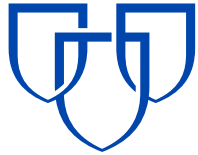


MAYO
CLINIC



Novel multiparametric magnetic resonance elastography (MRE) protocol accurately predicts NAS score for NASH diagnosis

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Background

- The lack of a reliable, noninvasive method to diagnose nonalcoholic steatohepatitis (NASH) before fibrosis is established remains a major unmet need in nonalcoholic fatty liver disease (NAFLD).
- Magnetic resonance elastography (MRE) is the most accurate noninvasive biomarker of liver fibrosis. However, the role of MRE in the detection of NASH has not been established

Can MR imaging give us the whole picture?

	ULTRASOUND	TRANSIENT ELASTOGRAPHY (Fibroscan®)	MAGNETIC RESONANCE IMAGING (MRE, MRI-PDFF, MRS)	BIOPSY
Steatosis	+	++	+++	+++
Inflammation/ ballooning	-	-	?	+++
Fibrosis	-	++	+++	+++
HCC screen	+	-	+++	-

Aim

To determine the diagnostic performance of a multiparametric MRE protocol for the detection of NASH and prediction of disease activity.

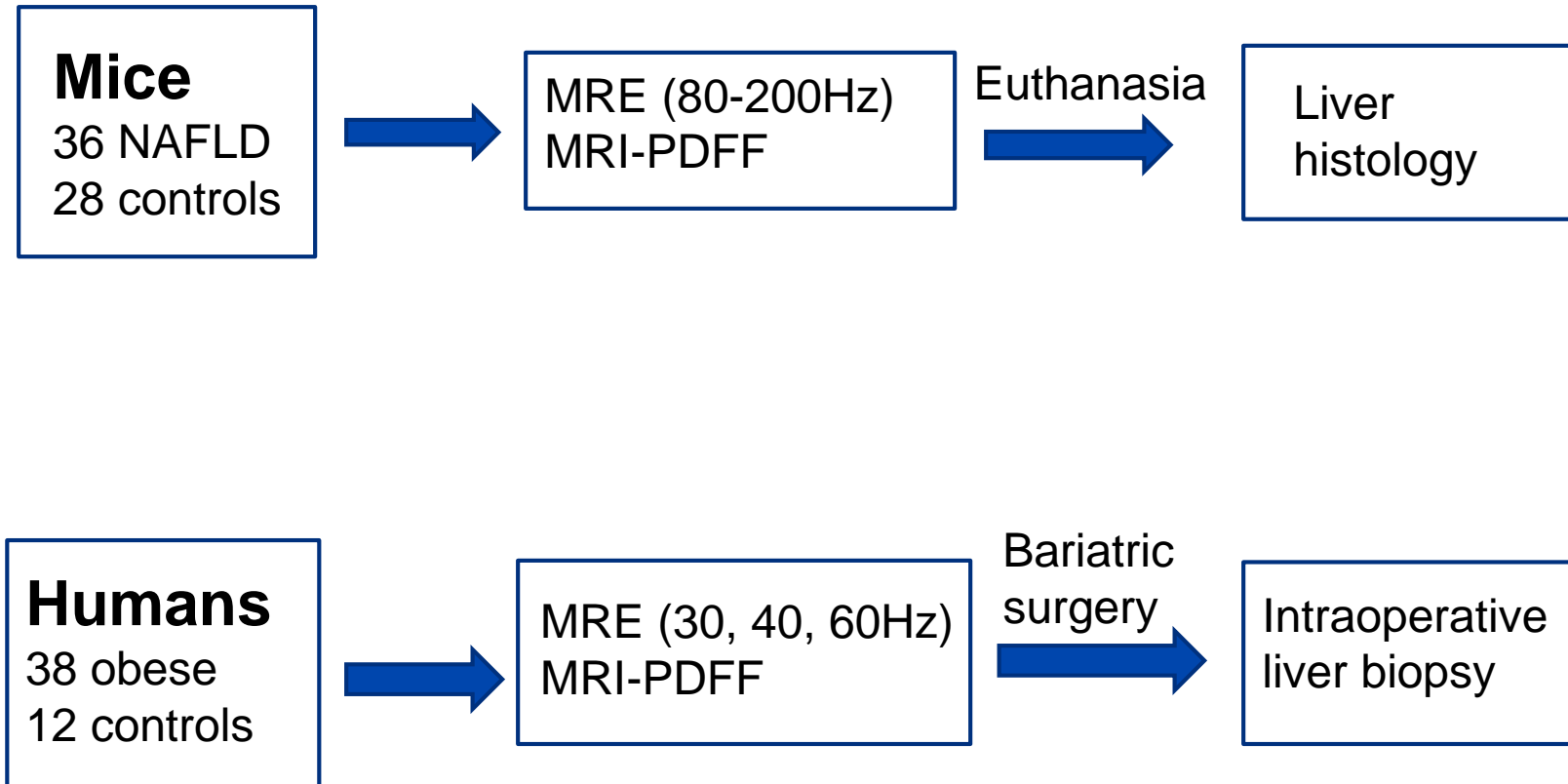
Hepatogram



Premise

- By generating the mechanical waves at different frequencies (30, 40 , 60 Hz), early histologic changes of NASH (lobular inflammation, cellular ballooning) that affect viscoelastic properties, such as interstitial fluid pressure and viscosity, can be detected.

Study protocol



Methods

- Liver biopsies were interpreted by a single pathologist for histologic changes of steatosis, lobular inflammation and ballooning, and NAFLD activity score (NAS) was calculated based on the NASH CRN criteria.
- From the complex shear modulus output generated by MRE at multiple mechanical frequencies, the parameters that best correlated with lobular inflammation and ballooning were selected.

