



Non-invasive imaging modalities for assessment of fibrosis, inflammation and steatosis in a Japanese NASH population



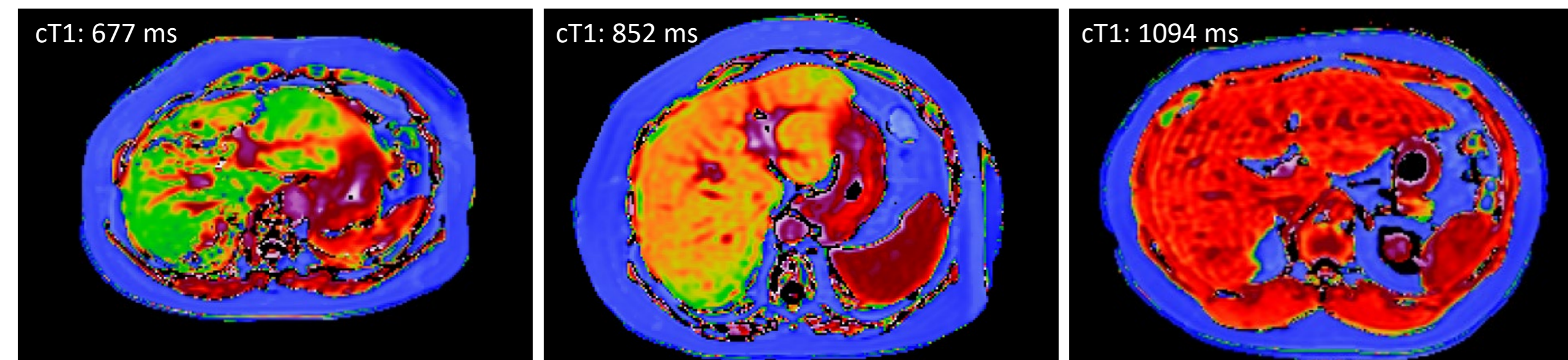
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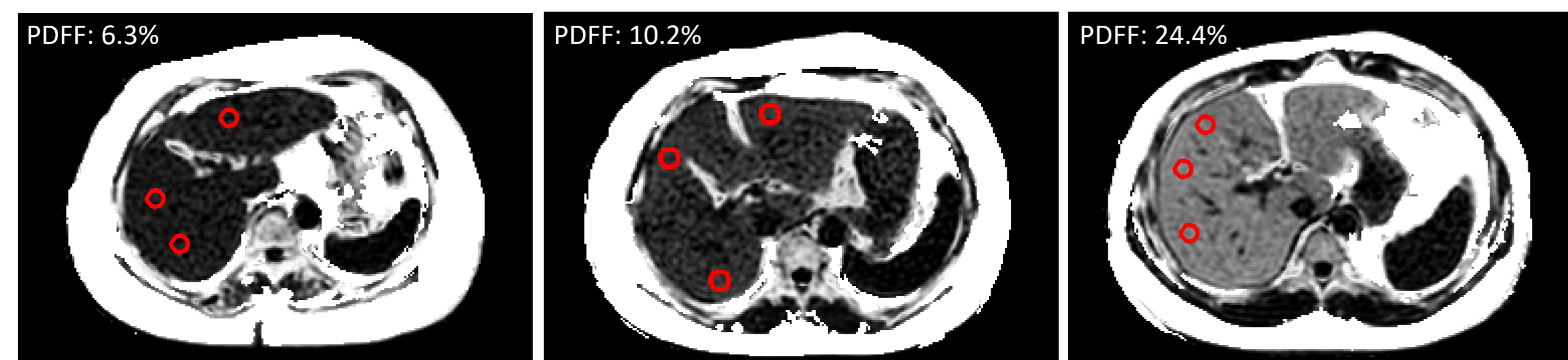
INTRODUCTION & AIM

- Current guidelines for diagnosis of non-alcoholic steatohepatitis (NASH) rely on liver biopsy which is limited by its costs and invasiveness.
- LiverMultiScan[®] is a non-invasive multiparametric MRI (mpMRI) diagnostic tool which includes two key measures for NASH assessment:

- cT1 (corrected T1)** is a quantitative measure of iron-corrected T1-relaxation time that has been shown to correlate with fibrosis and inflammation.¹⁻⁴



- PDFF (proton density fat fraction)** is a quantitative measure of fat that has been shown to correlate with hepatic fat.^{5,6}



- The first in a Japanese cohort, this prospective study aims to evaluate the diagnostic performance of mpMRI-based biomarkers (LMS-cT1 and LMS-PDFF) and other non-invasive imaging modalities compared to the gold standard, liver biopsy, for assessment of fibrosis, inflammation and steatosis in patients with suspected NASH.

