Understanding early stage fibrosis in NASH non-human primate model using AI digital pathology

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Abstract #132

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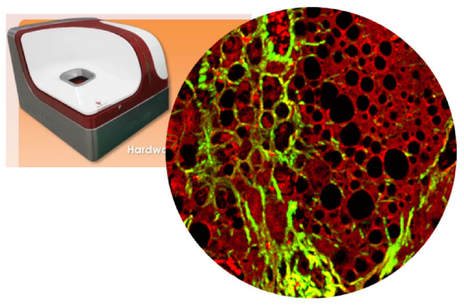
Background: Liver biopsy carries abundant information on the liver microenvironment, which may offer novel biological insights into disease progression, regression, or therapeutic response. Investigation into spatial biology is critical as NASH progression follows metabolic zonation system across the liver lobules.

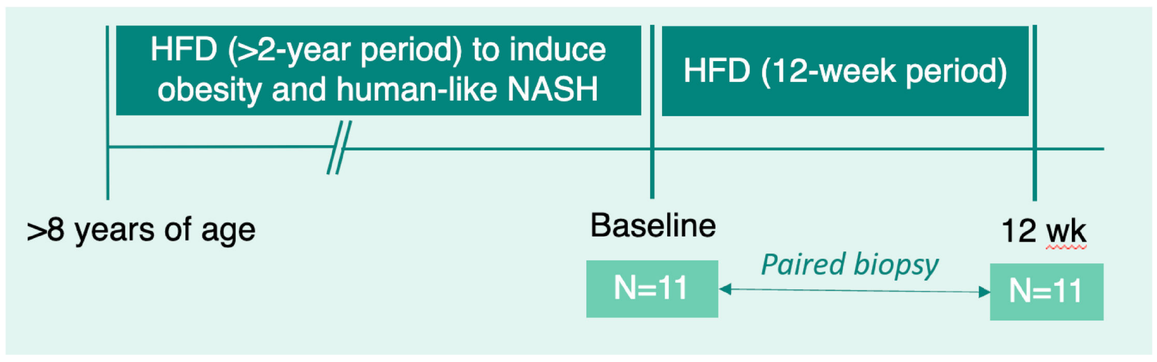
Objectives: Investigate changes in zone-specific liver microenvironment features in early-stage fibrosis in NASH non-human primate (NHP) model, leveraging HistoIndex AI digital pathology platform.

HistoIndex AI digital pathology: Stain-free second harmonic generation/two-photon excitation (SHG/TPE)



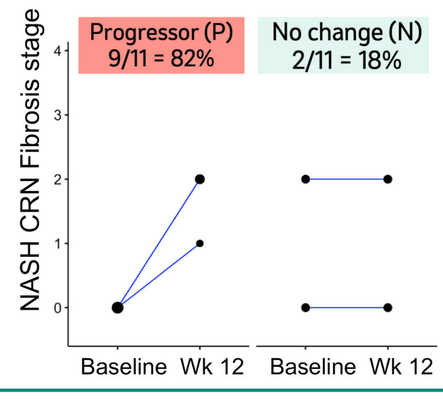
AI-derived zonal parameters
- 100+ fibrosis parameters
- 45+ steatosis parameters

