scanner

Analyzed offline by PD

- Quality control
- Results reporting
- Rapid turn around





MultiScan cT1



Type of biomarker:

Diagnostic enrichment biomarker

Context of use

Diagnostic enrichment biomarker that can be used, in conjunction with clinical risk factors, to identify patients who are more likely to have **liver histopathologic findings appropriate for inclusion in non-alcoholic steatohepatitis (NASH) clinical trials**

Letter of Intent
(LOI)

Initiates the qualification process of a biomarker for a proposed context of use (COU) in drug development



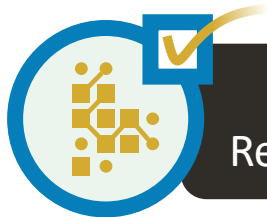
Qualification
Plan (QP)

Defines the intended development to generate the necessary supportive data to qualify the biomarker for the proposed COU



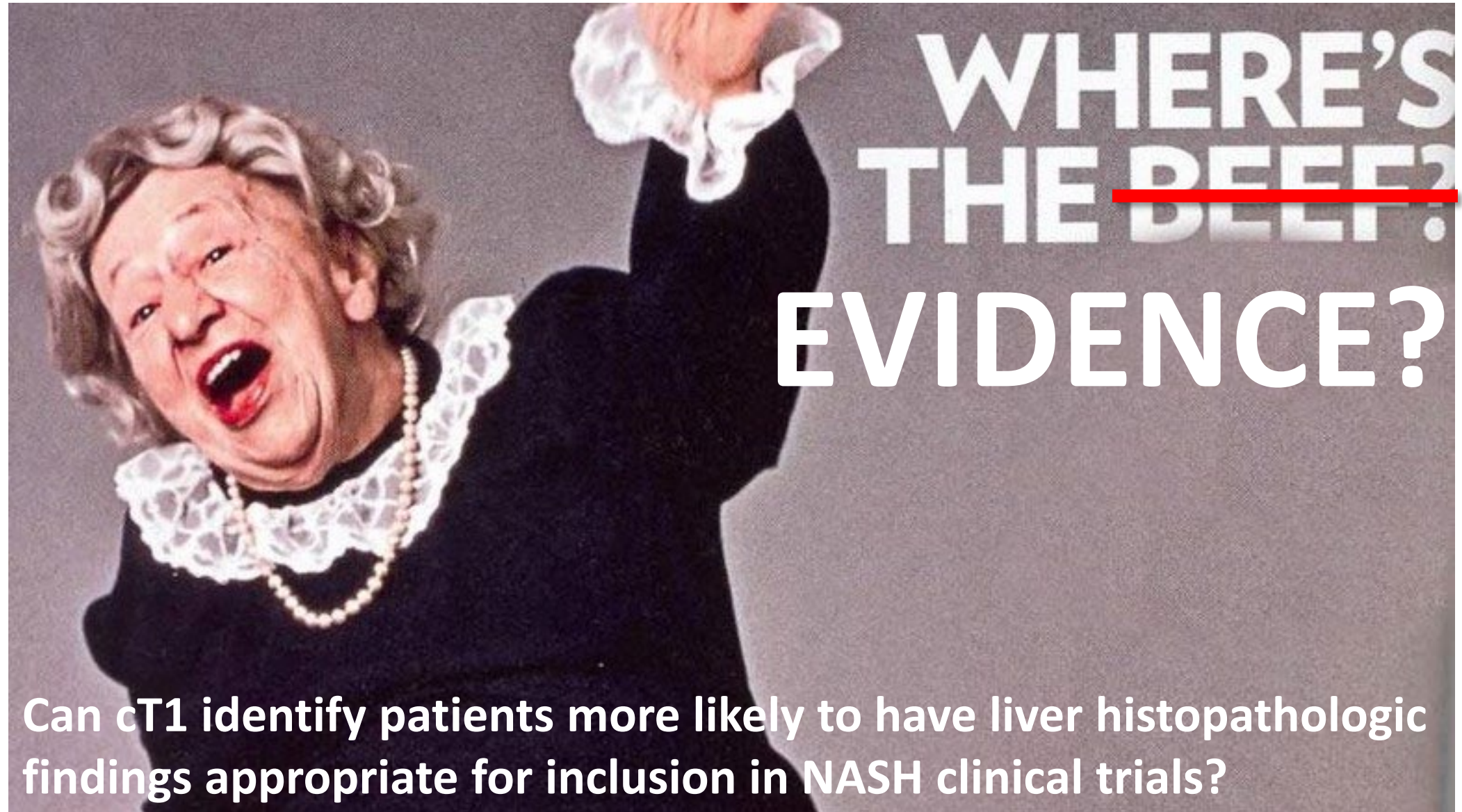
Full Qualification
Package (FQP)

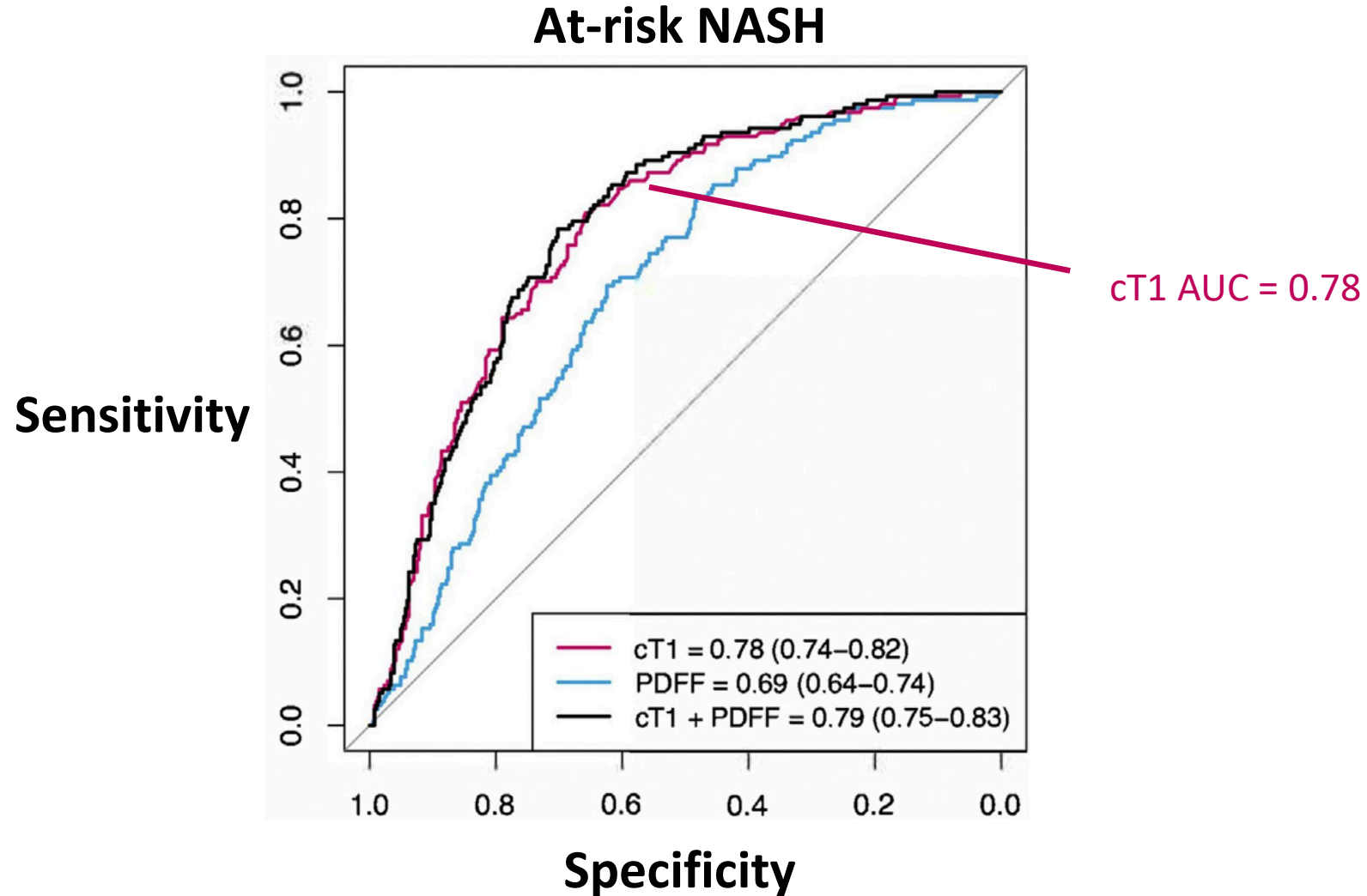
Contains all accumulated data to support the qualification of the biomarker for the proposed COU



Qualification
Recommendation

Contains FDA's determination on whether the biomarker is qualified for the proposed COU based on a comprehensive review of the FQP







MultiScan T1 has 39-86% sens. & 56-90% spec. for “at-risk” NASH



Cutoff	Sens	Spec	Youden
≥ 800 ms	86	56	142
≥ 825 ms	78	67	145
≥ 875 ms	59	81	140
≥ 900 ms	48	86	134
≥ 925 ms	39	90	129

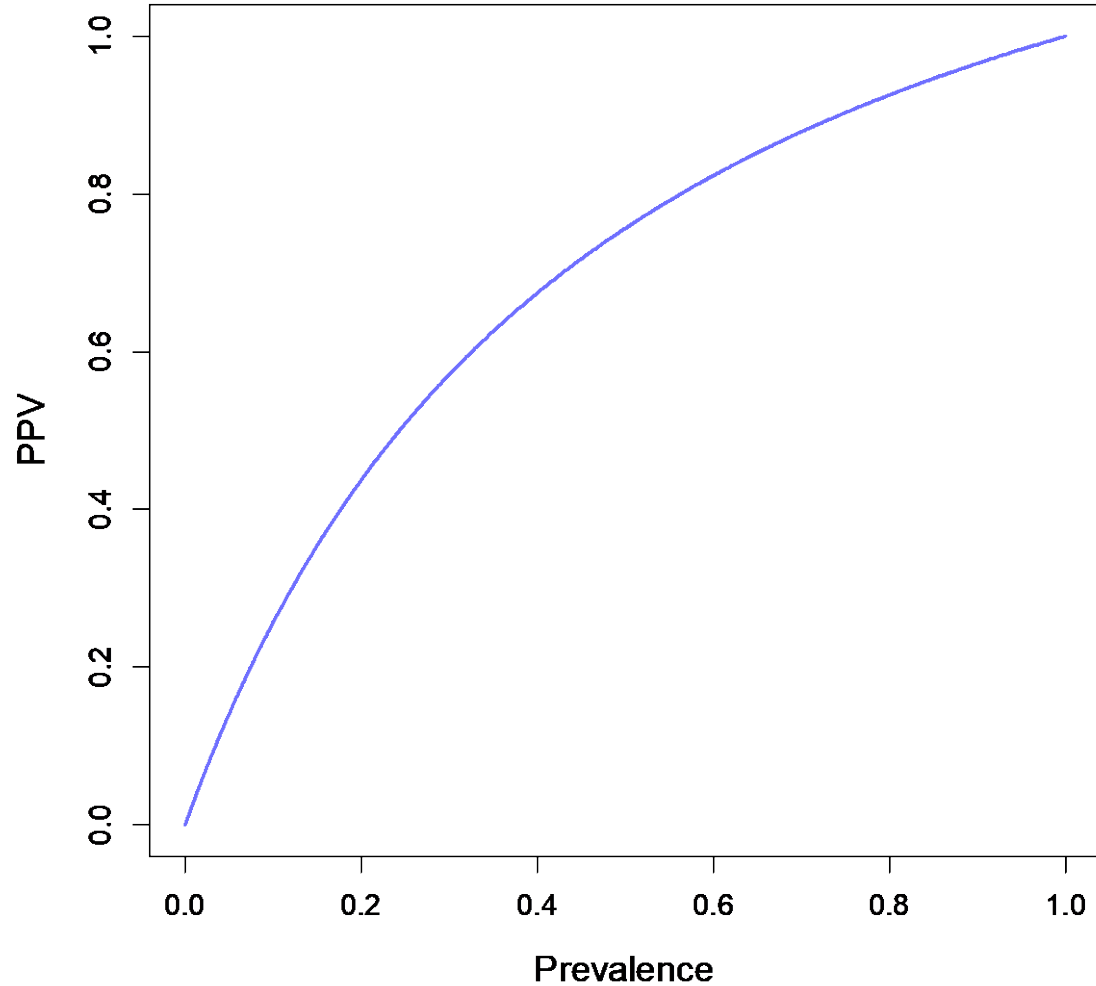
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MultiScan cT1 PPV and NPV simulation curves