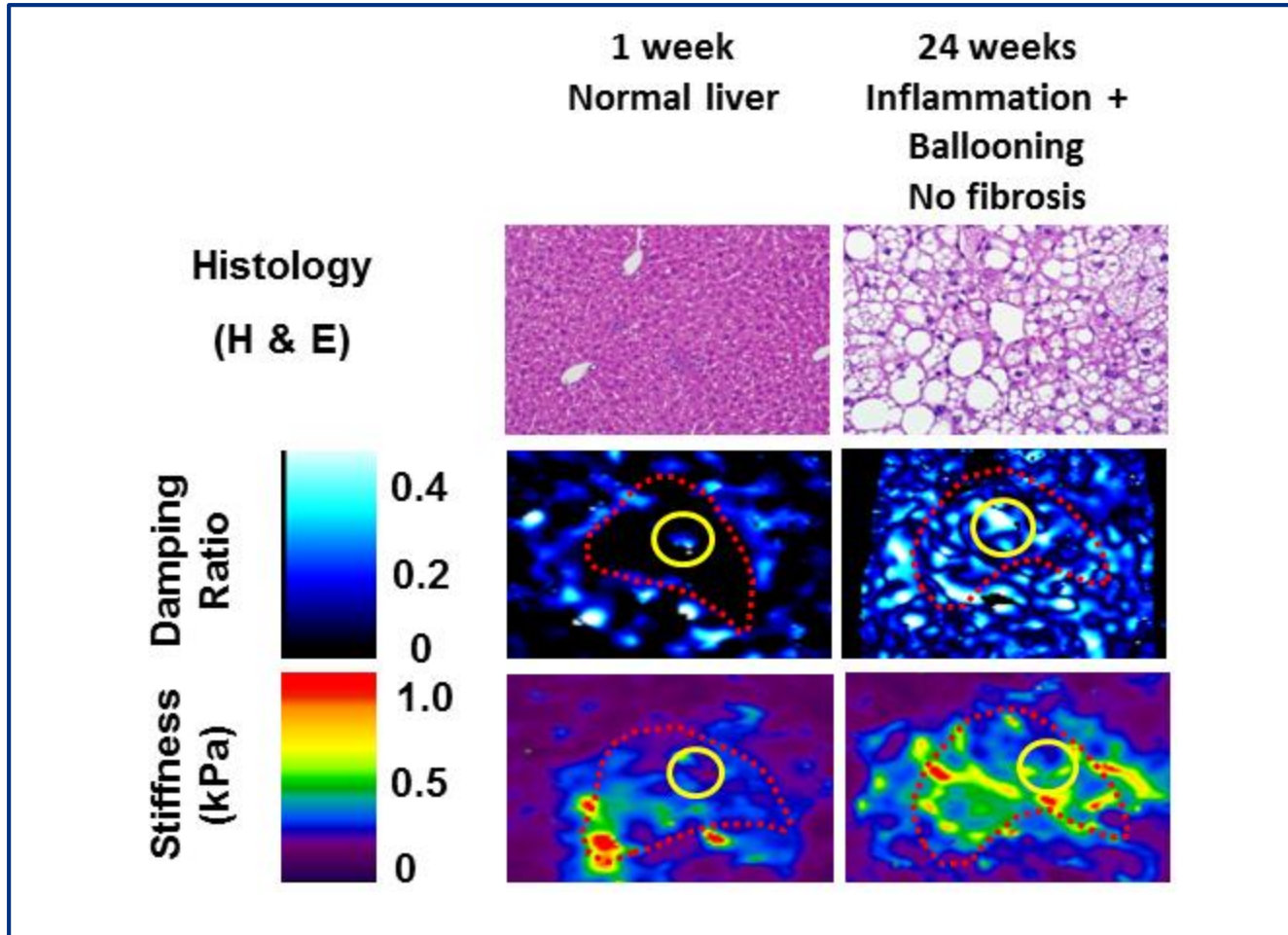
Statistical analysis

- We explored the predictive relation between imaging and histologic parameters using pairwise comparisons (nonparametric Dunn method for joint ranking)
- The imaging parameters with the strongest correlation with inflammation, ballooning and steatosis were included into a **predictive regression model of NAS.**
- Model performance: receiver operating curve (ROC) analysis using NAS score as a continuous output.

Results - Animal data

- The MRE parameters that showed the best correlation with NASH histology were:
 - **damping ratio** (loss modulus/storage modulus) with lobular inflammation
 - **complex shear modulus magnitude (shear stiffness)** with hepatocellular ballooning
 - **fat fraction** with steatosis ($p < 0.05$ for all parameters)

