



PARIS
MASH
MEETING

10th edition

September 5 & 6 2024
Institut Pasteur, Paris



Standardization and quantitative imaging biomarkers in care of MASLD

CLINICAL LECTURE

Friday September 6, 2024

1:30-2:00 pm

Claude B. Sirlin, MD
Liver Imaging Group
Dept. of Radiology
csirlin@health.ucsd.edu

UC San Diego





Disclosures



PARIS
MASH
MEETING

ACTIVE

INACTIVE

Research grants from industry
(Money paid to institution)

Bayer, GE

Gilead, Pfizer, Philips, Siemens

Equipment loans from industry
(Equipment given to institution)

GE (Logiq E10)
Butterfly (Butterfly IQ)

Material loans from industry
(Material given to institution)

Bayer (Eovist)

Lab service agreements
(Money paid to institution)

Orsobio

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)

Altimune

Ascelia Pharma AB, Blade, Boehringer,
Epigenomics, Guerbet

Position in company
(Stock and stock options to me)

Livivos
(Principal Scientific Advisor)

Member of advisory board
(Unpaid)

Quantix Bio

Royalties and educational
(Money paid to me)

Medscape, Wolters Kluwer

Quantitative Ultrasound

- Biomarkers of fat
- Biomarkers of fibrosis (stiffness)

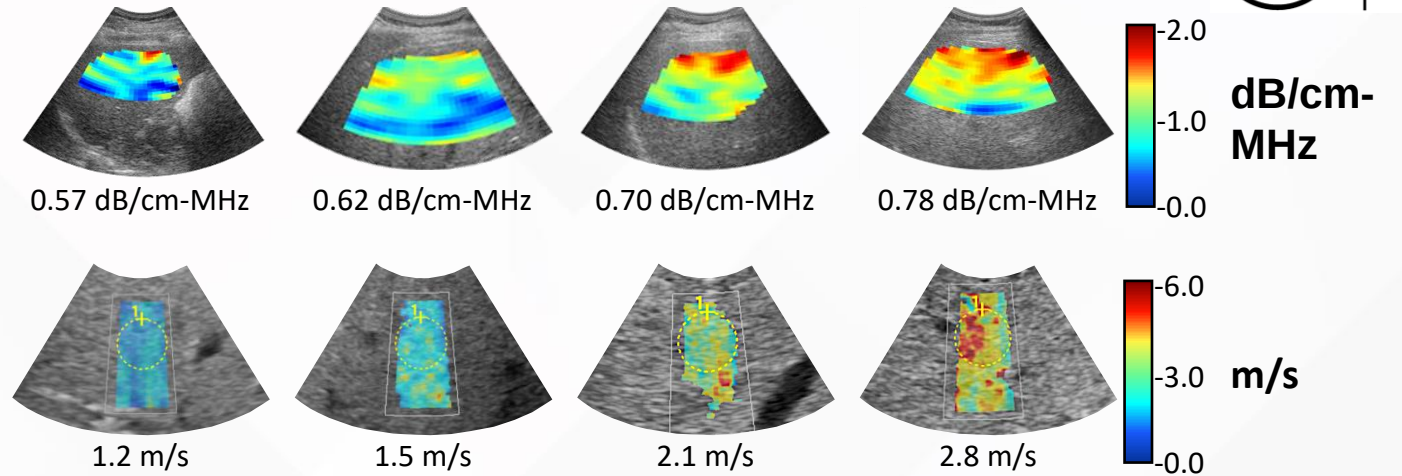
Quantitative MRI

- Biomarkers of fat
- Biomarkers of fibrosis (stiffness)

Quantitative Ultrasound

Attenuation
coefficient

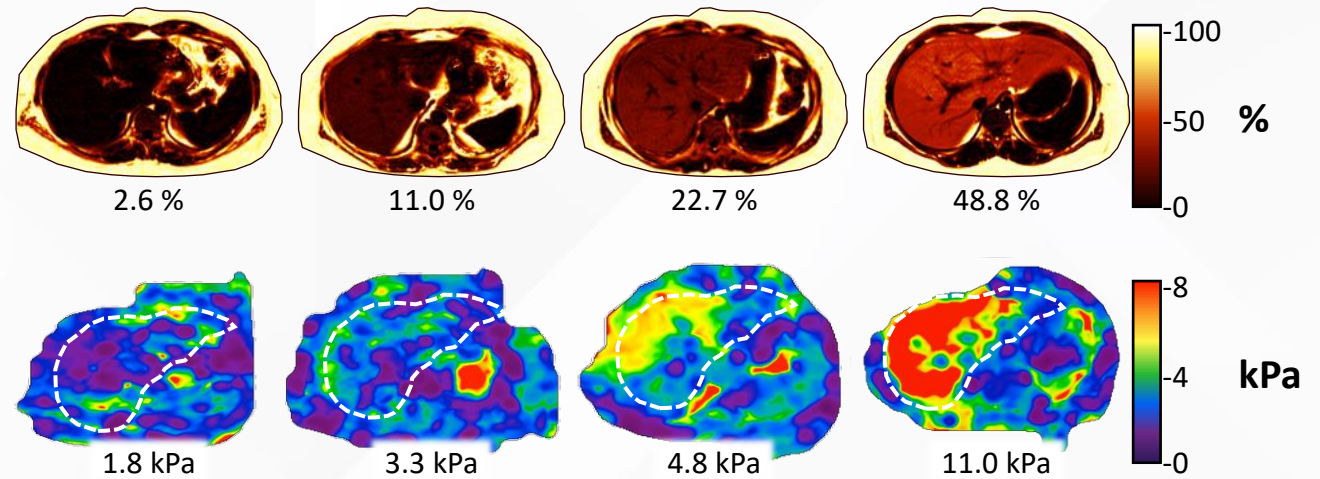
Shear wave
speed



Quantitative MRI

CSE-MRI
PDFF

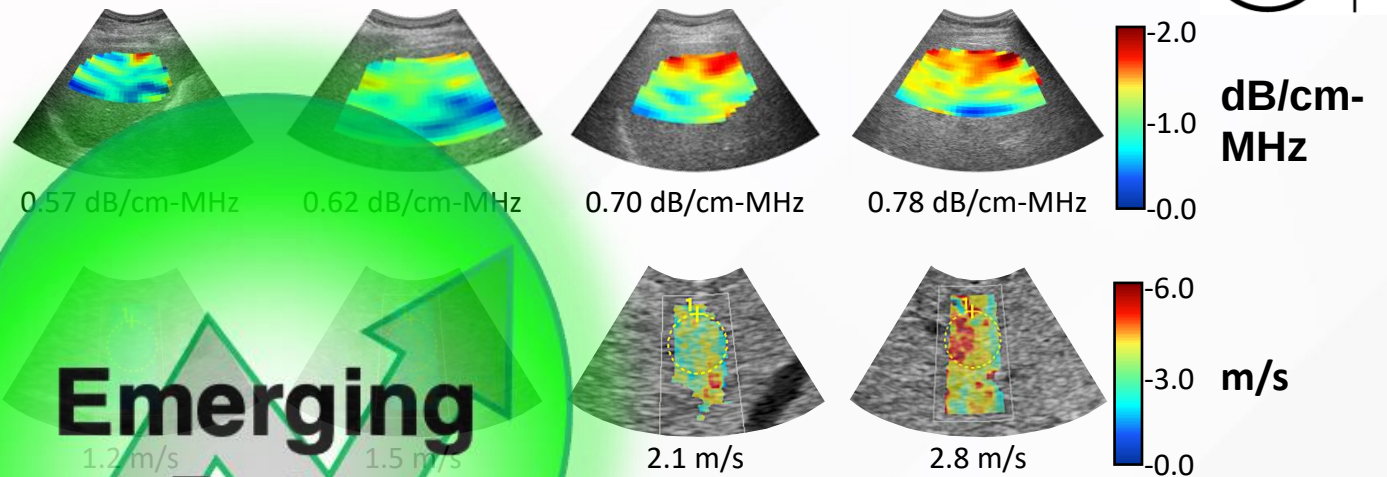
MRE-
stiffness



Quantitative Ultrasound

Attenuation
coefficient

Shear wave
speed

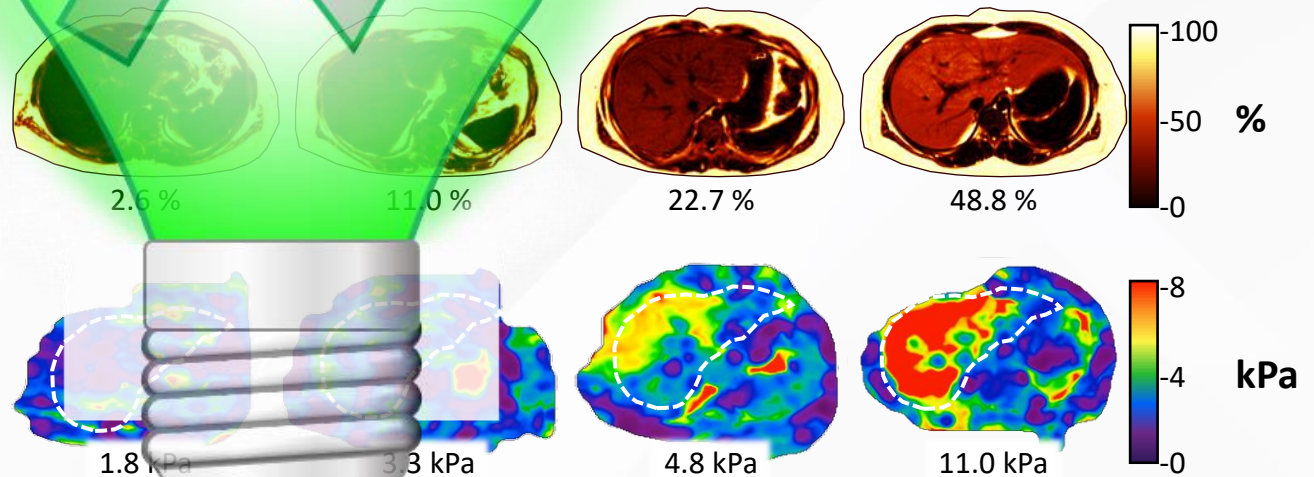


**Emerging
Data**

Quantitative MRI

CSE-MRI
PDFF

MRE-
stiffness



Circulating biomarkers

Vibration-controlled 1D Transient Elastography (e.g., VCTE™)

Vibration-controlled 2D Transient Elastography (e.g., Hepatoscope)

Native T1, “corrected” T1

Point-of-care MR (e.g., LiverScope®)

Outline

- A **question**
- A **definition**
- 6 **claims**
- **Summary**
- The **answer**
- The **Paris MASH Declaration of 2024**

Outline

- A **question**
- A **definition**
- 6 **claims**
- **Summary**
- The **answer**
- The **Paris MASH Declaration of 2024**

What happened in 1795 that needs to happen now?