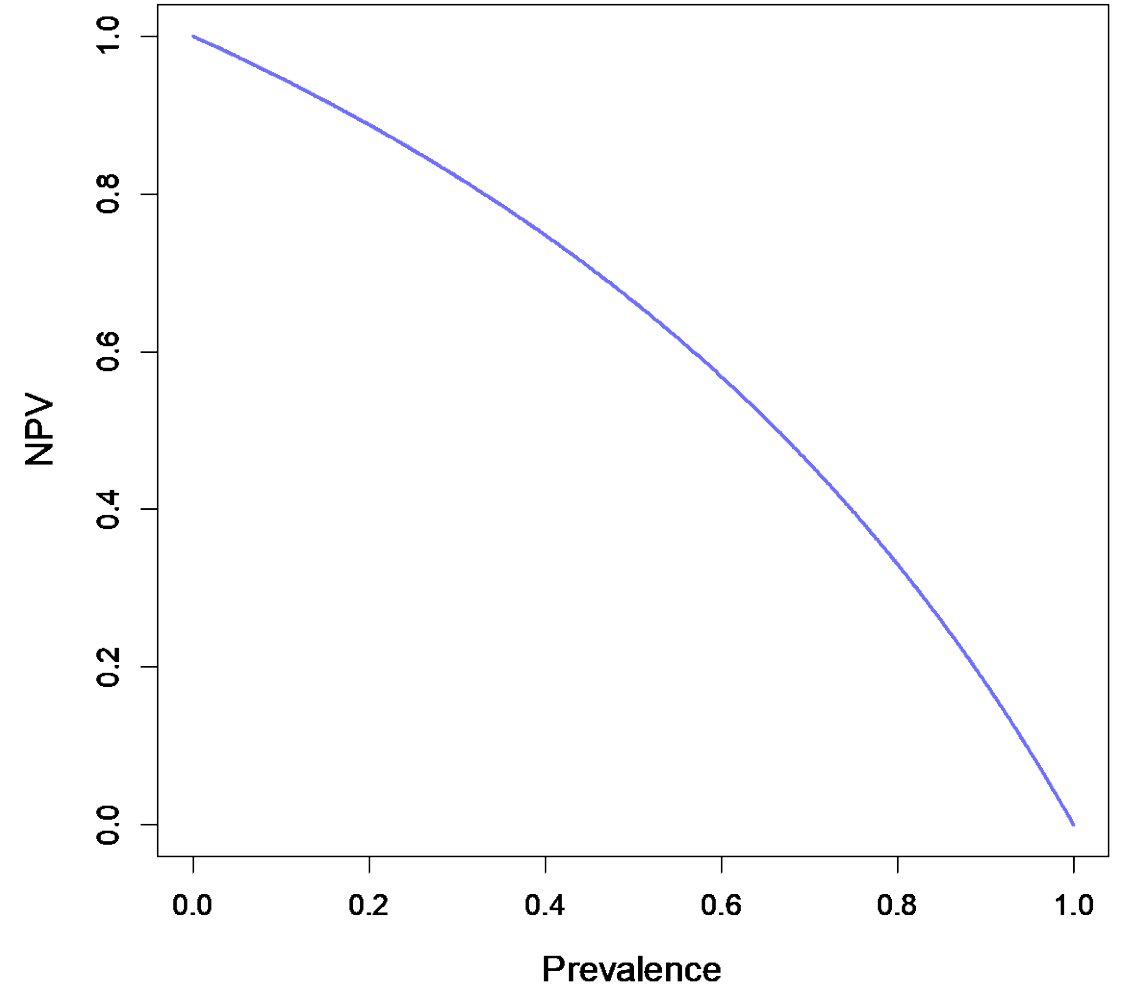
At risk NASH diagnosis

- 59% sensitivity
- 81% specificity

Corrected T1



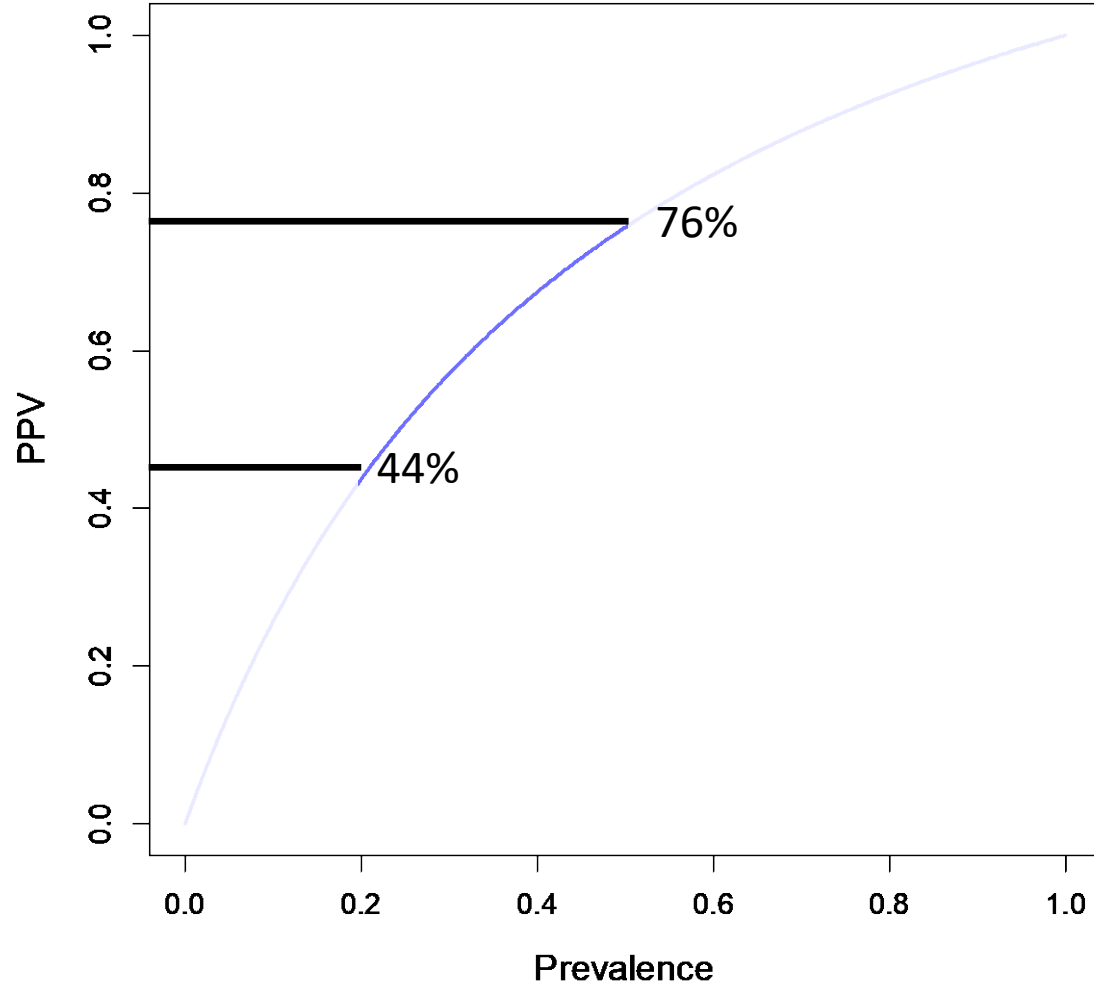
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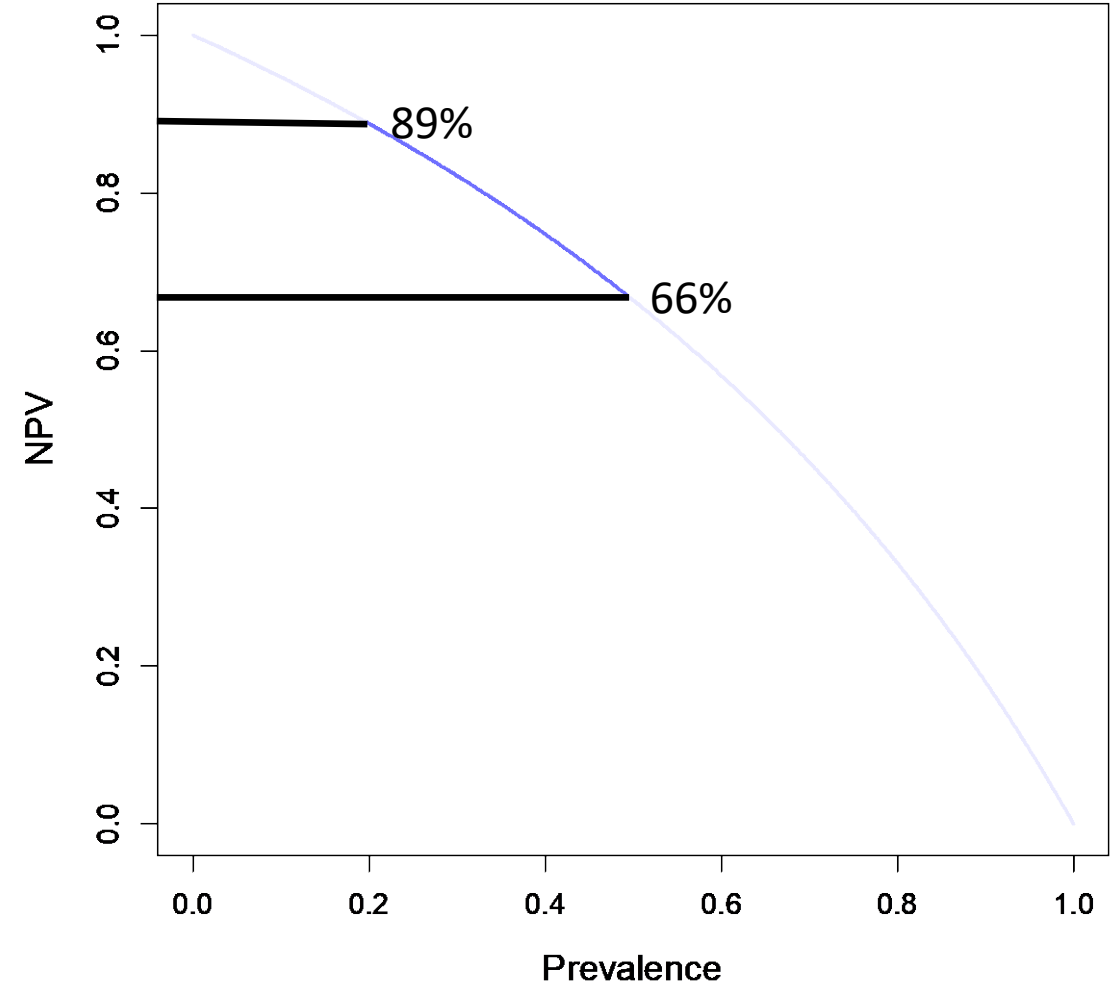
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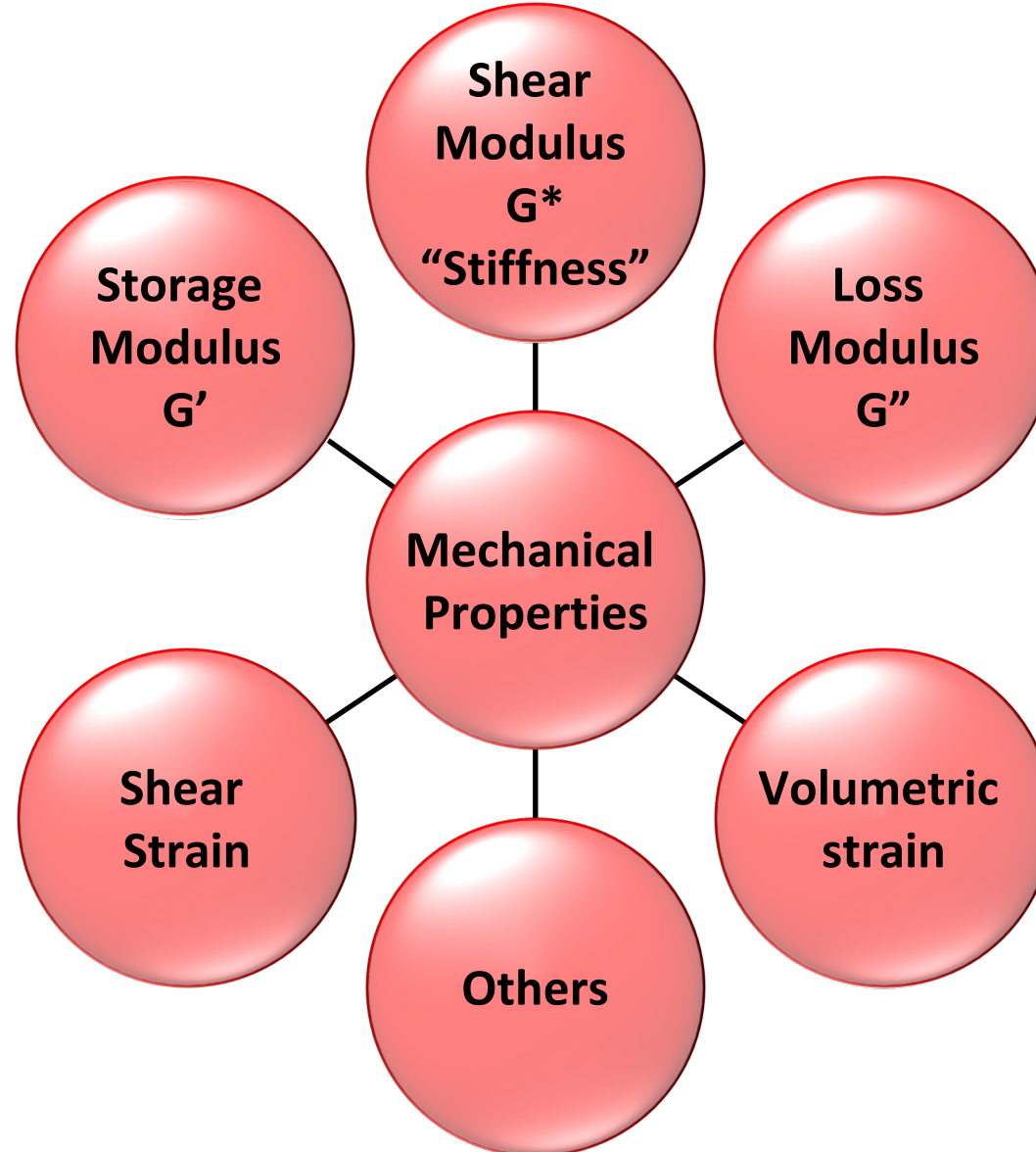
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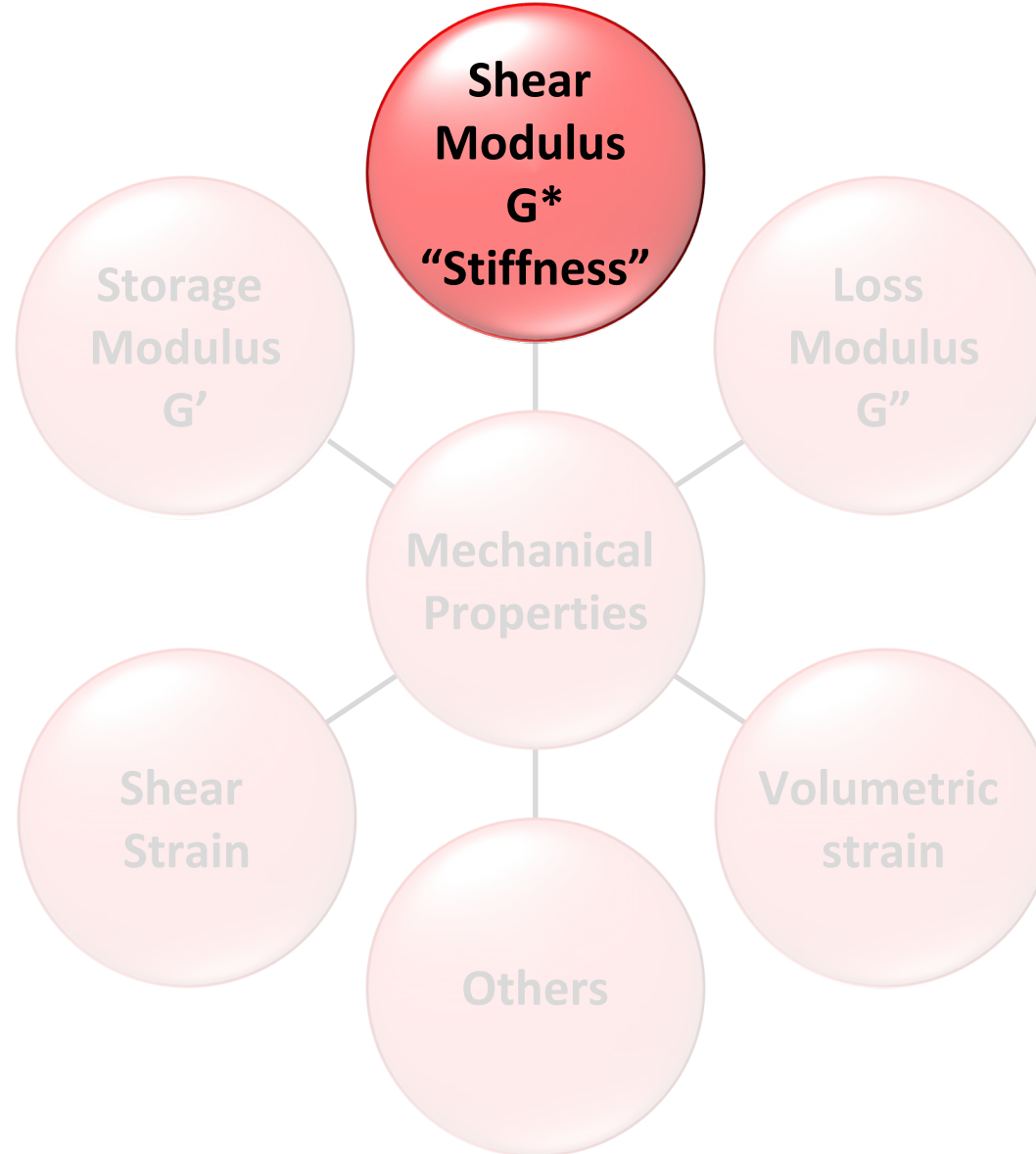
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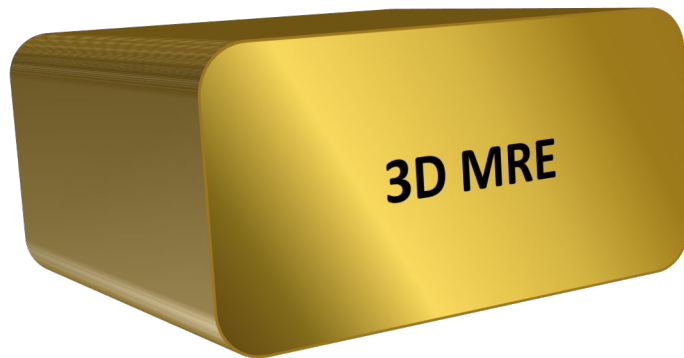
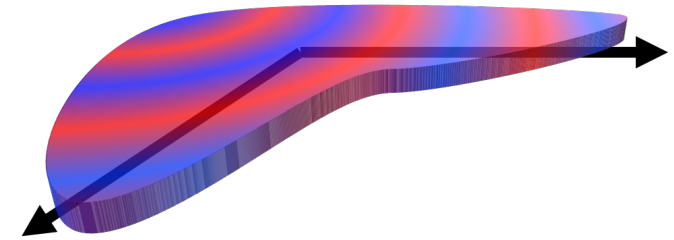




