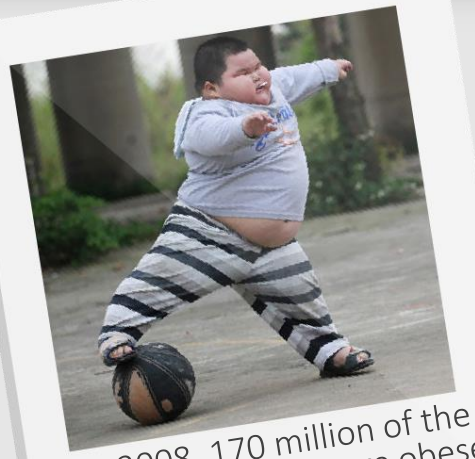
Global experts in diagnostic medicine, medical physics and image analysis

The looming pandemic

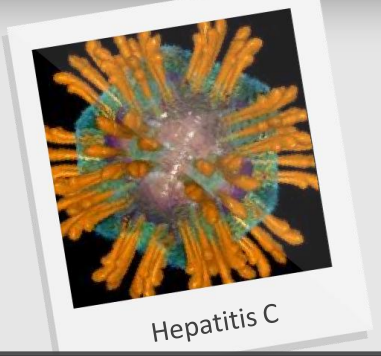
36% of US population is obese
24% UK population



In 2008, 170 million of the world's children were obese
20% EU kids and rising fast

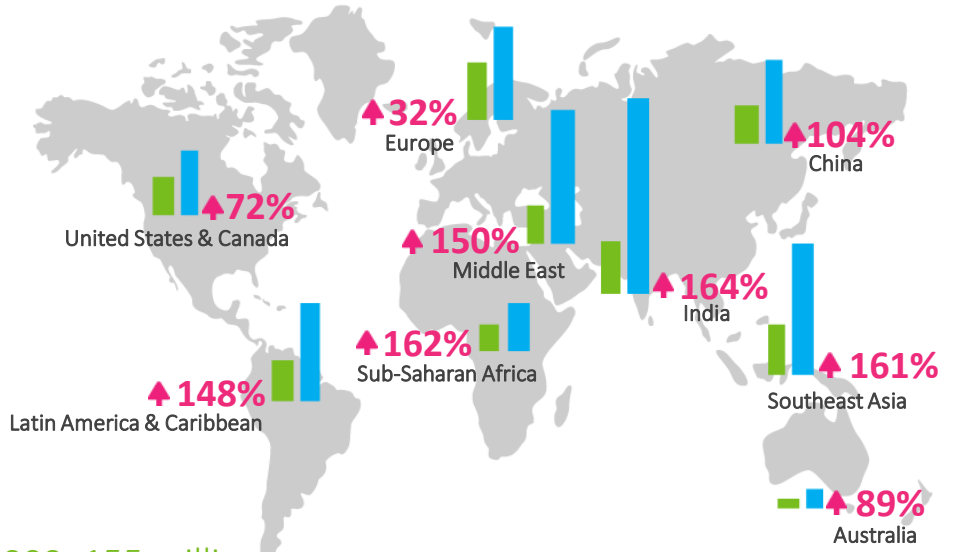
170 million

The world's favourite foods



Hepatitis C

Fatty liver disease in numbers



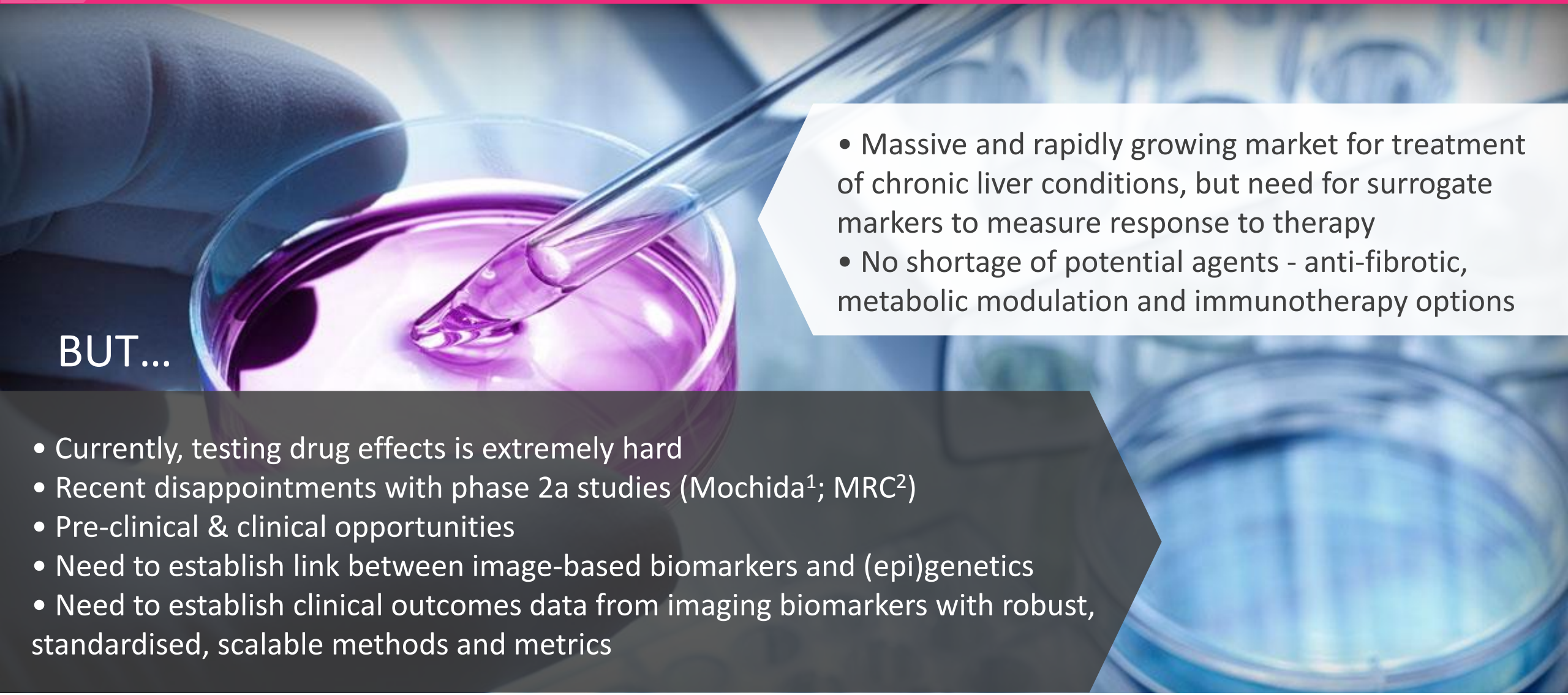
2000: 155 million
2030: 357 million

Massive growth in BRIC countries

- Cirrhosis = 2% risk of hepatocellular carcinoma *per year*
- Surge in (non-alcoholic) fatty liver disease and NASH
- 30% Western population has liver disease – ill defined
- Dame Sally Davies: liver disease is THE main priority[1]
- Leading cause of liver transplant by 2020
- Imaging biomarkers may act as surrogate endpoints in drug trials

1. Davies, S.C. "Annual Report of the Chief Medical Officer, Volume One, 2011, On the State of the Public's Health" London: Department of Health (November 2012)

Pharma's burgeoning interest…



- Massive and rapidly growing market for treatment of chronic liver conditions, but need for surrogate markers to measure response to therapy
- No shortage of potential agents - anti-fibrotic, metabolic modulation and immunotherapy options

BUT…

- Currently, testing drug effects is extremely hard
- Recent disappointments with phase 2a studies (Mochida[1]; MRC[2])
- Pre-clinical & clinical opportunities
- Need to establish link between image-based biomarkers and (epi)genetics
- Need to establish clinical outcomes data from imaging biomarkers with robust, standardised, scalable methods and metrics

1. No significant effects of Ethyl-Eicosapentanoic Acid on histologic features of Nonalcoholic Steatohepatitis in a Phase 2 Trial. Sanyal et al, *Gastroenterology* 147; p377-384,, August 2014.
2. http://www.controlled-trials.com/ISRCTN57849521

