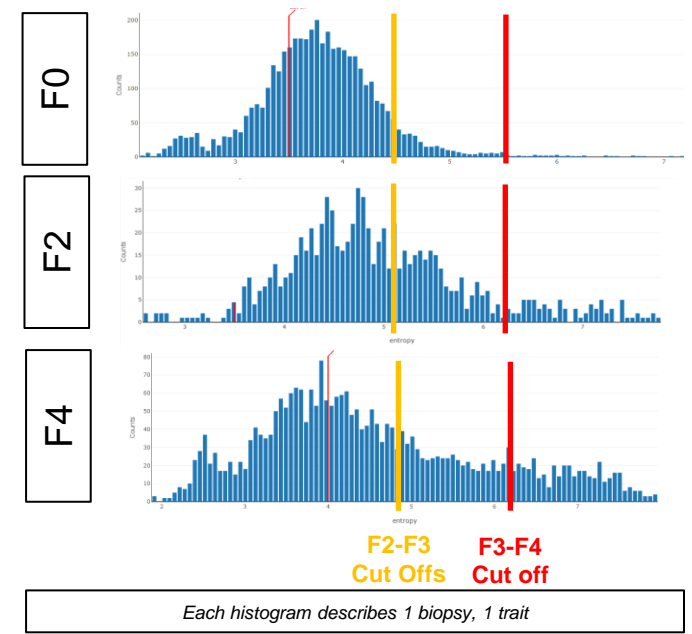
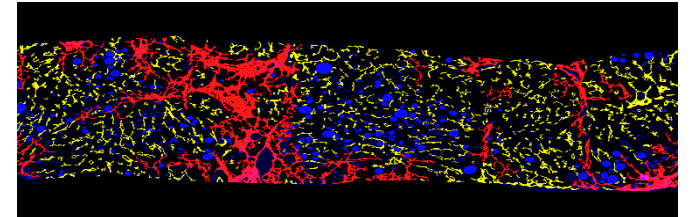
