Perspectum

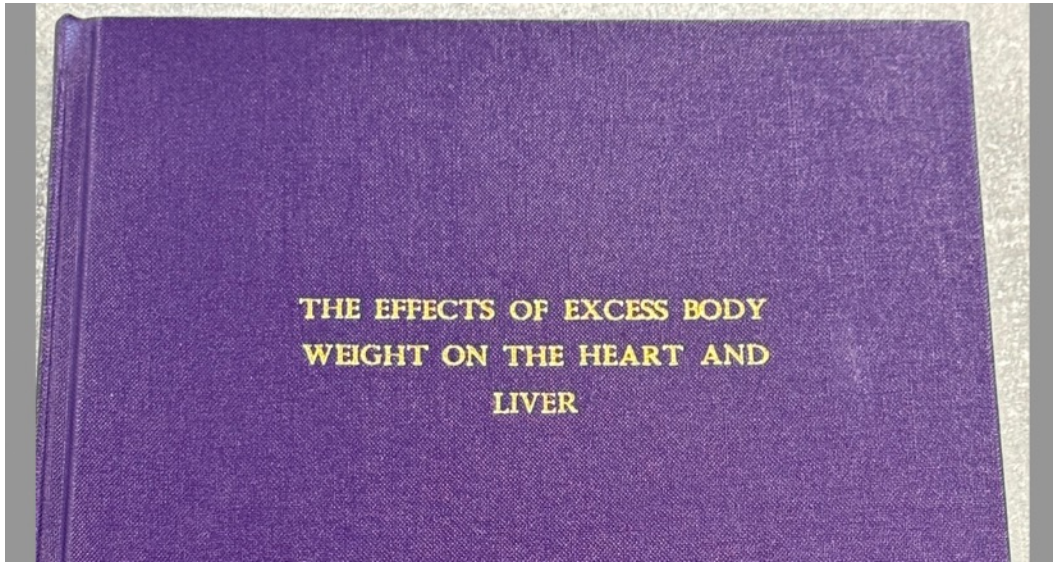
MASH and metabolic disease – Find it, Treat It, Fix It

Dr Rajarshi Banerjee

June 25th, 2024

Conflicts of Interest

- NHS Consultant – Oxford University Hospitals NHS Trust
- IP and Patent holder in multiparametric MRI
- Shareholder and director of Perspectum

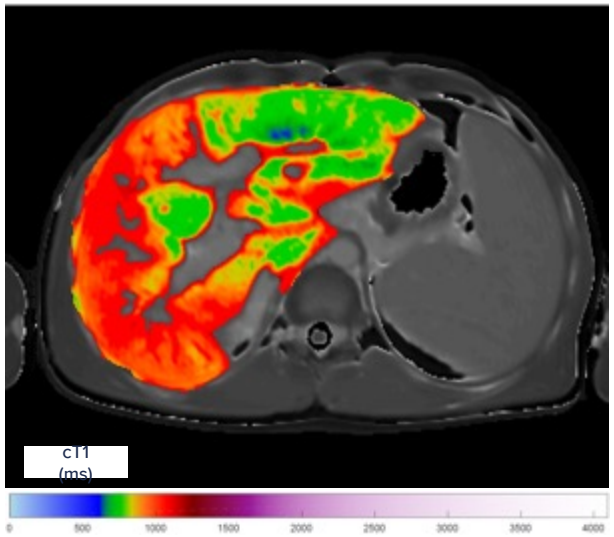


Key Points

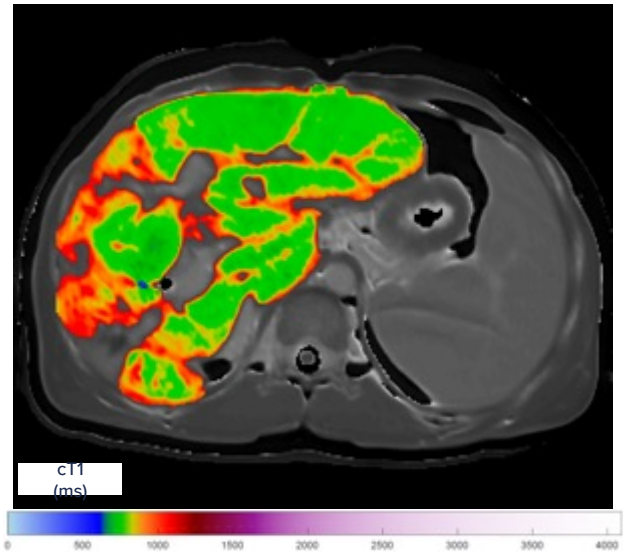
- MASH trials are expensive because they are slow
- Technology enables rapid recruitment and low ‘screen fail’ rates
- Standardisation and big data matter – allows scalability for reimbursement discussions, and data for FDA

Case Study: PSC/AIH patient on prednisolone and azathioprine

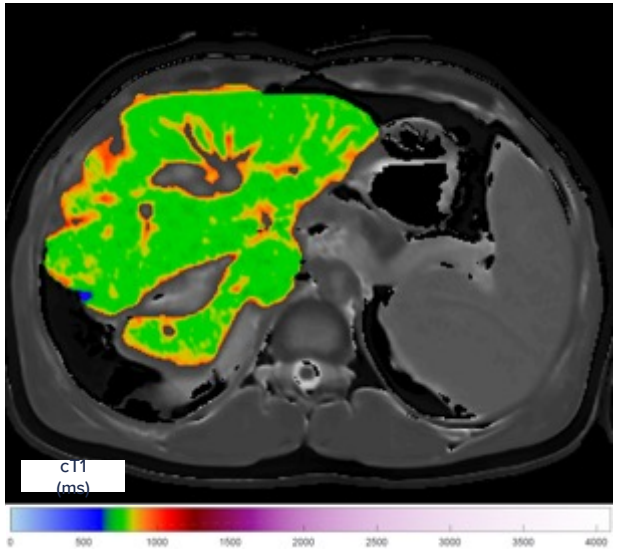
22-year-old male, with PSC and AIH overlap syndrome; responded to treatment.



Pre-treatment: February 2012

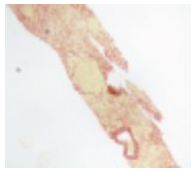


Post-treatment: October 2012



Post-treatment: October 2013

Pre-Treatment
Sirius Red



cT1: **960ms**
Liver fat 2%

cT1: **846ms**
Liver fat 4%

cT1: **824ms**
Liver fat 3%

Perspectum

A patient in Texas

December 2015

Good communication builds relationship

On 09/12/2015 22:22, "Harrison, Stephen A COL USARMY (US)" <stephen.a.harrison.mil@mail.mil> wrote:

Subject: Clinical LMS patient (UNCLASSIFIED)

Classification: UNCLASSIFIED

Caveats: NONE

Hi Banjo and Marija,

We scanned a clinical patient of Dr. Harrison's today. I just sent the scan over via amerdec safe. The patient is here TDY for just a couple days and they were hoping to be able to review his results prior to him departing San Antonio. Would it be possible to send over the result from that scan tomorrow as well? We would really appreciate it.

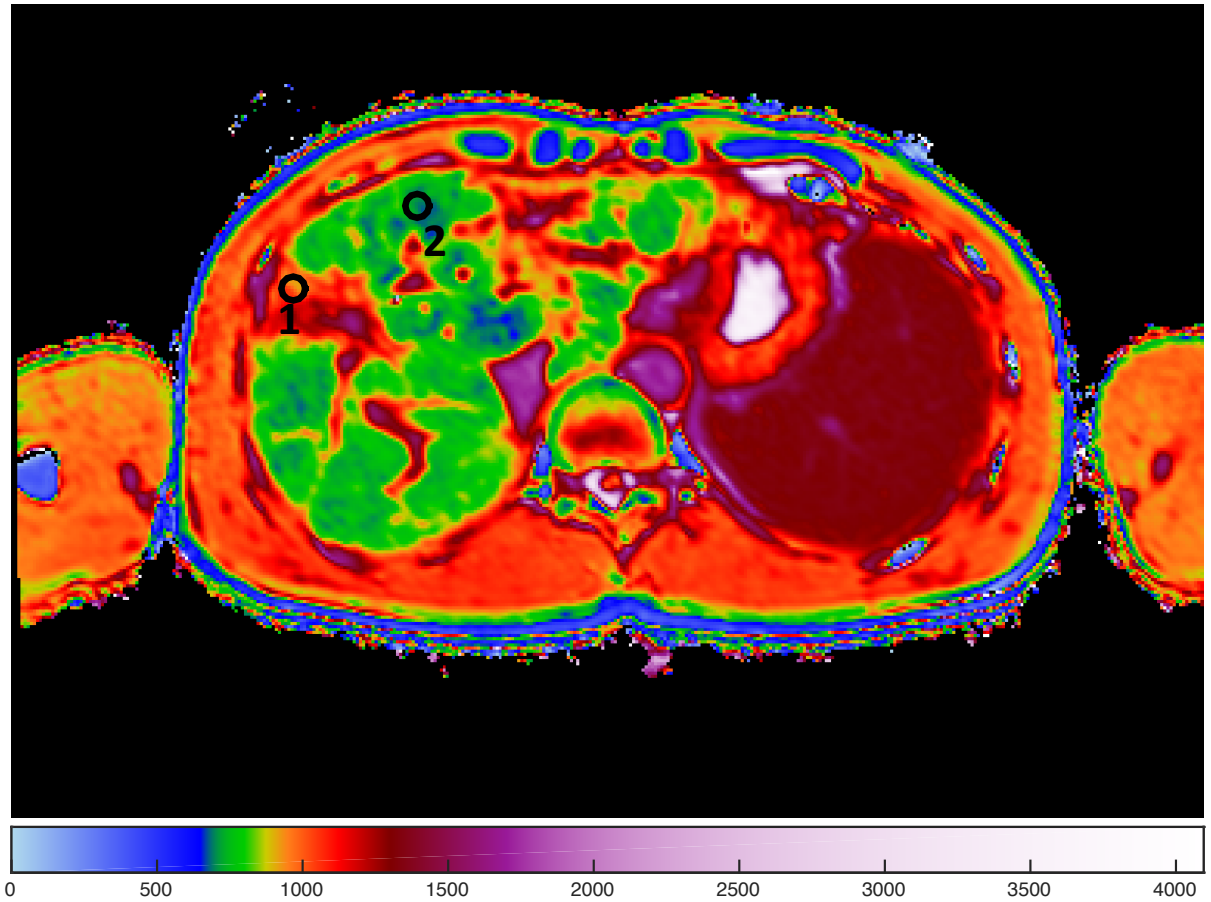
Thursday, 10 December 2015 13:23

Dear Stephen, Jen,

I have processed this patient's scans (both from August and new ones) - please find the reports attached. An ROI has been placed in healthy and diseased area in every slice.

The images are also compared in a short presentation.

PSC patient, Dec 2015



ROI 1

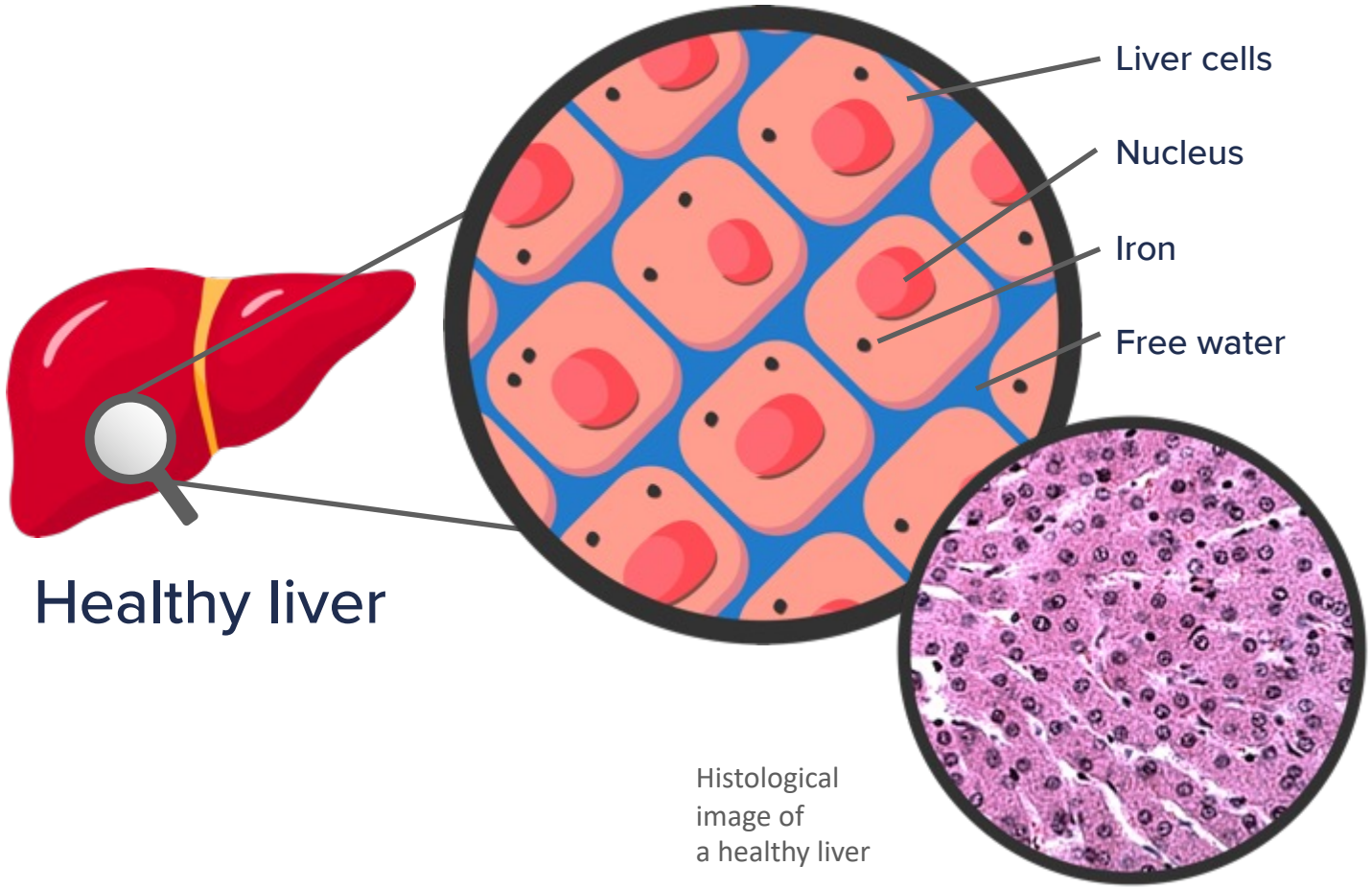
cT1 950ms

ROI 2

cT1 720ms

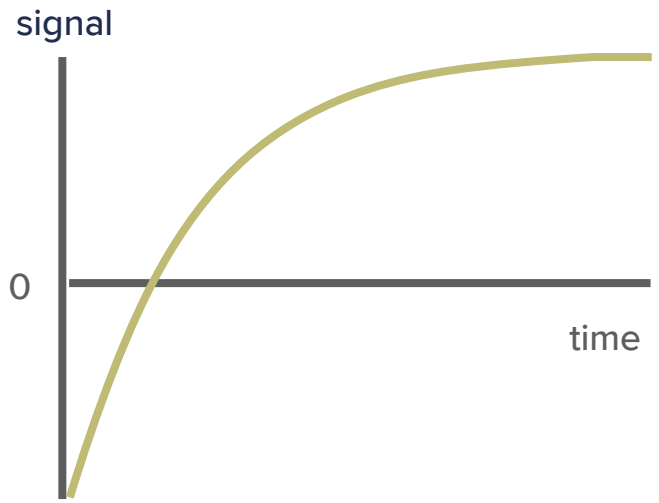
What is cT1?

T1 measurements and the liver



Healthy liver

Histological image of a healthy liver

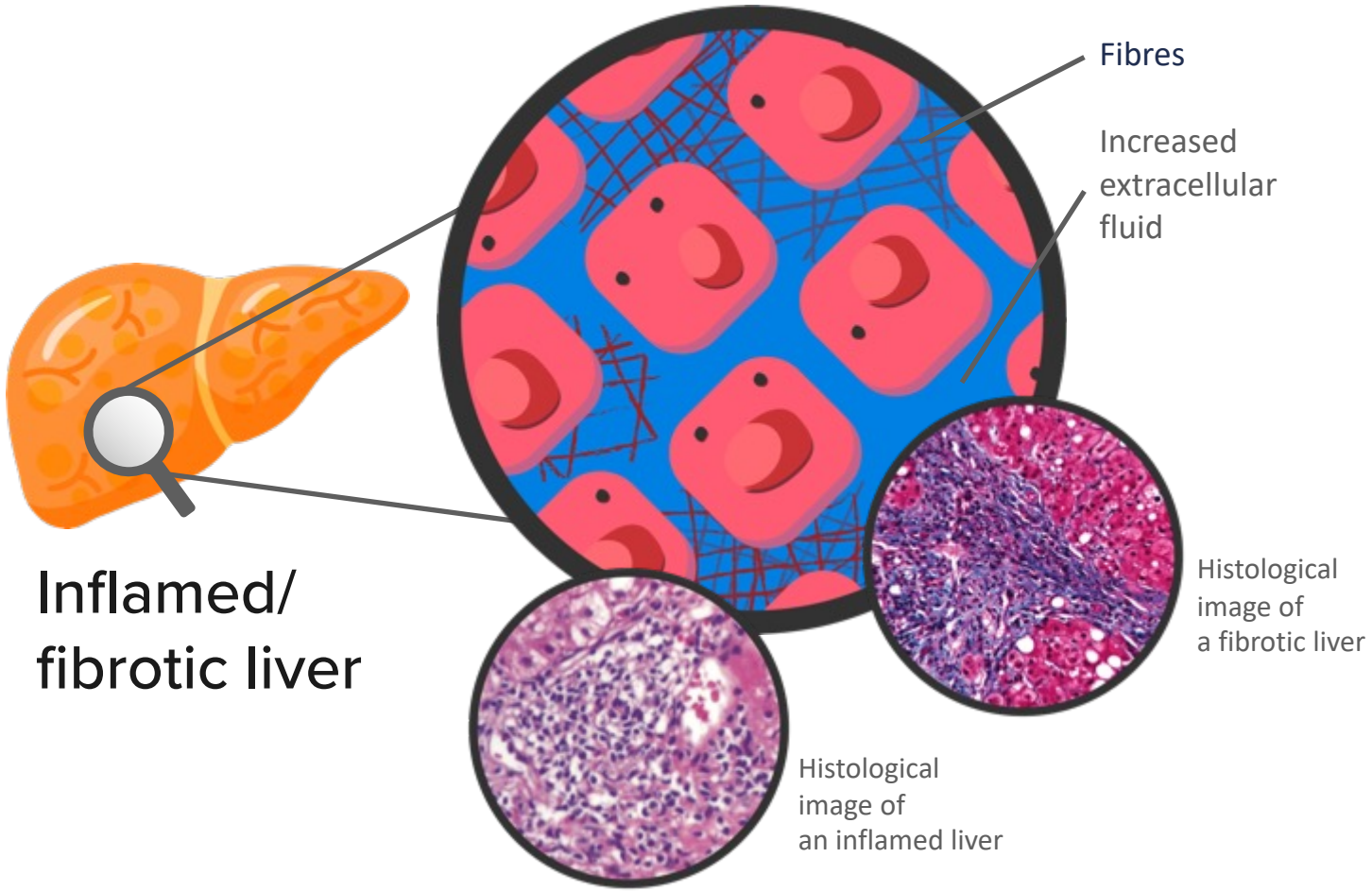


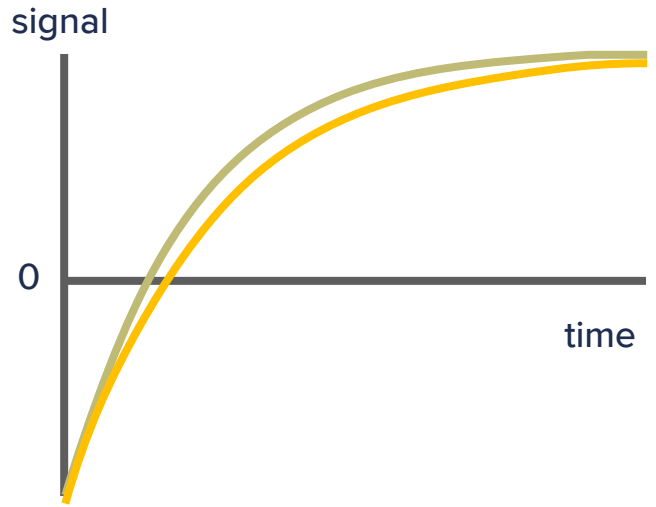
T1 relaxation

Tunnicliffe E. et al. JMRI, 2016

For illustration purposes only

T1 measurements and the liver





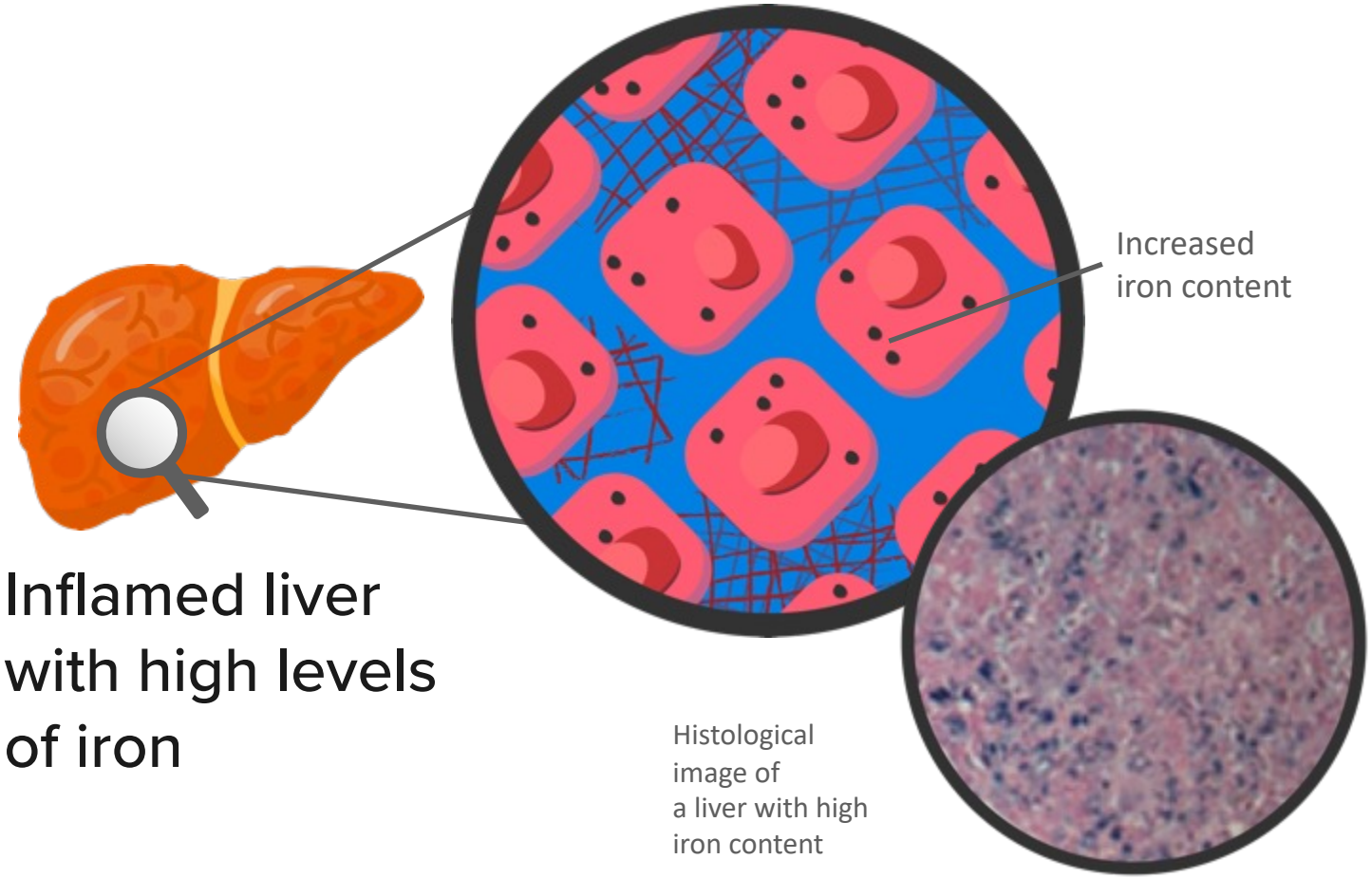
T1 relaxation

Changes in water content, lead to longer T1 relaxation times with increasing levels of fibroinflammation