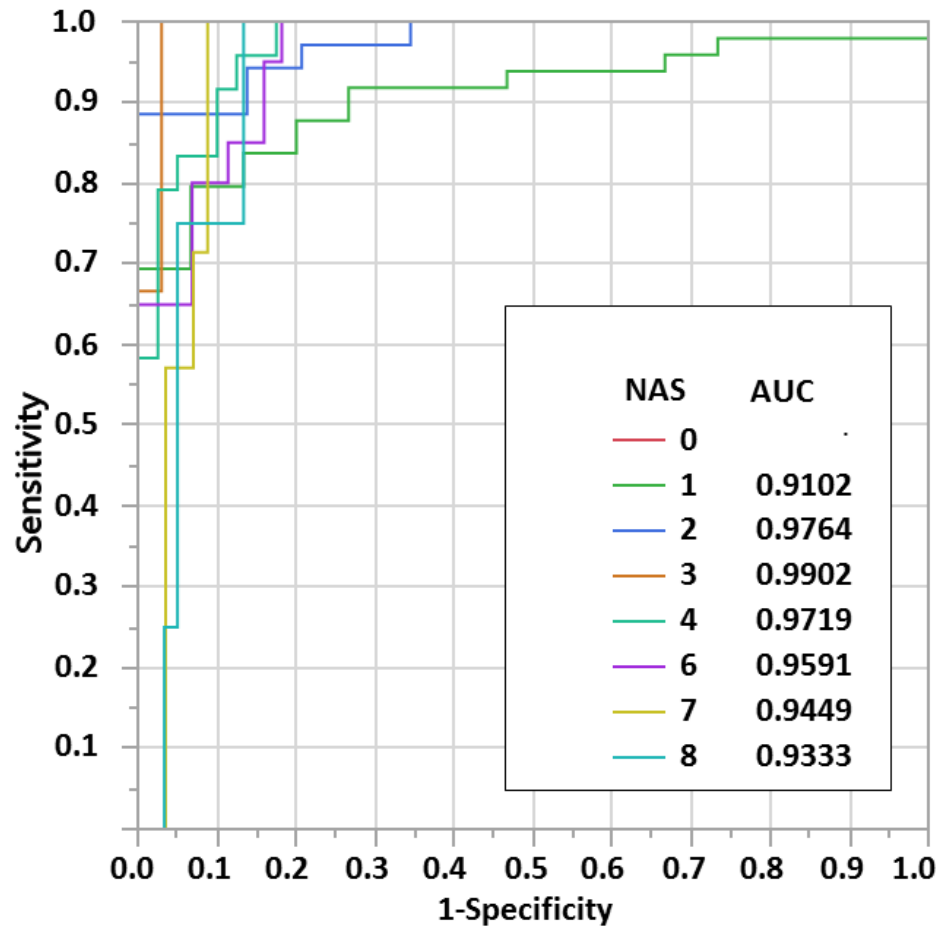
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