Perspectum Diagnostics

LiverMultiScan

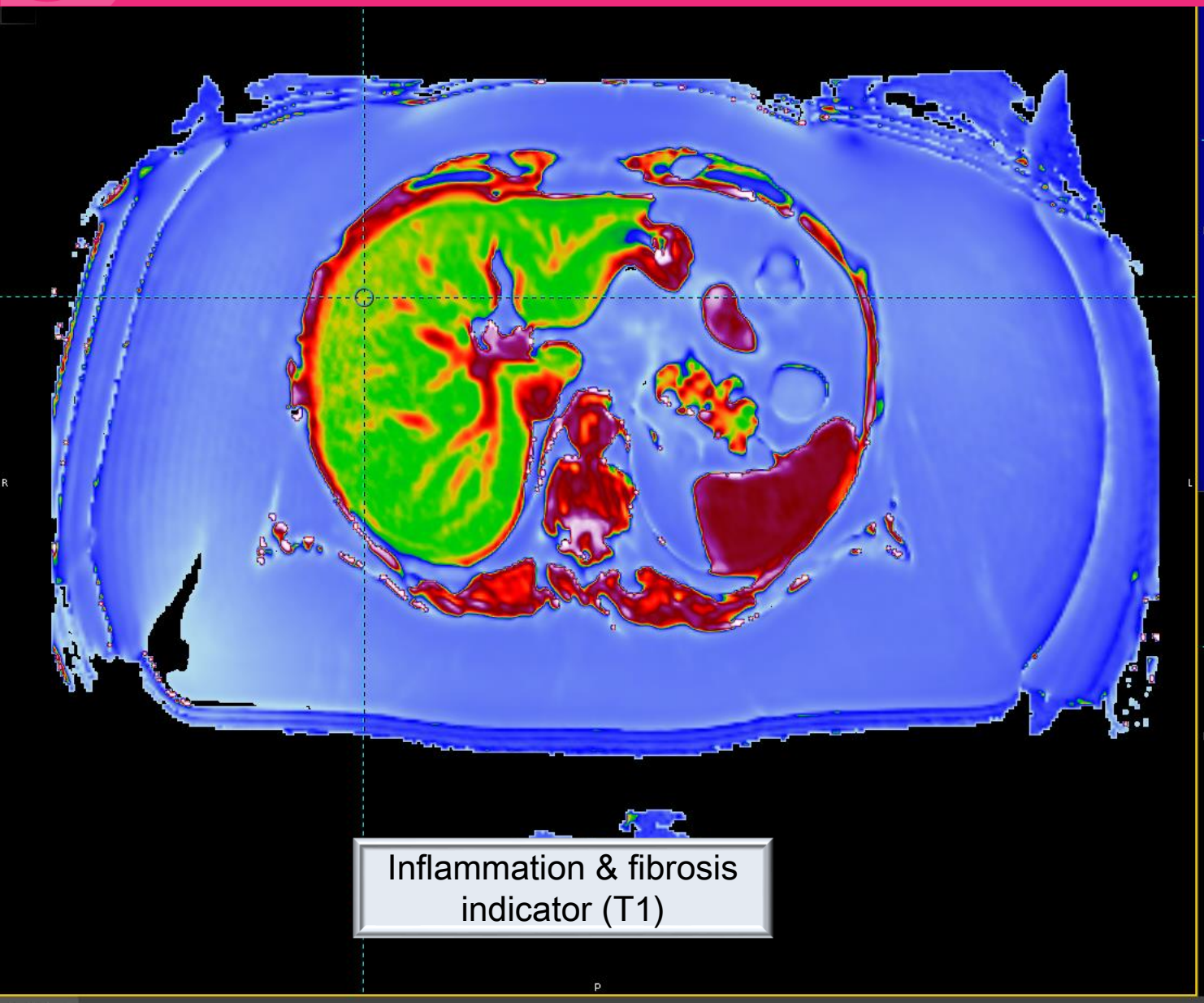
CE- marked software for the characterisation of liver tissue using MRI.

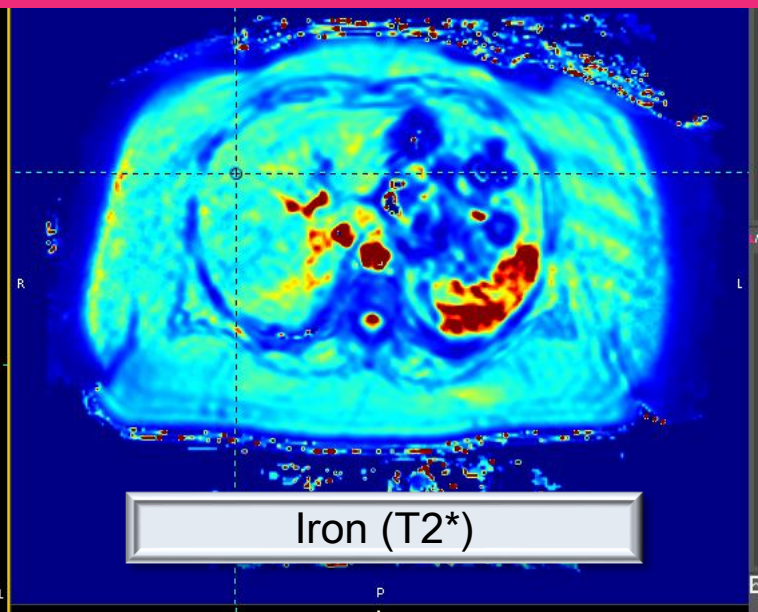
Key Benefits

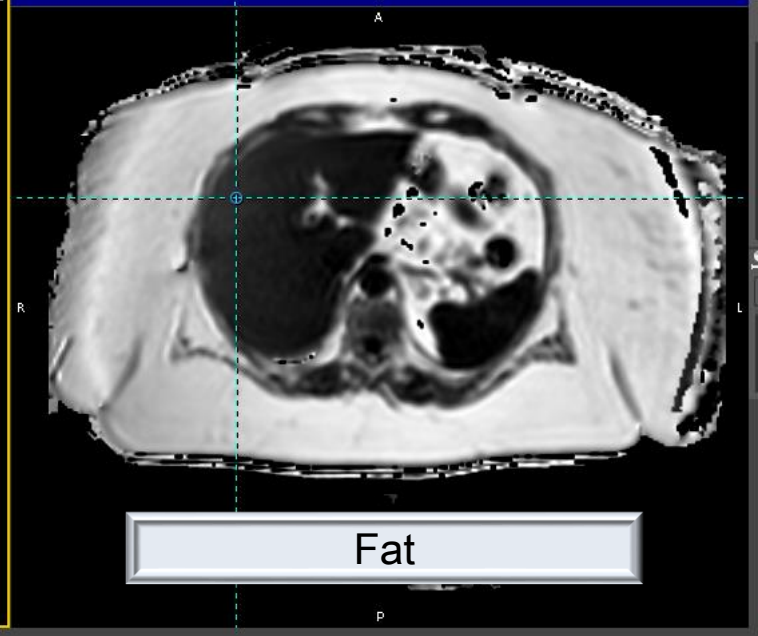
1. Provides metrics for **iron** and **fat fraction** with a novel, patented method for quantifying **inflammation and fibrosis (the 'LIF' score).**
2. **NO additional hardware required**. Can be deployed in any site offering MRCP.
3. Works on obese patients and those with ascites; **no contrast agents** needed.
4. **Fast** – 10min scan, 4–6 patients per hour, ideal for screening patients to enter trials.
5. High **sensitivity and reproducibility** – suitable for longitudinal monitoring.
6. **Whole liver assessment** – ideal for heterogeneous disease (PSC, NRH, cancer).

