AIM Explore: Assisting The Trials Vs Assisting The Clinician

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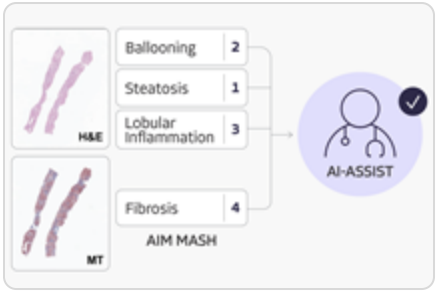
CEO and co-founder at PathAI
January 10, 2025

Acknowledgements

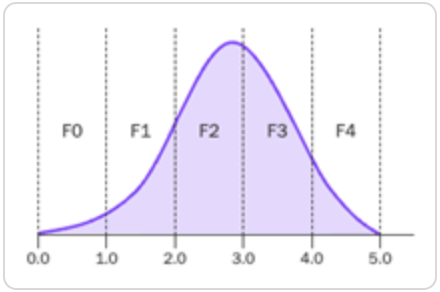
- We are grateful to patients, collaborators, and team members at PathAI for enabling this work
- Dr Stephen Harrison was a close collaborator and co-author on this work, and we dedicate this presentation to his memory and the lasting impact his work continues to have on the field.

From augmenting clinical trial enrollment and endpoint assessment w/AIM-MASH to driving biomarker discovery with Liver Explore



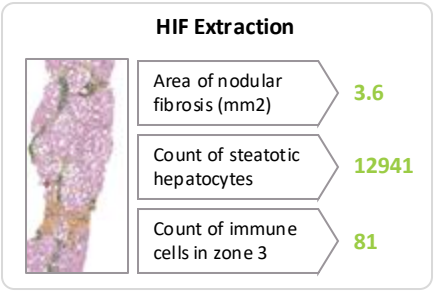
AIM MASH* AI Assist

Pathologist assist tool for clinical trial histology endpoint assessment to **reduce impact of reader variability and capture true drug effect.**



AIM MASH+

Ordinal and continuous MASH CRN scores to drive more **nuanced / deeper understanding** of changes within ordinal bins.



LiverExplore

AI-powered solution delivering histopathology features of tissue microarchitecture to uncover **insights into drug MOA and beyond.**

1. AIM-MASH and Liver Explore™ are for research use only. Not for use in diagnostic procedures
2. * Under review by FDA/EMA

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nature medicine

Article

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AI-based automation of enrollment criteria and endpoint assessment in clinical trials in liver diseases

Received: 2 May 2023

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Check for updates

A list of authors and their affiliations appears at the end of the paper

Clinical trials in metabolic dysfunction-associated steatohepatitis (MASH, formerly known as nonalcoholic steatohepatitis) require histologic scoring for assessment of inclusion criteria and endpoints. However, variability

FDA and EMA guidance recommend histologic endpoints for drug approval for MASH

MASLD Activity Score[1]

Inflammation

0	1	2	3
No foci	<2 foci per 20x field	2-4 foci per 20x field	>4 foci per 20x field

Variable and subjective approaches to counting foci

Ballooning

0	1	2
None	Few balloon cells	Many cells/prominent ballooning

Subjective interpretation

Steatosis

0	1	2	3
<5%	5-33%	>33-66%	>66%

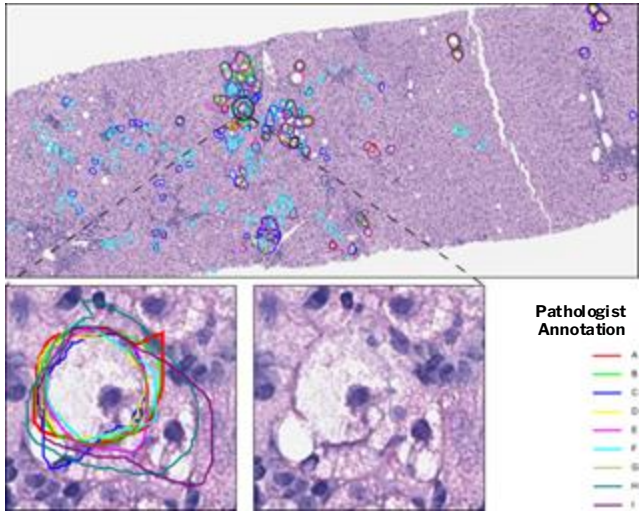
Arbitrary category boundaries

Fibrosis Stage

Fibrosis

F0	F1	F2	F3	F4
No fibrosis	Perisinusoidal or periportal	Perisinusoidal and periportal	Bridging fibrosis	Cirrhosis

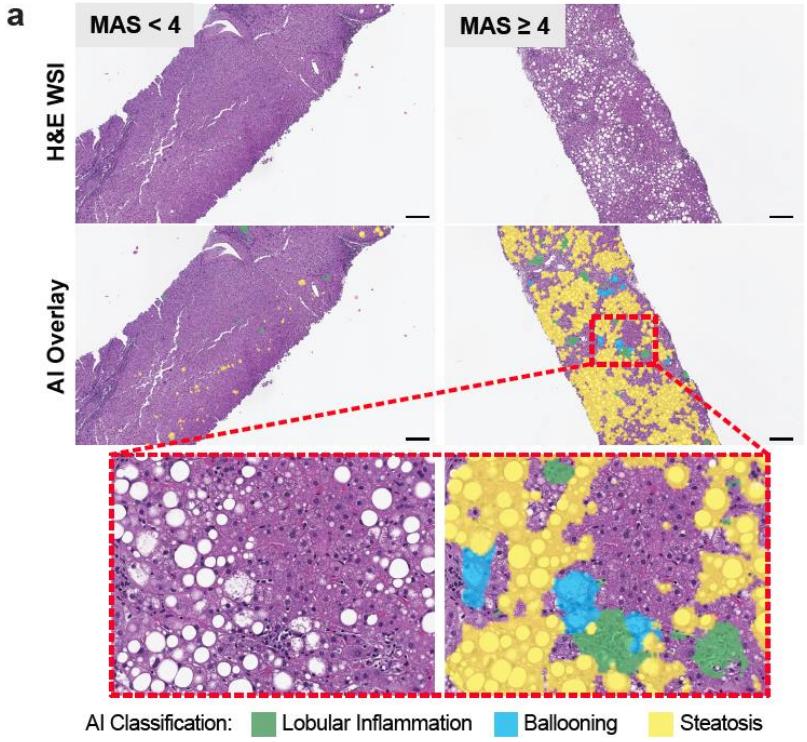
Subject to error around stage boundaries*

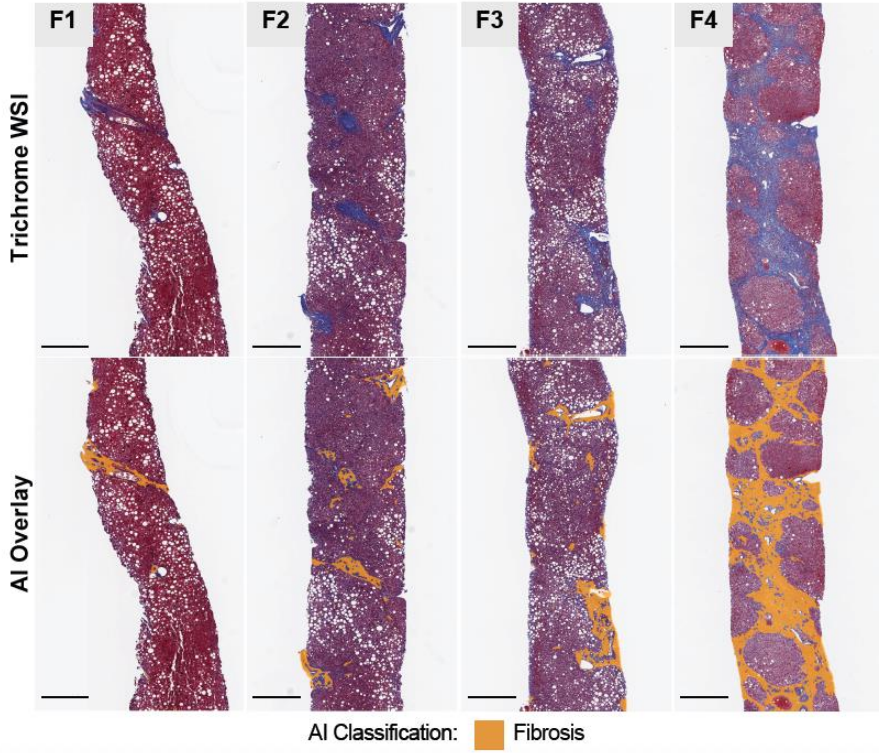


Only a single hepatocyte was considered to exhibit features consistent with ballooning by all 9 pathologists[3]