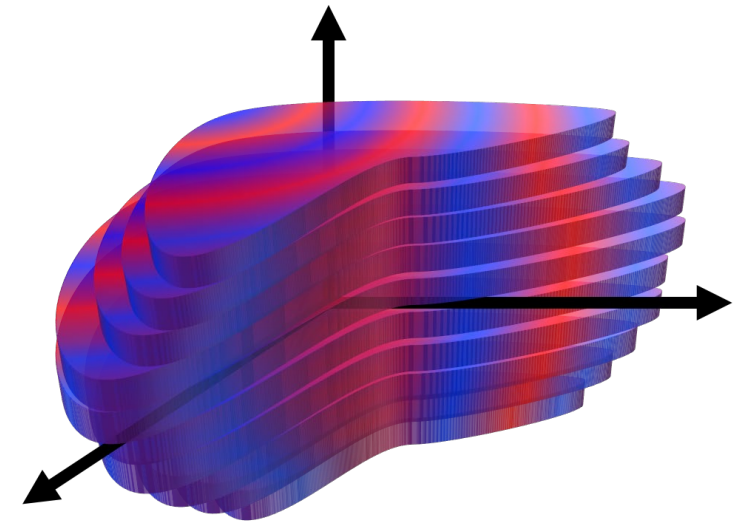
Two main flavors of MRE



2D wave motion
4 slices

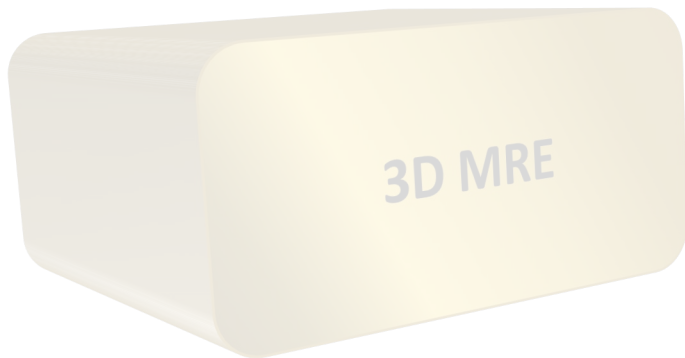


3D wave motion
Entire liver





2D wave motion
4 slices



3D wave motion
Entire liver

Image acquisition and reconstruction standardized across

- Feld strength
- Scanner

Soon: Optional automated cloud-based analysis by Resoundant

- Results reporting
- Rapid turn around

Type of biomarker:

Diagnostic biomarker

Context of use

A diagnostic biomarker to **pre-screen patients** with clinical risk factors for nonalcoholic fatty liver disease (NAFLD) or fibrotic nonalcoholic steatohepatitis (NASH) for enrollment in clinical trials to identify those at high risk of having histopathologic findings on liver biopsy of

- **significant fibrosis (\geq F2) or**
- **advanced fibrosis (\geq F3) or**
- **cirrhosis (F4)**

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PAR-21-178
(Drug Development Tools
Research Grants (U01)
awarded to Kay Pepin

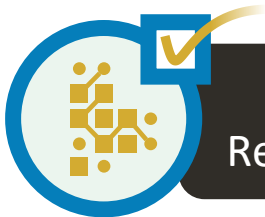



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WHERE'S
THE BEEF?
EVIDENCE?

Can MRE identify patients at high risk of having significant fibrosis ($F \geq 2$), advanced fibrosis ($F \geq 3$), or cirrhosis?



2D MRE |G*| Evidence: at least 12 relevant articles since 2020



THE FORUM

For Collaborative Research™

2020

ORIGINALS | HEPATOLOGY COMMUNICATIONS, VOL. 10, NO. 4

Multiparametric Magnetic Resonance Elastography Improves the Detection of NASH Regression Following Bariatric Surgery

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of multiparametric magnetic resonance elastography (MRE) in the diagnosis of nonalcoholic steatohepatitis (NASH) regression following bariatric surgery. The study included 100 patients who underwent MRE before and after bariatric surgery. The results showed that MRE improved the detection of NASH regression compared to conventional MRE. The study concluded that MRE is a valuable tool for the diagnosis of NASH regression following bariatric surgery.

HEPATOLOGY COMMUNICATIONS

The Role of Three-Dimensional Magnetic Resonance Elastography in the Diagnosis of Nonalcoholic Steatohepatitis in Obese Patients Undergoing Bariatric Surgery

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of three-dimensional magnetic resonance elastography (3D-MRE) in the diagnosis of nonalcoholic steatohepatitis (NASH) in obese patients undergoing bariatric surgery. The study included 100 patients who underwent 3D-MRE before and after bariatric surgery. The results showed that 3D-MRE improved the detection of NASH in obese patients compared to conventional MRE. The study concluded that 3D-MRE is a valuable tool for the diagnosis of NASH in obese patients undergoing bariatric surgery.

SCIENTIFIC REPORTS

Non-invasive Imaging Modalities for Assessment of Fibrosis, Inflammation and Steatosis in a Japanese NASH Population

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1038/s41598-020-14111-1](#))

Abstract: This study aimed to evaluate the role of non-invasive imaging modalities for the assessment of fibrosis, inflammation, and steatosis in a Japanese nonalcoholic steatohepatitis (NASH) population. The study included 100 patients who underwent various imaging modalities. The results showed that these modalities improved the assessment of fibrosis, inflammation, and steatosis in the Japanese NASH population. The study concluded that non-invasive imaging modalities are valuable tools for the assessment of NASH in a Japanese population.

SCIENTIFIC REPORTS

Multiparametric MR Index for the Diagnosis of Non-Alcoholic Steatohepatitis in Patients with Non-Alcoholic Fatty Liver Disease

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1038/s41598-020-14111-1](#))

Abstract: This study aimed to evaluate the role of a multiparametric MR index for the diagnosis of non-alcoholic steatohepatitis (NASH) in patients with non-alcoholic fatty liver disease (NAFLD). The study included 100 patients who underwent the multiparametric MR index. The results showed that the index improved the diagnosis of NASH in patients with NAFLD. The study concluded that the multiparametric MR index is a valuable tool for the diagnosis of NASH in patients with NAFLD.

ARTICLE

Multiparametric MR Is a Valuable Modality for Evaluating Disease Severity of Nonalcoholic Fatty Liver Disease

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of multiparametric magnetic resonance (MR) for the evaluation of disease severity in nonalcoholic fatty liver disease (NAFLD). The study included 100 patients who underwent multiparametric MR. The results showed that multiparametric MR improved the evaluation of disease severity in NAFLD. The study concluded that multiparametric MR is a valuable modality for the evaluation of disease severity in NAFLD.

ARTICLE

T1 mapping, T2 mapping and MR elastography of the liver for detection and staging of liver fibrosis

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of T1 mapping, T2 mapping, and MR elastography for the detection and staging of liver fibrosis. The study included 100 patients who underwent these modalities. The results showed that these modalities improved the detection and staging of liver fibrosis. The study concluded that T1 mapping, T2 mapping, and MR elastography are valuable tools for the detection and staging of liver fibrosis.

2021

RESEARCH ARTICLE

Diagnostic accuracy of elastography and magnetic resonance imaging in patients with NAFLD: A systematic review and meta-analysis

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This systematic review and meta-analysis aimed to evaluate the diagnostic accuracy of elastography and magnetic resonance imaging (MRI) in patients with nonalcoholic fatty liver disease (NAFLD). The study included 100 studies. The results showed that elastography and MRI improved the diagnostic accuracy of NAFLD. The study concluded that elastography and MRI are valuable tools for the diagnosis of NAFLD.

RESEARCH ARTICLE

The Combination of MR Elastography and Proton Density Fat Fraction Improves Diagnosis of Nonalcoholic Steatohepatitis

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of the combination of magnetic resonance elastography (MRE) and proton density fat fraction (PDF) for the diagnosis of nonalcoholic steatohepatitis (NASH). The study included 100 patients who underwent MRE and PDF. The results showed that the combination of MRE and PDF improved the diagnosis of NASH. The study concluded that the combination of MRE and PDF is a valuable tool for the diagnosis of NASH.

ORIGINAL RESEARCH

Automated Analysis of Multiparametric Magnetic Resonance Imaging/Magnetic Resonance Elastography Exams for Prediction of Nonalcoholic Steatohepatitis

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of automated analysis of multiparametric magnetic resonance imaging (MRI) and magnetic resonance elastography (MRE) exams for the prediction of nonalcoholic steatohepatitis (NASH). The study included 100 exams. The results showed that automated analysis improved the prediction of NASH. The study concluded that automated analysis is a valuable tool for the prediction of NASH.

RESEARCH ARTICLE

MRE combined with FIB-4 (MEFIB) index in detection of candidates for pharmacological treatment of NASH-related fibrosis

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of magnetic resonance elastography (MRE) combined with the FIB-4 index (MEFIB) for the detection of candidates for pharmacological treatment of nonalcoholic steatohepatitis (NASH)-related fibrosis. The study included 100 patients who underwent MRE and FIB-4. The results showed that MEFIB improved the detection of candidates for pharmacological treatment of NASH-related fibrosis. The study concluded that MEFIB is a valuable tool for the detection of candidates for pharmacological treatment of NASH-related fibrosis.

