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NOVEL ARTIFICIAL INTELLIGENCE-ASSISTED DIGITAL PATHOLOGY QUANTITATIVE IMAGE ANALYSIS PREDICTS THE OCCURRENCE OF LIVER-RELATED CLINICAL EVENTS IN THE MULTICENTRIC, EUROPEAN, HOTSURFR (HEPATIC OUTCOMES AND SURVIVAL FATTY LIVER REGISTRY) STUDY

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INTRODUCTION

Artificial intelligence-assisted digital pathology provides an automated, operator independent, sensitive and quantitative assessment of histological changes with the ability to identify patterns of fibrosis progression or regression. However, its value for predicting clinical events is unknown. We have previously shown that quantitative traits in collagen fiber parameters can be used to build a fibrosis score (Ph-FCS, Digital Pathology Fibrosis Biomarker) that is correlated with the semiquantitative histological NASH CRN stages.

STUDY AIM

To determine if quantitative fibrosis scores from baseline liver biopsies are correlated with incident liver-related events (LRE) in a large, multicentric, European cohort of NAFLD patients with long term follow-up.

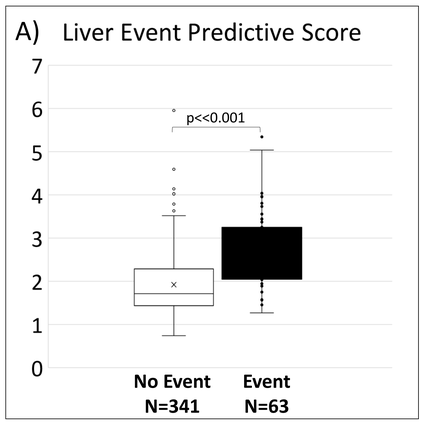
PATIENTS AND METHODS

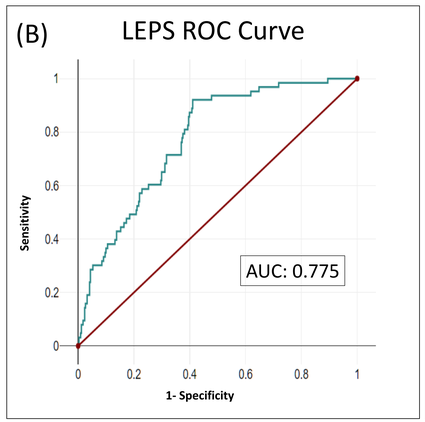
- 404 patients (pts) from 6 European centers with liver biopsy performed before 2011 for suspected NAFLD and clinical follow-up were retrospectively analyzed.
- Liver Related Events (LRE) were defined as occurrence of cirrhosis, cirrhosis decompensation events (occurrence of ascites, variceal bleeding, hepatic encephalopathy, jaundice) or hepatocellular carcinoma. The occurrence of the first LRE was analyzed.
- Digital Pathology images were acquired (40X) from retrospective glass slides of formalin-fixed, paraffin-embedded biopsies, stained with collagen stains (Masson Trichrome (n=119) or Picro Sirius Red (n=284)).
- Biopsies were read centrally by an expert pathologist (PB) and staged using the NASH CRN classification.
- Quantitative high resolution image analysis was performed to extract 315 single-fiber quantitative traits (qFTs) to assess fibrosis composition, morphometric and architectural histological phenotypes.
- The qFTs that exhibited a significant (>50%) mean change between patients with or without events were identified, normalized and combined in a Liver Event Predictive Score (LEPS).
- A quantitative fibrosis severity score, Ph-FCS, was previously optimized to model the F0-F4 fibrosis progression and this selection of the same 315 qFTs was also assessed.

