UNIVERSITY OF BIRMINGHAM | COLLEGE OF MEDICAL AND DENTAL SCIENCES

Validation Of Multi-Parametric MRI in the Assessment and Staging of Non-Alcoholic Fatty Liver Disease

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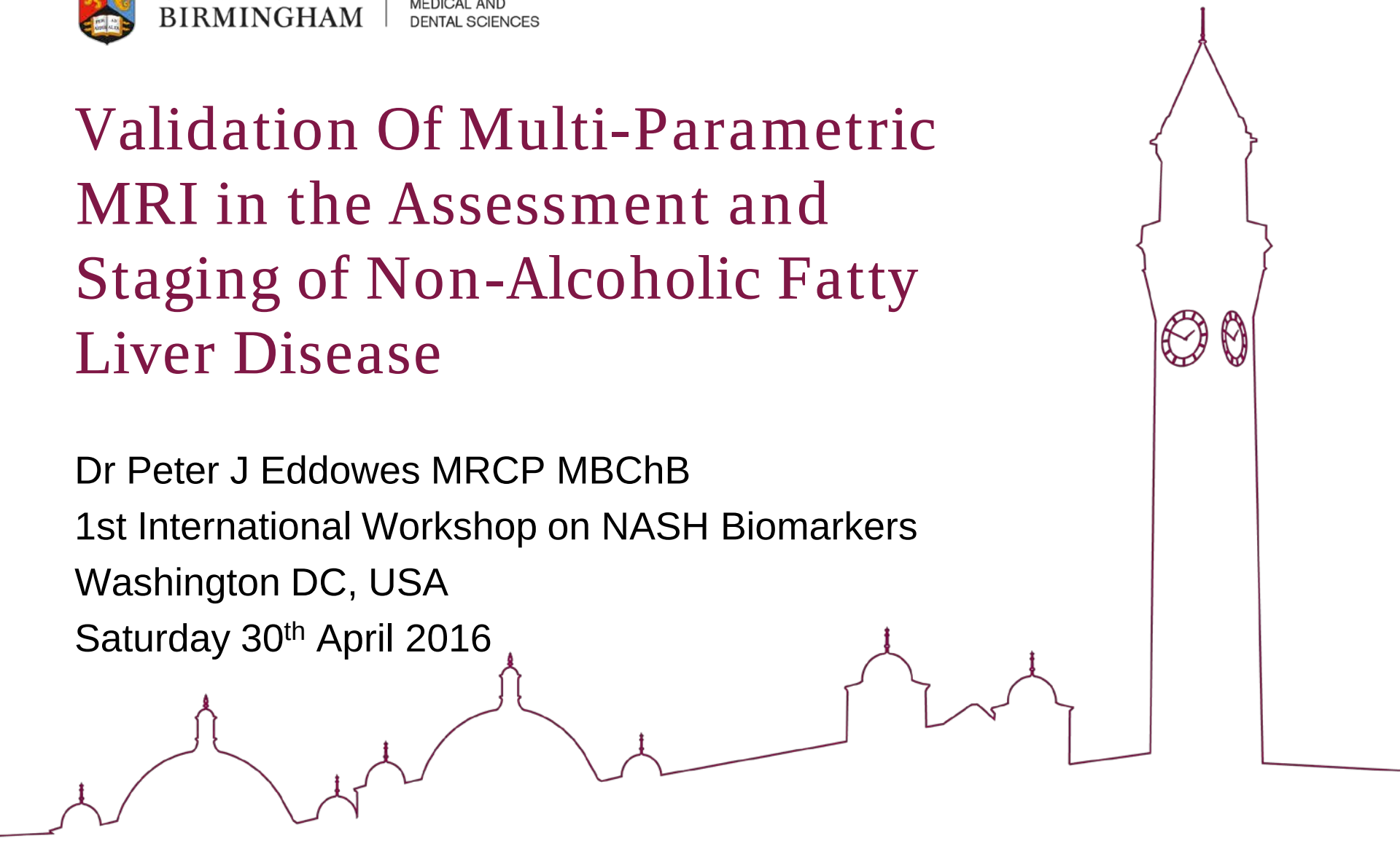
1st International Workshop on NASH Biomarkers

Washington DC, USA

Saturday 30th April 2016

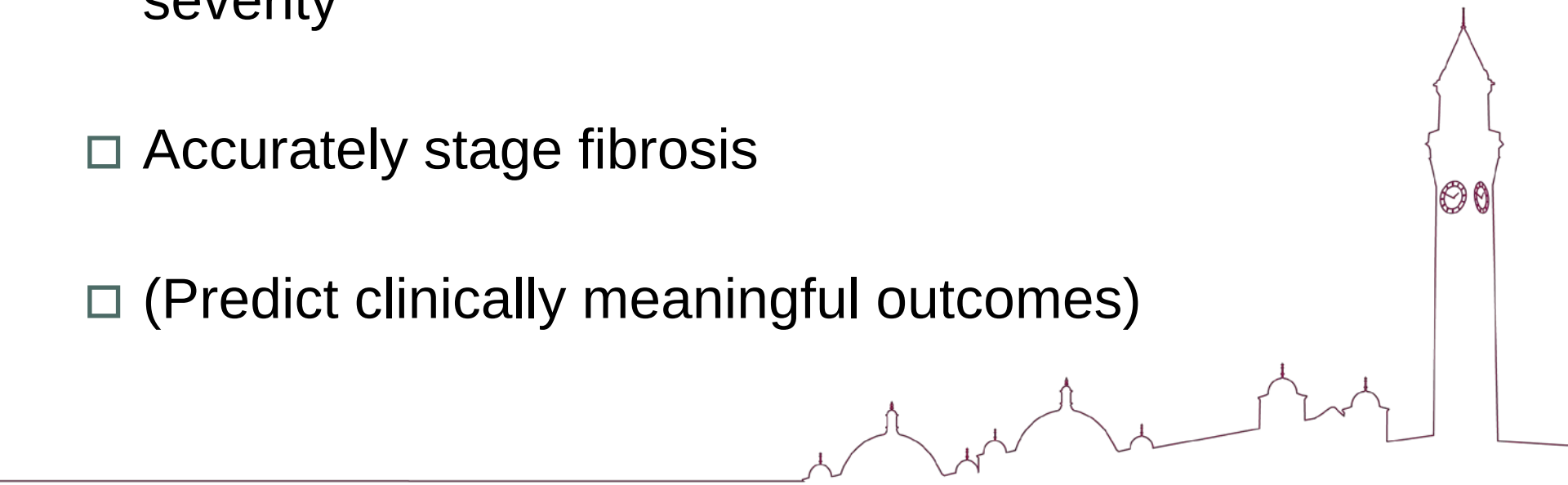


Disclosures

- This work is academic led and funded by Innovate-UK
- I have no financial interests in Perspectum Diagnostics Ltd