Outline

- A question
- **A definition**
- 6 claims
- Summary
- The answer
- The Paris MASH Declaration of 2024

Standardization

the process of making things of the same type all have the same basic features
(Cambridge Dictionary)

Standardization

the process of making things of the same type all have the same basic features
(Cambridge Dictionary)

Standardization of NITs

the process of making NITs of the same type agree with each other and with the “truth”
(adapted from Cambridge Dictionary)

Standardization

the process of making things of the same type all have the same basic features
(Cambridge Dictionary)

Standardization of NITs

the process of making NITs of the same type **agree with each other** and with the “truth”
(adapted from Cambridge Dictionary)

Today

Example: My Weight (kg)



Gold Standard

Example: My Weight (kg)



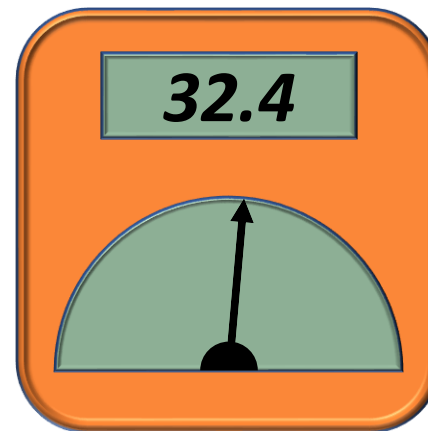
Gold Standard



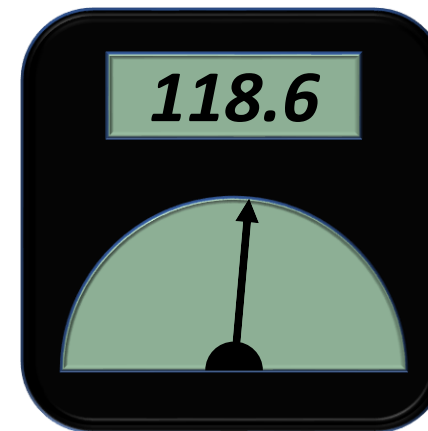
Vendor A



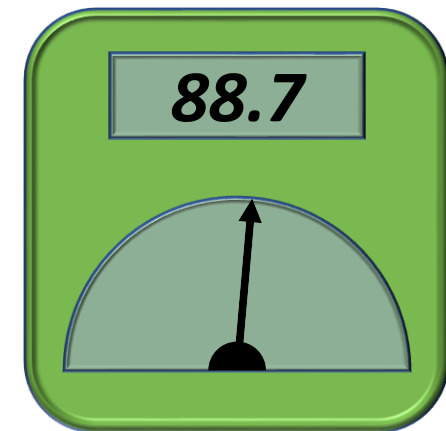
Vendor B



Vendor C



Vendor D



Vendor E

Outline

- A question
- A definition
- **6 claims**
- Summary
- The answer
- The Paris MASH Declaration of 2024

6 **Claims:** All Sound Reasonable

Claim 1. Different US vendors agree on measurement of **attenuation coefficient**

Claim 2. Different US vendors agree on measurement of **shear wave speed**

Claim 3. Different MR vendors agree on measurement of **proton density fat fraction**

Claim 4. Different MR vendors agree on measurement of **shear wave stiffness**

Claim 5. MRI-derived **proton density fat fraction** and **ultrasound-derived fat fraction** agree

Claim 6. MRE-derived **stiffness** and **shear wave elastography-derived stiffness** correlate

BENCHMARK. Correlation ≥ 0.90

6 **Claims:** All Sound Reasonable, but ...

Claim 1. Different US vendors agree on measurement of **attenuation coefficient**

Claim 2. Different US vendors agree on measurement of **shear wave speed**

Four of these claims are

Claim 3. Different MR vendors agree on measurement of **proton density fat fraction**

Claim 4. Different MR vendors agree on measurement of **shear wave stiffness**

Claim 5. MRI-derived **proton density fat fraction** and **ultrasound-derived fat fraction** agree

Two of these claims are

Claim 6. MRE-derived **stiffness** and **shear wave elastography-derived stiffness** correlate

BENCHMARK. Correlation ≥ 0.90



Claim 1. Different US vendors agree on **attenuation coefficient**
Benchmark: correlation ≥ 0.90



PARIS
MASH
MEETING

Claim 1. Different US vendors agree on **attenuation coefficient**

Benchmark: correlation ≥ 0.90

FNIH



Alex Pasek



Tania Kamphaus

Biostatistics core



Nancy Obuchowski



Tanya Wolfson

Imaging workstream



Anthony Samir



Arinc Ozturk



Katie Fowler



Michael Middleton



Sarah Sherlock



Sedi Shabanan



Teddy Pierce

Circulating workstream



Arun Sanyal



Roberto Calle



Rohit Loomba



Sudha Shankar

MGH/UCSD Team



Danielle Batakis



Guilherme Cunha



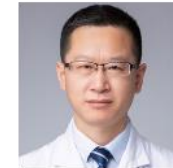
Jake Weeks



Lael Ceriani



Mina Trivedi



Qian Lee



Susi Price



Xiaohong Wang



Yesenia Covarrubias

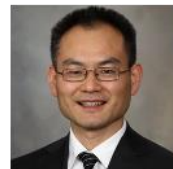
Mayo/Resoundant Team



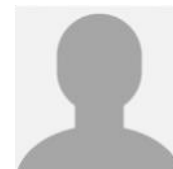
Dick Ehman



Jessica Magnusson



Jun Chen



Kathy J. Brown



Kay Pepin



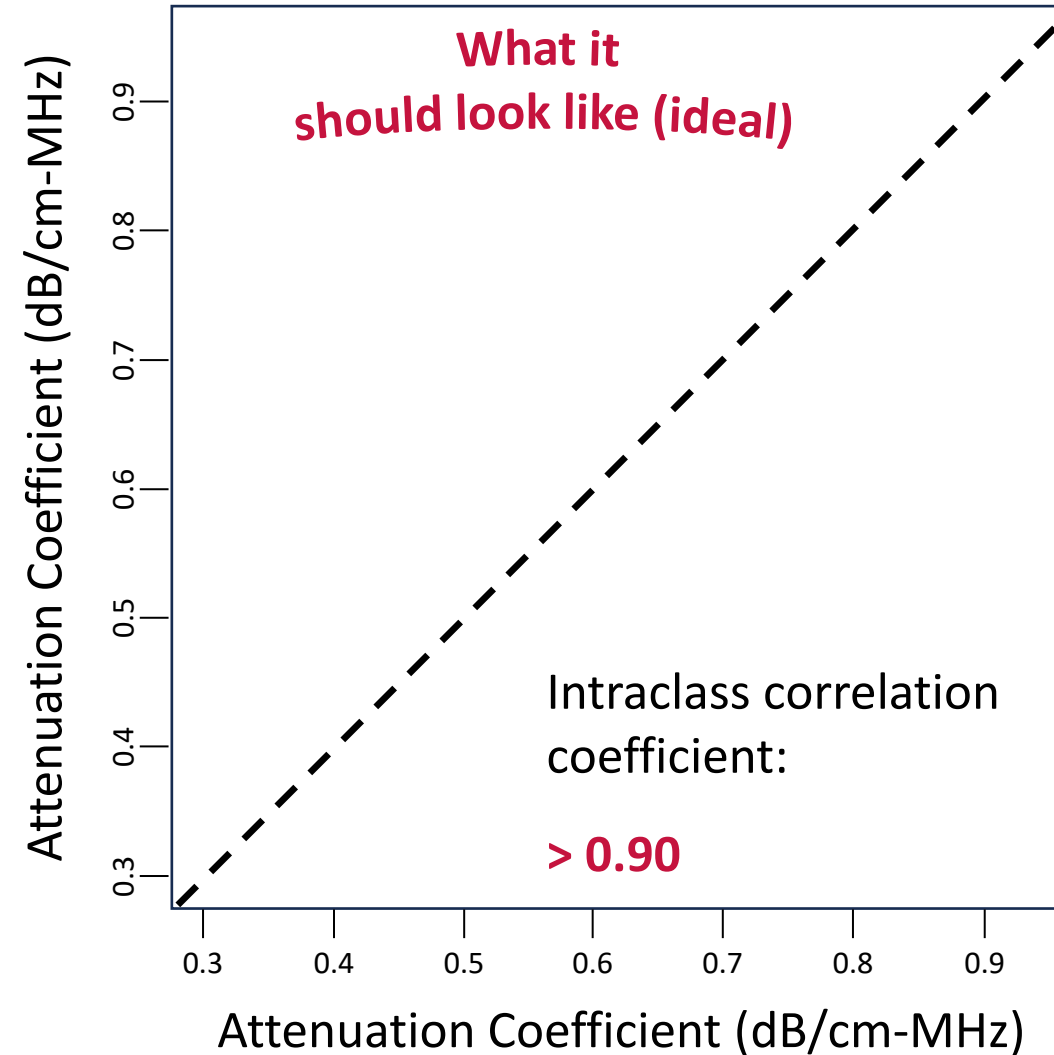
Sudhakar Venkatesh

Stage 1

Claim 1. Different US vendors agree on **attenuation coefficient**

Benchmark: correlation ≥ 0.90

● Vendor A vs B, N=39



Pairwise comparisons between vendors for **SAME** parameter (attenuation coefficient)



Slide courtesy of Sedi Shabanan and Tanya Wolfson

Stage 1

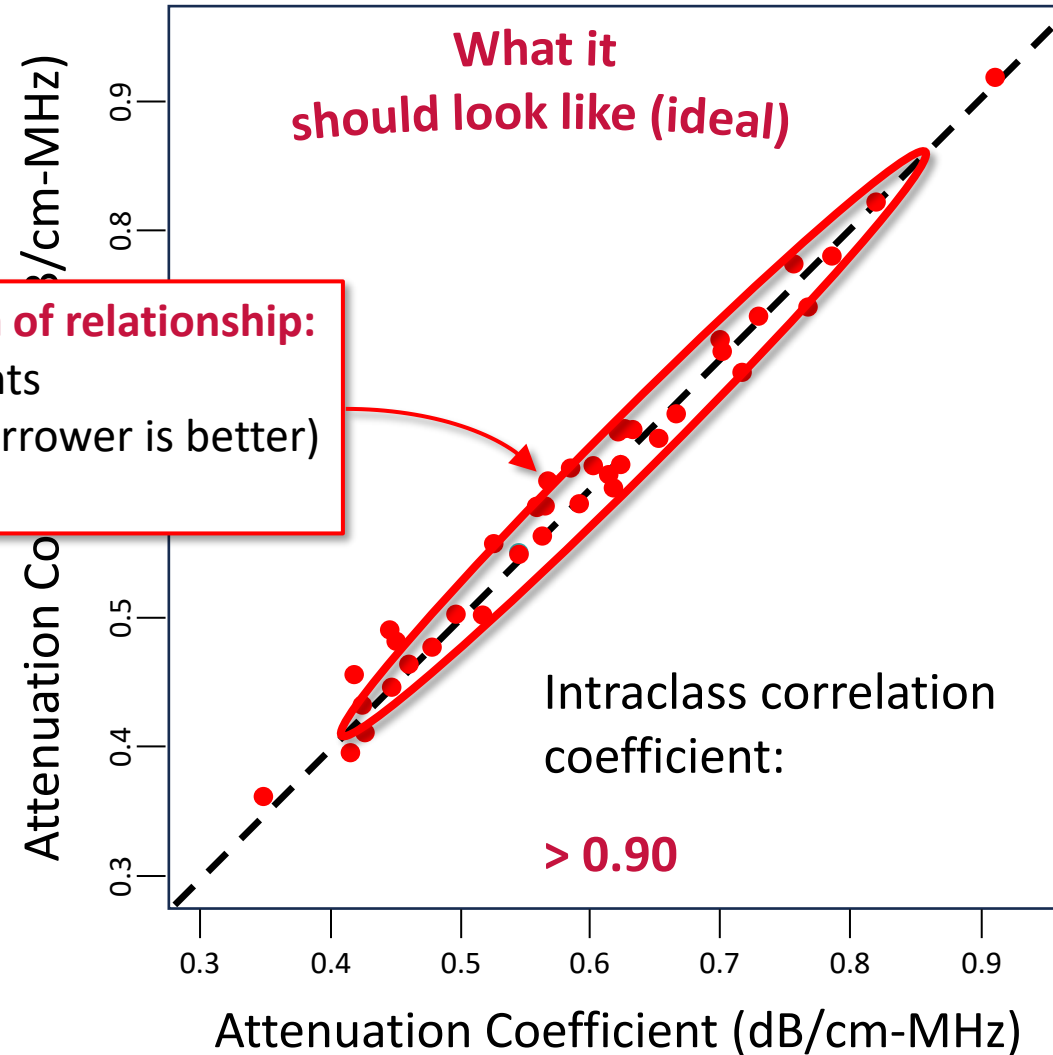
Claim 1. Different US vendors agree on **attenuation coefficient**