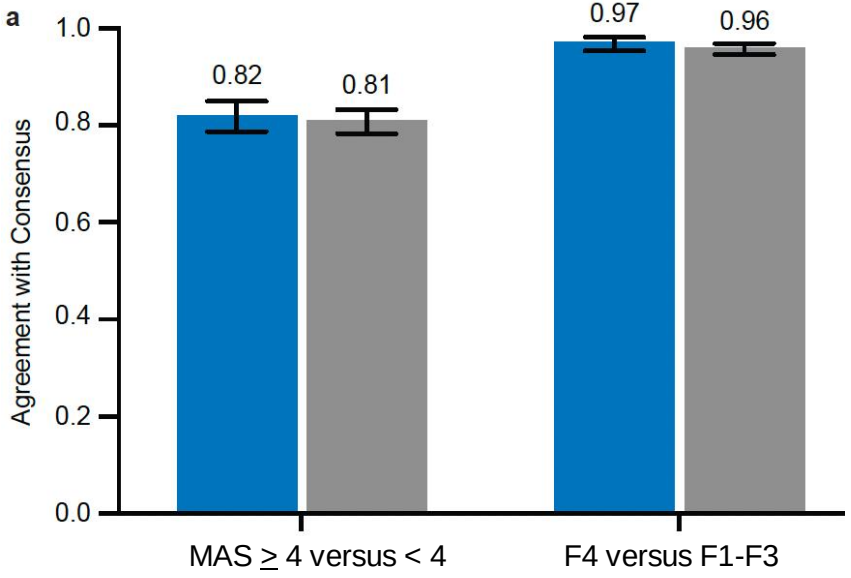
1 Kleiner DE, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology 2005 Jun; 41(6):1313-21.
2 Kleiner DE, et al. Association of Histologic Disease Activity with Progression of Nonalcoholic Fatty Liver Disease. JAMA Network Open 2019; 2:31912565
3 Brunt EM, et al. Complexity of ballooned hepatocyte feature recognition: Defining a training atlas for artificial intelligence-based imaging in NAFLD. Hepatology. 2022 May; 76(5): P1030-1041

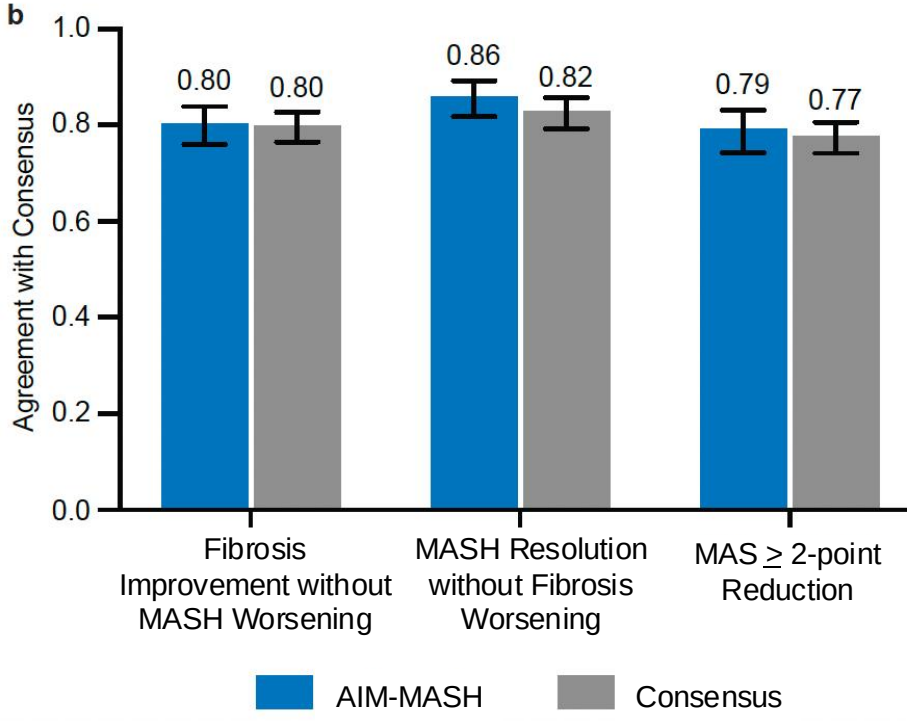
AI-based detection and scoring of MAS components and fibrosis enhanced by AI overlays of key histological features





AI-based grading/staging of enrollment criteria and efficacy endpoints on par with pathologist consensus





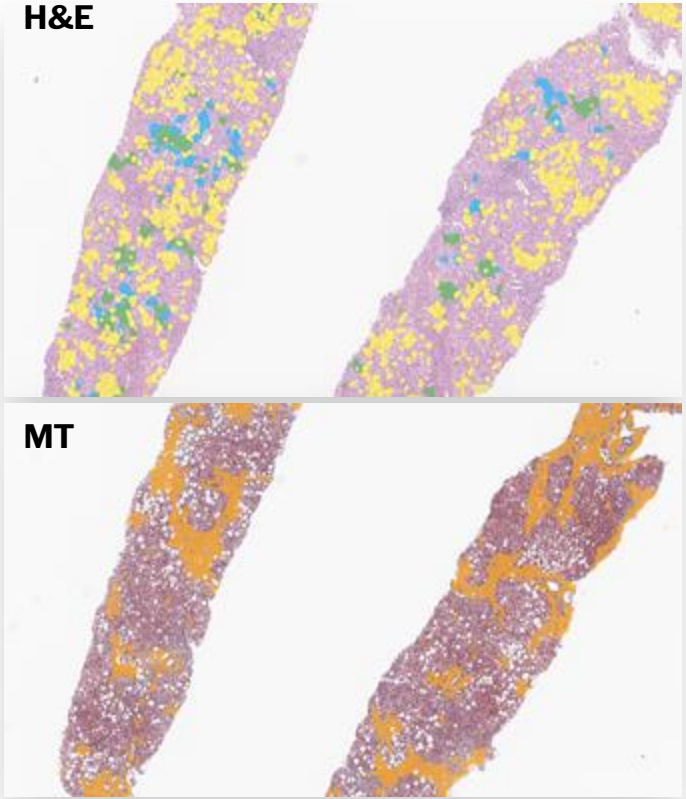
AI-based grading/staging is completely repeatable on the same whole slide image

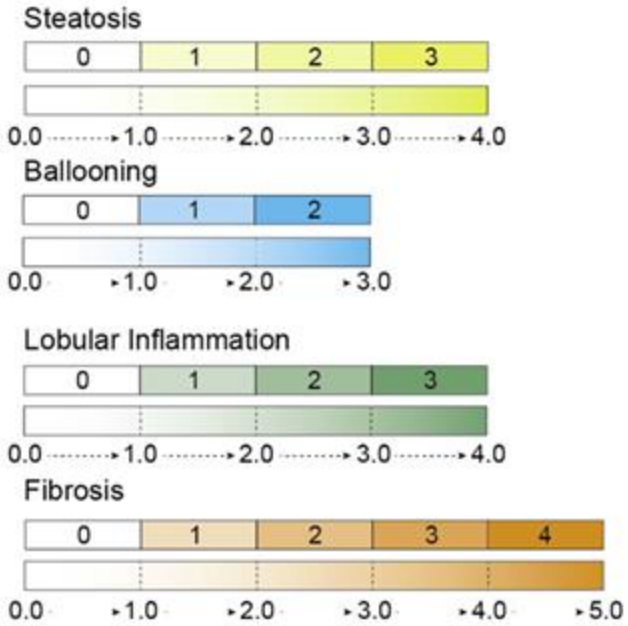
Supplementary Table 2. Algorithm repeatability assessment using 10 independent reads per WSI.

