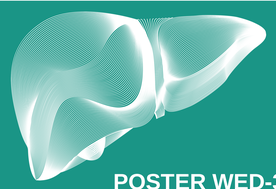

POSTER WED-374

Utilizing AI digital pathology for quantitative measurement, grading and differentiation of lobular and portal inflammation in MASH: preliminary analysis in liver histology

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Introduction

- Histological grading of inflammation is essential for evaluating treatment response in MASH clinical trials
- Differentiating lobular from portal inflammation by light microscopy can be subjective and variable
- AI digital pathology has the potential to offer objective, reproducible assessment through image analysis
- qFibrosis, qSteatosis, and qBallooning were validated using Second Harmonic Generation/Two Photon Excitation Fluorescence (SHG/TPEF) microscopy. However, qInflammation (qI) requires development on H&E images, as SHG/TPEF microscopy has limitations in visualizing inflammatory cells, and qI is more complex to develop and validate

Aim

- To develop and validate an AI-based qInflammation algorithm using H&E-stained liver biopsies
- To quantify and distinguish lobular and portal inflammation using objective morphometric features using the qI-algorithm

Method

- **Cohorts Utilised:** 269 liver biopsies from different sources (MASH clinical trials and clinical study samples)
  a) Randomly divided into training (n=180) and validation (n=89) cohorts
  b) Inflammatory foci were classified as described by Brunt et al [1] into portal and intra-acinar (lobular) inflammation ranging from grades 0-3 were used to define Inflammation zones and grades
- **Image Processing:**
  a) H&E-stained slides scanned using Leica Aperio scanner
  b) Digital images from Haematoxylin and eosin imaging channels of the scanner were processed to segment nuclei, detect inflammatory cells, and identify inflammatory foci
- **Portal Region Detection and Inflammatory Foci Classification:**
  a) Portal tracts localized via convolutional neural networks deep learning model trained on annotated blocks
  b) Inflammatory foci were classified as lobular or portal based on spatial overlay with portal regions
  c) Morphometric parameters, such as density, perimeter, and eccentricity were used to build qI-lobular and qI-portal indices using multiple linear regression on training cohorts and validated on the validation cohort
- **Statistical Analysis:**
  a) Spearman correlation with pathologist grades
  b) Concordance with pathologist based annotation on the validation cohort measured by Sensitivity (percentage of pathologist-identified inflammation also identified by qI) and Positive Predictive Value (PPV; percentage of qI-identified inflammation also identified by pathologist)
  c) Concordance with pathologist inflammation grades also calculated using weighted Kappa, Spearman's correlation, and the area under the receiver operating characteristic (AUROC) analysis.

Results

- **Pathologist Grading Distribution in n=269 biopsies**:
  a) Portal inflammation: I0 (14%), I1 (48%), I2 (36%), I3 (2%)
  b) Lobular inflammation: I0 (2%), I1 (44%), I2 (47%), I3 (7%)
- **qI detection Performance**:
  a) qI algorithm successfully distinguishes and quantifies portal and lobular inflammation from H&E images (Figure 1)
  b) Lobular inflammation: Sensitivity 83%, PPV 58%
  c) Portal inflammation: Sensitivity 89%, PPV 72%
- **Concordance with Pathologist Grading (Figure 2 and Table 1)**:
  a) qI-lobular index: Spearman's correlation = 0.556 (p<0.001), Weighted Kappa = 0.32, AUROCs = 0.80-0.88
  b) qI-portal index: Spearman's correlation = = 0.606 (p<0.001), Weighted Kappa = 0.38, AUROCs = 0.77-0.94

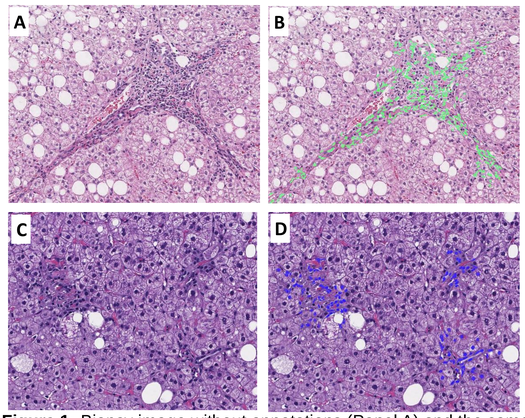

Figure 1: Biopsy image without annotations (Panel A) and the same image annotated using qInflammation algorithm (green annotations, Panel B) were both graded as **Grade 2 Portal Inflammation** by the pathologist and qInflammation. Biopsy image without annotations (Panel C) and the same image annotated using qInflammation algorithm (dark blue annotations, Panel D) were both graded as **Grade 3 Lobular Inflammation** by the pathologist and qInflammation

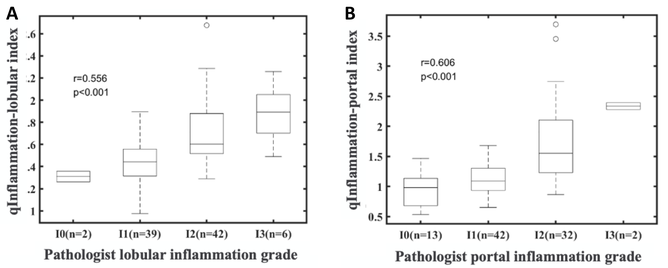

Figure 2: Validation cohort data for (A) qI-lobular and (B) qI-portal indices and their correlations with pathologist-based grading of inflammation

Table 1: Performances of the qI-lobular and qI-portal indices. Cutoff values were determined by Youden index. PPV: positive predictive value; NPV: negative predictive value

A

qI-lobular index	AUROC	Cut-off	Sensitivity	Specificity	PPV	NPV
I0 vs I1/2/3	0.88	1.37	82%	100%	100%	11%
I0/1 vs I2/3	0.80	1.55	67%	73%	74%	64%
I0/1/2 vs I3	0.82	1.83	67%	86%	20%	96%

B

qI-Portal index	AUROC	Cut-off	Sensitivity	Specificity	PPV	NPV
I0 vs I1/2/3	0.77	0.99	75%	46%	90%	27%
I0 vs I1/2/3	0.85	1.30	74%	78%	68%	83%
I0 vs I1/2/3	0.94	1.69	100%	84%	13%	100%

Conclusions

- Preliminary results show good correlation with pathologist grading and acceptable inter-rater agreement
- Ongoing improvements will focus on refining nuclear segmentation, reducing false positives, and identifying immune cell subtypes
- qI training and validation data completes the qFIBS panel (qFibrosis, qInflammation, qBallooning, qSteatosis), supporting comprehensive digital assessment of MASH histology for clinical trials

References

1. Brunt et al. Am J Gastroenterol. 1999;94(9):2467-74

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Metabolism, alcohol and toxicity
Kutbuddin Akbary

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