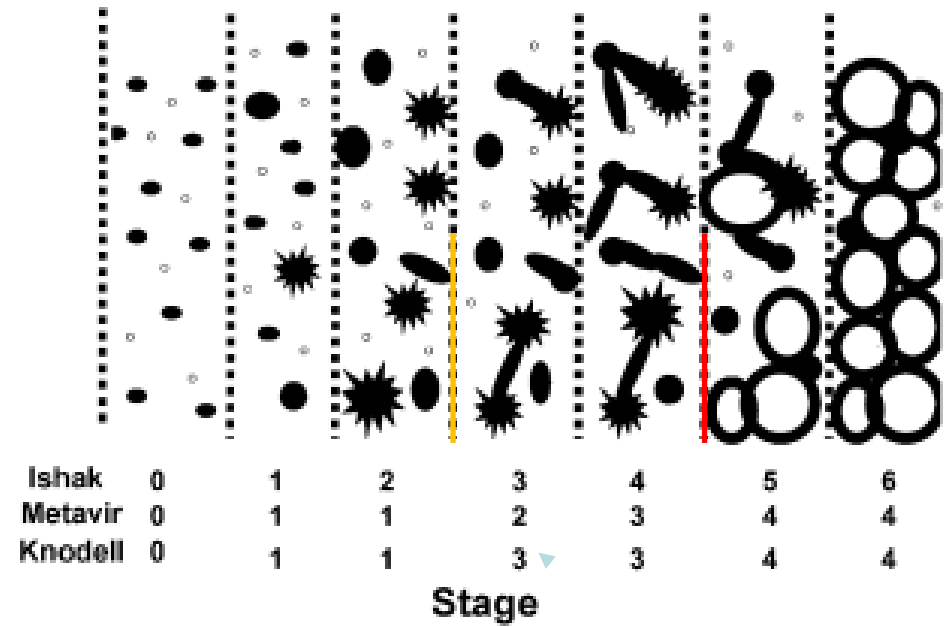
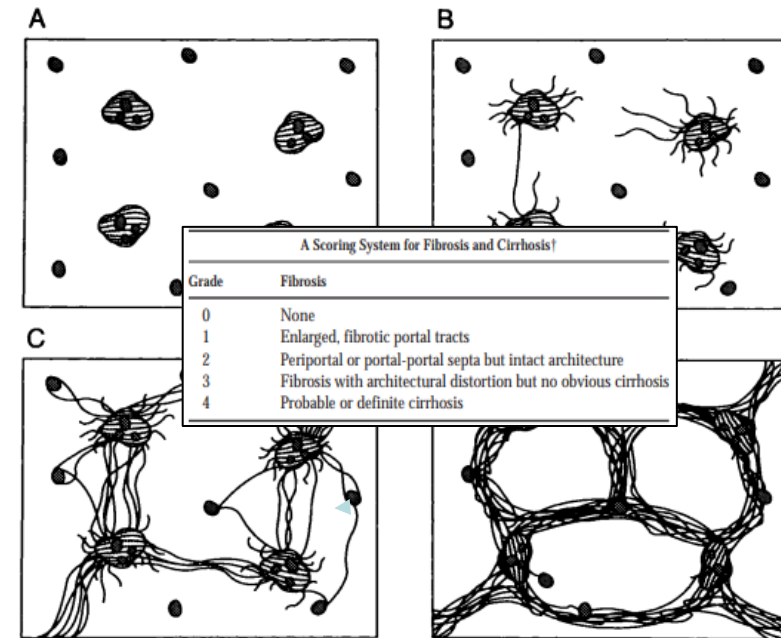