NASH-NHP model developed by Kunming Biomed International China



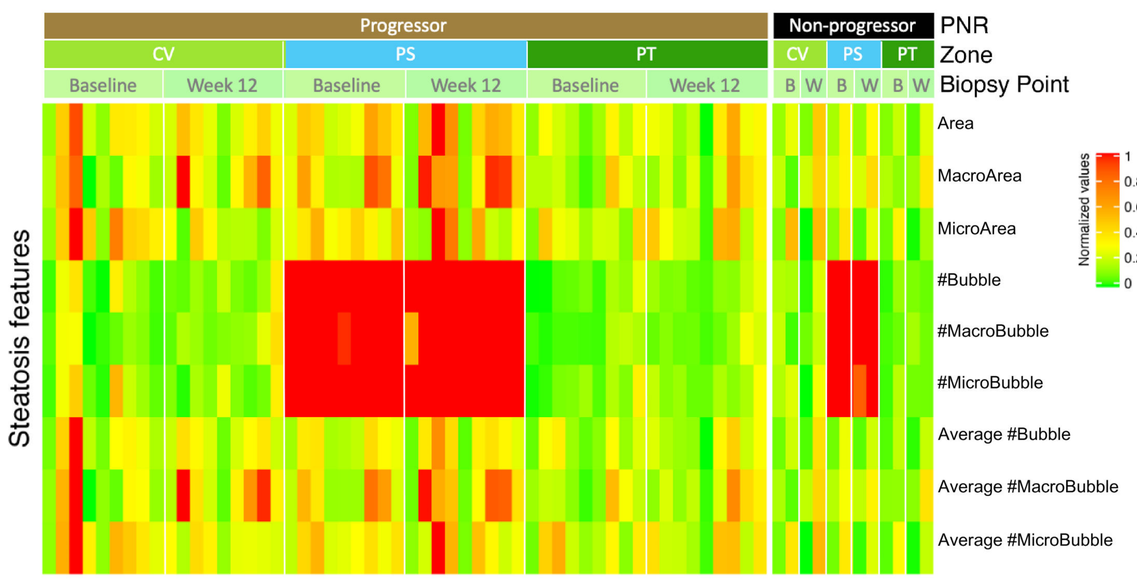
Disease progression based on median of 3 pathologists

NASH CRN fibrosis		Week 12				
		F0	F1	F2	F3	F4
Baseline	F0	1	3	6	0	0
	F1	0	0	0	0	0
	F2	0	0	1	0	0
	F3	0	0	0	0	0
	F4	0	0	0	0	0

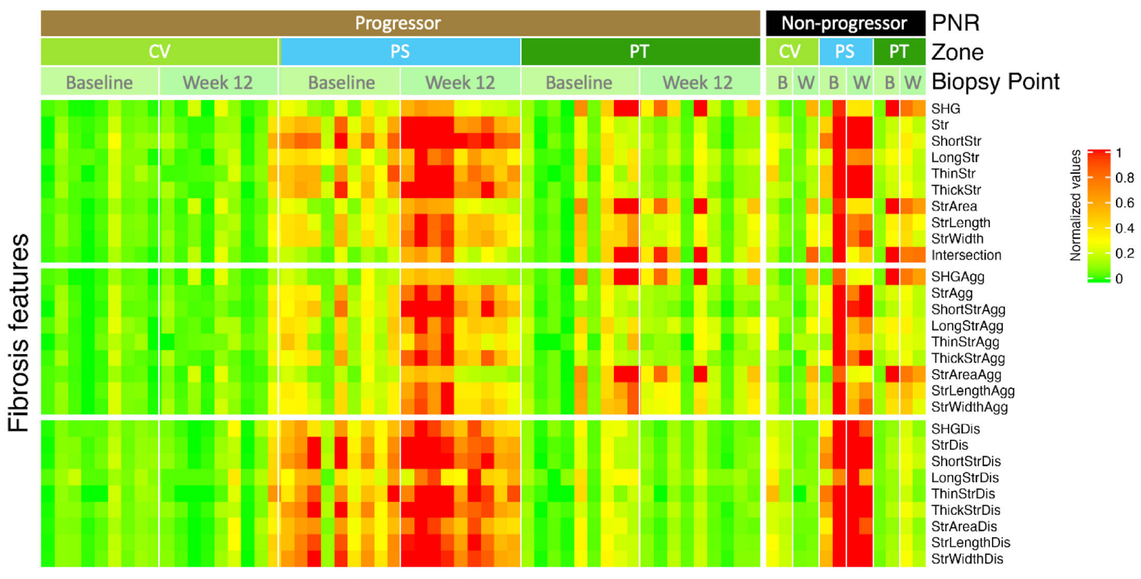


Results

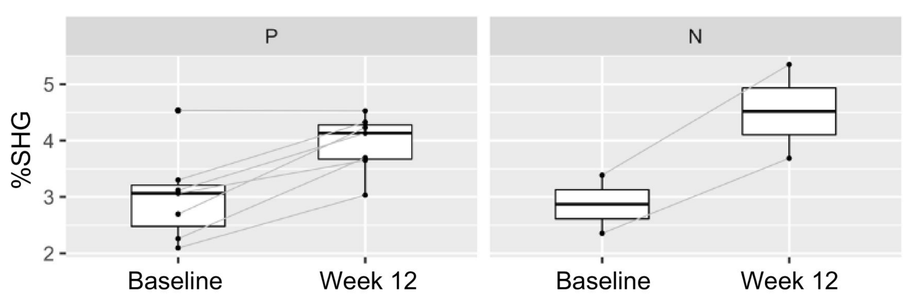
Increased macrosteatosis in central vein (CV) and perisinusoidal (PS) zone at week 12 compared to baseline