RESEARCH ARTICLE

MRI-based (MAST) score accurately identifies patients with NASH and significant fibrosis

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of the MRI-based MAST score for the identification of patients with nonalcoholic steatohepatitis (NASH) and significant fibrosis. The study included 100 patients who underwent the MAST score. The results showed that the MAST score improved the identification of patients with NASH and significant fibrosis. The study concluded that the MAST score is a valuable tool for the identification of patients with NASH and significant fibrosis.

RESEARCH ARTICLE

Magnetic resonance elastography plus FibroScan 4 versus FibroScan-apartate aminotransferase in detection of candidates for pharmacological treatment of NASH-related fibrosis

Shen M, Han Y, Wang M, et al. (See Full Paper: [https://doi.org/10.1002/hep4.1411](#))

Abstract: This study aimed to evaluate the role of magnetic resonance elastography (MRE) plus FibroScan 4 versus FibroScan-apartate aminotransferase (FibroScan-AAT) for the detection of candidates for pharmacological treatment of nonalcoholic steatohepatitis (NASH)-related fibrosis. The study included 100 patients who underwent MRE, FibroScan 4, and FibroScan-AAT. The results showed that MRE plus FibroScan 4 improved the detection of candidates for pharmacological treatment of NASH-related fibrosis. The study concluded that MRE plus FibroScan 4 is a valuable tool for the detection of candidates for pharmacological treatment of NASH-related fibrosis.



2D MRE | G* | Eviden

2020

ORIGINALS | HEPATOLOGY COMMUNICATIONS, VOL. 1, NO. 1

Multiparametric Magnetic Resonance Elastography Improves the Detection of NASH Regression Following Bariatric Surgery

Shahzad Ahmad, MD, PhD, et al. | Hepatic Fibrosis, Elastography, Bariatric Surgery, NASH Regression

These findings in multiparametric MR elastography (MRE) as a tool to detect and monitor regression of non-alcoholic steatohepatitis (NASH) after bariatric surgery are promising. MRE may be a valuable tool to assess the degree of NASH regression after bariatric surgery. This is a high-quality prospective study that is the first to show that MRE can detect and monitor regression of NASH after bariatric surgery. MRE may be a valuable tool to assess the degree of NASH regression after bariatric surgery. This is a high-quality prospective study that is the first to show that MRE can detect and monitor regression of NASH after bariatric surgery.

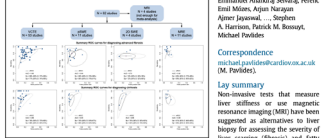
Non-invasive tests that measure liver stiffness or use magnetic resonance imaging (MRI) have been suggested as alternatives to liver biopsy for assessing the severity of liver scarring (fibrosis) and fatty inflammation (steatohepatitis) in patients with non-alcoholic fatty liver disease (NAFLD). In this study, we summarize the results of previously published studies on how accurately these non-invasive tests can diagnose liver fibrosis and inflammation, using liver biopsy as the reference. We found that some techniques that measure liver stiffness had a good performance for the diagnosis of severe liver scarring.

2021

Research Article | NAFLD and Alcohol-Related Liver Diseases | JOURNAL OF HEPATOLOGY

Diagnostic accuracy of elastography and magnetic resonance imaging in patients with NAFLD: A systematic review and meta-analysis

Emmanuel Anandraj Selvaraj, Ferenc Ajmer Mózés, Arjun Narayan, et al.



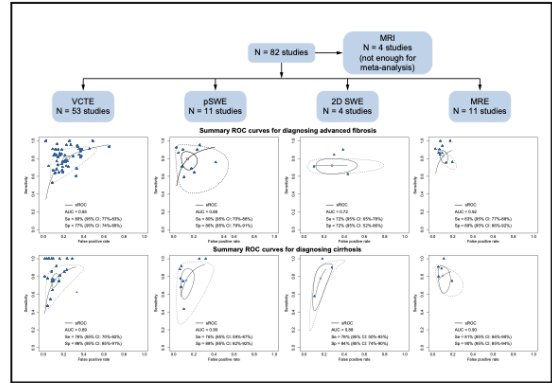
Highlights
• This is the largest systematic review of imaging/elastography biomarkers in NAFLD.
• Meta-analysis of 1 MR elastography and 3 ultrasound techniques.
• Elastography may help in fibrosis evaluation in those with NAFLD and valid readings.
• Clinical utility of these tests cannot be assessed fully as intention-to-diagnose analyses and validation of pre-specified cut-offs are lacking.

Research Article
NAFLD and Alcohol-Related Liver Diseases

JOURNAL OF HEPATOLOGY

Diagnostic accuracy of elastography and magnetic resonance imaging in patients with NAFLD: A systematic review and meta-analysis

Graphical abstract



Authors

Emmanuel Anandraj Selvaraj, Ferenc Ajmer Mózés, Arjun Narayan, Ajmer Jayaswal, ..., Stephen A. Harrison, Patrick M. Bossuyt, Michael Pavlides

Correspondence

michael.pavlides@cardiov.ox.ac.uk (M. Pavlides).

Lay summary

Non-invasive tests that measure liver stiffness or use magnetic resonance imaging (MRI) have been suggested as alternatives to liver biopsy for assessing the severity of liver scarring (fibrosis) and fatty inflammation (steatohepatitis) in patients with non-alcoholic fatty liver disease (NAFLD). In this study, we summarise the results of previously published studies on how accurately these non-invasive tests can diagnose liver fibrosis and inflammation, using liver biopsy as the reference. We found that some techniques that measure liver stiffness had a good performance for the diagnosis of severe liver scarring.

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<https://doi.org/10.1016/j.jhep.2021.04.044>
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THE FORUM
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Meta-analysis