PharmaNest

FibroNest Engine

37 phenotypic traits, each quantified in 7 statistical dimensions



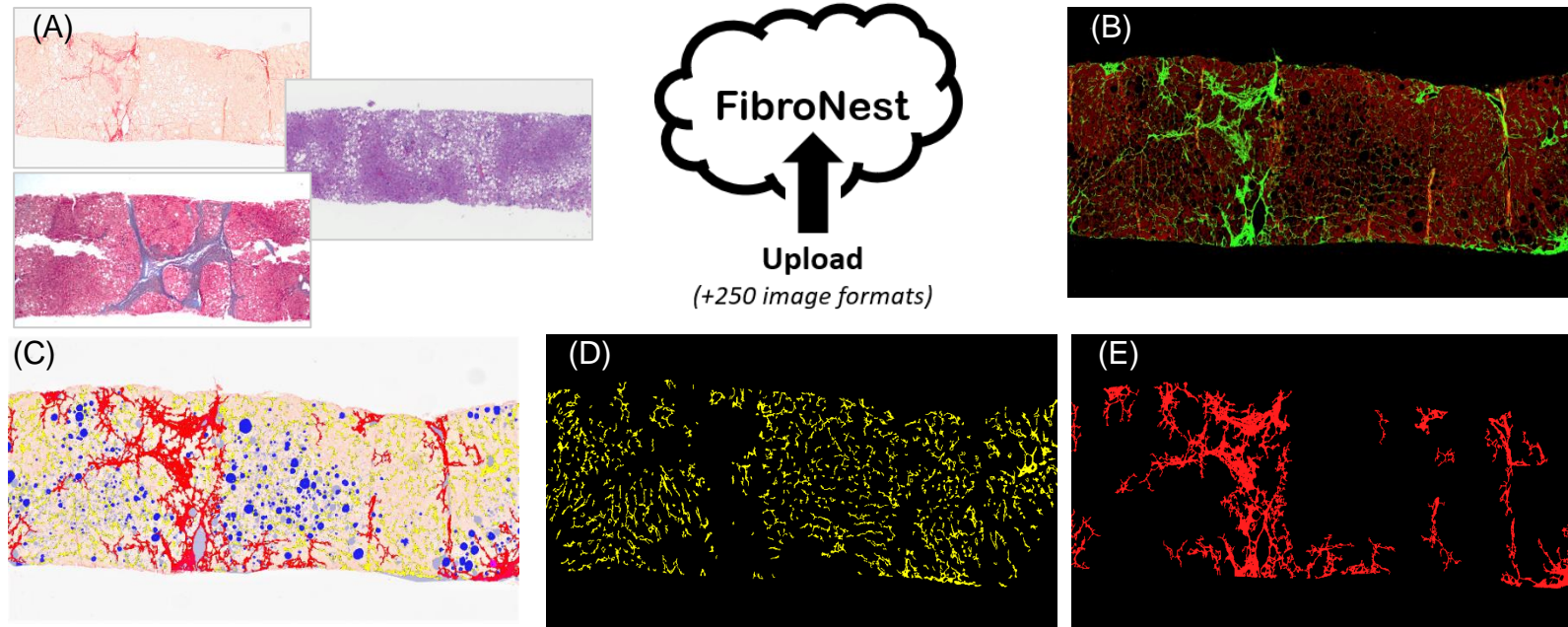
FibroNest is based on the hypothesis that fibrosis expresses multiple and different histology phenotypes
We quantify them across 3 phenotypic dimensions with Signal-to-Noise >100