Tunnicliffe E. et al. JMRI, 2016

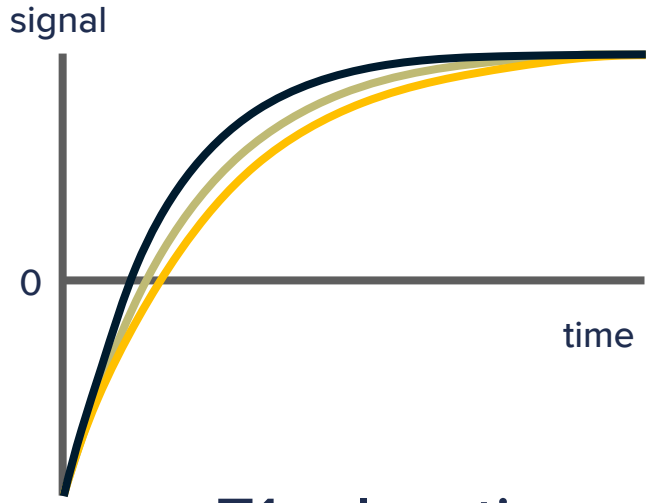
For illustration purposes only

T1 measurement and iron



Inflamed liver with high levels of iron

Histological image of a liver with high iron content



T1 relaxation

Iron also accumulates in inflamed liver and artificially shortens T1 values

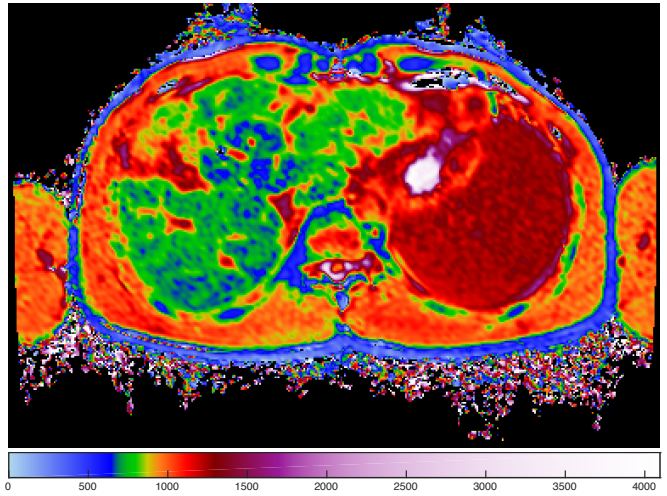
Tunnicliffe E. et al. JMRI, 2016

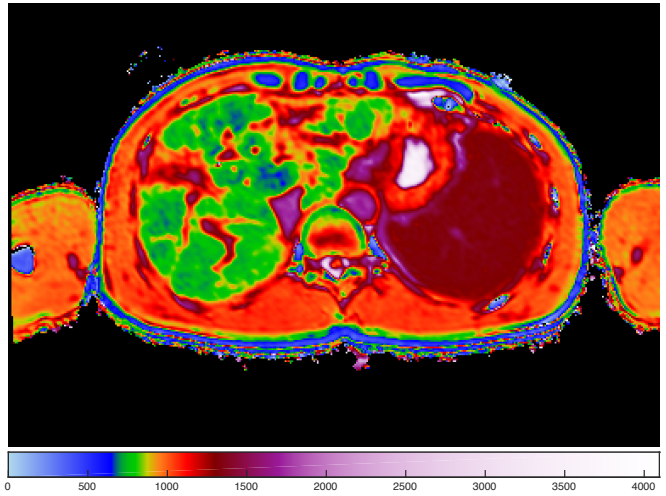
PSC patient cT1 comparison

July 2015

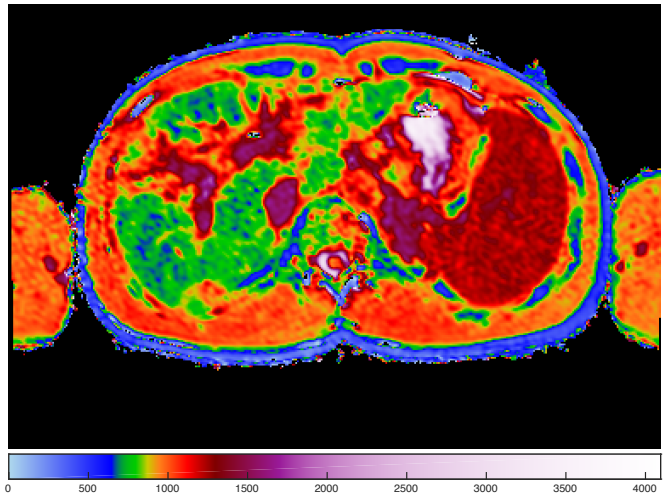
Dec 2015

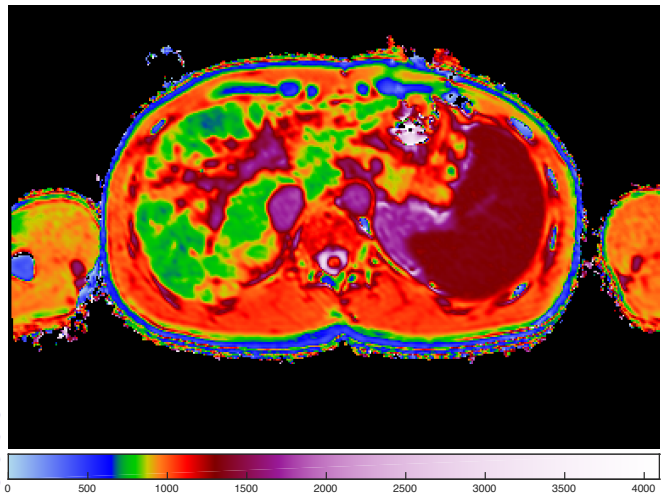
Slice 1





Slice 2



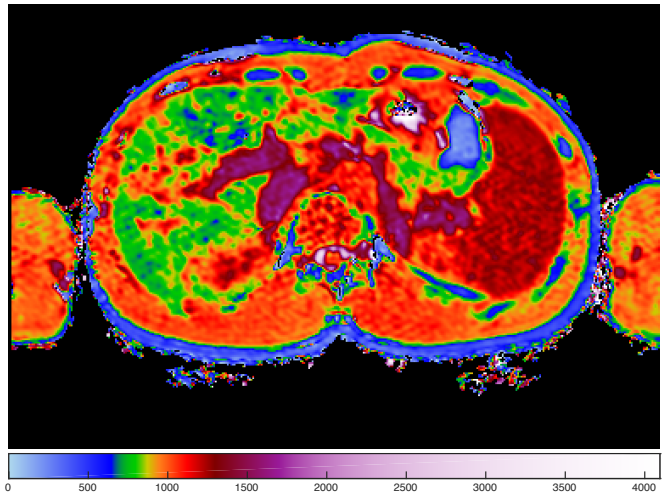


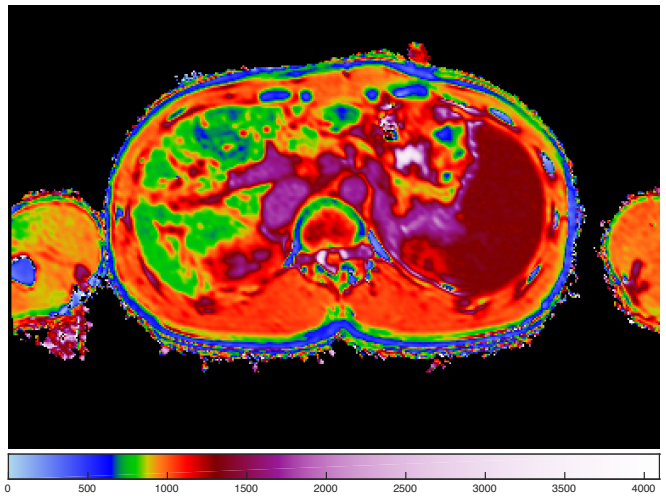
PSC patient cT1 comparison

July 2015

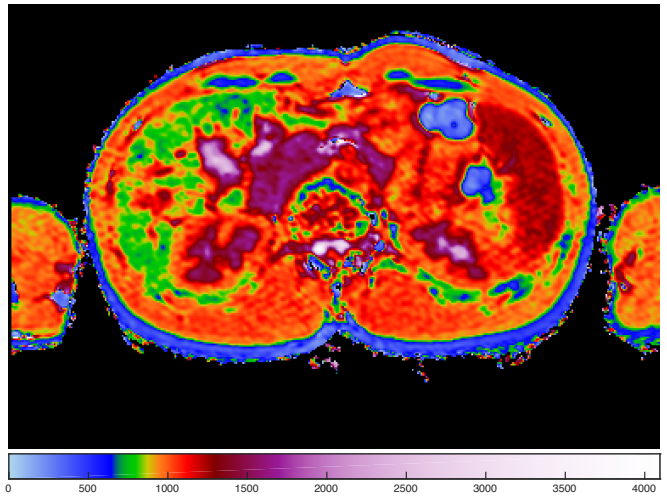
Dec 2015

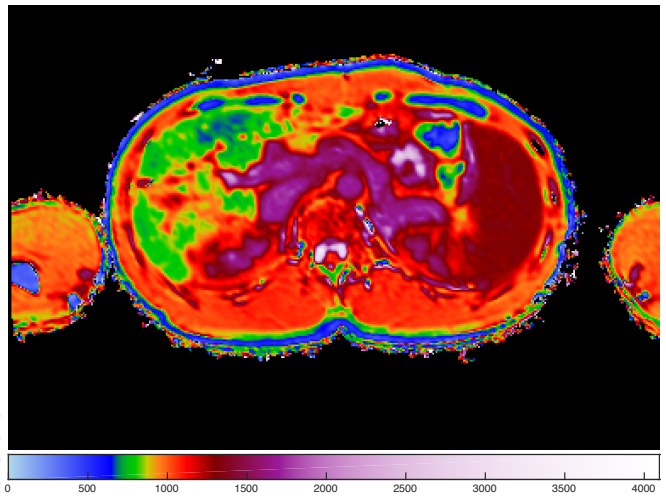
Slice 3





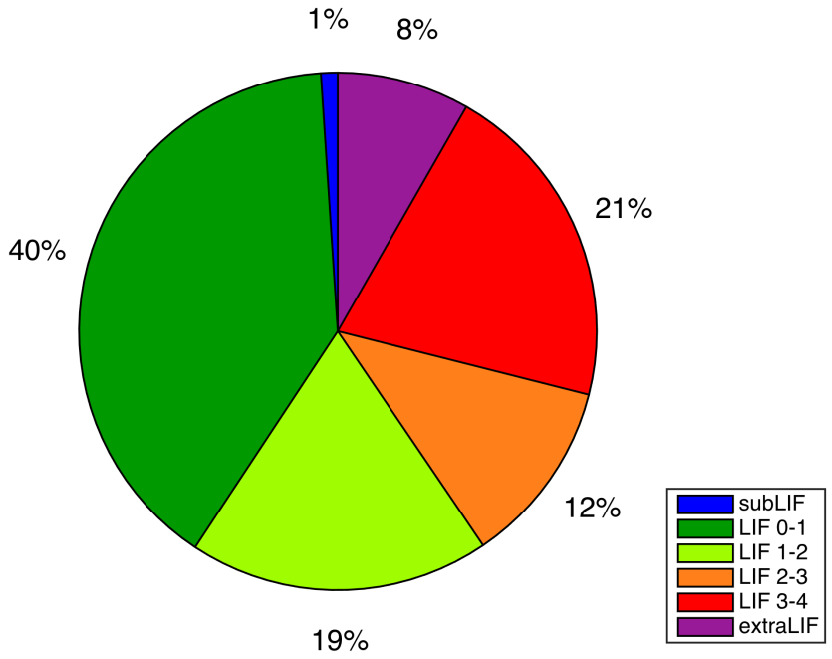
Slice 4



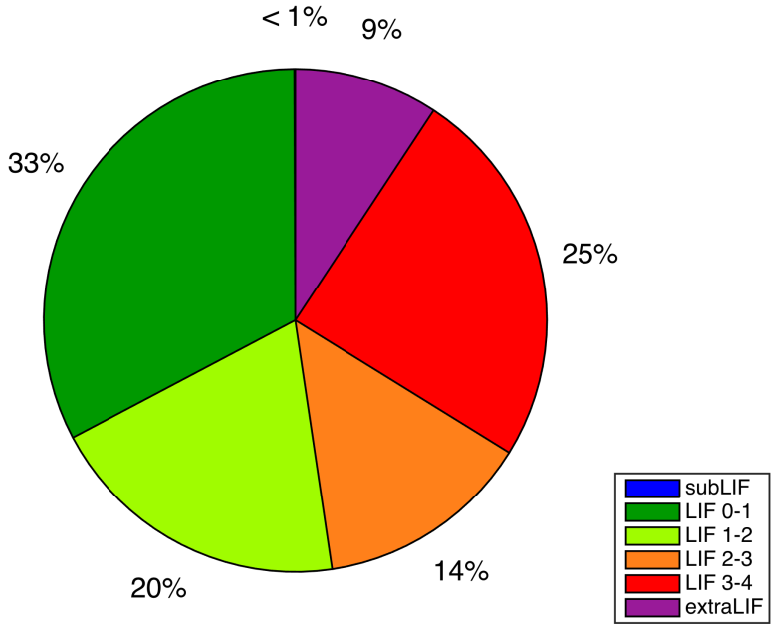


Distribution of disease
in all four slices – no improvement in the liver

July 2015



December 2015



Professor Stephen Harrison, pioneer and clinical triallist.

A Global Medical Imaging & Decision Support Platform

240 **Employees**
across our offices in Oxford, San Francisco, Boston, Dallas, Singapore and Lisbon

70+ **PhDs**
across disciplines inc: oncology, medical imaging, machine learning, genetics

700+ **Scanners**
Worldwide enabled with Perspectum technology

>70 **Clinical trials**
Have used our imaging

100+ **Papers published**

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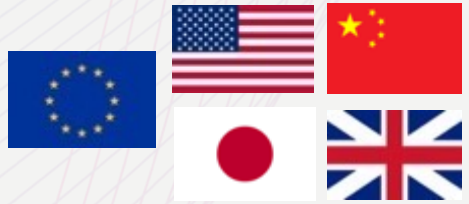
>100,000 **Data sets** paired with biochemistry and genetics

26 **Regulatory Clearances**

20+ **Perspectum-led trials**

18 **Patent families**

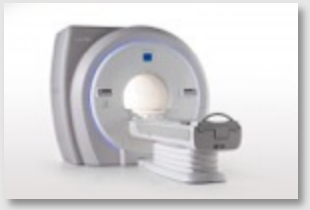


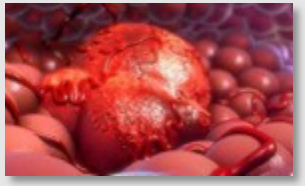
AI in cancer - imaging and decision support

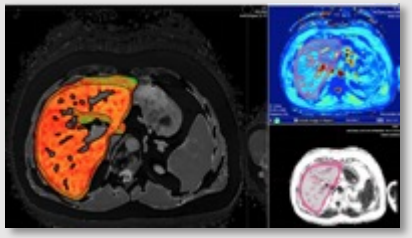
Faster clinical outcomes, and the bulk of the investment in medical imaging

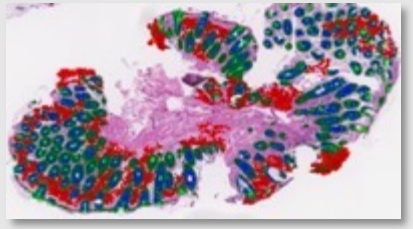

MERRY

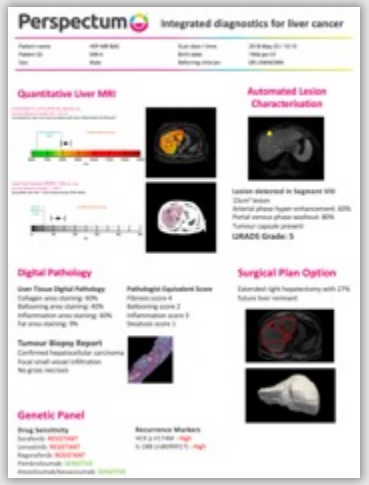
Delivering Precision Health in Chronic Disease and Cancer











Regulatory clearance
Payor coverage
CPT codes
Reimbursement

Multimodality, qualitative inputs

Digital, quantitative biomarkers

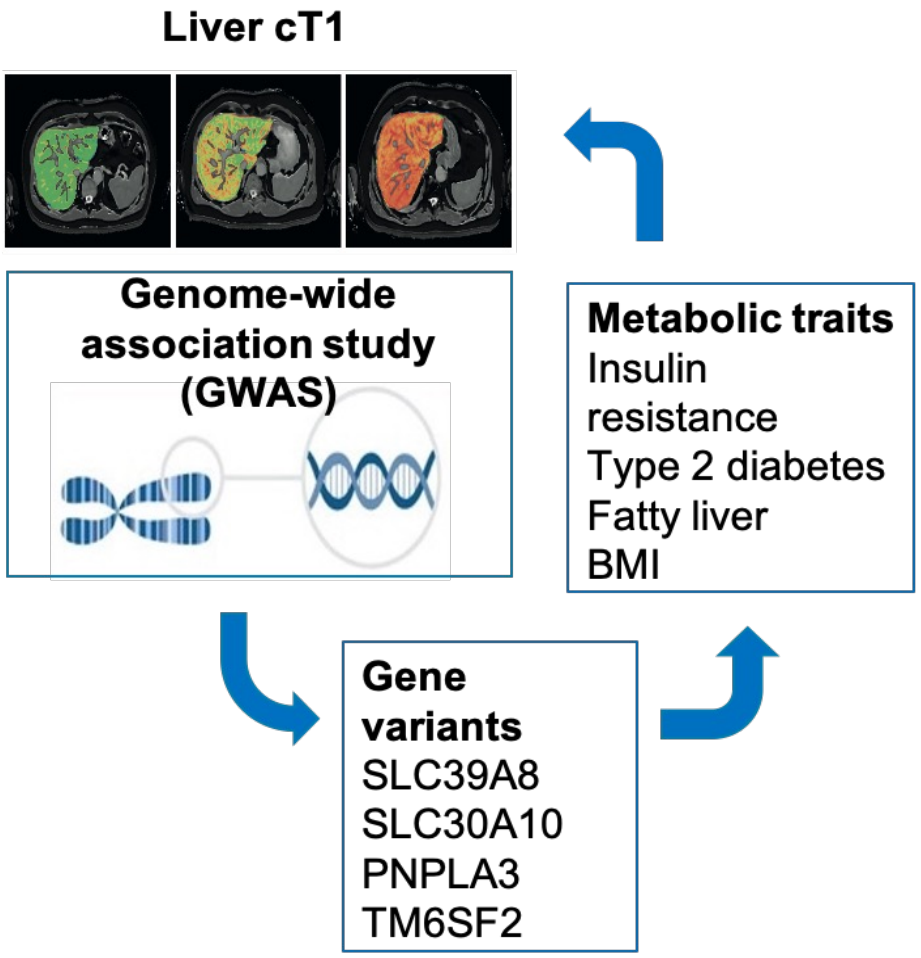
Actionable, integrated results

Better decision support and care

cT1 helped identify new genetic target for drug development

GWAS in 14,440 Europeans from UK Biobank with cT1 measures

JOURNAL OF HEPATOLOGY



Insulin resistance, T2D, fatty liver and BMI are causally linked with increased cT1 as a marker of fibro-inflammatory disease.

Genetic variant	Risk factors
SLC39A8	New risk factor for steatohepatitis and fibrosis
SLC39A8	New risk factor for steatohepatitis and fibrosis
PNPLA3	Known risk factor for steatosis (also influenced PDFF)
TM6SF2	Known risk factor for steatosis (also influenced PDFF)

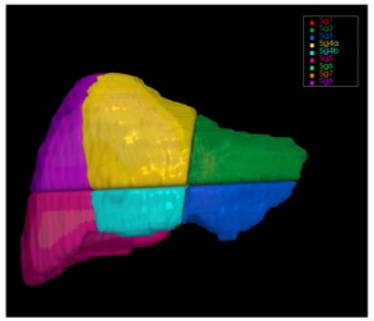
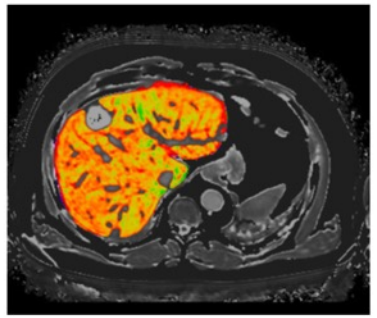
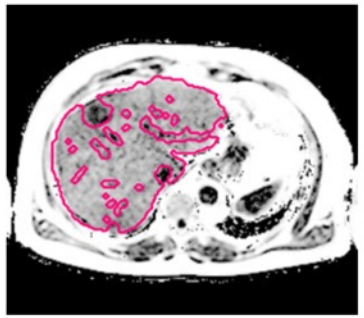
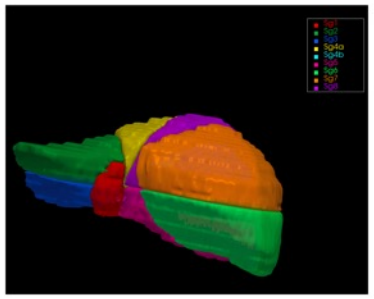
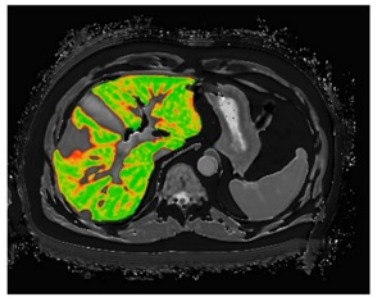
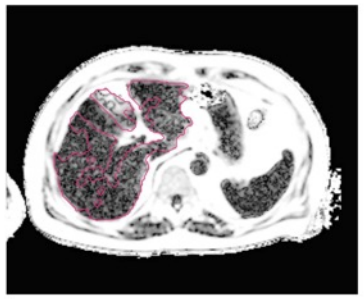
Four genetic variants influencing liver cT1 were correlated with blood tests and metabolic traits.

cT1, corrected T1; GWAS, genome wide association study; T2D, type 2 diabetes; BMI, body mass index

Parisinos et al. (2020). *Journal of Hepatology*, *73*(2), 241-251.

Improving patient outcomes by helping to plan safer surgeries

Two patients with similar pre-operative characteristics had liver resection but different post-operative outcomes

Volume	Disease activity Reference range: 688-794 ms	Fat Reference range: <5.6 %
		
Volume = 1506 mL	cT1 = 829 ms	PDFF = 14 %
		
Volume = 2188 mL	cT1 = 728 ms	PDFF = 3 %

Patient 1

- MRI showed high disease activity (cT1) and fat (PDFF)
- Future liver remnant: 23%
- Post-hepatectomy liver failure, 14 days in hospital

Patient 2

- MRI showed normal disease activity (cT1) and liver fat (PDFF)
- Future liver remnant: 29%
- Uneventful post-operative course, 3 days in hospital

Supporting surgeons to make more informed pre-operative decisions

cT1 – corrected T1; PDFF – proton density fat fraction

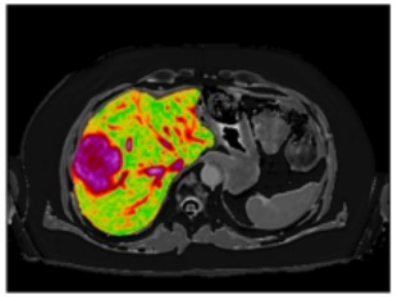
Sethi, P., et al. (2021). *BJR | Case Reports*, 6, 20200172.

Significant cost-savings through early identification of patients at risk of poor post-operative outcomes

Pre-operative cT1 is predictive of duration of post-operative hospital stay

Small estimated FLR

Normal cT1 (cT1<795ms)

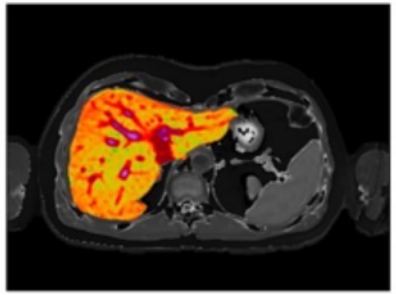


Augmented clinical decision:

- In favour of surgery
- Potential for extended hepatectomy

Large estimated FLR

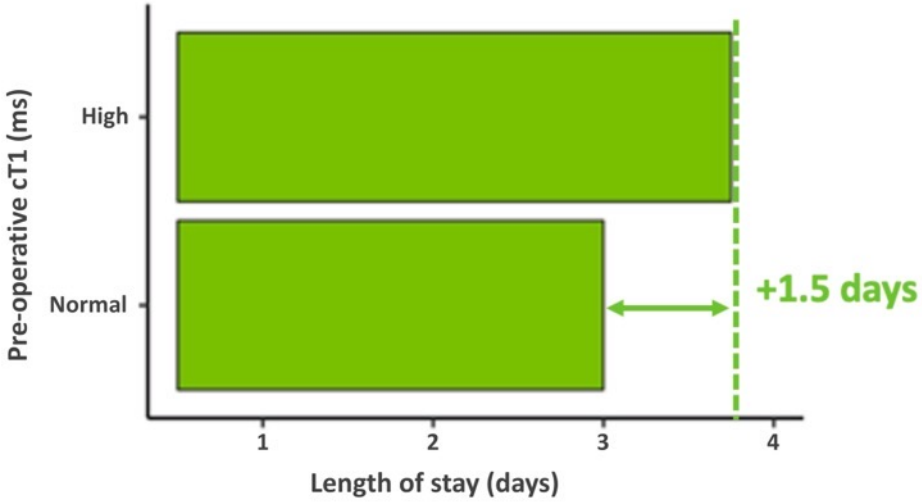
High cT1 (cT1 ≥ 795ms)



Augmented clinical decision:

- Consider alternatives to surgery
- Counsel patient of increased risk of hepatectomy

Median length of post-operative hospital stay was 1.5 days longer in patients with high pre-operative cT1 (cT1 ≥795ms), than those presenting with normal cT1.