	Number of WSIs	Model versus model agreement rate
Steatosis	639	100%
Lobular inflammation	639	100%
Ballooning	639	100%
Fibrosis	633	100%

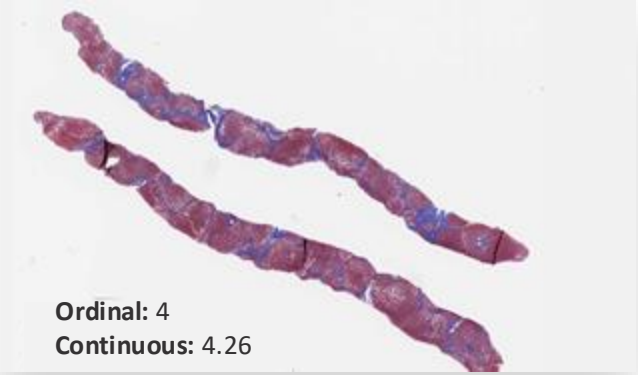
WSI, whole slide image.

AIM-MASH outputs continuous MAS and CRN grades/stages, enabling measurement of sub-ordinal changes in disease severity

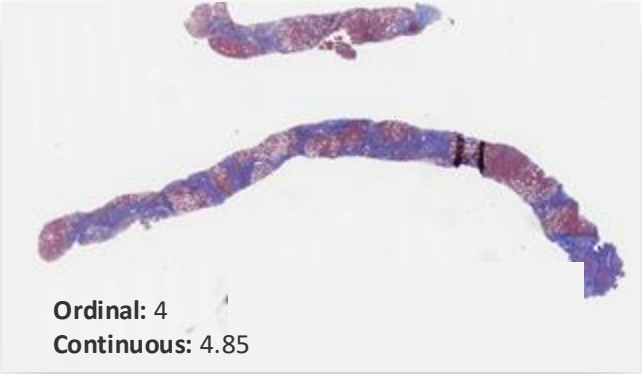




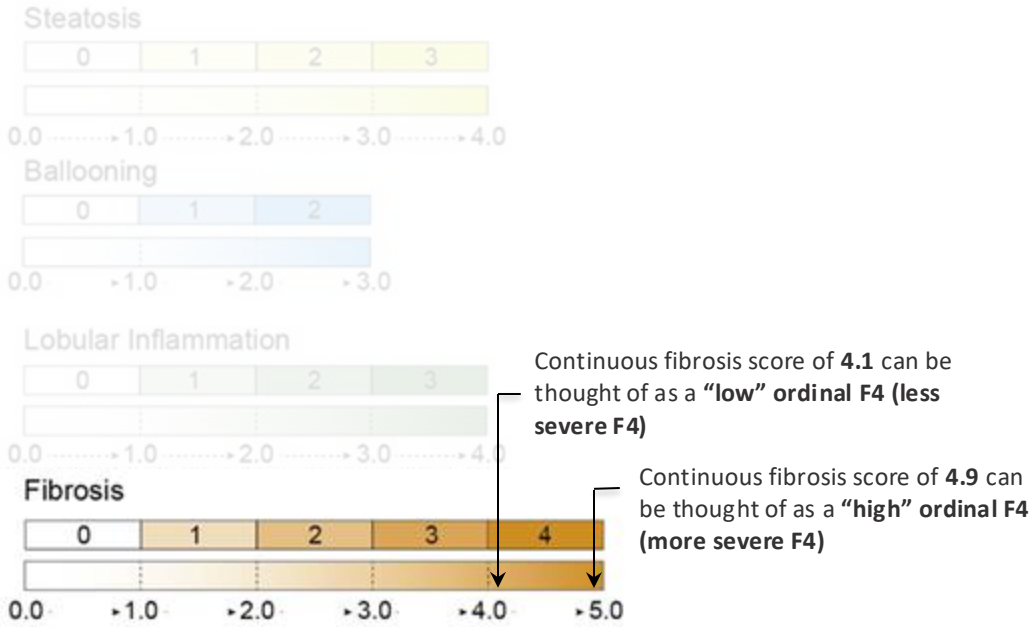
AIM-MASH outputs continuous MAS and CRN grades/stages, enabling measurement of sub-ordinal changes in disease severity



Ordinal: 4
Continuous: 4.26



Ordinal: 4
Continuous: 4.85

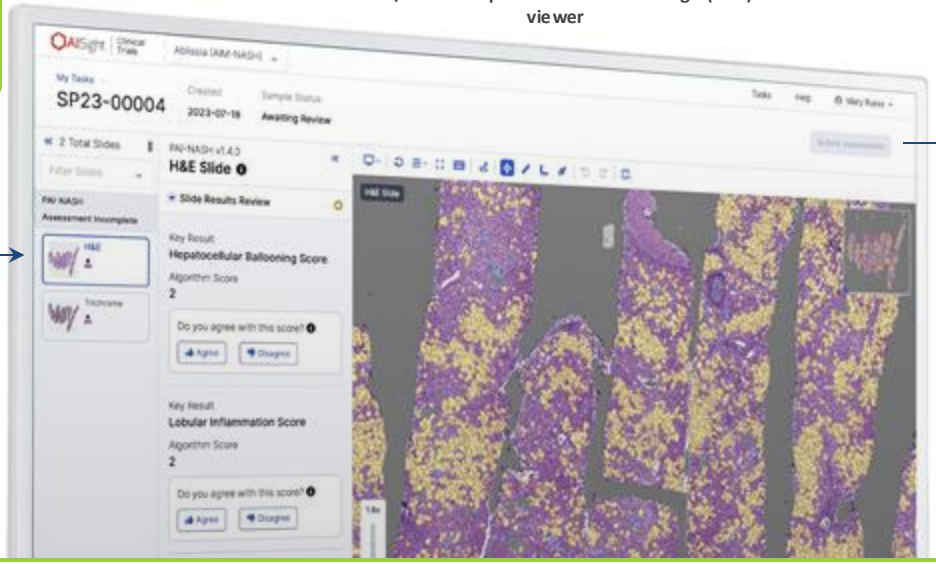


AIM-MASH Drug Development Tool for Assisting Pathologists for MASH Trial Biopsy Scoring

AISight Clinical Trials, validated for pathologist evaluation of biopsies in MASH trials.

AISight | Clinical Trials

GCP/GCLP compliant Whole Slide Image (WSI) viewer



Digitized WSIs of liver biopsy (H&E and Trichrome)

AIM-MASH Deployment

Pathologist review of AIM-MASH scores

- MASLD activity score
- CRN fibrosis stage

Overlay features validated for accuracy in highlighting the MAS and CRN fibrosis scores

Context of Use for which a Qualification is requested: A monitoring biomarker as an adjunct that aids the pathologist in assessing MAS score (steatosis, hepatocellular ballooning, lobular inflammation) and fibrosis stage (at baseline and follow-up time points) in liver biopsies in MASH clinical trials.