Batts KP, Ludwig J. Chronic hepatitis. An update on terminology and reporting. Am J Surg Pathol 1995;19:1409-1417
Grading and staging systems for inflammation and fibrosis in chronic liver diseases, Zachary D. Goodman* Journal of Hepatology 47 (2007) 598-607

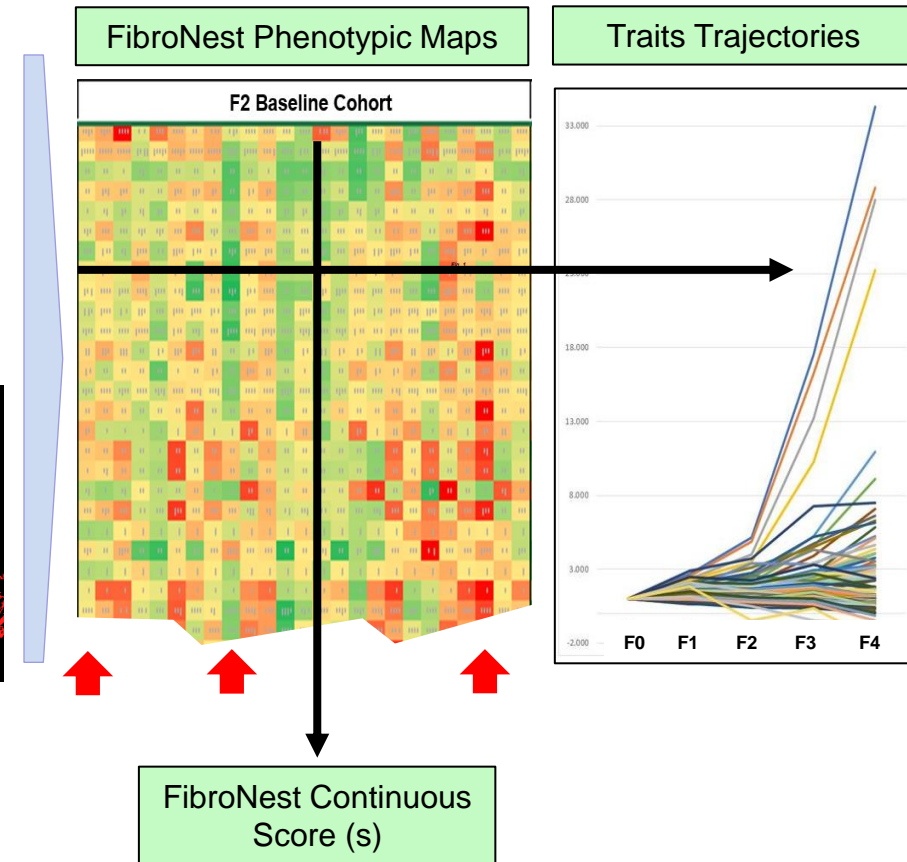
PharmaNest

FibroNest Workflow

Delivered Worldwide via the cloud



(A) 20x Biopsy (Sirius red or Mass Trichrome, H&E) (B) FibroNest Color Normalization and deconvolution Green: collagens, Red: tissue (C) Augmented visualization of the Digital Image (aid to adjudication) - FibroNest quantification Red: assembled collagen, Yellow : interstitial collagen, Blue: steatosis (D) Yellow : interstitial collagen alone (E) Red: assembled collagen. The coalescence of interstitial collagen (yellow) into assembled collagen (Red) is a marker of fibrosis progression.



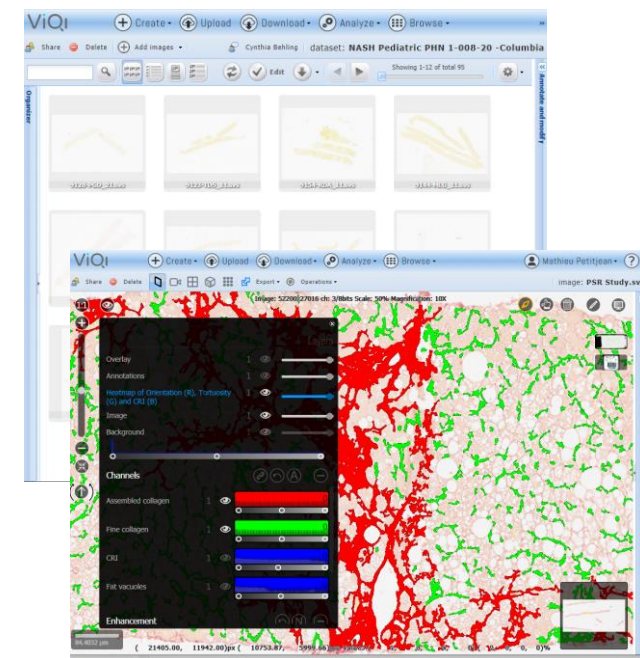
“Non-invasive Workflow”

Once Calibrated, the FibroNest Phenotypic Assay is “Frozen” and kept constant for every model

