Machine learning histology model in NASH cirrhosis may improve the assessment of key outcome changes

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Derivation of machine learning histologic scores correlating with portal pressures and the development of varices in NASH patients with cirrhosis

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1 Introduction

Previous studies from Hepatitis C using semi-quantitative methods have found that considering features including fibrosis area, septal thickness, size and number of nodules can be useful in correlating histology with portal pressure in cirrhotic patients. However, these semi-quantitative techniques are subjective and prone to variabilities.

2 Aim

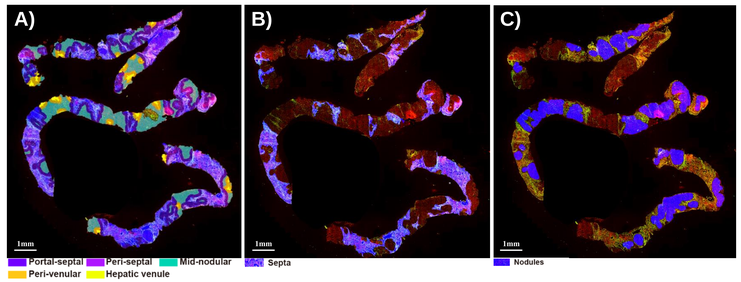
- To examine if a machine learning model can accurately predict hepatic venous pressure gradient (HVPG) and presence of varices based on liver histology in NASH cirrhotic patients
- Using second harmonic generation/two-photon excitation fluorescence (SHG/TPEF), a machine learning algorithm was developed based key histologic features in NASH cirrhosis; (a) Fibrosis, (b) Septa, (c) Nodule.

3 Method

- NASH patients with compensated cirrhosis and HVPG ≥ 6 mm Hg (n = 143) were included from the Belapectin phase 2b trial (NCT02462967).
- Liver biopsies, HVPG measurements, and upper endoscopy were performed at baseline (BL) and at end of treatment (EOT).
- SHG/TPEF imaging-based tool provided an automated quantitative assessment of histologic features: 457 histologic variables related to key cirrhosis architectural features: septa, nodules, and fibrosis (SNOF).
- We then combined these features to assess correlation with clinically meaningful changes of HVPG (SNOF-C), i.e., related to HVPG change of >20% or ≤20%.

4 Results

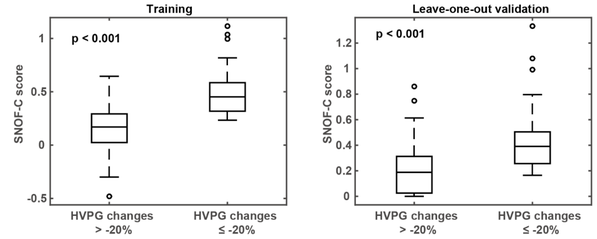
Figure 1: SHG/TPE image showing the AI annotations of (A) Fibrosis, (B) Septa and (C) Nodules



- The visualization of fibrosis, as well as septa and nodules are shown in Figure 1.
- Using the machine learning model, fibrosis was quantified (1A) in regions specific to cirrhotic samples, including the portal-septa, peri-septal, mid-nodular, peri-venular, and hepatic venule regions; and 18 septa (1B) and 19 nodules (1C) were detected.

4 Results continued

Figure 2: Boxplots showing the training and validation of SNOF-C score on patients with HVPG change of >20% or ≤20% between BL and EOT irrespective of the treatment arm.



- A machine learning score, SNOF-Change (SNOF-C) score was built based on the top 15 significant morphological parameters that correlated with 20% changes in HVPG.
- We found that the combination of septa, nodules and fibrosis (SNOF) in an index outperforms using just septa, or nodule, or fibrosis separately.

Table 1: Performances of SNOF-C in detecting clinically meaningful HVPG changes

	Training					Leave-one-out validation				
	AUC	Sensitivity	Specificity	PPV	NPV	AUC	Sensitivity	Specificity	PPV	NPV
SNOF-C score>0.257 to predict HVPG changes ≤ -20%	0.89	97%	69%	50%	99%	0.79	75%	63%	40%	89%

- The SNOF-C score performed well in differentiating those who had >20% change in HVPG versus those who did not, with AUROC of 0.89 in the training cohort and 0.79 in the validation cohort.
- Limitation of the study includes the variability of HVPG measurements in NASH cirrhosis although the HVPG measurements were conducted according to a rigorous protocol, and clinical events did not occur often enough in our study to be correlated with the machine learning model.

5 Conclusions

- Incorporating septa and nodules detection into machine learning algorithms can accurately detect septa and nodules in NASH cirrhotic patients.
- This can be used to develop more sophisticated algorithms to correlate with HVPG and study the natural history of NASH cirrhosis and treatment response.

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7 References

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