Perspectum provides a non-invasive, quantitative, individualised indicator of surgical risk, with potential to inform clinical decisions drove patient outcomes

Mole et al. PLOS ONE 2020

Sequencing and MRI in metastatic colorectal cancer patients

35

Whole Genome Sequencing

mpMRI

18 Actionable mutations in clinical practice

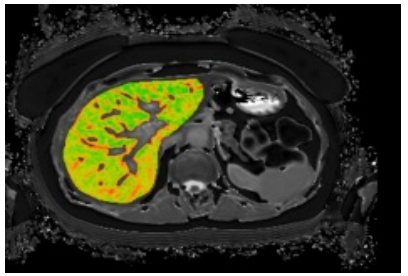
6 Actionable mutations NOT in clinical practice

20 Eligible for clinical trials

7 Mutations with prognostic significance

Multidisciplinary Team

mpMRI



Low risk

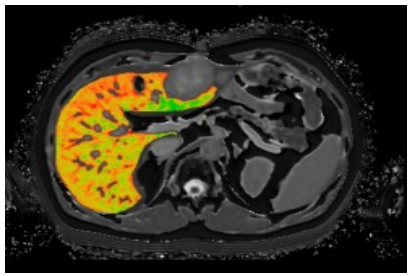
WGS

APC *KRAS*

Good prognosis

Outcome Recovered well

mpMRI



Steatohepatitis

WGS

APC *TP53* *KRAS* *POLQ* *ATM*

Poor prognosis

Outcome RIP < 1 year

The combination of genomic and imaging information supports clinical decisions

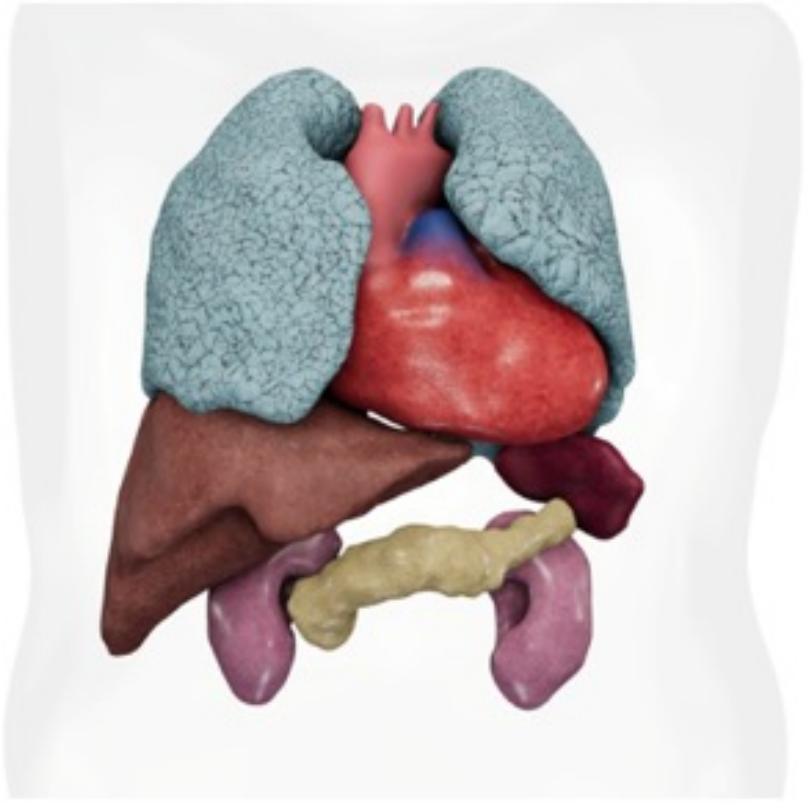
Perspectum

WGS: whole genome sequencing; mpMRI: multiparametric magnetic resonance imaging; OS: overall survival

AI in cardiometabolic disease - imaging and decision support

More patients, need scalability and data collection of clinical outcomes

Moving beyond glucocentric/weight-based care



GLP-1s have reported significant improvements in the following organs:

- Liver
- Heart
- Kidney
- Pancreas

What can you measure with multiorgan imaging at scale

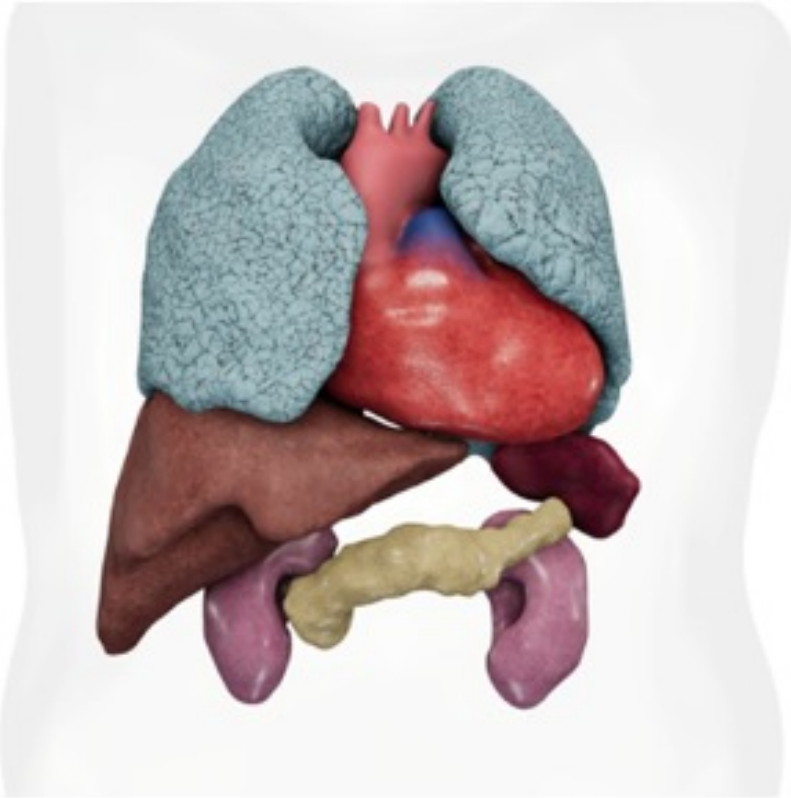
40 min acquisition, FDA cleared software as a medical device (SAMD)

Liver
Fat
Fibro Inflammation
Iron Load
Volume
Stiffness
Biliary health

Pancreas
Fibrosis
Fat
Volume

Kidneys
Fibrosis (T1)
Function (DWI)
Blood Oxygenation (BOLD)
Volume (TKV)

Lungs
Fractional Area Change
Volume



Aorta
Distensibility
Lumen Diameter
Wall Thickness

Heart
Atrioventricular Function
LV Mass, Thickness, Thickening
Ejection Fraction
LV T1 and T2 Mapping
LV Strain

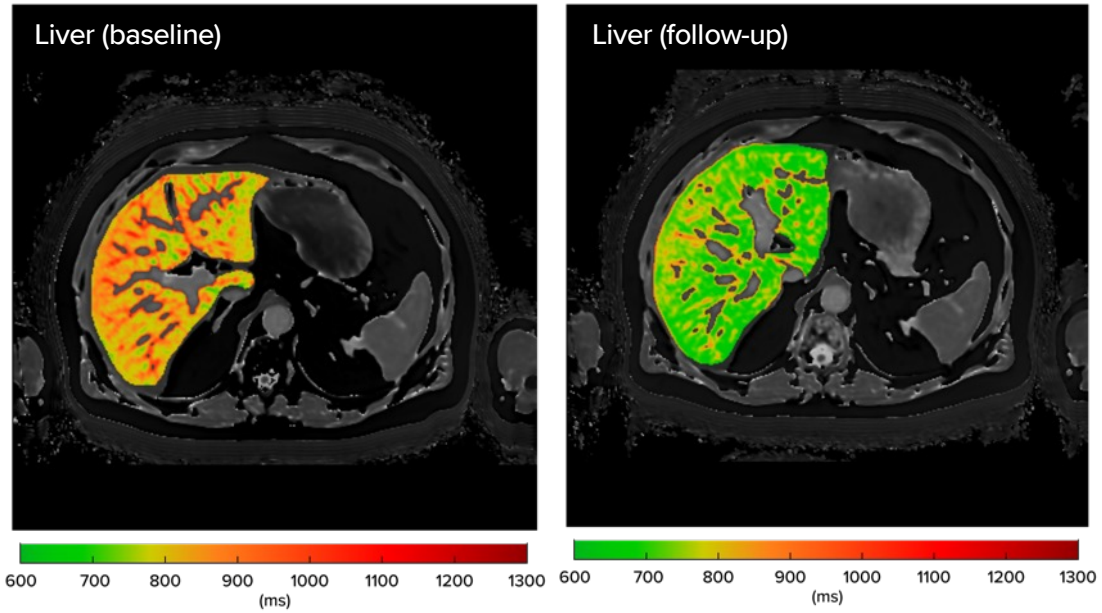
Spleen
Fibrosis
Volume
Portal Hypertension

Body Composition
Visceral Adipose Tissue (VAT)
Subcutaneous Adipose Tissue (SAT)
Lean Muscle Mass
Muscle Fat Infiltration (MFI)

Is it all about weight loss?

- 62 yr-old male, BMI of 30 kg/m^2, living with type 2 diabetes for 12 years, being treated with **metformin**, **sulphonylurea** and **SGLT2 inhibitors** in secondary care.

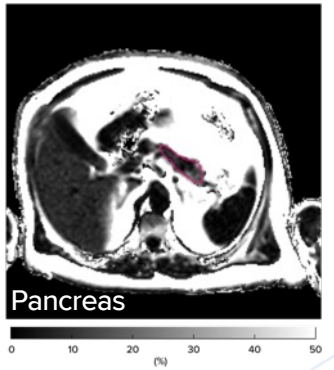
- Clinically significant reduction in liver disease activity (cT1) over 7 months, **despite no weight change**.

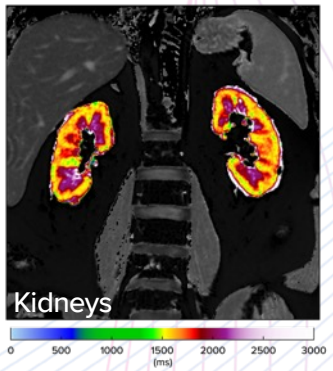


High liver cT1
(828ms)
Reference range:
<800ms

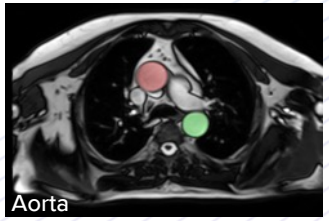
Normal liver cT1
(722ms)
Reference range:
<800ms

High pancreatic fat
(7.1%)
Reference range:
<4%

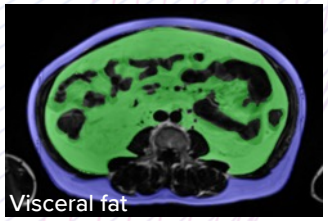




High cortical T1
(L: 1520ms;
R: 1580ms)
Reference range:
L: <1527ms
R: <1516ms



Low aortic distensibility
(Ascending [red]: 0.37 x10^{-3} mmHg^{-1}
Descending [green]: 0.80 x10^{-3} mmHg^{-1})
Reference range:
Ascending: >1.44 x10^{-3} mmHg^{-1}
Descending: >2.91 x10^{-3} mmHg^{-1}



High VAT [green] (361cm^2)
Normal SAT [blue] (156cm^2)
Reference range:
VAT <217cm^2
SAT <238cm^2

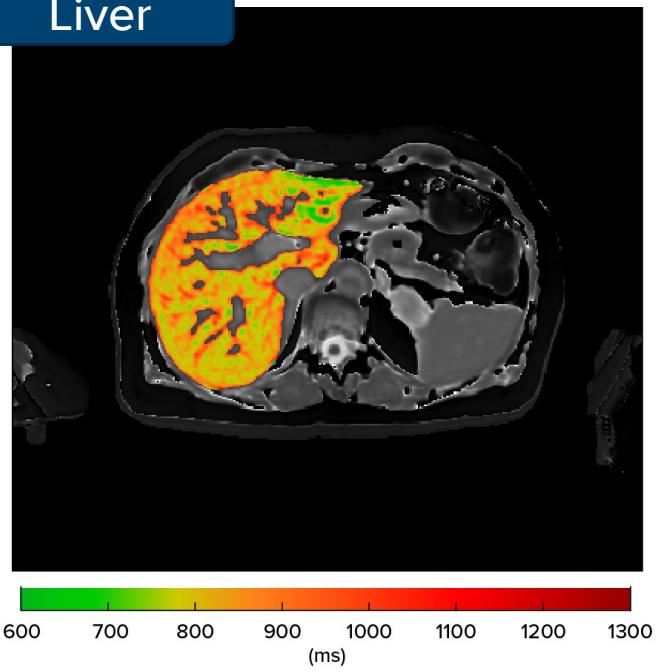
Case study: Disease activity without obesity

- 57-year-old female, smoker, BMI = 25 kg/m^2.
- Patient diagnosed with type 2 diabetes and retinopathy for 4 years.

Liver

High liver cT1 (825 ms)

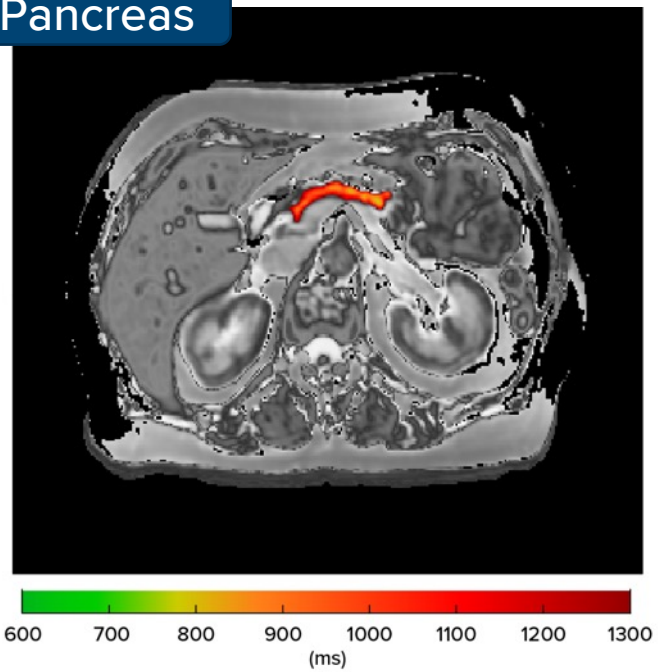
Normal reference range: < 800ms



Pancreas

High pancreas srT1 (909 ms)

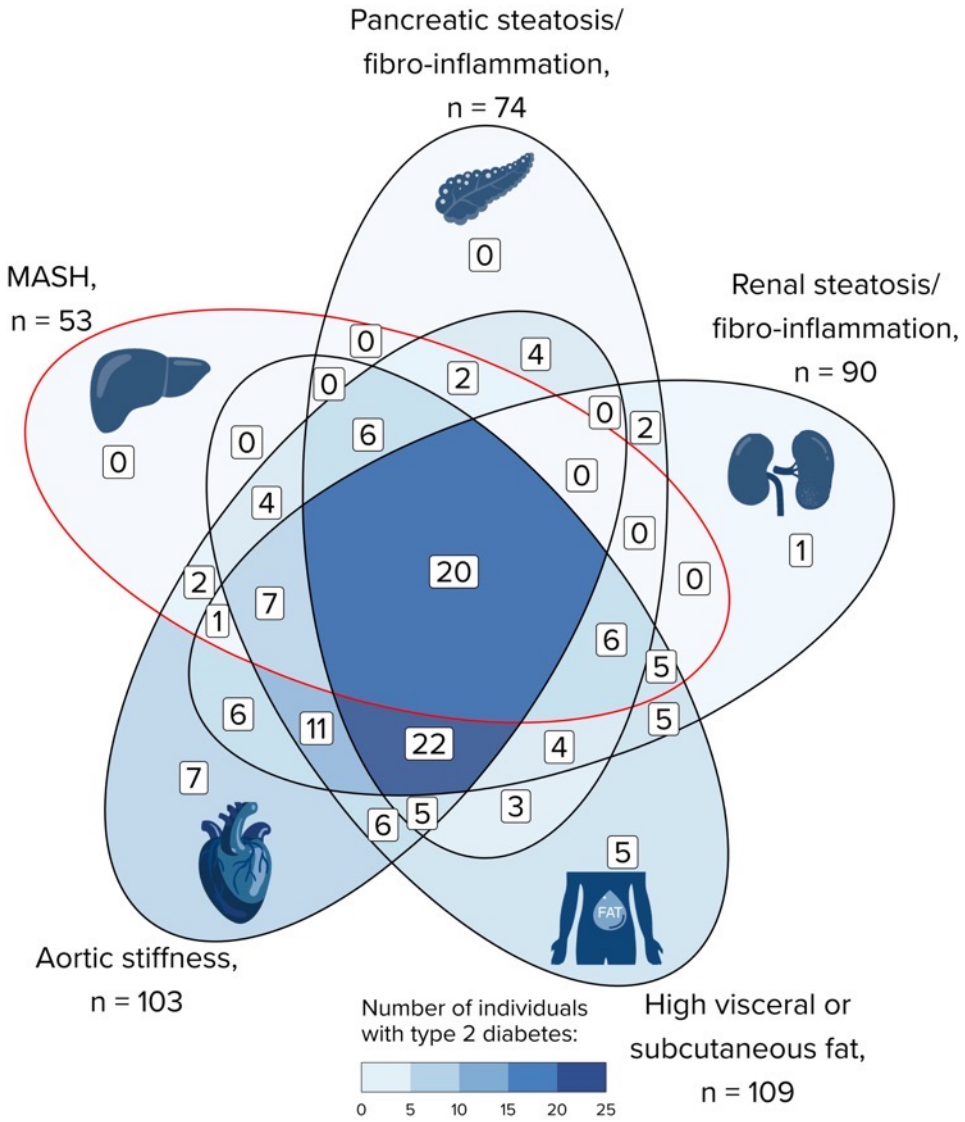
Normal reference range: < 836ms



CoverScan identified liver and pancreas disease activity without high BMI.

cT1: iron-corrected T1; srT1 scanner referenced T1; BMI: body mass index

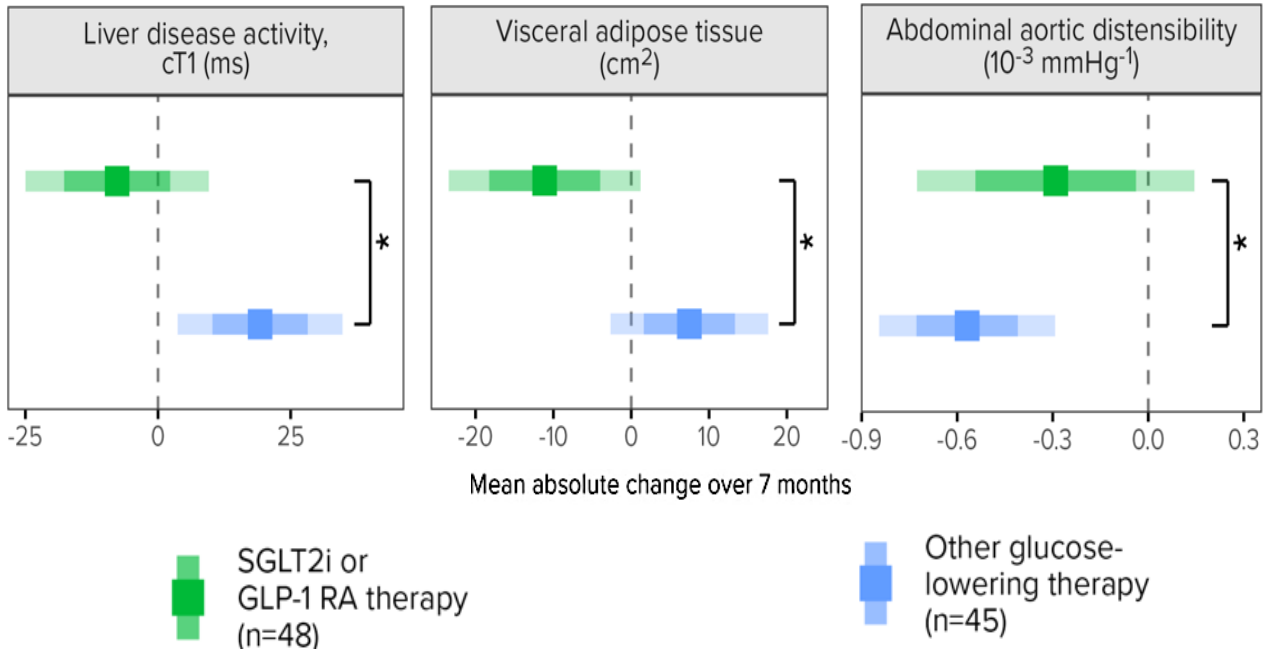
Multi-organ imaging can stratify and monitor metabolic disease



diabetes

- 134 patients scanned and followed up.

After 7 months, **multi-organ imaging** showed improvements with SGLT2i or GLP-1 RA therapies, *but NOT with other therapies*.

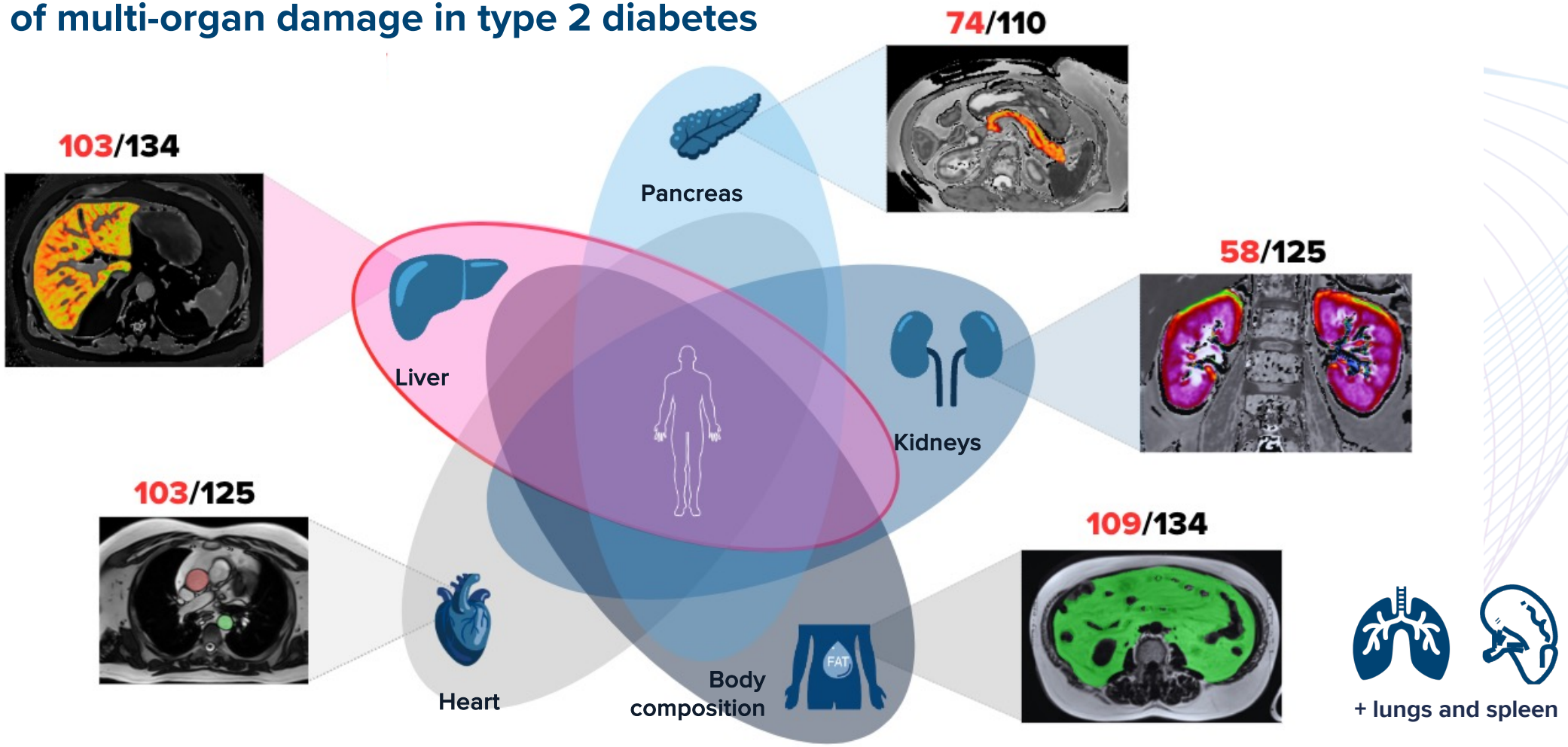


Perspectum

Quantitative imaging reveals steatosis and fibro-inflammation in multiple organs in people with type 2 diabetes; Diamond, et al. (2023)

Profiling Metabolic Disease in a Single Scan

High burden of multi-organ damage in type 2 diabetes

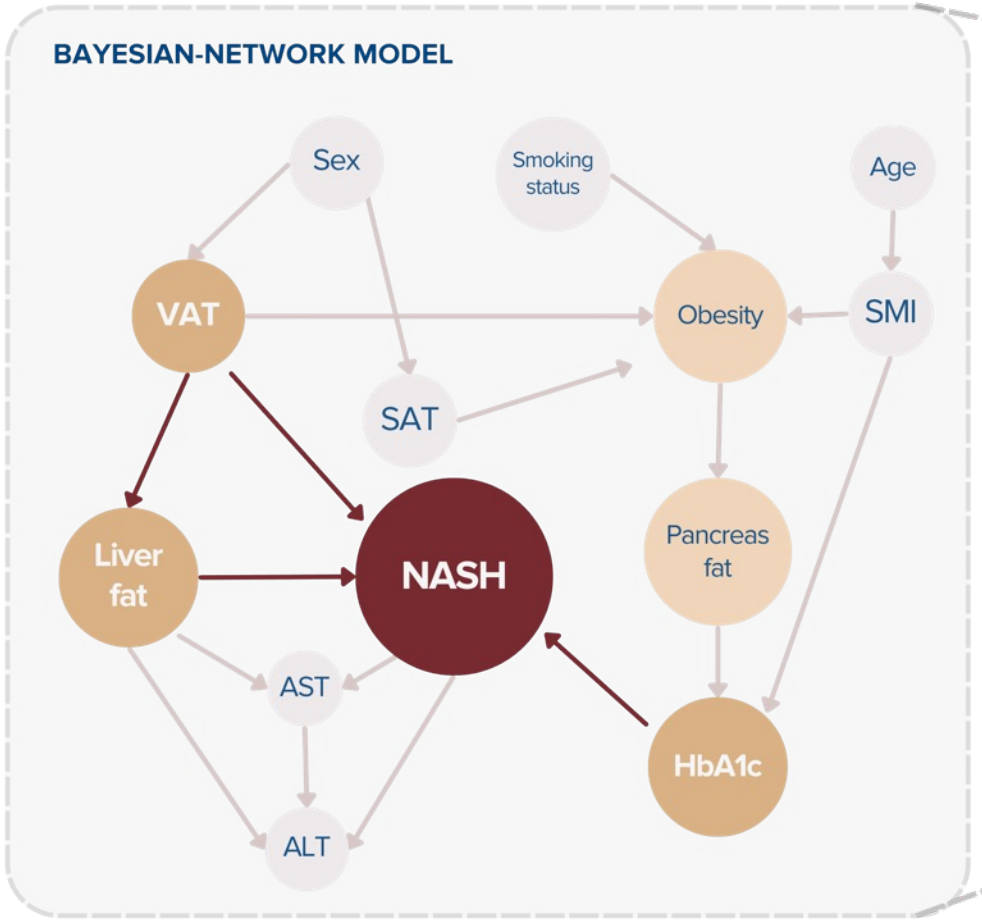


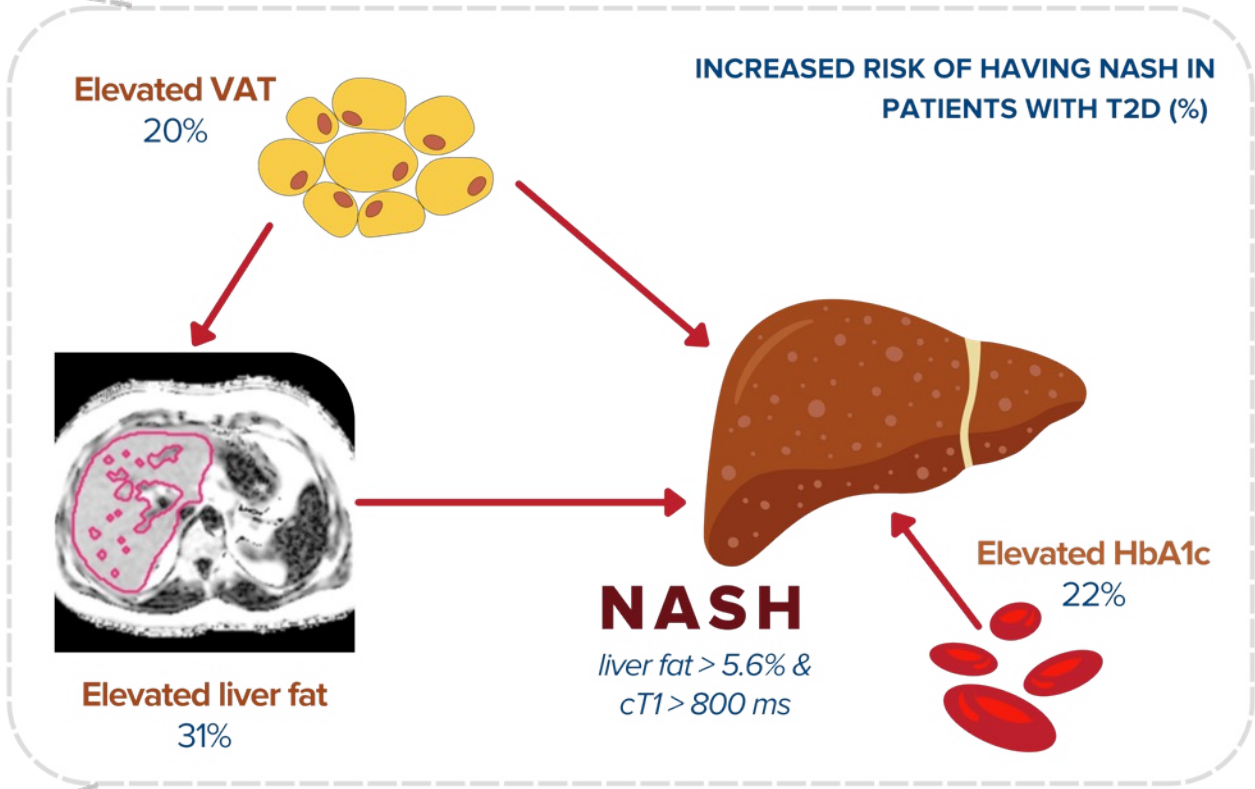
N = T2DM patients with organ abnormality
N = total T2DM patients

Routine T2DM treatments → Minimal effects on end-organs at follow-up (7 months)

Quantitative imaging reveals steatosis and fibro-inflammation in multiple organs in people with type 2 diabetes; Diamond, et al. (2023)

Multi-organ imaging shows that the risk of NASH increases with elevated ectopic fat and poor glycaemic control





cT1, corrected T1; T2D, type 2 diabetes; VAT, visceral adipose tissue; HbA1c, glycated haemoglobin

Study findings may have important implications for the development of targeted drug therapies to prevent NASH in high-risk populations with T2D.

