Digital Pathology Quantification of Cirrhosis Severity Continuum in Human HCV Liver Biopsies and its Correspondence with Laennec and Beijing stages

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INTRODUCTION

Cirrhosis severity is defined histologically as a continuous process in which the normal anatomical lobules are replaced by architecturally abnormal nodules separated by fibrous tissue of different morphological phenotypes. The Laennec system, and, more recently the Beijing classification, have been used to subclassify various histological degrees of cirrhosis severity and activity. These methods lack intra-operator reproducibility and have poor detection thresholds.

AIM

We report on the development of an automated quantitative Digital Pathology and AI method (FibroNest™) to quantify cirrhosis severity and activity and assess its correspondence with Laennec and Beijing scores.

METHOD

• 20 consecutive hepatitis C (HCV) patients undergoing liver transplantation consented to participate in an IRB-approved protocol
• 5 core biopsies were taken from five segments of the liver immediately after explantation.
• Formalin-fixed, paraffin embedded sections of the biopsies were stained with Masson trichrome and scanned at 20X for Digital Pathology.
• 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].
• The NASH-CRN (F0 to F4), Laennec system (4A-4C indicating increasing degrees of cirrhosis [3]) and Beijing classification (P-active, I-indeterminate, R-regressive [4]) were assessed by an expert pathologist (MiF).
• This HCV cohort (n=100) demonstrated a large variety of severity stages [5].
• Quantitative image analysis was performed to extract single fiber quantitative traits (qFTs, N=335) to describe the collagen, the fiber morphometric and fibrosis architectural phenotypic dimensions.
• Principal components of the qFT dataset were automatically identified to account for variability along (a) the full spectrum of fibrosis severity, (b) the Laennec, and (c) the Beijing stages, and then assembled into normalized:
  - (a) Fibrosis Severity Phenotypic Score (Ph-FCS)
  - (b) a Cirrhosis Severity composite Score (CFS) and
  - (c) a Cirrhosis Activity composite Score (CAS).

RESULTS

CONCLUSIONS

The automated quantification of multiple histological phenotypic traits resolves the complexity of the histological assessment of severity and the activity in the cirrhosis continuum with a performance that benchmarks pathologist assessments.