Benchmark: correlation ≥ 0.90

● Vendor A vs B, N=39

Ellipse is visual reflection of relationship:

- **Length** = range of points
- **Width** = variability (narrower is better)
- **Angle** = direction



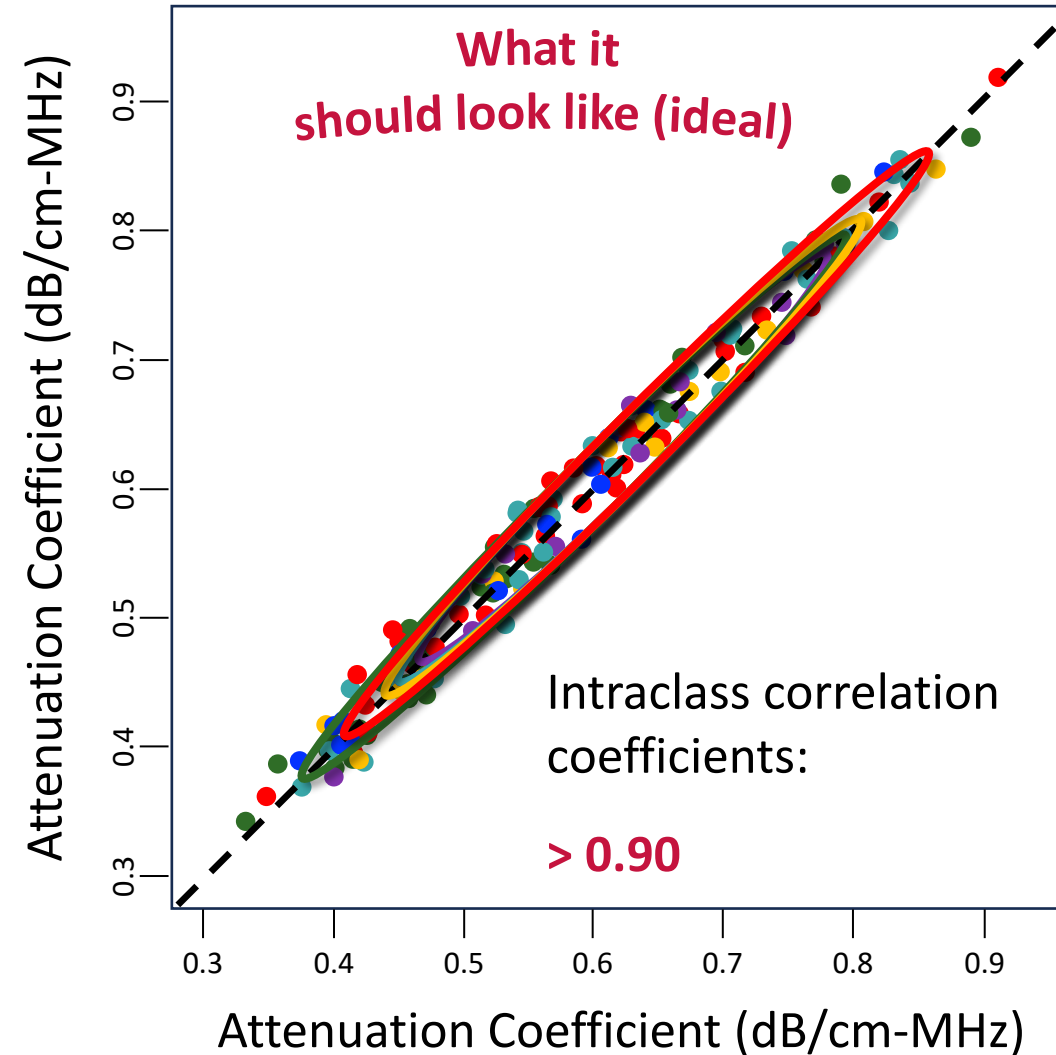
Pairwise comparisons between vendors for **SAME** parameter (attenuation coefficient)

Stage 1

Claim 1. Different US vendors agree on **attenuation coefficient**

Benchmark: correlation ≥ 0.90

- Vendor A vs B, N=39
- Vendor A vs C, N=15
- Vendor A vs D, N=40
- Vendor B vs C, N=37
- Vendor B vs D, N=16
- Vendor C vs D, N=16



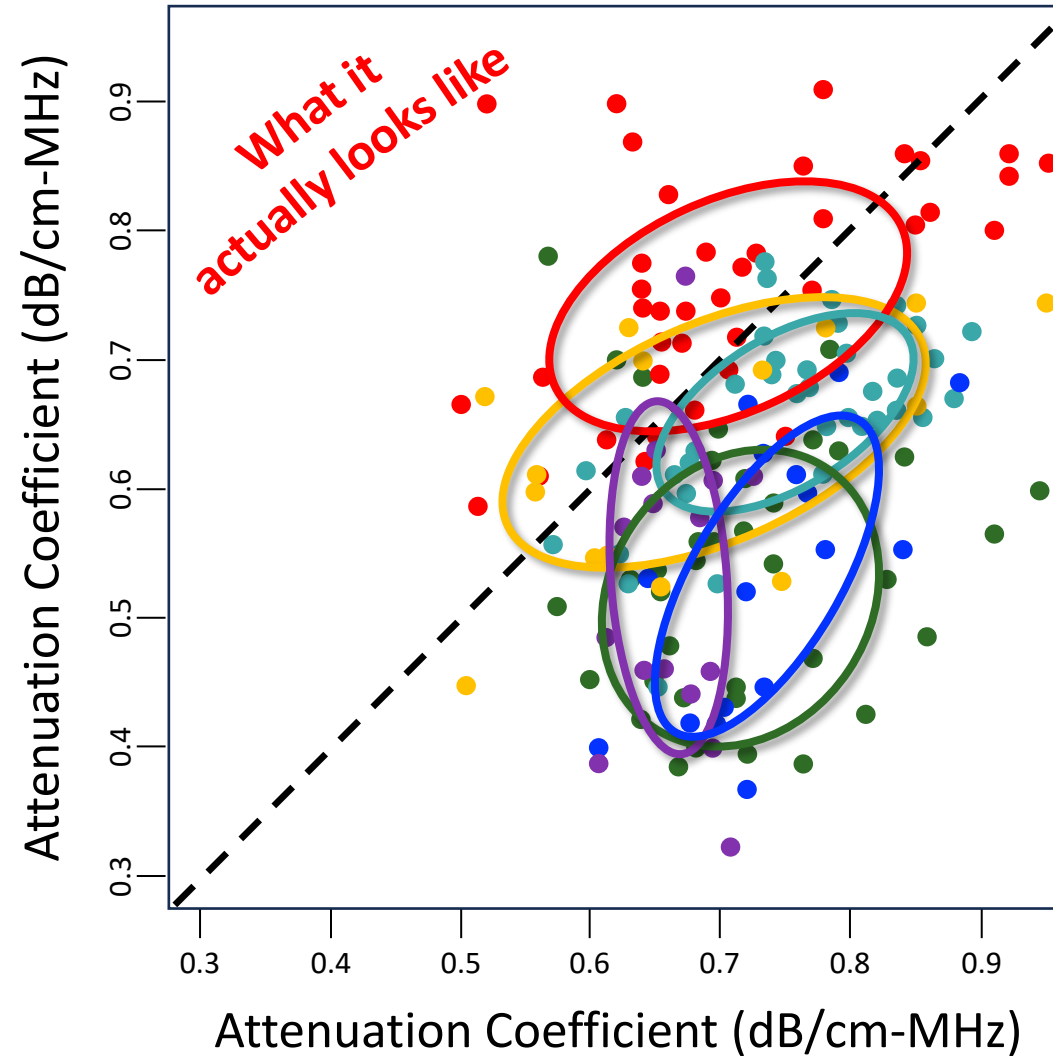
Pairwise comparisons between vendors for **SAME** parameter (attenuation coefficient)

Stage 1

Claim 1. Different US vendors agree on **attenuation coefficient**

Benchmark: correlation ≥ 0.90

- Vendor A vs B, N=39
- Vendor A vs C, N=15
- Vendor A vs D, N=40
- Vendor B vs C, N=37
- Vendor B vs D, N=16
- Vendor C vs D, N=16



Pairwise comparisons between vendors for **SAME** parameter (attenuation coefficient)