METHODS

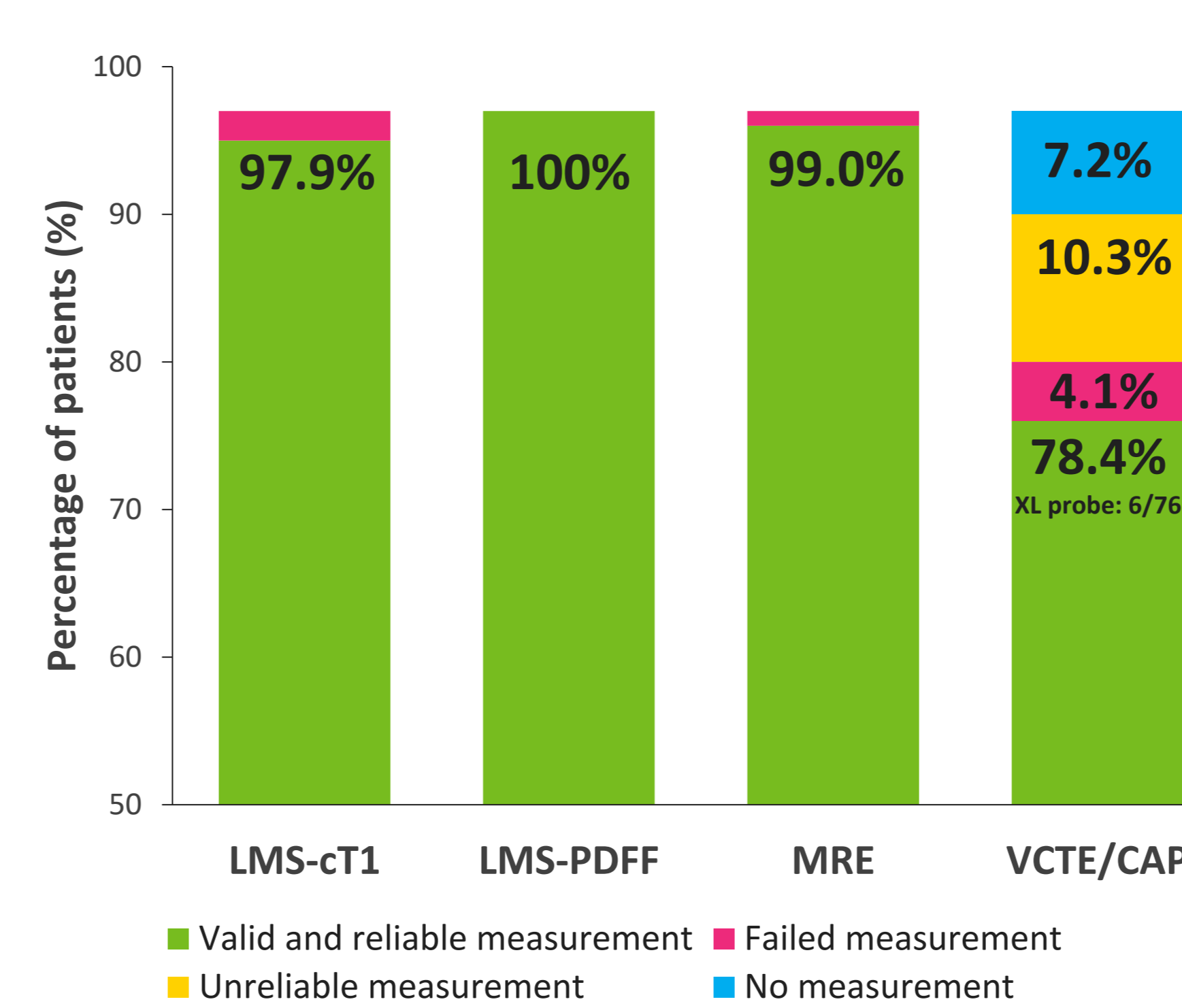
- 97 adult patients suspected of NASH were recruited from a liver clinic in Yokohama, Japan.
- Liver biopsies were assessed by two pathologists in a double-blind manner with consensus using the NASH CRN scoring system where NAFLD activity score (NAS) ranged from 0 to 8 according to steatosis (0-3), lobular inflammation (0-3) and hepatocellular ballooning (0-2); while stage of liver fibrosis was assessed according to the Kleiner-Brunt (KB) criteria (0-4).
- Patients were screened with cT1 and PDFF using LiverMultiScan (LMS), Liver Stiffness Measurement (LSM) using magnetic resonance elastography (MRE), LSM and Controlled Attenuation Parameter (CAP) using vibration-controlled transient elastography (VCTE).
- MRI-based data were collected on a 3T GE Discovery 750w.
- VCTE-based data were collected with M and XL probes. Failure is defined as zero valid readings. Unreliable result is defined as <10 valid readings, <60% success rate and interquartile range >30% of median value. Where available, result from XL probe were considered when M probe reading failed/was unreliable.
- Diagnostic performance were assessed based on valid and reliable measurements using area under receiver operating curve (AUROC). Cut-offs applied were as previously reported.^{2,3,4,6-10}