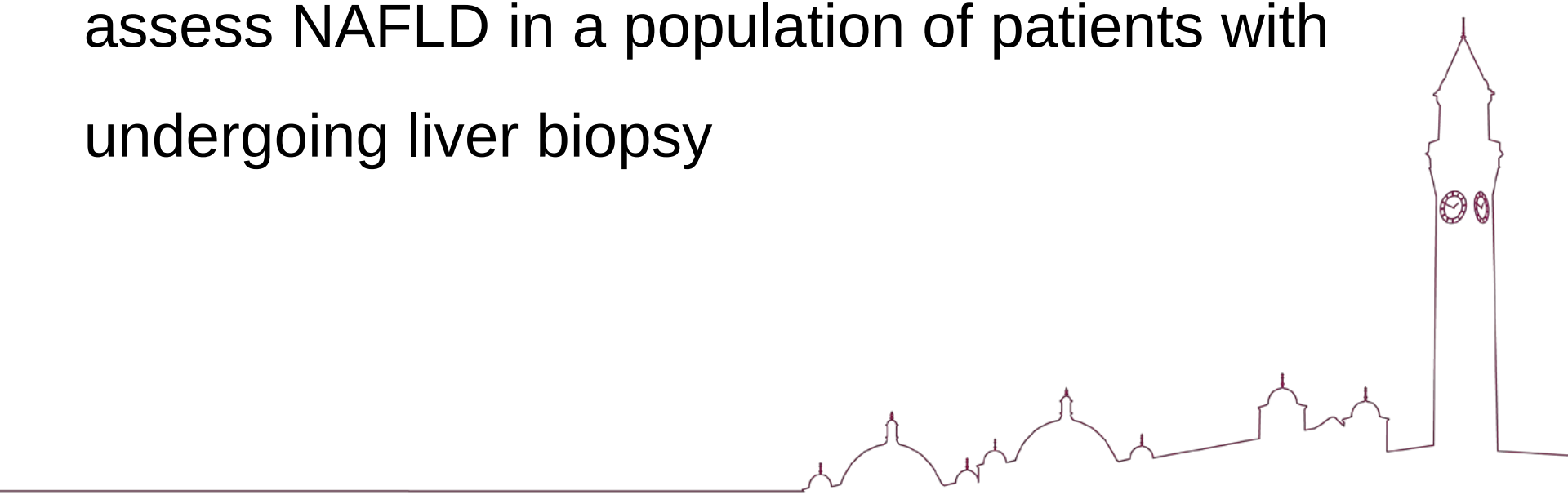
Non-invasive testing seeks to:

- Detect steatosis
- Diagnose NASH
- Be sensitive enough to monitor changes in NASH severity
- Accurately stage fibrosis
- (Predict clinically meaningful outcomes)



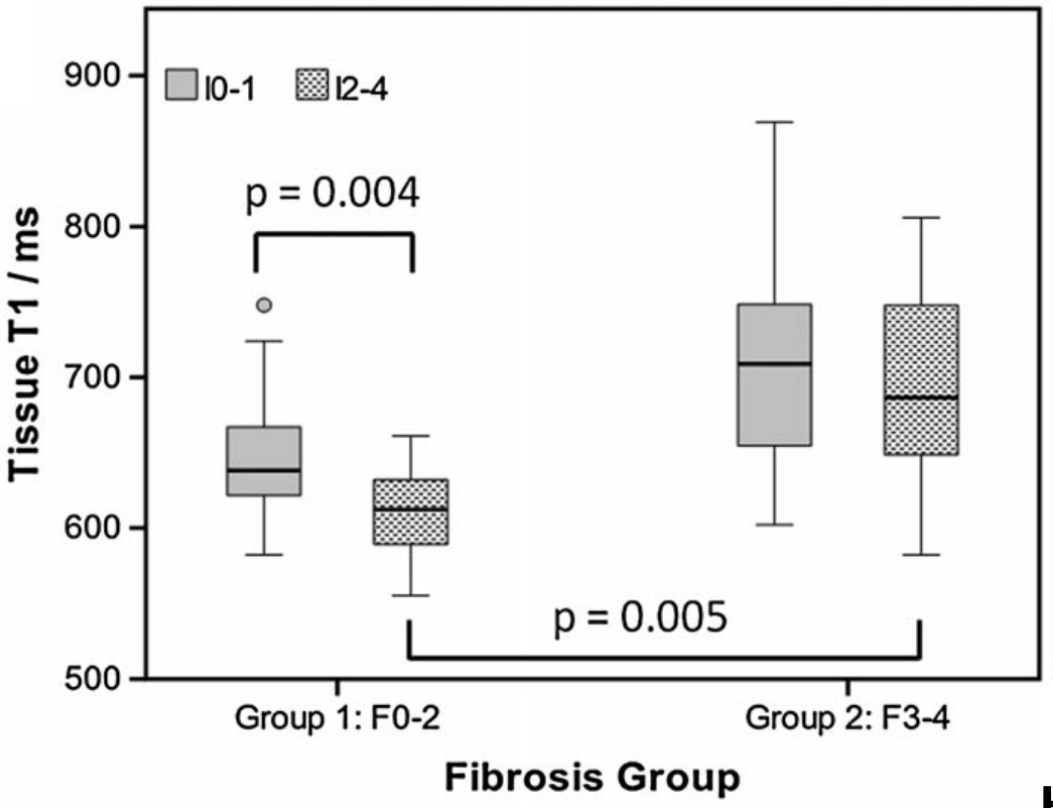
Aims

Prospective assessment and validation of multi-parametric MRI as a non-invasive test to assess NAFLD in a population of patients with undergoing liver biopsy



T1 Mapping

Hypothesis that hepatic T1 is proportional to extracellular water content, which is elevated in fibrosis



Hepatic iron content inversely proportional to T1

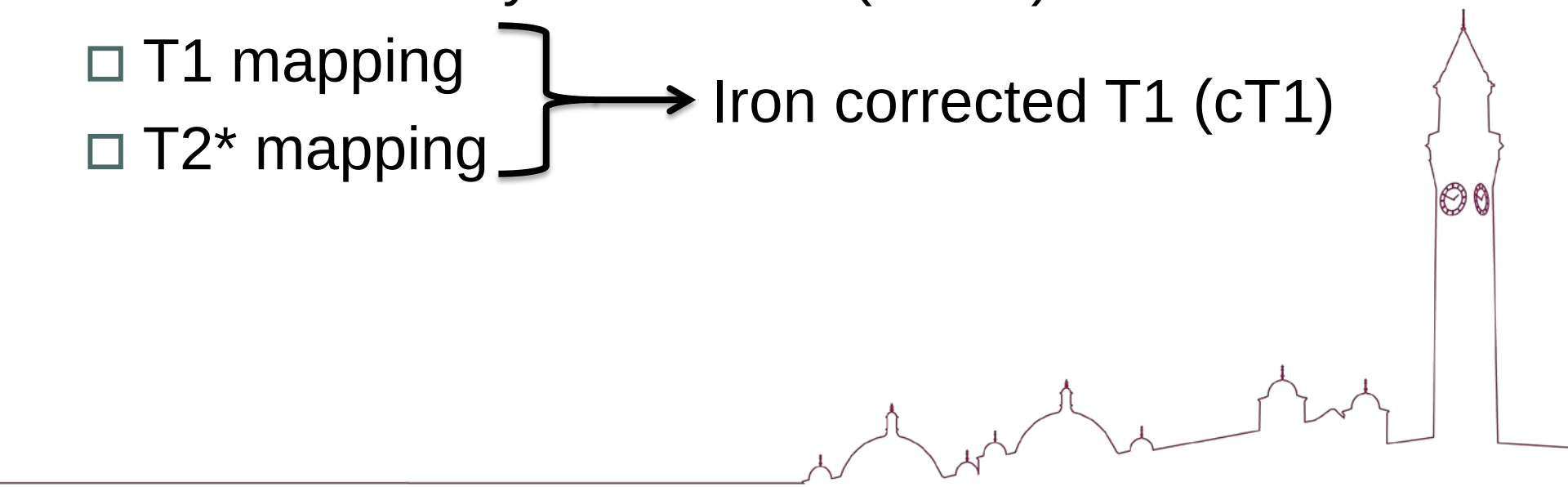
Hoad C et al, NMR Biomed, 2015

Multi-Parametric MRI

- Proprietary algorithm developed by Perspectum Diagnostics Ltd uses T2* to adjust T1 to compensate for the effects of iron

