PathAI: Liver Forum
October 27, 2020

Company Overview

PathAI's platform promises substantial improvements to the accuracy of diagnosis and the measurement of therapeutic efficacy for complex diseases like cancer, IBD and NASH, leveraging modern approaches in machine learning

SUMMARY

- Founded in 2016 by Andy Beck, MD PhD and Aditya Khosla, PhD
- Headquartered in Boston with offices in New York & Austin
- World class team of >150 people

CLIENTS

- Research with majority of top 20 pharma companies
- Signed industry first AI-driven CDx program in early 2020
- 11 Presentations on Liver Diseases in 2019-2020

INVESTORS

GENERAL CATALYST

GENERAL ATLANTIC

Bristol Myers Squibb

LabCorp

Merck Global Health Innovation

OUR MISSION

Improve patient outcomes with AI-powered pathology

PathAI has made Significant Progress in NASH: 2019-2020

Grading and Staging NASH

- AASLD - *Machine Learning Models Accurately Interpret Liver Histology In Patients With Nonalcoholic Steatohepatitis (NASH)*
- AASLD - *Machine Learning Fibrosis Models Based on Liver Histology Images Accurately Characterize the Heterogeneity of Cirrhosis due to Nonalcoholic Steatohepatitis (NASH)*
- EASL - *Machine learning models identify novel histologic features predictive of clinical disease progression in patients with advanced fibrosis due to nonalcoholic steatohepatitis*
- AASLD - *A machine learning model based on liver histology predicts the hepatic venous pressure gradient (HVPG) in patients with compensated cirrhosis due to nonalcoholic steatohepatitis (NASH)*
- AASLD - *Integration of AI-powered Liver Histopathology with RNA-seq Identifies Gene Network Signatures Associated with Prognosis in Patients with Nonalcoholic Steatohepatitis (NASH)*

Monitoring Treatment Response in NASH

- EASL (late breaker) - *Safety and efficacy of combination therapies including cilofexor/firsocostat in patients with bridging fibrosis and cirrhosis due to NASH: Results of the phase 2b ATLAS trial*
- AASLD - *Validation of a machine learning-based approach (DELTA Liver Fibrosis Score) for the assessment of histologic response in patients with advanced fibrosis due to NASH*

Grading, Staging, and Monitoring Treatment Response in PSC & HBV

- EASL - *Machine learning models accurately interpret liver histology and are associated with disease progression in patients with primary sclerosing cholangitis*
- EASL (late breaker) - *Machine Learning Identifies Histologic Features Associated with Regression of Cirrhosis in Treatment for Chronic Hepatitis B*
- AASLD - *Machine learning enables quantitative assessment of histopathologic signatures associated with ALT normalization in chronic hepatitis B patients treated with tenofovir disoproxil fumarate (TDF)*
- AASLD - *Machine learning based quantification of histology from patients treated for chronic hepatitis B identifies features associated with viral DNA suppression and e-antigen loss*

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Machine Learning Models Identify Novel Histologic Features Predictive of Clinical Disease Progression in Patients With Advanced Fibrosis Due to Nonalcoholic Steatohepatitis

Harsha Pokkalla, Kishalve Pethia, Amaro Taylor-Weiner, Benjamin Glass, Hunter Elliott, Ling Han, Catherine Jia, Ryan S. Huss, Chuhan Chung, G. Mani Subramanian, Robert P. Myers, Stephen A. Harrison, Zachary Goodman, Murray Resnick, Aditya Khosla, Andrew Beck, Ilan Wapinksi, Arun J. Sanyal, Zobair M. Younossi