Waddell, T., et al. (2023). *Frontiers in Endocrinology*, *14*, 412.

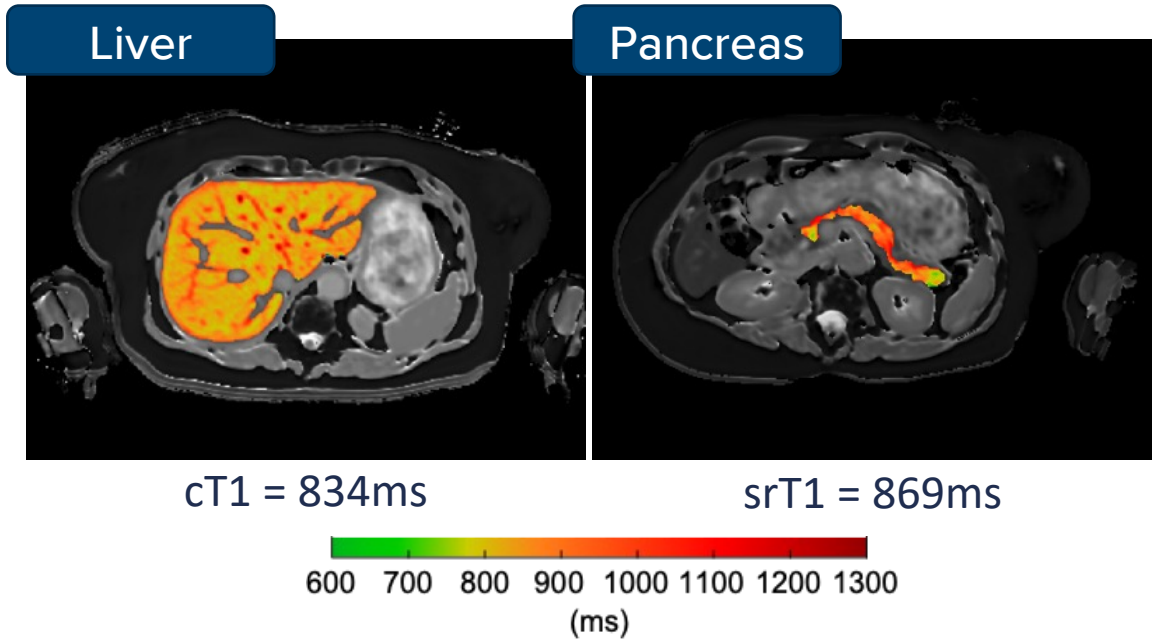
Fibro-inflammation in both liver and pancreas is associated with increased risk of cardiovascular and liver hospitalisation

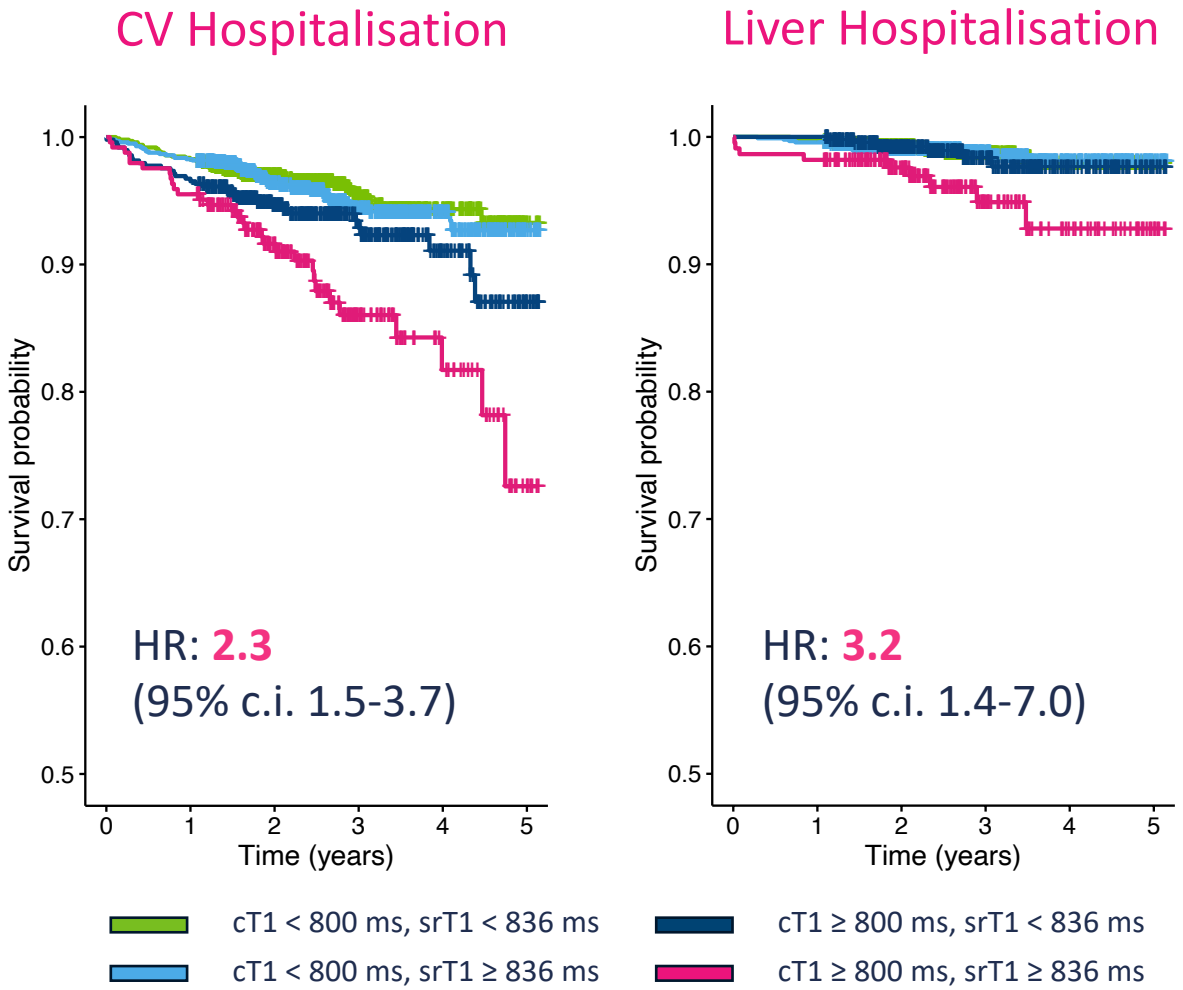
28,859

UK Biobank participants over **5 year** follow up

245

participants with fibro-inflammation in **liver** and **pancreas**:





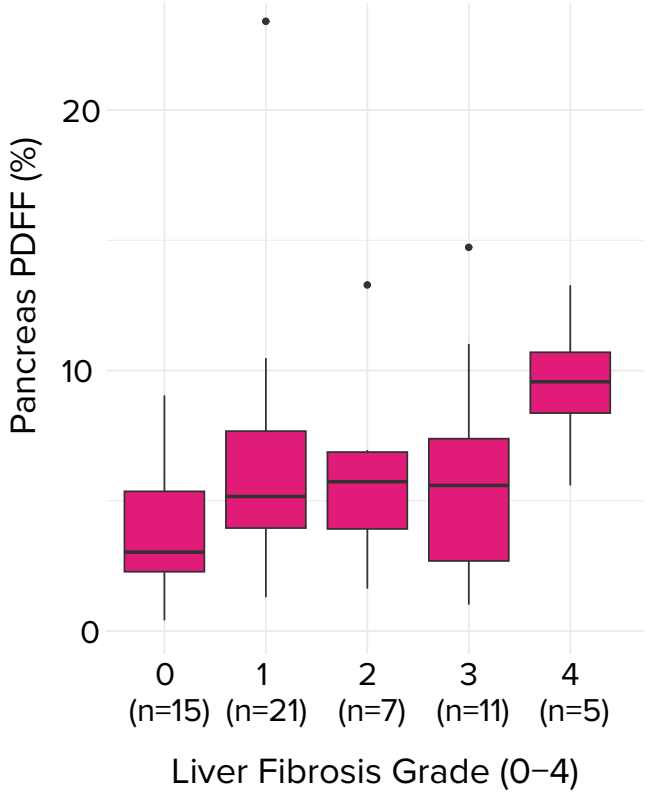
Perspectum

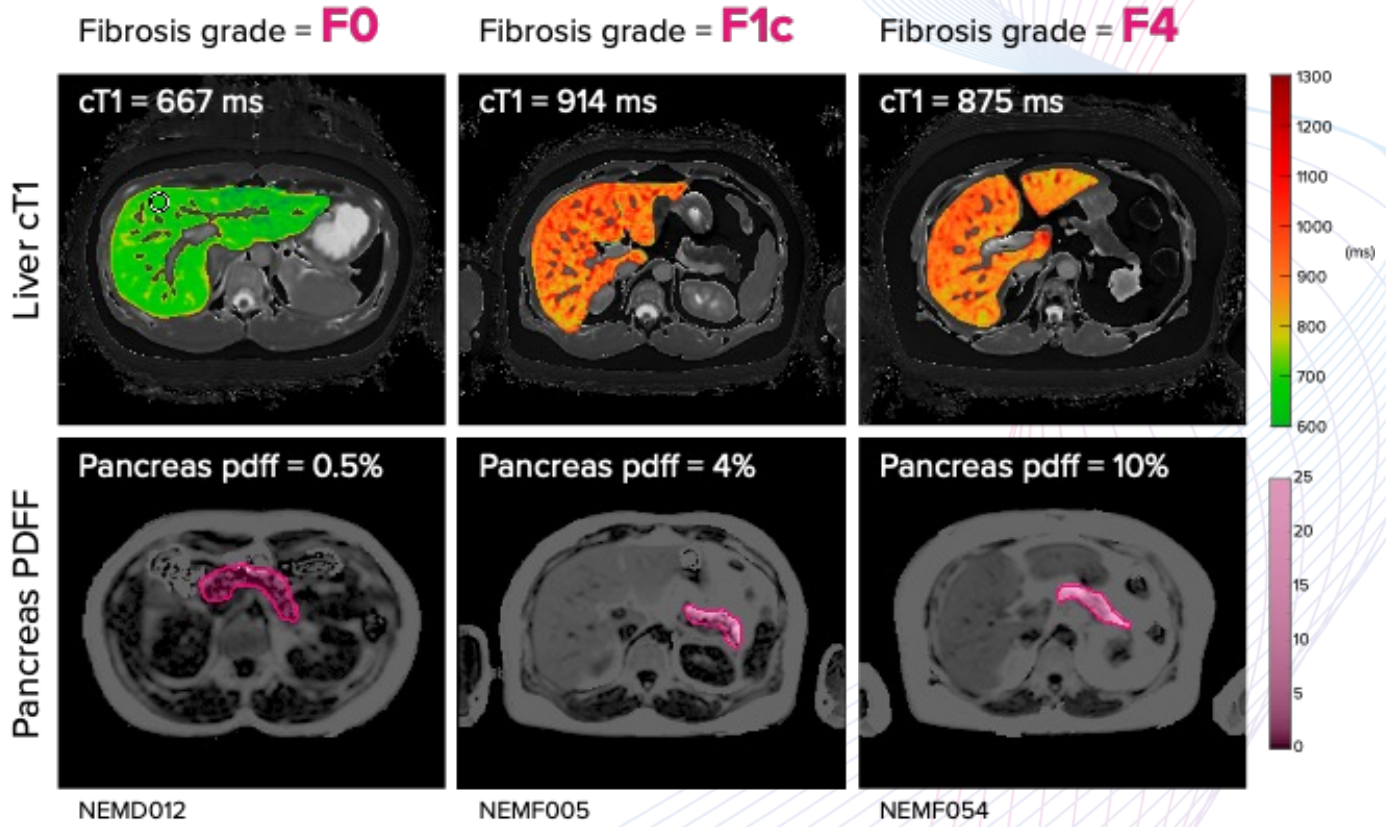
Jackson E. et al., Multi-organ pathophysiology in the liver and pancreas increases risk of liver and cardiovascular events: results from the UK Biobank (Poster, Innovations in SLD Think Tank 2024)

High pancreatic fat identifies patients with most severe metabolic liver disease

59 **INDIVIDUALS**

South-east Asian individuals
(19% Malaysian, 61% Chinese, 12% Indian, 46% male, median BMI 29 kg/m^2, median age 38 years)
with biopsy-proven MASLD.





Measuring pancreatic health matters

Perspectum

Jackson, E., et al. High pancreatic fat and reduced volume stratify patients with F4 liver fibrosis (2024).

NUS National University of Singapore

MRI cT1 predicts liver and cardiac outcomes

197 CLD PATIENTS: 693 PATIENT-YEARS

In a study of 197 patients over a median of 43 months, cT1 was shown to be the best noninvasive predictor of clinical outcomes in CLD.

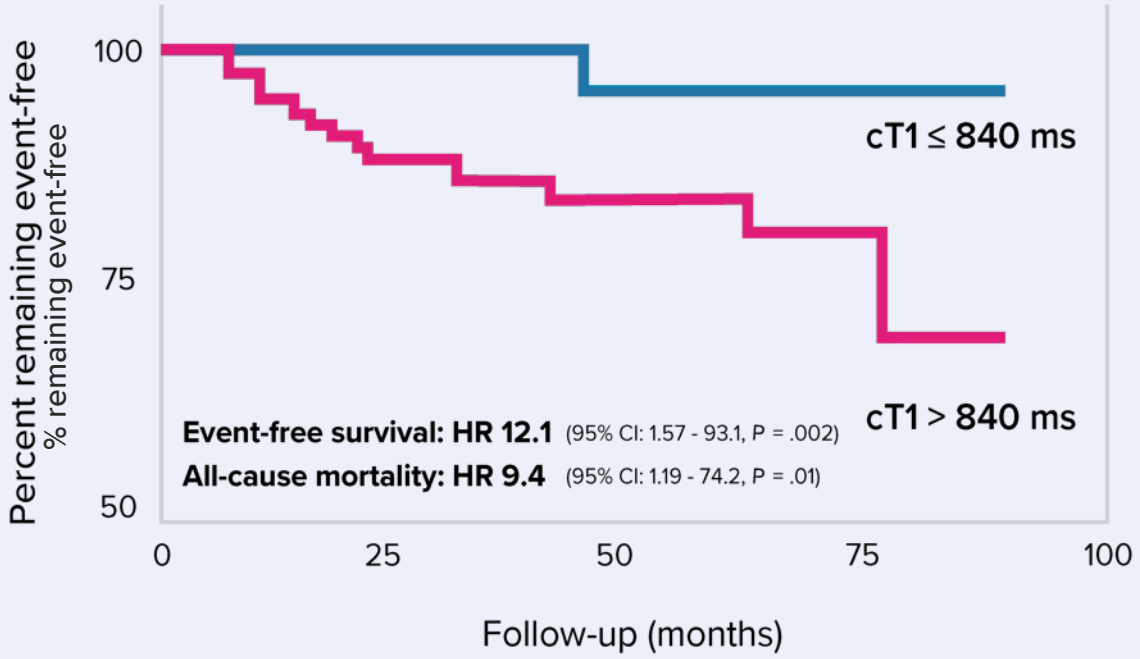
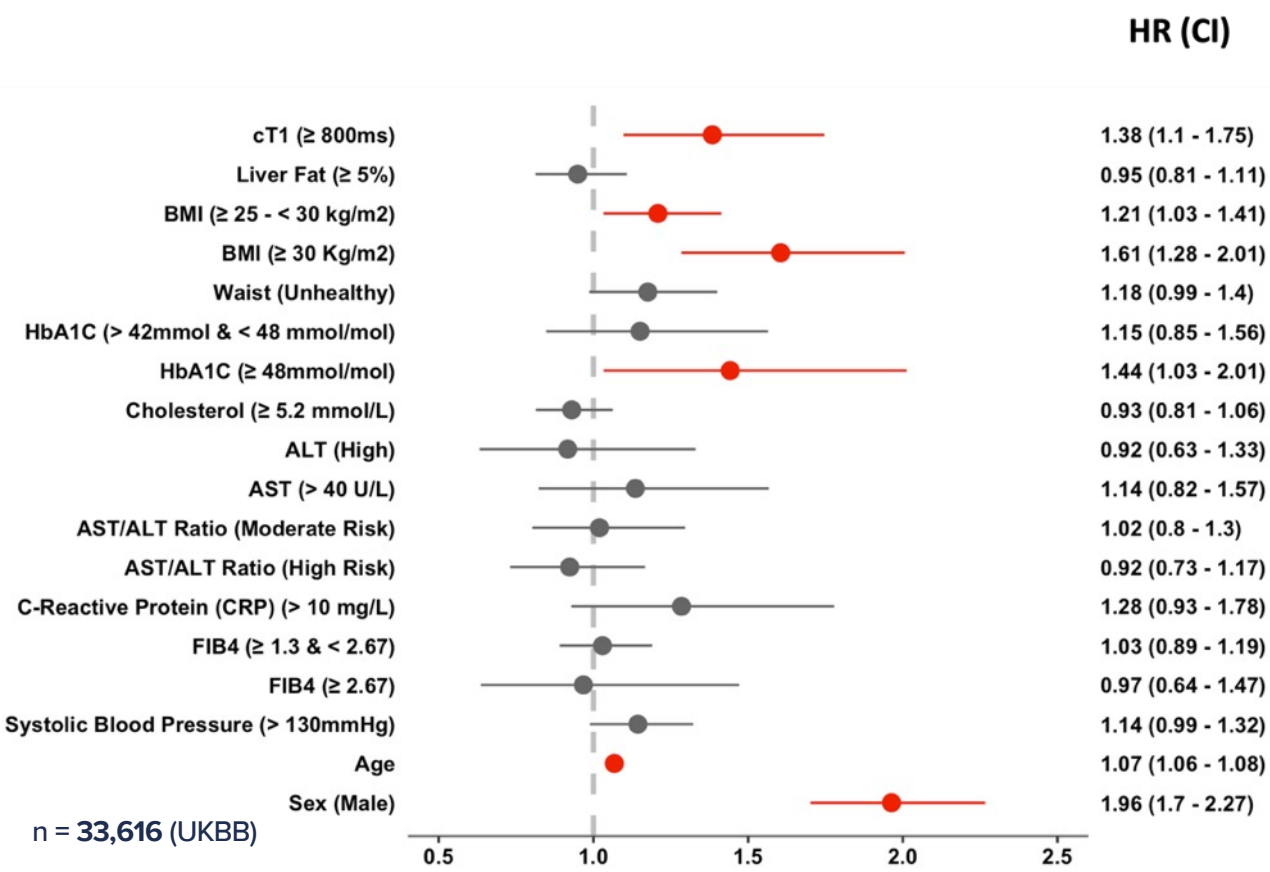


Figure: Kaplan-Meier plots of the percentage of chronic liver disease (CLD) patients remaining event-free, stratified by cT1 > 840 ms, demonstrates how cT1 can help to predict clinical outcomes. Adapted from Jayaswal et al, 2020[10]

cT1 ≥ 800 MS PREDICTS HOSPITALIZATION DUE TO CVD IN THE GENERAL POPULATION; PDFF AND FIB-4 DO NOT



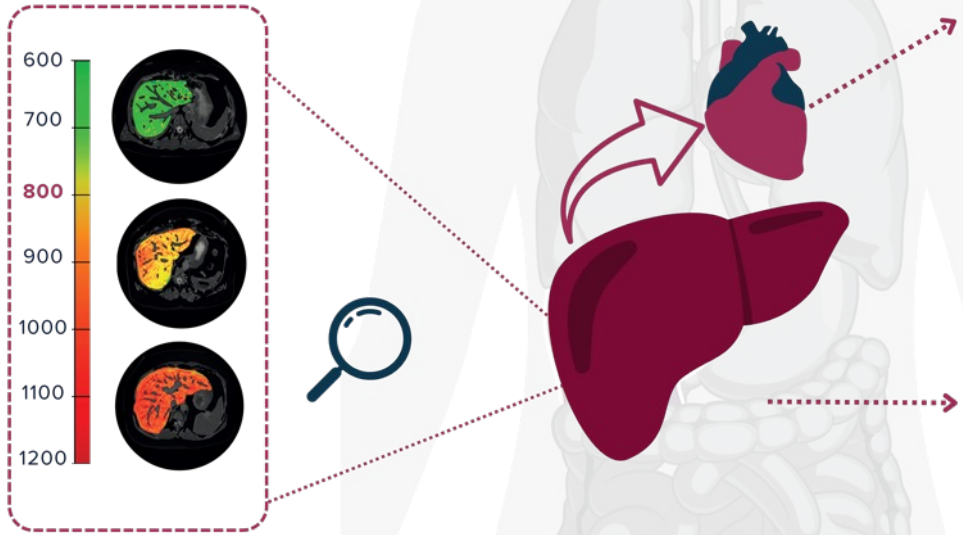
n = **33,616** (UKBB)

CVD: cardiovascular disease

Jayaswal et al., Liver Intern. 2020; Roca-Fernandez et al., JHEP. 2023

Early liver disease is a modifiable risk factor for heart disease

JOURNAL OF HEPATOLOGY



LiverMultiScan results from 33,316 UK Biobank participants revealed that **INCREASING cT1 was associated with an INCREASED RISK of developing:**

Cardiovascular events:

Hospitalization:	1.27 (1.18 - 1.37)
Atrial fibrillation:	1.3 (1.12 - 1.51)
Heart failure:	1.3 (1.08 - 1.58)
Any cardiac event:	1.14 (1.03 - 1.26)

All-cause MORTALITY: 1.19 (1.02 - 1.38)

Hazard ratios (with 95% confidence intervals)

The association of cT1 with higher risk of future CVD events, independent of blood biomarkers and FIB4, highlights liver disease activity as a risk factor for heart disease.

