PRELIMINARY STUDY TO IDENTIFY THE SEVERITY OF HEPATIC FIBROSIS IN PATIENTS WITH NON-ALCOHOLIC STEATOHEPATITIS (NASH) USING IBIOPSY®

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Background

According to the World Health Organization (WHO), Non-Alcoholic Fatty Liver Disease (NAFLD) is a pandemic affecting 25% of the global population [1]. For 20% of patients, NAFLD leads to a more severe disease, Non-Alcoholic Steatohepatitis (NASH). Within the high-risk population of NASH patients, disease evolution can lead to cirrhosis and liver cancer. NASH prognosis mostly depends on the hepatic fibrosis grade.

Hepatic biopsy is a method used to measure hepatic fibrosis severity. However, due to its invasiveness, and sampling errors related to small sample size as well as spatial variation in degree of fibrosis, hepatic biopsy is not used as first indication for diagnostic purposes. In routine clinical practice, the assessment of the absence of advanced fibrosis of the liver is done by non-invasive tests such as blood tests and hepatic elastography. The biopsy is however essential for the diagnosis of advanced NASH. In its early stages, the disease remains reversible by a change in eating habits and lifestyle.

The objective of this study was to quantify the ability of iBiopsy®'s algorithms to discriminate between early and advanced fibrosis grade in NASH patients using clinically available tests and images.

Approach

This preliminary study tests the feasibility of our iBiopsy Liver® platform to accurately and non-invasively distinguish patients with early fibrosis from patients with advanced fibrosis at risk of progressing to cirrhosis and liver cancer. In this retrospective study, features on the images were extracted using a CNN-type Deep Learning architecture, enriched with image processing and clinical measurements before applying a binary classifier.

References

[1] Cotter Thomas G., Rinella Mary, Gastroenterology, Volume 158, Issue 7, 2020, Pages 1851-1864

[2] Krizhevsky Alex, Ilya Sutskever, and Geoffrey E. Hinton. NIPS (2012)

[3] Long Jonathan, Evan Shelhamer, and Trevor Darrell. ICVPR (2015)

Materials and Methods

Sixty-three patients have been included on this study. MR Elastography, MRI (PDFF, T2*) was acquired at Baseline, week 12 and week 24 alongside to Fibroscan® and blood markers (Alkaline Phosphatase, Alanine Aminotransferase, Aspartate Aminotransferase, Bilirubin (mg/dL), Gamma Glutamyl Transferase and Platelets). Patients get a biopsy to measure NASH CRN score (F0-F4). After organs segmentations (liver and spleen), morphological features were extracted.

A proprietary Deep Learning method (iBiopsy® DL) using a similar architecture as [2, 3] is employed to generate fibrosis score map.

Patients were affiliated to dichotomic classes: 1st group -NASH CRN score ≤ F2; 2nd group- NASH CRN score ≥ F3. The train/test split has been performed at patient level by prioritizing the training set.

A random forest algorithm was trained and Area Under Receiver Operating Characteristic (AUROC) used to compare clinical strategies in order to discriminate between early and advanced fibrosis grade in NASH patients.
Sensitivity (True Positive rate, TPR), Specificity (True Negative rate, TNR), positive predictive value (PPV), negative predictive value (NPV), false positive rate (FPR), false negative rate (FDR), false discovery rate (FDR) were also computed.

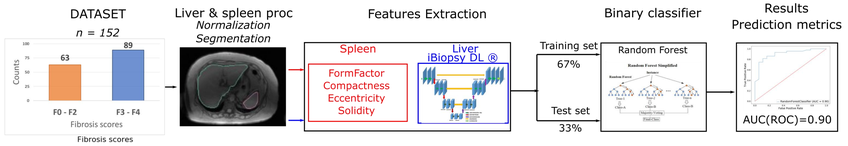

Fig.1: Pipeline of processing

Four scenarios were considered:

A: conventional Fibroscan® and Blood;

B: conventional Fibroscan® and Blood; + basic MRI features;

C: conventional Fibroscan® and Blood; + basic MRI features; + iBiopsy DL without Fibroscan®;

D: conventional Fibroscan® and Blood; + basic MRI features; + iBiopsy DL with Fibroscan®;

Results

The dataset has 63 series in group 1 and 89 in group 2. The training subset has a repartition of 45/46 whereas the test subset has 17/44 for group1/group2 respectively.

On the Fig1, the ROC curves for the 4 clinical set up and Table1 provides insights regarding the performance for each situation. Adding MRI features increase the performance. By using all information available (scenario D: Fibroscan® + MRE + MRI + Blood) the best performance is achieved in terms of both precision, sensibility and accuracy.

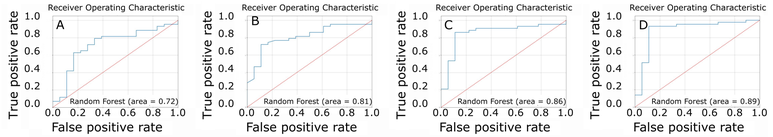

Fig.2: Receiver Operating Characteristic for the 4 scenarios considered.

	TPR	TNR	PPV	NPV	FPR	FNR	FDR	AUROC
A	0.63	0.83	0.90	0.48	0.17	0.37	0.10	**0.72**
B	0.72	0.89	0.94	0.57	0.11	0.28	0.06	**0.81**
C	0.86	0.89	0.95	0.73	0.11	0.14	0.05	**0.86**
D	0.93	0.89	0.95	0.84	0.11	0.07	0.05	**0.90**

Table. 1: Performance of the classifier for the 4 scenarios considered.

Conclusions

Our preliminary results demonstrate the iBiopsy® non-invasive fibrosis biomarker for NASH could allow for the discrimination between early and advanced fibrosis. Initial results are very encouraging, yet an independent validation study should be conducted to assess the generalization power of our model.