A Deep Learning Algorithm to Quantify Liver Fat Content in Humans

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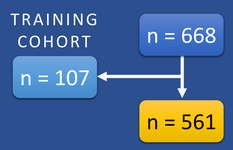
1 Background & Aims

Deep learning (DL) algorithms are computational paradigms that are inspired by the biological function of neurons[1]. DL algorithms are powerful tools for automatic image analysis[2]. In histological diagnosis and classification of liver disease, visual evaluation by a hepatopathologist is considered to be the gold standard. Observer-related factors are well known to cause significant variability in pathologists' evaluations[3-6]. There is a need for observer-independent methods for accurate, rapid and automated quantification of liver histology.

We determined whether DL can be used to automatically quantify hepatic steatosis in human liver biopsies. We developed and validated a DL algorithm to analyse liver histology using the Aiforia™ platform in a large cohort of liver biopsies, and compared the algorithm's performance against human observers.

2 Patients & Methods

LIVER BIOPSIES FROM BARIATRIC SURGERY PATIENTS



Patient characteristics	
Age (years)	48.6 ± 0.3
Females (%)	71.8
BMI (kg/m^2)	42.7 ± 0.3
Liver fat (%)	10 (0-30)
NAFLD (%)	67.6
NASH (%)	12.4

Data are in %, mean ± SEM or median (IQR).

- We acquired digital hi-res whole-slide images (WSI) of Herovici-stained liver specimens, which we then uploaded to the cloud-based Aiforia™ image processing platform[7].
- Using hand-drawn annotations, the DL algorithm was trained by pathologists and trained operators to recognise different histological structures.
- Algorithm calculates the percentage of macrovesicular steatosis, in addition to the number, size, diameter and surface area of lipid droplets (LD) and other structures, and the distribution of LDs in hepatic acini.
- We compared the algorithm's results to manual human counting and to pathologists' conventional assessments of steatosis.

3 Results

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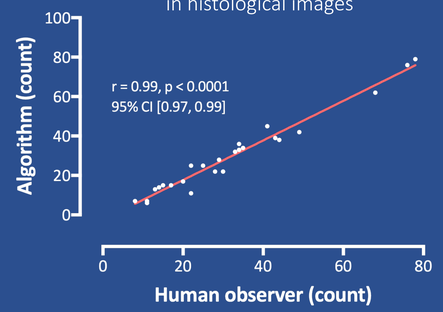
Algorithm recognises lipid droplets with high sensitivity and precision in comparison to manual human counting

Count of LDs in random scoring regions in histological images



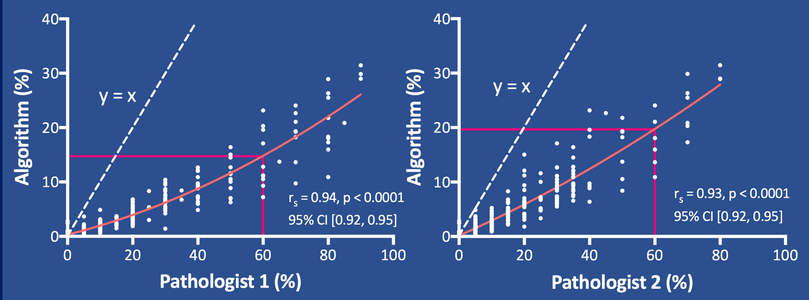
Performance metrics of LD recognition

Metric	%	Formula
Precision	96.8	TP/(TP+FP)
Recall*	89.8	TP/(TP+FN)
F_1-score†	**93.1**	2*P*R/(P+R)

TP, true positive; FP, false positive; FN, false negative; P, precision; R, recall (*sensitivity)

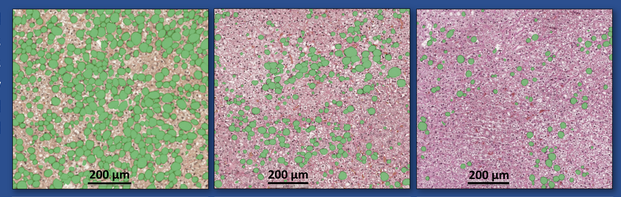
† the F-measure reflects overall accuracy of the algorithm

Pathologists' assessments of steatosis correlate higly significantly with algorithm's quantitation but pathologists consistently report higher percentage of fat in a given specimen

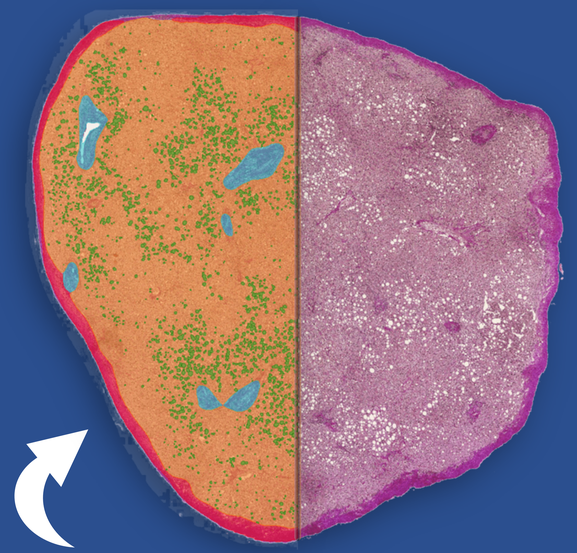


The human eye overemphasizes the degree of steatosis in liver biopsies

Manually selected homogenous areas from three biopsies containing mainly hepatocytes and macrovesicular lipid droplets.



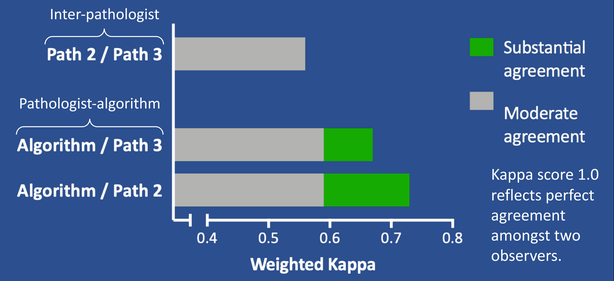
Algorithm	48 %	16 %	5 %
Pathologists	80/70 %	40/30 %	10/7 %



The deep learning algorithm automatically segments hepatic **parenchyma**, **capsule**, **portal tracts**, and **lipid droplets** in WSIs. We also implemented a method for automatically quantifying the **distribution** of LDs in the hepatic acini by measuring the distance of individual LDs to the edge of the nearest portal tract (see figure in the lower right corner).

Analysis speed was on average 3.5 seconds per single WSI or 50 mm^2 per second. Thus, it takes **one hour to analyse 1000 histological sections**.

Steatosis grading by the algorithm achieves higher agreement with pathologists than pathologists achieve with each other



Kappa score 1.0 reflects perfect agreement amongst two observers.

4 Conclusions

1. **Deep learning** is a fundamentally different method of analysing liver histology compared to traditional histological assessment by pathologists. It provides rapid, consistent and accurate metrics regarding hepatic steatosis.
2. Detection of lipid droplets by DL compared to a human is both **sensitive and precise**.
3. Steatosis quantitation using DL **correlates** well with estimatied steatosis perentage by experienced hepatopathologists.
4. **Pathologists consistently overestimated** the degree of steatosis in liver specimens. Previous data published by others support the notion that the human eye overemphasizes the degree of steatosis in liver biopsies[8-10].
5. Use of computerised analysis **eliminates observer-related variability** in histological assessments, improving consistency.
6. These novel metrics can be used to further characterize the emerging **subtypes of NAFLD**.

5 References

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