

Automated analysis of biopsy samples enables rapid and reproducible quantification of NASH disease activity

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Deep-learning approaches to pattern recognition in liver biopsy samples have moved one step closer to clinical application, with a new study reporting a good correlation between an automated image analysis system and an expert reviewer for the identification of key markers of disease activity in a pre-clinical model of non-alcoholic steatohepatitis (NASH). The study reported today at The International Liver Congress 2018 in Paris, France, found that deep-learning algorithms applied using open-source pathology software (QuPath) could accurately identify cell histology patterns consistent with lobular inflammation and hepatocellular ballooning—markers of disease activity that are essential to establish the diagnosis and severity of NASH.

Non-alcoholic steatohepatitis is the progressive form of non-alcoholic fatty [liver](#) disease (NAFLD), in which excessive fat accumulates in the liver of individuals who do not have a history of alcohol abuse. NAFLD is regarded as a hepatic manifestation of metabolic syndrome, with the number of individuals with NAFLD/NASH increasing rapidly worldwide, in parallel with the increasing prevalence of obesity. Although clinical algorithms based on blood test results are being developed to identify patients with progressive NASH, liver biopsy remains essential to establish both the diagnosis of NASH and the severity of the disease.²

'The histological evaluation of NASH by microscopy is time consuming

and limited by inter- and intra-observer variability', explained Mr John Brozek from the French biotechnology company, GENFIT, which is developing the deep-learning system. 'We have been working to eliminate the subjectivity associated with interpreting histological images and have recently used deep-learning technologies to quantify histological patterns associated with NASH in an animal model'.

In the study presented today by Mr Brozek, animal models (rats or mice fed a choline-deficient, L-amino-acid-defined diet supplemented with cholesterol) were used to evaluate hepatocellular ballooning and lobular [inflammation](#) in liver biopsy samples. An expert histopathologist determined the ballooning and inflammation scores for all the animals included in the study, and deep-learning models were constructed to detect and analyze these histological features. An initial training set (n=31) was used to calibrate ballooning and inflammation for subsequent prediction of these histological features in four independent cohorts (n=271).

According to Mr Brozek, the deep-learning system was able to predict cell histological patterns relating to ballooning and inflammation with accuracies of 98% and 91%, respectively. Excellent agreement was observed between the expert and fully automated scores of ballooning at a cellular level for each of the cohorts ($k=0.84$ and $k=0.81$). An excellent correlation was also observed with the full tissue samples ($k=0.71$), and between whole slide imaging-based automatic scoring of inflammation on the training cohort ($Rho=0.907$).

'Deep-learning-based scoring systems allow an exhaustive and reproducible analysis of all cells in a biopsy sample, and they can analyze specific regions of cells that can be difficult to interpret manually, even if you are an expert', said Mr Brozek. 'Our automated scoring system for ballooning and inflammation showed a high correlation with expert evaluation and it is ready to be used for high-throughput activity scoring

in pre-clinical studies or, in the near future, as a companion diagnostic tool for [clinical application](#)'.

'There are key challenges in the consistency of [liver biopsy](#) interpretation and machine learning offers the promise of a more standardized, objective approach that allows for the analysis of biopsies in clinical trials', said Prof. Phil Newsome from the Queen Elizabeth Hospital and University of Birmingham, UK, and EASL Governing Board Member.

Provided by European Association for the Study of the Liver

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