Quantitative Multimodal Anisotropy Imaging enables machine learning prediction of NASH CRN fibrosis stage without manual annotation

Abstract #36650

BACKGROUND

Staging fibrosis severity in non-alcoholic steatohepatitis (NASH) requires pathologist review of tissue stained to visualize collagen. The accuracy of staging can be affected by both stain quality and variability of pathologists' interpretation of the stain.

PathAI's Quantitative Multimodal Anisotropy Imaging (QMAI) can highlight collagen in tissue and can be used in quantification and staging of NASH fibrosis (1). AIM-NASH is a machine learning model developed by PathAI using 26,000 pathologist annotations on whole slide images (WSI) of Masson's Trichrome (MT)-stained tissue to accurately and reproducibly predict NASH Clinical Research Network (CRN) fibrosis stage (2; *manuscript in preparation*). Here, QMAI provides detailed, unbiased annotations of fibrosis on MT-stained tissue that are used to train deep neural network (DNN)-based ML models to infer a QMAI fibrosis pattern (iQMAI), which is then used by graph neural networks (GNNs) to predict slide level CRN fibrosis scores.

CONCLUSIONS

- QMAI, which provides unbiased annotations of fibrosis with high sensitivity and specificity, may enable more accurate ML modeling of NASH histology.
- These results show that QMAI can be used to train ML models to predict CRN fibrosis stage with accuracy comparable to that of models (like AIM-NASH) trained with thousands of expert pathologist annotations of fibrosis in MT-stained tissue.
- QMAI-derived fibrosis annotations in H&E-stained NASH slides are now being validated. If CRN fibrosis stage predictions derived from these models are concordant with CP scores, this methods may eliminate the need for MT staining in clinical trials.

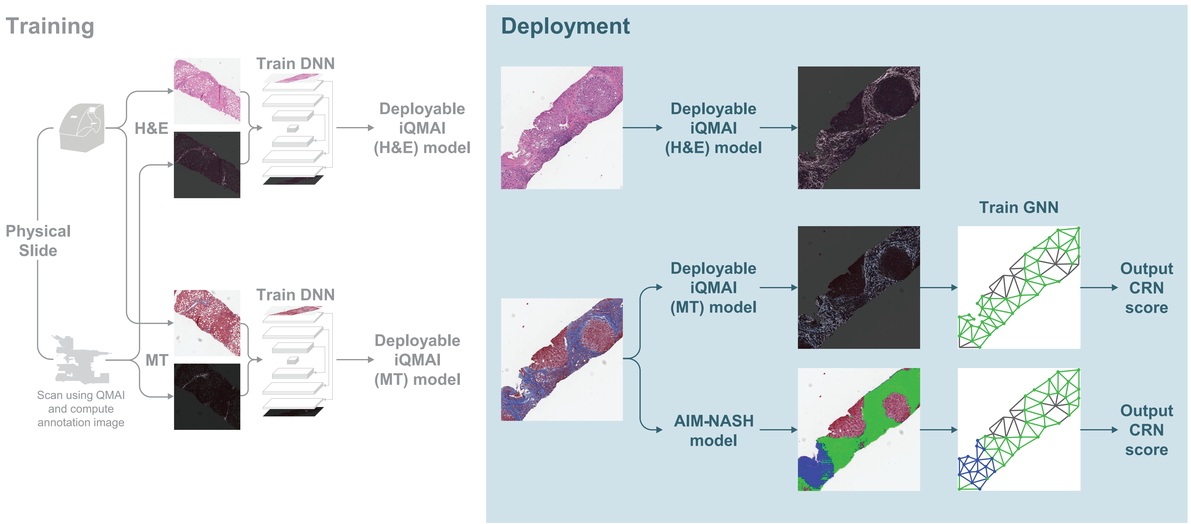
METHODS

Model Training

ML models based on DNNs were trained to predict a QMAI-like fibrosis pattern in tissue using 14 slides of liver tissue from patients with NASH from a clinical laboratory (PathAI Diagnostics, Memphis, TN). All sides were stained with MT and scanned on a Leica Aperio AT2 scanner and imaged by QMAI imaging to create paired digitized images of the same slide. DNNs were trained using the paired QMAI and AT2 scanned WSI, as shown in. Figure 1 also shows that separate DNNs were trained to infer QMAI-fibrosis in tissue stained with hematoxylin and eosin (H&E).

Models based on GNNs were trained to predict slide-level CRN fibrosis score from iQMAI using, 500 MT-stained whole-slide images (split evenly across CRN 0-4) from two completed NASH clinical trials were divided into training (70%), validation (15%), and test (15%) sets.

Figure 1. iQMAI Model Development, Deployment and Comparison with AIM-NASH



Paired QMAI and WSI of H&E- or MT-stained tissue is used to train iQMAI (Training), which are then deployed to generate inferred QMAI-like images (Deployment). GNNs, trained on CNN-generated pixel-level overlays of NASH fibrosis or on inferred QMAI images, predict slide-level CRN fibrosis score.

RESULTS

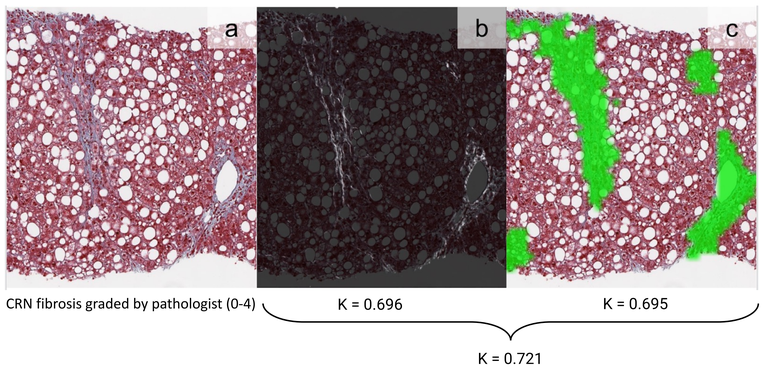
Model Deployment

Fibrosis overlays were generated for each slide via ML-QMAI and AIM-NASH. GNNs predicted CRN fibrosis stage based on these overlays.

Test set performance was assessed by comparing model CRN fibrosis grade predictions against scores provided by the trials' central pathologist (CP) via kappa statistics (linear Cohen's).

In the test set, concordance between CP assessment and ML-QMAI fibrosis stage predictions was moderately high (kappa = 0.696). Furthermore, ML-QMAI predictions as concordant with CP as AIM-NASH and CP (kappa = 0.695). Utilizing QMAI fibrosis overlays in conjunction with MT-ML-overlays to train the GNNs (not shown in Figure 1) yielded improved concordance with CP scoring (kappa = 0.721).

Figure 2. Imaging Fibrosis in NASH Tissue



A region of interest highlighting fibrosis in NASH tissue is shown here (a) stained with MT, (b) as an ML-QMAI overlay, and (c) as an AIM-NASH generated overlay.

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REFERENCES

1. . Zhang et al. Quantitative multimodal anisotropy imaging enables automated fibrosis assessment of H&E-stained tissue, Poster Presented at The International Liver Congress, 22-26 June 2022.

2. Carrasco-Zevallos et al., AI-based histologic measurement of NASH (AIM-NASH): A drug development tool for assessing clinical trial endpoints, Oral Presentation at The International Liver Congress, 23-26 June 2021.

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DISCLOSURES

W.T., T.N., M.G.D., Y.Z., J.Z., J.S.I., V.M., M.R., I.W., A.B., and J.L. are employees of and hold stock in PathAI. A.B. is a cofounder of PathAI.

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