Digital Pathology Quantification of Cirrhosis Severity Continuum in Human HCV Liver Biopsies and its Correspondence with Laennec and Beijing stages

LOUIS C. PETITJEAN[1], XIAOFEI ZHANG[2], THOMAS D. SCHIANO[3], MATHIEU M. PETITJEAN[1], MARIA ISABEL FIEL[3]

[1] PharmaNest Inc, Princeton, NJ, USA,
[2] Department of Pathology, NYU Long Island School of Medicine, NY,
[3] Icahn School of Medicine at Mount Sinai, New York, NY, USA

EASL CONGRESS 2023
Vienna, Austria
21–24 June

INTRODUCTION

Cirrhosis severity is defined histologically as a continuous process in which the normal anatomical lobules are replaced by architecturally abnormal nodules separated by fibrous tissue of different morphological phenotypes. The Laennec system, and, more recently the Beijing classification, have been used to sub-classify various histological degrees of cirrhosis severity and activity. These methods lack intra-operator reproducibility and have poor detection thresholds

AIM

We report on the development of an automated quantitative Digital Pathology and AI method (FibroNest™) to quantify cirrhosis severity and activity and assess its correspondence with Laennec and Beijing scores.

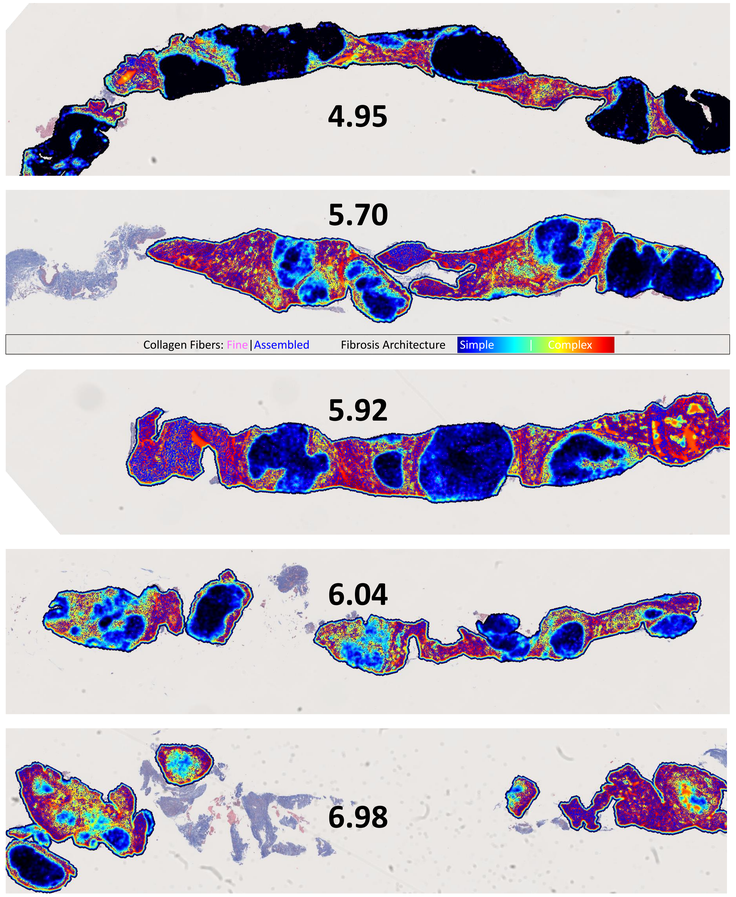
METHOD

- 20 consecutive hepatitis C (HCV) patients undergoing liver transplantation consented to participate in an IRB-approved protocol
- 5 core biopsies were taken from five segments of the liver immediately after explantation.
- Formalin-fixed, paraffin embedded sections of the biopsies were stained with Masson trichrome and scanned at 20X for Digital Pathology.
- This F4/Cirrhosis (HCV F-Stage) cohort (n=100 biopsies) was enriched with a fibrosis severity progression cohort (NASH Fibrosis stages: F0, n=15, F1=20, F2=19, F3=16) described elsewhere [1,2].
- The NASH-CRN (F0 to F4), Laennec system (4A-4C indicating increasing degrees of cirrhosis [3]) and Beijing classification (P-progressive, I-indeterminate, R-regressive [4]) were assessed by an expert pathologist (MIF).

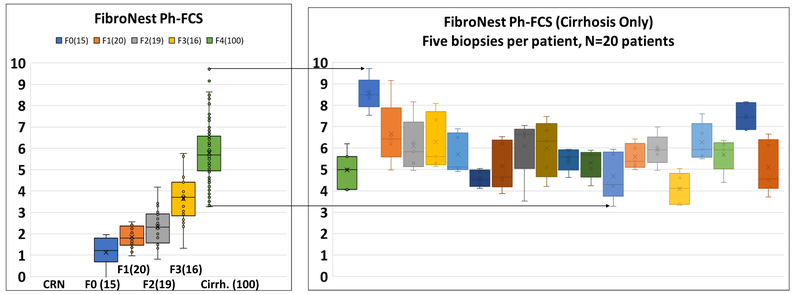
- This HCV cohort (n=100) demonstrated a large variety of severity stages [5]
- Quantitative image analysis was performed to extract single fiber quantitative traits (qFTs, N=335) to describe the collagen, the fiber morphometric and fibrosis architectural phenotypic dimensions.