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nature medicine

Article

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Clinical validation of an AI-based pathology tool for scoring of metabolic dysfunction-associated steatohepatitis

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Check for updates

Hanna Pulaski[1,19], Stephen A. Harrison[2,19], Shraddha S. Mehta[1,12], Arun J. Sanyal[3], Marlena C. Vitali[1,13], Laryssa C. Manigat[1], Hypatia Hou[1], Susan P. Madasu Christudoss[1,14], Sara M. Hoffman[1,15], Adam Stanford-Moore[1], Robert Egger[1], Jonathan Glickman[1,16], Murray Resnick[1,17], Neel Patel[1], Cristin E. Taylor[1], Robert P. Myers[4], Chuhan Chung[5], Scott D. Patterson[6], Anne-Sophie Sejling[7], Anne Minnich[8], Vipul Baxi[8], G. Mani Subramaniam[4], Quentin M. Anstee[9], Rohit Loomba[10], Vlad Ratziu[11], Michael C. Montalto[1,18], Nick P. Anderson[1], Andrew H. Beck[1] & Katy E. Wack[1]

Today’s paradigm for MASH clinical trial histology assessment

Today’s paradigm

Three individual pathologists, each need to read every case
Intra- and inter-reader reproducibility is a challenge

~10% of cases require consensus panel

AIM-MASH AI-assisted solution

Single AI-assisted pathologist reads each case with equivalent accuracy to consensus panel and are aided by a highly reproducible tool

< 2% of cases require consensus reads

AIM-MASH AI Assist has the potential to enhance turnaround time, reduce complexity without compromising gold standard consensus-level trial readouts

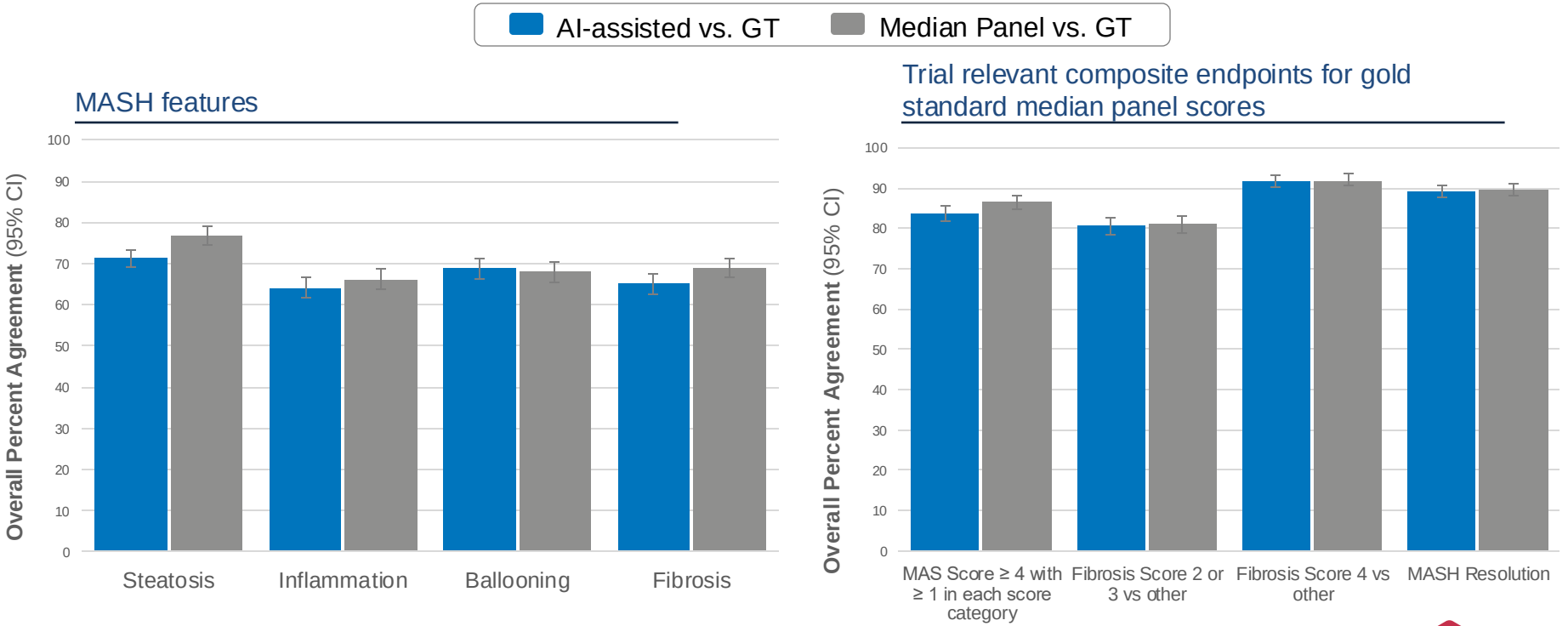
AIM-MASH Achieves Superior Agreement to Ground Truth (GT) for Scoring MASH Phenotypes Compared to Unaided Pathologist

Average AI-assisted pathologist compared to average individual pathologists' linearly weighted kappa with ground truth (GT) panel - algorithm score was modified by pathologist in only 1.8% of all cases.

CV Datasets: Two Phase 2b Trials (F2/3, F4) + one Phase 3 Trial, (~1,480 cases)

Single AIM MASH AI Assist -aided pathologist is equivalent to gold standard panel

Average AI-assisted pathologist compared to median panel of pathologists' overall percent agreement with ground truth (GT) panel



CV Datasets: Two Phase 2b Trials (F2/3, F4) + one Phase 3 Trial, (~1,480 cases)

AIM-MASH-assisted scoring is superior to traditional manual pathology scoring for enrollment and endpoint assessment

Pathologists aided by AIM-MASH are as good as the gold standard consensus panel at all MASH CRN components and clinical trial relevant assessments

Pathologists aided by AIM-MASH are **more accurate** in their assessment of **hepatocellular ballooning**, and **lobular inflammation** and non-inferior in their assessment of steatosis and fibrosis compared to unaided pathologists.

Pathologists aided by AIM-MASH are **superior** to unaided pathologists in accuracy in their assessment **of inclusion criteria, NAS >=4, F2/3, and relevant endpoint assessment, NASH resolution**.

AIM-MASH is **highly reproducible** and substantially improves scoring reproducibility compared with unassisted manual scoring

For further information, please refer to two recent publications on the development and clinical validation of AIM-MASH

nature medicine

AI-based automation of enrollment criteria and endpoint assessment in clinical trials in liver diseases

Iyer, J.S., Juyal, D., Le, Q. et al. Nat Med 30, 2914–2923 (2024).
https://doi.org/10.1038/s41591-024-03172-7