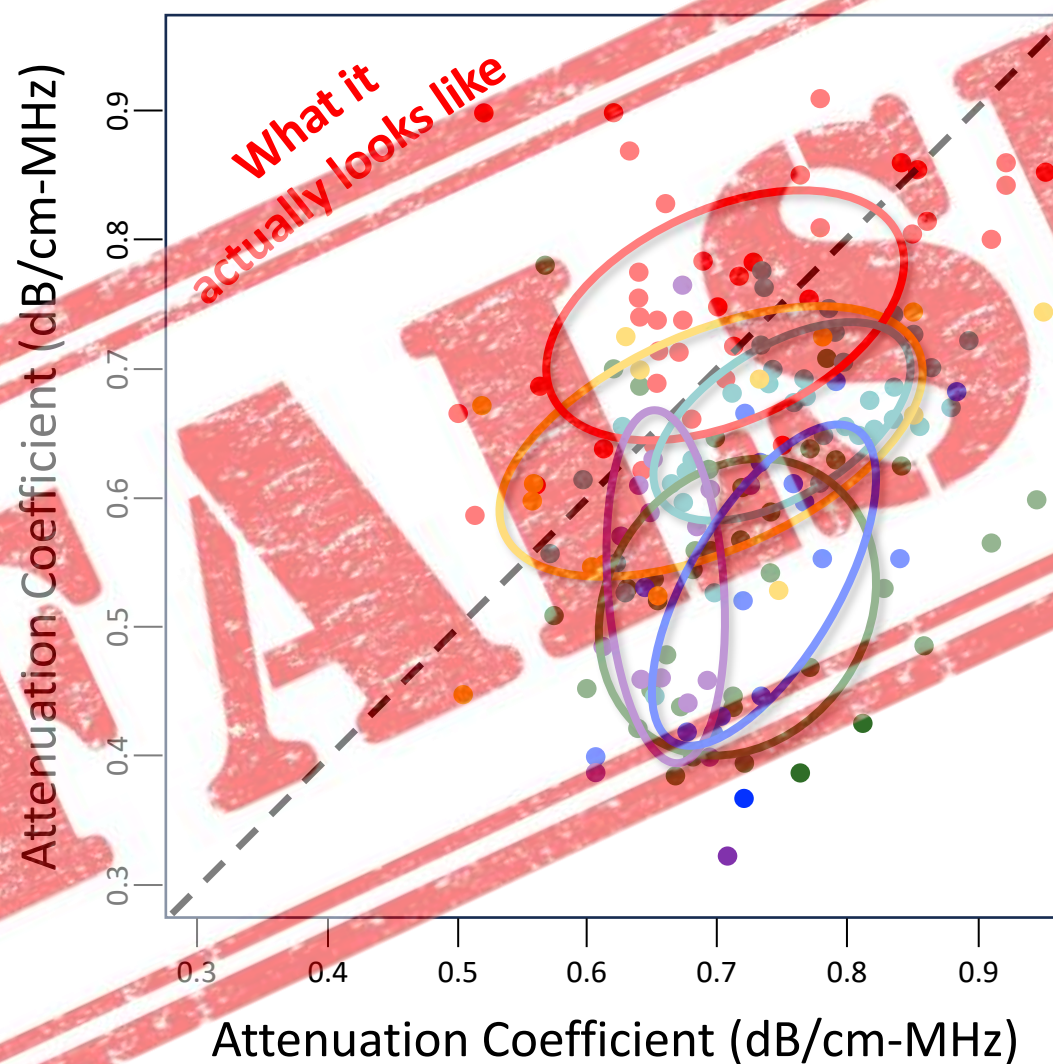
Stage 1



Claim 1. Different US vendors agree on **attenuation coefficient**

Benchmark: correlation ≥ 0.90

- Vendor A vs B, N=39
- Vendor A vs C, N=15
- Vendor A vs D, N=40
- Vendor B vs C, N=37
- Vendor B vs D, N=16
- Vendor C vs D, N=16



Intraclass correlation coefficient (ICC)

0.48

0.49

0.02

0.36

0.16

0.00

Range 0.00 to 0.49

Average 0.25



Claim 2. Different US vendors agree on **shear wave speed**

Benchmark: correlation ≥ 0.90

FNIH



Alex Pasek



Tania Kamphaus

Biostatistics core



Nancy Obuchowski



Tanya Wolfson

Imaging workstream



Anthony Samir



Arinc Ozturk



Katie Fowler



Michael Middleton



Sarah Sherlock



Sedi Shabanan



Teddy Pierce

Circulating workstream



Arun Sanyal



Roberto Calle



Rohit Loomba



Sudha Shankar

MGH/UCSD Team



Danielle Batakis



Guilherme Cunha



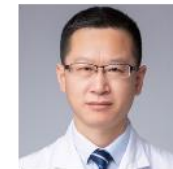
Jake Weeks



Lael Ceriani



Mina Trivedi



Qian Lee



Susi Price



Xiaohong Wang



Yesenia Covarrubias

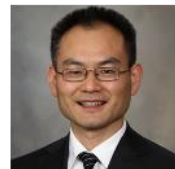
Mayo/Resoundant Team



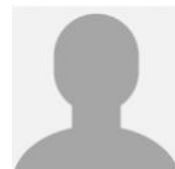
Dick Ehman



Jessica Magnusson



Jun Chen



Kathy J. Brown



Kay Pepin



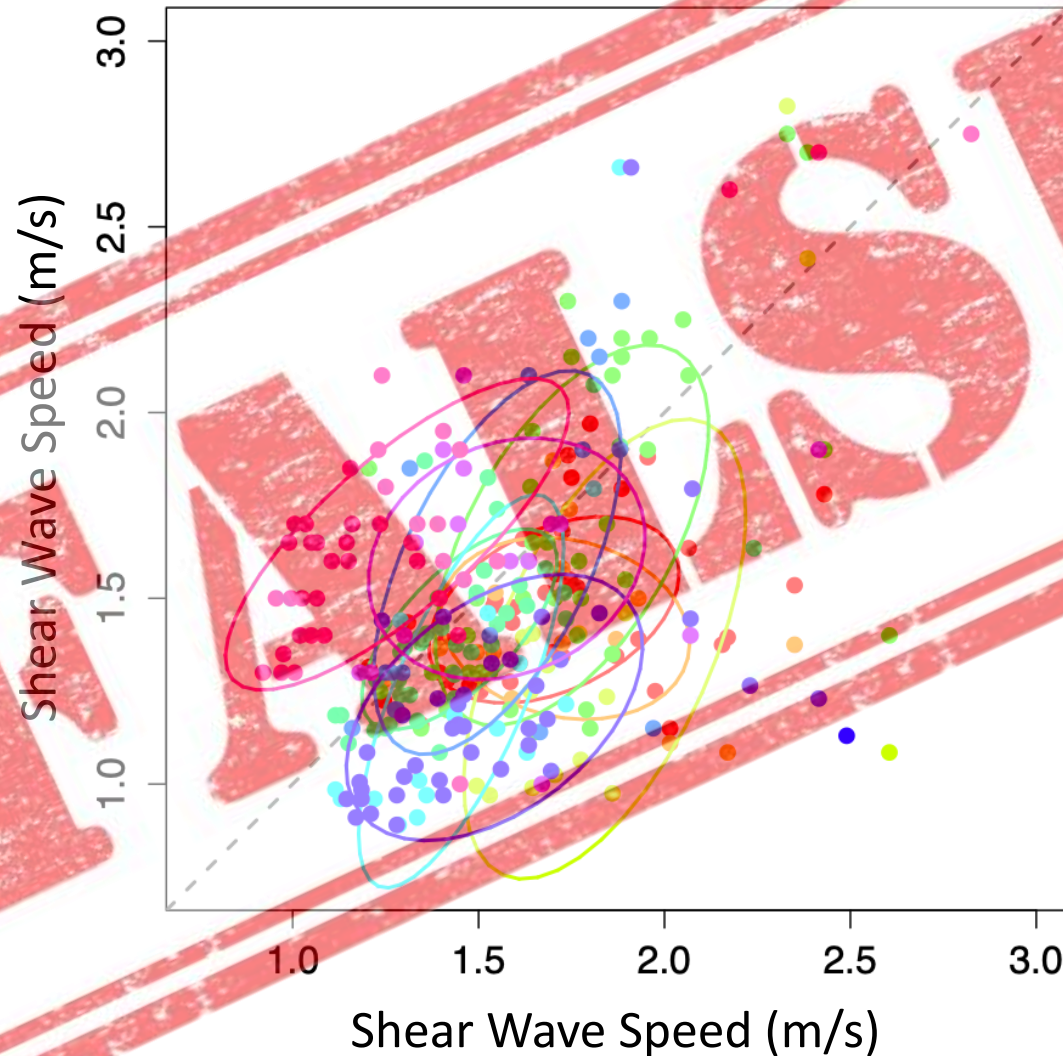
Sudhakar Venkatesh

Stage 1

Claim 2. Different US vendors agree on shear wave speed

Benchmark: correlation ≥ 0.90

- Vendor A vs B, N=40
- Vendor A vs C, N=16
- Vendor A vs D, N=16
- Vendor A vs E, N=40
- Vendor B vs C, N=40
- Vendor B vs D, N=16
- Vendor B vs E, N=16
- Vendor C vs D, N=40
- Vendor C vs E, N=16
- Vendor D vs E, N=40



Intraclass correlation coefficient (ICC)

0.27

0.00

0.33

0.53

0.68

0.53

0.55

0.30

0.19

0.51

Range 0.00 to 0.68

Average 0.39



Claim 3. Different MR vendors agree on **proton density fat fraction**

Benchmark: correlation ≥ 0.90

FNIH



Alex Pasek



Tania Kamphaus

Biostatistics core



Nancy Obuchowski



Tanya Wolfson

Imaging workstream



Anthony Samir



Arinc Ozturk



Katie Fowler



Michael Middleton



Sarah Sherlock



Sedi Shabanan



Teddy Pierce

Circulating workstream



Arun Sanyal



Roberto Calle



Rohit Loomba



Sudha Shankar

MGH/UCSD Team



Danielle Batakis



Guilherme Cunha



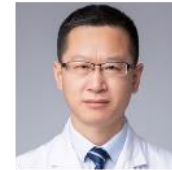
Jake Weeks



Lael Ceriani



Mina Trivedi



Qian Lee



Susi Price



Xiaohong Wang



Yesenia Covarrubias

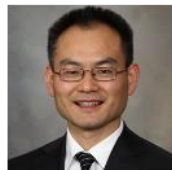
Mayo/Resoundant Team



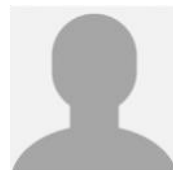
Dick Ehman



Jessica Magnusson



Jun Chen



Kathy J. Brown



Kay Pepin



Sudhakar Venkatesh

Stage 1



FNIH | THE biomarkers CONSORTIUM



Claim 3. Different MR vendors agree on **proton density fat fraction**

Benchmark: correlation ≥ 0.90

● Vendor X vs Y (n=8)

● 1.5T

● 3T

● Vendor X vs Z (n=12)