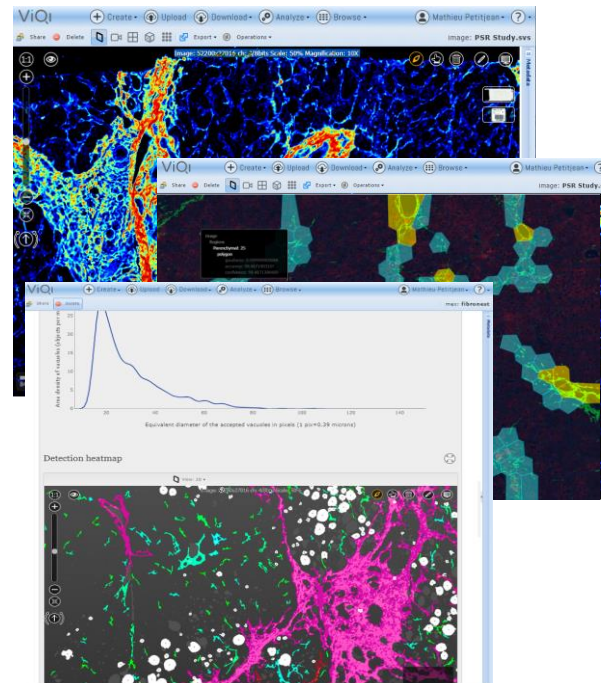
PharmaNest – ViQI Platform

Using Next Generation of Cloud-based Bioimaging and Computation Infrastructures

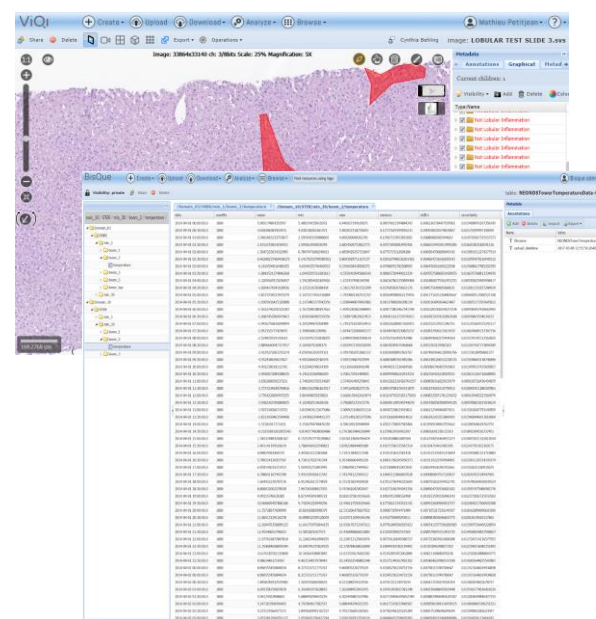
Web-based viewers and collaboration



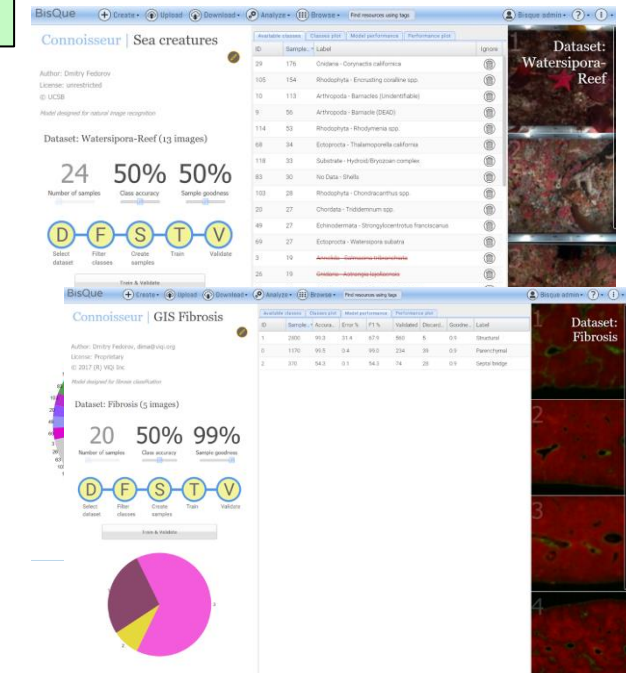
FibroNest Analysis



Annotations and metadata e.g. Biomarker



AI & ML



**Unlimited Computing Power applied to Fibrosis, Disease Activity and NASH Challenges
Designed to enable Pathomic Fusion**