Presented at The Digital International Liver Congress, 27–29 August 2020

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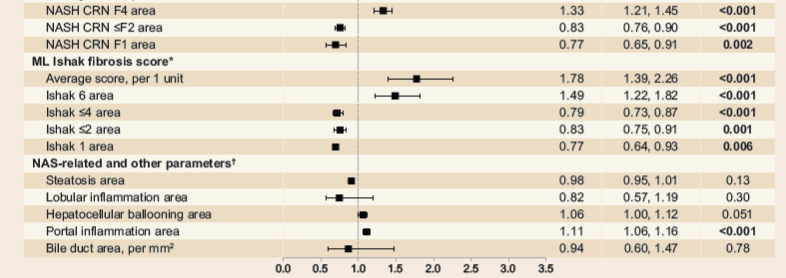
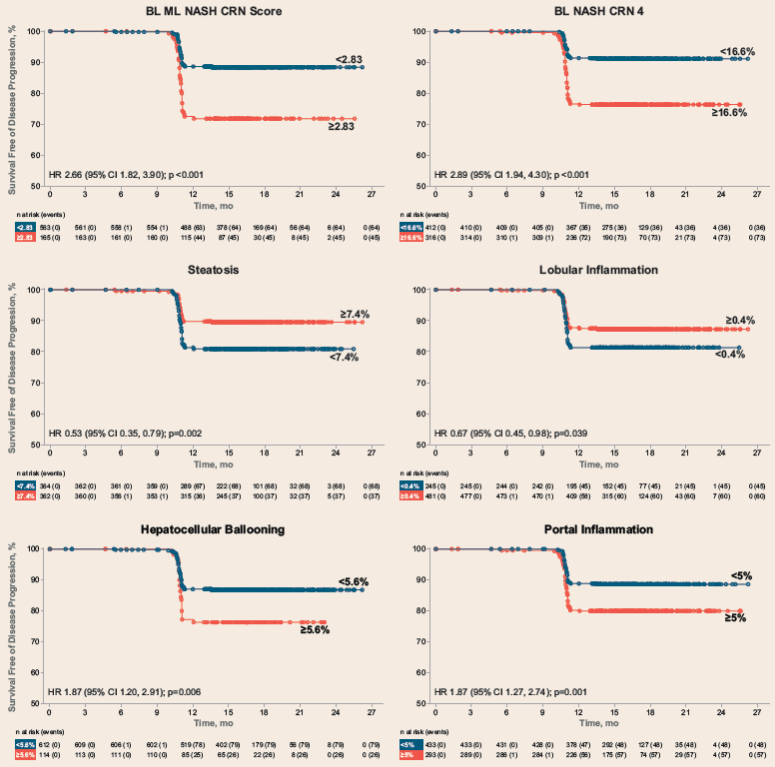
ML-Based Histologic Features Predicted Disease Progression in Patients With Bridging Fibrosis (F3)

- During median follow-up of 16.5 mo, 15% of patients with F3 fibrosis progressed to cirrhosis (n=112) or experienced a liver decompensation event (n=1)

	Bridging Fibrosis (clinical disease progression; n=113/755)		
	HR	95% CI	p-Value
ML NASH CRN fibrosis score*			
Average score, per 1 unit	2.18	1.56, 3.06	**<0.001**
NASH CRN F4 area	1.33	1.21, 1.45	**<0.001**
NASH CRN ≤F2 area	0.83	0.76, 0.90	**<0.001**
NASH CRN F1 area	0.77	0.65, 0.91	**0.002**
ML Ishak fibrosis score*			
Average score, per 1 unit	1.78	1.39, 2.26	**<0.001**
Ishak 6 area	1.49	1.22, 1.82	**<0.001**
Ishak ≤4 area	0.79	0.73, 0.87	**<0.001**
Ishak ≤2 area	0.83	0.75, 0.91	**0.001**
Ishak 1 area	0.77	0.64, 0.93	**0.006**
NAS-related and other parameters†			
Steatosis area	0.98	0.95, 1.01	0.13
Lobular inflammation area	0.82	0.57, 1.19	0.30
Hepatocellular ballooning area	1.06	1.00, 1.12	0.051
Portal inflammation area	1.11	1.06, 1.16	**<0.001**
Bile duct area, per mm²	0.94	0.60, 1.47	0.78



- Progression to cirrhosis was associated with higher ML NASH CRN and Ishak fibrosis scores, higher proportionate areas of NASH CRN F4 and Ishak stage 6 fibrosis, and lower proportionate areas of mild fibrosis (all p <0.05)
- Among nonfibrosis-related parameters, higher proportionate areas of hepatocellular ballooning and portal inflammation were associated with progression to cirrhosis