nature medicine

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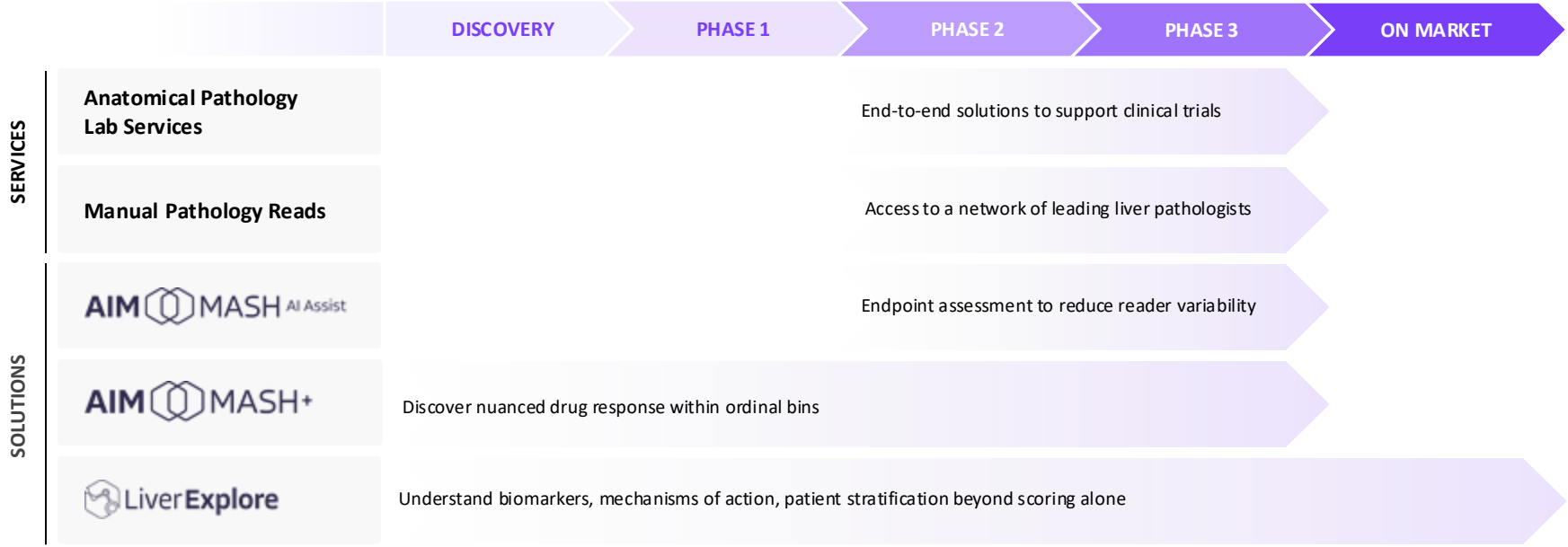
Pulaski, H., Harrison, S.A., Mehta, S.S. et al. Nat Med (2024).
https://doi.org/10.1038/s41591-024-03301-2

PathAI provides support throughout clinical development

Integrating unique solutions to your most pressing clinical challenges



Leveraging **quantitative insights** to uncover liver biology with Liver Explore™

Drug MOA, disease progression and beyond

Liver Explore features can address hypothesized mechanisms

Mechanism	Liver Explore features
Reduced fat deposition	
Reduced inflammatory response	
Reduced fibrogenesis	
Recovery of hepatocyte function	

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Liver Explore features can address hypothesized mechanisms

Mechanism	Liver Explore features
Reduced fat deposition	•Proportionate area of steatosis •Density of steatotic hepatocytes
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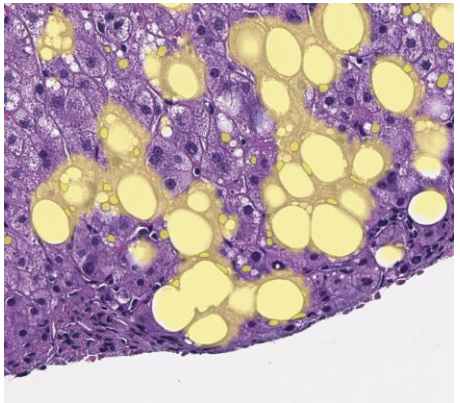

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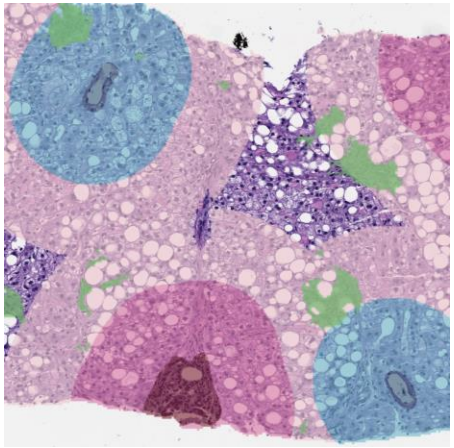
Liver Explore features can address hypothesized mechanisms

Mechanism	Liver Explore features
Reduced fat deposition	•Proportionate area of steatosis •Density of steatotic hepatocytes
Reduced inflammatory response	•Density of immune cell types •Relative density of immune cells in fibrotic regions •Proportionate area of lobular inflammation in Zones 1-3
Reduced fibrogenesis	
Recovery of hepatocyte function	



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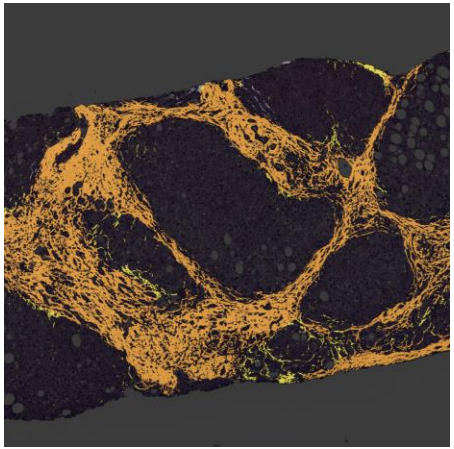
Recovery of hepatocyte function	



Liver Explore is for research use only. Not for use in diagnostic procedures

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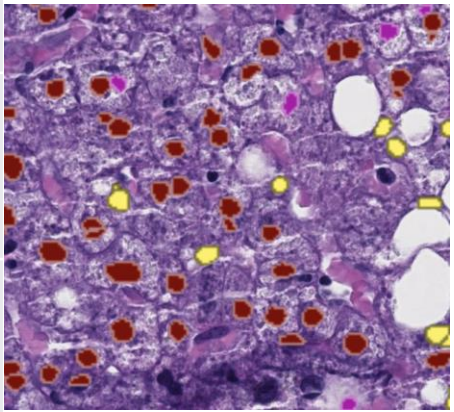

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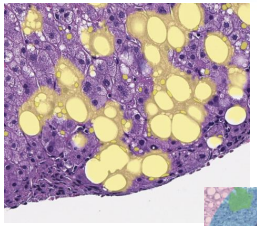
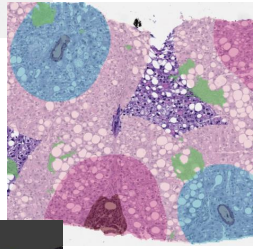
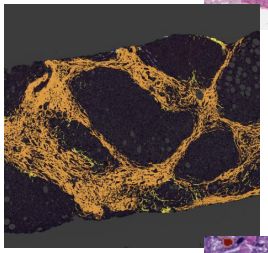
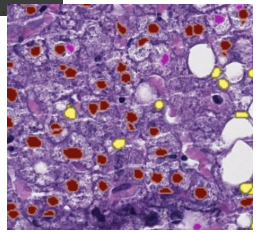
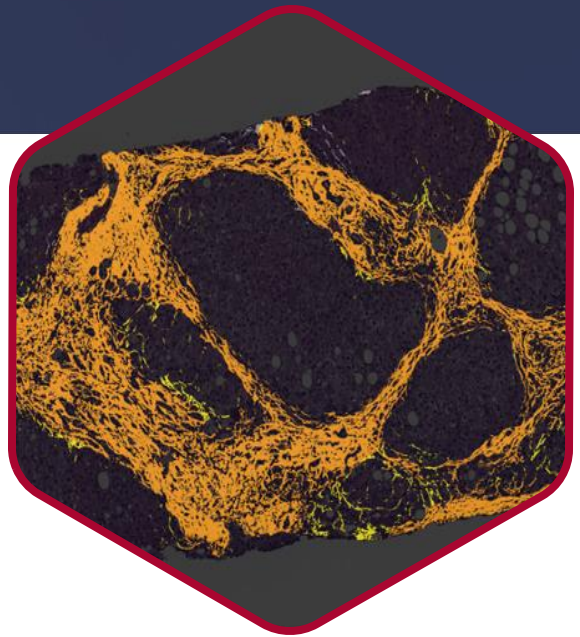