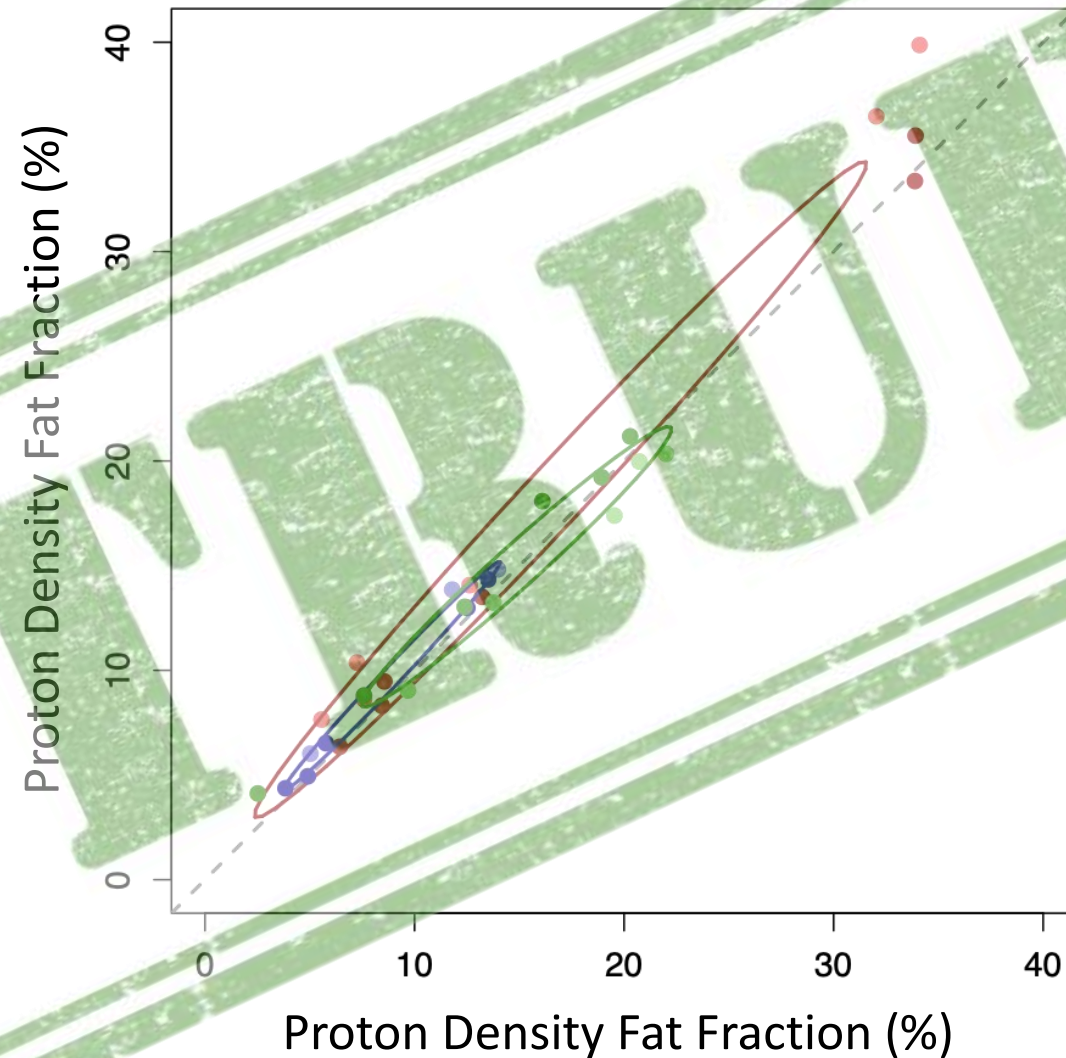
● 1.5T

● 3T

● Vendor Y vs Z (n=11)

● 1.5T

● 3T



Intraclass correlation coefficient (ICC)

0.982

0.977

0.977

Range 0.977 to 0.982

Average 0.979

Claim 4. Different MR vendors agree on **shear stiffness**

Benchmark: correlation ≥ 0.90

FNIH



Alex Pasek



Tania Kamphaus

Biostatistics core



Nancy Obuchowski



Tanya Wolfson

Imaging workstream



Anthony Samir



Arinc Ozturk



Katie Fowler



Michael Middleton



Sarah Sherlock



Sedi Shabanan



Teddy Pierce

Circulating workstream



Arun Sanyal



Roberto Calle



Rohit Loomba



Sudha Shankar

MGH/UCSD Team



Danielle Batakis



Guilherme Cunha



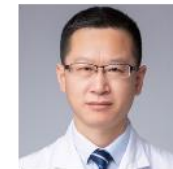
Jake Weeks



Lael Ceriani



Mina Trivedi



Qian Lee



Susi Price



Xiaohong Wang



Yesenia Covarrubias

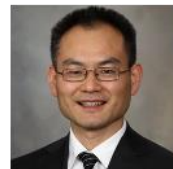
Mayo/Resoundant Team



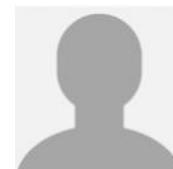
Dick Ehman



Jessica Magnusson



Jun Chen



Kathy J. Brown



Kay Pepin



Sudhakar Venkatesh

Stage 1

Claim 4. Different MR vendors agree on **shear stiffness**

Benchmark: correlation ≥ 0.90

● Vendor X vs Y (n=8)

● 1.5T

● 3T

● Vendor X vs Z (n=12)

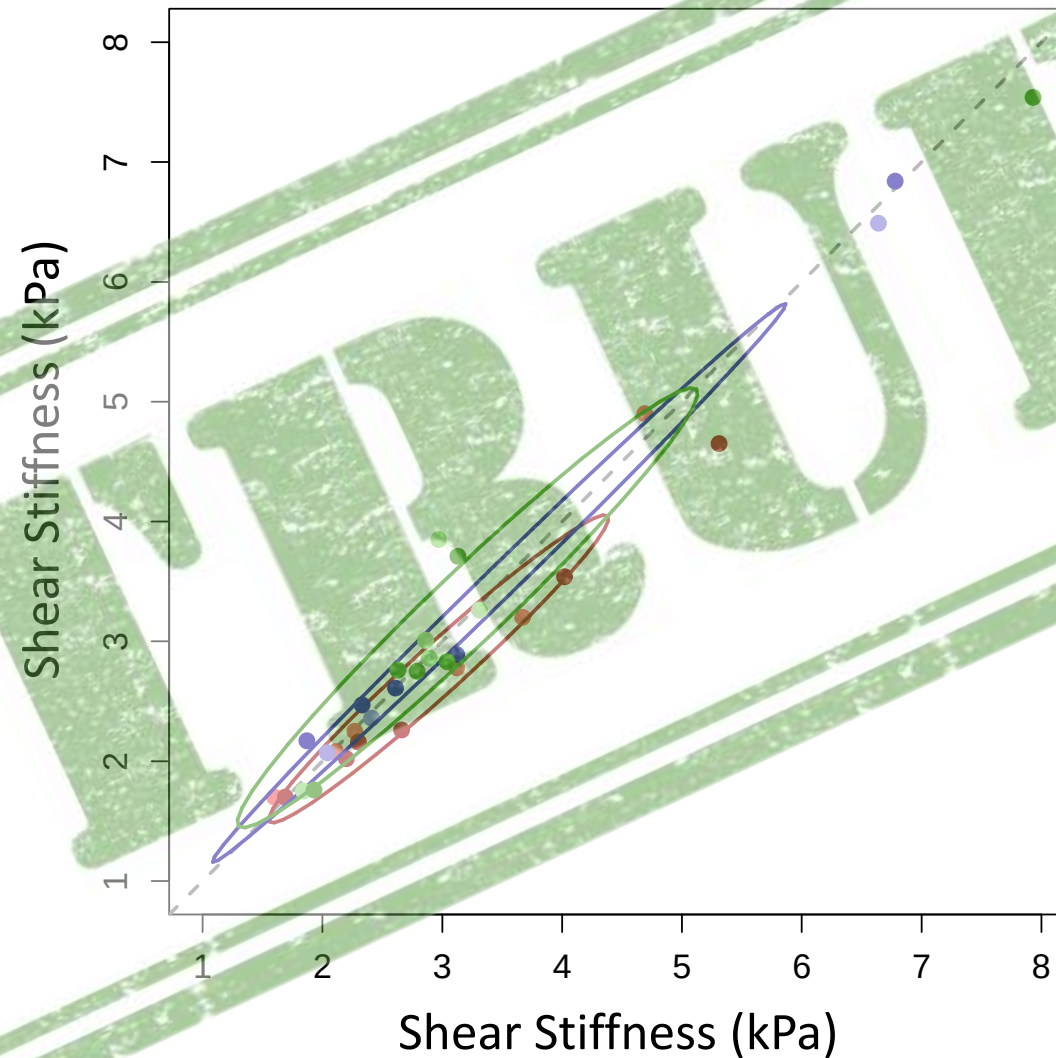
● 1.5T

● 3T

● Vendor Y vs Z (n=11)

● 1.5T

● 3T



Intraclass correlation coefficient (ICC)

0.960

0.997

0.975

Range 0.960 to 0.997

Average 0.977

Claim 5. MRI-PDFF and ultrasound-derived fat fraction agree

Benchmark: correlation ≥ 0.90

R01 DK088925

Unpublished Data



108 adults w/ severe obesity (BMI ≥ 35 kg/m²)

- Prospective study, up to 5 visits
- Total of 462 visits
- Mean age 44 years
- Mean BMI 46 kg/m²

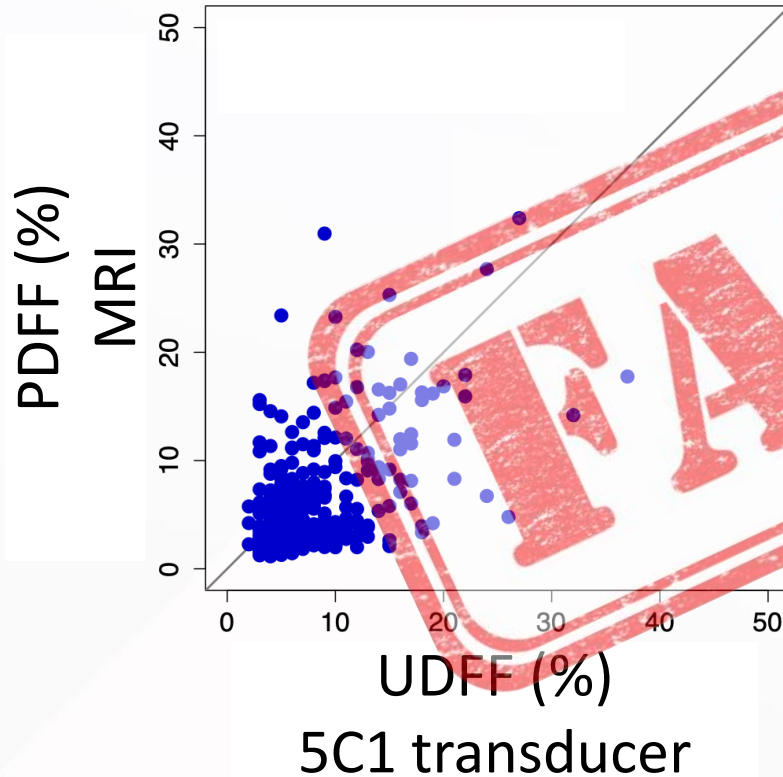
- **PDFF**
- **UDFF - 5C1**
- **UDFF - DAX**

**At each visit
(same day)**

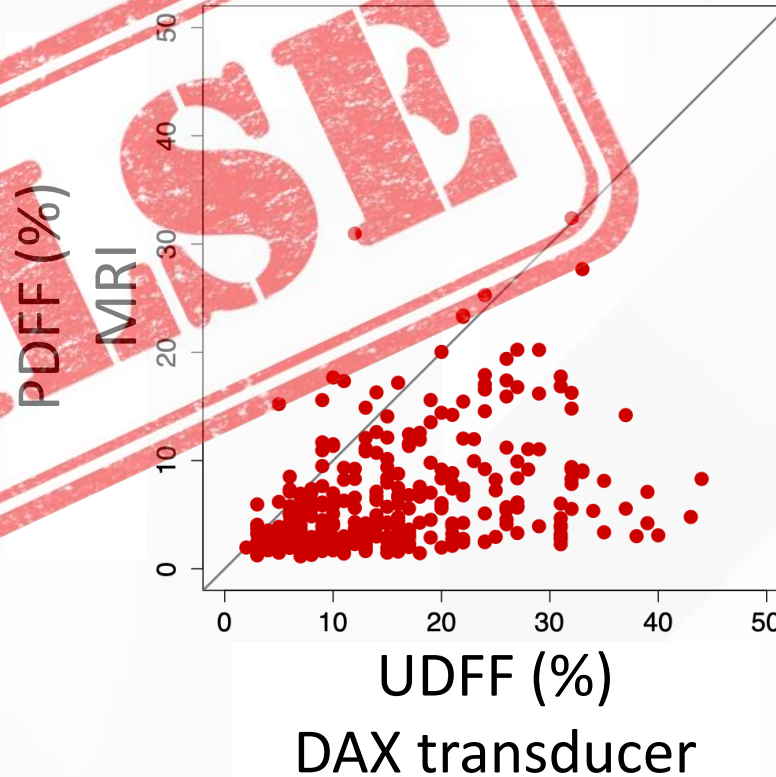
Claim 5. MRI-PDFF and ultrasound-derived fat fraction agree