Perspectum Diagnostics

LiverMultiScan







T1: 863.4ms ± 18.2
T2*: 21.5ms (20.7;23.0)
Fat: 17.2%

cT1: 863.7ms

LIF Score

LIF 1.8

4
3
2
1
0

Image Gallery

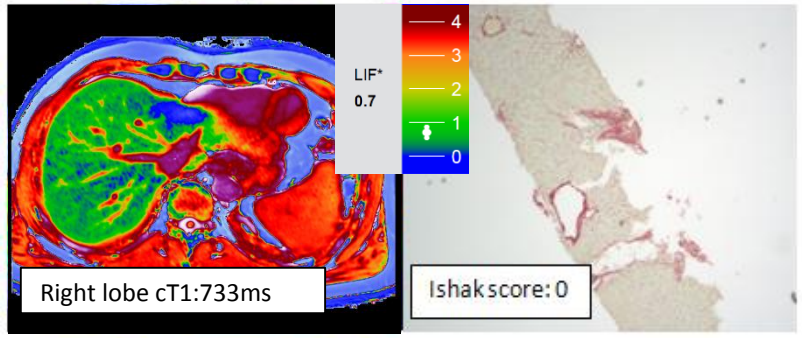
ROI List

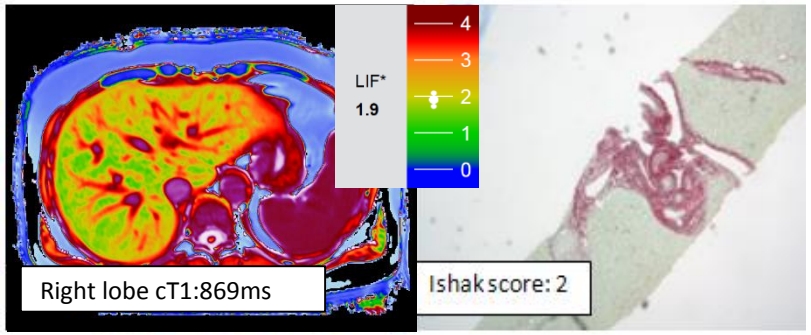
Delete ROI

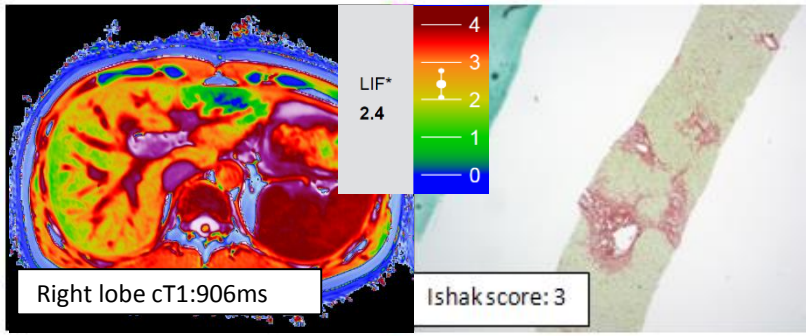
New Region

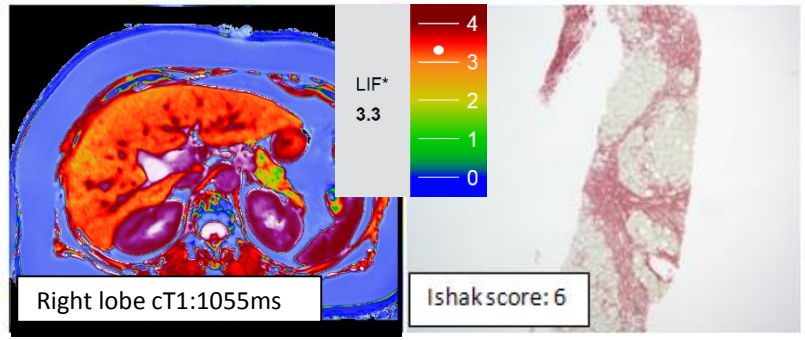
LiverMultiScan

Multi-parametric MRI stages adult patients with chronic disease (n=79)

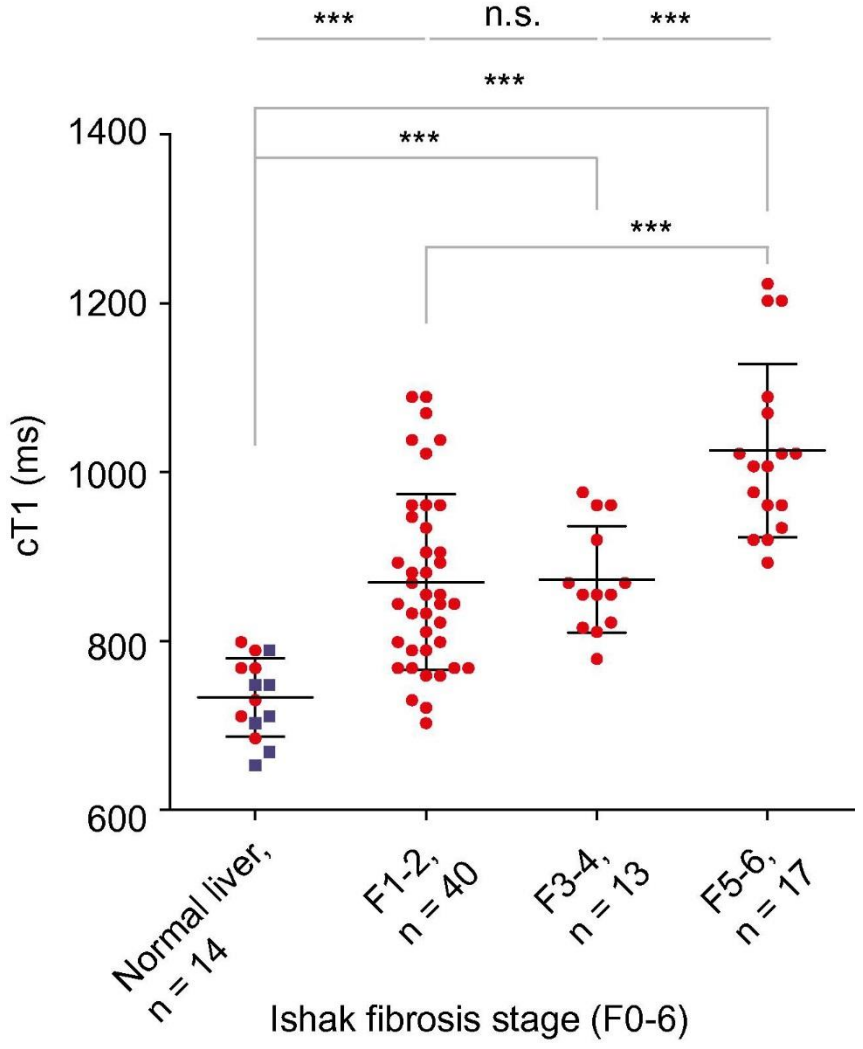








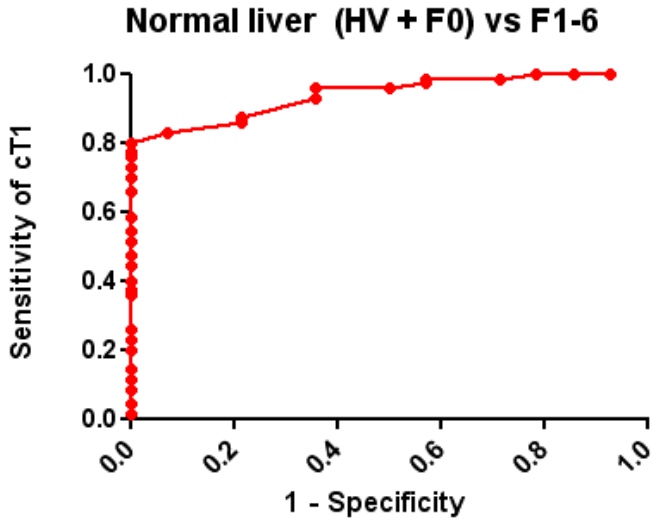
JOURNAL OF HEPATOLOGY Volume 60(1): 69-77 (2014)