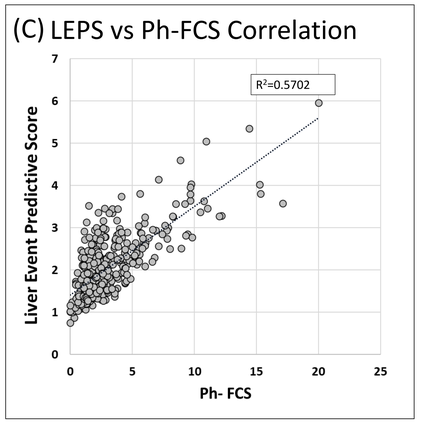
RESULTS

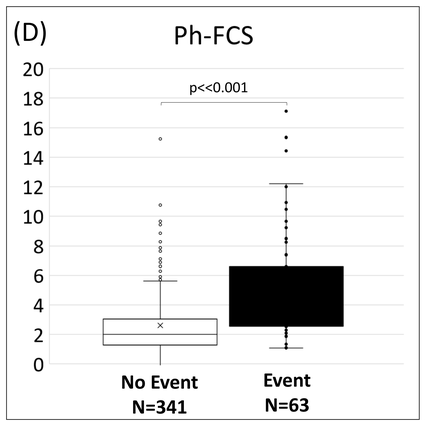
Patient Characteristics

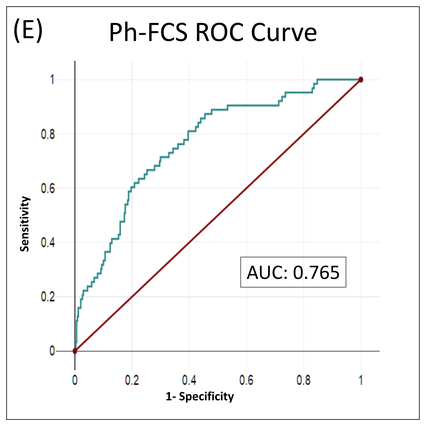
Males, n (%)	234 (58%)
Age, years, mean	53,7
BMI, kg/m², mean	31.2
T2D, n (%)	150 (37%)
HTA, n (%)	242 (60%)
Smokers, n (%)	73 (25%)
Median follow-up, yrs	11.4
At least one LRE, n (%)	63 (16%)
Fibrosis stages	%
Stage 0	53
Stage 1	19
Stage 2	8
Stage 3	13
Stage 4	7
Diagnosis, %	%
Cirrhosis	7
NASH+ fibrosis stage 2/3	16
NASH + fibrosis stage 0/1	9,1
NAFL + fibrosis stage 0/1	51
NAFL + fibrosis stage 2/3	4,6
Normal liver	11

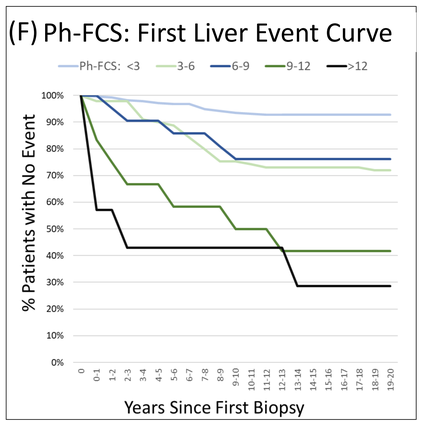












- The LEPS Score was developed by training FibroNest™'s Digital Pathology ML engine based on Liver Related outcomes. Its performance as a diagnostic test to predict long term Liver Events is moderate with an AUROC=0.775
- The FibroNest Digital Pathology Fibrosis Biomarker (Ph-FCS) developed to measure the histological phenotype of fibrosis severity can also be used as diagnostic test to predict long term Liver Events with an AUROC=0.765
- We have reported elsewhere that Ph-FCS can be used as a diagnostic test to classify Early Fibrosis (=<NASH CRN F2) from Advanced Fibrosis (>=NASH CRN F3) with an AUROC=0.926

CONCLUSION

Quantitative image analysis by digital pathology performed on stained liver slides using FibroNest™ provides continuous scores that identify NAFLD patients at risk of incident hepatic clinical outcomes.

Further validation on additional cases is ongoing. Quantitative image analysis may provide automated, continuous and sensitive histological biomarkers for therapeutic trials.

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