Benchmark: correlation ≥ 0.90

$r = 0.44$



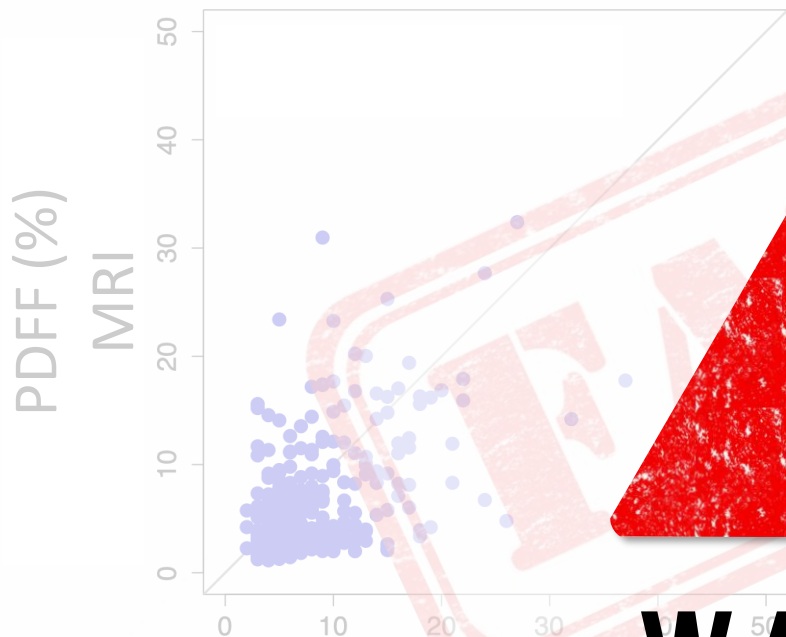
$r = 0.36$



Claim 5. MRI-PDFF and ultrasound-derived fat fraction agree

Benchmark: correlation ≥ 0.90

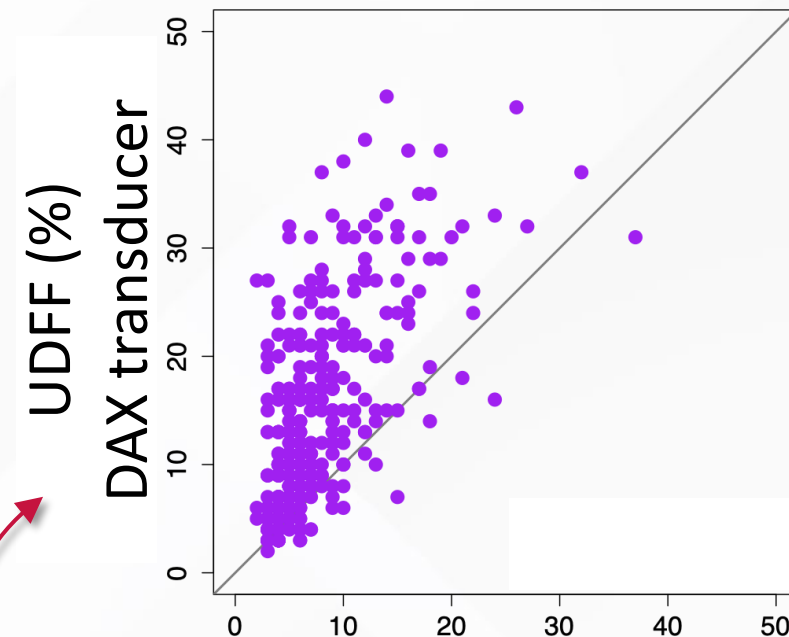
$r = 0.44$



$r = 0.36$



$r = 0.65$



WARNING

Don't agree

Claim 6. MRE-derived stiffness and SWE-derived stiffness correlate

Benchmark: correlation ≥ 0.90

Study in progress



UC San Diego

Adults with cirrhosis undergoing HCC screening

- Prospective study, 1 visit

Prelim results in first 55 participants (27 men)

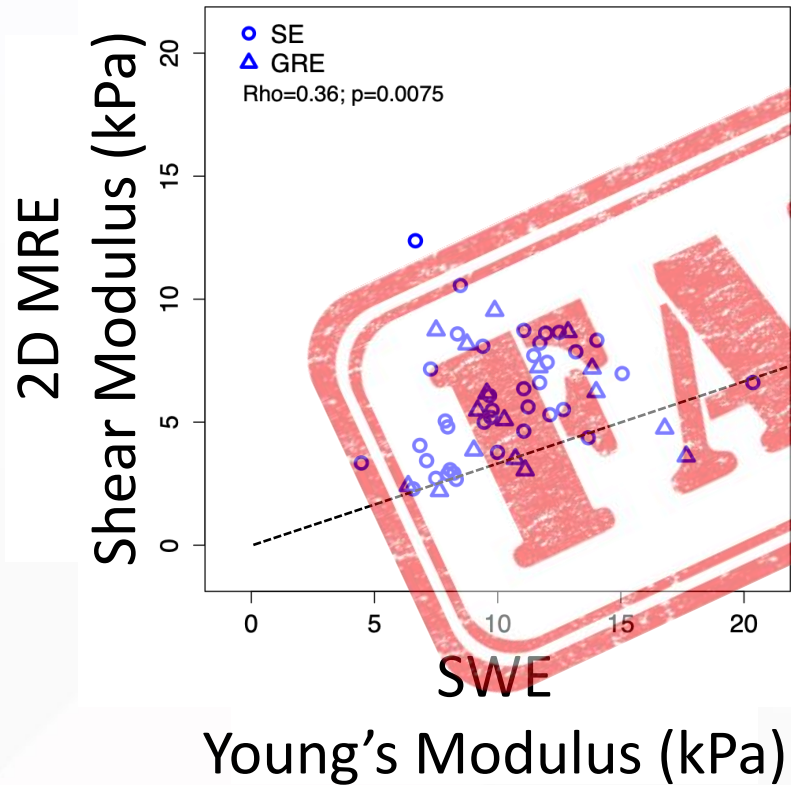
- Mean age 58 years
- Mean BMI 30 kg/m²
- **2D MRE-GRE or 2D MRE-SE**
- **3D MRE**
- **2D SWE**

Same day

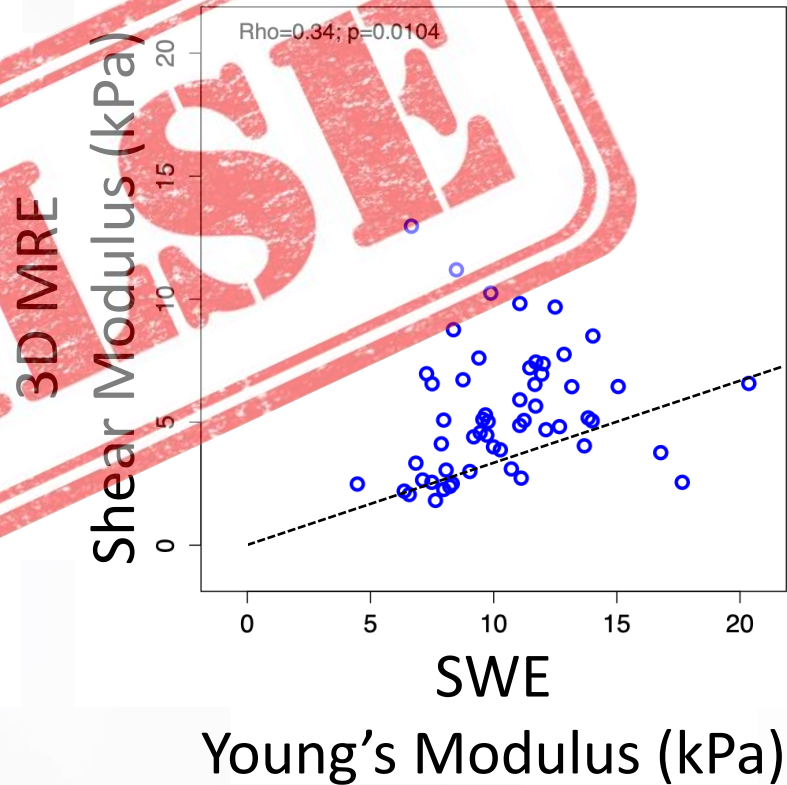
Claim 6. MRE-derived stiffness and SWE-derived stiffness correlate

Benchmark: correlation ≥ 0.90

Rho = 0.36



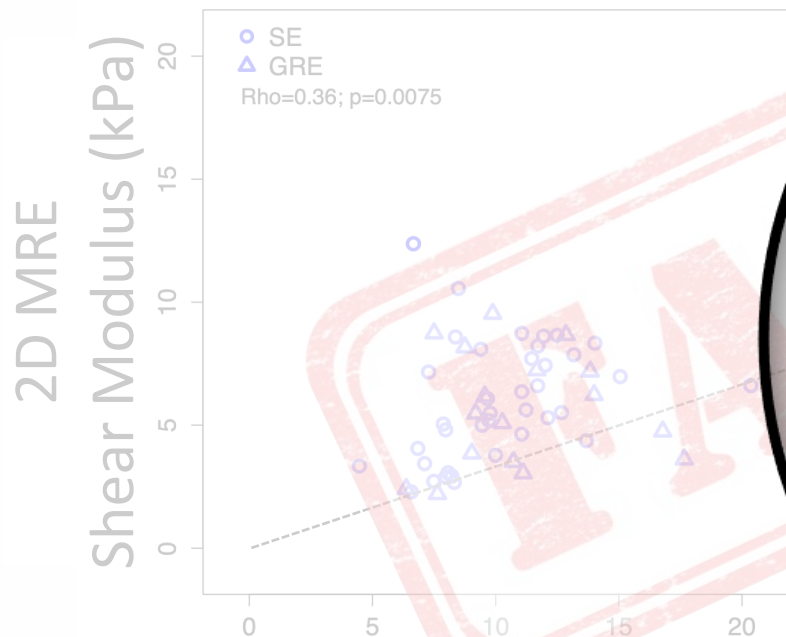
Rho = 0.34



Claim 6. MRE-derived stiffness and SWE-derived stiffness correlate

Benchmark: correlation ≥ 0.90

Rho = 0.36

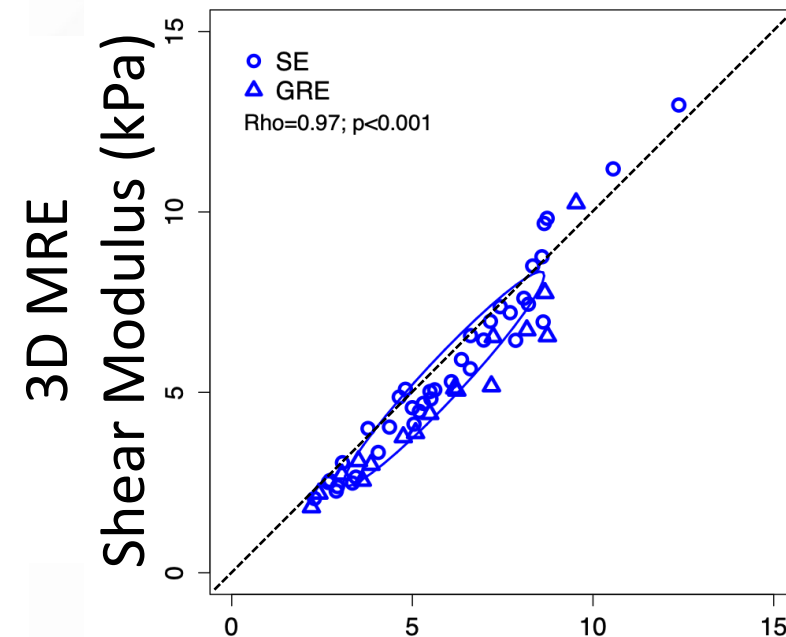


Rho = 0.34



Sanity check!