*The LIF scale represents the range of focus for cT1 values in the liver

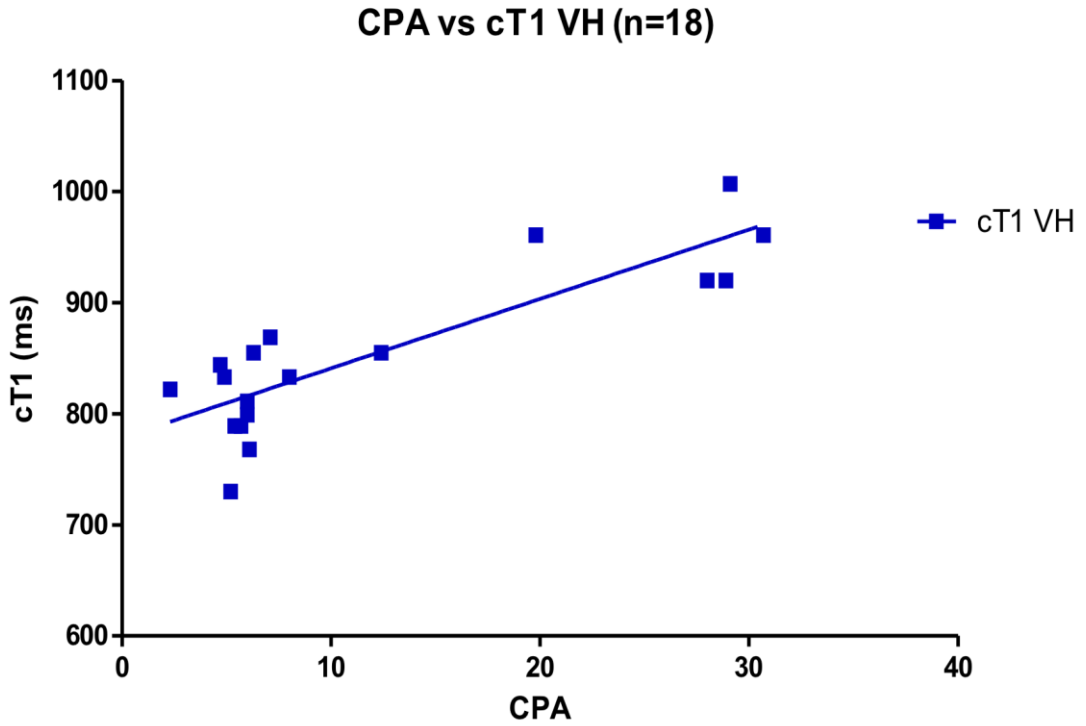
'The first non-invasive test to clearly identify even early fibrosis'

AUROC is 0·94 (95% CI 0·89 – 0·99) to detect **any disease** in a general population (viral hepatitis n=31, FLD n=31, other n=17); sensitivity 86%, specificity 93%



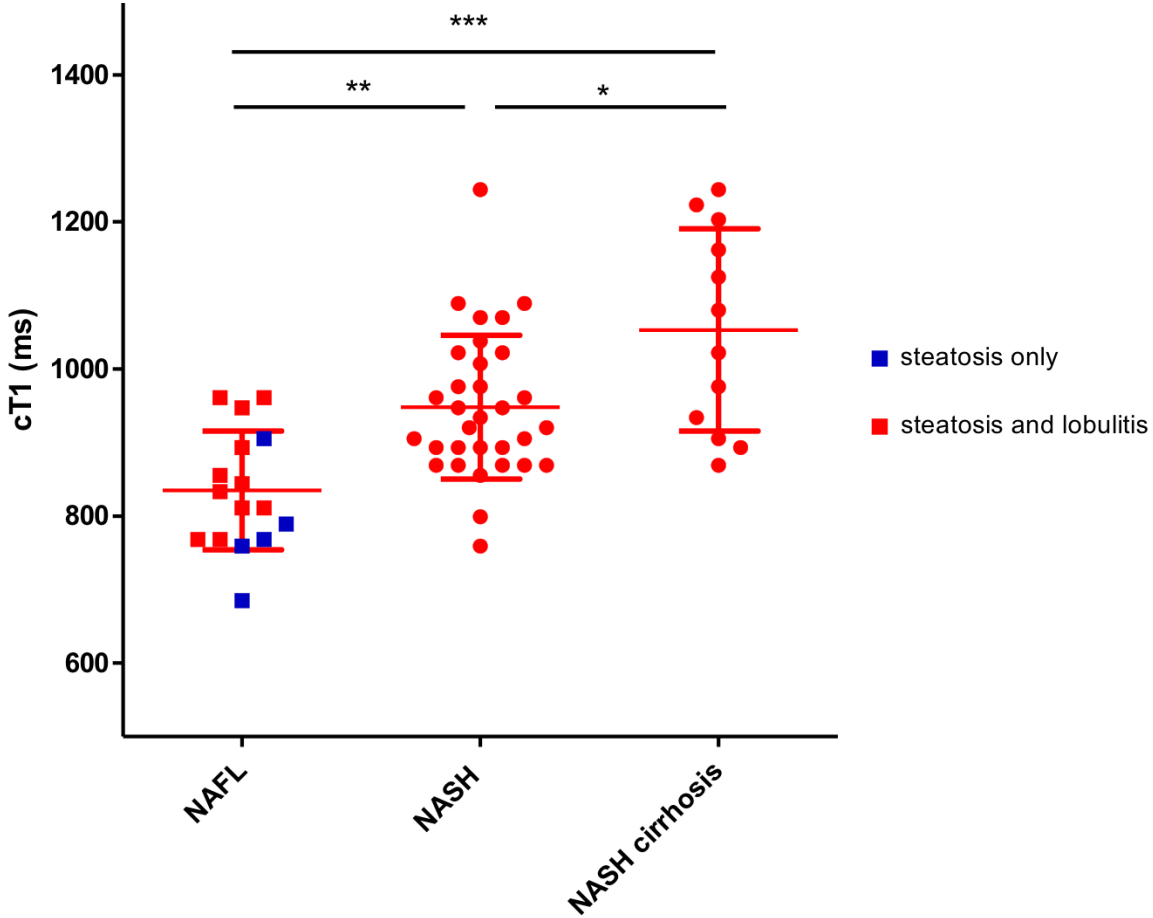
Perspectum Diagnostics

Comparisons with other histological scoring systems



Collagen – proportionate area in patients with viral hepatitis: R = 0.85, p < 0.001

Banerjee et al, J Hepatology 2014



AUROC distinguishing NAFL from NASH = 0.84

Pavlides et al, J Hepatology 2014

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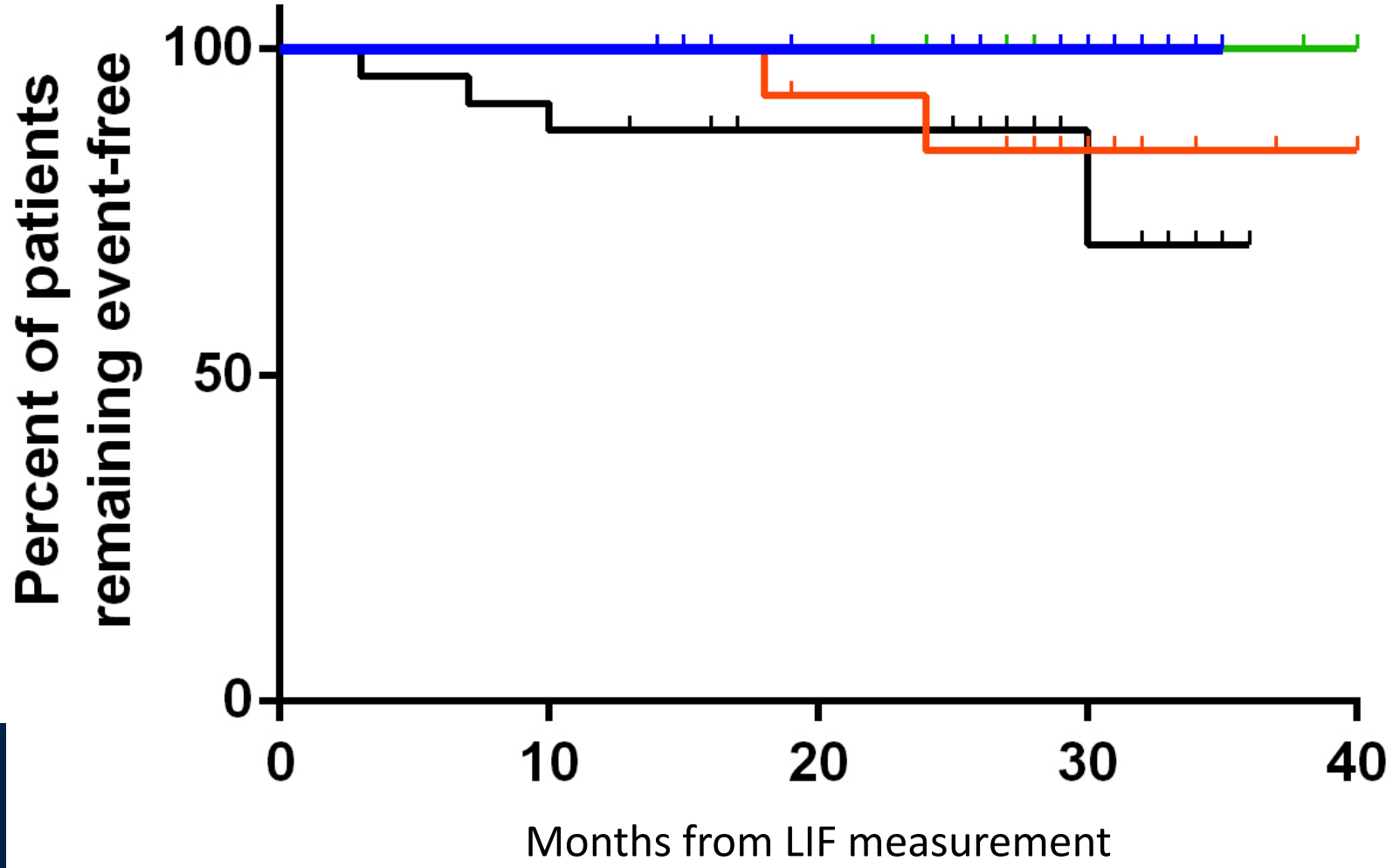
Perspectum Diagnostics

