Prevalence and stratification of NAFLD/NASH in a UK and US cohort using non-invasive multiparametric MRI

Stephen Harrison[1], Henry R. Wilman[2,3], Matthew D. Kelly[3], Andrea Dennis[3], Cat J. Kelly[3], Angelo Paredes[4], Jennifer Whitehead[4], Stefan Neubauer[1], Rajarshi Banerjee[3].

[1]University of Oxford, UK [2]University of Westminster, London, UK [3]Perspectum Diagnostics, Oxford, UK [4]San Antonio Military Medical Center, San Antonio, US

Background

- There is a clear need to assess the prevalence of NAFLD and NASH in the general population.
- MRI iron corrected T1 (cT1) and has been shown to correlate with liver inflammation and fibrosis, and liver-related outcomes [1], and distinguish NASH from simple steatosis [2].
- Proton density fat fraction (PDFF) and cT1 are being collected as part of the UK Biobank imaging study of 100,000 individuals, and as a part of the US Prevalence study [3].

Aim

To investigate the effectiveness of multiparametric MRI for the assessment and stratification of NAFLD/NASH in two large UK and US cohorts

Inflammation and/or fibrosis, no steatosis

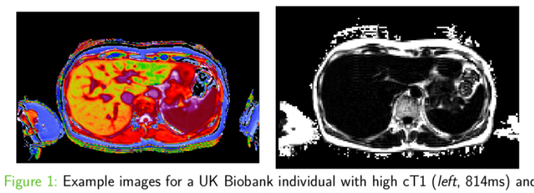

Figure 1: Example images for a UK Biobank individual with high cT1 (*left*, 814ms) and low PDFF (*right*, 0.8%).

No inflammation, fibrosis or steatosis

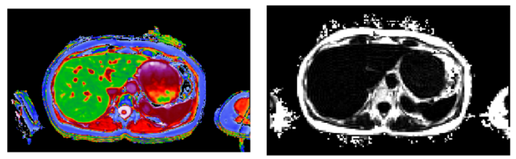

Figure 2: Example images for a UK Biobank individual with low cT1 (*left*, 602ms) and low PDFF (*right*, 0.7%).

Methods

Data is presented for 2895 individuals from the UK Biobank cohort. Each individual received multiparametric MRI (Liver*MultiScan*^{TM} protocol, $<$ 5 min.) to estimate liver fat fraction (PDFF) and cT1. Liver*MultiScan*^{TM} uses MRI T2* combined with T1 to derive cT1. Values presented here are based on Liver*MultiScan*^{TM} v2.0. High cT1 has been shown to correlate with inflammation, fibrosis, and liver-related outcomes [1]. The PDFF and cT1 values from the UK Biobank cohort were compared to those obtained in a general population study in the San Antonio (TX) area [3]. Patients were recruited from those referred for routine colon cancer screening with no prior history of liver disease or alcohol abuse. Patients were invited for a biopsy if any of the four non-invasive markers they were at risk of liver disease (FibroScan Liver Stiffness Measurement ($\geq$ 7kpa), MR elastography ($\geq$ 3kpa), and Liver*MultiScan*^{TM} PDFF ($\geq$ 5%) and LIF ($\geq$ 2). Fibrosis was staged on the Kleiner-Brunt scale, with >F1 classed as significant fibrosis. Liver biopsies were double-blind evaluated with consensus using the NASH CRN scoring system by two expert pathologists.

MRI identifies high risk NASH

- Of the biopsied subjects (n=139) from the US cohort, 98% (98%) with PDFF $\geq$ 5% & cT1 $\geq$ 800ms (750ms) had NAFLD, and 67% (67%) had NASH. (Figure 3).
- 29% (25%) of subjects with PDFF $\geq$ 5% & cT1 $\geq$ 800ms (750ms) had high risk NASH (NASH and fibrosis F2-3).
- 36% (44%) of the US cohort with PDFF $\geq$ 5% & cT1 $<$ 800ms (750ms) had NASH, and only 6% (11%) had high risk NASH
- 62.5% (92%) of high risk NASH subjects had PDFF $\geq$ 5% & cT1 $\geq$ 800ms (750ms).
- Adding cT1 ($\geq$800ms) improved PDFF-based stratification for NASH and high risk NASH with enrichment ratios of 116% and 253% respectively.

UK Biobank participants at high risk of NASH

- There is no biopsy data for the UK Biobank cohort but PDFF alone identifies patients with steatosis [4].
- Applying the prevalences from the US cohort to the UK Biobank cohort, we would expect a NASH prevalence of 12%.
- Similarly, we would expect 49% of Biobank participants with PDFF $\geq$ 5 to have NASH, and 15% to have high risk NASH.
- The US and UK cohort are ethnically different (27% Latino, 73% non-Latino vs 96% white), and the US cohort has a higher prevalence of diabetes (14.5% vs 5.4%), hypertension (41% vs 26%), and has a higher mean BMI (30 vs 26 kg/m^2).