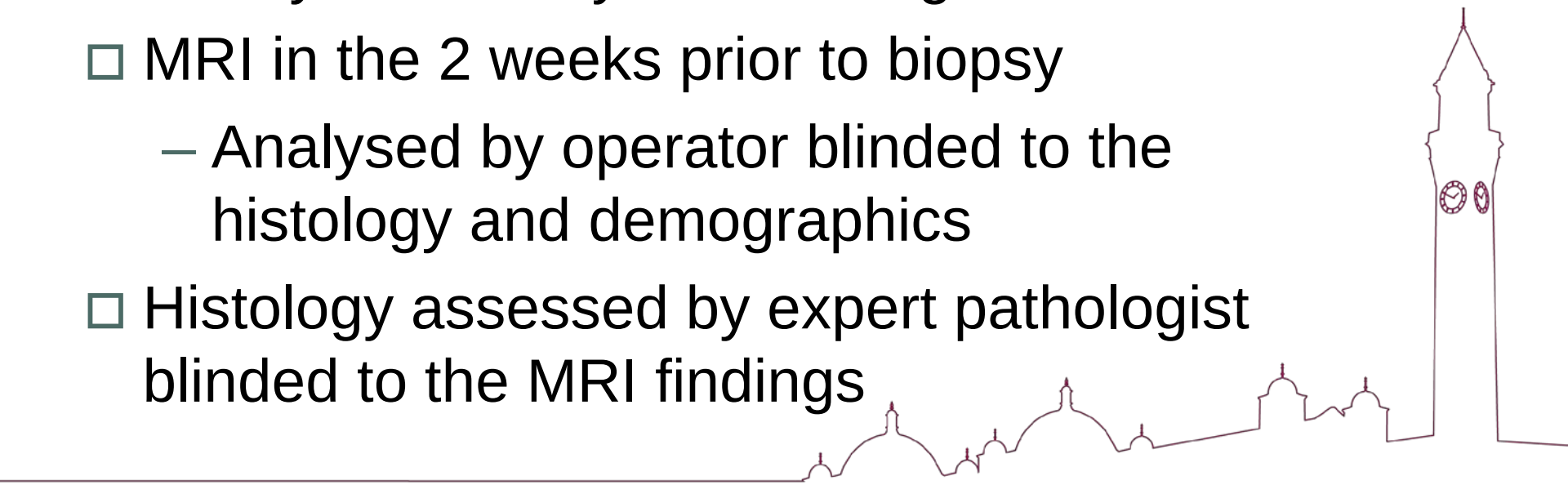
- Proton density fat fraction (PDFF)
- T1 mapping
- T2* mapping

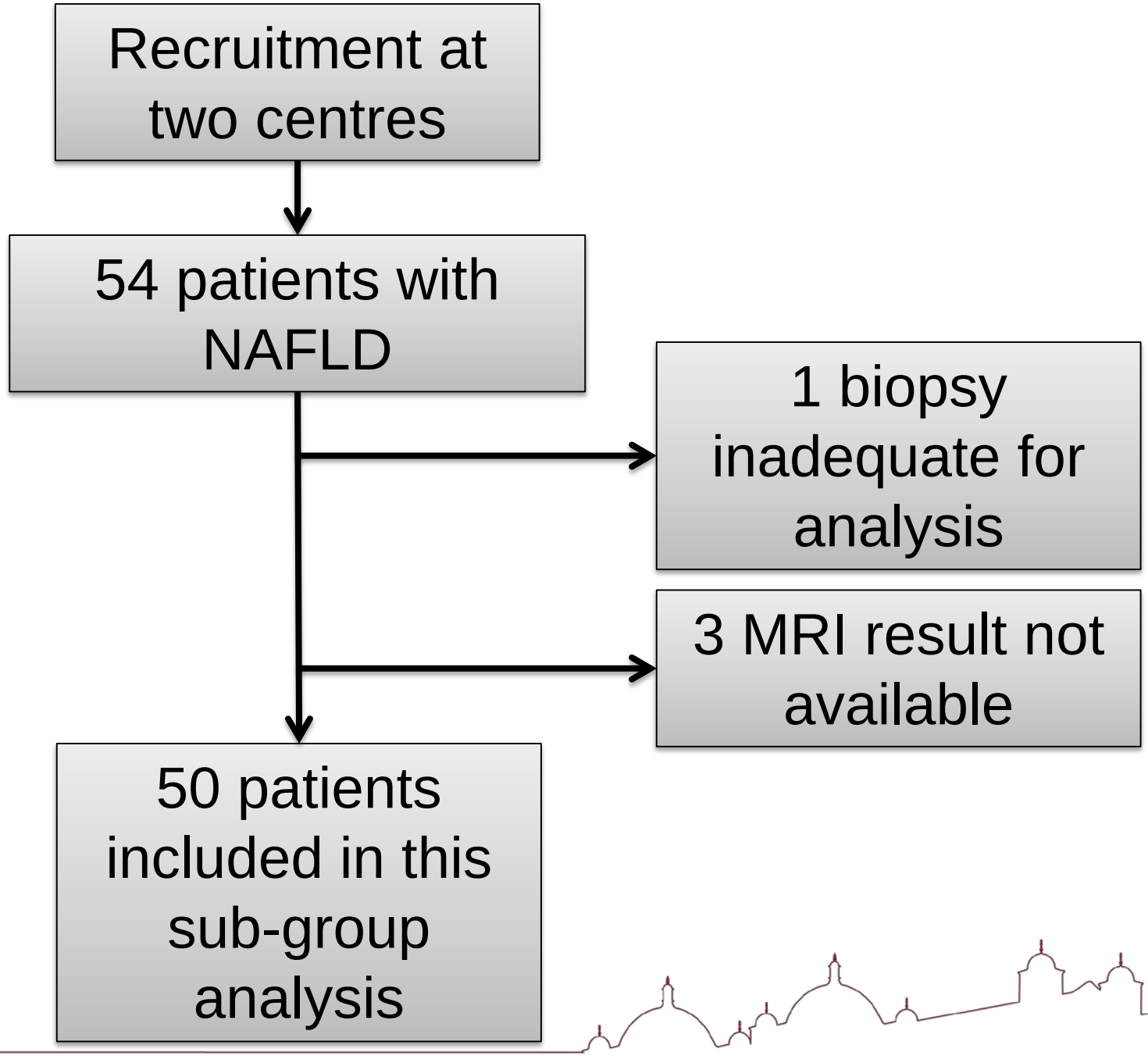
→ Iron corrected T1 (cT1)