2D MRE

• 11 studies

VCTE

• 53 studies

pSWE

• 11 studies

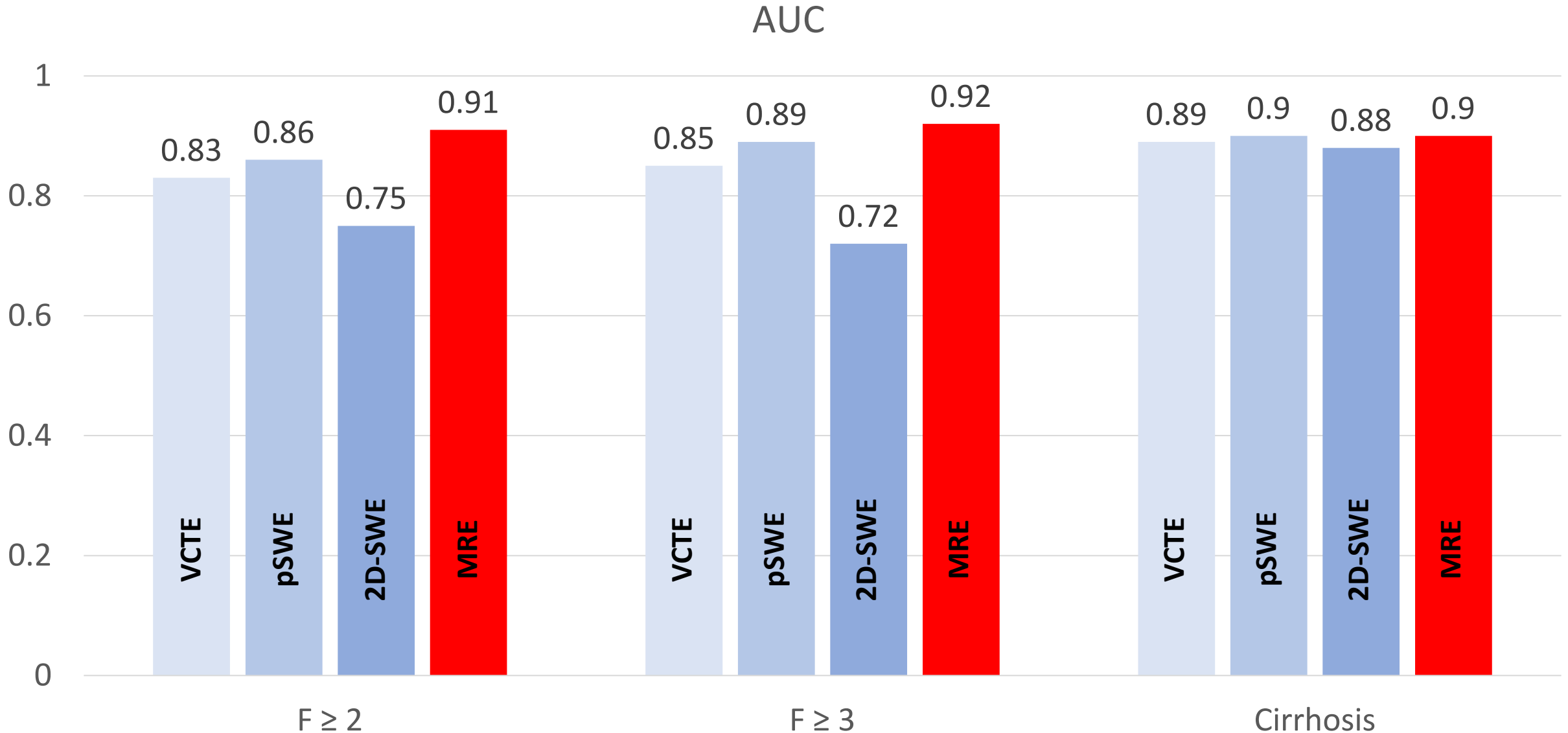
2D SWE

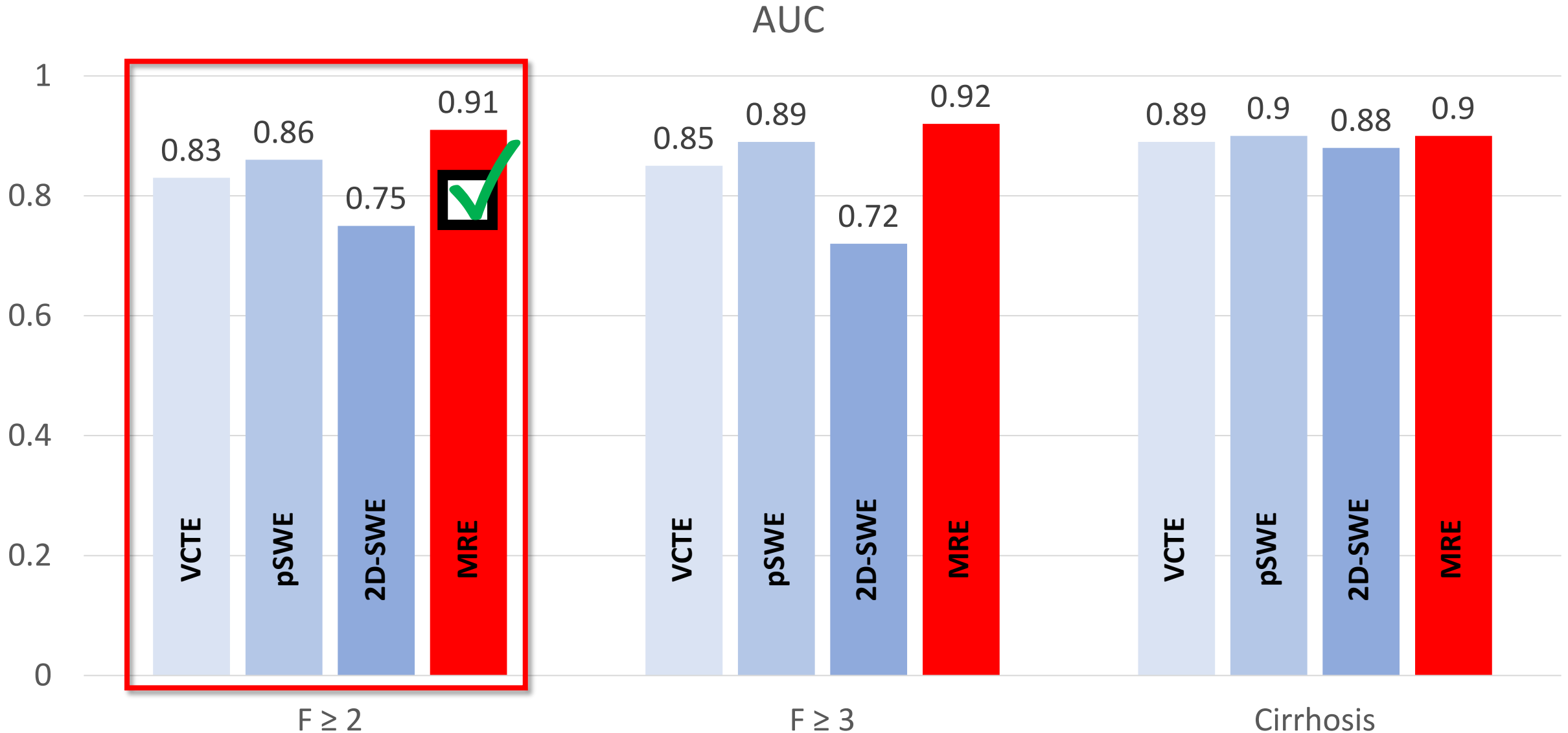
• 4 studies

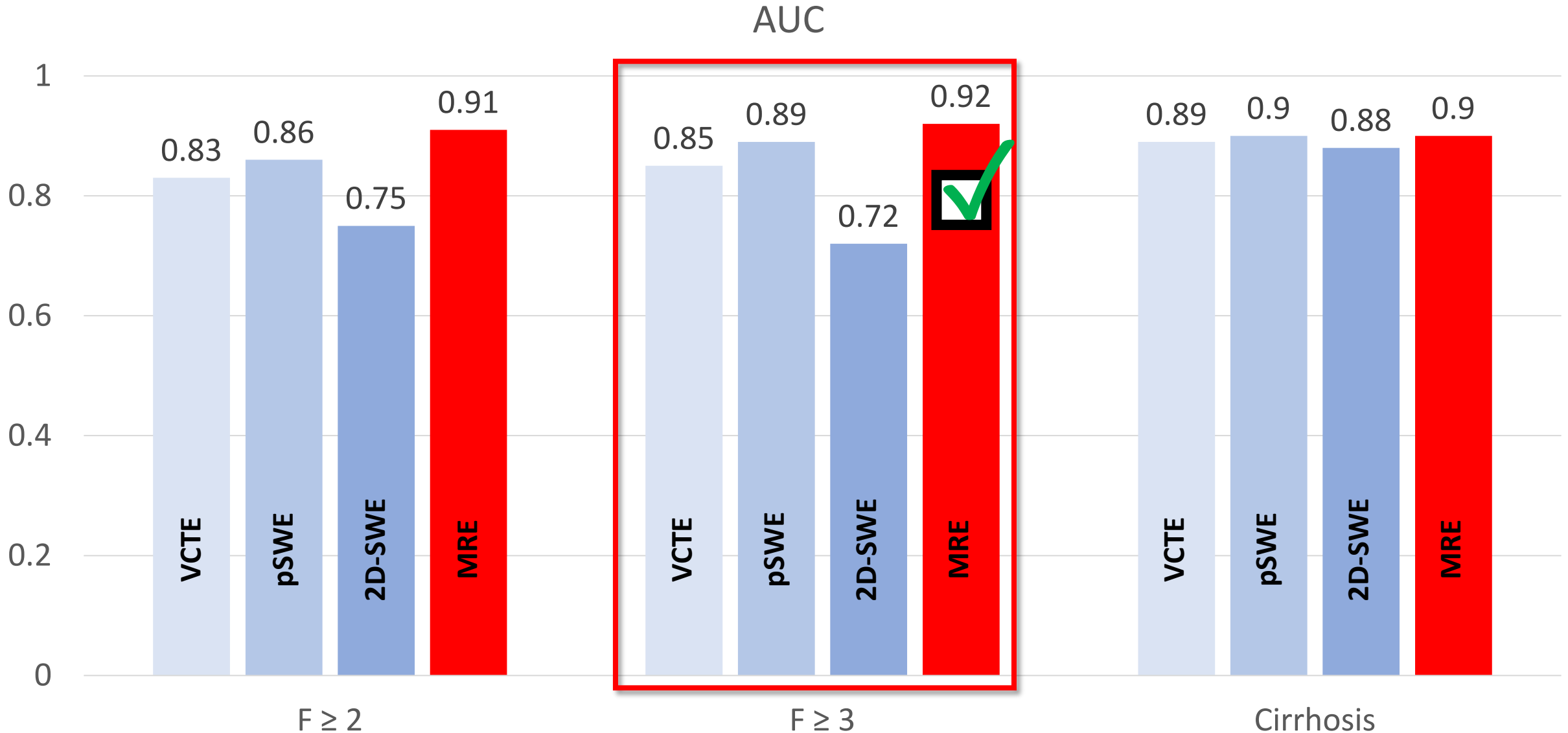
2D MRE

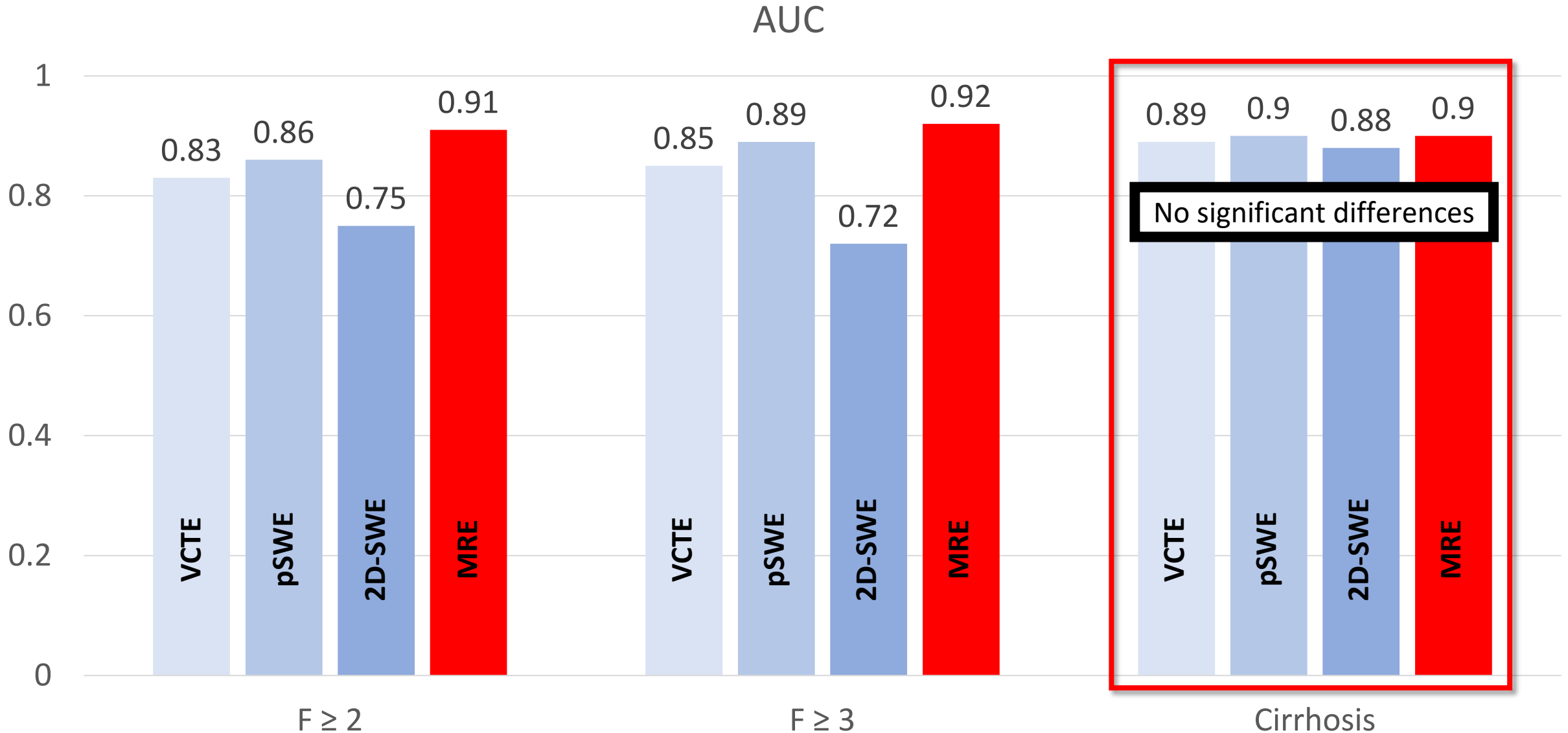
• 11 studies

Biopsy reference









Modality	Fibrosis Stage	Sens	Spec	Youden
VCTE	F ≥ 2	80	73	153
	F ≥ 3	80	77	157
	Cirrhosis	76	88	164
pSWE	F ≥ 2	69	85	154
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2D SWE	F ≥ 2	71	67	138
	F ≥ 3	72	72	144
	Cirrhosis	78	84	162
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	F ≥ 3	83	89	172
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MRE-stiffness has higher sens/spec for stage ≥ 2 , ≥ 3 , 4

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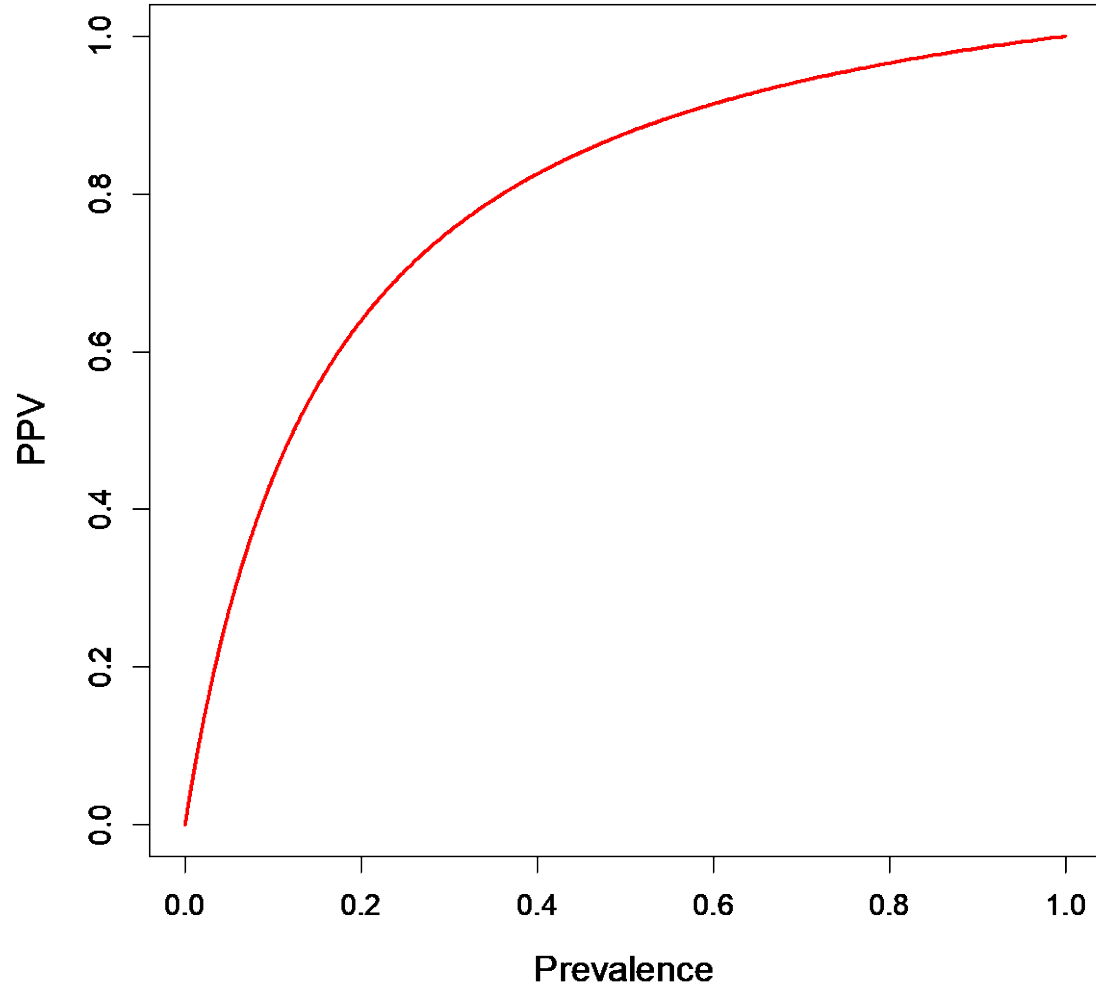
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	$F \geq 3$	80	77	157
	$F = 4$	76	88	164
pSWE	$F \geq 2$	69	85	154
	$F \geq 3$	80	86	166
	$F = 4$	76	88	164
2D SWE	$F \geq 2$	71	67	138
	$F \geq 3$	72	72	144
	$F = 4$	78	84	162
MRE	$F \geq 2$	78	89	167
	$F \geq 3$	83	89	172
	$F = 4$	81	90	171