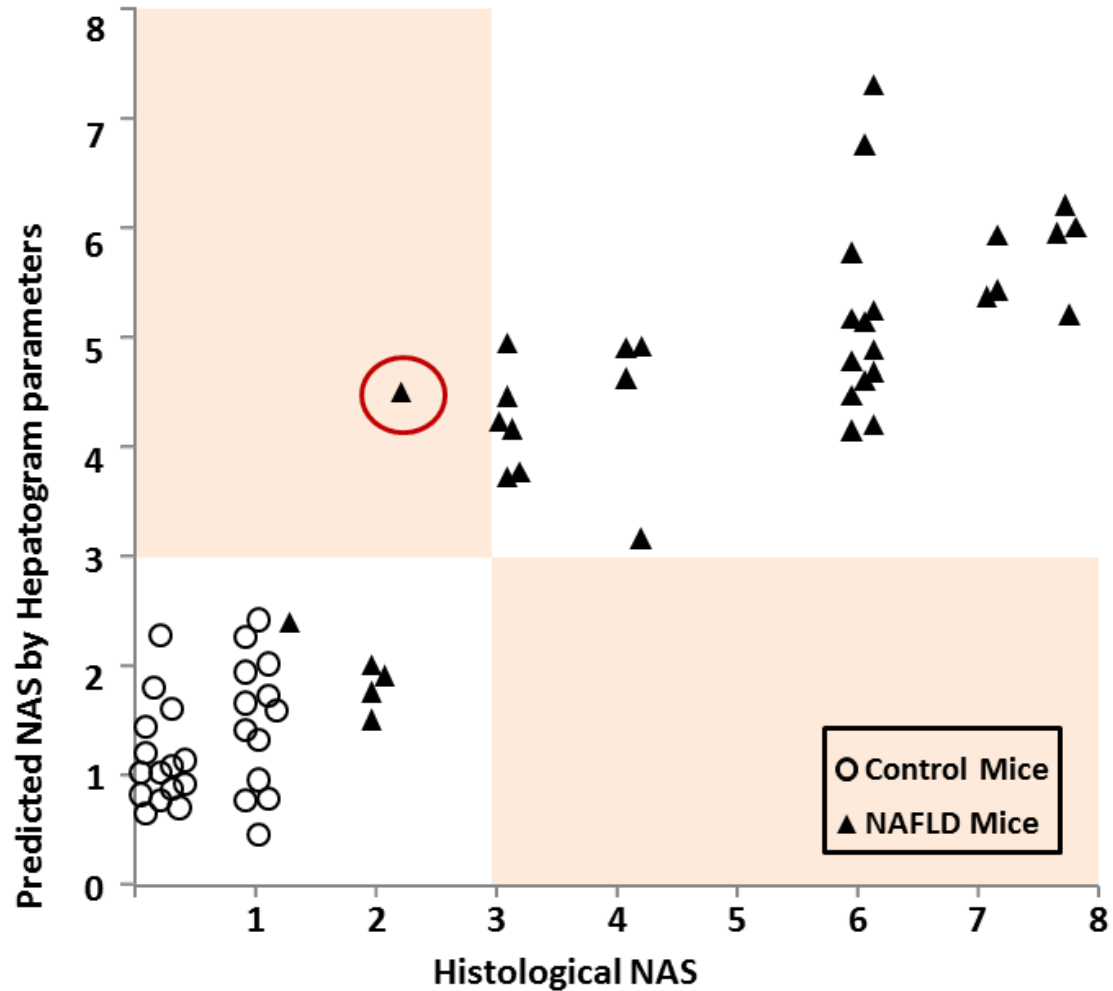
Logistic regression model of NAS prediction