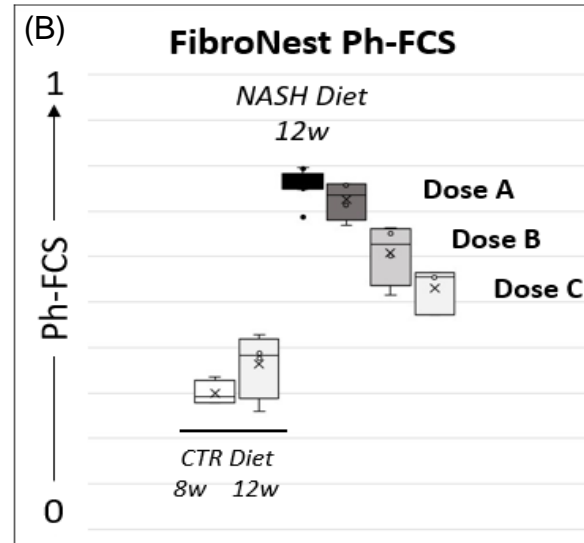
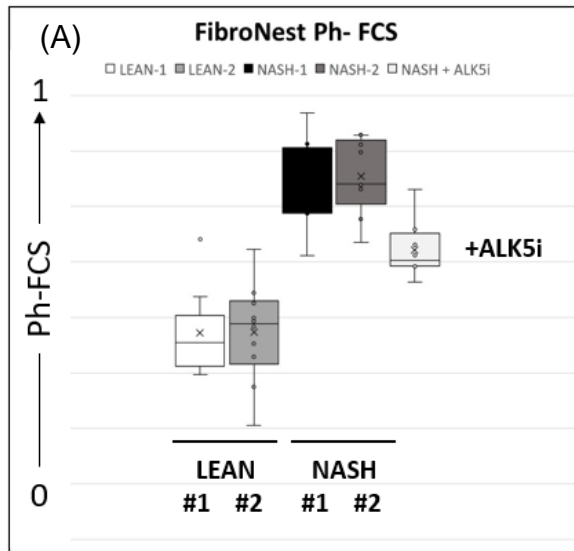
Is FibroNest Validated to quantify NASH Severity and Drug Response?

NASH Spheroids

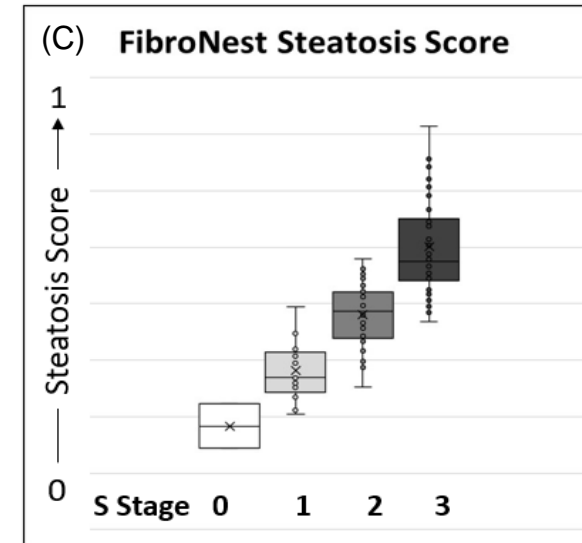
Rodent Fibrosis & NASH

Pediatric NASH

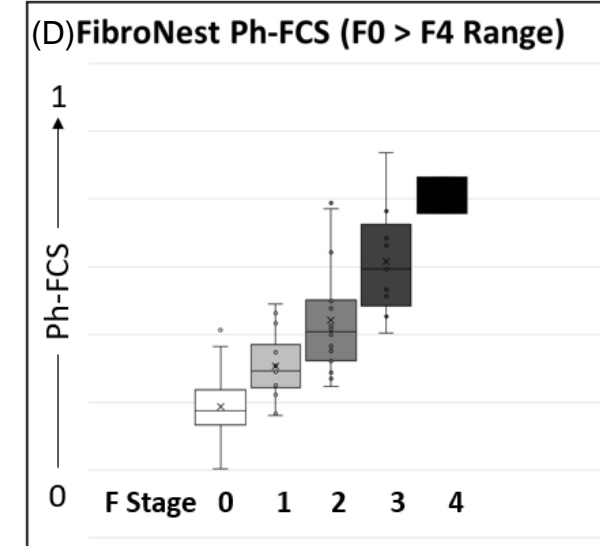
Adult NASH



FibroNest is validated on +20 Animal Models Including several KO models



FibroNest Classifies NASH-1 vs NASH-2 patients based on their Fibrosis Phenotype (E) and Correlates with NASH-CRN stages (F)