2D MRE-|G*| PPV and NPV simulation curves

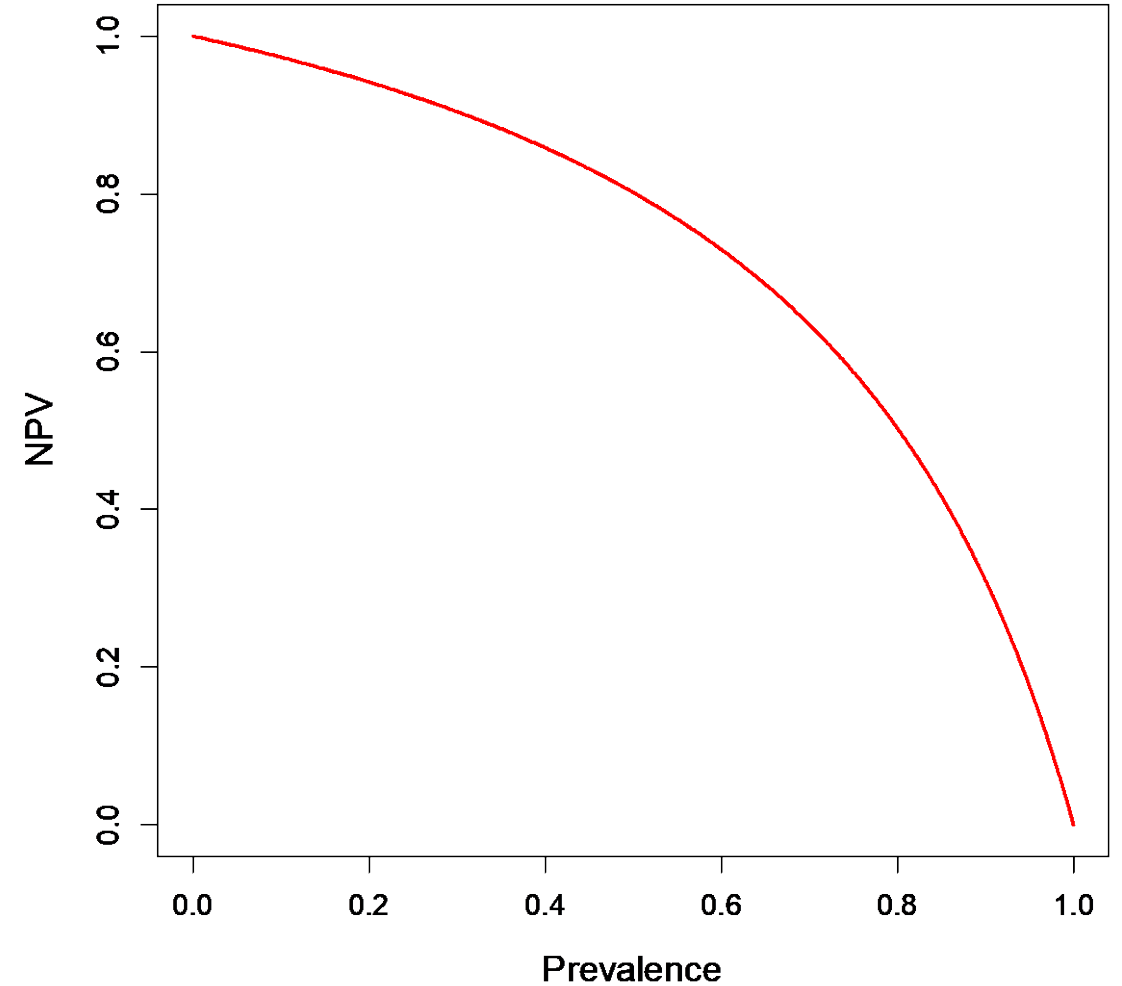
F ≥ 2 diagnosis

- 78% sensitivity
- 89% specificity

MRE



MRE

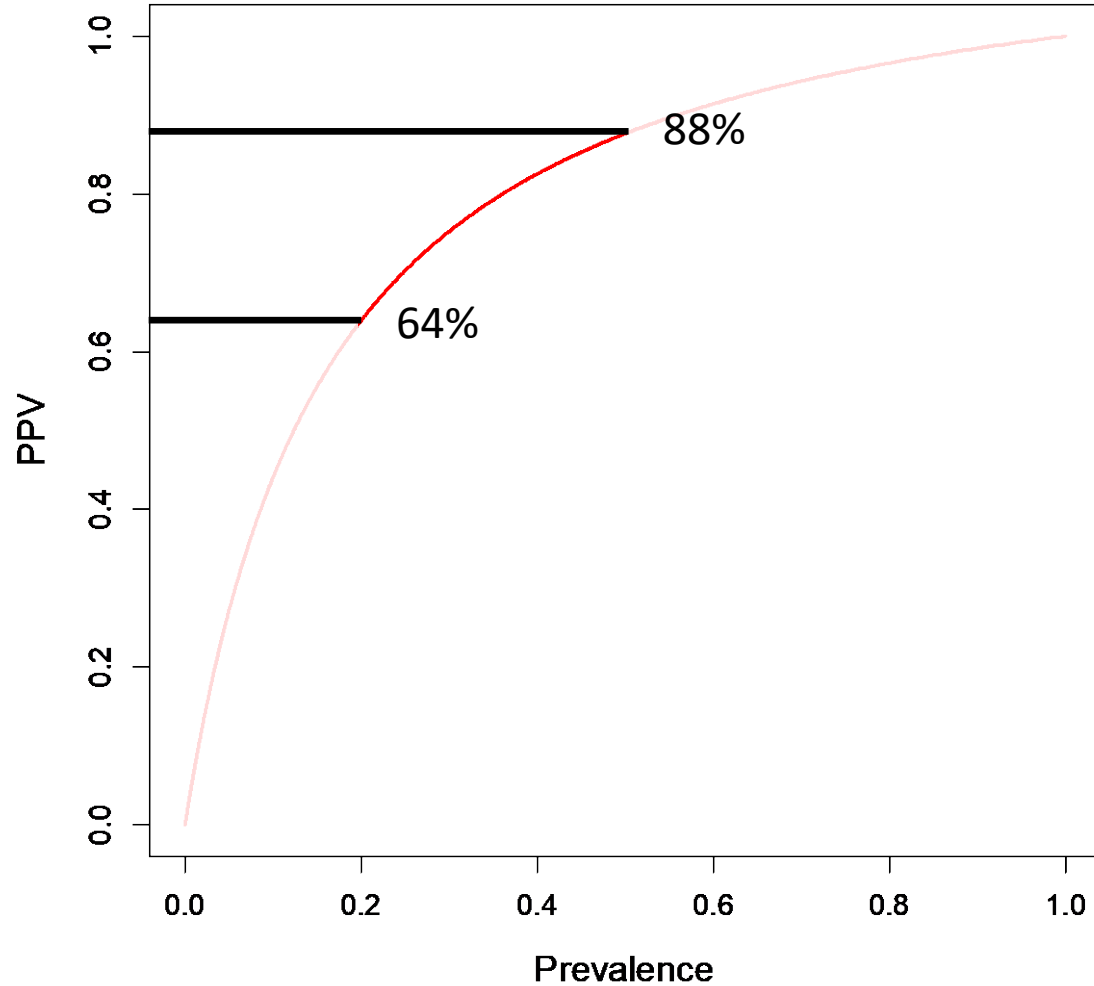


For prevalence between 20-50%: PPVs 64-88%; NPVs 80-94%

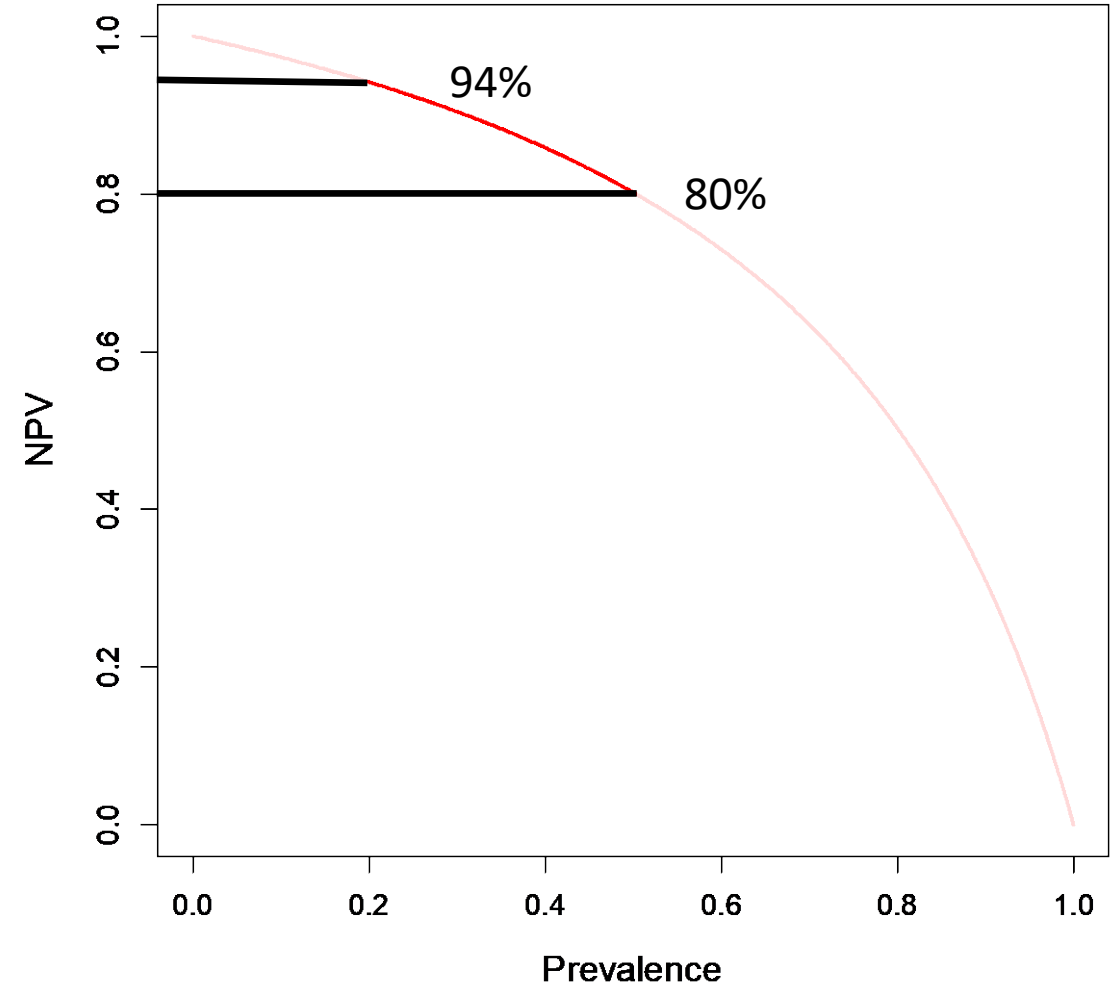
MRE $F \geq 2$ diagnosis

- 78% sensitivity
- 89% specificity

MRE



MRE



Outline

● **Diagnostic biomarkers**
in NAFLD clinical trials

● **MultiScan: iron-corrected T1 (cT1)**
as a diagnostic enrichment biomarker in NAFLD clinical trials

● **MR elastography: magnitude of complex modulus ($|G^*|$), “shear stiffness”**
as a diagnostic biomarker in NAFLD clinical trials

● **MultiScan-cT1 and MRE- $|G^*|$**
friend or foe?

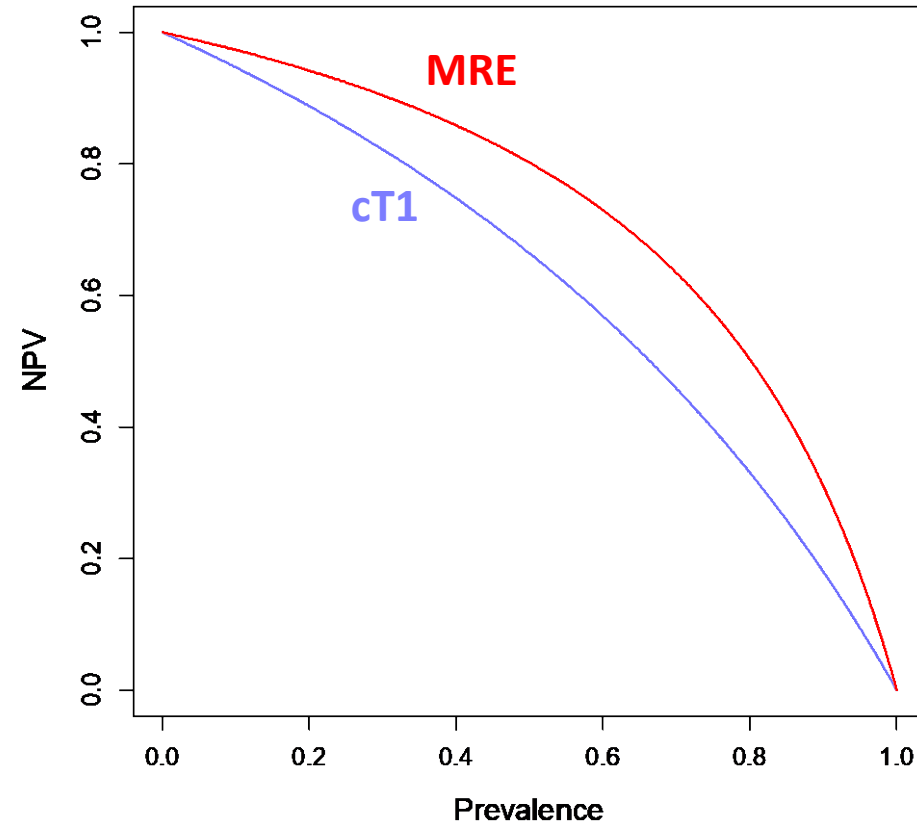
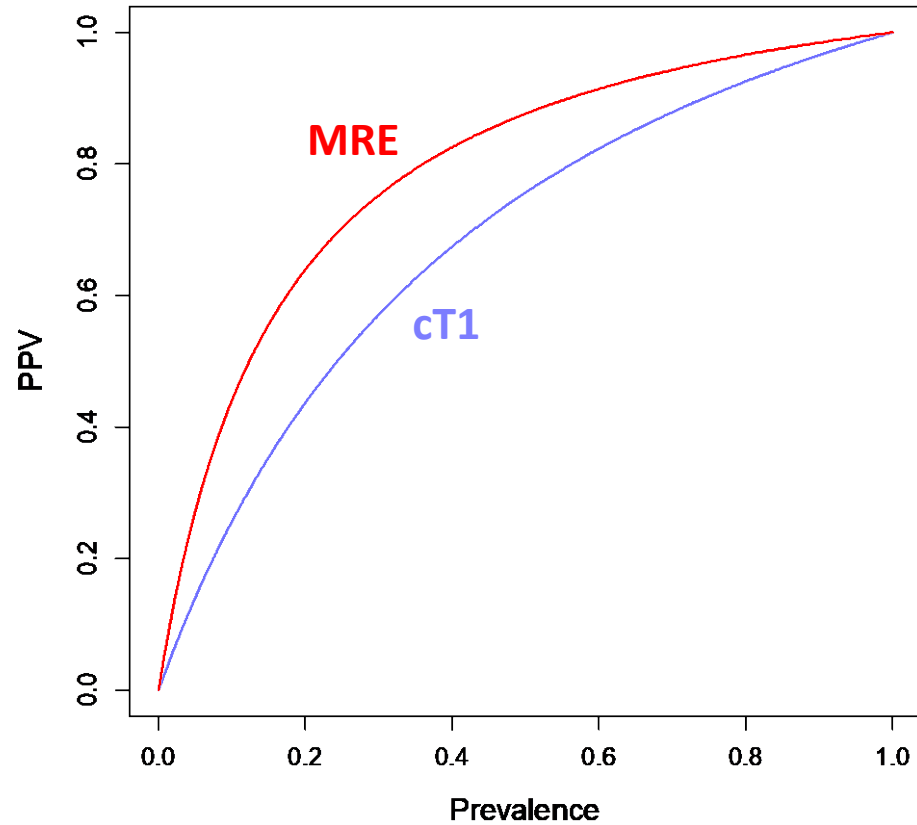
PPV and NPV simulation curves: cT1 vs. MRE