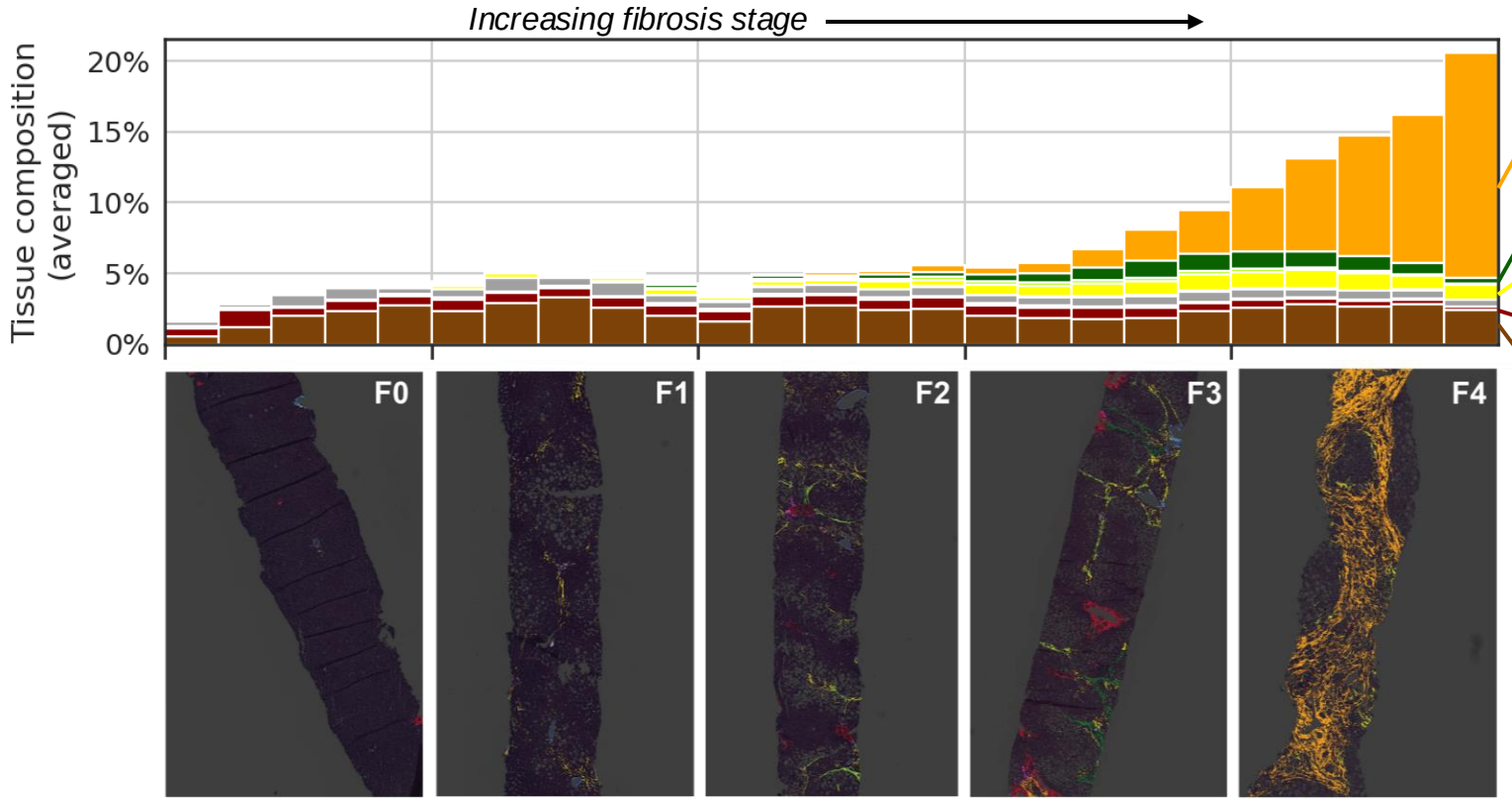
Case studies



Applying Liver Explore features to test hypotheses across liver disease indications

1. **MASH: fibrosis insights and spatial insights** (quantitative characterization)
   - *Collaboration with Gilead (STELLAR-3 and STELLAR-4 datasets), results presented at AASLD 2023 and EASL 2024*
2. **Bariatric surgery: histologic response to treatment**
   - *Collaboration with Unitat de Recerca Biomèdica, Universitat Rovira i Virgili (Step 2 cohort), results submitted to EASL 2025*
3. **ASH: correlation with outcomes** (novel insights)
   - *Collaboration with the Mayo Clinic, results presented at AASLD 2024*

Liver Explore fibrosis subtyping features offer granular resolution within MASH CRN fibrosis stages



Nodular fibrosis

Complete septal fibrosis

Perisinusoidal fibrosis

Portal collagen

Structural collagen

Posters presented at AASLD 2023 & EASL 2024

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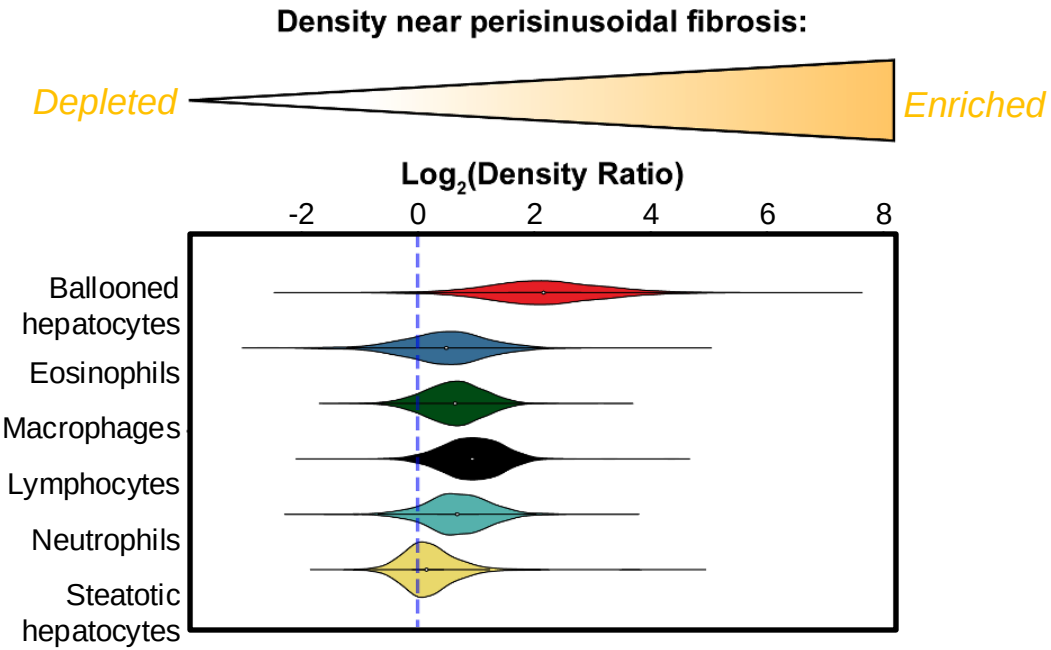
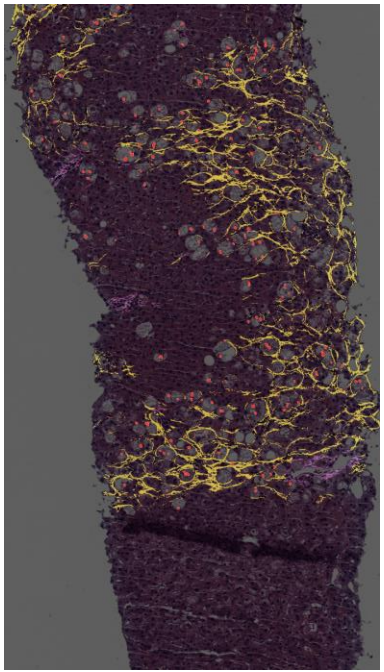
Spatial association revealed between cell types and fibrotic features