FibroNest can calculate Specific scores to better resolve F2<->F3 if and F3<->F4 if needed

“Disease Activity” Quantification (inc. Tissue & Lobular Inflammation, Hep. Ballooning) in Q1 - 2021

(A) Novel phenotypic image analysis of 3D NASH model generate quantitative and continuous scores for the evaluation of fibrosis in vitro. Mathieu M. Petitjean¹, Radina Kostadinova², Li Chen¹, Simon Ströbel², Eva Thoma² (1) PharmaNest, Princeton, NJ, USA (2) InSphero AG, Schlieren, Switzerland (AASLD2020) (B) Automated Steatosis Morphometric Scores Benchmark the Pathology-Based Quantification of Steatosis in Pediatric NASH/NAFLD Populations. Zachary Pitkowski¹, Li Chen², Elena Reynoso¹, Mathieu Petitjean², Cynthia Behling³, Joel Lavine¹ - 1 Pediatric Gastroenterology, Hepatology & Nutrition, Columbia Vagelos College of Physicians and Surgeons, New York, NY 2 - PharmaNest Princeton, NJ - 3 University of California, San Diego, NAFLD Research Center, Division of Gastroenterology. (AASLD 2019) (D) Evaluation of a novel histology-based fibrosis phenotypic composite score and its correlation with NASH-CRN Fibrosis scores in patients with NASH. Li Chen⁽¹⁾, Michael Lung⁽²⁾, Cynthia Behling⁽²⁾, Arun Sanyal⁽³⁾, Mathieu Petitjean⁽¹⁾. 1 - PharmaNest, Princeton, NJ, USA; 2 - University of California, San Diego, NAFLD Research Center, Division of Gastroenterology. 3-Virginia Commonwealth University, Richmond, VA, USA. (EASL2020) (E) Automated Morphometric Fibrosis Phenotyping of NAFLD Biopsies Digital Images Helps Classify NASH-Type 1 Vs NASH-Type 2 in Early Fibrosis Pediatric Patients. Mathieu Petitjean¹, Li Chen¹, Elena Reynoso², Cynthia Behling³, Joel E. Lavine². - 1 PharmaNest Princeton, NJ - 2 Pediatric Gastroenterology, Hepatology & Nutrition, Columbia Vagelos College of Physicians and Surgeons, New York, NY - 3 University of California, San Diego, NAFLD Research Center, Division of Gastroenterology. Poster presentation at AASLD 2019.

FibroNest @ Clinical Studies

Noise and Controls

Inspired From.....

The Journal of Pathology: Clinical Research
 J Pathol Clin Res; April 2019; 5: 91–99
 Published online 29 November 2018 in Wiley Online Library
 (wileyonlinelibrary.com). DOI: 10.1002/cjcr.2.121

PERSPECTIVE

Quality assurance guidance for scoring and reporting for pathologists and laboratories undertaking clinical trial work

Clinical Trial Imaging Endpoint Process Standards Guidance for Industry

Additional copies are available from:
 Office of Communications, Division of Drug Information
 Center for Drug Evaluation and Research
 Food and Drug Administration
 10801 New Hampshire Ave., Silver Spring, MD, 20910-4477
 Phone: 855-545-7734 or 301-796-3400; Fax: 301-414-6133; Email: druginfo@fdhva.gov
 https://www.fda.gov/oc/communications/clinical-trial-imaging-endpoint-process-standards-guidance-for-industry

U.S. Department of Health and Human Services
 Food and Drug Administration
 Center for Drug Evaluation and Research (CDER)
 Center for Biologics Evaluation and Research (CBER)

April 2018
 Clinical Medical

Considerations for Use of Histopathology and Its Associated Methodologies to Support Biomarker Qualification Guidance for Industry