- Principal components of the qFT dataset were automatically identified to account for variability along (a) the full spectrum of fibrosis severity, (b) the Laennec, and (c) the Beijing stages, and then assembled into normalized:
  - (a) Fibrosis Severity Phenotypic Score (Ph-FCS)
  - (b) a Cirrhosis Severity composite Score (CFS) and
  - (c) a Cirrhosis Activity composite Score (CAS).

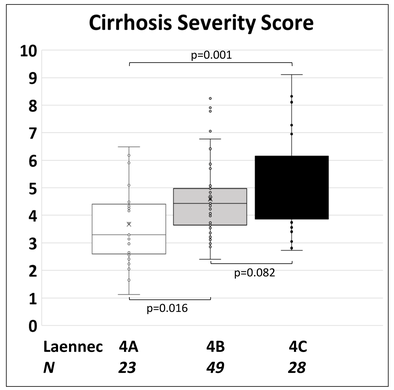
RESULTS

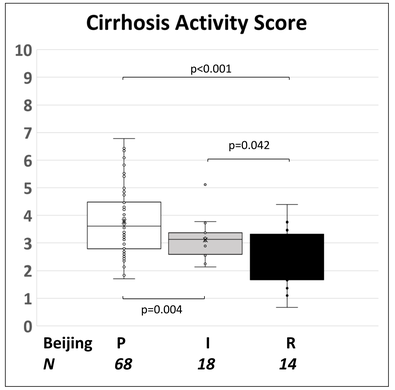


Augmented Digital Pathology images showing the tow of the 335 Single-Fiber analysis and Fibrosis Texture Analysis quantitative traits used to generate the qFT dataset, later exploited by AI to extract the phenotypic traits needed for the buildup of the composite scores. In black, for each image, the Ph-FCS used to quantify for fibrosis severity along the F0 to cirrhosis spectrum



- The Ph-FCS score segregates F4 from F3 biopsies with p-value (<<0.001).
- For each liver explant with 5 biopsies, Ph-FCS Coefficient of Variability (CoV) ranged from 8.4% to 24.1% (mean=16.7%, SE=1.3%)
- SEs ranged from 0.10 to 0.36 (mean=0.24, SE=0.017).





- The AI-enabled CFS and CAS scores classify extreme stages (4A vs 4C, P vs R) with strong statistical significance (p=0.0011 and p=0.0004 respectively) in contrast to earlier studies where the Collagen Proportional Area did not correlate with Laennec and Beijing histological scores [5]).
- The intermediate stages (4A vs 4B; 4B vs 4C; P vs I; I vs R) are classified by with moderate performance (p values =0.016; 0.082; 0.004; 0.042 respectively) but it is not clear if the uncertainty is driven by the computational method of the pathologist's scoring accuracy.
- All the three sub-phenotypic layers (for which specific sub-scores are also created) play complementary roles. For instance, the Architecture-CFS classifies 4A vs 4B groups with a p-value of 0.001 (figure not shown)

CONCLUSIONS

The automated quantification of multiple histological phenotypic traits resolves the complexity of the histological assessment of severity and the activity in the cirrhosis continuum with a performance that benchmarks pathologist assessments.

REFERENCES: [1] **Petitjean, L.** et al. Evaluation of the performance of a novel Digital Pathology method for the continuous quantification of Steatosis, Ballooning and Inflammation in liver biopsies and its correlation with NASH-CRN scores in patients with NASH. International Liver Congress, EASL (2022) - [2] **Chen, L.** et al. Evaluation of a novel histology-based fibrosis phenotypic composite score and its correlation with NASH-CRN Fibrosis scores in patients with NASH. International Liver Congress, EASL (2020) - [3] **Kutami R** et al."The Laennec grading system for assessment of hepatic fibrosis: validation by correlation with wedged hepatic vein pressure and clinical features." features. Hepatology. 2000; 32: 407A [4] **Sun Y et al.** "New classification of liver biopsy assessment for fibrosis in chronic hepatitis B patients before and after treatment."Hepatology. 2017; 65: 1438-1450 10.1002/hep.29009 [5] **Zhang, Xiaofei** et al. "A comparative study of cirrhosis sub-staging using the Laennec system, Beijing classification, and morphometry." Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc vol. 34,12 (2021): 2175-2182.

CONTACT: louis.Petitjean@pharmanest.com