RESULTS

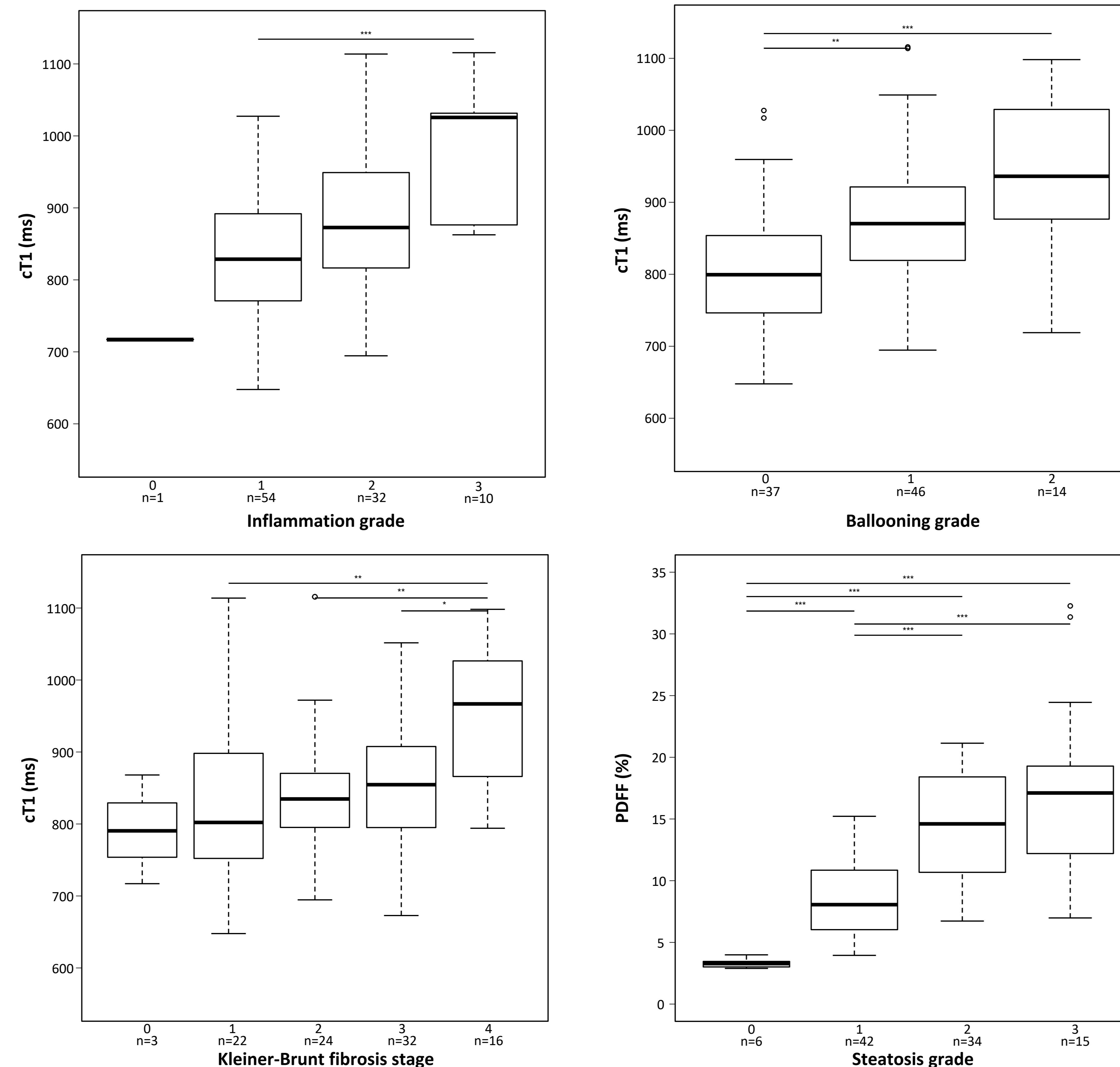
Patient Characteristics

Variable	NASH (n=60)	non-NASH (n=37)
Age, years (mean±SD)	61.3±14.3	58.3±12.9
Male, n (%)	34 (57)	26 (70)
Weight, kg (mean±SD)	78.5±15.2	76.6±18.6
BMI, kg/m ² (mean±SD)	29.6±4.4	28.0±5.1
Obesity (BMI ≥25), n (%)	50 (83)	27 (73)
T2DM, n (%)	42 (70)	25 (68)
Hypertension, n (%)	30 (50)	18 (49)
Dyslipidemia, n (%)	48 (80)	27 (73)

Success rates of imaging modalities



Box plots of cT1 vs ballooning, lobular inflammation, fibrosis and PDFF vs steatosis



Assessment of steatosis compared to liver biopsy

Steatosis grade (Prevalence, %)	Quantifier	AUROC	95% CI	Cut-off	Sens (%)	Spec (%)
S≥1 (93.8%)	LMS-PDFF	1.00	0.99-1	6.4	84	100
	CAP	0.95	0.87-1	233.5	97	60
S≥2 (50.5%)	LMS-PDFF	0.89	0.83-0.95	17.4	37	100
	CAP	0.65	0.52-0.78	268.5	91	41
S3 (15.5%)	LMS-PDFF	0.79	0.67-0.91	22.1	20	100
	CAP	0.66	0.49-0.83	301.2	67	56

Assessment of NASH compared to liver biopsy

Presence of NASH (Prevalence, %)	Quantifier	AUROC	95% CI	Cut-off	Sens (%)	Spec (%)
NAS≥4 (55.7%)	LMS-cT1	0.77	0.67-0.86	815	82	55
	MRE-LSM	0.58	0.46-0.70	2.7	89	33
	VCTE-LSM	0.60	0.47-0.73	6.2	89	28
Ballooning≥1 (61.9%)	LMS-cT1	0.74	0.64-0.85	815	81	59
