AUTOMATED QUANTITATION OF STEATOSIS, FIBROSIS AND BALLOONING USING MACHINE LEARNING IN ROUTINE HISTOLOGICAL IMAGES OF LIVER BIOPSIES OF PATIENTS WITH NAFLD

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Background: Histology remains the gold standard for diagnosis of Non-Alcoholic Fatty Liver Disease. It is reported using semi-quantitative scores, with high intra and inter-observer variability. Ballooning is a key histological feature in Non-Alcoholic Steatohepatitis (NASH), however its diagnosis is still challenging.
We aimed to develop an automated method based on machine learning for the quantitation of ballooning, fat and fibrosis using routine histological images of patients with NAFLD.

Methods: We evaluated retrospectively consecutive liver biopsies with NAFLD. Biopsies were stained with H&E and Sirius Red and scored by two liver pathologists for NASH CRN scoring system. Images were digitalized and areas of ballooning were annotated manually using NDP.view2 to facilitate machine learning. Ballooning quantitation followed 3 stages: each component of the image was isolated by texture (fat droplets, ballooned cells, veins, sinusoids) using automatic threshold techniques. Finally, ballooning was identified after analysing the distribution of intensity. Results were expressed as % ballooned area vs whole core (Figure 1). Accuracy was defined as number of annotated cells detected by the software divided by number of manually annotated cells. Concordance between results and manual annotations was measured using interclass correlation coefficient (ICC).
Fat Percentage (Fat%) and Collagen Proportionate Area (CPA) were obtained using image analysis as published by our group.

Results: Up to now, 54 liver biopsies have been analyzed. As per CRN scoring system, steatosis grade was mild in 12 (22%), moderate in 18 (33%) and severe in 24 (44%) cases. Fibrosis was staged as F1-F2 in 14 (26%) cases, F3 in 15 (28%) and F4 in 4 (7%). Lobular inflammation was reported as grade 1 in 26 (48%), grade 2 in 7 (13%) and grade 3 in 2 (37%) cases. Ballooning was reported as score 0 in 14 (26%), score 1 in 26 (48%) and score 2 in 14 (26%) cases. 11 (20%) patients had no NASH, 23 (43%) borderline NASH and 20 (37%) definite NASH.
According to image analysis, median Fat% was 3.85% ± 1.5 for grade 1, 12% ± 8.8 for grade 2 and 27.9% ± 3.3 for grade 3. Median CPA was 2.2% ± 2.9 in stage 1, 2.9% ± 1.3 in stage 2, 5% ± 4 in stage 3 and 15.1% ± 5 in stage 4. Median ballooning% was 8% ± 2.3 for score 0, 14.9% ± 6 for score 1 and 16.4 ± 5.3% for score 2.
Ballooning quantitation showed an accuracy of 82.7%. Concordance between manual and automatic measurements was excellent with an ICC: 0.95, 95%CI=0.69-0.98, F value=13.2, p=0.001.

Conclusion: We have developed and validated a novel technique for high-throughput, objective quantitation of ballooning, steatosis and fibrosis in liver biopsies of NAFLD. Uniquely, this technique is fully-automated – employing machine-learning software – and requires no specialised equipment, making it applicable to clinical practice. As such, the ability to assess key histological outcomes and differences in NAFLD more objectively, would be to great clinical advantage.
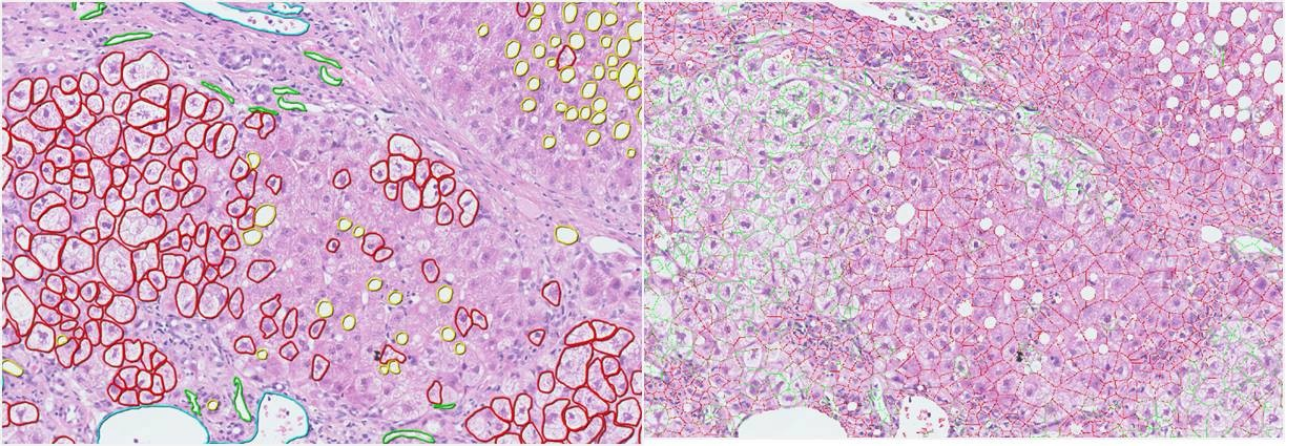
Figures:

Figure 1: Ballooning quantitation: on the left manual annotations, on the right automated quantitation's results (Fat% 8%, Ballooning% 13%). Fat droplets appear in green, ballooned hepatocytes in red.