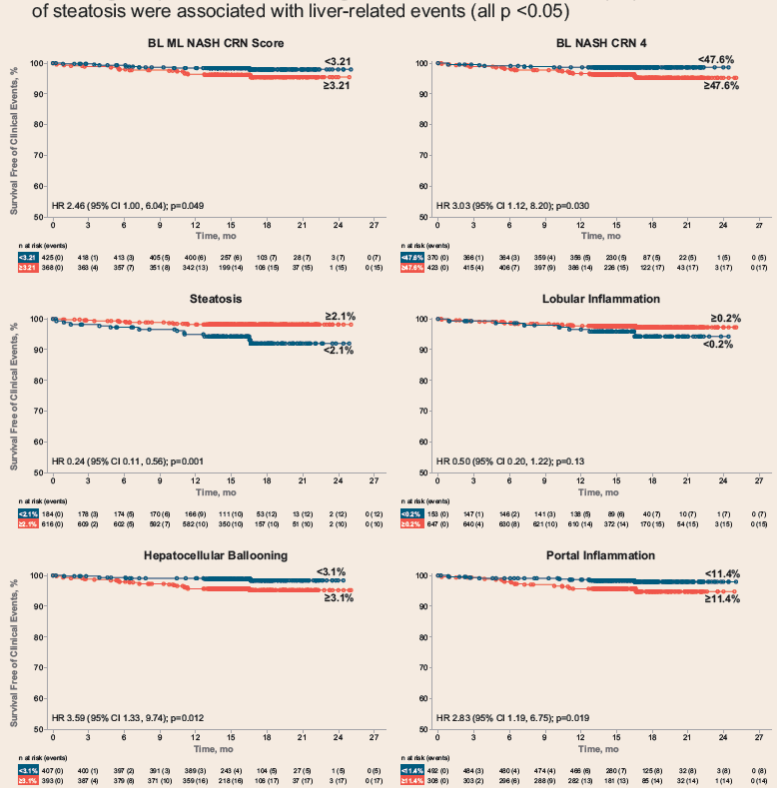
*Unless otherwise specified, hazard ratio (HR) reflects per 10% difference in parameter; †Unless otherwise specified, HR reflects per 1% difference in parameter. CI, confidence interval.

ML-Based Histologic Features Predicted Disease Progression in Patients With Cirrhosis (F4)

- During median follow-up of 15.8 mo, 3% (22/838) of F4 patients had liver-related clinical events

	Cirrhosis (clinical disease progression; n=22/838)		
	HR	95% CI	p-Value
ML NASH CRN fibrosis score*			
Average score, per 1 unit	2.94	1.04, 8.33	**0.043**
NASH CRN F4 area	1.23	1.00, 1.51	0.050
NASH CRN ≤F2 area	0.69	0.49, 0.97	**0.034**
NASH CRN F1 area	0.46	0.20, 1.08	0.08
ML Ishak fibrosis score*			
Average score, per 1 unit	3.36	1.61, 7.02	**0.001**
Ishak 6 area	1.31	1.10, 1.55	**0.002**
Ishak ≤4 area	0.64	0.49, 0.82	**<0.001**
Ishak ≤2 area	0.55	0.32, 0.94	**0.029**
Ishak 1 area	0.39	0.15, 1.02	0.06
NAS-related and other parameters†			
Steatosis area	0.84	0.73, 0.97	**0.017**
Lobular inflammation area	0.56	0.15, 2.16	0.40
Hepatocellular ballooning area	1.11	1.02, 1.21	**0.016**
Portal inflammation area	1.10	1.04, 1.17	**<0.001**
Bile duct area, per mm²	1.98	1.15, 3.41	**0.014**

- Liver-related events were associated with higher ML NASH CRN and Ishak fibrosis scores, higher proportionate areas of NASH CRN F4 and Ishak stage 6 fibrosis, and lower proportionate areas of mild fibrosis
- Among nonfibrosis-related parameters, higher proportionate areas of hepatocellular ballooning and portal inflammation, higher bile duct area, and a lower proportionate area of steatosis were associated with liver-related events (all p <0.05)