CVD: cardiovascular disease; cT1: corrected T1; FIB4: fibrosis 4

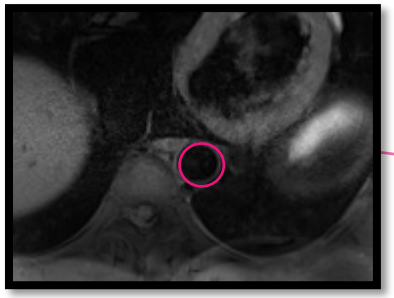
Roca-Fernandez et al, J Hepatol. 2023. 20:S0168-8278(23)00420-8

Tissue characterization without needles

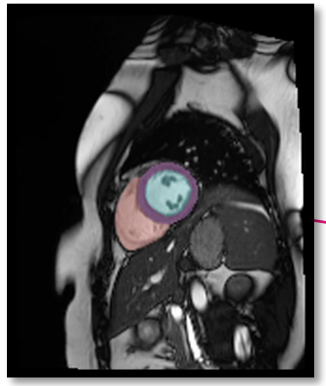
Let’s look at the heart, pancreas and kidneys

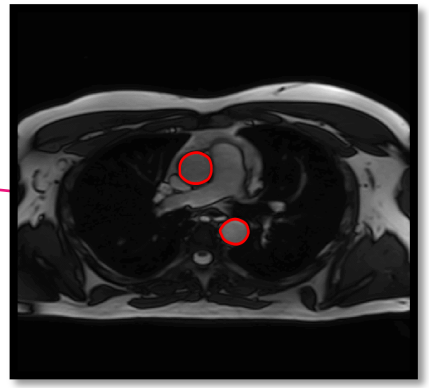
Cardiac MRI for Structural and Functional Assessment

Lumen Diameter
Wall Thickness

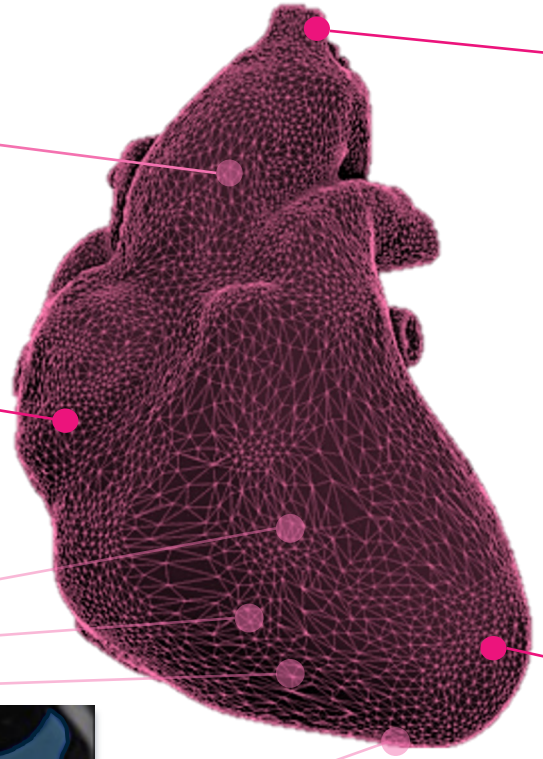


Diastolic Function



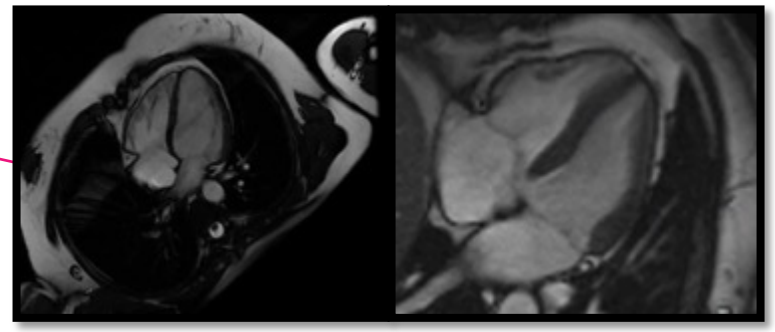


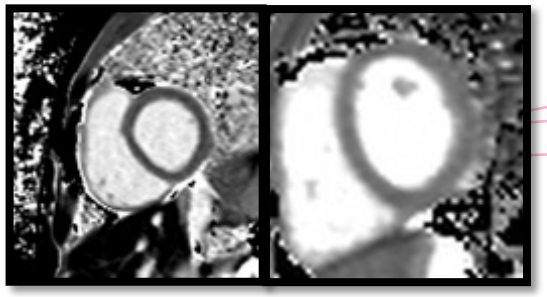
Aortic Strain
Aortic Distensibility



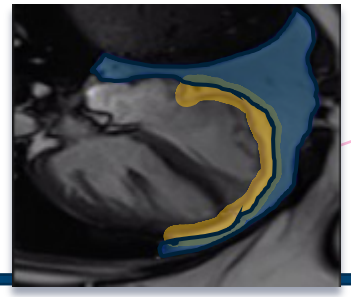
Mass
Wall Thickness
Wall Thickening

Systolic Function
Ejection Fraction
Cardiac Strain
Volume Index





T1, T2 Mapping
(16 segments)



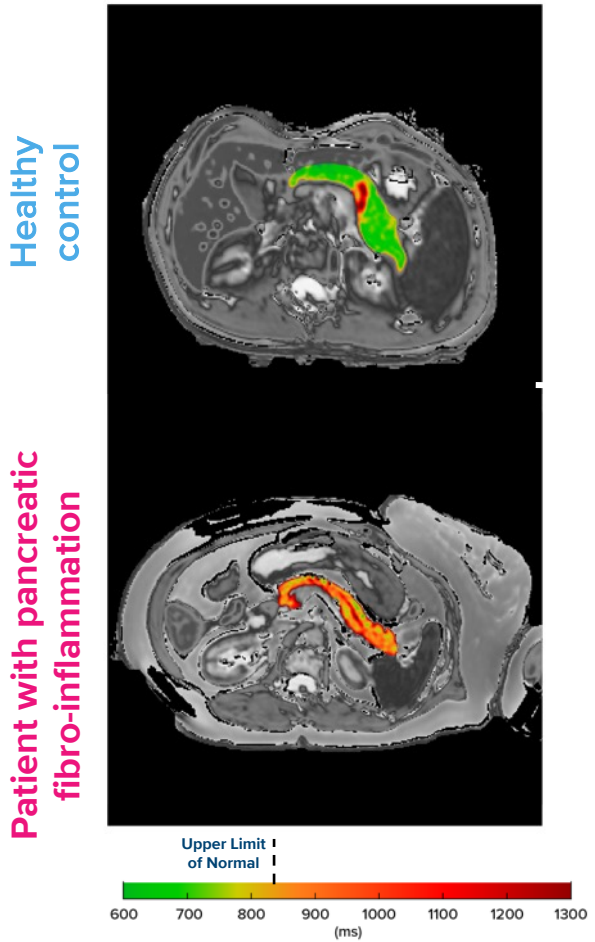
Pericardial Fat
Epicardial Fat

Metrics consolidated following the 2020 guidance of Society for Cardiovascular Magnetic Resonance regarding image interpretation and post-processing

Pancreas Imaging Metrics

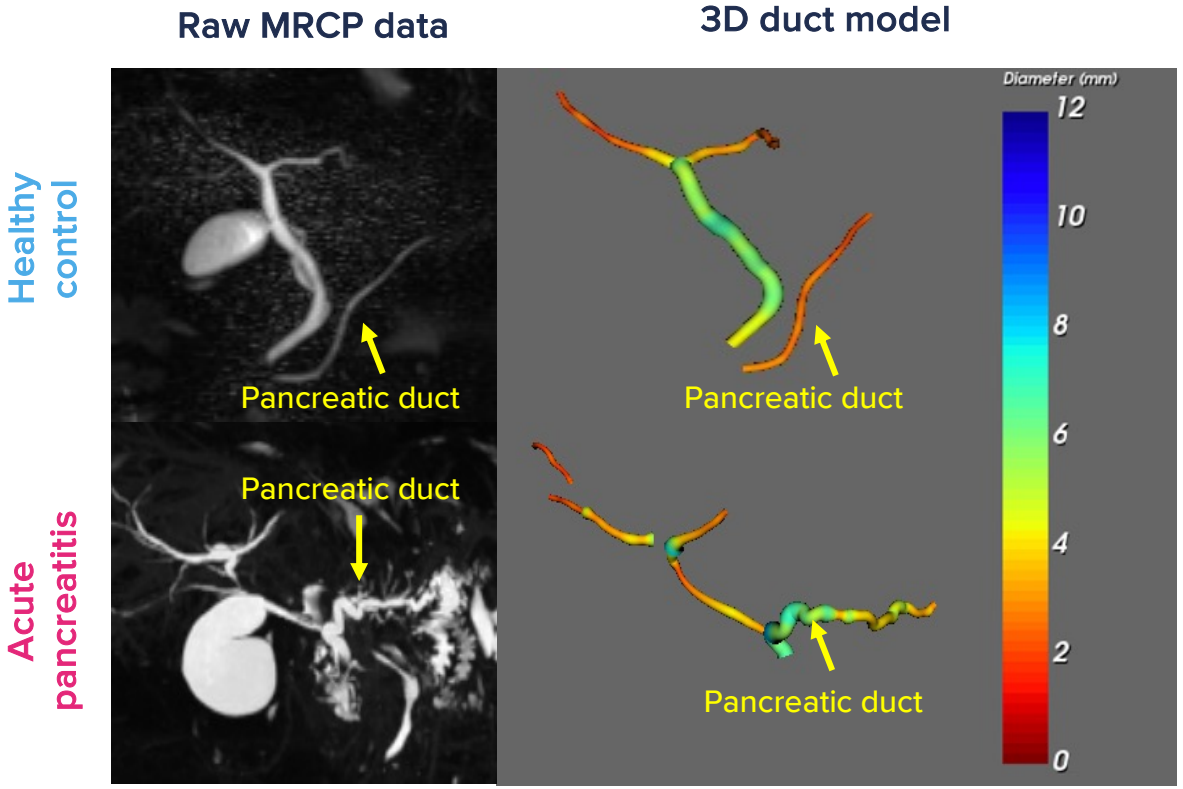
Pancreatic srT1:

- Elevation can indicate oedema or fibrosis
- Discriminates acute pancreatitis and resolves in response to anti-inflammatory tx[1]
- Can stage chronic pancreatitis[2] and pancreatic fibrosis[3]
- Correlates with reduced exocrine function in PDAC and chronic or autoimmune pancreatitis[4]



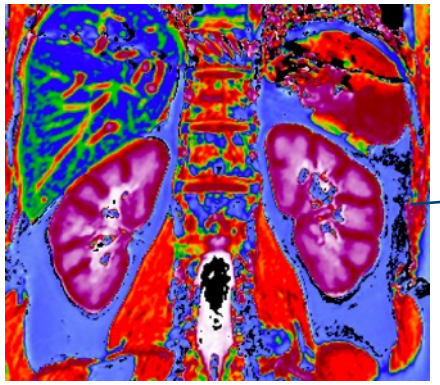
Ductal morphology:

- Quantifies enlargement of pancreatic and common bile duct[5]
- Measures median and maximum duct diameter

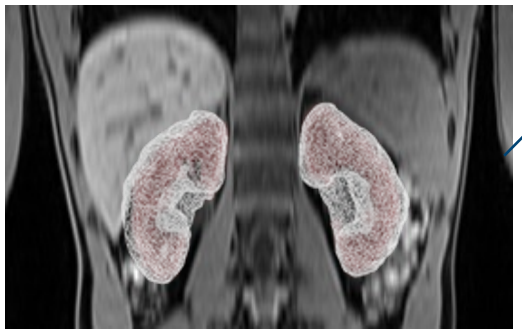


1. Zhu, et al., 2019 2. Wang, et al., 2020; 3. Liu, et al., 2021; 4. Ashihara, et al., 2020; 5. Goldfinger, et al., 2020

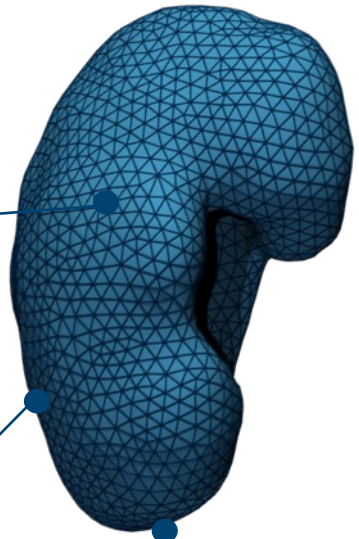
Renal MRI for Functional and Structural Assessment



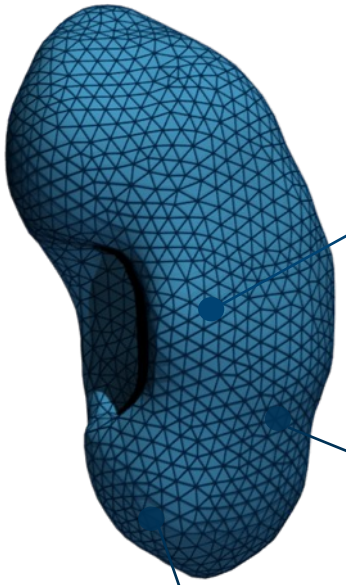
Cortex & Medulla T1



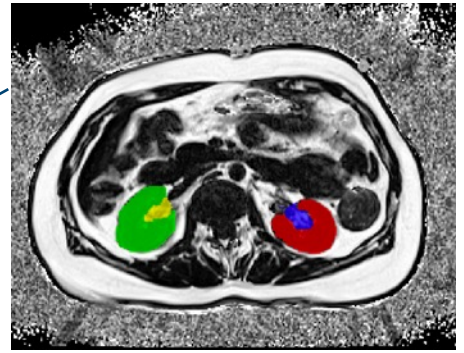
Total Kidney Volume



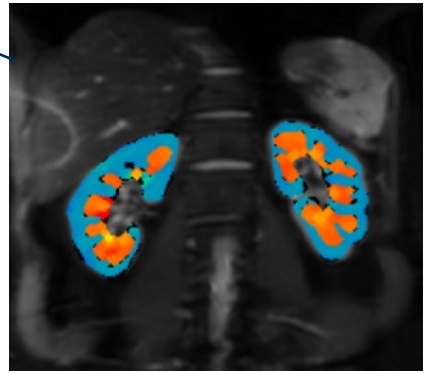
Cyst Volume



Cortex & Medulla BOLD



Peri-renal fat &
Renal sinus fat



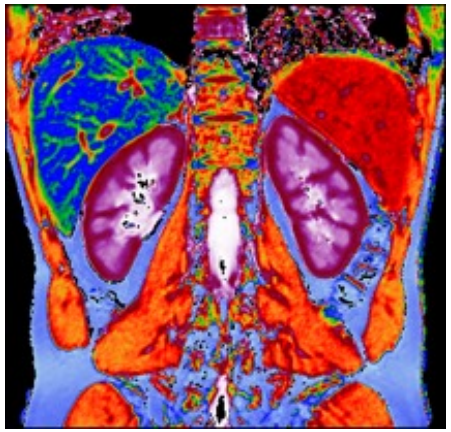
Cortex & Medulla ADC

Example of Typical Renal Protocol

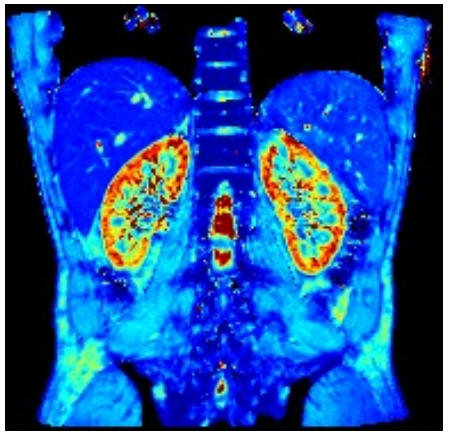
All kidney metrics can be acquired directly via a single, non-contrast MRI scan

Patient Preparation	Localizer	T1 Acquisition	BOLD Acquisition	DWI Acquisition	Post Scanning
2 minutes	1 minute	11 seconds	15 seconds	3 minutes	1 minute

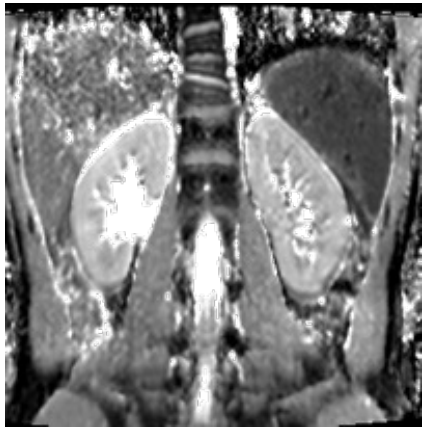
Fast Data Acquisition



T1 Map



BOLD Map



Diffusivity Map

List of renal metrics acquired over the duration of the scan:

- ❑ Volume (TKV)
- ❑ Length
- ❑ Presence of Cysts
- ❑ Cortex T1
- ❑ Cortex thickness
- ❑ Medulla T1
- ❑ Medulla ADC (DWI)
- ❑ Cortex ADC (DWI)
- ❑ Kidney Oxygenation (BOLD)

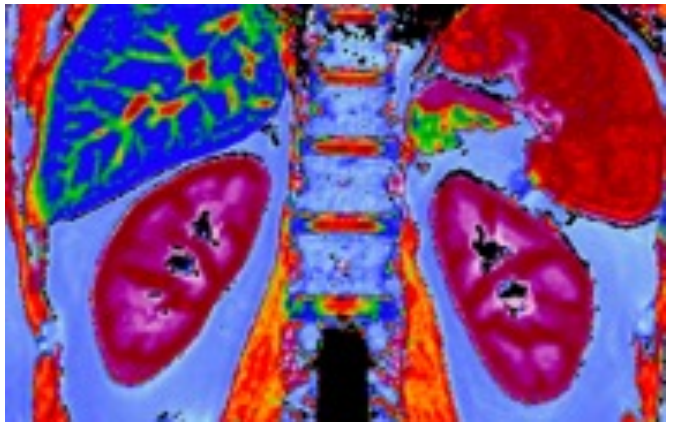
Required

Optional

Comprehensive kidney characterization

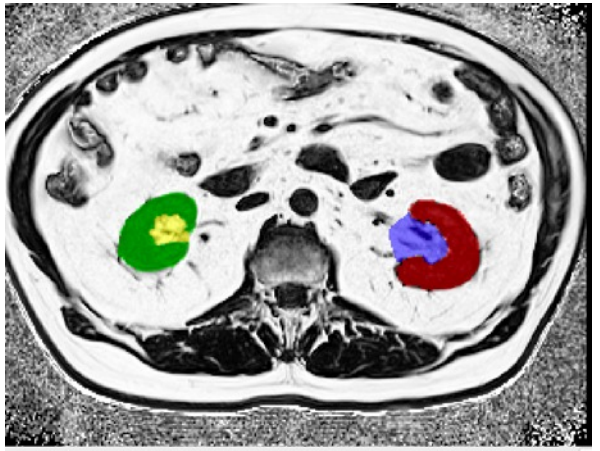
Fibrosis, Inflammation, Oedema (T1)

- **Metrics: Cortex T1, Medulla T1, ΔT1**
- Correlates with eGFR[1,4]
- Correlates with kidney fibrosis[1,4]
- Staging of CKD[4]
- Significantly increased in patients with IgAN[5]



Fat Content (Dixon)

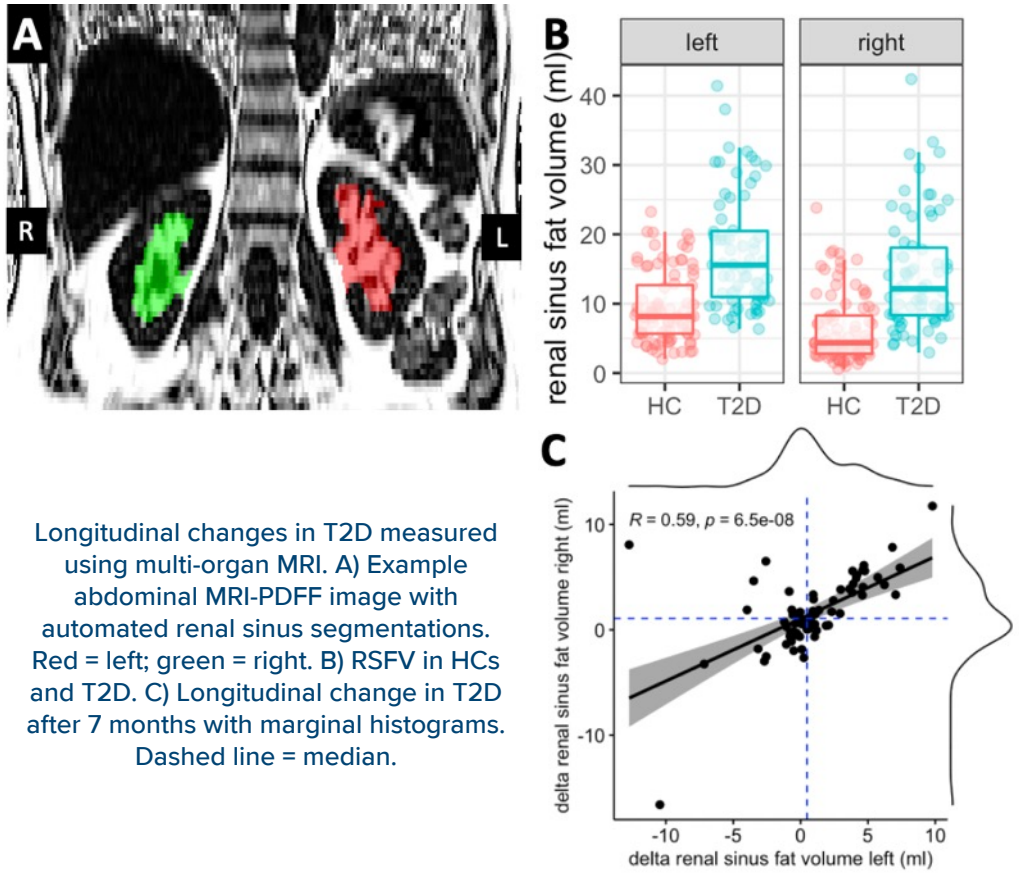
- **Metrics: Peri-Renal Fat, Sinus Fat Volume, Renal Sinus Fat, Volume/Parenchyma Volume ratio**
- Kidney fat independently associated with increased risk of CKD (OR 1.86)[6]
- Peri-renal fat might act as a marker of poor prognosis in IgAN[3]
- Correlates with eGFR[8], albumin-creatinine ratio and HbA1c[7]



1. Berchtold et al. 2019, Nephrol Dial Transplant; 3. Hu et al. 2023. Kidney Diseases 4. Wu et al. 2021. Frontiers in Medicine; 5. Graham-Brown et al. 2019. BMC Nephrol.; 6. Foster et al. 2011, Hypertension; 7. Lin. Et al., Journal of Diabetes and its Complication 2021; 8. Spit et al. Magnetic Resonance Materials in Physics, Biology and Medicine, 2019; 9. Notoohamiprodjo et al. Plos One, 2020; 10. Fujioka et al. 2023, Clinical and Experimental Nephrology; 11. Zelicha et al 2018, Clinical Nutrition

Automated, repeatable MRI method can monitor fat around the kidney in patients with diabetes

- Renal sinus was defined by automatic segmentation of the kidneys to provide organ-specific measures of size and fat deposition using **multi-organ MRI** with potential as indicators of subclinical nephropathy.
- Renal sinus fat volume **was significantly higher in patients with T2D** compared to HC.
- **65%** of patients displayed increases in fatty infiltration to kidneys over seven months that were above scan rescan variability.



Longitudinal changes in T2D measured using multi-organ MRI. A) Example abdominal MRI-PDFF image with automated renal sinus segmentations. Red = left; green = right. B) RSFV in HCs and T2D. C) Longitudinal change in T2D after 7 months with marginal histograms. Dashed line = median.

Using multi-organ MRI to monitor kidney sinus fat in patients with diabetes can potentially improve their clinical management.

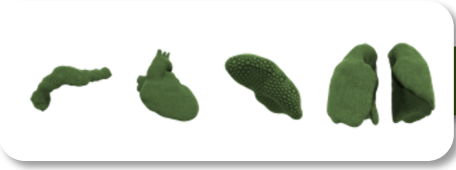
T2D: type 2 diabetes; HC: healthy control; RSFV: renal sinus fat volume

Perspectum

Eichert, N., et al. (2022). *Quantitative measurement of renal sinus fat volume using non-invasive MRI: A repeatable biomarker for monitoring kidney health in type 2 diabetes.* RSNA. [Oral presentation].

CoverScan

Case study 1: **Liver and Kidney Disease Activity**



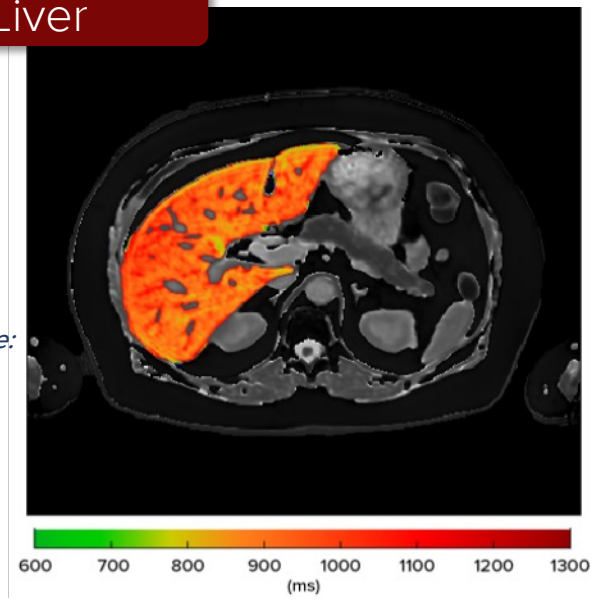
All other organs within reference ranges

- 61-year-old female, BMI = 34 kg/m^2.
- Patient with type 2 diabetes diagnosed 7 years ago, on metformin and statins.
- FIB4 and eGFR normal.

Liver

High Liver cT1: 913 ms

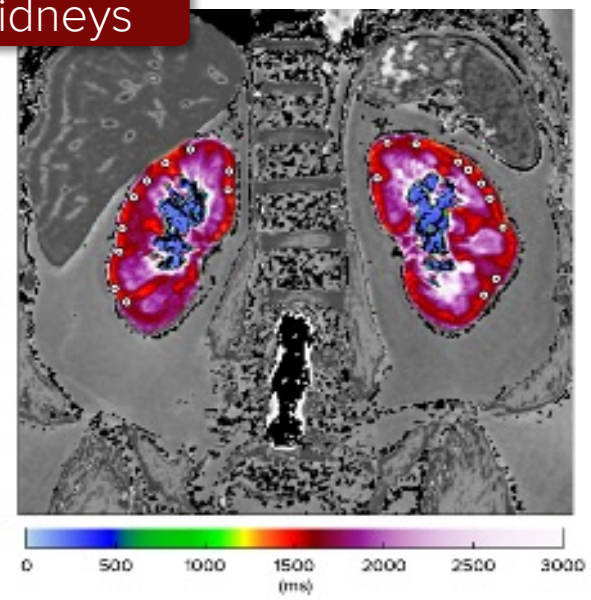
Normal Reference: < 800 ms



Kidneys

High Cortical T1: L: 1538ms; R: 1519ms

Normal Reference: L: 1288ms to 1527ms R: 1278 ms to 1516ms



CoverScan identified liver and kidney disease activity undetected by standard-of-care blood tests.

