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DIGITAL EXPERIENCE

Evaluation of the multivendor performance of a novel histology-based fibrosis phenotypic composite score and its correlation with NASH-CRN Fibrosis scores in patients with NASH

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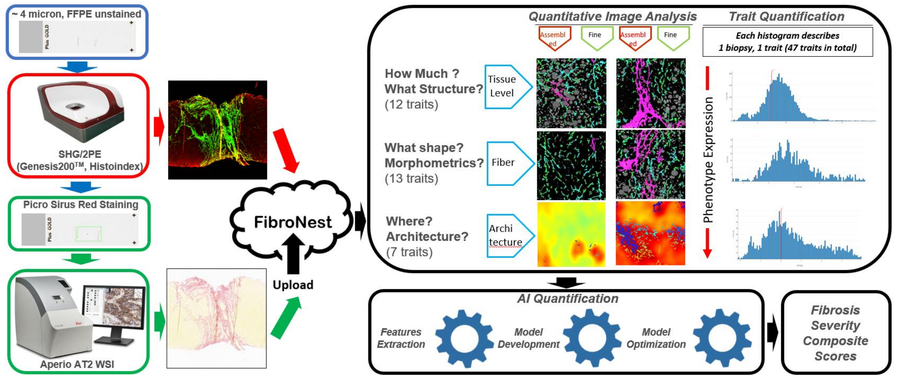
BACKGROUND and AIMS

We have previously shown that the Phenotypic Fibrosis Composite Score (Ph-FCS) calculated by the FibroNest image analysis platform from second harmonic generation (SHG) images correlates with the NASH-CRN fibrosis scores. In this study, the same sections imaged non-destructively by SHG have been stained, digitized and then quantified with FibroNest. We compare performance of the Ph-FCS obtained from these two imaging methods.

METHOD

TISSUE PREPARATION, INSTRUMENTATION, AND WORKFLOW

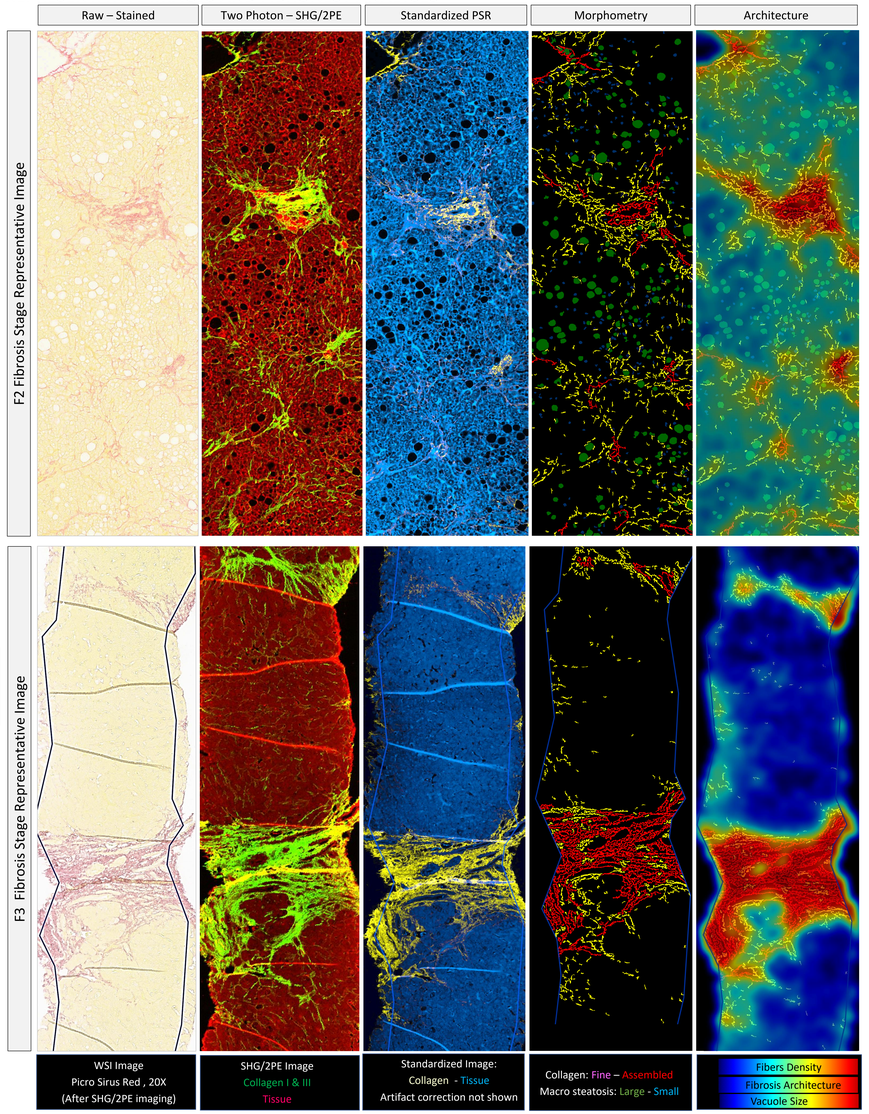


Description	Histological Assessment	Total N= 77
Patients with histological diagnosis of NASH and fibrosis stages 0 to 4	Histologic assessment and Fibrosis severity stage was assessed by pathologists according to NASH CRN	F0 (N= 21), F1 (N=17), F2 (N=20), F3 (N=15), F4 (N=4)

