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Unlock the Potential of Digital Pathology and AI

Identifying the ASH/MASH Spectrum in Liver Biopsies Using Weakly Supervising

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Introduction

Metabolic dysfunction-associated steatohepatitis (MASH) and alcoholic steatohepatitis (ASH) are challenging to distinguish due to their overlapping histological features, making accurate diagnosis difficult.

The traditional labeling approach, which typically selects either ASH or MASH, fails to recognize the **coexistence** of these conditions, leading to the need for a new category, **MetALD (ASH+MASH)**.

Algorithms need modification to identify the coexistence and to accurately locate a patient within the ASH/MASH spectrum using weak supervision.

Objective

1. Develop a convolution neural network (CNN) which can differentiate ASH and MASH
2. Identify ASH/MASH spectrum using weakly supervising learning method

Method

1. Obtained liver biopsy slides (ASH 150 + MASH 158).
2. Slides were digitalized with their diagnosis.
3. Cropped 256x256 patches from region of interesting (ROI).

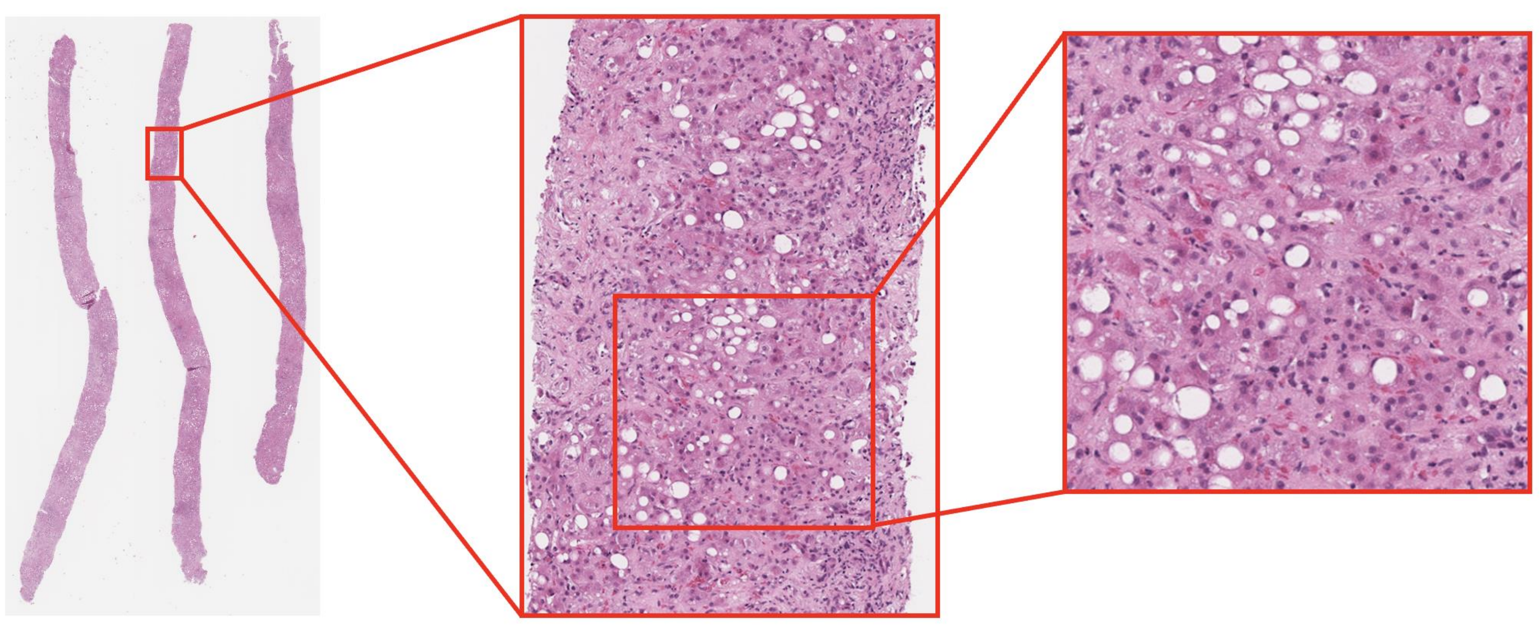

Figure 1. Processing of WSI to patches for train and testing

4. Train CNN model with patches using cross entropy loss and positive unlabeled (PU) loss.

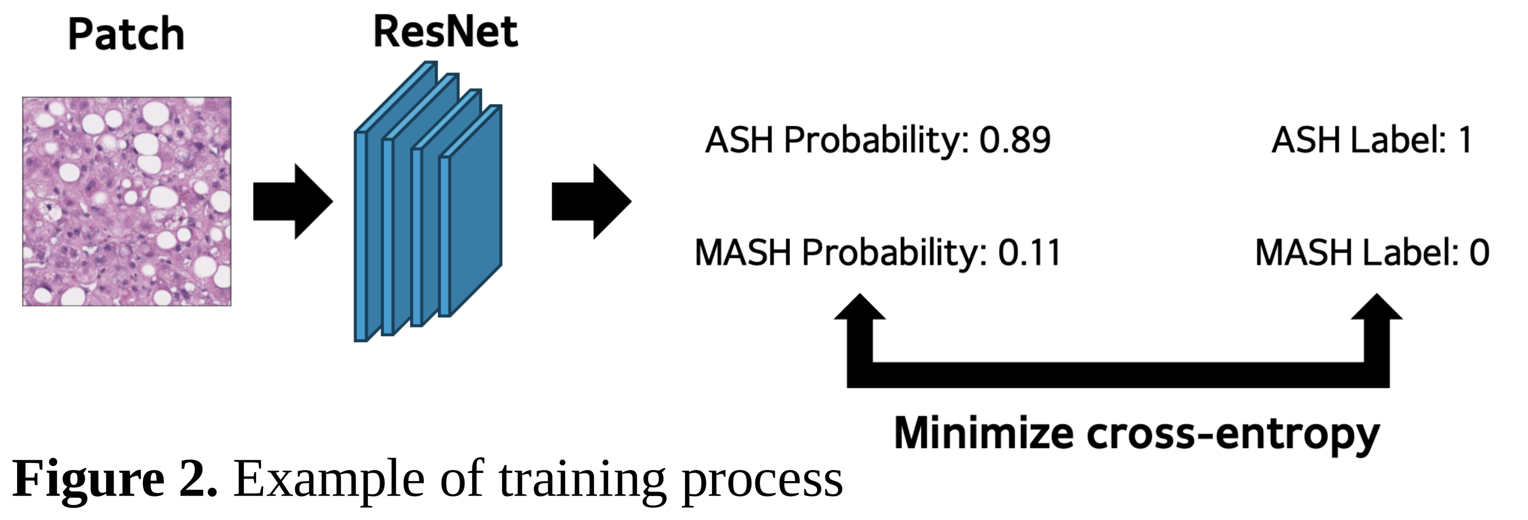

Figure 2. Example of training process

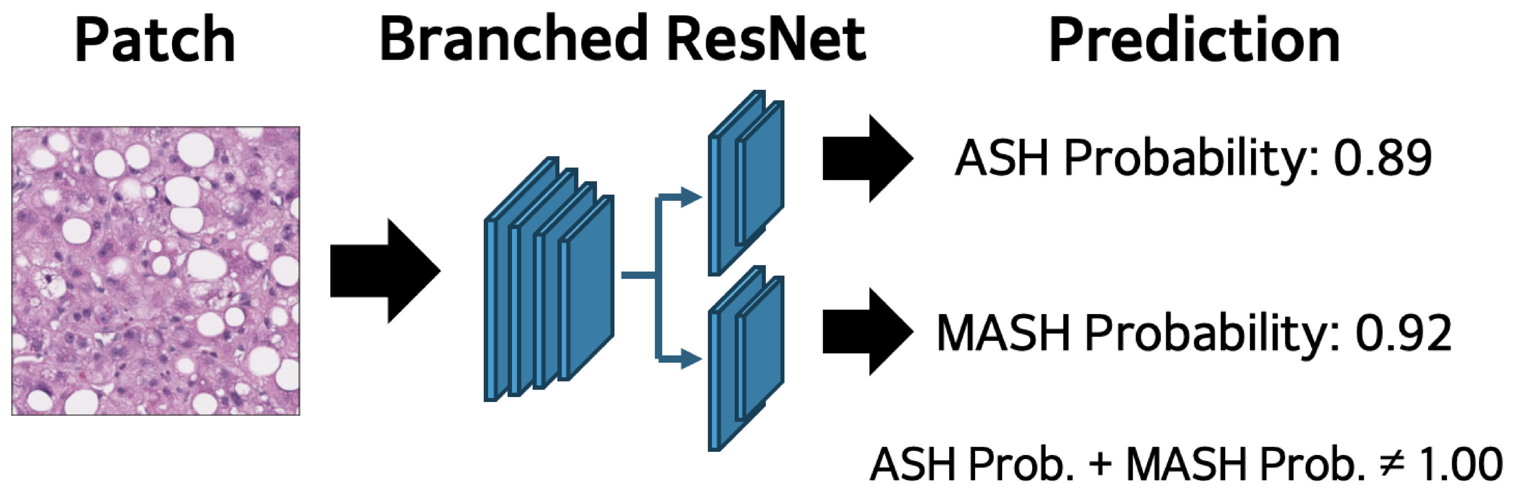

Figure 3. Example of model's prediction process.