Methods

- Sequential patients undergoing standard of care liver biopsies for the diagnosis or assessment of NAFLD
  - Queen Elizabeth Hospital Birmingham
  - Royal Infirmary of Edinburgh
- MRI in the 2 weeks prior to biopsy
  - Analysed by operator blinded to the histology and demographics
- Histology assessed by expert pathologist blinded to the MRI findings




Recruitment at two centres
54 patients with NAFLD
1 biopsy inadequate for analysis
3 MRI result not available
50 patients included in this sub-group analysis

Baseline Demographics

Age (years)	54 (18-73)	Median (range)
Male	28 (56%)	n (%)
Caucasian	43 (86%)	n (%)
BMI (Kg/m^2)	33.6 (+/-5.1)	Mean (+/-SD)
Male Waist:Hip ratio	0.98 (+/-0.07)	Mean (+/-SD)
Female Waist:Hip ratio	0.90 (+/-0.06)	Mean (+/-SD)
Post transplant	5 (10%)	n (%)
Type 2 diabetes	26 (52%)	n (%)
Consume alcohol	13 (26%)	n (%)
Alcohol intake (UK units/week)	8 (1-20)	Median (range)

Histology

Median (range) length 25 (15—50) mm

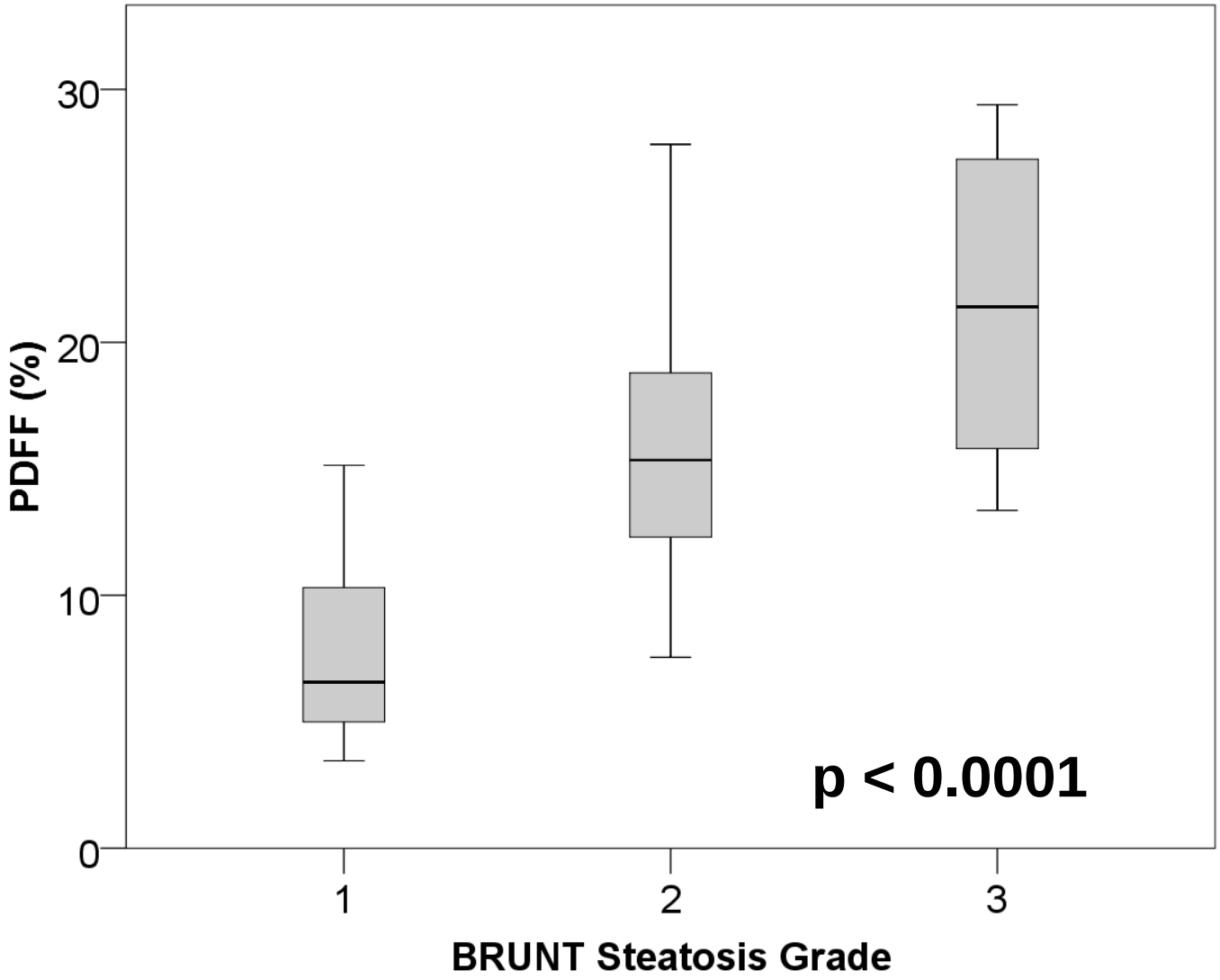
Confirmed diagnosis of NASH 38 (76%)