Ballooned hepatocytes

Perisinusoidal fibrosis

Poster presented at AASLD 2023

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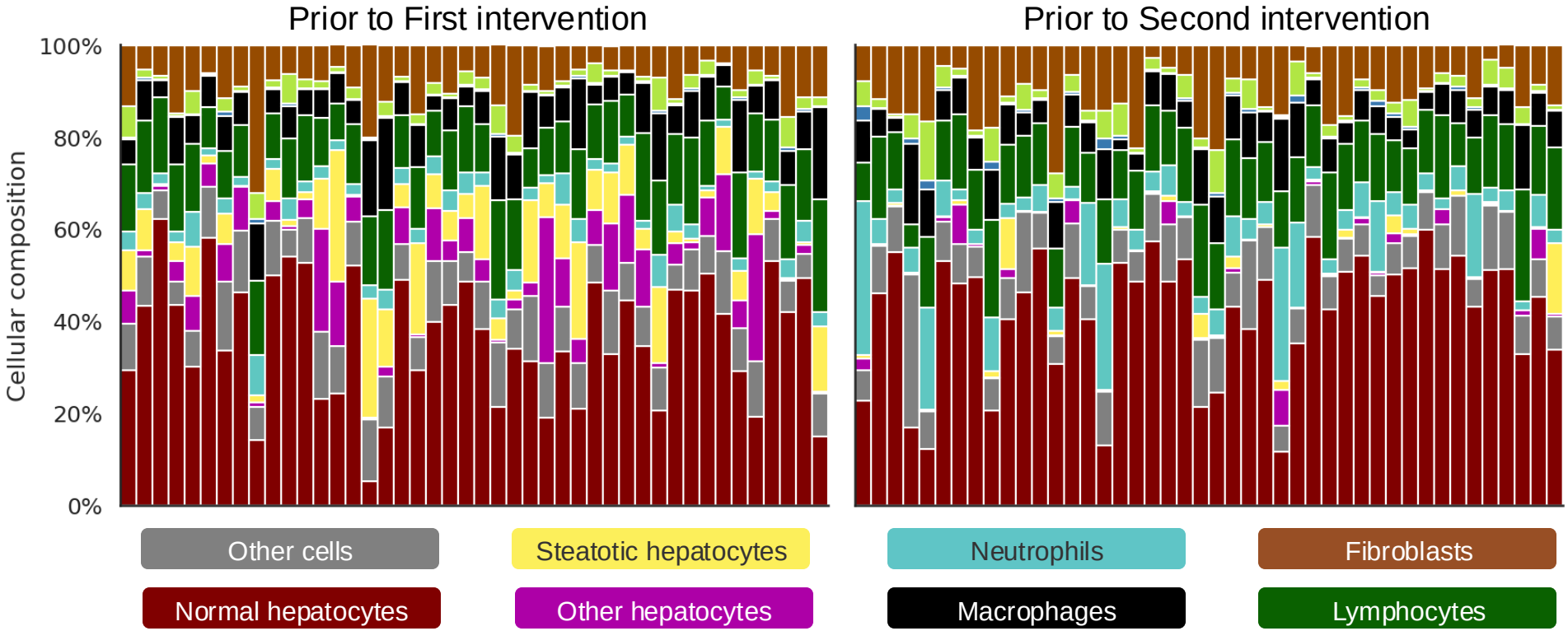
Bariatric surgery results in cellular composition changes



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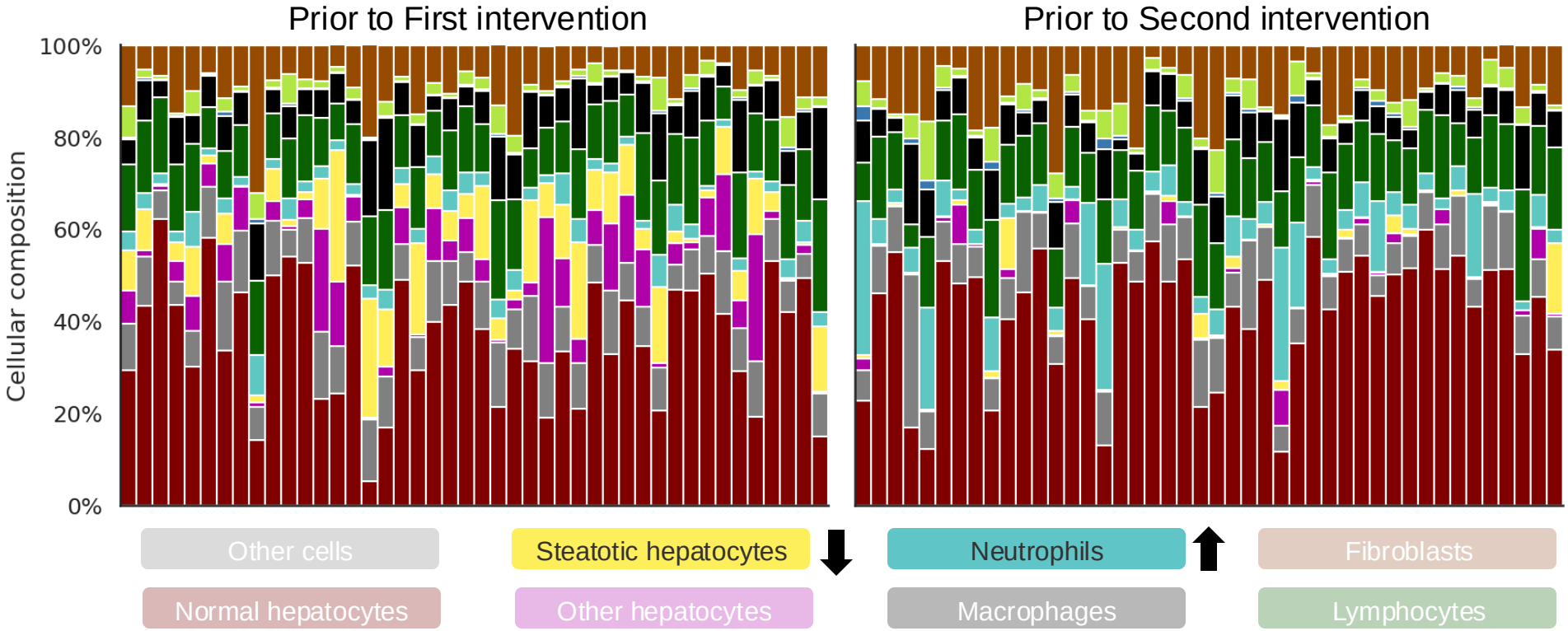

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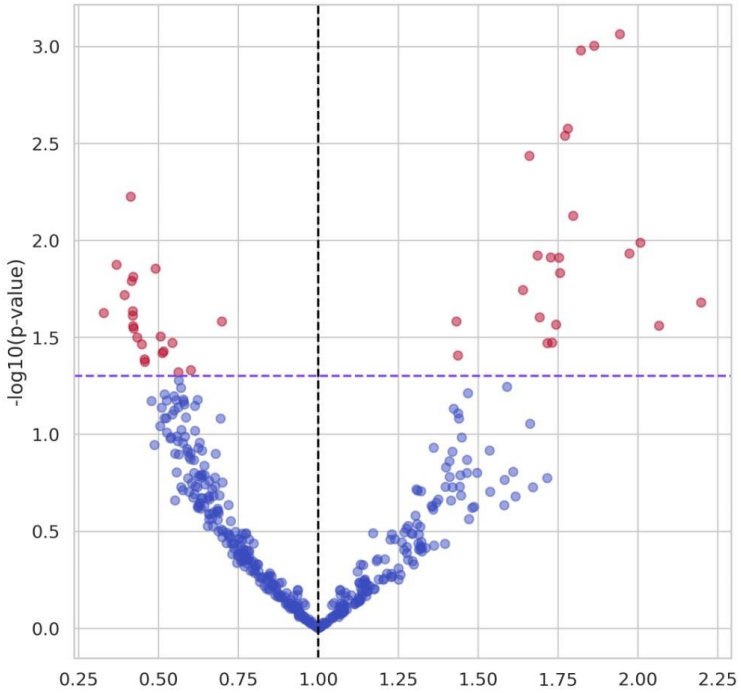
High-throughput biomarker discovery in ASH