Rho = 0.97



Outline

- A question
- A definition
- 6 claims
- **Summary**
- The answer
- The Paris MASH Declaration of 2024

6 **Claims:** All Sound Reasonable, but ... **Four are False**

Claim 1. Different US vendors agree on measurement of **attenuation coefficient**

Claim 2. Different US vendors agree on measurement of **shear wave speed**

Claim 3. Different MR vendors agree on measurement of **proton density fat fraction**

Claim 4. Different MR vendors agree on measurement of **shear wave stiffness**

Claim 5. MRI-derived **proton density fat fraction** and **ultrasound-derived fat fraction** agree

Claim 6. MRE-derived **stiffness** and **shear wave elastography-derived stiffness** correlate

BENCHMARK. Correlation ≥ 0.90

Outline

- A question
- A definition
- 6 claims
- Summary
- The **answer**
- The Paris MASH Declaration of 2024

What happened in 1795 that needs to happen now?



DU *cinquantième* jour de *juin* l'an troisième de
la République française une et indivisible.

[illegible][illegible]

The metric system was adopted in France



**> 250,000 different units
of weights and measures in France alone**

Status of the metric system, 2024

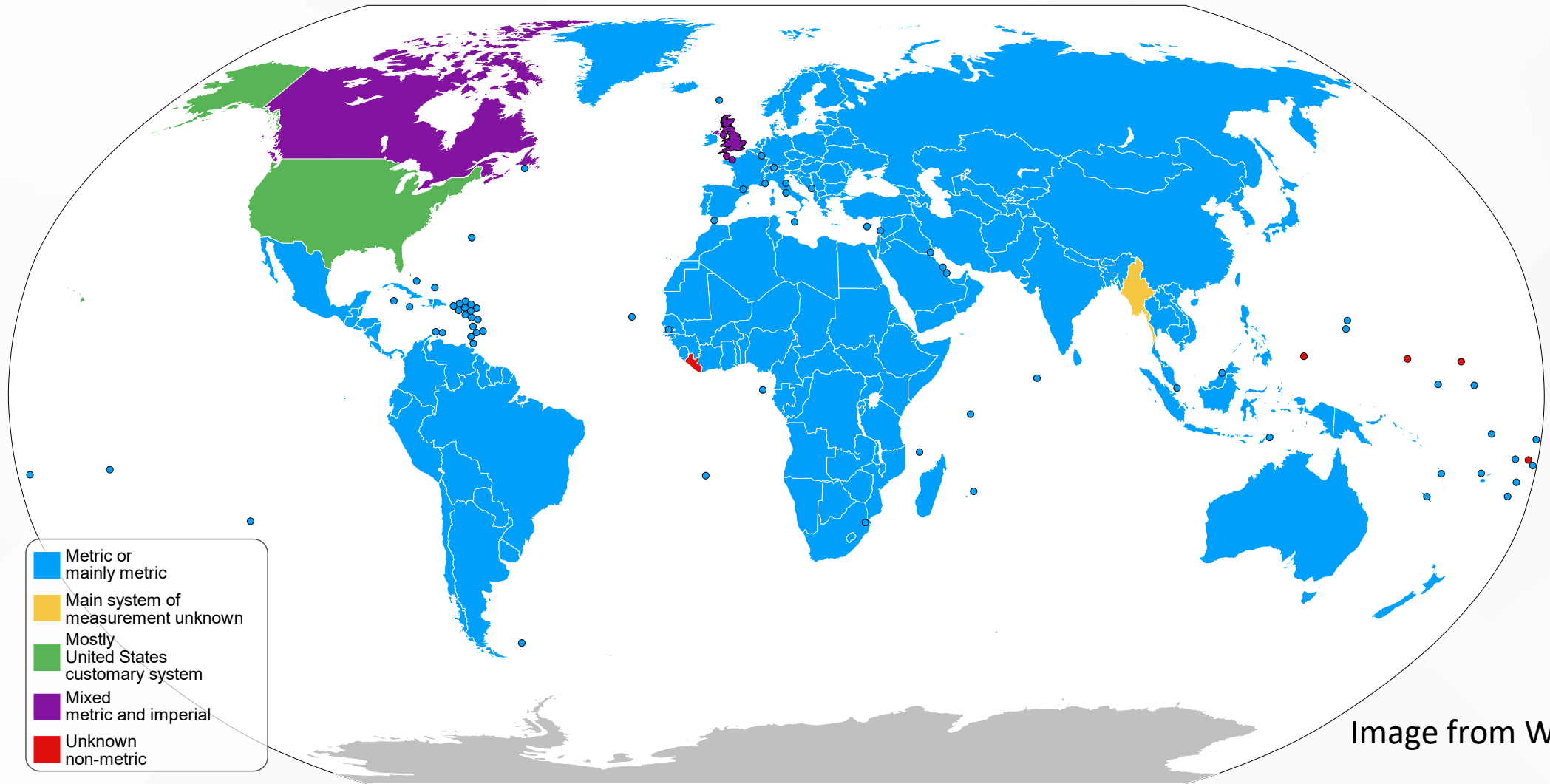


Image from Wikipedia

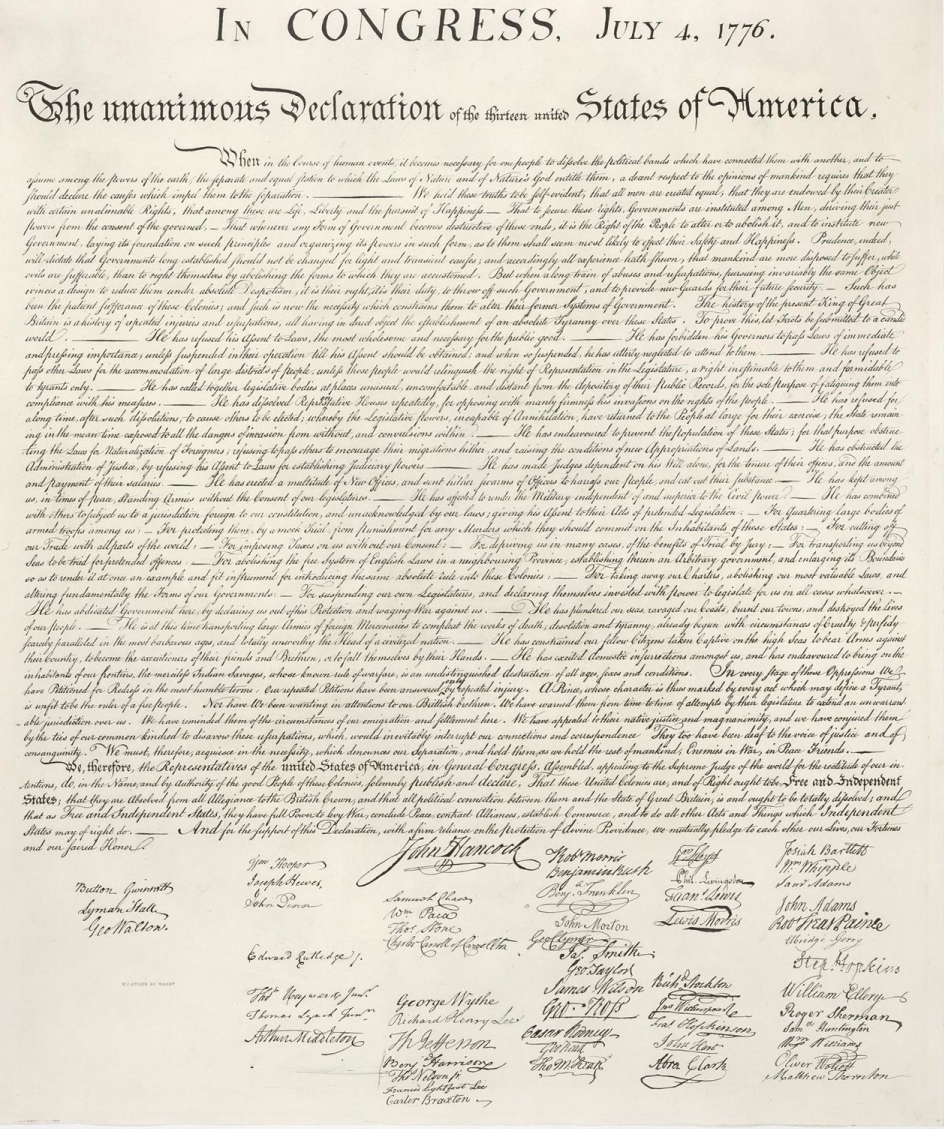
We need standardization of NITs

Outline

- A question
- A definition
- 6 claims
- Summary
- The answer
- The **Paris MASH Declaration of 2024**