Kleiner Fibrosis Stage		
0	6	12%
1	10	20%
2	9	18%
3	20	40%
4	5	10%

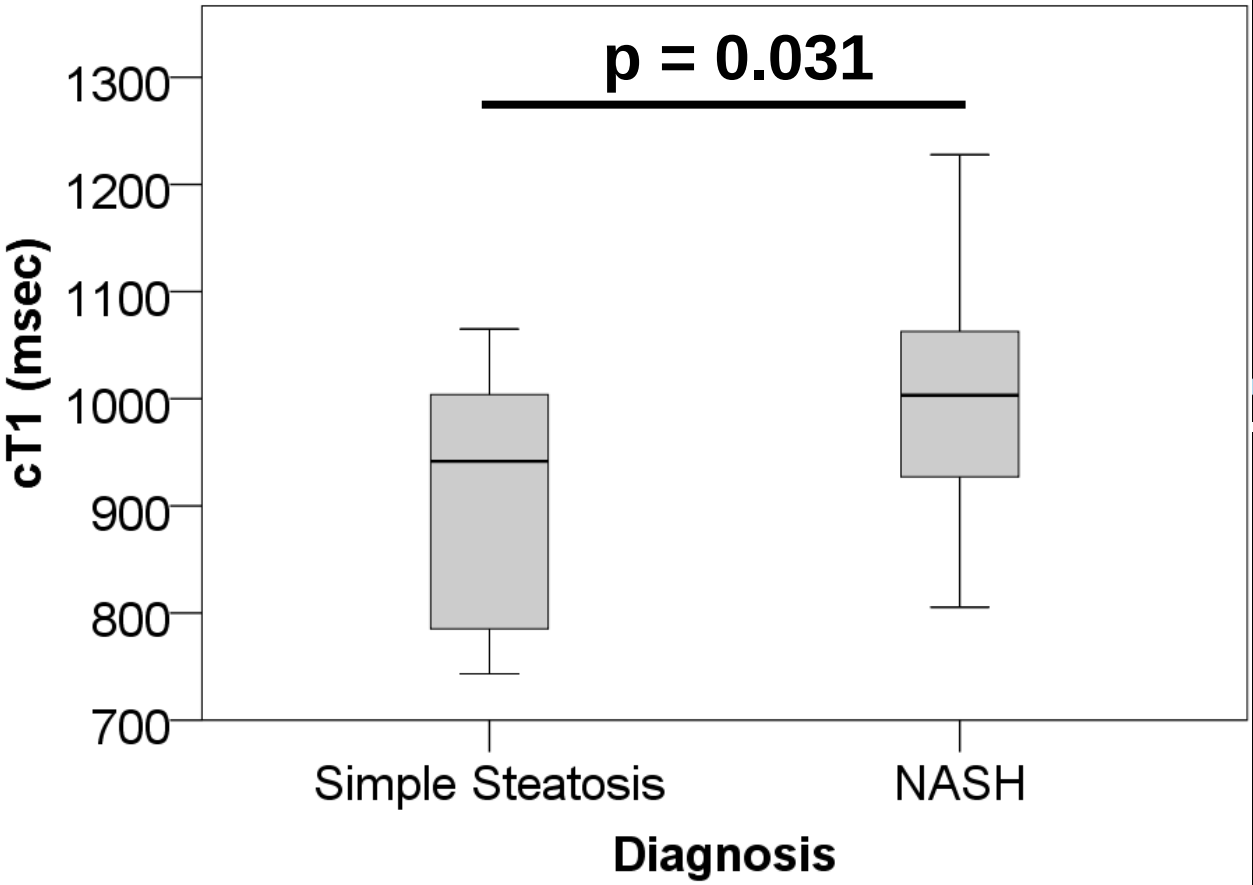
Total NAS score		
1-2	9	18%
3-4	16	32%
5-6	22	44%
7-8	3	6%

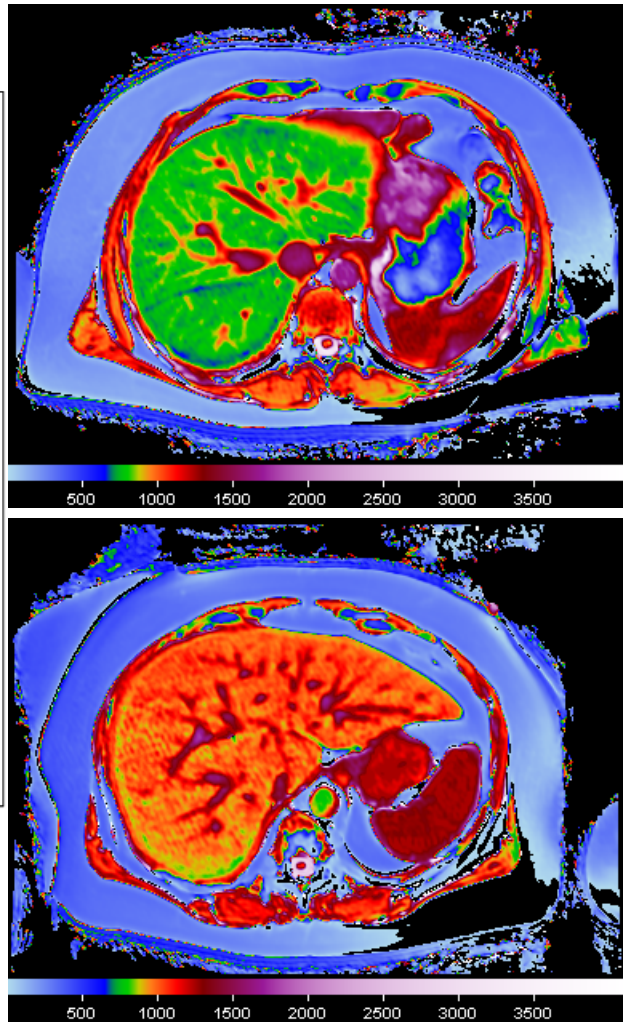
Brunt Steatosis Grade		
0	0	0%
1	23	46%
2	17	34%
3	10	20%