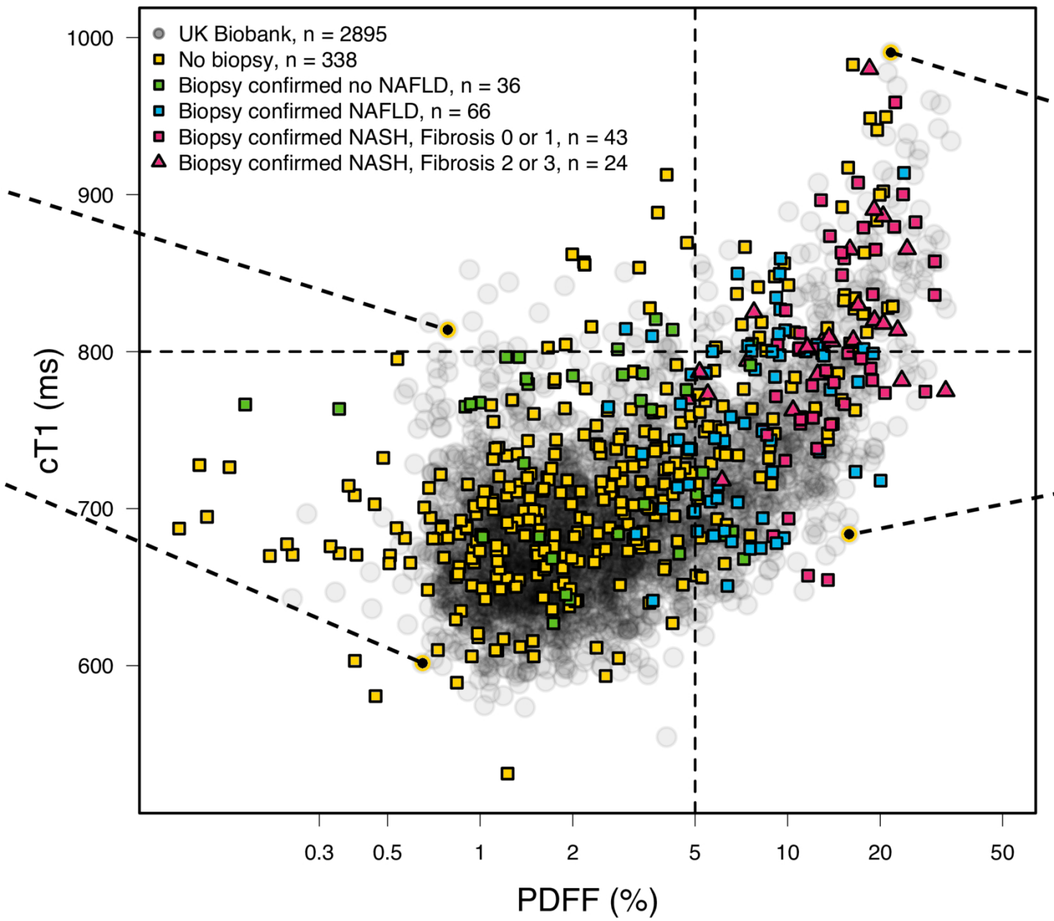

Figure 3: Distribution of cT1* and PDFF for UK Biobank individuals (black circles). Overlayed are cT1* and PDFF plotted for 338 US patients (square points), coloured by their biopsy proven NASH status. Dashed lines at PDFF = 5% (widely accepted clinical threshold) and cT1* = 800. Yellow circles indicate the four UK Biobank participants displayed in Figures 1, 2, 4, and 5. *cT1 values displayed here are equivalent to those calculated by Liver*MultiScan*^{TM} v2.0.

Conclusions

- Multiparametric MRI (Liver*MultiScan*^{TM}) is an effective non-invasive method to identify and stratify individuals with NAFLD and NASH at a population level.
- Liver*MultiScan*^{TM} acquisition takes $<$ 5 minutes, requires no contrast, can be used for high throughput analysis of a general population, and can identify individuals less likely to benefit from a liver biopsy.
- Iron corrected T1 can be used in addition to PDFF to further enrich a population for NASH with significant fibrosis.

Inflammation and/or fibrosis, and steatosis

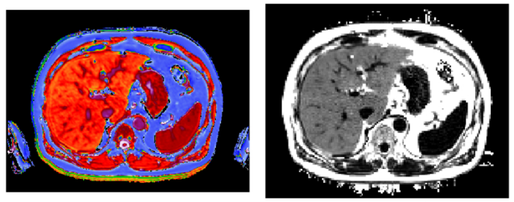

Figure 4: Example images for a UK Biobank individual with high cT1 (*left*, 990ms) and high PDFF (*right*, 22%).

No inflammation or fibrosis, steatosis

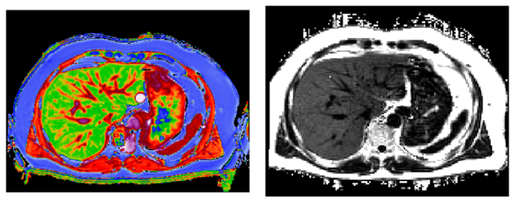

Figure 5: Example images for a UK Biobank individual with low cT1 (*left*, 684ms) and high PDFF (*right*, 16%).

References and acknowledgements

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Perspectum Diagnostics

biobank uk Imaging study

UNIVERSITY OF WESTMINSTER

Contact: henry.wilman@perspectum-diagnostics.com