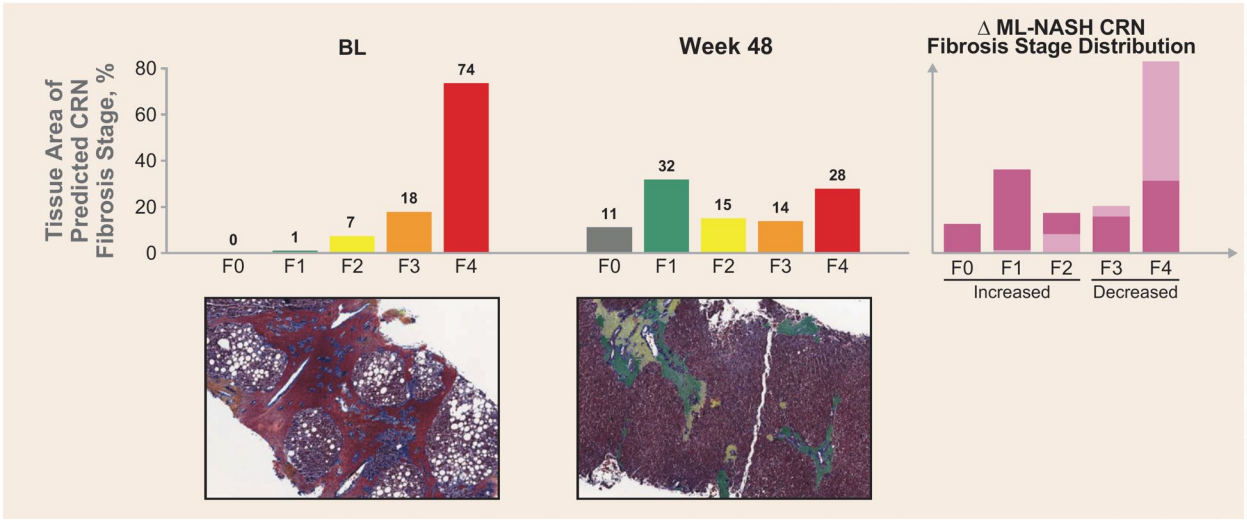


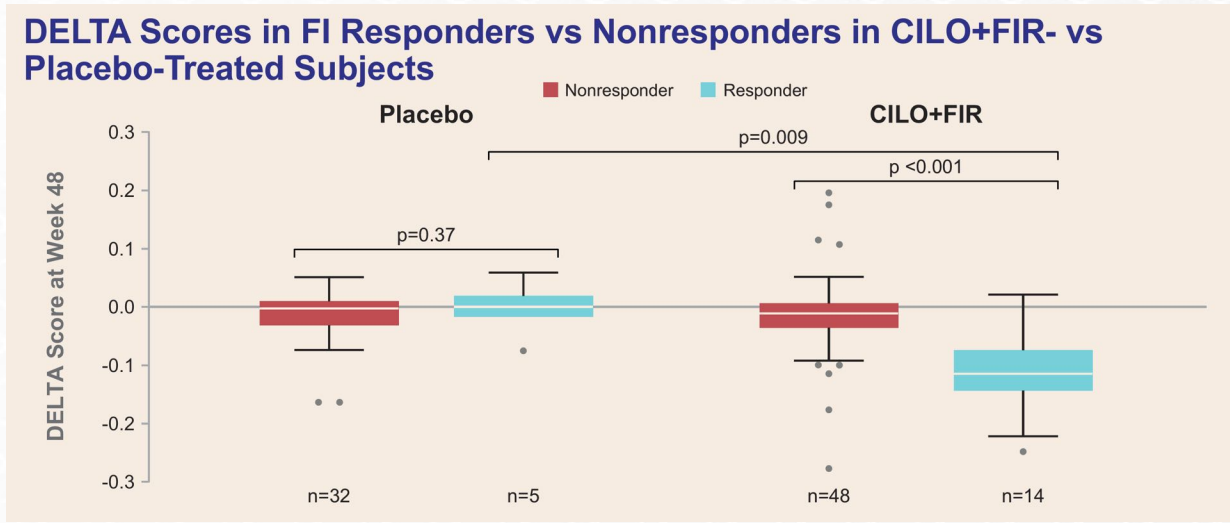
*Unless otherwise specified, HR reflects per 10% difference in parameter; †Unless otherwise specified, HR reflects per 1% difference in parameter.

Validation of a Machine Learning-Based Approach (DELTA Liver Fibrosis Score) for the Assessment of Histologic Response in Patients With Advanced Fibrosis Due to NASH

Amaro Taylor-Weiner,[1] Harsha Pokkalla,[1] Ling Han,[2] Catherine Jia,[2] Ryan Huss,[2] Chuhan Chung,[2] Hunter Elliott,[1] Benjamin Glass,[1] Kishalve Pethia,[1] Oscar Carrasco-Zevallos,[1] Chinmay Shukla,[1] G. Mani Subramanian,[2] Robert P. Myers,[2] Ilan Wapinski,[1] Aditya Khosla,[1] Murray Resnick,[1,3] Michael C. Montalto,[1] Quentin M. Anstee,[4] Vincent Wai-Sun Wong,[5] Michael Trauner,[6] Eric J. Lawitz,[7] Stephen A. Harrison,[8] Takeshi Okanoue,[9] Manuel Romero-Gomez,[10] Zachary Goodman,[11] Rohit Loomba,[12] Andrew H. Beck,[1] Zobair M. Younossi[11]

[1]PathAI, Inc., Boston, MA; [2]Gilead Sciences, Inc., Foster City, CA; [3]The Warren Alpert Medical School, Brown University, Providence, RI; [4]Institute of Cellular Medicine, Newcastle University Faculty of Medical Sciences, Newcastle upon Tyne, UK; [5]The Chinese University of Hong Kong, People's Republic of China; [6]Medical University of Vienna, Austria; [7]Texas Liver Institute, UT Health San Antonio, TX; [8]Pinnacle Clinical Research, San Antonio; [9]Saiseikai Suita Hospital, Suita, Japan; [10]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [11]Inova Fairfax Hospital, Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA; [12]UC San Diego NAFLD Research Center, La Jolla, CA