	MRE-LSM	0.61	0.48-0.74	2.7	90	38
	VCTE-LSM	0.60	0.46-0.74	6.2	88	26

Assessment of fibrosis compared to liver biopsy

KB fibrosis stage (Prevalence, %)	Quantifier	AUROC	95% CI	Cut-off	Sens (%)	Spec (%)
F≥1 (96.9%)	LMS-cT1	0.71	0.42-1	800	71	67
	MRE-LSM	0.97	0.93-1	2.88	80	100
	VCTE-LSM	0.95	0.89-1	5.8	86	100
F≥2 (74.2%)	LMS-cT1	0.65	0.50-0.79	825	69	61
	MRE-LSM	0.91	0.86-0.97	3.54	71	84
	VCTE-LSM	0.90	0.83-0.97	7.0	89	68
F≥3 (49.5%)	LMS-cT1	0.66	0.54-0.77	875	54	74
	MRE-LSM	0.93	0.88-0.98	3.77	85	86
	VCTE-LSM	0.86	0.78-0.95	8.7	92	60
F4 (16.5%)	LMS-cT1	0.79	0.67-0.91	950	56	89
	MRE-LSM	0.96	0.92-0.99	4.09	100	74
	VCTE-LSM	0.95	0.89-0.99	10.3	100	63

CONCLUSION

- Multiparametric MRI using LiverMultiScan is the best-performing modality with high success rates for assessment of steatosis and NASH.
- MRE-LSM and VCTE-LSM are good imaging modalities for assessment of fibrosis; VCTE however, has lower success rates.
- High specificity of cT1 shows potential for ruling in severe fibrosis (F4).
- Study highlights complementarity of techniques for non-invasive assessment for histopathological features of NASH.

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