qVessel, a Machine Learning-based Algorithm, Accurately Stages Liver Biopsies with Chronic Liver Disease, Based on Automated Vessel Counting

Zheng-xin Li[1],Tingting Zhu[1],Zhao zhi-min[1],Qiang Yang[2],Xiao Teng[3],Ya-yun Ren[2],Dean Tai[3],Ian Wanless[4],Cheng-hai Liu[1],

1. Institute of Liver Diseases, Shuguang Hospital,Shanghai University of Traditional Chinese Medicine
2. Hangzhou Choutu Technology Co., Ltd, China
3. Histoindex Pte Ltd (HistoIndex), Singapore
4. Department of Pathology, Dalhousie University, Halifax, Nova Scotia, Canada

AASLD The Liver Meeting® Nov. 12-15, 2021
DIGITAL EXPERIENCE

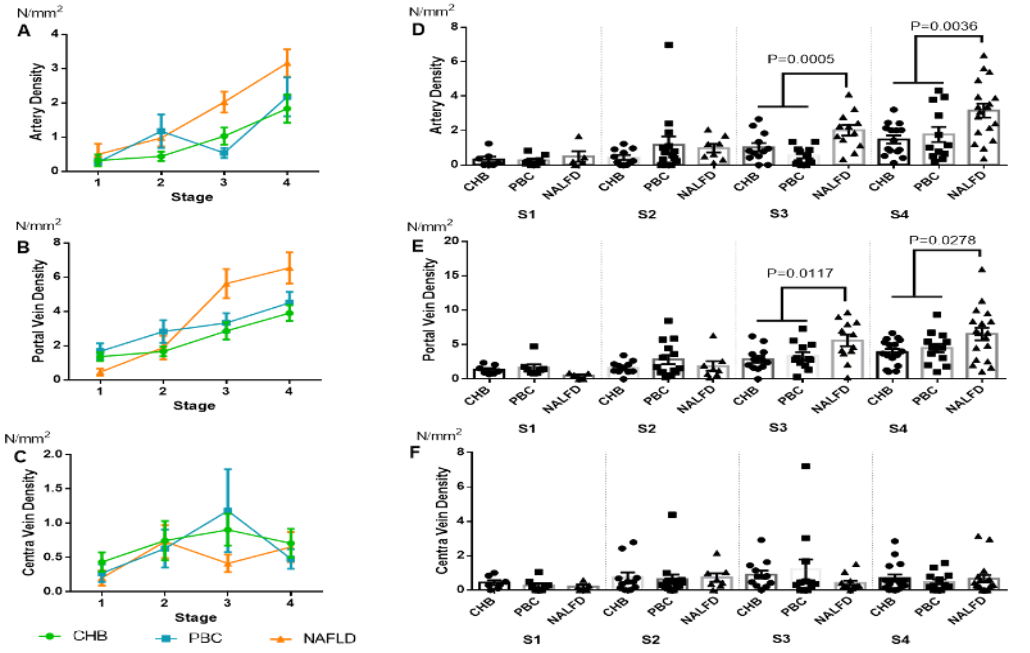
HISTOINDEX® New Standard | New Life

A major histologic feature of cirrhosis is the loss of hepatocytes that causes a collapse of tissue and an increased number of portal tract structures per unit area (i.e., density). We have previously shown that artery and duct density correlates with histologic stage by METAVIR, Ishak, or Laennec systems[1,2]. When quantifying fibrosis stage, these standard systems suffer from severe inter-observer variation that can be ameliorated with quantitative image analysis, as performed with our earlier product, qFibrosis. qFibrosis is a machine learning-based algorithm that quantifies collagen density using stain-free Second Harmonic Generation/Two-photon Excitation Fluorescence (SHG-TPEF) microscopy[3].

In the present study, we evaluated qVessel, a new machine learning-based algorithm using SHG-TPEF, to quantify the density of vessels in liver biopsies with a chronic disease of varied etiology and stage.

Needle biopsies from patients with Chronic Hepatitis B (CHB, n=46), Primary Biliary Cholangitis (PBC, n=49), and Non-alcoholic Fatty Liver Disease (NAFLD, n=43) were collected from Shuguang Hospital and Beijing Friendship Hospital.

The METAVIR system was used to assess stages on trichrome-stained tissues. The SHG-TPEF images were generated from unstained slides of the same biopsies. Vessels were counted using qVessel (previously trained on manually labeled vessels on stained slides (CD34/aSMA/CK19) and evaluated by a decision tree algorithm). The qVessel-detected counts were compared using one-way ANOVA.



The figure shows vascular density in three chronic liver diseases vs METAVIR stage. A: Arteries. B: Portal veins. C: Central veins. D-F: Comparisons of vascular density when divided into etiologic groups.

The number of arteries increased with advancing METAVIR stage (CHB P=0.002, PBC P=0.009, NAFLD P=0.000). A similar increase was observed in the number of portal veins (CHB P=0.003, PBC P=0.028, NALFD P=0.000). The number of central veins did not change in stage for any of the etiologic groups ($P > 0.05$). The numbers of arteries and portal veins in NAFLD was higher than with other etiologies ($P < 0.05$).

Using the qVessel algorithm, we observed that both the number of arteries and portal veins correlated with METAVIR stages in all three etiologies. Our results show that vessel density (portal veins and arteries) can be the basis of a new staging system, with the major advantage of objectivity gained by a machine-learning-based algorithm.

The qVessel platform may be useful for evaluation of anti-fibrosis or pro-regeneration therapies.

We thank the National Major Science and Technology Special Project of China for their financial support.

1) Wanless IR, et al.. Importance of tissue collapse and unmasking of reticulin on the assessment of fibrosis in acute and chronic liver disease. Hepatology 2016;63:214A.
2) Sun Y, et al. Artery density in human liver: A valuable measure for staging chronic liver disease. J Hepatol (suppl 1), 2019.
3) Feng Liu,et al. "qFIBS: A Novel Automated Technique for Quantitative Evaluation of Fibrosis, Inflammation, Ballooning, and Steatosis in Patients with Non-Alcoholic Steatohepatitis." Hepatology 2020

Q.Y, X.T, Y.R and D.T are employees of HistoIndex or its subsidiary, X.T and Y.R hold stock options and D.T owns stock in HistoIndex.

Cheng-hai Liu, chenghai.liu@outlook.com