Significant association between PDFF and Brunt steatosis grade

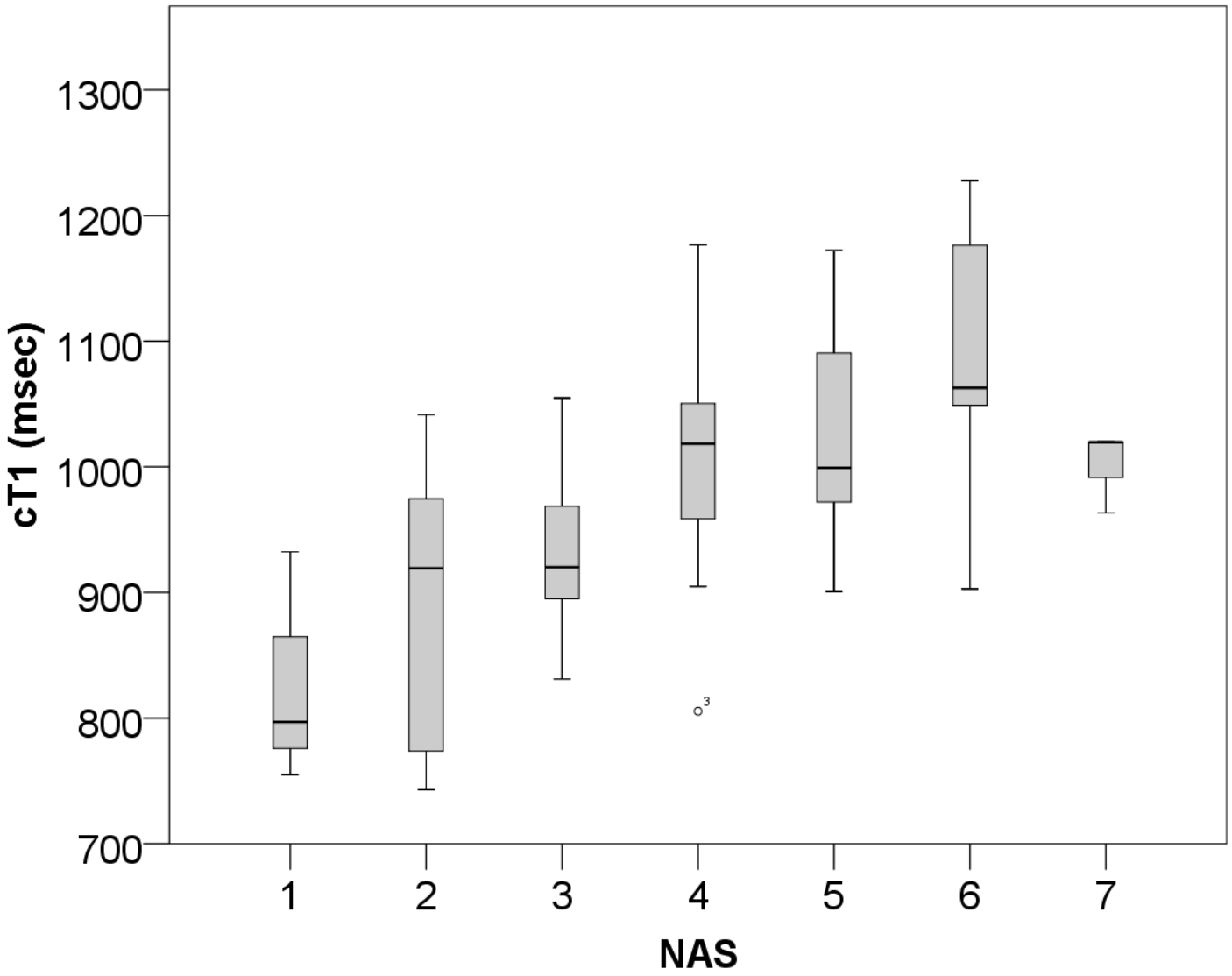


cT1 is significantly elevated in those diagnosed with NASH



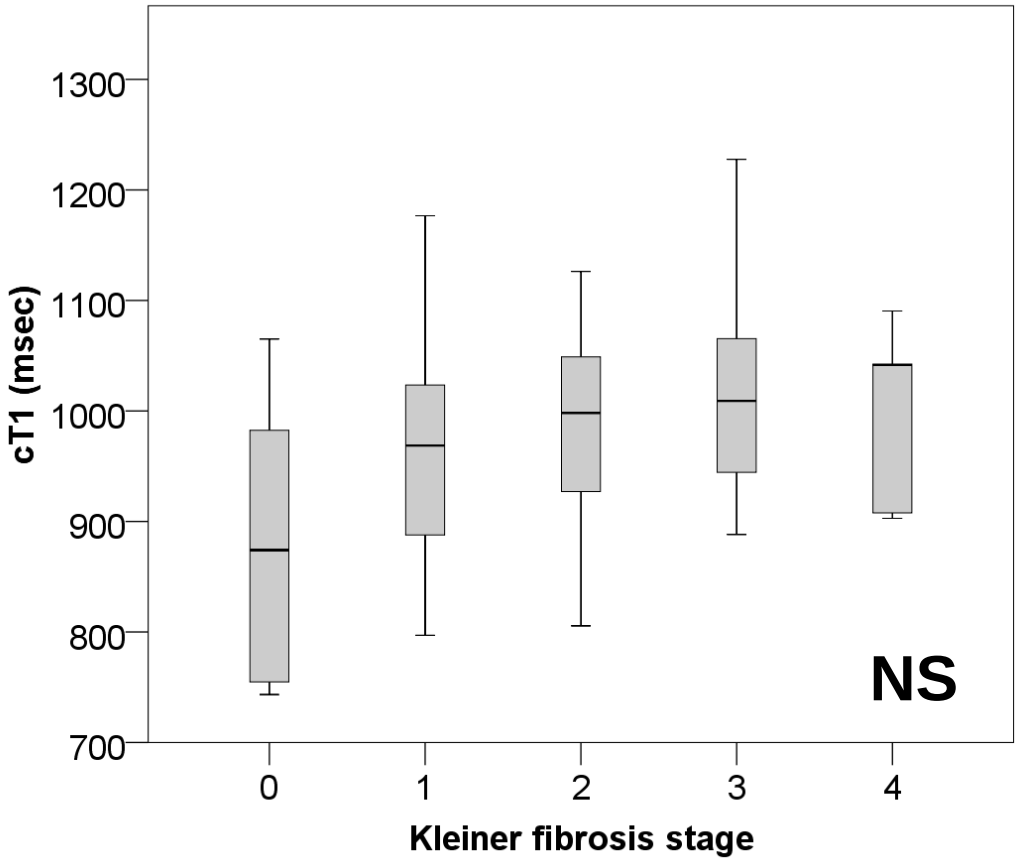


Significant association between cT1 and total NAS score



p = 0.013

No significant association between cT1 and fibrosis



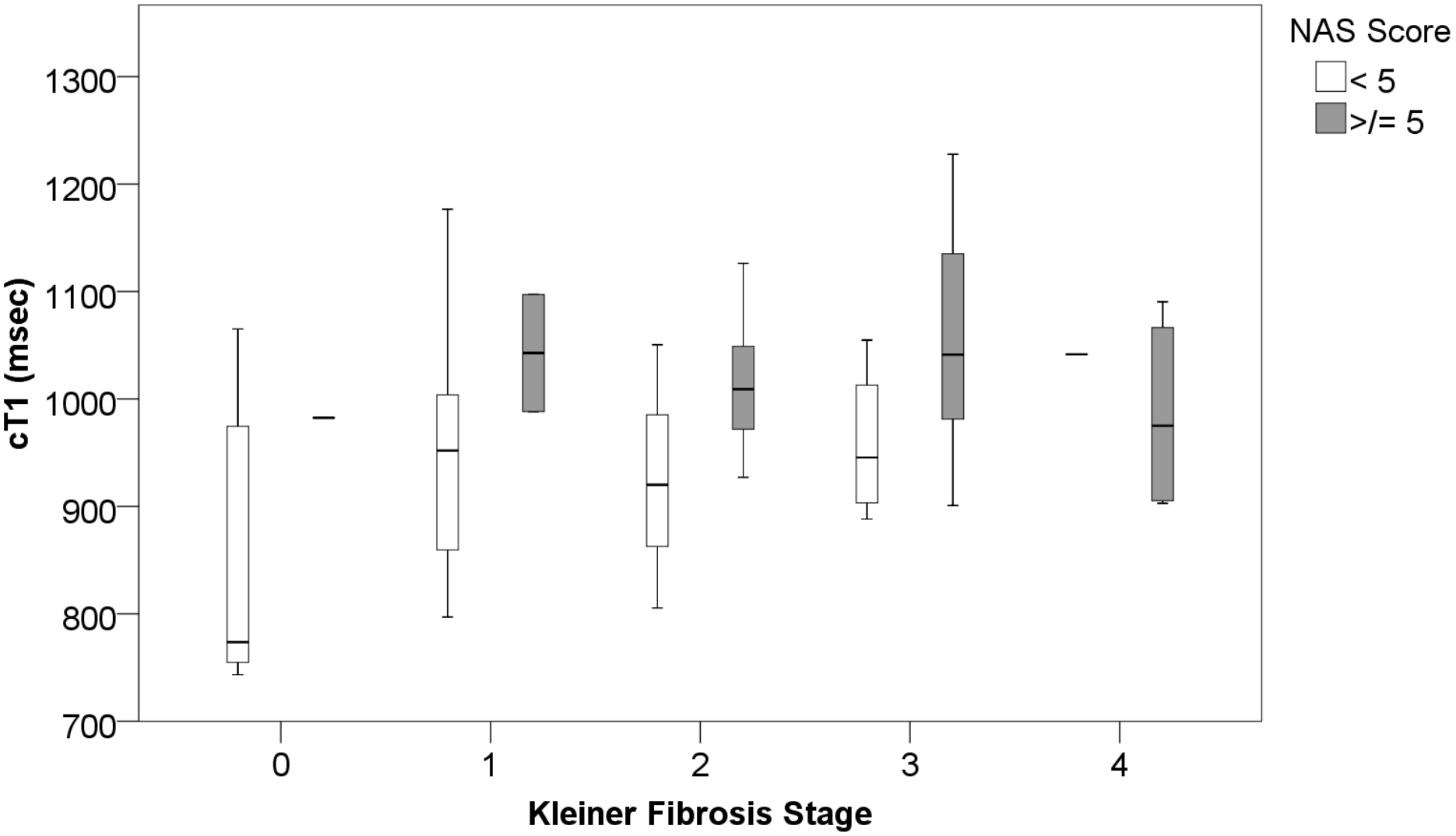
≥ F1

AUROC 0.72 (0.47 – 0.97)