cT1 at risk NASH diagnosis

- 59% sensitivity
- 81% specificity

MRE $F \geq 2$ diagnosis

- 78% sensitivity
- 89% specificity



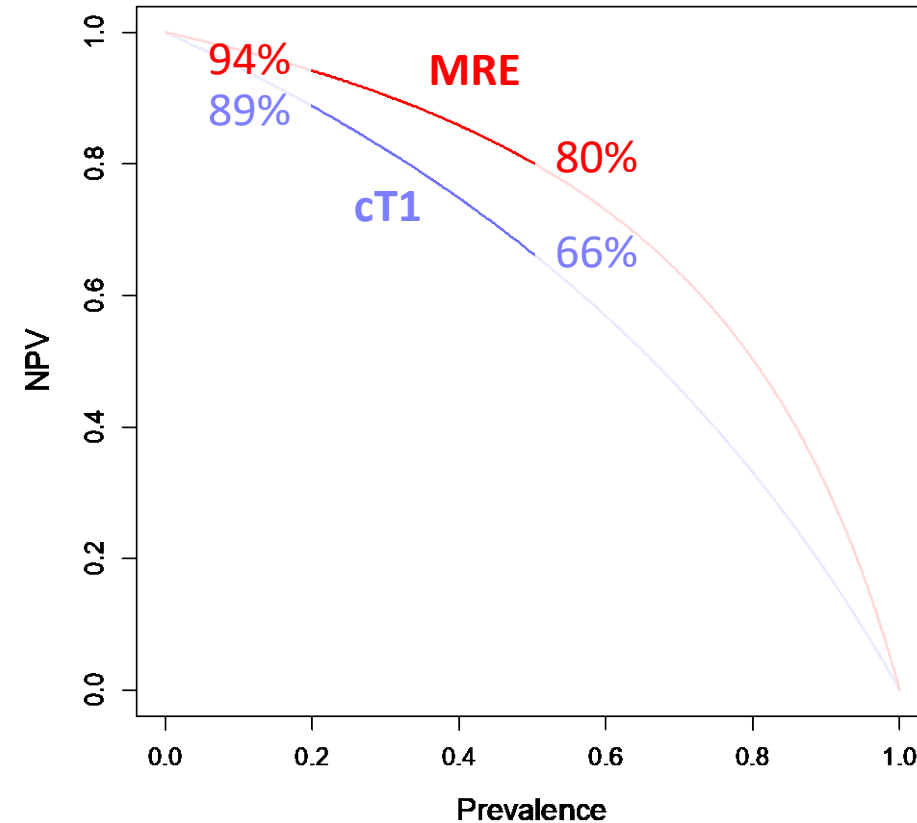
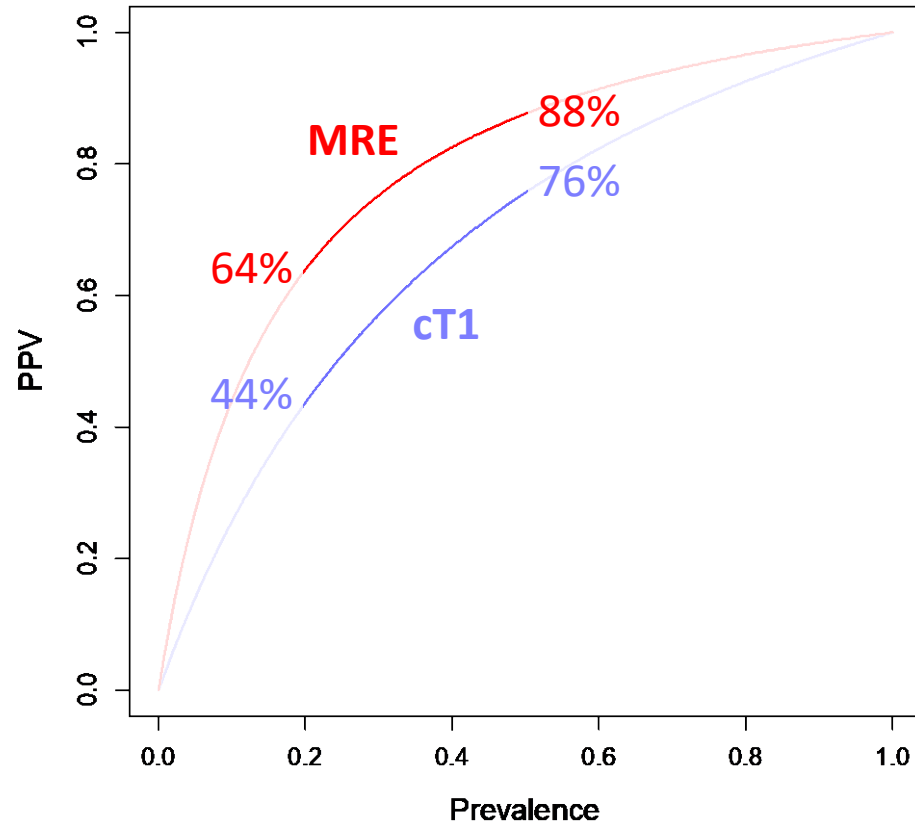
PPV and NPV simulation curves: 20-50% prevalence cT1 vs. MRE

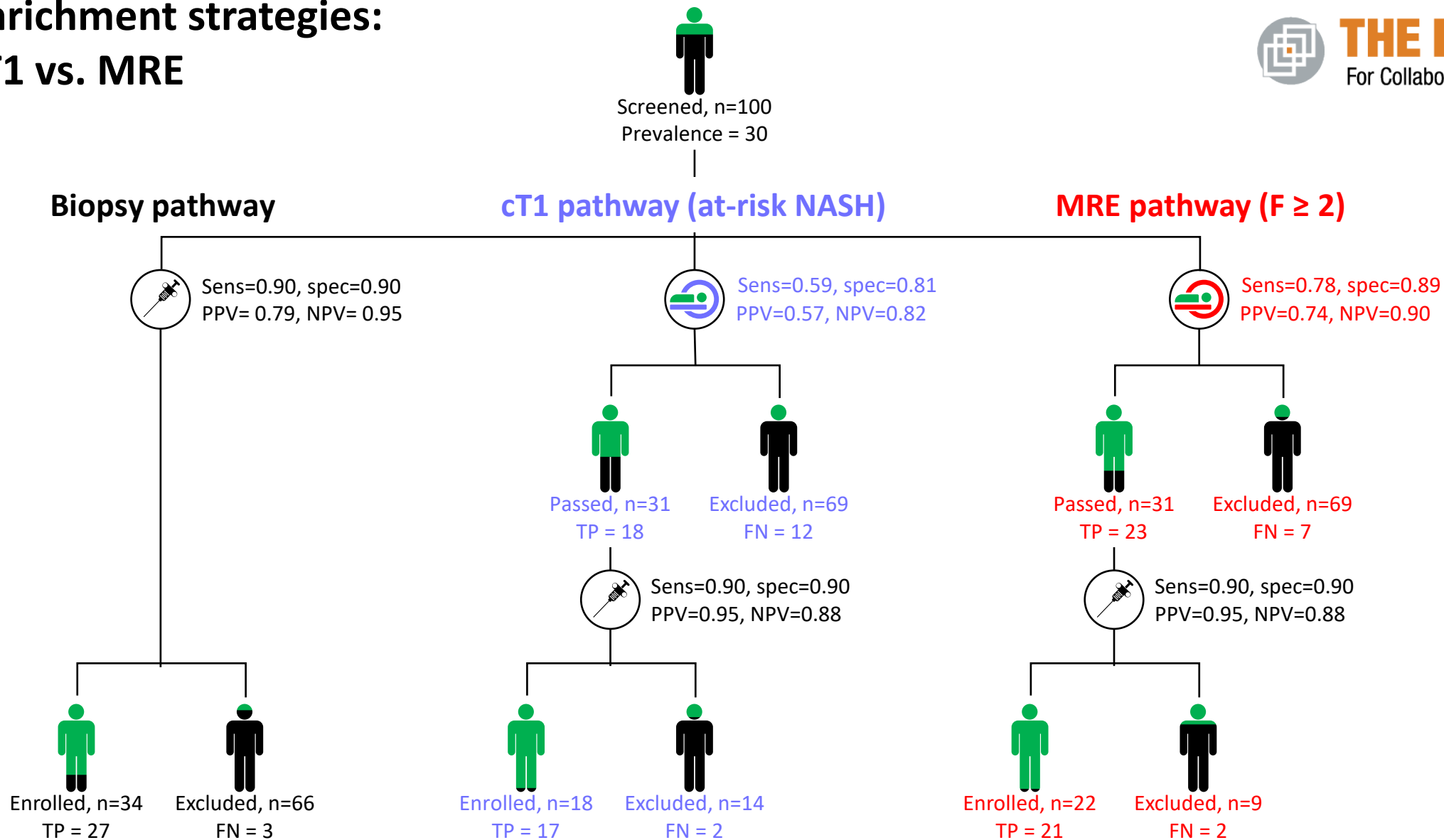
cT1 at risk NASH diagnosis

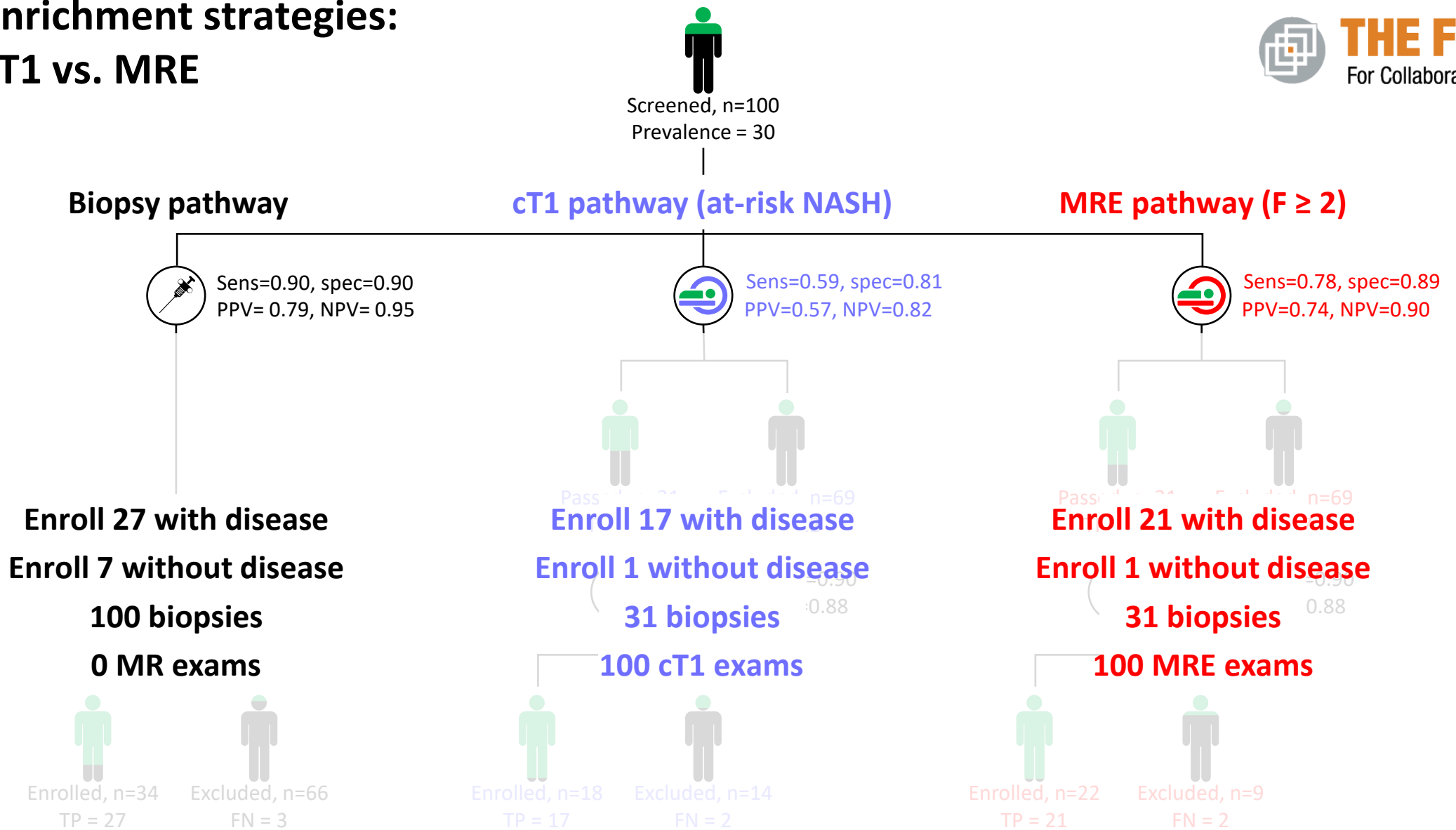
- 59% sensitivity
- 81% specificity

MRE $F \geq 2$ diagnosis

- 78% sensitivity
- 89% specificity











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ORIGINAL ARTICLE

Clinical and Translational Research

Quantitative multiparametric magnetic resonance imaging can aid non-alcoholic steatohepatitis diagnosis in a Japanese cohort

Kento Imajo, Louise Tetlow, Andrea Dennis, Elizabeth Shumbayawonda, Sofia Mouchti, Timothy J Kendall, Eve Fryer, Shogi Yamanaka, Yasushi Honda, Takaomi Kessoku, Yuji Ogawa, Masato Yoneda, Satoru Saito, Catherine Kelly, Matt D Kelly, Rajarshi Banerjee, Atsushi Nakajima

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Author contributions: Imajo K and Nakajima A developed the study concept, protocols and initiated the project; Kelly MD and Banerjee R assisted in the further development of the protocol and drafting the clinical study protocol; Imajo K, Nakajima A, Fryer E, Kendall TJ, Yamanaka S, Honda Y, Kessoku T, Ogawa Y, Yoneda M and Saito S contributed to the data collection; Tetlow L, Dennis AM, Shumbayawonda E to the data analysis; Imajo K, Tetlow L, Nakajima A, Dennis AM, Shumbayawonda E, Kelly C, Kelly

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Abstract

BACKGROUND

Non-invasive assessment of non-alcoholic steatohepatitis (NASH) is increasing in desirability due to the invasive nature and costs associated with the current form of assessment; liver biopsy. Quantitative multiparametric magnetic resonance imaging (mpMRI) to measure liver fat (proton density fat fraction) and fibroinflammatory disease [iron-corrected T1 (cT1)], as well as elastography techniques [vibration-controlled transient elastography (VCTE) liver stiffness measure], magnetic resonance elastography (MRE) and 2D Shear-Wave elastography (SWE) to measure stiffness and fat (controlled attenuated parameter, CAP) are emerging alternatives which could be utilised as safe surrogates to liver biopsy.


