Automated Fibrosis Phenotyping of NASH non-tumorous lesions digital images helps classify HCC and non-HCC NASH patients who underwent liver transplantation

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BACKGROUND

The incidence of Hepatocellular carcinoma (HCC) arising from NAFLD has been increasing worldwide. Advanced liver fibrosis, especially liver cirrhosis, is a risk factor for HCC development in NASH/NAFLD. However, it is not known whether there is a distinct fibrosis histological pattern (or phenotype) that is related to development of HCC in patients with liver cirrhosis. In this study, we evaluated the performance of analysis of fibrosis histological phenotypic features to identify traits that differentiate HCC and non-HCC primary liver malignancy in NASH liver cirrhosis patients who underwent liver transplantation.

METHOD

Tissue Preparation, Instrumentation, and Workflow

- FFPE sections (3-4 microns) of patient liver non-tumorous tissue were deparaffinised, stained with Picosirius Red (no Hematoxylin bath) for Collagen and digitized at 40x (Aperio AT2)
- Using FibreMark™ 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 / texture traits (7). In each image, each morphometric and texture trait is represented by a histogram distribution (e.g. Fiber Skeleton Length histogram).
- 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.
- Principal qFPs are automatically detected if their group distribution (H vs N=H) significantly different (p<0.001, T- TEST), and normalized mean group value ratio greater than 1.2
- Principal qFPs are used individually and collectively to describe the differences in phenotypes between the two groups. They are combined into a normalized Phenotypic Composite Fibrosis Score (Ph-CFS), a continuous quantifier of the HCC fibrosis phenotype.
- Cut-off values are selected to optimize the performance of a test to classify the patients (HCC or non-HCC) based on their Ph-CFS. The performance of the test is evaluated using a confusion matrix and its related sensitivity and specificity values.

RESULTS

Representative Images and FibroNest Analyses

Phenotypic Quantification

The Phenotypic Composite score is assembed from Principal qFPs and helps classify the HCC and non-HCC Patients

Conclusion

Fibrosis histological phenotypic quantification helps to distinguish between HCC and non-HCC in NASH liver cirrhosis patients who underwent liver transplant. These data show that phenotypic analysis of collagen with FibreMark™ is an effective and automated method to classify HCC from non-HCC in histopathology imaging studies. This can be of clinical importance for appropriate guidance of treatment strategy.