Derivation of PU loss from cross entropy loss.

When π is class prior and $p(x,y) = \pi p(x|y=1) + (1-\pi)p(x|y=0)$,

$$L = \mathrm{E}_{p(x,y)}[-\log \hat{q}(y|x)]$$
$$= (1-\pi)\mathrm{E}_{\boxed{p(x|y=0)}}[-\log \hat{q}(y=0|x)] + \pi \mathrm{E}_{p(x|y=1)}[-\log \hat{q}(y=1|x)]$$

Substitue $\boxed{p(x|y=0) = \frac{1}{(1-\pi)}p(x,y) - \frac{\pi}{(1-\pi)}p(x|y=1)}$.

$$L = \pi \mathrm{E}_{p(x|y=1)}[-\log \hat{q}(y=0|x) + \log \hat{q}(y=1|x)] + \mathrm{E}_{p(x,y)}[-\log \hat{q}(y=0|x)]$$

Using PU Loss provides flexibility in model's prediction.

Results

We found some ASH slides have both ASH and MASH properties.

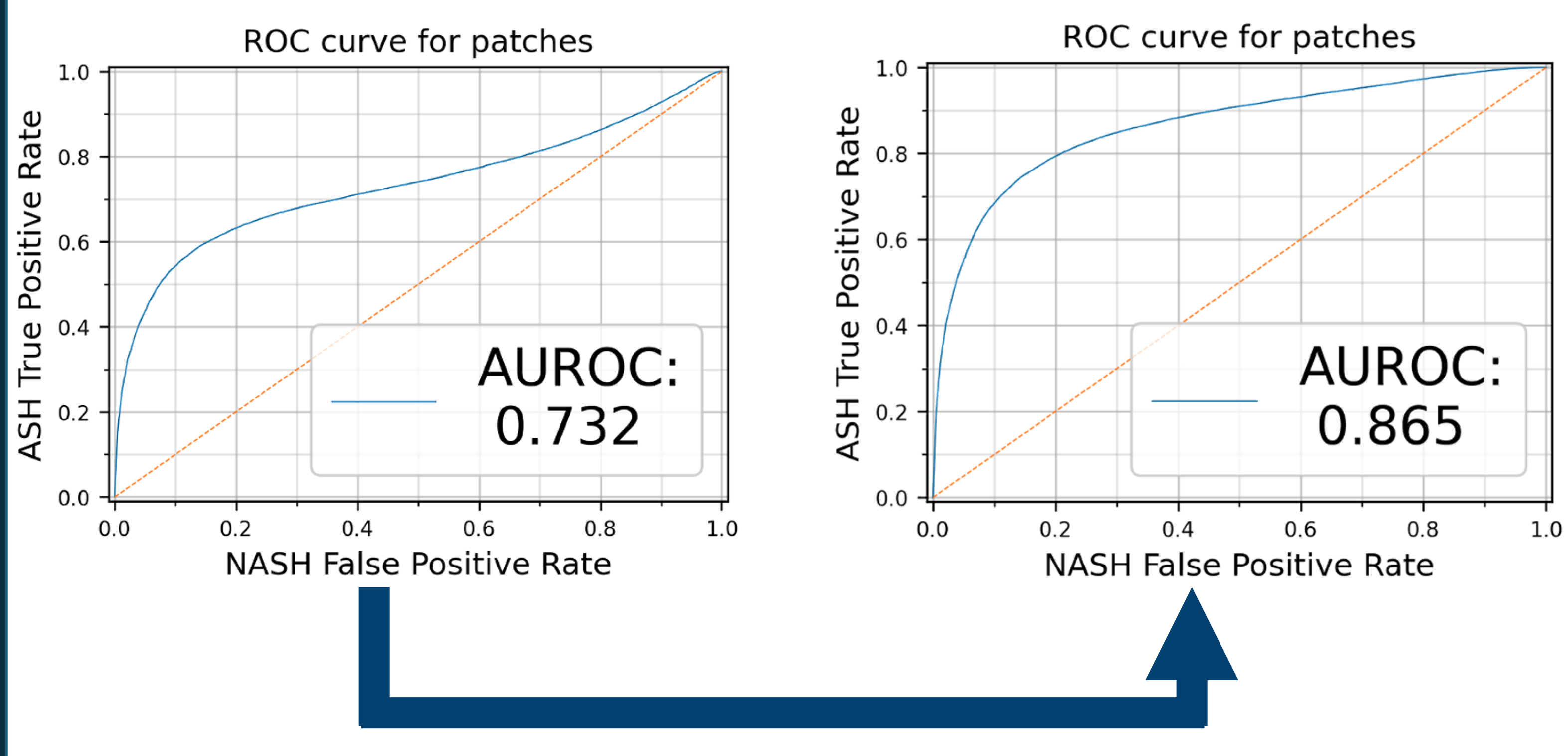

Figure 4. AUROC improve by changing 20 ASH labels to MASH.

We assessed our model's performance by 3 fold validation

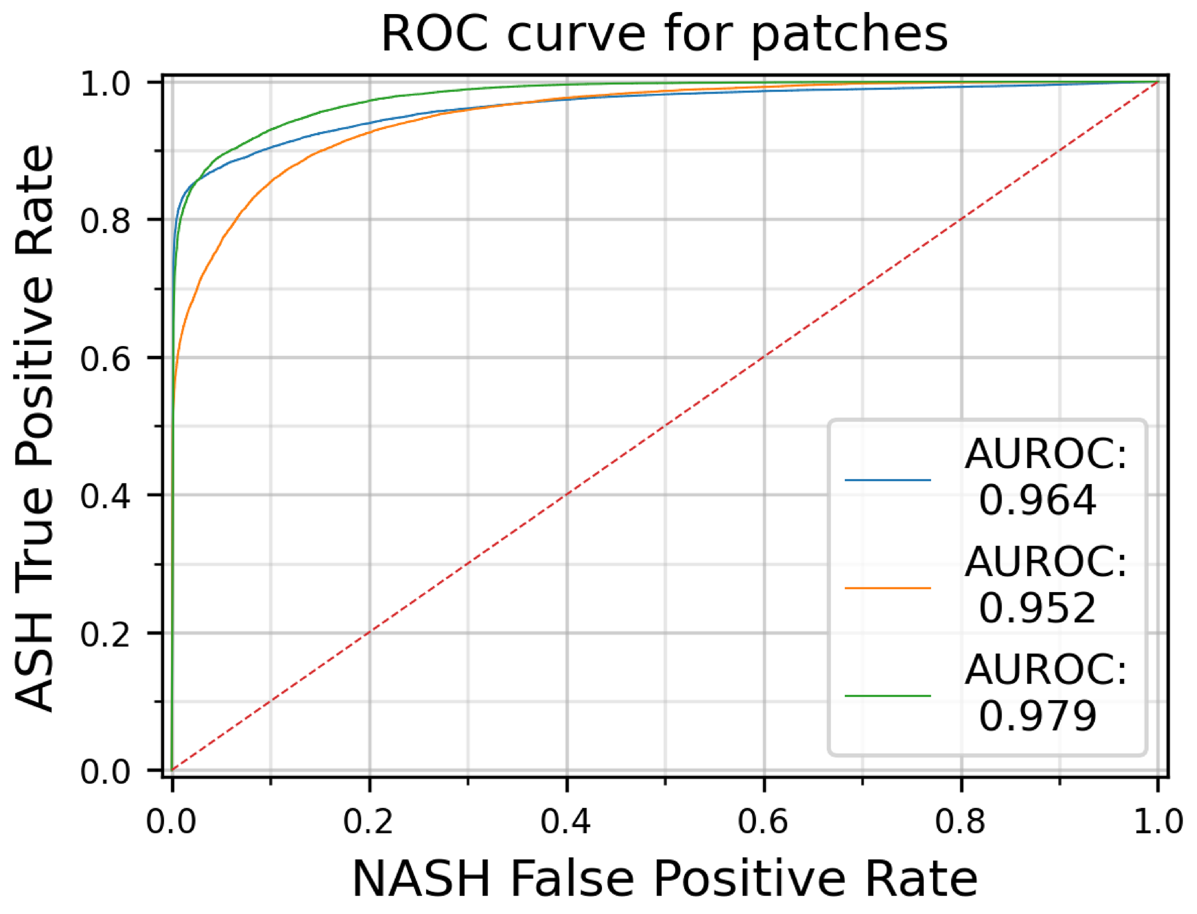

Figure 5. AUROC curve of 3 fold validation.