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N

- 145 suspected NASH

1 site

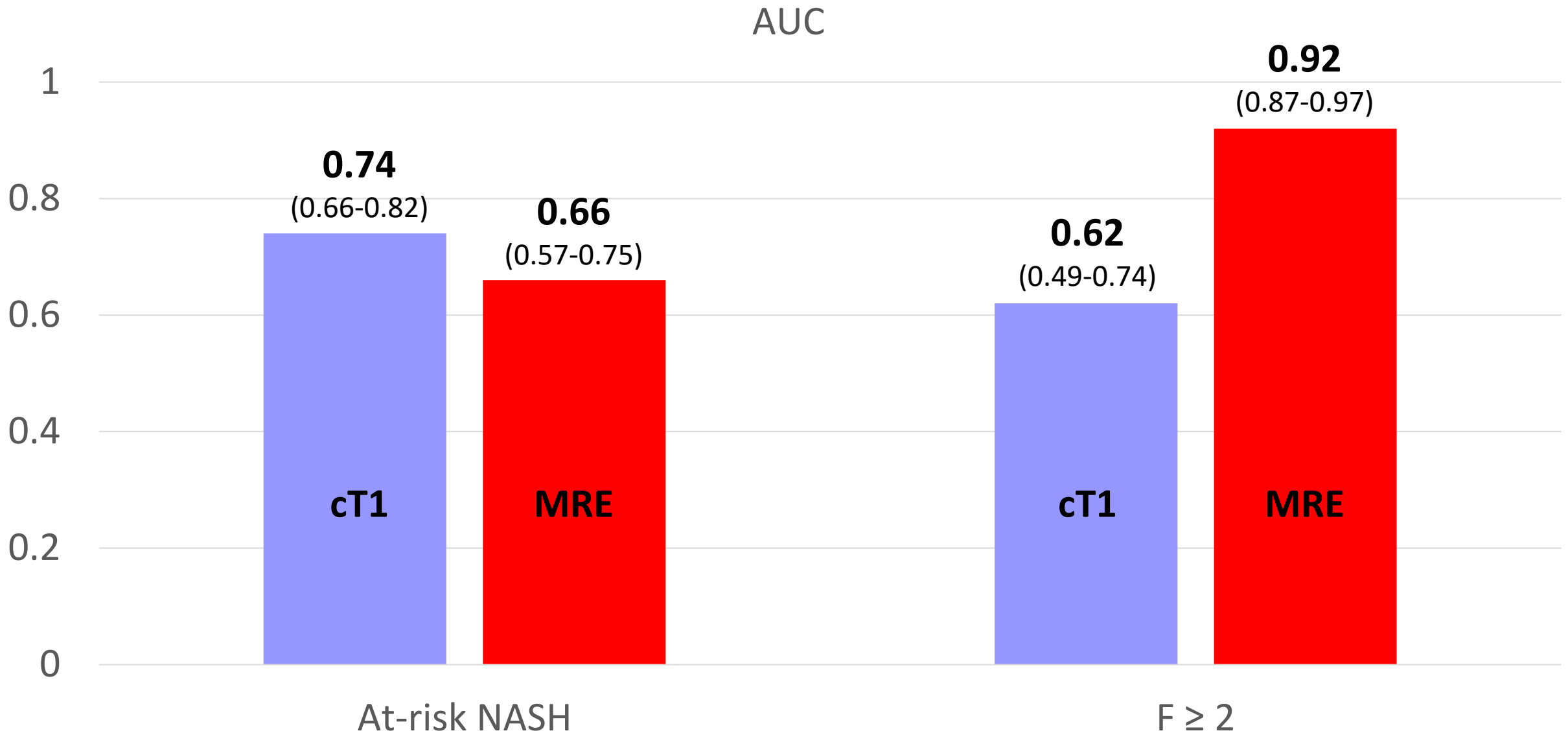
- Japan

3 MR Biomarkers

- cT1
- PDFFF
- 2D MRE-|G*|

(Also VCTE, CAP)

Biopsy reference



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SCIENTIFIC REPORTS
nature research

OPEN **Multiparametric MR Index for the Diagnosis of Non-Alcoholic Steatohepatitis in Patients with Non-Alcoholic Fatty Liver Disease**

Jeong Woo Kim^{1,2,5}, Young-Sun Lee^{3,5}, Yang Shin Park¹, Baek-Hui Kim⁴, Soo Yeon Lee⁴, Jong Eun Yeon² & Chang Hee Lee^{1*}

Non-alcoholic steatohepatitis (NASH) is a complex disease consisting of various components including steatosis, lobular inflammation, and ballooning degeneration, with or without fibrosis. Therefore, it is difficult to diagnose NASH with only one imaging modality. This study was aimed to evaluate the feasibility of magnetic resonance imaging (MRI) for predicting NASH and to develop a non-invasive multiparametric MR index for the detection of NASH in non-alcoholic fatty liver disease (NAFLD) patients. This prospective study included 47 NAFLD patients who were scheduled to undergo or underwent ultrasound-guided liver biopsy within 2 months. Biopsy specimens were graded as NASH or non-NASH. All patients underwent non-enhanced MRI including MR spectroscopy (MRS), MR elastography (MRE), and T1 mapping. Diagnostic performances of MRS, MRE, and T1 mapping for grading steatosis, activity, and fibrosis were evaluated. A multiparametric MR index combining fat fraction (FF), liver stiffness (LS) value, and T1 relaxation time was developed using linear regression analysis. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the diagnostic performance of the newly devised MR index. Twenty NASH patients and 27 non-NASH patients were included. Using MRS, MRE, and T1 mapping, the mean areas under the curve (AUCs) for grading steatosis, fibrosis, and activity were 0.870, 0.951, and 0.664, respectively. The multiparametric MR index was determined as $0.037 \times \text{FF} (\%) + 1.4 \times \text{LS value (kPa)} + 0.004 \times \text{T1 relaxation time (msec)} - 3.819$. ROC curve analysis of the MR index revealed an AUC of 0.883. The cut-off value of 6 had a sensitivity of 80.0% and specificity of 85.2%. The multiparametric MR index combining FF, LS value, and T1 relaxation time showed high diagnostic performance for detecting NASH in NAFLD patients.

Non-alcoholic fatty liver disease (NAFLD) is a leading cause of chronic liver disease with increasing prevalence worldwide¹. NAFLD encompasses a wide spectrum of diseases, ranging from simple steatosis and non-alcoholic steatohepatitis (NASH) to liver cirrhosis. NASH increases the risk of hepatocellular carcinoma (HCC) and death from cardiovascular disease^{2,3}. Therefore, it is crucial to differentiate NASH from simple steatosis. Liver biopsy is regarded as the gold standard for the diagnosis of NASH^{4,5}. However, liver biopsy is an invasive and costly procedure with the risk of pain, bleeding, and although extremely rarely, even death. As a liver biopsy specimen represents only about 0.0002% of the whole liver, sampling error with inter- and intra-observer variability is another potential problem. Therefore, there have been substantial clinical demands for alternative and noninvasive methods to diagnose NASH.

With recent advances in MRI, MR spectroscopy (MRS), and MR elastography (MRE) have emerged as promising methods for detecting and grading fat and fibrosis, respectively⁶⁻⁹. MRS enables the direct measurement of the fat proton signal fraction and is considered the method of choice for accurate non-invasive quantification of liver fat¹⁰. MRE has shown promising results for staging hepatic fibrosis and detecting NASH in NAFLD

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N

- 20 NASH
- 27 non-NASH

1 site

- Korea

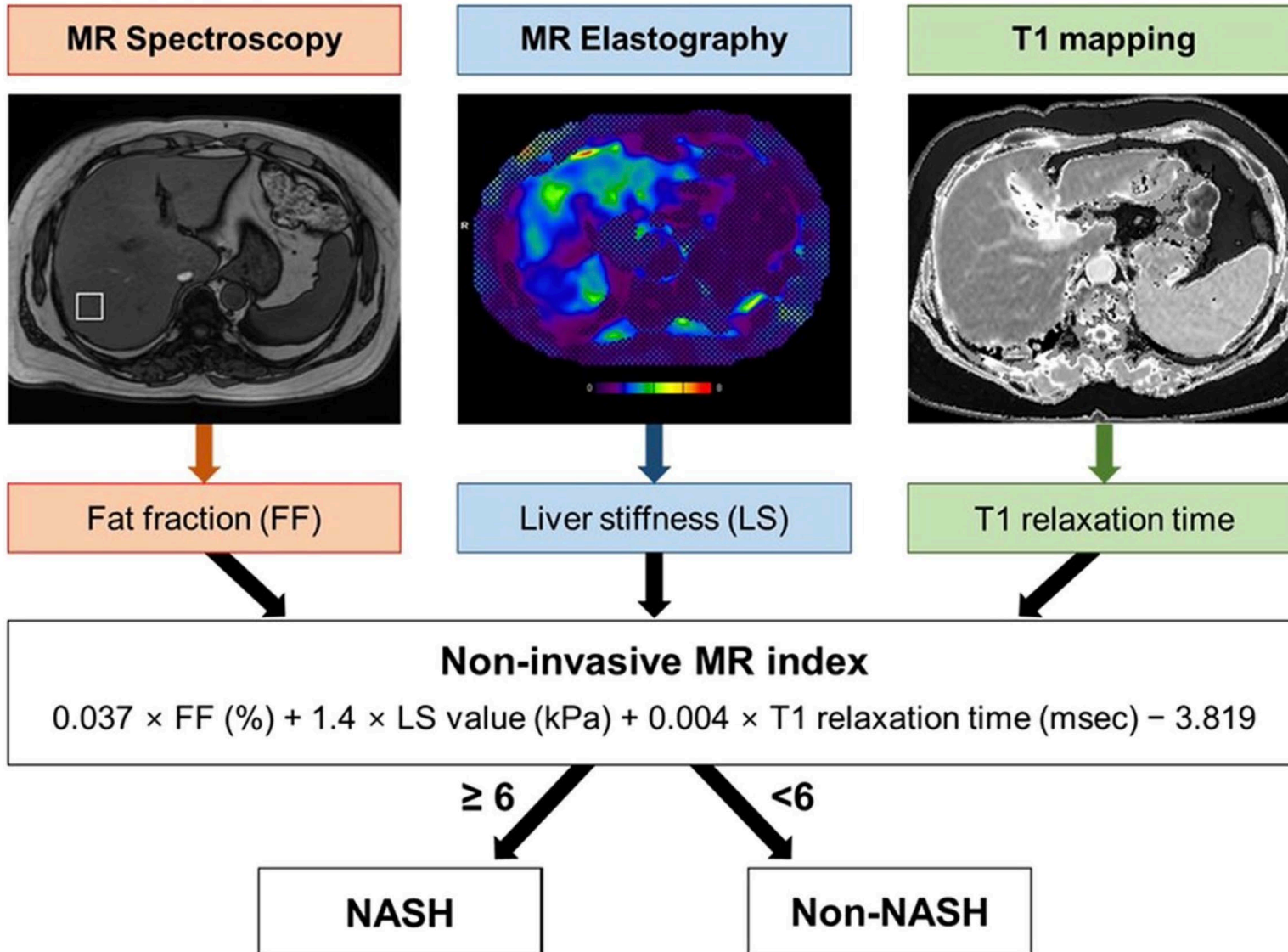
3 MR Biomarkers

- T1 (no iron correction)
- MRS-FF
- 2D MRE-|G*|

(Also VCTE, CAP)

Biopsy reference

Complementarity?



For diagnosis of NASH

- **AUC 0.88**
- **Cutoff ≥ 6**
- **Sens 80**
- **Spec 85**

NIMBLE – Non-Invasive BioMarkers for Metabolic Liver Disease

Team Science: The Key to Non Invasive
Biomarkers Development for NASH

Outline



Diagnostic biomarkers
in NAFLD clinical trials

MultiScan: iron-corrected T1 (cT1)
as a diagnostic enrichment biomarker in NAFLD clinical trials

MR elastography: magnitude of complex modulus ($|G^*|$), “shear stiffness”
as a diagnostic biomarker in NAFLD clinical trials

MultiScan-cT1 and MRE-stiffness
friend or foe?



THE FORUM

For Collaborative ResearchSM

MRI:

YOU

Diagnostic Application of cT1 & Elastography
Through the Lens of Regulatory Science

Thank
Diagnostic Context of Use
Friday April 22, 2022

Claude B. Sirlin, MD
csirlin@health.ucsd.edu

UC San Diego