Animal data

$$\text{NAS} = 10.8 \times \text{SS} + 24.4 \times \text{DR} + 9.9 \times \text{FF} - 3.4$$



Model performance in mice



Results- Human pilot data

Characteristics of bariatric subjects (N=38)	No steatosis N= 9	Nonalcoholic fatty liver N=29		
		NAS=1-2 N=12	NAS=3-4 N=12	NAS=5-8 N=5
Subjects with NASH	0	2	11	5
Steatosis grade	0	1	1.58	1.75
Ballooning grade	0	0.17	0.83	1.75
Lobular inflammation grade	0.22	0.30	1	2
Fibrosis stage 0-1	9	12	8	1
Fibrosis stage 2-3	0	1	4	2
Fibrosis stage 4	0	0	0	1
Damping ratio (DR)	0.07	0.09	0.10	0.11
Shear stiffness (LS), kPa	2.38	2.42	2.51	3.85
Fat fraction (FF), %	5.91	11.96	20.36	21.47

Mean age 46

Female 84%

Mean BMI=46 kg/m²

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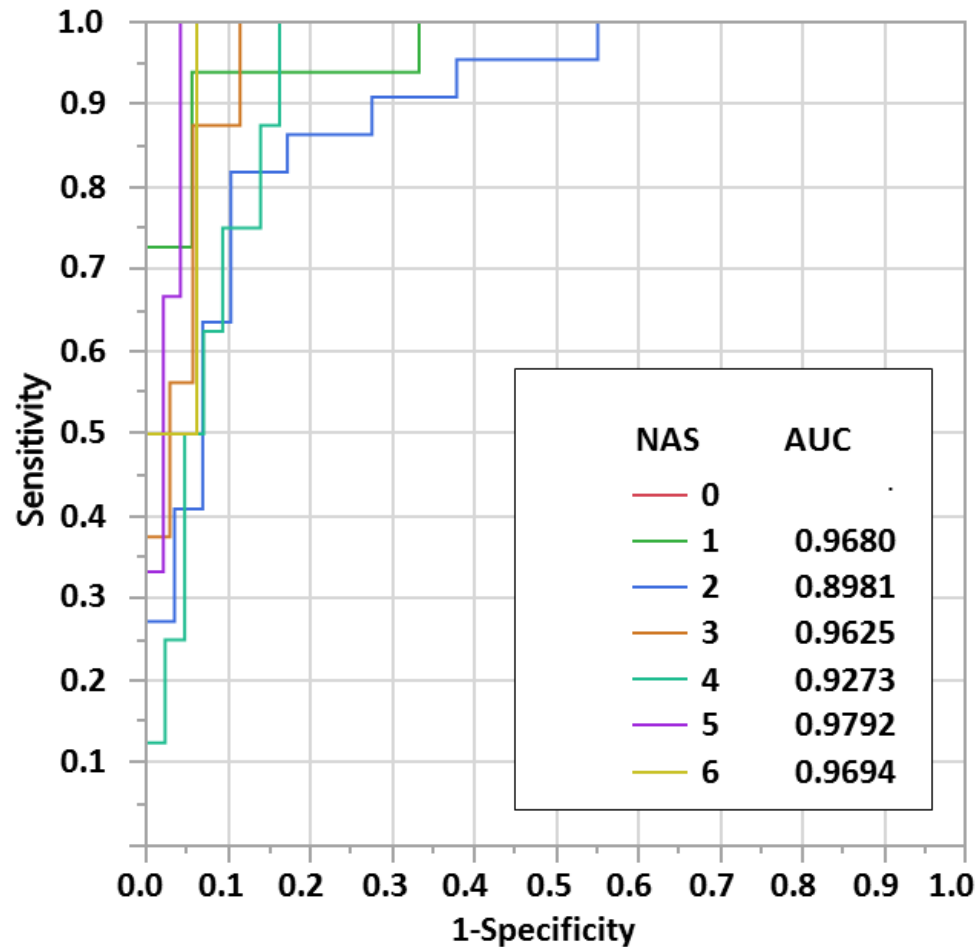
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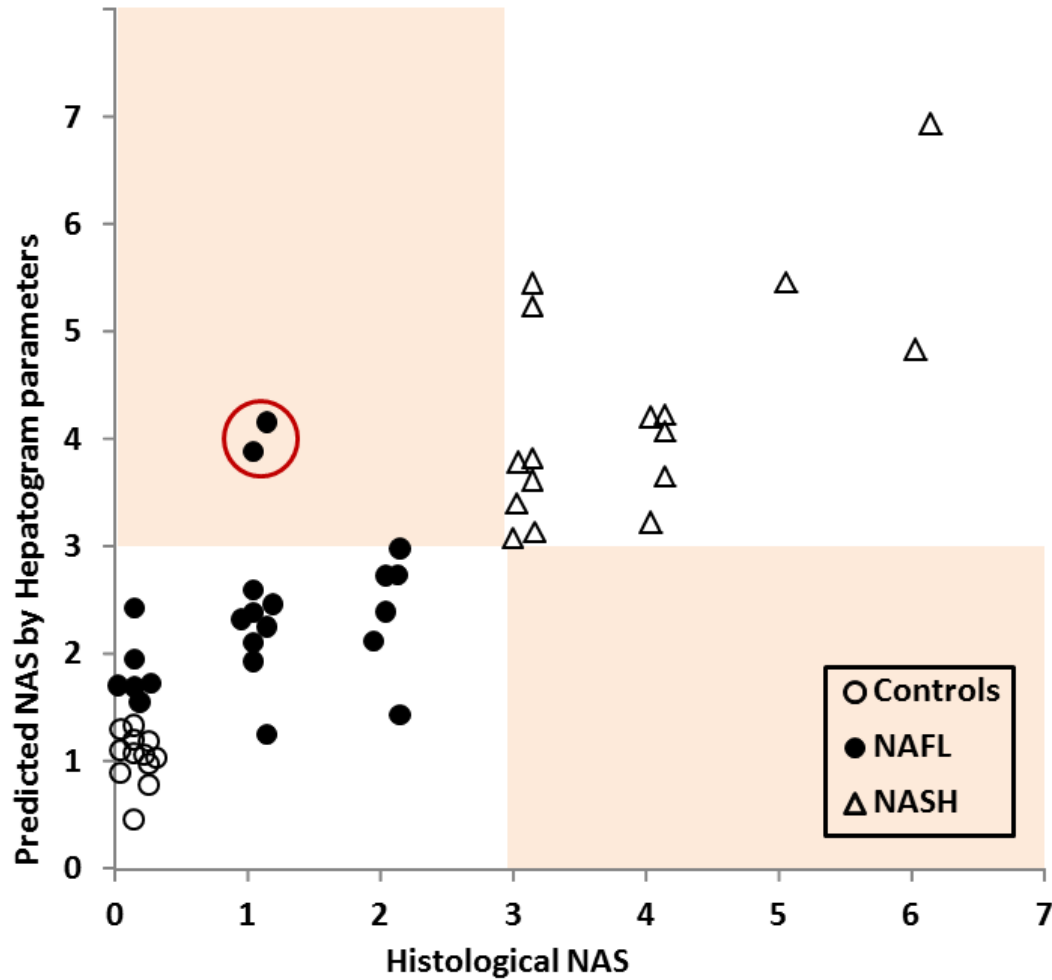
Logistic regression model of NAS prediction

Human data

$$\text{NAS} = 1.5 \times \text{SS} + 4.6 \times \text{DR} + 0.1 \times \text{FF} - 3.8$$



Model performance in human subjects



Conclusions

This novel MRE methodology enables:

- Detection of **inflammation/ballooning** in NASH before onset of fibrosis.
- Prediction of **disease activity** → promising alternative to liver biopsy for NASH diagnosis and monitoring.
- Useful method to estimate the key histologic parameters for NASH diagnosis and **disease monitoring in clinical trials and practice.**
- Hepatogram has the potential to provide a **comprehensive** liver evaluation in one setting, including presence of NASH, degree of steatosis, fibrosis stage and liver masses.
- Further testing on larger sample size and validation in independent patient cohorts are necessary.