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 fibrosis scores that are correlated with the semiquantitative histological NASH CRN stages

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

- 304 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 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=185)).
- 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, ranging from 1 to 10, previously optimized to model the F0-F4 fibrosis progression, and derived from a selection of the same 315 qFTs was also assessed.

CONCLUSION

- Quantitative image analysis by digital pathology performed on stained liver slides 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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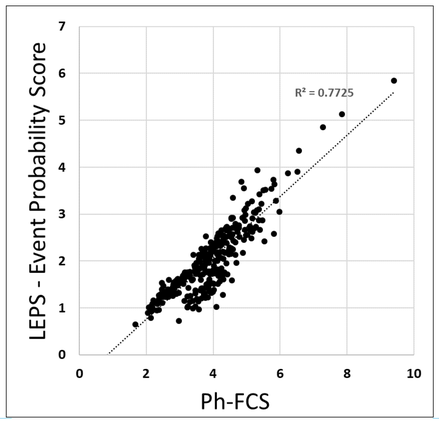
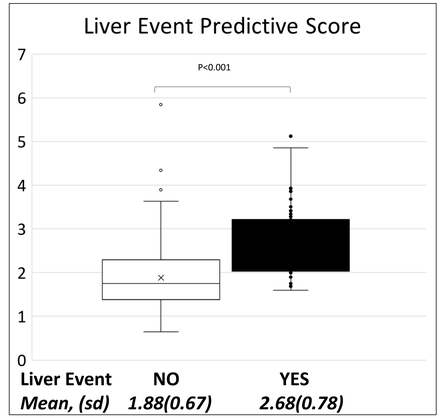
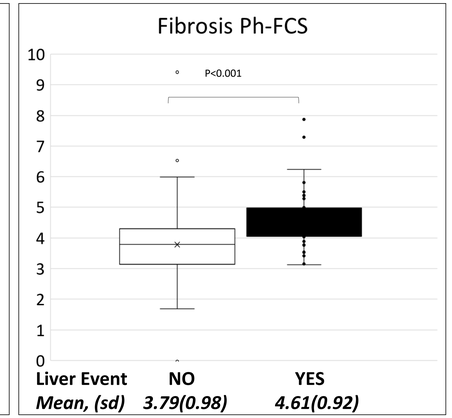
Patient Characteristics	
Males, n (%)	130 (42.8%)
Age, yrs, mean (sd)	55.2 (12.6)
BMI, kg/m², mean (sd)	30.5 (5.16)
T2D, n (%)	125 (41.1%)
HTA, n (%)	190 (62.5%)
Smokers, n (%)	73 (25%)
Median follow-up, yrs	11.4
At least one LRE, n (%)	52 (17%)
Fibrosis stages	%
Stage 0	53,4
Stage 1	17,4
Stage 2	7,4
Stage 3	13,4
Stage 4	8,3
Diagnosis, %	
Cirrhosis	8,3
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



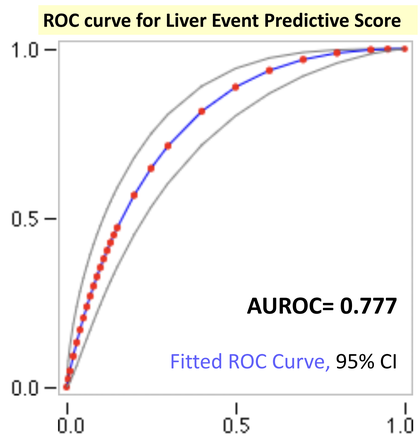
RESULTS

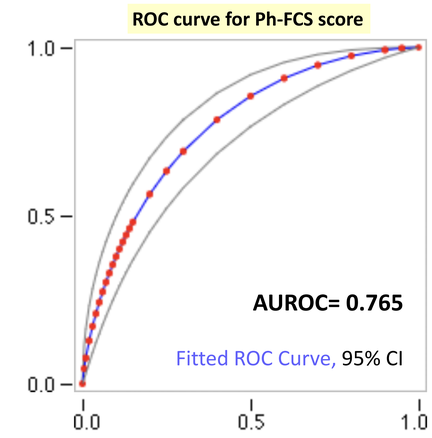




LEPS Prognostic Performance		
Cut off	Sensitivity	Specificity
2.90	67%	72%

Ph-FCS LRE Prognostic Performance		
Cut off	Sensitivity	Specificity
4	79%	62%





There was a strong correlation between LEPS and Ph-FCS (r=0.77, p<0.001), confirming that the fibrosis severity score is a major predictor of clinical events.

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