Oral presentation at AASLD 2024



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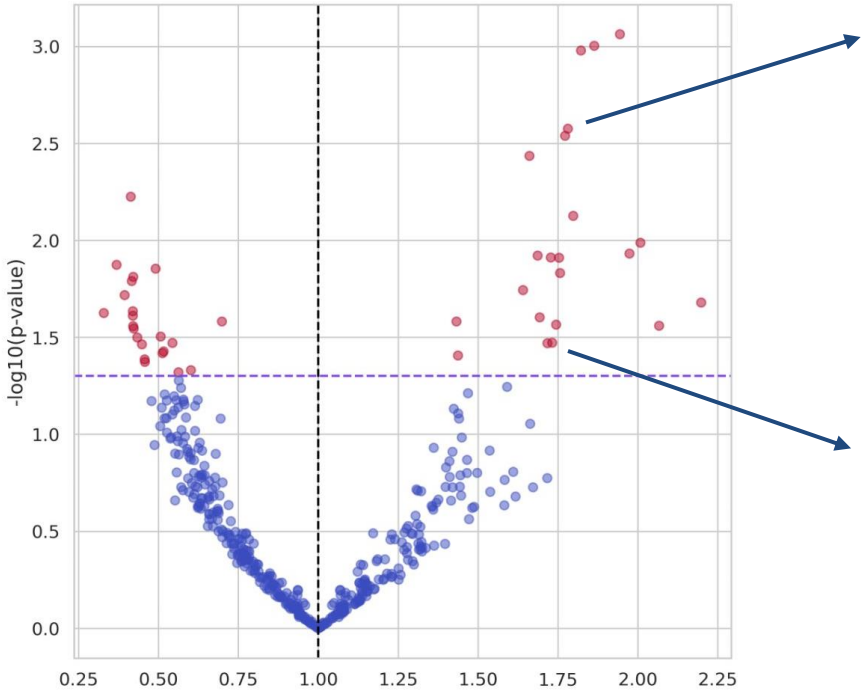
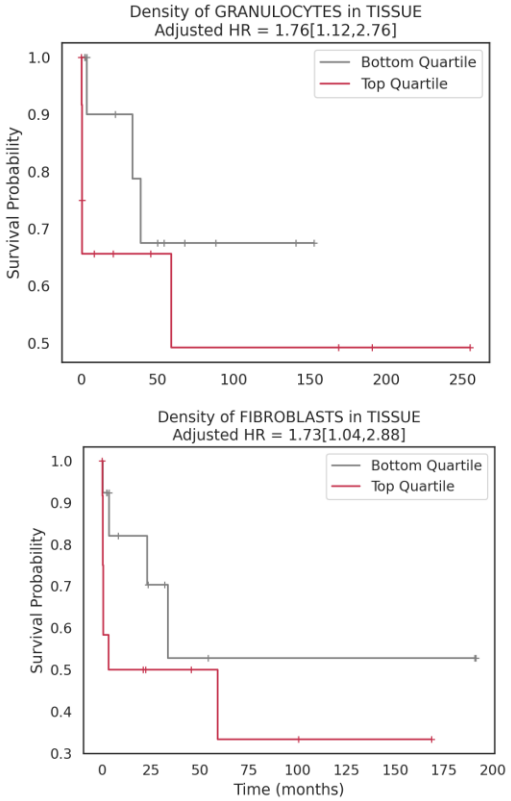
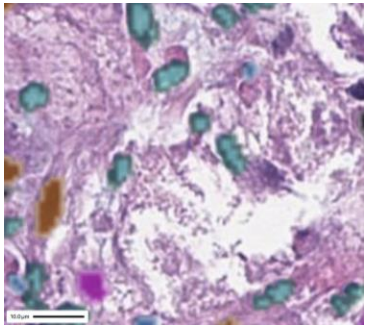
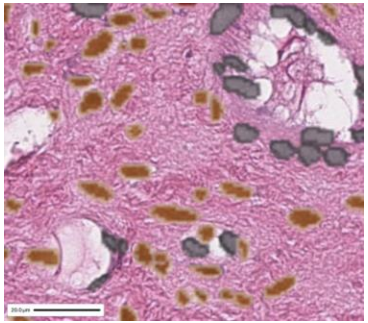




Granulocytes



Fibroblasts



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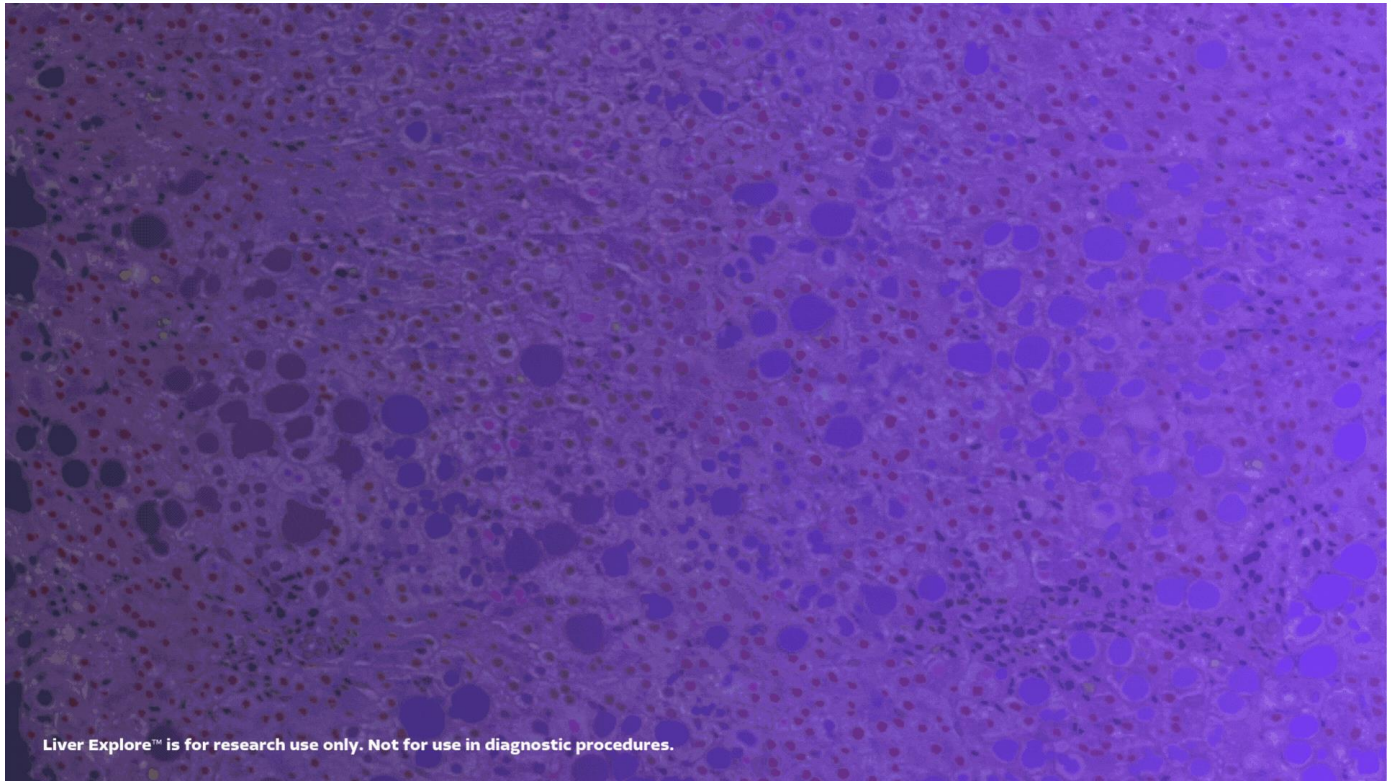
Liver Explore™ at your fingertips



Demo Registration

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