Perspectum

cT1: corrected T1; FIB4: fibrosis-4 index; BMI: body mass index; eGFR: estimated glomerular filtration rate; L: left; R: right

CoverScan

Case study 2: **Inflammation without steatosis**

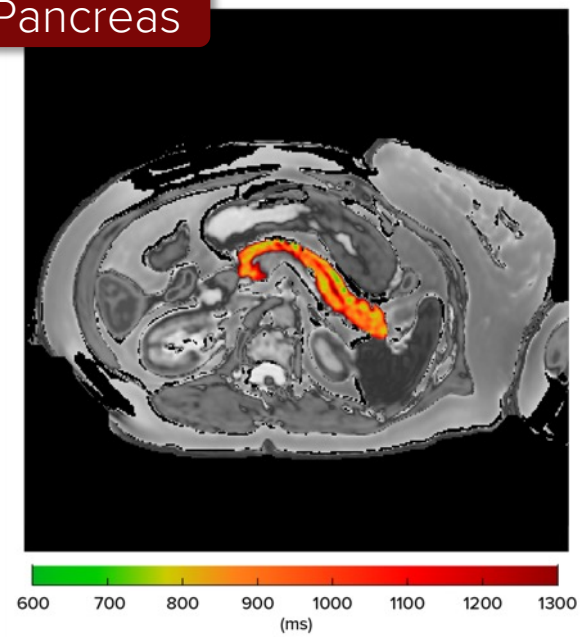
All other organs within reference ranges

- 47-year-old female, smoker, BMI = 27 kg/m2
- Patient with type 2 diabetes diagnosed 1.5 years ago, on metformin, DPP4 inhibitors and SGLT2 inhibitors.
- Hba1c is high. Normal eGFR, pancreas fat and kidney fat.

Pancreas

High
Pancreas srT1:
888 ms

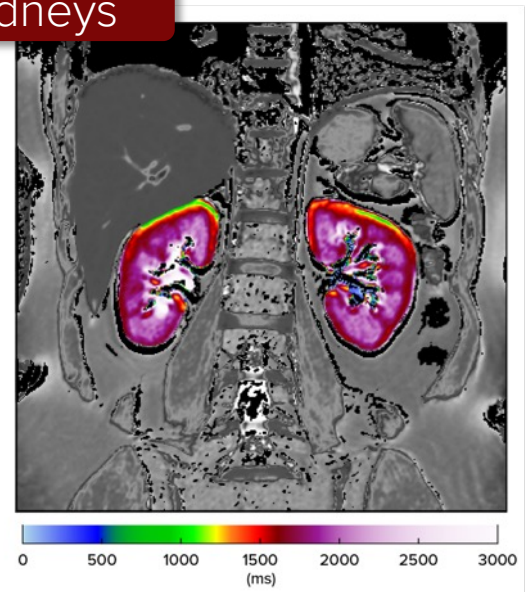
Normal Reference:
< 836 ms



Kidneys

High
Cortical T1:
L: 1555 ms;
R: 1585ms

Normal Reference:
L: 1288ms to 1527ms
R: 1278 ms to 1516ms



Disease activity in type 2 diabetes can appear without obesity or organ fat.

Perspectum

srT1: scanner referenced T1; BMI: body mass index; HbA1c: hemoglobin A1c; eGFR: estimated glomerular filtration rate; DPP4: Dipeptidyl-peptidase 4; SGLT2: sodium glucose co-transporter-2


Kidney cortical T1
0001
0003
0004
0006
0007
0010
0011
0013
0017
0018
0020
0022
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0025
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Big data

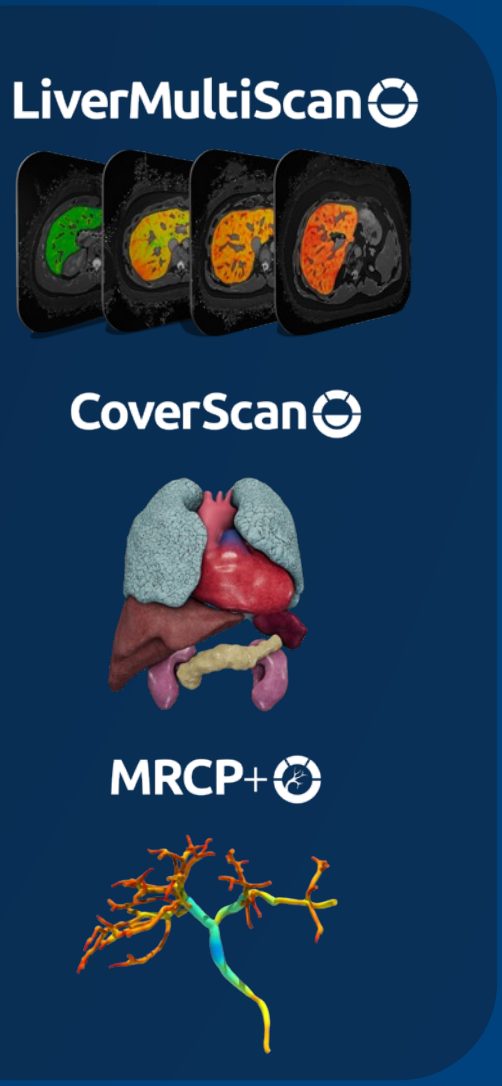
Faster clinical outcomes, and the bulk of the investment in medical imaging

The NEW ENGLAND JOURNAL of MEDICINE

AI is big in medical imaging

Table 1. Summary of AI CPT Codes.*

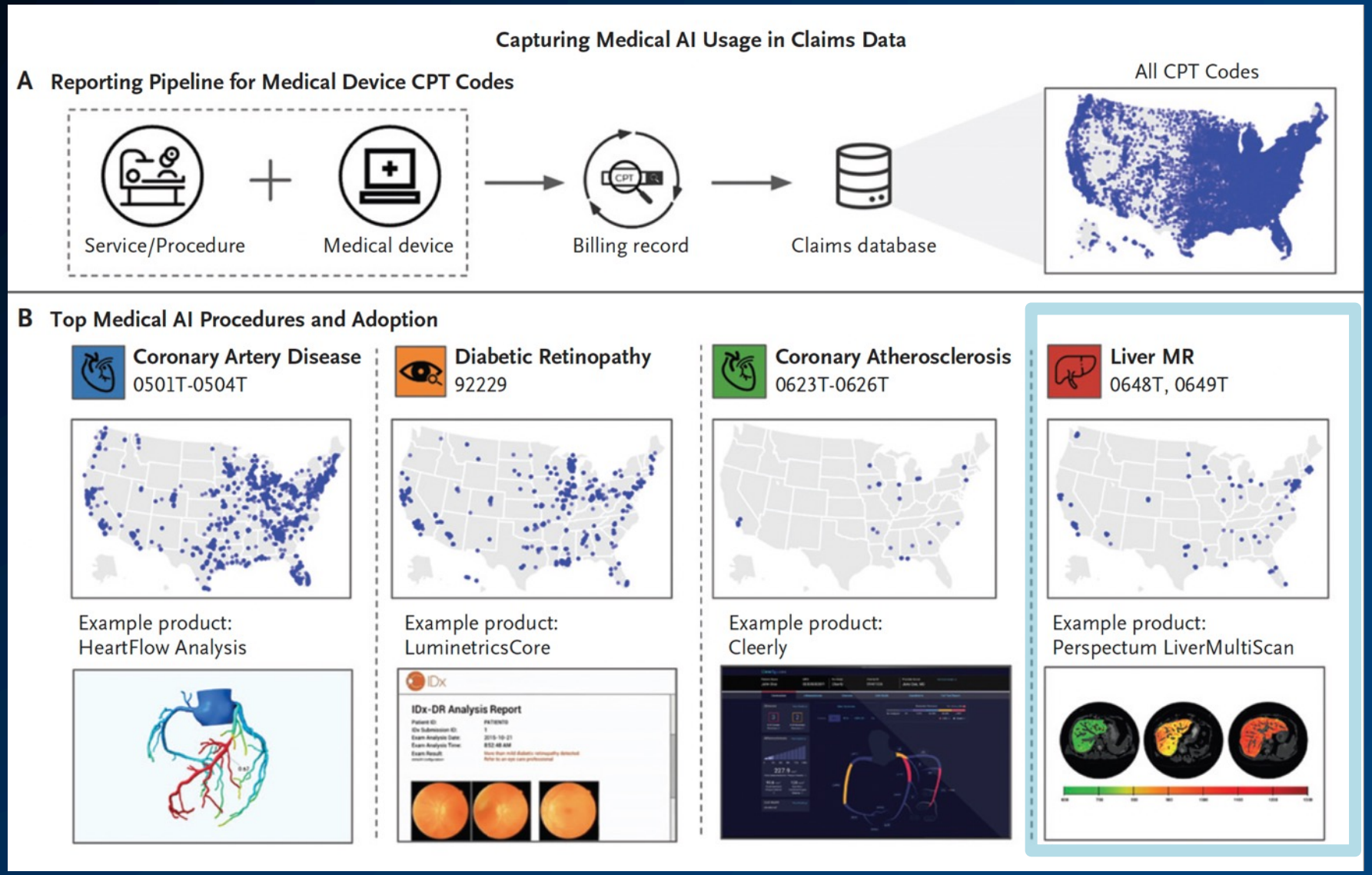
Total Claims	Condition or Medical AI Procedure	CPT Code(s)	Example Product Name	Effective Date
67,306	Coronary artery disease	0501T–0504T	HeartFlow Analysis[48]	June 1, 2018
15,097	Diabetic retinopathy	92229	LumineticsCore[49]	January 1, 2021
4,459	Coronary atherosclerosis	0623T–0626T	Cleerly[50]	January 1, 2021
2,428	Liver MR	0648T–0649T	Perspectum LiverMultiScan[51]	January 1, 2021
591	Multiorgan MRI	0697T–0698T	Perspectum CoverScan[52]	January 1, 2022
552	Breast ultrasound	0689T–0690T	Koios DS[53]	January 1, 2022
435	ECG cardiac dysfunction	0764T–0765T	Anumana[50]	January 1, 2023
331	Cardiac acoustic waveform recording	0716T	CADScor[50]	July 1, 2022
237	Quantitative MR cholangiopancreatography	0723T–0724T	Perspectum MRCP+[54]	July 1, 2022
67	Epidural infusion	0777T	CompuFlo[55]	January 1, 2023
4	Quantitative CT tissue characterization	0721T–0722T	Optellum Virtual Nodule Clinic[56]	July 1, 2022
1	Autonomous insulin dosage	0740T–0741T	d-Nav[57]	January 1, 2023
1	CT vertebral fracture assessment	0691T	HealthVCF[50]	January 1, 2022
1	Noninvasive arterial plaque analysis	0710T–0713T	ElucidVivo[50]	January 1, 2022
0	Facial phenotype analysis	0731T	Face2Gene[50]	July 1, 2022
0	X-ray bone density	0749T	OsteoApp[50]	January 1, 2023



Wu, K., Wu, E., Theodorou, B., Liang, W., Mack, C., Glass, L., Sun, J. and Zou, J., 2023. Characterizing the clinical adoption of medical AI through US insurance claims. NEJM AI.

Perspectum

The NEW ENGLAND JOURNAL of MEDICINE

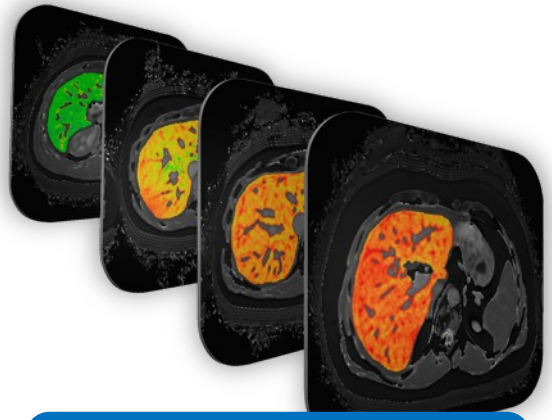


Perspectum

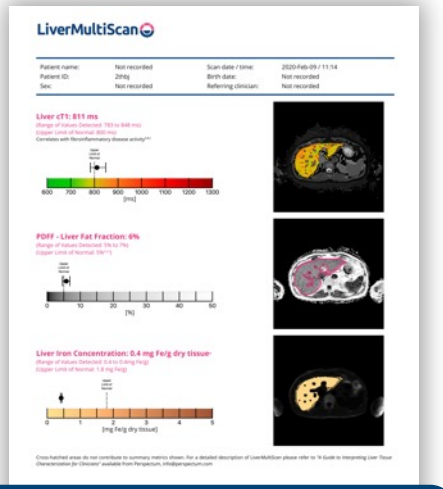
Wu, K., Wu, E., Theodorou, B., Liang, W., Mack, C., Glass, L., Sun, J. and Zou, J., 2023. Characterizing the clinical adoption of medical AI through US insurance claims. NEJM AI.

Perspectum Extracts Quantitative, Actionable and Objective Information from Images to Inform Clinical Decision Making

Non-contrast MRI scan



Digital, quantitative biomarkers

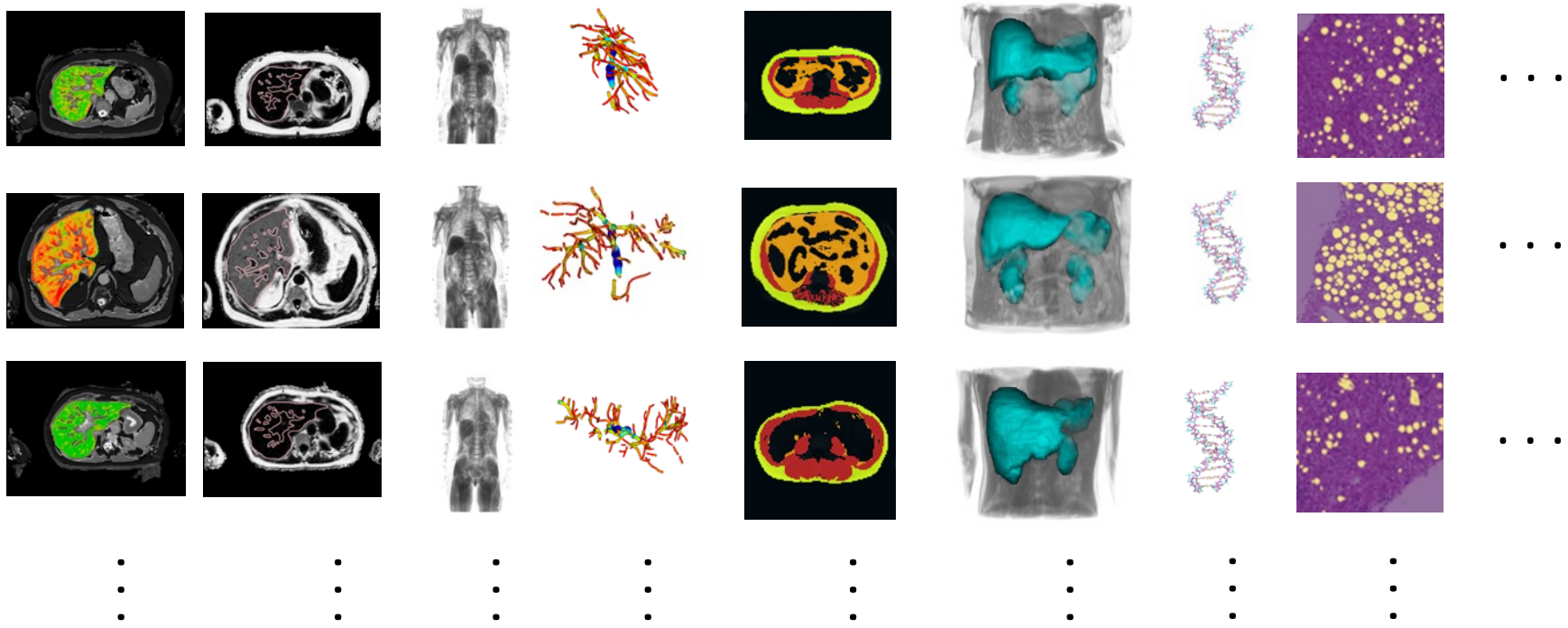


Actionable reports

Better decision support and care

rich information in a single individual

population level disease profiling



Quantifying fat in specific depots across the body

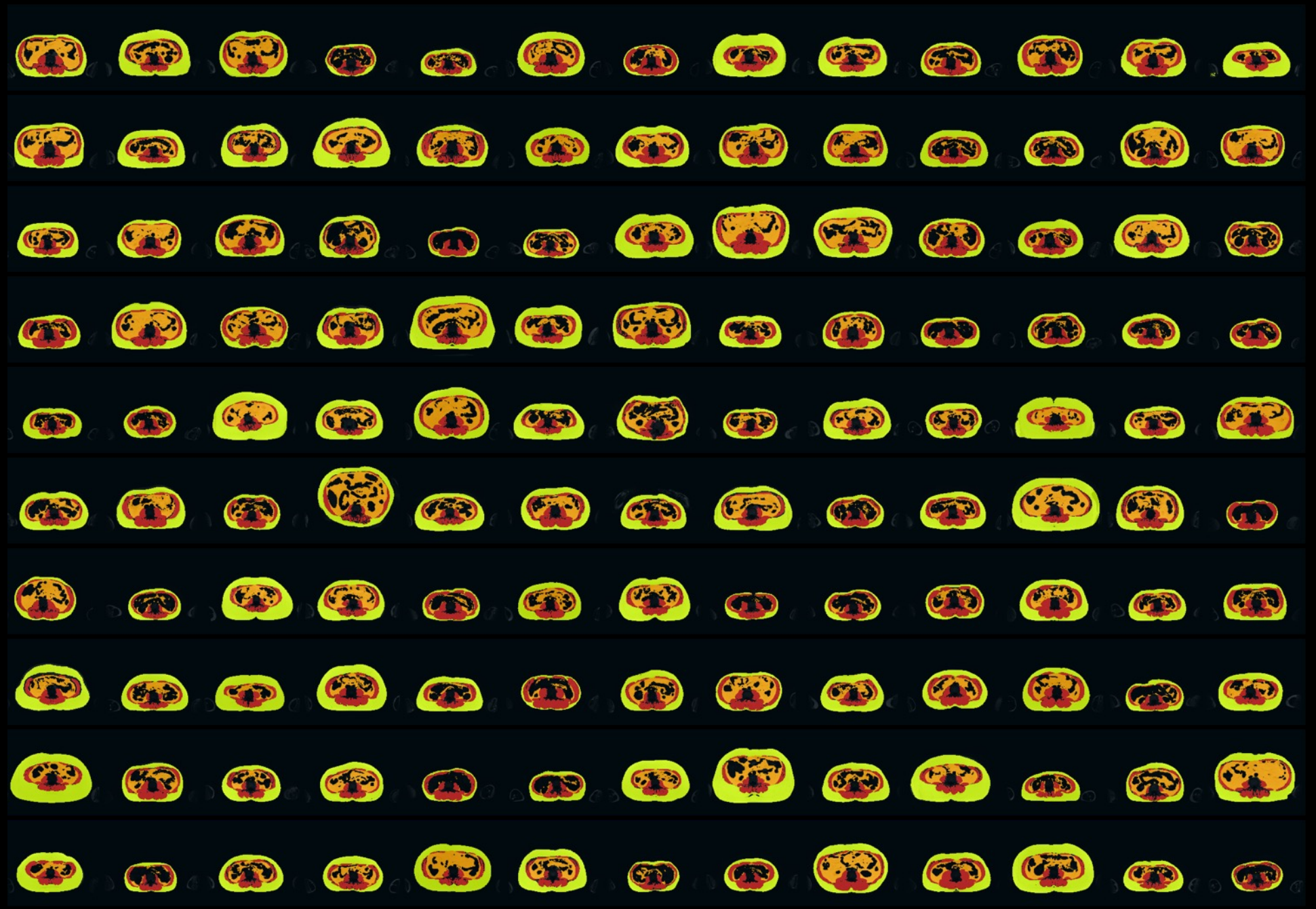
MRI

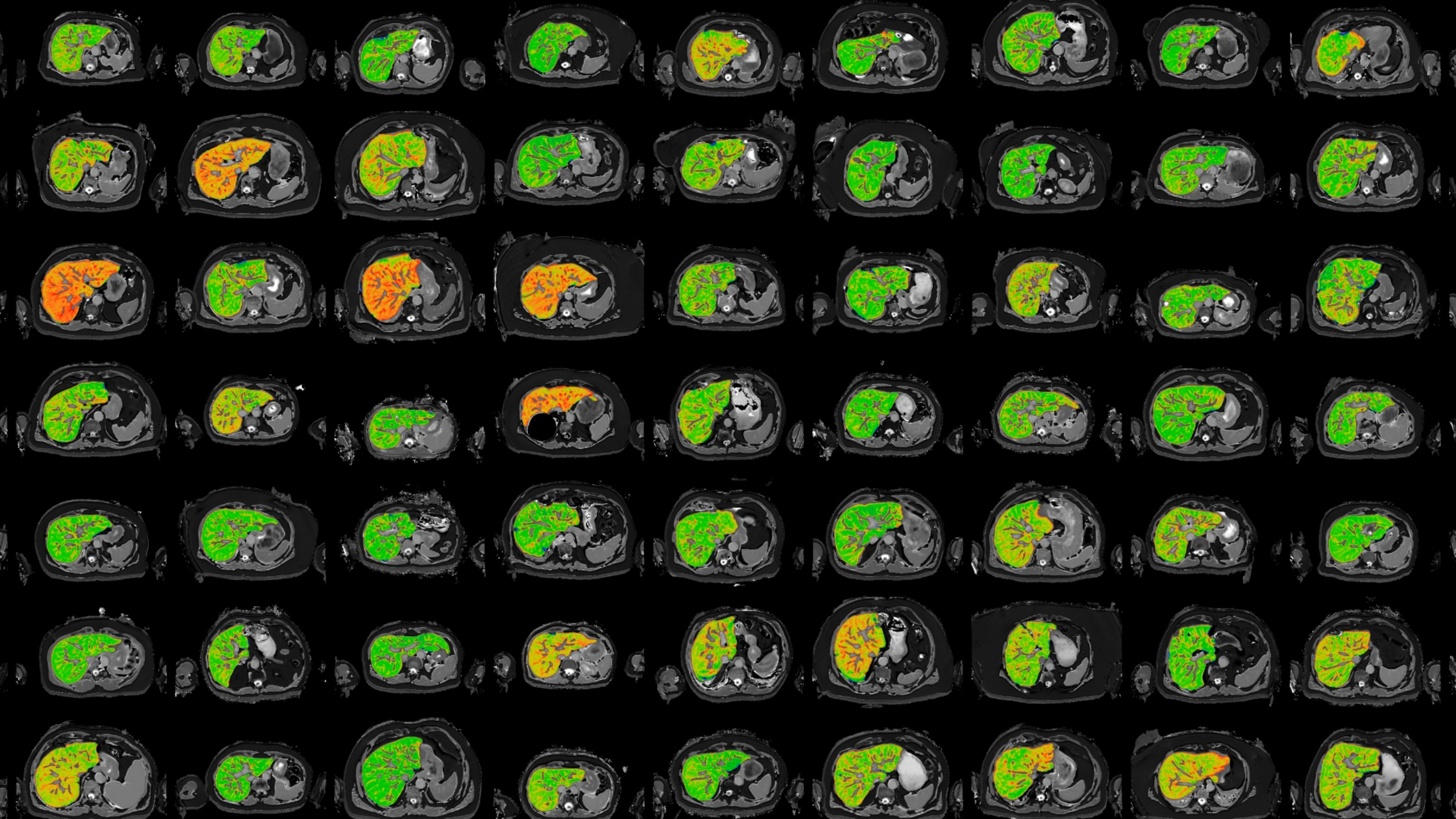
- tongue
- neck
- thymus
- clavicular suspected brown fat
- paracardial
- epicardial
- liver
  LiverMultiScan - 510(k)
- erector spinae muscle fat infiltration
- pancreas
  CoverScan - 510(k)
- perirenal
- abdominal subcutaneous
- vertebrae bone marrow
- renal sinus
- visceral
- thigh muscle fat infiltration
- femur bone marrow

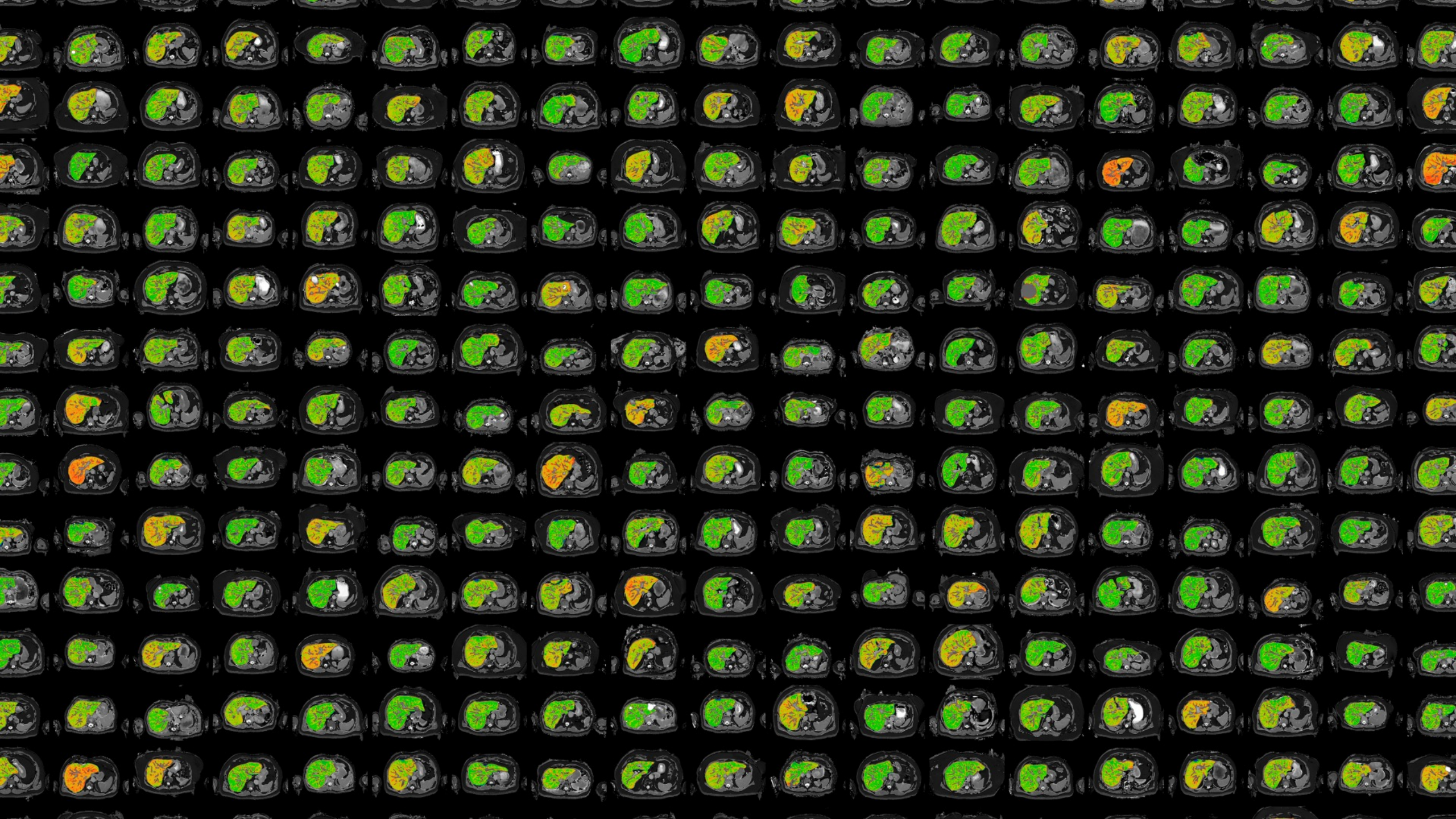
DXA
510(k)