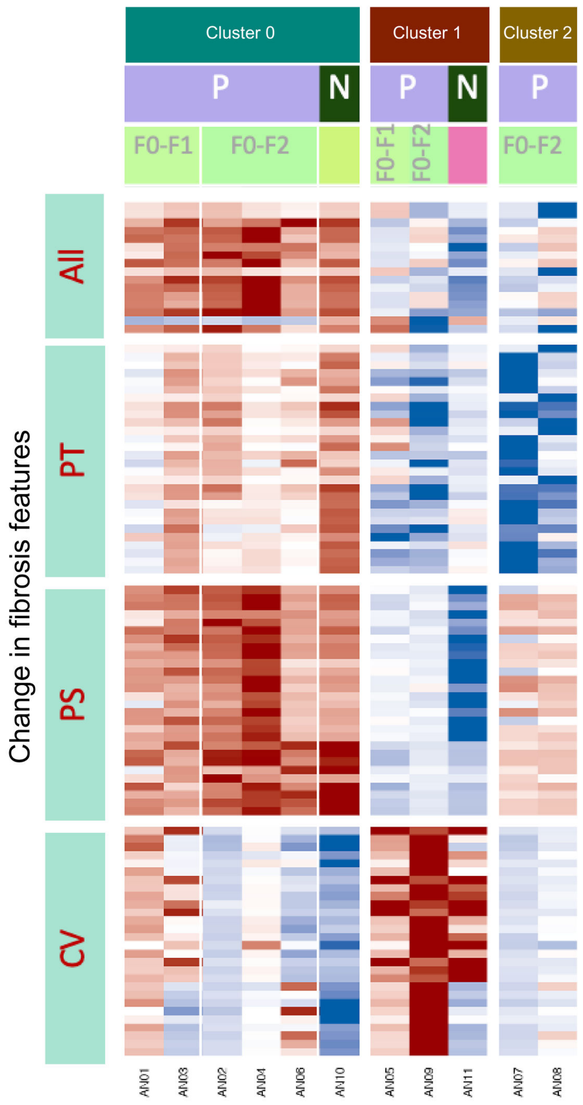
Increased PS fibrosis at week 12 compared to baseline

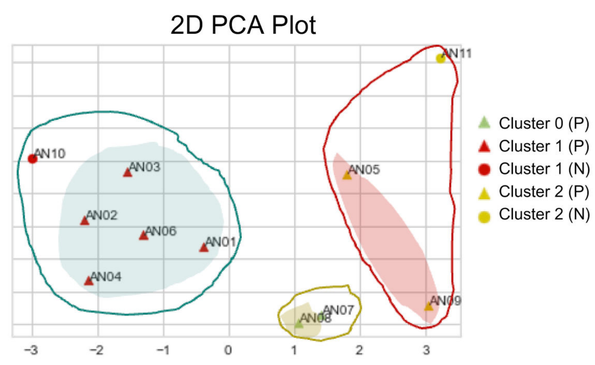


Increased fibrosis/steatosis colocalization at week 12



Identifying pattern of disease progression using k-means clustering based on changes in fibrosis features





3 clusters identified, as seen in the PCA plot as well as the delta heatmap

- K-means clusters for progressor (P):
  - Cluster 0: Most increase PS, some increase in PT
  - Cluster 1: Most increase in CV
  - Cluster 2: Mild increase in PS
  - *The different clusters for progressors cannot be explained by the change from pathologist scores*
- K-means clusters for no-change (N): This may highlight underlying changes which are not detected by pathologist scores

Conclusion:
- Findings: Study demonstrated the metabolic relevance of the NASH KBI-NHP model in studying early-stage fibrosis.
- Significance of AI digital pathology: Powerful tool for studying changes in spatial biology.

Future direction:
Validate results in larger datasets to differentiate progressors & non-progressors, at early-stage as well as late-stage fibrosis.