"LIF score accurately predicts clinical outcomes*"

The first non-invasive imaging test to do so.



Patients from earlier paper (ie a general population), followed up for minimum 12 months (median 28 months)

AASLD 2014 late-breaker no. 13

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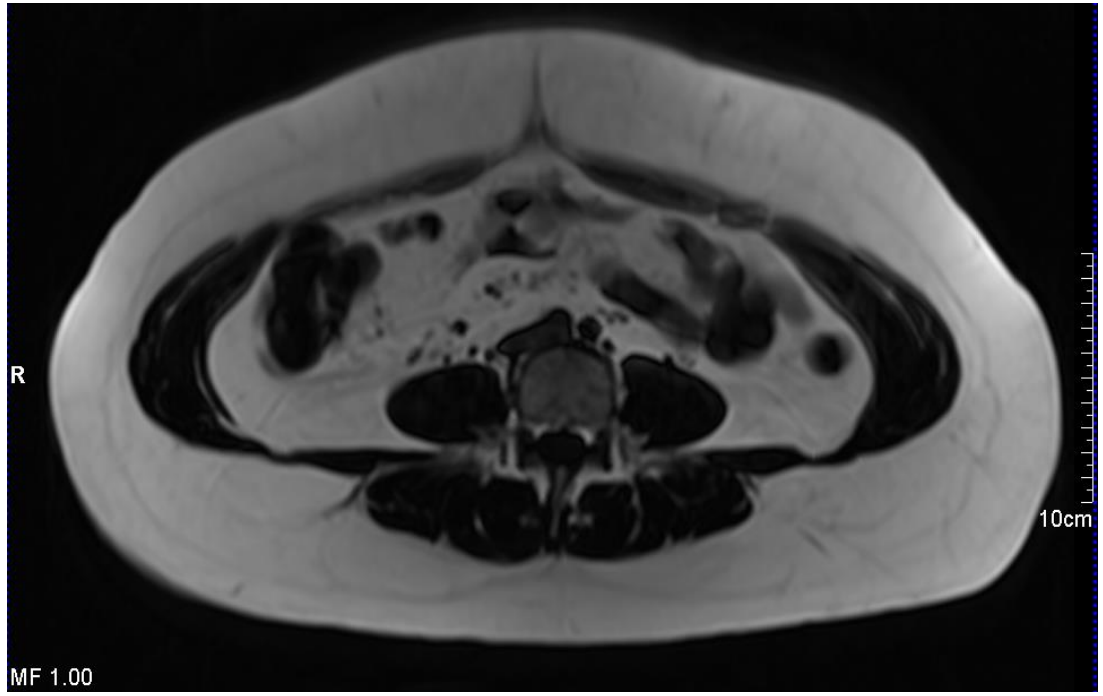
Perspectum Diagnostics

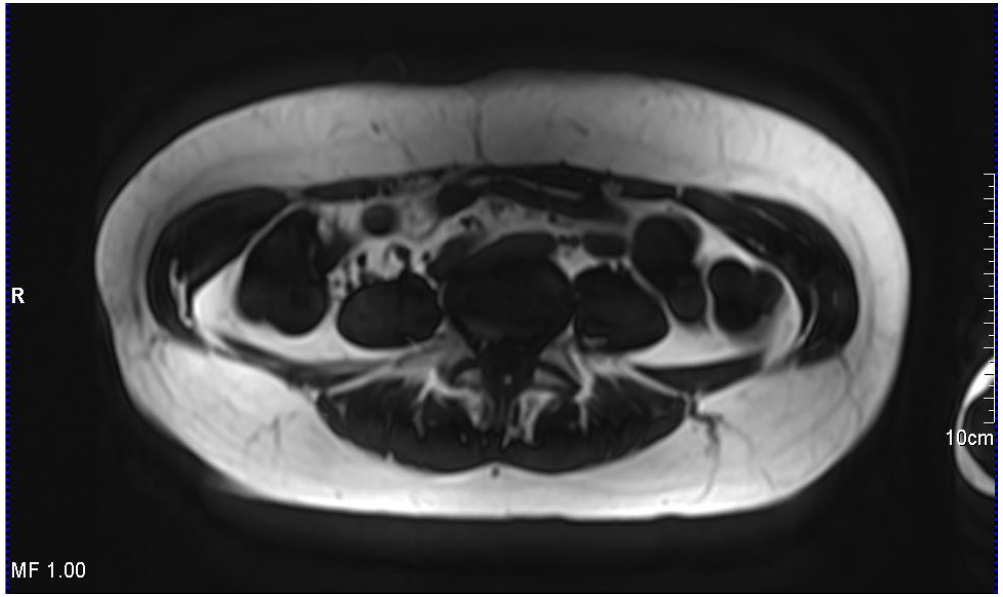
Measuring change

Fatty liver

44 yr old lady, worked fulltime, no overt symptoms.
Pre (left) and post (right) gastric bypass surgery images at L4, (same scale).



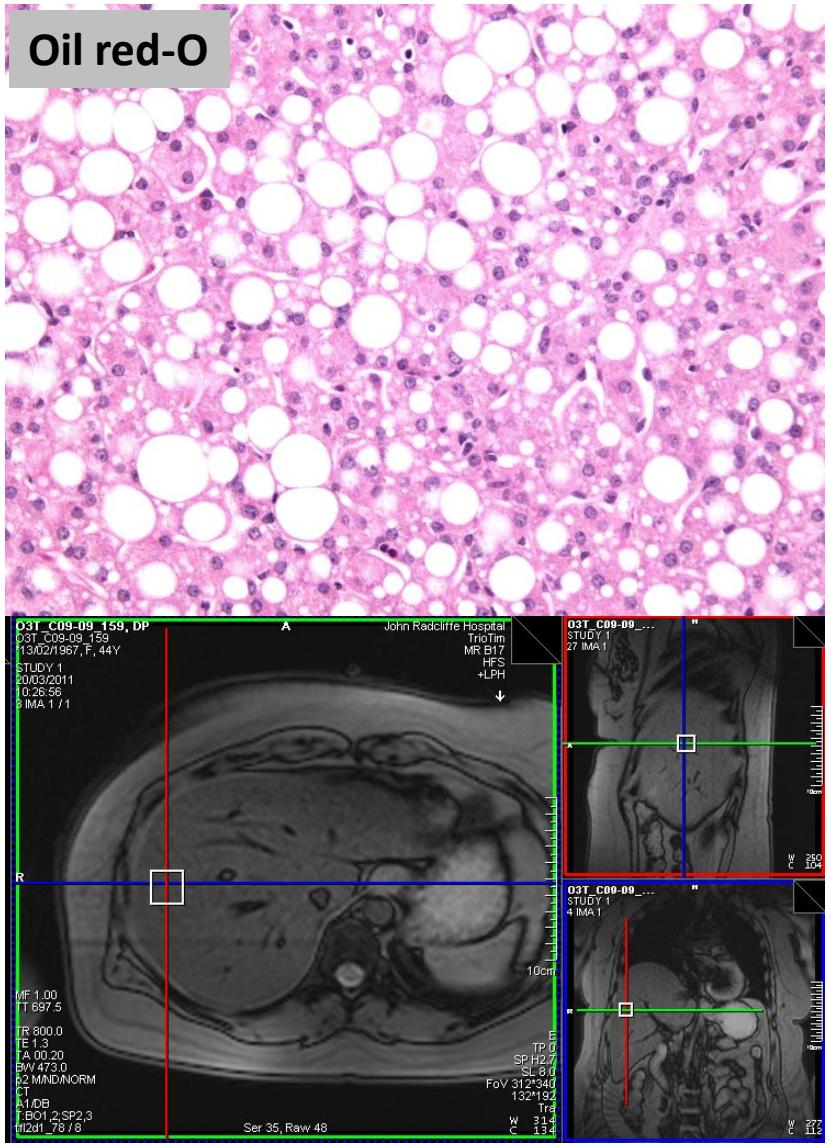
Preop BMI 34.3 kg/m^2 & visceral fat 131cm^2.