- android
- gynoid
- total
- arms
- legs
- trunk
- head

MRI (white=fat)



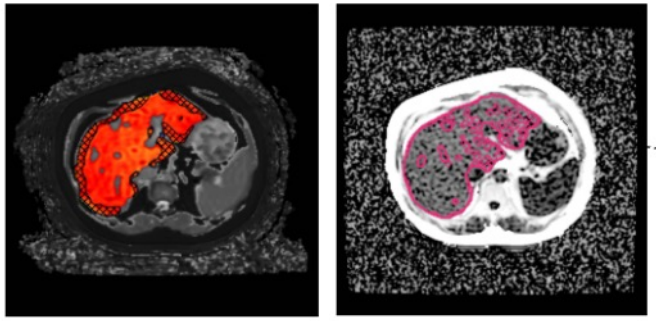




LiverMultiScan for detection & stratification

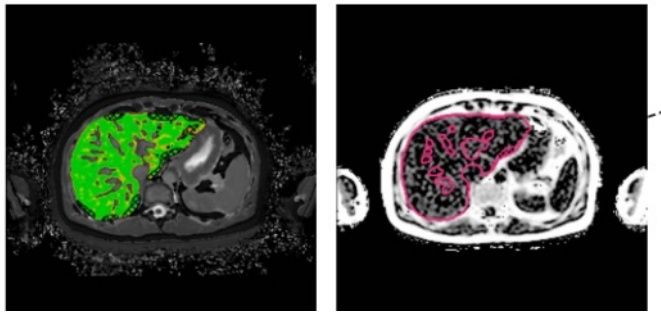
Disease activity without steatosis

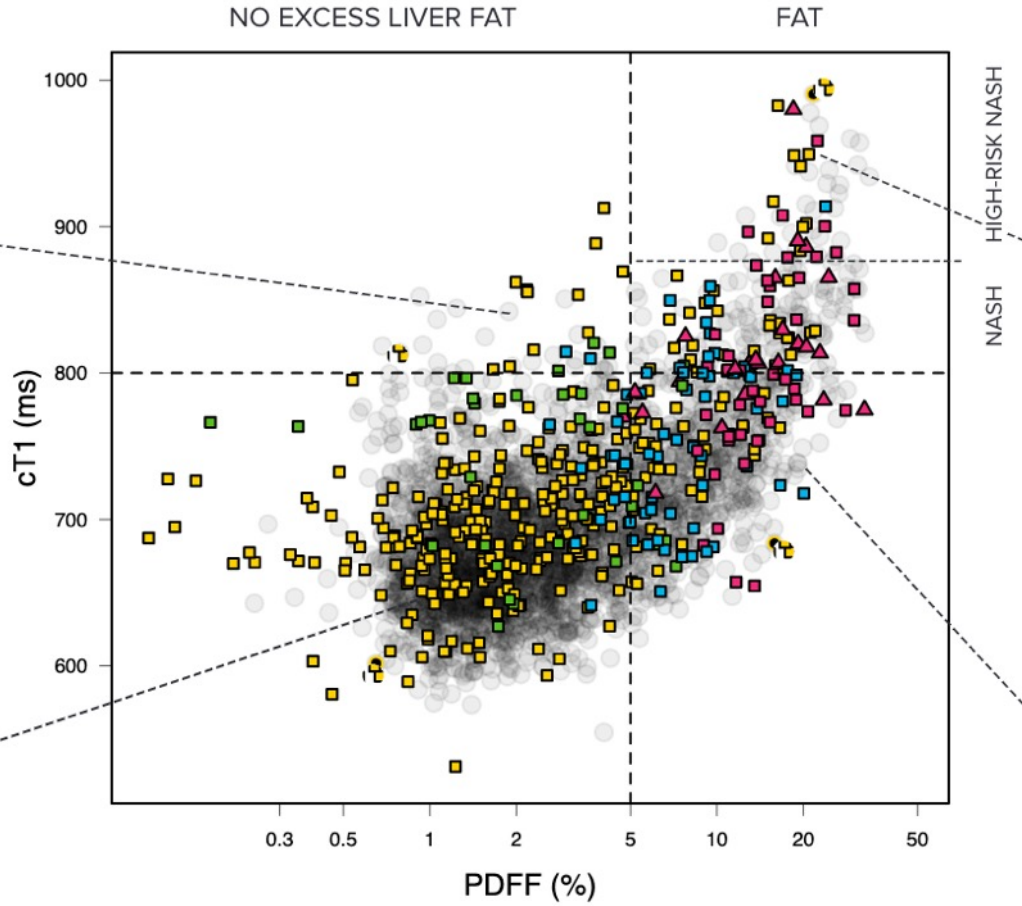
Consider differential diagnosis of autoimmune or viral liver disease



No disease activity, no steatosis

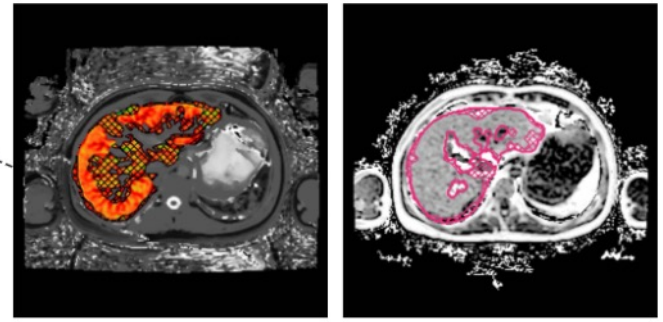
Low-risk patient, unlikely to have significant parenchymal disease





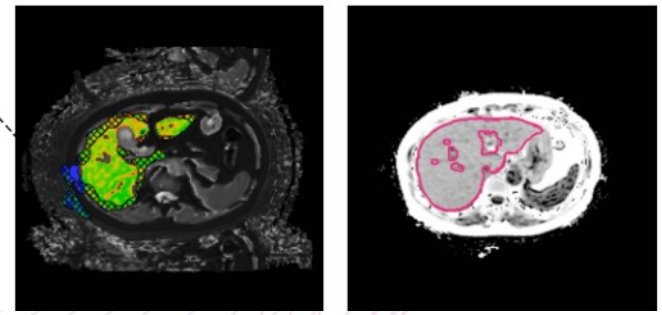
Disease activity with steatosis

Highly likely to have biopsy-proven steatohepatitis



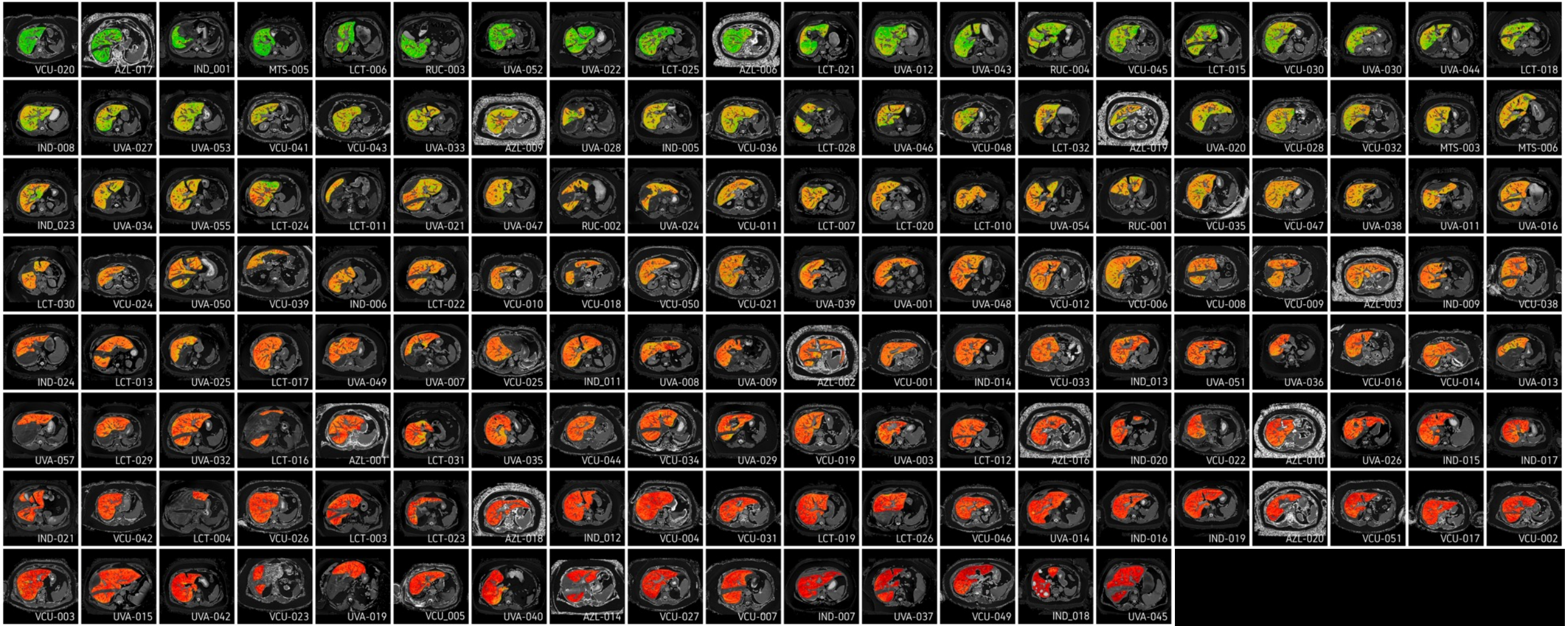
No disease activity with steatosis

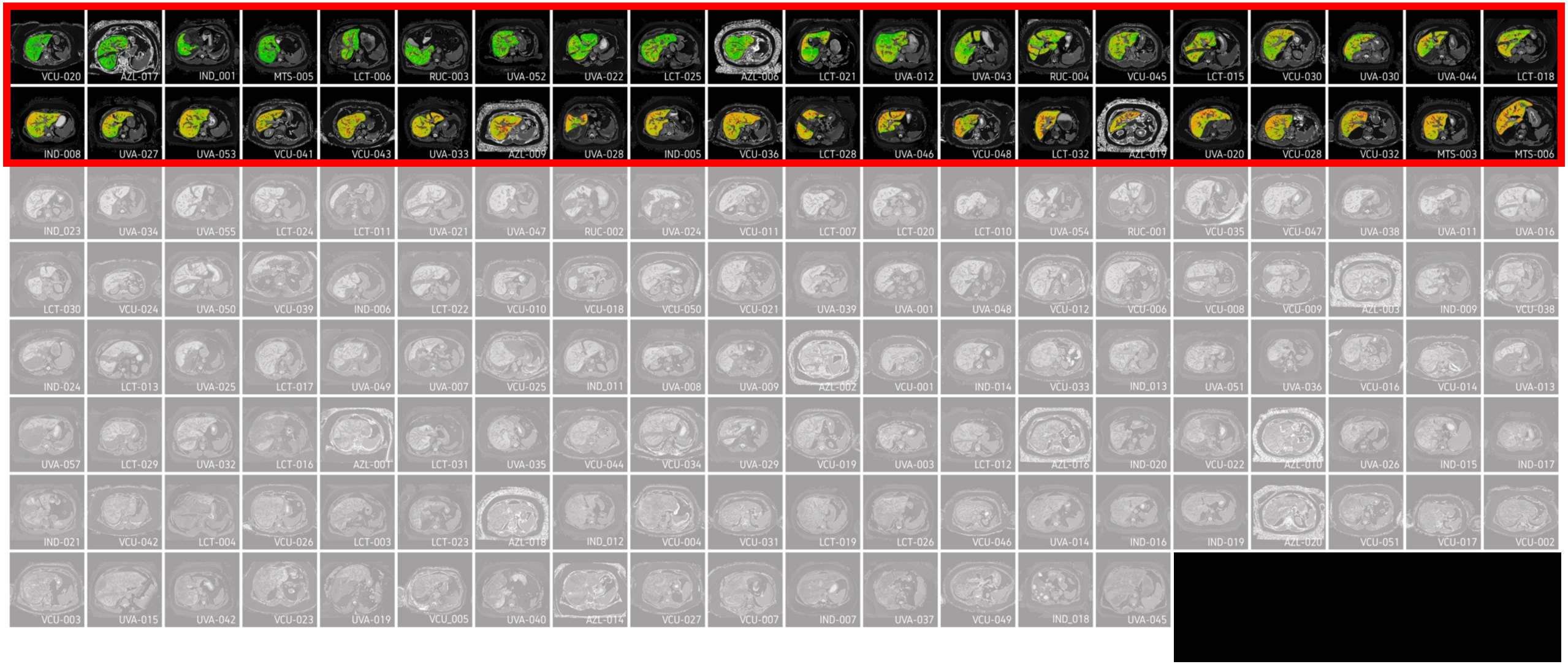
Often fatty liver disease without aggressive inflammation



N-QUAN: An FDA funded prospective validation study of cT1's diagnostic accuracy for MASH

Site	PI	Enrolment	Months open	Enrolment /month
Indiana University Health	Raj Vuppalanchi	24	10	2.4
University of Virginia	Zachery Henry	57	43	1.3
Virginia Commonwealth University	Arun Sanyal	51	42	1.2
Arizona Liver health	Naim Alkouri	23	21	1.1
Liver Centre of Texas	Abdullah Mubarek	32	43	0.7
Rush University Medical Centre	Nancy Reau	4	10	0.4
Mount Sinai	Douglas Dieterich	10	36	0.3


VCU-020 AZL-017 IND_001 MTS-005 LCT-006 RUC-003 UVA-052 UVA-022 LCT-025 AZL-006 LCT-021 UVA-012 UVA-043 RUC-004 VCU-045 LCT-015 VCU-030 UVA-030 UVA-044 LCT-018
IND-008 UVA-027 UVA-053 VCU-041 VCU-043 UVA-033 AZL-009 UVA-028 IND-005 VCU-036 LCT-028 UVA-046 VCU-048 LCT-032 AZL-019 UVA-020 VCU-028 VCU-032 MTS-003 MTS-006
IND_023 UVA-034 UVA-055 LCT-024 LCT-011 UVA-021 UVA-047 RUC-002 UVA-024 VCU-011 LCT-007 LCT-020 LCT-010 UVA-054 RUC-001 VCU-035 VCU-047 UVA-038 UVA-011 UVA-016
LCT-030 VCU-024 UVA-050 VCU-039 IND-006 LCT-022 VCU-010 VCU-018 VCU-050 VCU-021 UVA-039 UVA-001 UVA-048 VCU-012 VCU-006 VCU-008 VCU-009 AZL-003 IND-009 VCU-038
IND-024 LCT-013 UVA-025 LCT-017 UVA-049 UVA-007 VCU-025 IND_011 UVA-008 UVA-009 AZL-002 VCU-001 IND-014 VCU-033 IND_013 UVA-051 UVA-036 VCU-016 VCU-014 UVA-013
UVA-057 LCT-029 UVA-032 LCT-016 AZL-001 LCT-031 UVA-035 VCU-044 VCU-034 UVA-029 VCU-019 UVA-003 LCT-012 AZL-016 IND-020 VCU-022 AZL-010 UVA-026 IND-015 IND-017
IND-021 VCU-042 LCT-004 VCU-026 LCT-003 LCT-023 AZL-018 IND_012 VCU-004 VCU-031 LCT-019 LCT-026 VCU-046 UVA-014 IND-016 IND-019 AZL-020 VCU-051 VCU-017 VCU-002
VCU-003 UVA-015 UVA-042 VCU-023 UVA-019 VCU_005 UVA-040 AZL-014 VCU-027 VCU-007 IND-007 UVA-037 VCU-049 IND_018 UVA-045


VCU-020 AZL-017 IND_001 MTS-005 LCT-006 RUC-003 UVA-052 UVA-022 LCT-025 AZL-006 LCT-021 UVA-012 UVA-043 RUC-004 VCU-045 LCT-015 VCU-030 UVA-030 UVA-044 LCT-018
IND-008 UVA-027 UVA-053 VCU-041 VCU-043 UVA-033 AZL-009 UVA-028 IND-005 VCU-036 LCT-028 UVA-046 VCU-048 LCT-032 AZL-019 UVA-020 VCU-028 VCU-032 MTS-003 MTS-006
IND_023 UVA-034 UVA-055 LCT-024 LCT-011 UVA-021 UVA-047 RUC-002 UVA-024 VCU-011 LCT-007 LCT-020 LCT-010 UVA-054 RUC-001 VCU-035 VCU-047 UVA-038 UVA-011 UVA-016
LCT-030 VCU-024 UVA-050 VCU-039 IND-006 LCT-022 VCU-010 VCU-018 VCU-050 VCU-021 UVA-039 UVA-001 UVA-048 VCU-012 VCU-006 VCU-008 VCU-009 AZL-003 IND-009 VCU-038
IND-024 LCT-013 UVA-025 LCT-017 UVA-049 UVA-007 VCU-025 IND_011 UVA-008 UVA-009 AZL-002 VCU-001 IND-014 VCU-033 IND_013 UVA-051 UVA-036 VCU-016 VCU-014 UVA-013
UVA-057 LCT-029 UVA-032 LCT-016 AZL-001 LCT-031 UVA-035 VCU-044 VCU-034 UVA-029 VCU-019 UVA-003 LCT-012 AZL-016 IND-020 VCU-022 AZL-010 UVA-026 IND-015 IND-017
IND-021 VCU-042 LCT-004 VCU-026 LCT-003 LCT-023 AZL-018 IND_012 VCU-004 VCU-031 LCT-019 LCT-026 VCU-046 UVA-014 IND-016 IND-019 AZL-020 VCU-051 VCU-017 VCU-002
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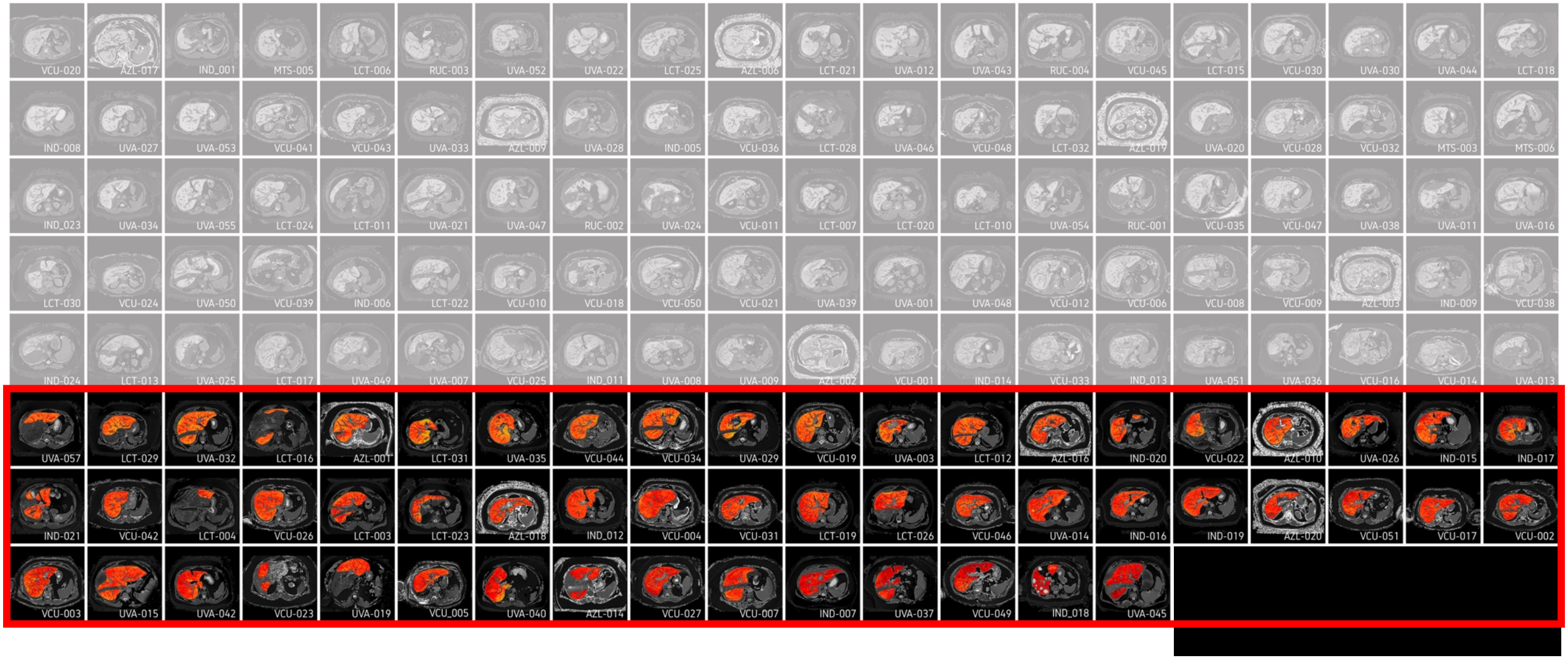
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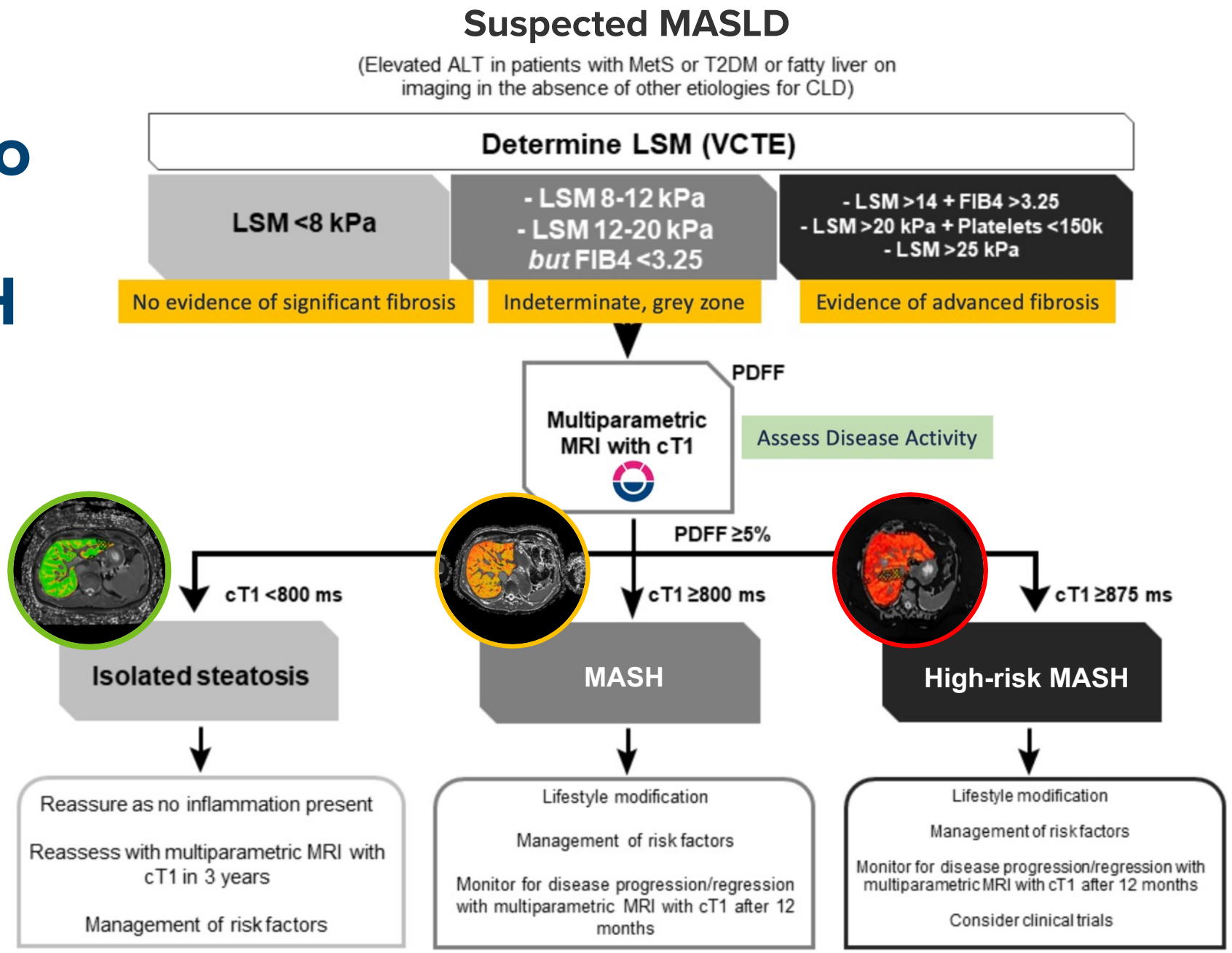
IND-008 UVA-027 UVA-053 VCU-041 VCU-043 UVA-033 AZL-009 UVA-028 IND-005 VCU-036 LCT-028 UVA-046 VCU-048 LCT-032 AZL-019 UVA-020 VCU-028 VCU-032 MTS-003 MTS-006
IND_023 UVA-034 UVA-055 LCT-024 LCT-011 UVA-021 UVA-047 RUC-002 UVA-024 VCU-011 LCT-007 LCT-020 LCT-010 UVA-054 RUC-001 VCU-035 VCU-047 UVA-038 UVA-011 UVA-016
LCT-030 VCU-024 UVA-050 VCU-039 IND-006 LCT-022 VCU-010 VCU-018 VCU-050 VCU-021 UVA-039 UVA-001 UVA-048 VCU-012 VCU-006 VCU-008 VCU-009 AZL-003 IND-009 VCU-038
IND-024 LCT-013 UVA-025 LCT-017 UVA-049 UVA-007 VCU-025 IND_011 UVA-008 UVA-009 AZL-002 VCU-001 IND-014 VCU-033 IND_013 UVA-051 UVA-036 VCU-016 VCU-014 UVA-013
UVA-057 LCT-029 UVA-032 LCT-016 AZL-001 LCT-031 UVA-035 VCU-044 VCU-034 UVA-029 VCU-019 UVA-003 LCT-012 AZL-016 IND-020 VCU-022 AZL-010 UVA-026 IND-015 IND-017
IND-021 VCU-042 LCT-004 VCU-026 LCT-003 LCT-023 AZL-018 IND_012 VCU-004 VCU-031 LCT-019 LCT-026 VCU-046 UVA-014 IND-016 IND-019 AZL-020 VCU-051 VCU-017 VCU-002
VCU-003 UVA-015 UVA-042 VCU-023 UVA-019 VCU_005 UVA-040 AZL-014 VCU-027 VCU-007 IND-007 UVA-037 VCU-049 IND_018 UVA-045

Integrating LiverMultiScan into the clinical care pathway for MASH

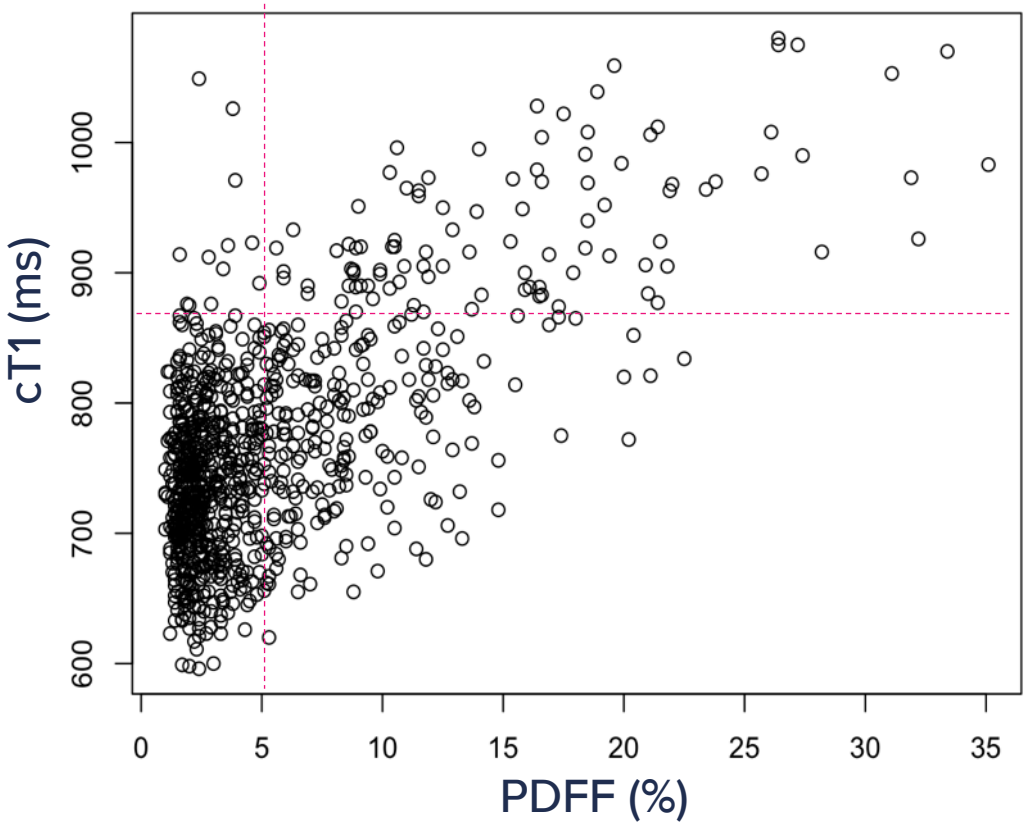
The cT1 score may be used instead of or prior to liver biopsy in all patients at intermediate/ high risk of fibrosis, but this decision should be made by a hepatologist.