#1572 at AASLD: The Liver Meeting® Digital Experience, November 13–16, 2020

https://aasldpubs.onlinelibrary.wiley.com/doi/epdf/10.1002/hep.31579

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PathAI supports all phases of biomarker and diagnostic development

Translational Research

- Retrospective exploratory analysis
- Drug target identification
- Mechanisms of action
- Hypothesis generation: patient selection and stratification
- Trial design / indication selection

Clinical Trial Services

- Prospective/Scalable Quantitative Pathology Data
- Hypothesis Generation/Testing
- Dose Selection/PD
- Selection/Stratification

Device Development

- FDA approved IVD/CDx
- Lab Developed Test (CLIA)
- Drug Development Tool (DDT)

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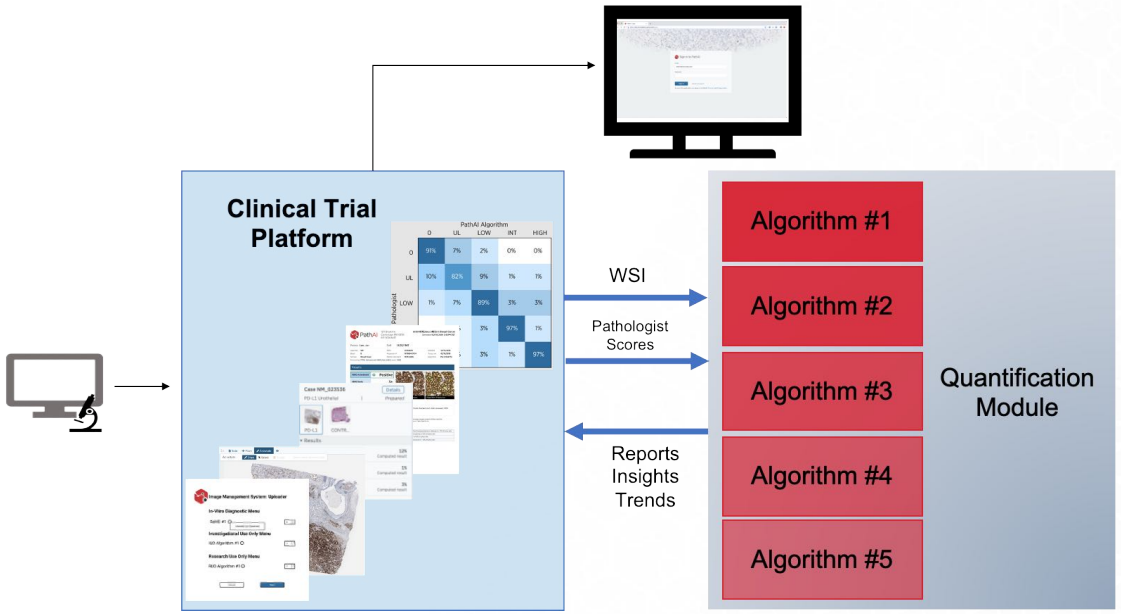
PathAI Clinical Trial Platform



Product offerings

- Fit for purpose locked algorithms
- Pre-configured custom project-specific workflows
- Pre-configured interactive analytics module

Key platform features

- Upload WSI and pathology scores (as needed)
- One click algorithm initiation
- Standardized, quantitative biomarker results
- Study-level data organization
- Participant level & cumulative reporting
- Automated trend analysis for quality control
  - Drifts in data
  - Variability across sites / pathologist scores
- Monitoring capabilities

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PathAI is Well Positioned for Regulatory Success with Active FDA Engagement and Quality Achievements

Industry Progress: FDA's approach advanced regarding Digital Pathology

- >30 510(k) clearances for product codes NOT, NQN, OEO (image analysis for IHC)
- 4x 510(k) clearances for WSI Primary Diagnosis on Digital Pathology Devices
- FDA Draft Guidance for WSI: Technical Performance Assessment Guidance Document

PathAI FDA Interactions

- 3 x pre-subs meetings w FDA regarding "follow-on" and CDx products, 3 more planned
- Breakthrough Designation Status Submission in progress
- FDA accepted LOI for Biomarker Qualification Program for PathAI NASH Drug Development Tool (DDT) (2020)

PathAI Quality and Regulatory

- PathAI has achieved ISO27001 and ISO13485 certification as well as 21 CFR Part 820 compliance to ensure the highest quality and standards to achieve regulatory approval

Thank You

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