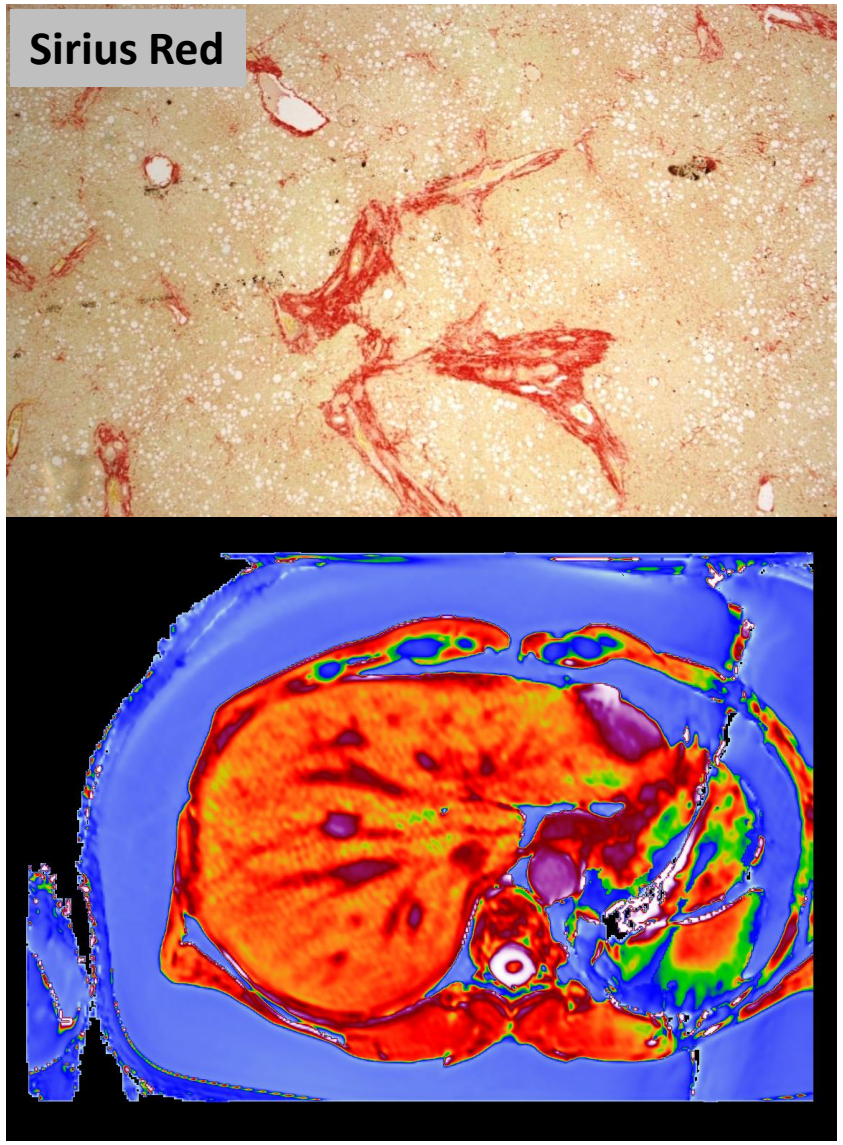


Postop BMI 24.4kg/m^2 & visceral fat 28.3cm^2.

Perspectum Diagnostics

Measuring change





Histology showed 90% of hepatocytes had lipid inclusions, and an ISHAK score of 3, with marked pericellular fibrosis as well.

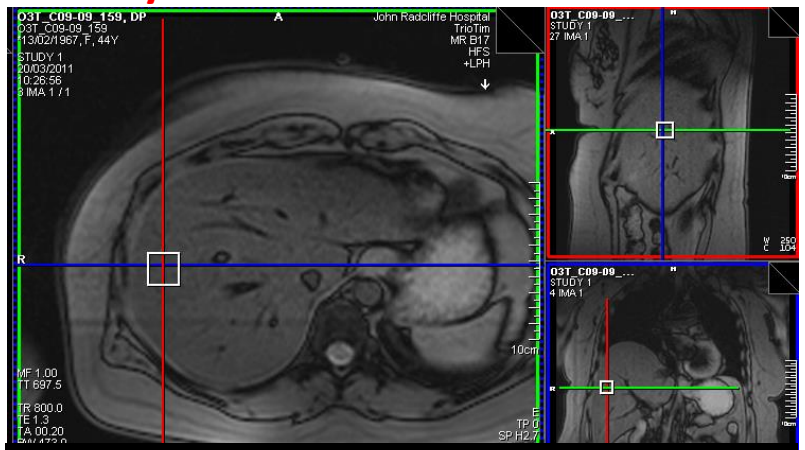
Diagnosis = NASH

Bottom row: MRS (left) and Liver*MultiScan* cT1 image (right) of patient at baseline