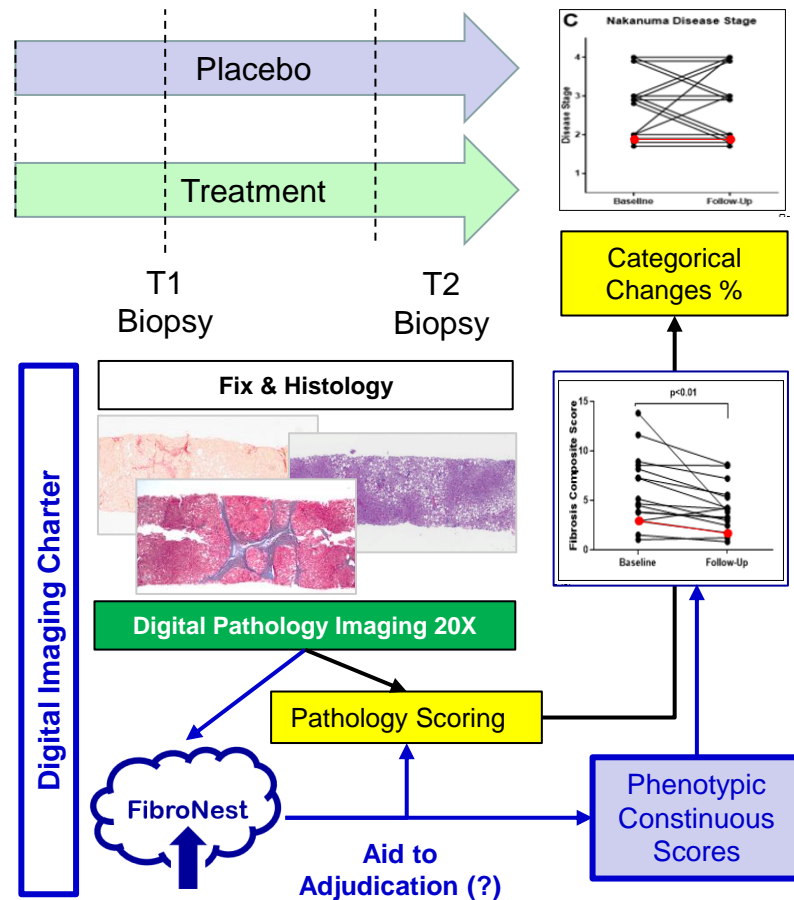
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 Phone: 855-545-7734 or 301-796-3400; Fax: 301-414-6133; Email: druginfo@fdhva.gov
 https://www.fda.gov/oc/communications/considerations-for-use-of-histopathology-and-its-associated-methodologies-to-support-biomarker-qualification-guidance-for-industry

U.S. Department of Health and Human Services
 Food and Drug Administration
 Center for Drug Evaluation and Research (CDER)
 Center for Biologics Evaluation and Research (CBER)

May 2016
 Procedural

FibroNest Digital Pathology Imaging Charter

FibroNest Workflow (same slide)



Images & Data

Secure: Attack Vulnerability Audits Passed

Dual Site Back Up of data “As Generated”

Full Audit Trail

Raw Data (~8000 features per biopsy) stored as long as needed

Analyses images available to clients and their pathologists

Ready for Pathomic Fusion

FibroNest benefits (Today)

Translate Fibrosis and associated features knowledge from Discovery to the clinic, and across organs.

Quantify fibrosis when no quantification system exist

Aid Pathologists in the assessment of “grey zone stages” and reduce the variability of Gold Standard

Resolve subtitle changes in **Fibrosis** and **Disease Activity**

Support the development of novel NIT

Areas of Industry & Regulatory Discussion / Innovation (SIG ?)

NASH Clinical Trial NASH Digital Pathology Endpoint process Standards – Guidance ?

Adequate Digital Liver Biopsy?

Should “Robotic Pathology” participate in the Adjudication process for the Gold Standard?