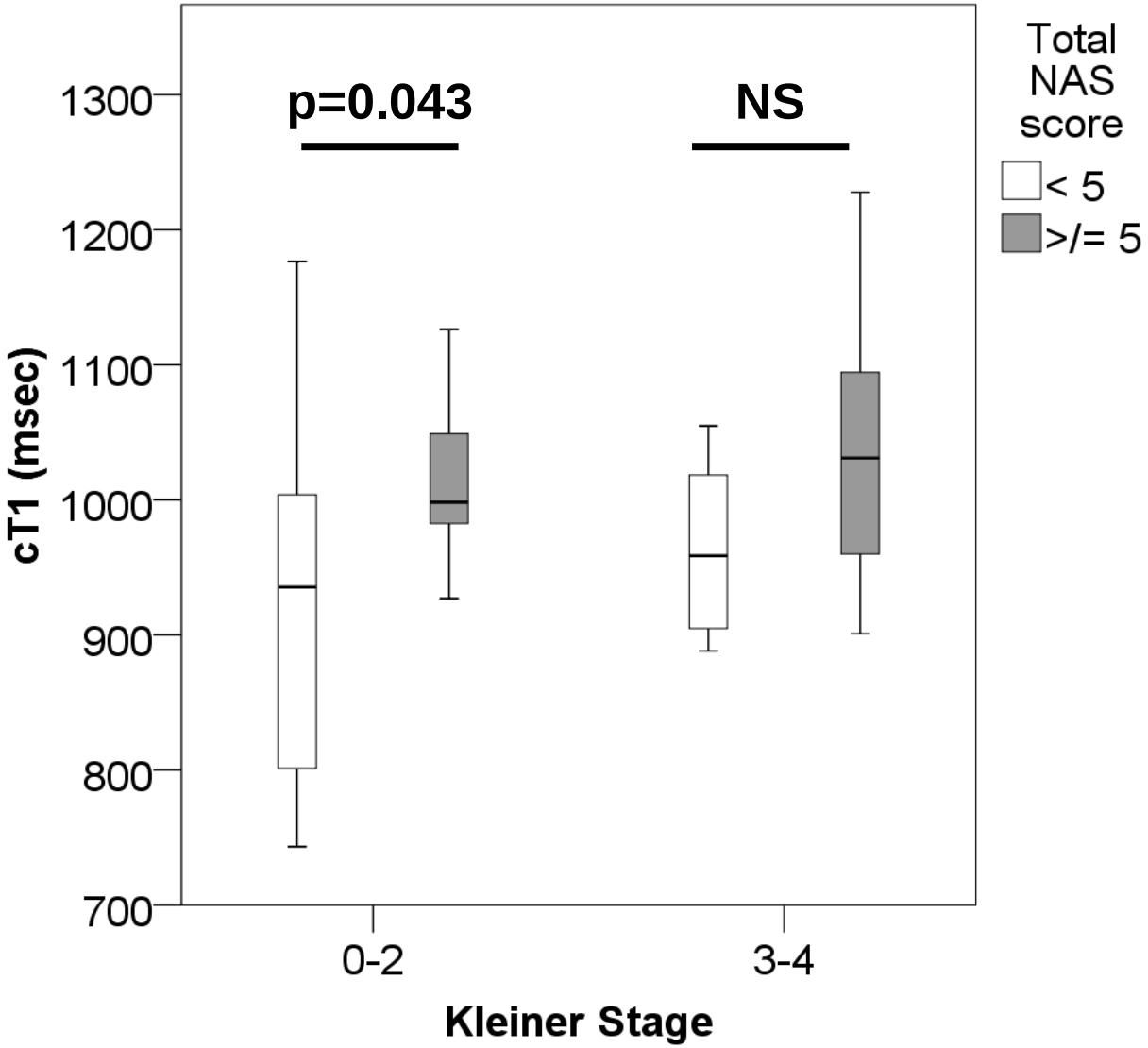
≥ F3

AUROC 0.62 (0.47-0.78)

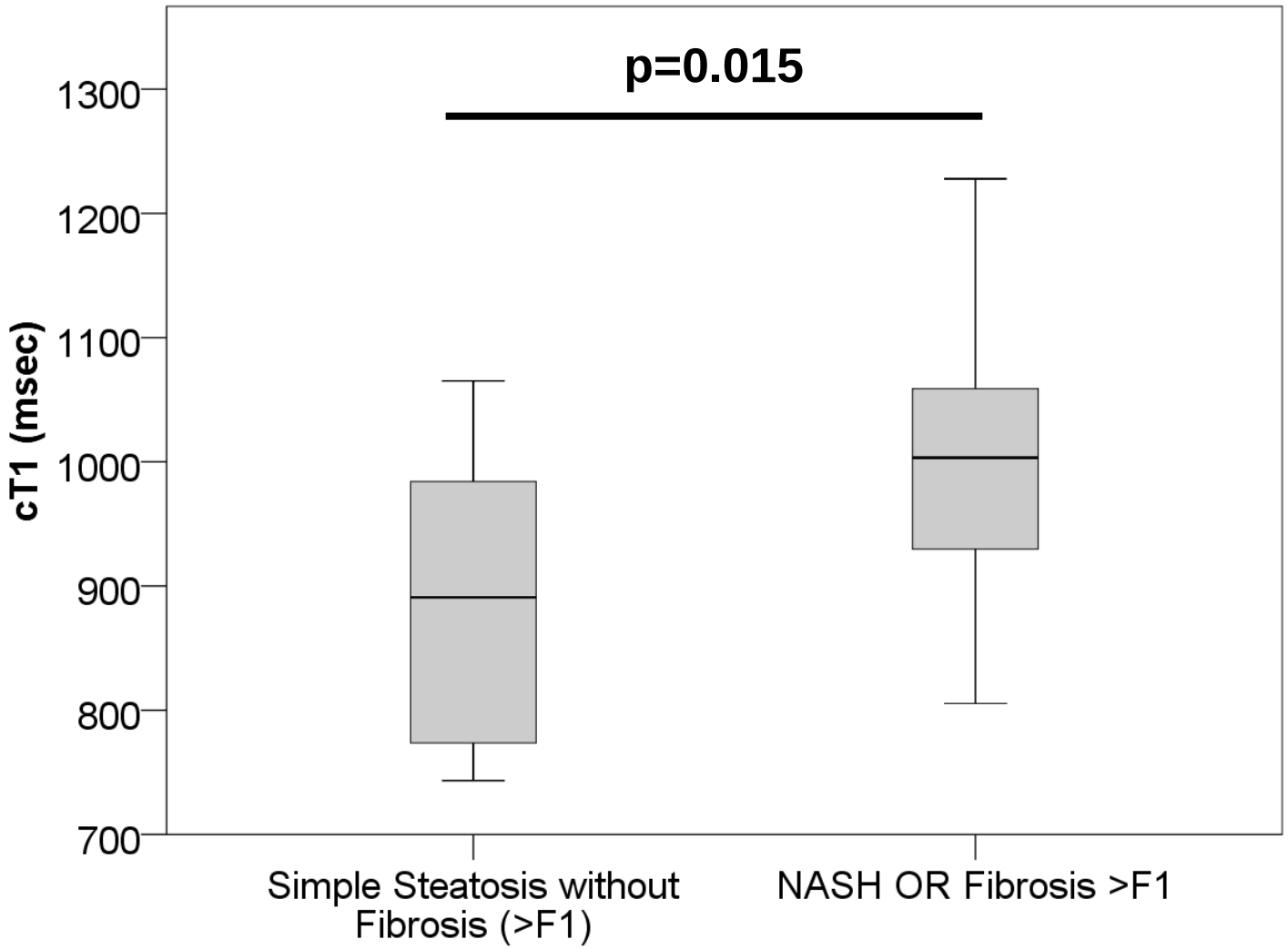
Fibrosis assessment confounded by presence of inflammation