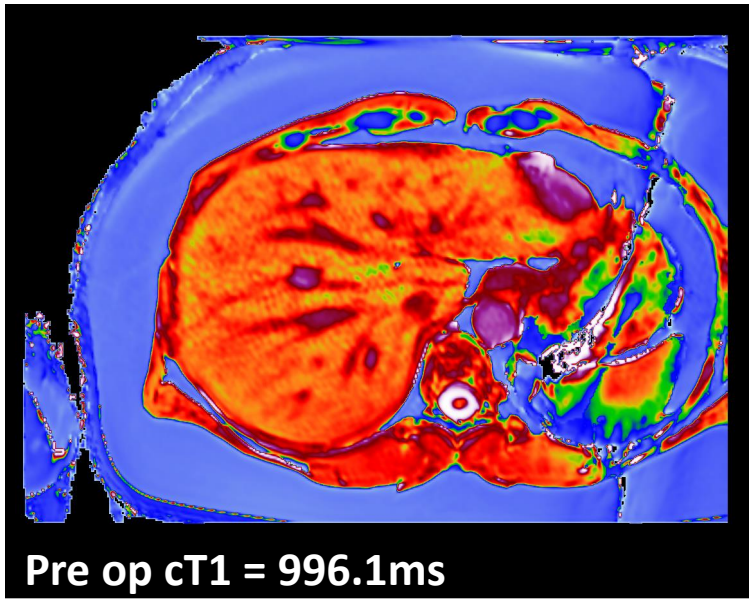
Perspectum Diagnostics

Measuring change

Liver fat (as measured with MR) is clearly reduced

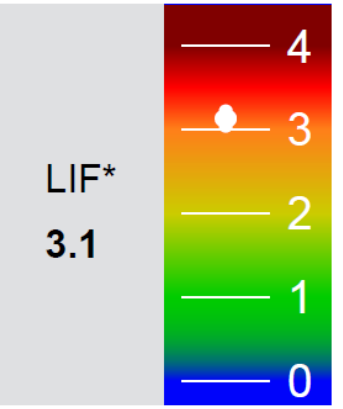


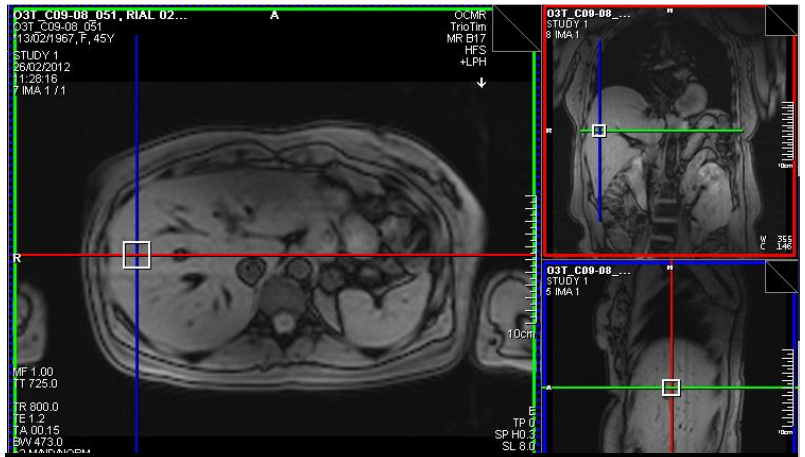
Pre op liver fat = 20.4%



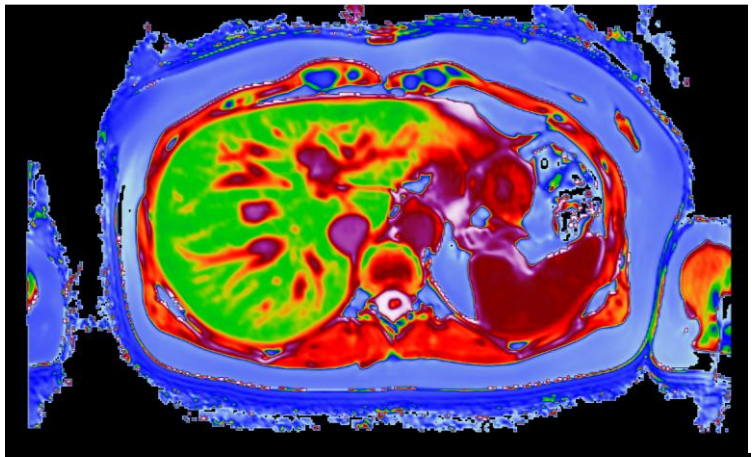
Pre op cT1 = 996.1ms

Clear change in cT1. No follow-up biopsy; no clinical indication

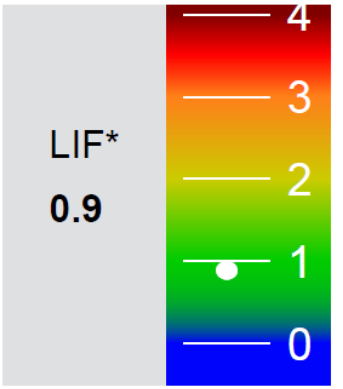




After weight loss liver fat = 1.7%



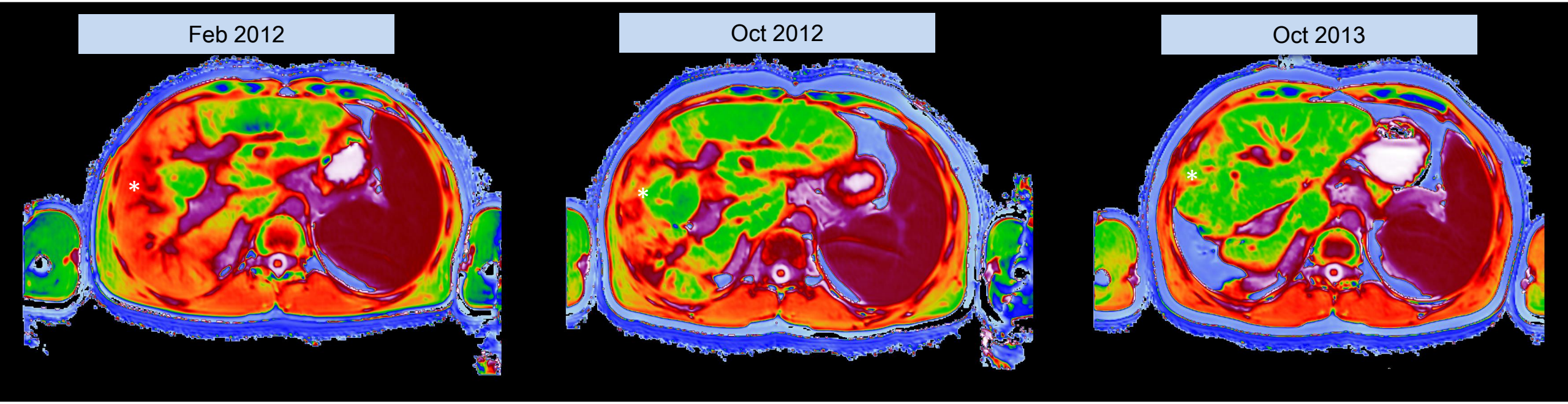
After weight loss cT1 = 783.5ms



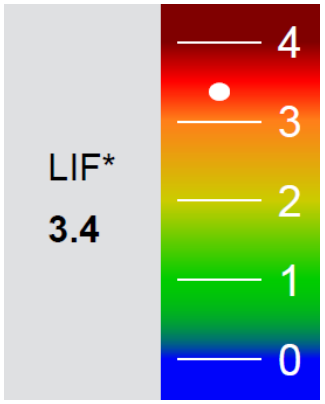
Perspectum Diagnostics

Measuring change

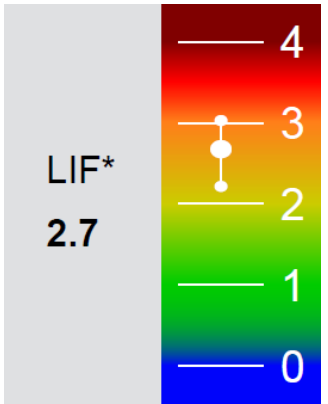
Treated with response to prednisolone and azathioprine over 20 months