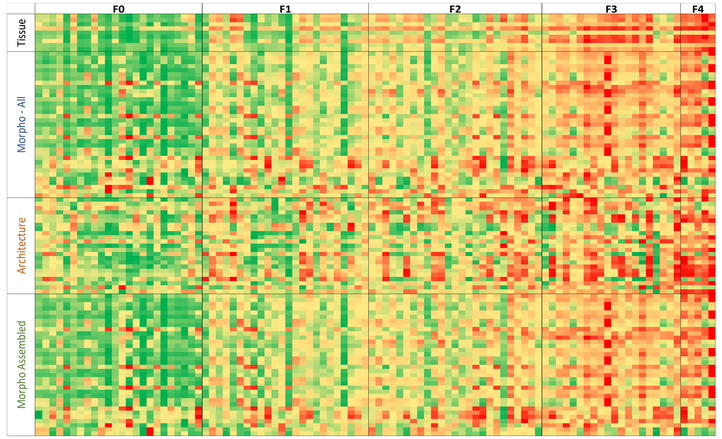
- FFPE sections (~4 microns) of patient liver biopsies (unguided) are mounted on (no coverslip), deparaffinized and imaged ("SHG Image") on the Genesis200™ SHG/2PE microscope from Histoindex, at 20X (0.37 micron per pixel). This imaging method is non-destructive.
- The same slides are subsequently stained for collagen using picrosirius red, and imaged at 20X (0.50 micron per pixel) on the Aperio AT2 Digital Pathology system ("WSI Image").
- Both sets of Digital Images are analyzed and quantified using the FibroNest method:
  - Using Quantitative Image Analysis (FibroNest™) the fibrosis phenotype is described for its collagen content and structure (12 traits), the morphometric traits of the collagen fibers (13 traits), and fibrosis architecture traits (7). In each image, each morphometric and texture trait is represented by a histogram distribution (e.g. Fiber Skeleton Length)
  - The histogram for each trait is described by up to seven quantitative fibrosis parameters (qFPs, 315 in total) to account for mean, variance, distortion and progression.
  - To detect phenotypic differences between the F sub-groups, principal qFPs are automatically detected if their group mean value difference is statistically (P<0.05, T-Test) greater than 20%.
  - Principal qFPS are used individually and collectively to describe the differences in phenotypes between groups. They are combined into a normalized Phenotypic Composite Fibrosis Score, a continuous quantifier of the fibrosis phenotype.
  - The composite fibrosis scores are compared to the Pathologist assessment.

RESULTS

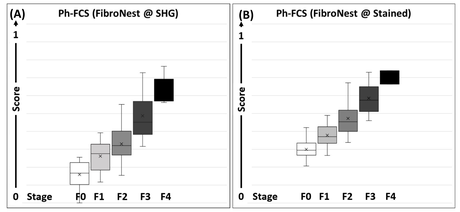
REPRESENTATIVE IMAGES AND FIBRONEST ANALYSES

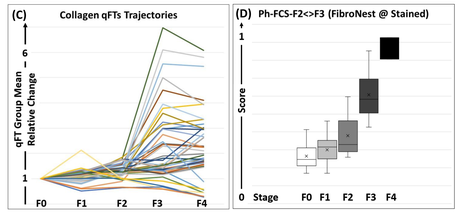


FIBROSIS PHENOTYPIC HEAT MAPS AND COMPOSITE SCORES



For each patient (column) the Fibrosis Phenotypic maps (above) visualizes the relative severity (green to red) of the quantitative fibrosis traits (qFTs) as quantified from the image, and automatically selected to account for variability between groups. Each raw represents a quantifiable trait. The normalized quantitative traits values are combined to generate a phenotypic Fibrosis composite score for each patient. The phenotypic map and augmented images can be used to assist pathologists for staging and reduce their Categorical Staging Incertitude.





Using FibroNest, there is no significant difference between the performance of the Ph-CSF obtained from SHG (Fig. A) and conventional stained slides (Fig. B). In both cases the scores correlate with fibrosis stages ($p<0.001$) and differentiates between fibrosis F1 to F4 stages.

The performance of the correlation is slightly superior at low F stage values, due to the superior performance of PSR staining and the Aperio scanner.

Several traits related to the morphometric and architectural phenotypes are specifically characteristics of the F2->F3 transition (Fig. C). The are used generate a sPh-FCS-F2<>F3 score (Fig. D) which exhibits a remarkably high detection threshold and classifies patients below F2 or above F3 (cut-off 0.5) with a sensitivity [specificity] or 91% [92%].

Conclusion

The phenotype of Fibrosis in NASH does not depend on the staining and imaging method and is well quantified by FibroNest. The FibroNest composite scores correlate well with NASH-CRN stages and can be tailored to answer specific phenotypic questions in NASH.

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