cT1 is a marker of fibrosis and inflammation

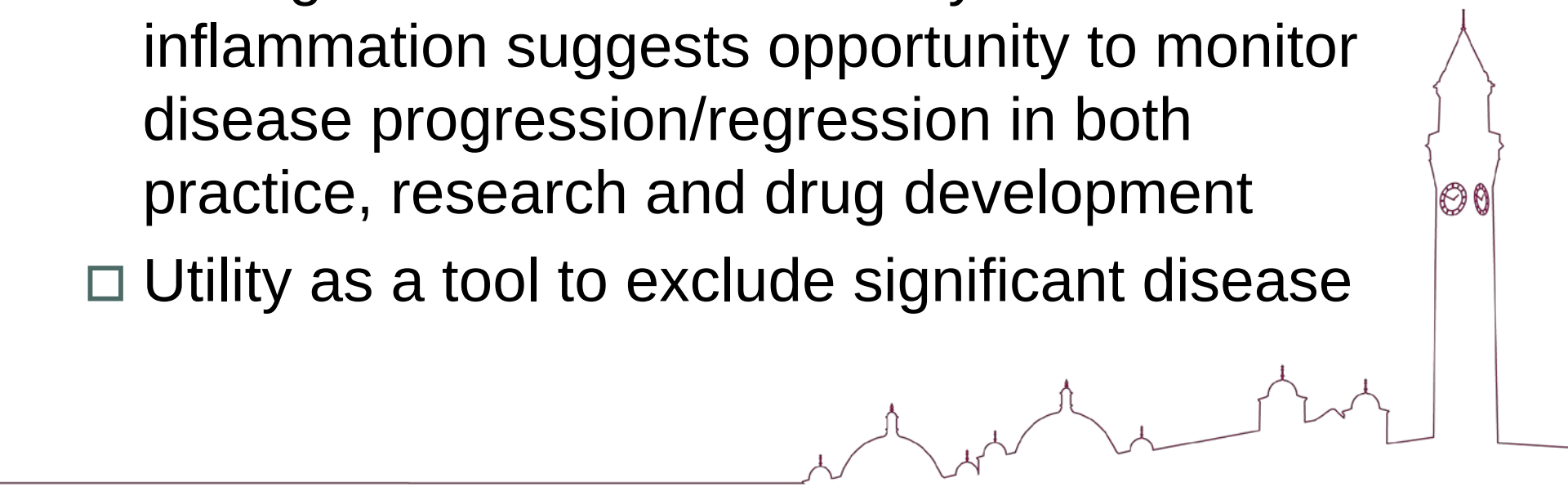


Multi-parametric MRI has potential to exclude disease



Conclusions

- Multi-parametric MRI has potential for identification of steatosis
- Multi-parametric MRI has potential to differentiate NASH from simple steatosis
- Strong correlation with severity of inflammation suggests opportunity to monitor disease progression/regression in both practice, research and drug development
- Utility as a tool to exclude significant disease

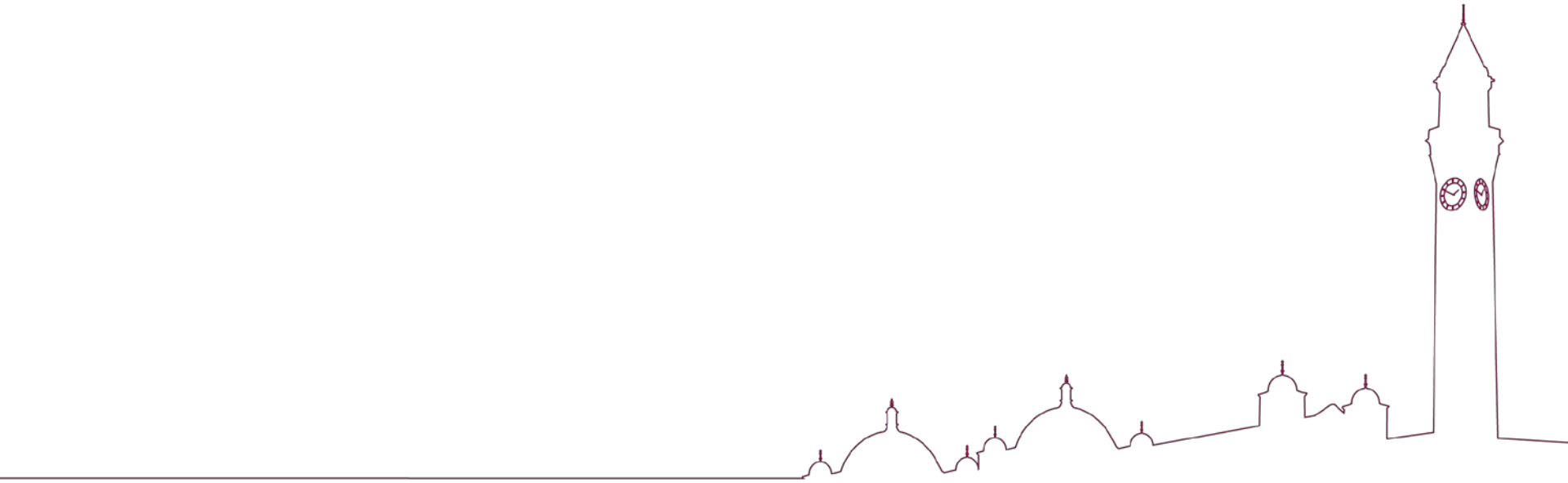


Research Article

EASL | JOURNAL OF HEPATOLOGY

Multiparametric magnetic resonance imaging predicts clinical outcomes in patients with chronic liver disease

Michael Pavlides[1,2,†], Rajarshi Banerjee[3,†], Joanne Sellwood[2], Catherine J. Kelly[3], Matthew D. Robson[2], Jonathan C. Booth[4], Jane Collier[1], Stefan Neubauer[2,‡], Eleanor Barnes[1,5,*,‡]



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