Zhang

Traits that drove intra("geographic") variability were normalized and FibroNest was able to quantify A previously validated selection of principal quantitative traits (qFTs) to generate continuous fibrosis severity scores to assess intra("geographic")-liver variability.

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 evaluate intra("geographic")-liver variability.

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.

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

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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.

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].

RESULTS

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%) and SEs ranged from 0.10 to 0.36 (mean=0.24, SE=0.017).

The F4 Range, the SE of the FibroNest scores was 0.073

Four 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.

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).

LIVER TISSUE HISTOLOGY

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

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

CoV

FibroNest Ph-FCS

Statistical Analysis

• 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 FPC 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


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