Perspectum

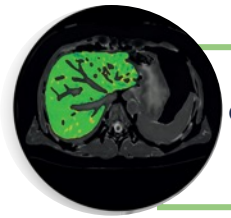
Kugelmas et al., Liver International. 2023.

Finding MASH patients in Dallas

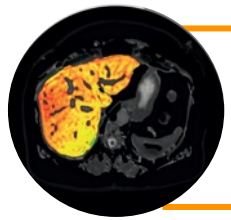


Dallas Hearts and Minds
N=914

PDFF >=5%
N= 314

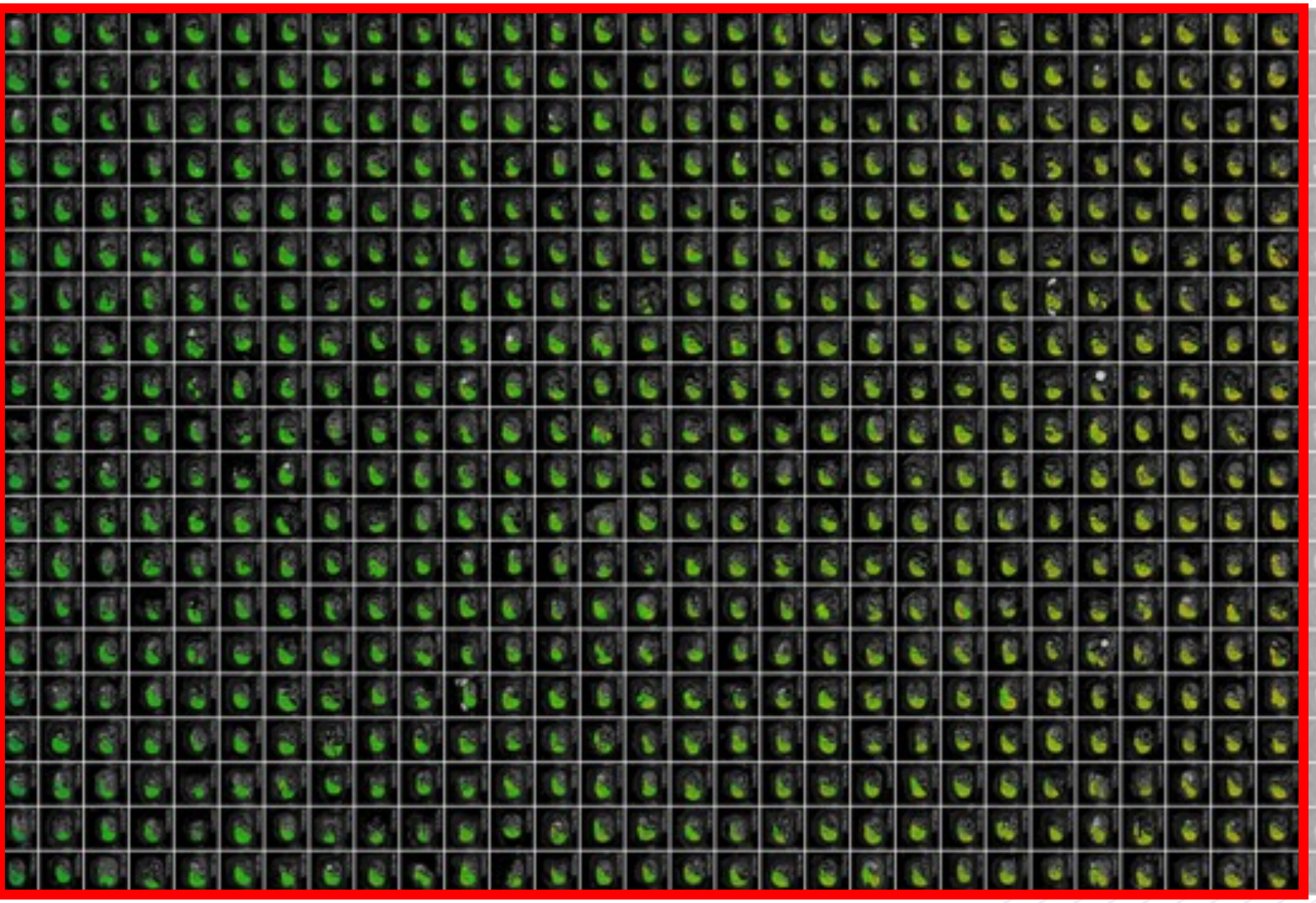


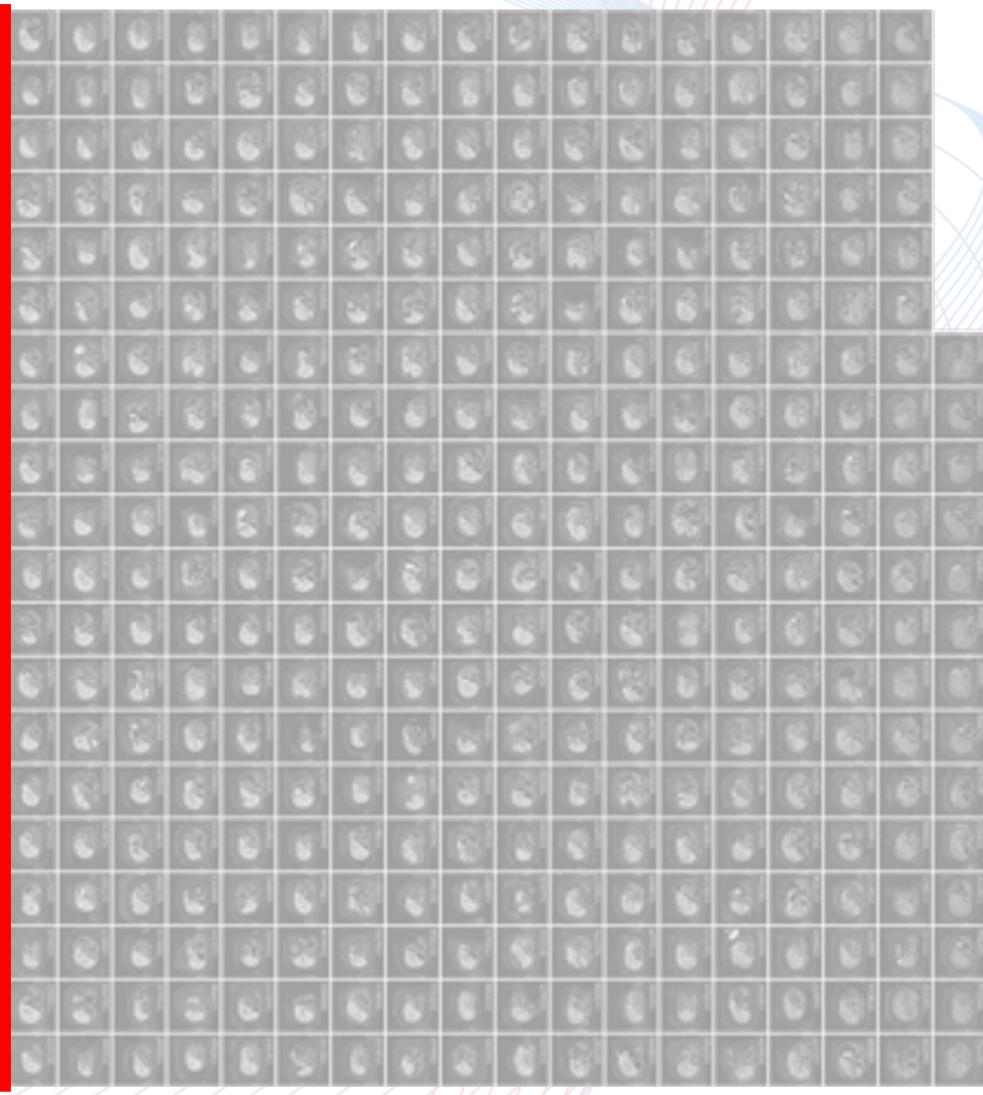
cT1 <800ms
N = 128

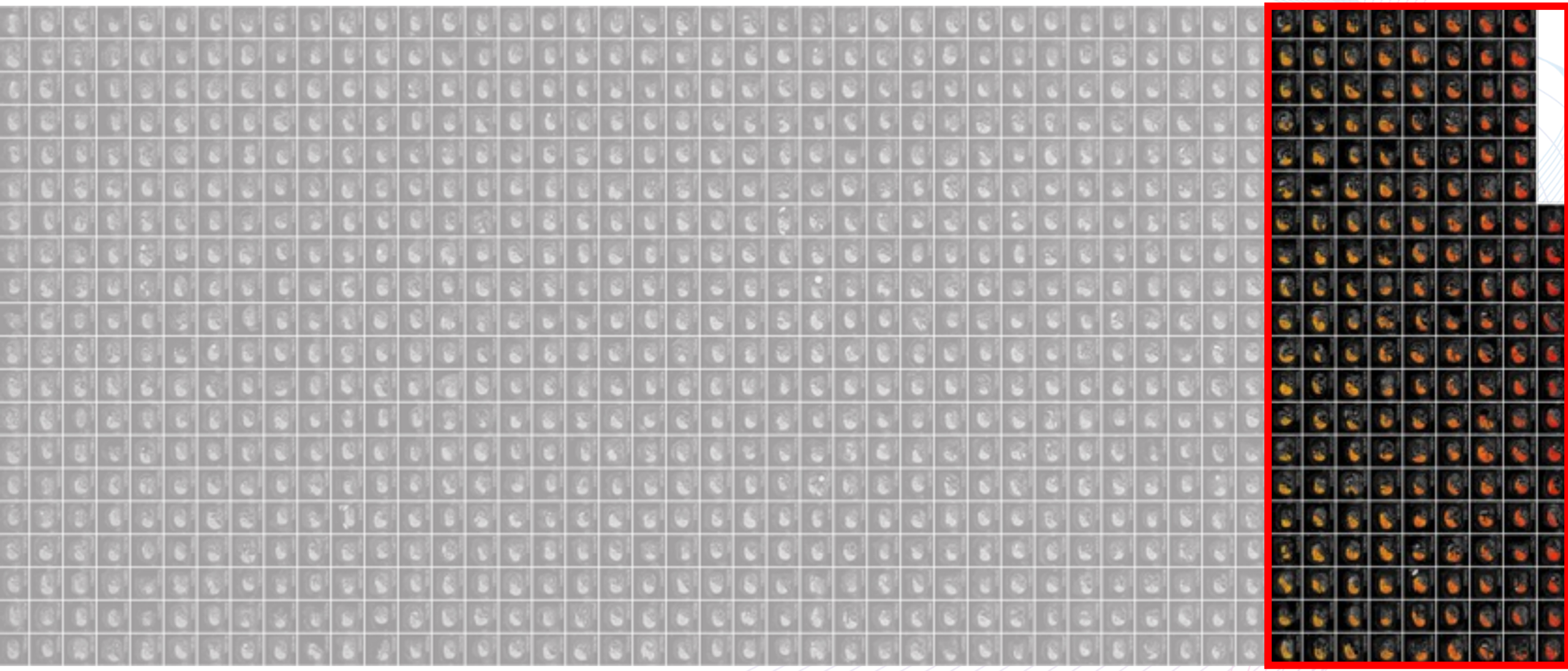


cT1: 800-875ms
N = 93

cT1 >875ms
N = 93



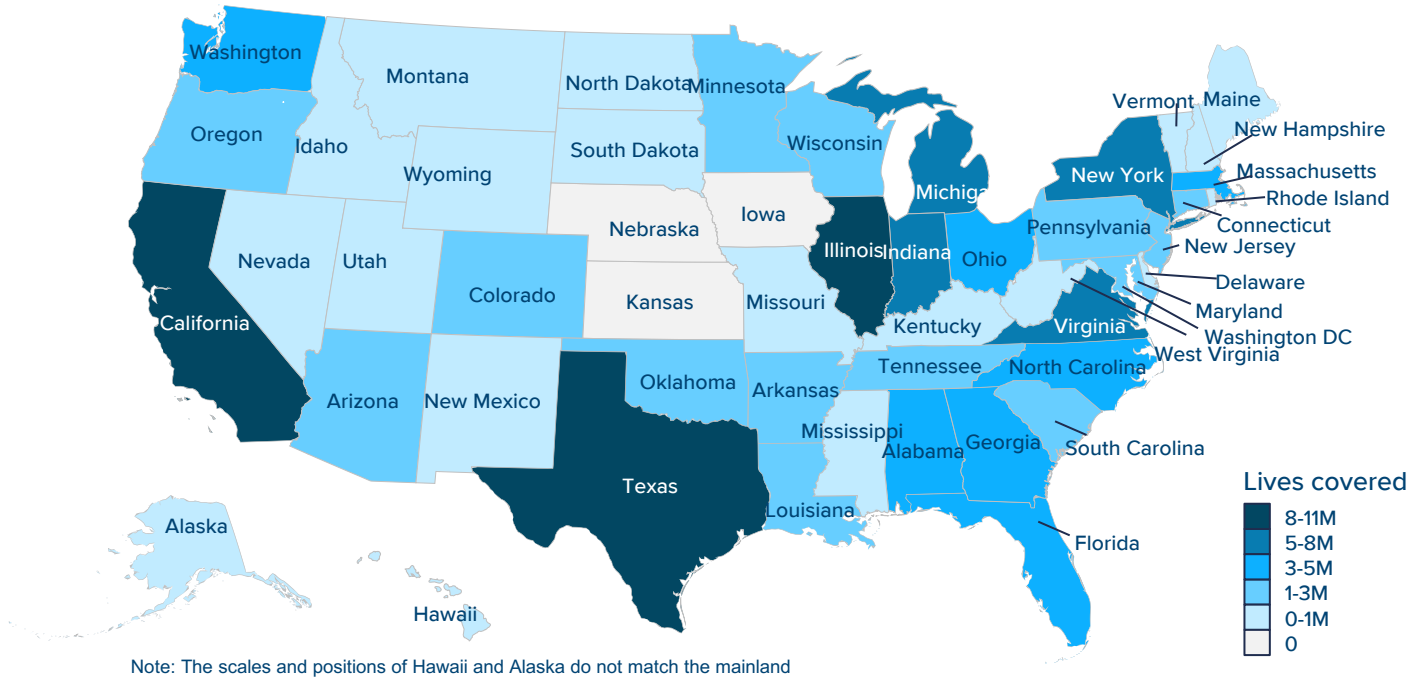




Real world data & reimbursement

Payors care about real benefits, not trial benefits

Nationwide payer coverage for diagnosis & management of MASLD



Note: The scales and positions of Hawaii and Alaska do not match the mainland

0648T / +0649T

Quantitative MR for analysis of tissue composition obtained without diagnostic MRI examination of the same anatomy during the same session

47 states — US States covered*
(incl. DC and Puerto Rico)

109 million — People covered
(1/3 of US population)

$950 — Medicare reimbursement for hospitals

$2,100 — Commercial Reimbursement
(Technical + Professional)

Wu et al., MedRxiv. 2023; OPPS Payment by HCPCS Code for CY 2022, Addendum B.- PFS Payment by HCPCS Code for CY 2022, Clinical Diagnostic Laboratory Fee Schedule for 2022; Policy Reporter, effective March 13, 2022

LiverMultiScan is Medically Necessary for Management of Chronic Liver Diseases

LiverMultiScan is **medically necessary** for diagnosis and management of any of the following:

- Diagnosis and management of **advanced hepatic fibrosis/cirrhosis** in patients with established chronic liver disease:
  - **Nonalcoholic fatty liver disease (NAFLD)*** in patients with high risk for cirrhosis due to advanced age, obesity, diabetes, or alanine aminotransferase (ALT) level more than twice the upper limit of normal
  - **Other established chronic liver diseases** when ultrasound elastography cannot be performed or is nondiagnostic
- **Iron overload** in hemochromatosis

National Payer

❖ Anthem (14 state affiliates):

- California
- New York
- Colorado
- Connecticut
- Georgia
- Indiana
- Kentucky
- Missouri
- Ohio
- Wisconsin
- Maine
- New Hampshire
- Nevada
- Virginia

Anthem

Arkansas

BlueCross BlueShield of Texas

BlueCross BlueShield of Illinois

BlueCross BlueShield of North Carolina

BlueCross BlueShield of Oklahoma

BlueCross BlueShield of New Mexico

MASSACHUSETTS

BlueCross BlueShield of Louisiana

BlueCross BlueShield of Alabama

BlueCross BlueShield of Montana

Regional Payer

- HCSC
  - BCBS Texas, Illinois, Montana, New Mexico, Oklahoma
- BCBS Massachusetts
- BCBS North Carolina
- BCBS Louisiana
- BCBS Alabama
- BCBS Arkansas
- Premera
- LifeWise Health Plans
- Pacificsource

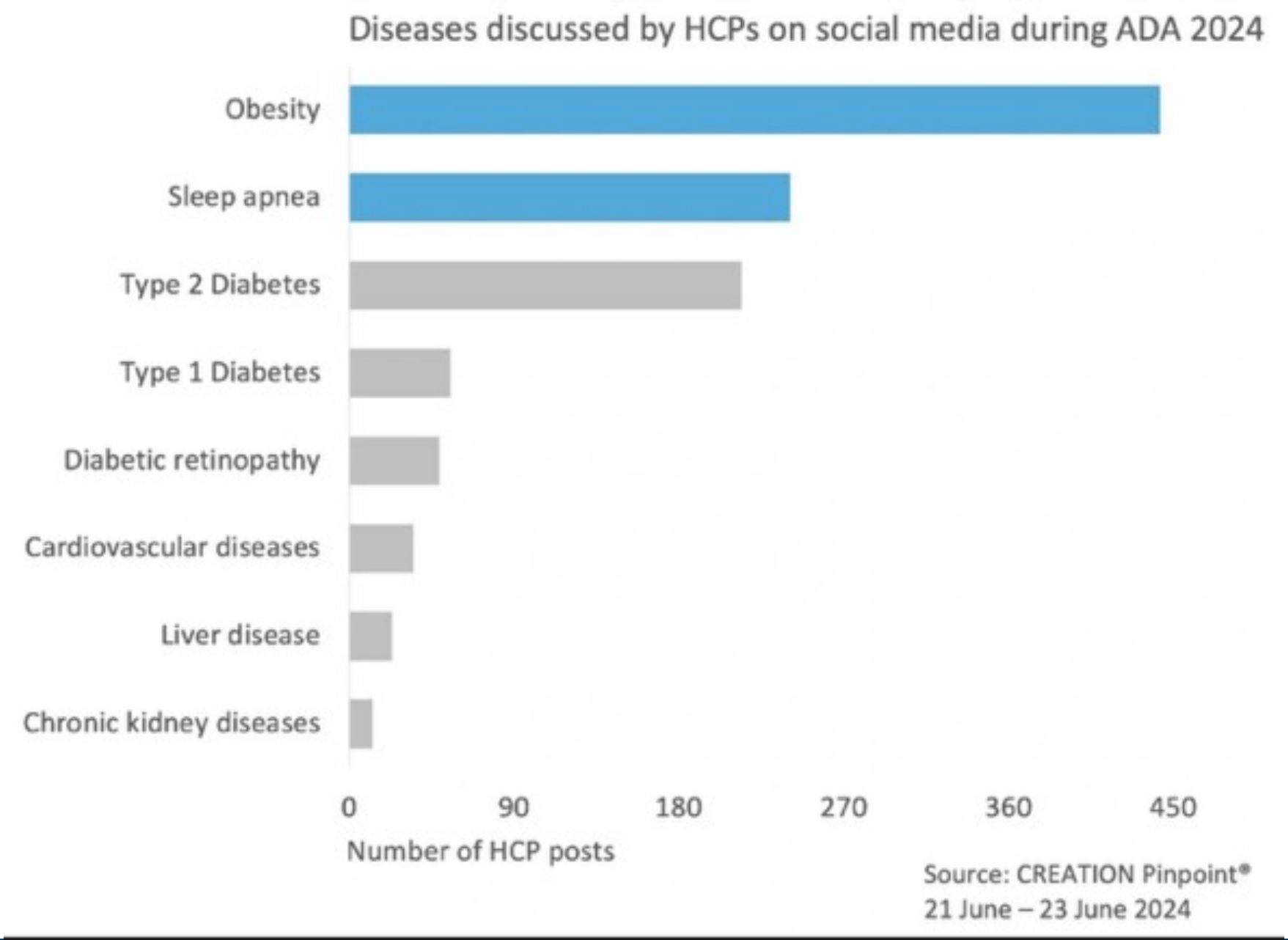
SUMMARY

- Speed matters – time is money (and a lot of it)
- Technology enables rapid recruitment and low ‘screen fail’ rates
- Getting medicine right in chronic disease is hard without technology
- Big data – expensive to get, but needed for reimbursement

Perspectum

Thank you for listening

Rajarshi.Banerjee@Perspectum.com


Diseases discussed by HCPs on social media during ADA 2024
Obesity
Sleep apnea
Type 2 Diabetes
Type 1 Diabetes
Diabetic retinopathy
Cardiovascular diseases
Liver disease
Chronic kidney diseases
0
90
180
270
360
450
Number of HCP posts
Source: CREATION Pinpoint®
21 June – 23 June 2024

Semaglutide Reduced Risk for Major Kidney Disease Events by 24% for Patients with Type 2 Diabetes and Kidney Disease

American Diabetes Association Symposium Showcases New Potential Solution for Patients at High-Risk of Kidney Outcomes

ORLANDO, FL. (JUNE 24, 2024) – Today, findings from the landmark FLOW trial, the first dedicated kidney outcomes trial with a GLP-1 (glucagon-like peptide-1) receptor agonist were reported, demonstrating semaglutide significantly reduces the risk of major kidney disease events and cardiovascular outcomes in patients with type 2 diabetes and chronic kidney disease. New data presented here also highlighted the likely benefits of combined therapy with SGLT2 inhibitors. The results were presented at a symposium at the American Diabetes Association's® (ADA) 84th Scientific Sessions in Orlando, FL, and were simultaneously published in *Nature Medicine*.

The double-blind, randomized, placebo-controlled international trial enrolled 3,533 participants with a median follow-up period of 3.4 years. The trial compared injectable semaglutide (1.0 mg) once weekly with a placebo as an adjunct to the standard of care for the prevention of major kidney outcomes, specifically kidney failure, substantial loss of kidney function, and death from kidney or cardiovascular causes.

Compared to those who received a placebo, participants who received Semaglutide experienced:

- **Composite Primary Endpoint**: 24% risk reduction (including kidney outcomes and death due to cardiovascular and kidney causes)
- **Secondary Endpoints**:
  - slower eGFR slope of 1.16 ml/min/1.73m2/year
  - reduction of major cardiovascular events by 18%
  - reduction of the risk of all-cause death by 20%.