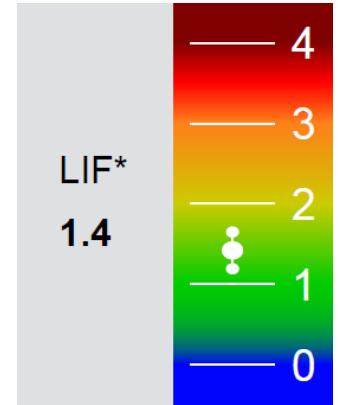
Pre treatment
cT1 = 1008.7
+/- 12ms



After treatment
cT1 = 919.8 +/-
46ms

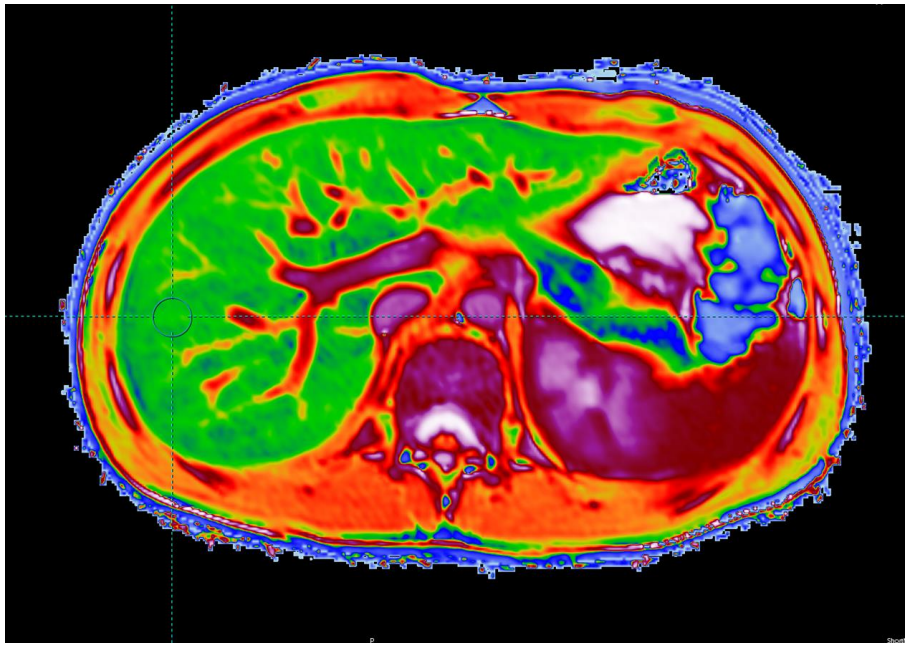


After treatment
cT1 = 826.4 +/-
24.7ms



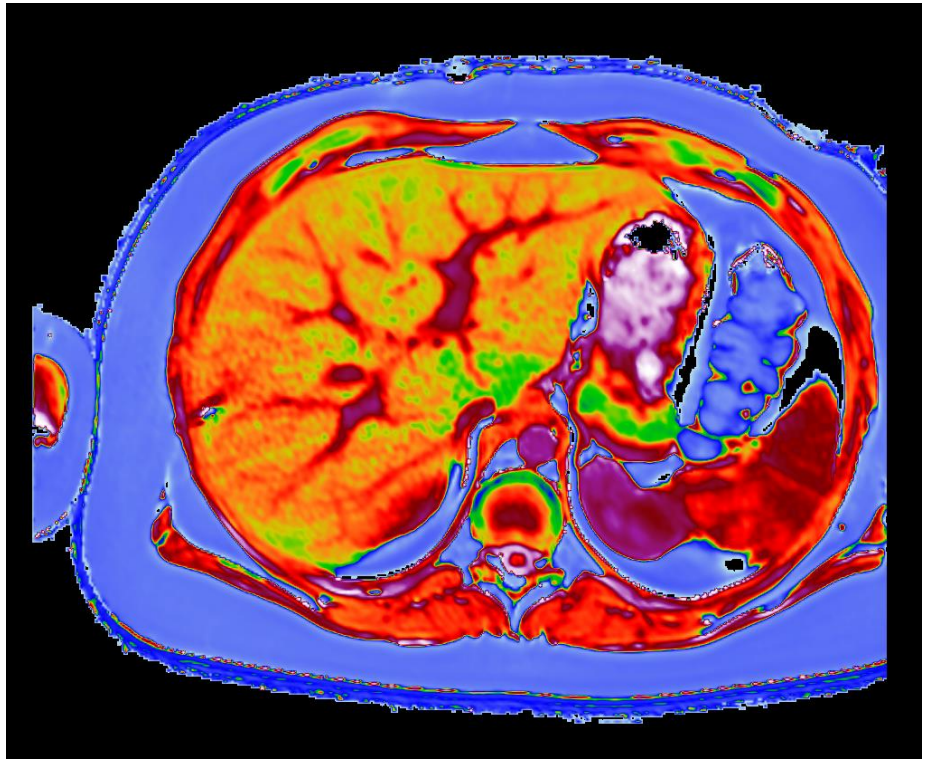
Adolescent imaging

Normal 12 year old



cT1 = 767.3 ms (LIF = 0.8)

12 year old with NASH + MetS



HLC 18%, glucose 6.5mmol/l, TG 1.15mmol/l, waist circumference 104cm, BP 133/77

cT1 = 990.1 ms (LIF = 3.1)

Perspectum Diagnostics

Changing the diagnostic pathway for patients

Symptoms / abnormal blood tests

Repeat blood tests — 2-6 weeks

Liver ultrasound — 4-8 weeks

Liver clinic appointment — 4-8 weeks

Liver biopsy — 2-6 weeks

Appointment for diagnosis — 4 weeks

16- 32 weeks

Multiparametric MR to diagnose and stage disease

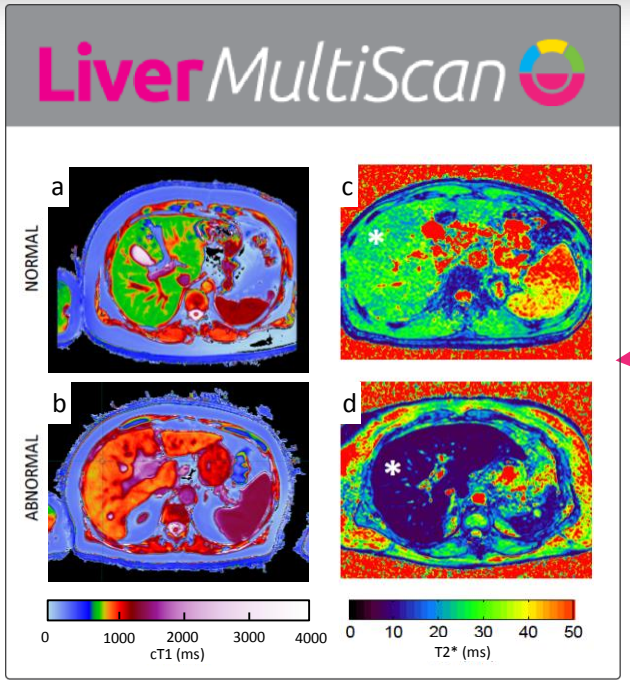
Same day diagnosis

- Saving up to 32 weeks per patient - diagnosis & management begin earlier
- Saving patients from unnecessary and painful liver biopsy
- Less disruptive to the patient's life, fewer visits to hospital, less anxiety
- **Saving over £1000 in cost per NHS patient**

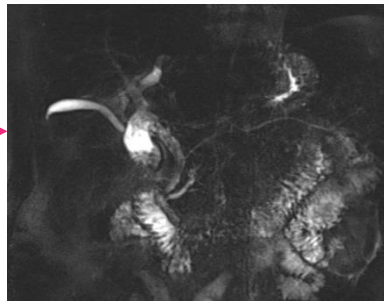
Perspectum Diagnostics

What we offer for drug development

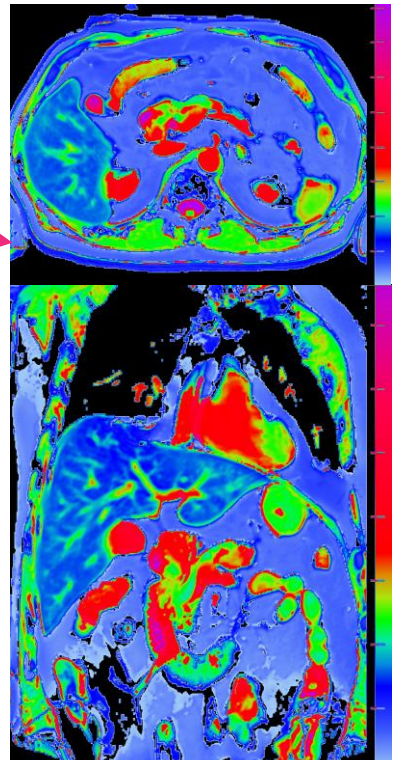
Quantitative MR Biomarkers In Clinical Trials



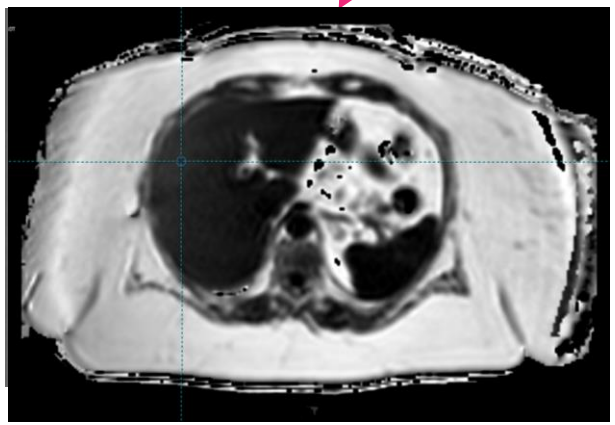
BILIARY TREE



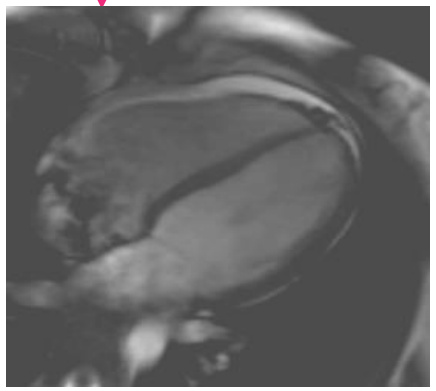
PANCREATIC CHARACTERISATION



VISCERAL & SUBCUTANEOUS FAT DISTRIBUTION



CARDIAC MASS & FUNCTION



Perspectum Diagnostics

Please visit
www.perspectum-diagnostics.com