AASLD The Liver Meeting® Nov. 4–8, 2022

Digital Pathology Quantification of Intra("geographic")-Liver Variation in Human HCV F4 | Cirrhosis Liver Biopsies

Louis Petitjean[1], Xiaofei Zhang[2], Maria Isabel Fiel[3], Thomas D. Schiano[3], Arun J. Sanyal[4], Mathieu M. Petitjean[1]

[1]PharmaNest, Princeton, NJ, USA, [2]University of Wisconsin at Madison, WI, USA, [3]The Mount Sinai Medical Center, NY, USA, [4]Virginia Commonwealth University, VA, USA

BACKGROUND and AIMS

The degree of variability between biopsies taken from the same liver is not well established. Herein, we use a novel digital pathology quantitative image analysis and artificial intelligence platform, FibroNest™, to generate continuous fibrosis severity scores to assess intra("geographic")-liver variability.

METHOD

STUDY DESIGN

- Twenty (20) hepatitis C (HCV) patients with 5 needle liver biopsies each, taken during liver transplantation.
- Five (5) core biopsies were taken from segments 8, 6, 4, 2, and 1 of the liver immediately after explantation using 14 gauge (2mm width) needles used .
- 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].

LIVER TISSUE HISTOLOGY

- FFPE sections (~4 microns) of adequate liver biopsies were stained with Masson Trichrome for collagen

DIGITAL PATHOLOGY AND ARTIFICIAL INTELLIGENCE

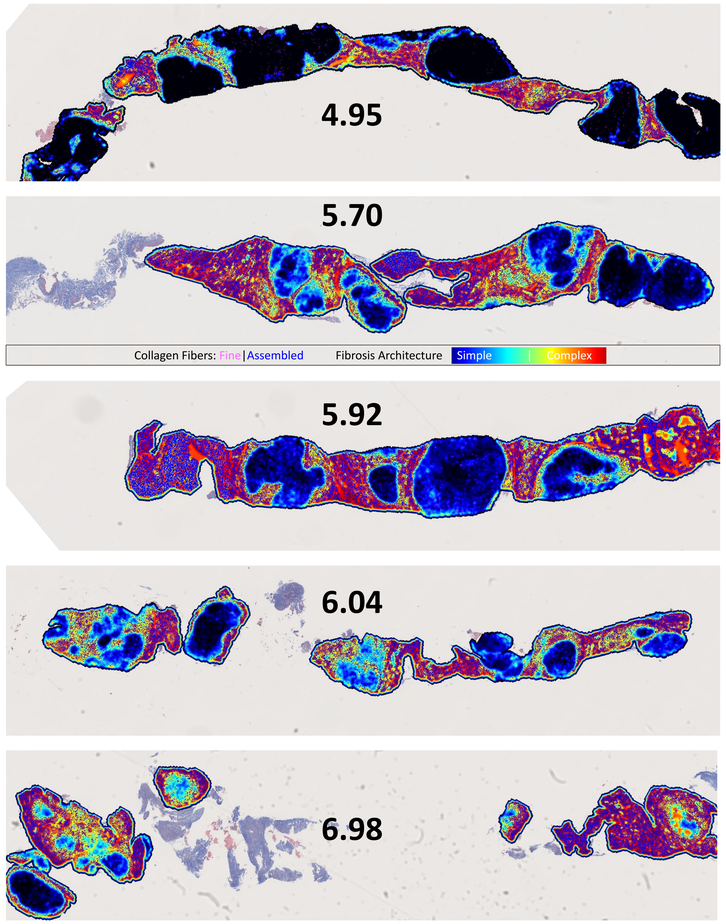
- The same slides prepared for and reviewed by pathologists were digitized at 20X (0.50 micron/pixel) on a Aperio AT WSI system.
- The Masson Trichrome digital images were read using FibroNest, a single-fiber, high-content quantitative Digital Pathology image analysis and AI automated, full-tissue method.
- Quantitative image analysis was performed to extract single-fiber quantitative traits (qFTs, N=315).
- A previously validated selection of principal qFTs was normalized and combined into a fibrosis severity score (Ph-FCS, 1 to 10).

STATISTICAL ANALYSIS

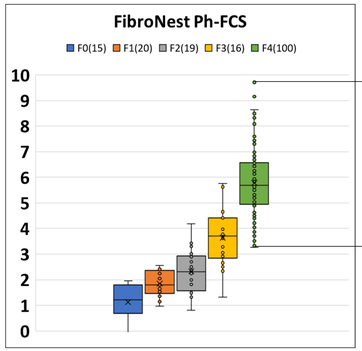
- For each patient, the coefficient of variation (CoV) and standard error (SE) of the Ph-FCS were calculated to evaluate the intra("geographic")-liver variability
- qFTs with high intra("geographic")-liver CoVs were identified and reported as an aid for pathologist practice.

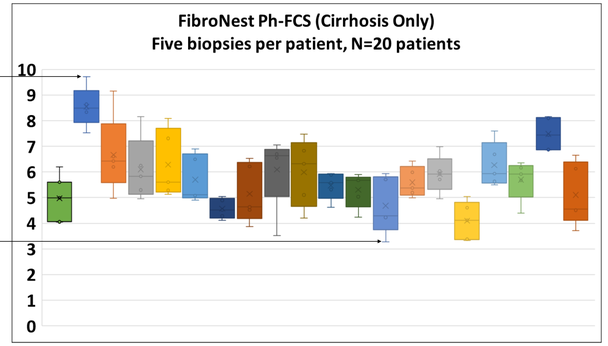
RESULTS

IMAGING VS DIGITAL PATHOLOGY PERFORMANCE (Ph-FCS , Same Liver – 5 Biopsies)

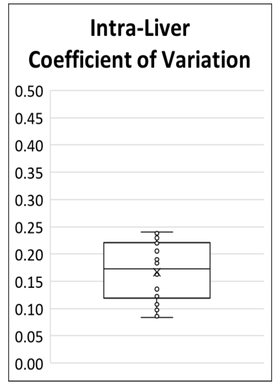


STATISTICAL ANALYSIS





- The Ph-FCS score **segregates F4 from F3** biopsies with strong p-value (p-val=1.57e-05).
- For each liver explant with 5 biopsies, Ph-FCS **CoVs** 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).
- In the F4 Range, the SE of the FibroNest scores was 0.073
- **24 qFTs drive the intra("geographic")-liver variability**:
  - The median of fiber perimeter
  - The skewness (distortion of the distribution) of length, filled to area ratio, and density,
  - The standard deviation of fiber width,
  - The kurtosis (distortion of the distribution) of the number of branches in a fiber
  - Several architectural traits, all of which can be visualized in augmented pathology images.



Conclusion

- FibroNest was able to quantify **the severity of fibrosis** from *moderate* NASH fibrosis levels to *complex phenotypes* within the HCV F4/ Cirrhosis spectrum.
- Ph-FCS scores in the HCV F4 cohort **is as wide as between NASH F0-F3**, consistent with histological scores that describe the substages of cirrhosis.
- **The average intra("geographic")-liver Ph-FCS variability was 16.6**±1.3. This is significantly *smaller* than previously reported CoVs of 47.3±4.5%, using collagen proportionate area (CPA) due to the comprehensive scope of measurements that form the Ph-FCS.
- Traits that drove intra("geographic")-liver variability are identified by Digital Pathology: augmented pathology images may assist pathologists in the more robust assignment of fibrosis stages in the cirrhosis spectrum.

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)

Contact and presenting author: louis.petitjean@pharmanest.com