

HISTOPATHOLOGICAL ASSESSMENT OF SJÖGREN'S DISEASE WITH HISTOMIL

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1. BACKGROUND

Primary Sjögren's (pSS) is a systemic autoimmune disease characterized by impaired function of the exocrine glands, pain and fatigue, greatly affecting patients' quality of life [1].

Histopathological assessment of labial salivary gland (LSG) biopsies is a key part of the diagnostic process, however their interpretation requires expert analysis, limiting access. Moreover, studies have shown there exists high inter-observer classification variability [2].

Deep learning can help automate and benchmark analysis to improve diagnostic capabilities and inter-observer concordance, ultimately leading to improved patient care.

AIM: To design a deep learning tool classifying LSG biopsies into pSS– (sicca) and + (sjögren), providing support to the diagnostic process.

2. METHODS

117 LSG biopsies were sampled, stained with H&E, digitized as Whole Slide Images (WSIs) and classified following 2016 ACR-EULAR Classification Criteria¹, 36 as pSS– and 81 as pSS+.

A gated-attention, deep multiple instance learning pipeline was implemented, modified from AttMIL/CLAM [3, 4] with a previously finetuned VGG16 backbone and attention score heatmap overlays². Training was conducted using a 70/30% train/test split, with strict separation of patients between splits.

3. RESULTS

The model correctly classifies 89% of WSIs (Fig. 1A) and shows high diagnostic potential, correctly ranking patients (AUC = 88%) with a low rate of false negatives (Sensitivity = 90%).

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¹Ethics approval: sample collection was approved by ethics committees (REC 05/Q0702/1, REC 17WS0172) for Rheumatology/Oral medicine clinic, Queen Mary University London.

²All code, implementation details and training schedule available at: <https://github.com/AmayaGS/HistoMIL>

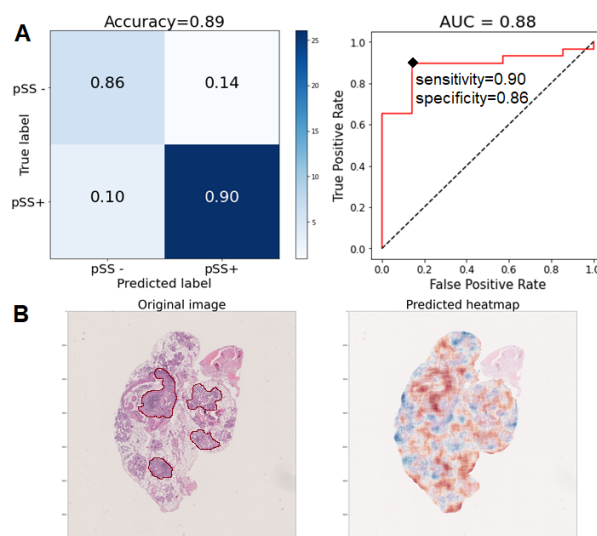


Fig. 1. A. Confusion matrix and Area Under the ROC Curve plot. B. Left: original WSI with areas of diagnostic relevance demarcated in red; Right: predicted heatmap overlay, with higher/lower attention scores in red/blue.

The attention heatmap (Fig. 1B) successfully highlights areas of diagnostic importance, corresponding to aggregates of lymphocytic infiltration. An in depth study of predicted heatmaps and incorrect predictions with pathologists/immunologists will help pinpoint where the model can be improved.

NEXT STEPS: Integrating further clinical data part of diagnostic criteria, such as presence of circulating auto-antibodies and salivary gland transcriptomics, to improve patient diagnosis and stratification.

4. REFERENCES

- [1] F. Chowdhury, A. Tappuni, and M. Bombardieri, "Biological Therapy in Primary Sjögren's Syndrome: Effect on Salivary Gland Function and Inflammation," *Front. Med.*, vol. 8, pp. 707104, 2021.
- [2] D. Lucchesi, E. Pontarini, V. Donati, et al., "The use of digital image analysis in the histological assessment of Sjögren's syndrome salivary glands improves inter-rater agreement and facilitates multicentre data harmonisation," *Clin. and Exp. Rheumatology*, vol. 38 Suppl 126, no. 4, pp. 180–188, 2020.
- [3] M. Y. Lu, D. F. K. Williamson, T. Y. Chen, et al., "Data-efficient and weakly supervised computational pathology on whole-slide images," *Nat. Biomed. Eng.*, vol. 5, no. 6, pp. 555–570, June 2021.
- [4] M. Ilse, J. Tomczak, and M. Welling, "Attention-based deep multiple instance learning," in *Proc. 35th ICML*, 2018, vol. 80, pp. 2127–2136.