Declaration of Independence by the United States

July 4, 1776



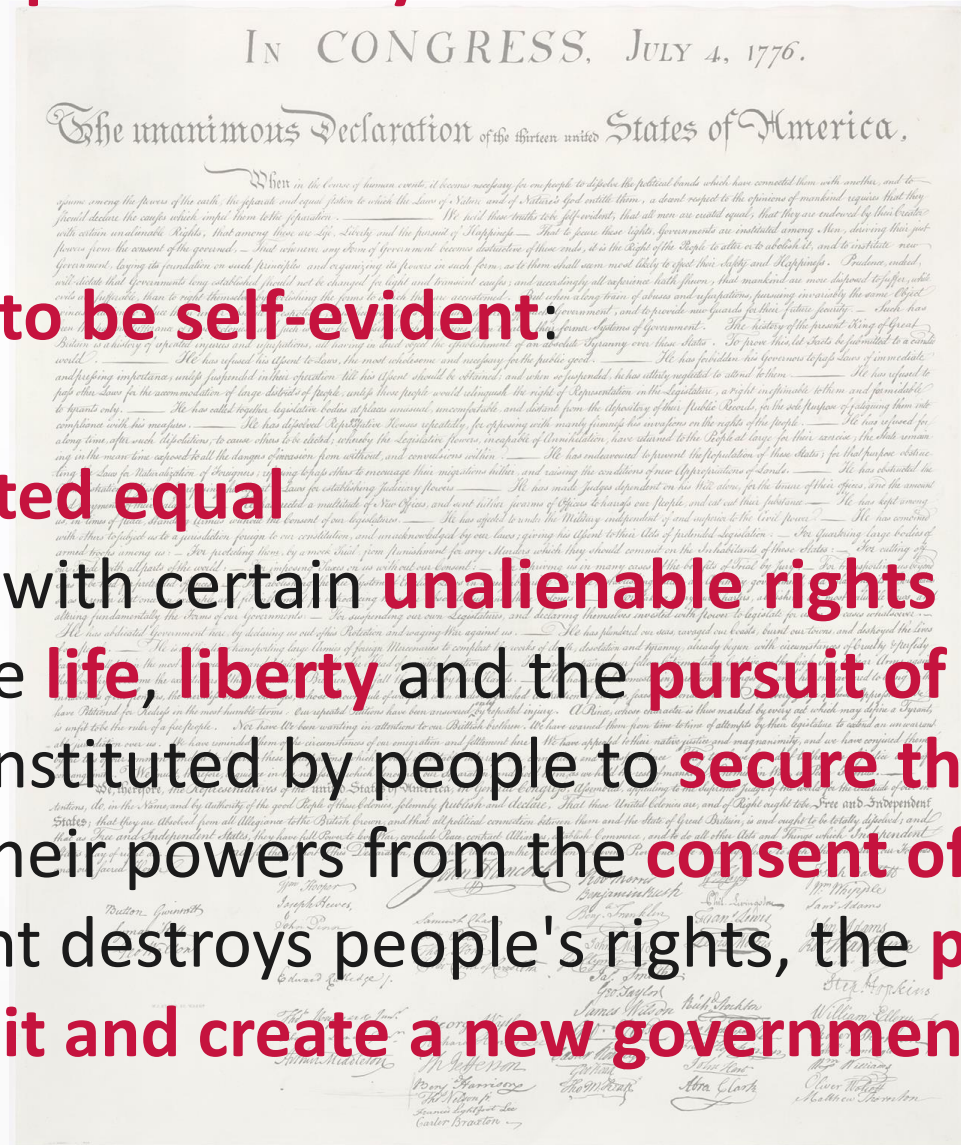
Declaration of Independence by the United States

July 4, 1776



We hold these **truths to be self-evident**:

- all people are **created equal**
- they are endowed with certain **unalienable rights**
- these rights include **life, liberty** and the **pursuit of happiness**
- **governments** are instituted by people to **secure these rights**
- governments get their powers from the **consent of the governed**
- when a government destroys people's rights, the **people have the right to alter or abolish it and create a new government**

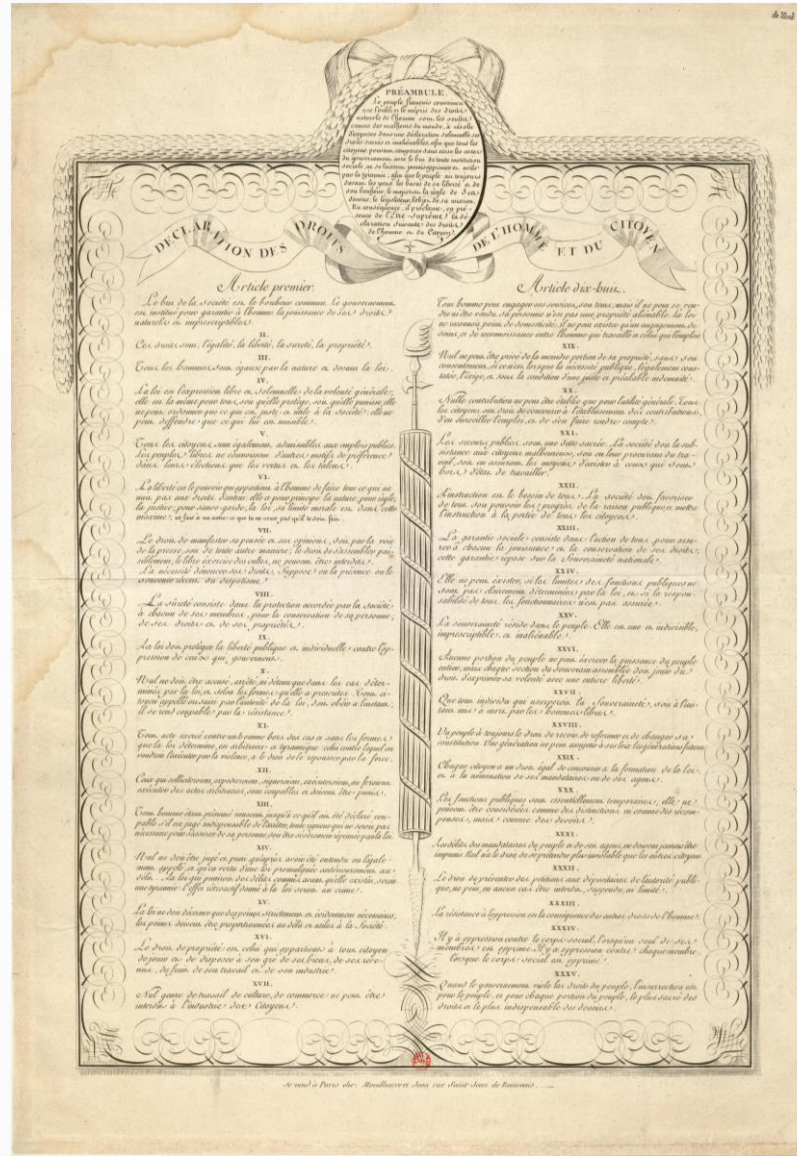


Original text
paraphrased for
brevity and style



Declaration of the National Assembly of France

August 26, 1789



Natural, unalienable, and sacred **rights of human beings:**

Article 1. People are born and remain **free and equal in rights**

Article 2. Governments must **preserve liberty, property, safety, and resistance to oppression**

Article 3. Sovereignty **arises from the nation**

Article 4. Liberty is the freedom to anything that **does not harm others**

Article 5. Laws can forbid only those **actions that injure society**

Article 6. Laws are the expression of the **general will**

Article 7. No one can be accused, arrested, or detained **outside the law**

Article 8. Laws can prescribe only **necessary punishments**

Article 9. Every one is **presumed innocent**

Article 10. No one can be disturbed based on their **opinions**

Article 11. People have the **right to communicate ideas and opinions**

Article 12. A **public force** is needed to guarantee the rights of people

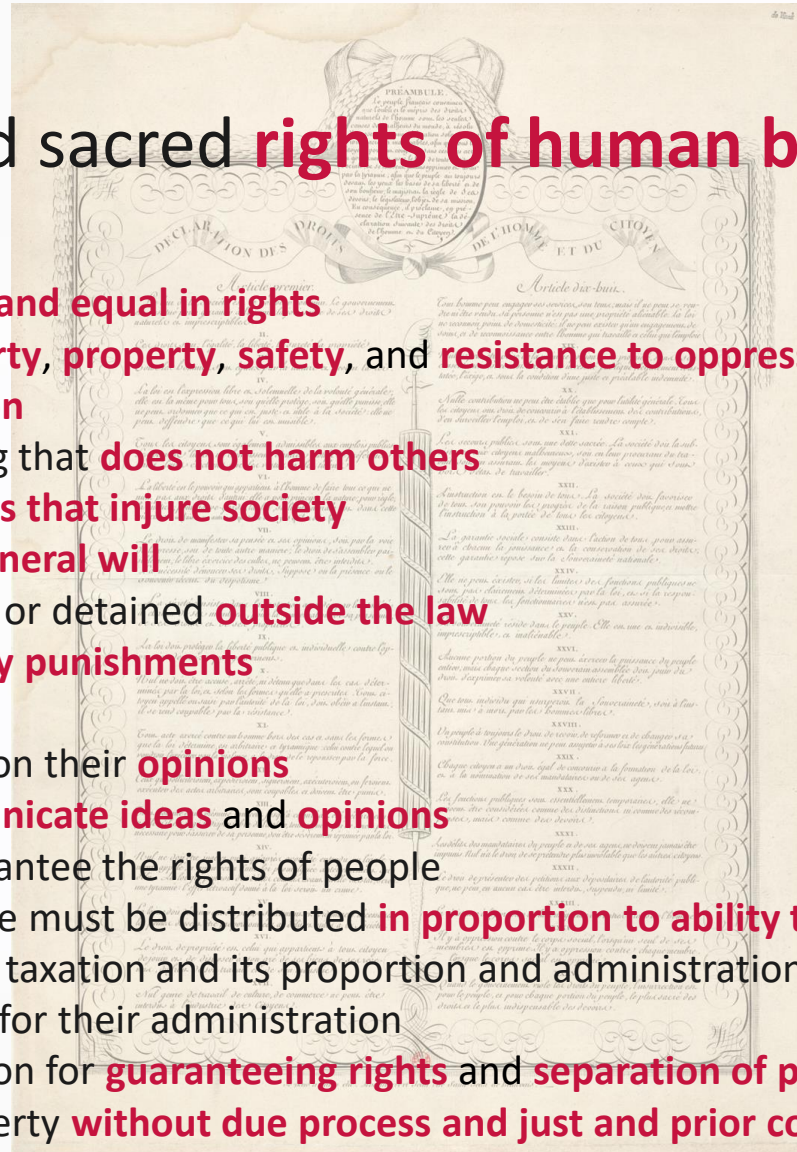
Article 13. A **tax** to maintain the public force must be distributed **in proportion to ability to pay**

Article 14. **Citizens determine** the need for taxation and its proportion and administration

Article 15. **Public officials are accountable** for their administration

Article 16. A constitution requires a provision for **guaranteeing rights and separation of powers**

Article 17. No one can be deprived of property **without due process and just and prior compensation**



Original text
paraphrased for
brevity and style



Declaration of the 10th Paris MASH Conference

September 6, 2024



PARIS
MASH
MEETING



PARIS MASH MEETING

10th edition

Noninvasive tests are not people and they do not have rights, unalienable or otherwise

10th edition

Noninvasive tests have **standardization requirements**

Article 1. NITs of the same type must **agree with each other (i.e., inter-changeable)**

Article 2. NITs must **agree with the “truth”** Stay tuned for Stage 2



10th edition



PARIS
MASH
MEETING

10th edition

September 5 & 6 2024
Institut Pasteur, Paris

Standardization and quantitative imaging biomarkers in care of MASLD

Thank You!

CLINICAL LECTURE

Friday September 6, 2024

1:30-2:00 pm

Claude B. Sirlin, MD

Liver Imaging Group

Dept. of Radiology

csirlin@health.ucsd.edu

UC San Diego