The CNNs' average accuracy was **91.5%**

Average sensitivity – 84.6%

Average specificity – 98.1%

We trained branched CNN model using PU loss to identify ASH/MASH spectrum.

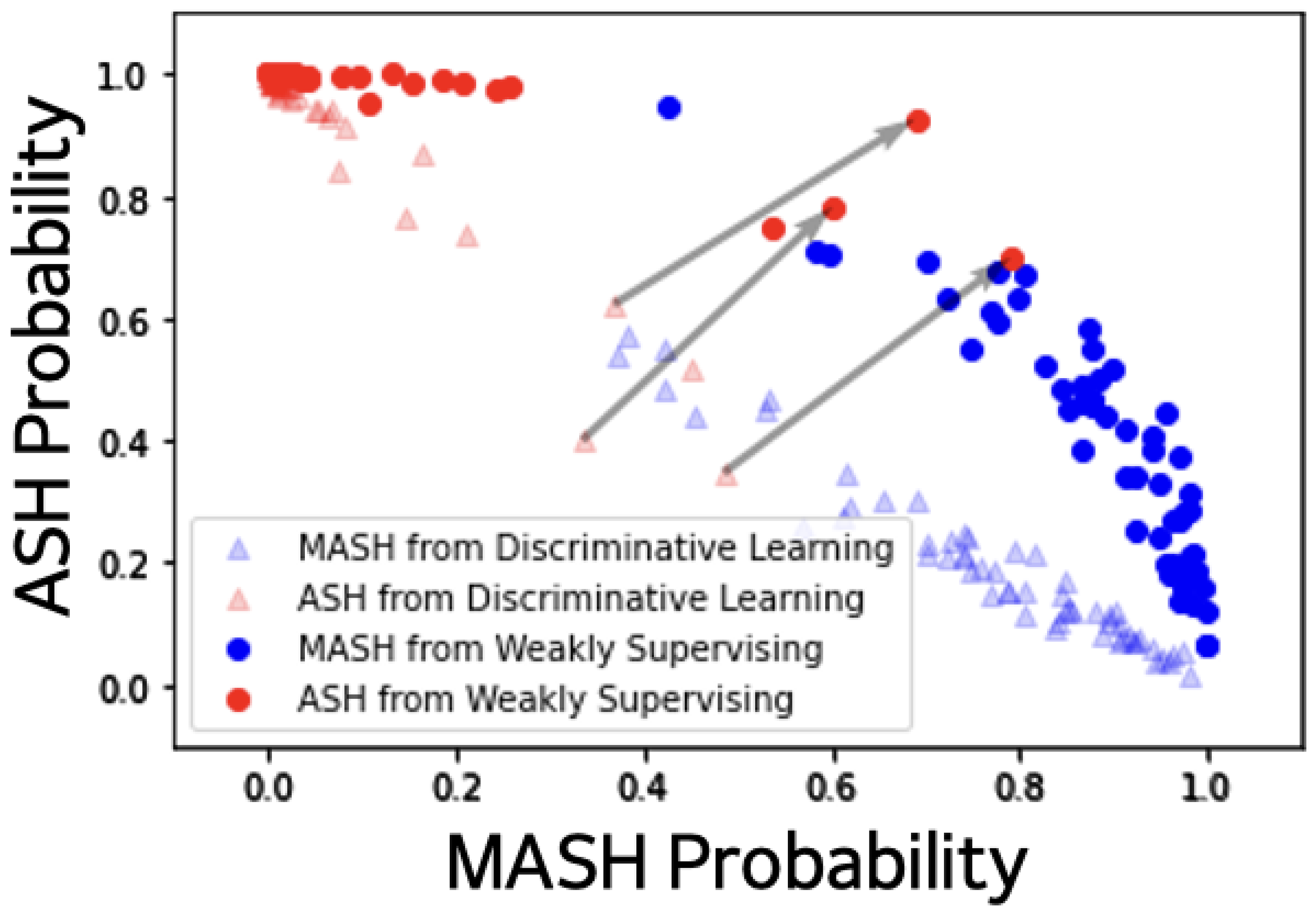

Figure 6. Distribution difference of discriminative learning and weakly supervising.

Conclusion

Our CNN-based experiment demonstrated the **coexistence** of ASH and MASH in patients labeled with only one, achieving 0.915 prediction accuracy for slide level classification after considering the coexistence.

PU learning with weak supervision and its output spectrum confirmed the coexistence.