“Morphologic criteria and CD138-positive cells counting for chronic endometritis: manual versus AI-based algorithms”

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INTRODUCTION

Chronic endometritis (CE) is one of the most impactful causes of female infertility. So accurate CE diagnosis is extremely important for proper management of such patients. The most significant feature of CE is the plasma cell in the endometrium. They can be identified on hematoxylin and eosin-stained slides, but immunohistochemistry with CD138 expression provides more accurate and reproducible results. Thus, the goal of our survey was to develop a reproducible neural network (NN)-based algorithm for accurate plasma cell detection on histological images stained with CD138. Previously established NNs developed for this purpose could not rule out stained CD138 glandular cells and squamous cells in endometrial curettage samples, so we tried to avoid this disadvantage in our NN (fig. 1).

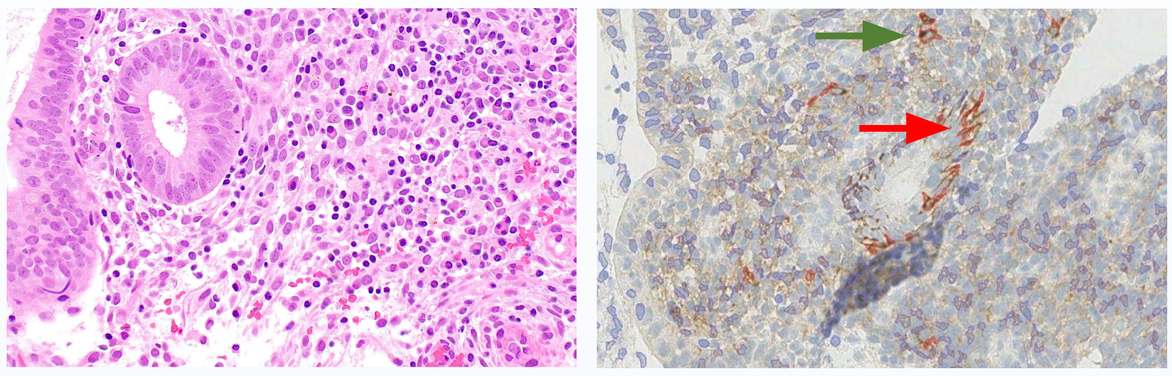

Figure 1. Plasma cells on h/e slide (left) and on IHC slide (CD 138) (right) Plasma cells marked green arrow, glandular cells marked with red arrow.

MATERIALS AND METHODS

Three pathologists independently evaluated 50 endometrial biopsies morphologically and immunohistochemically (CD138). The cut-off for EC diagnosis was 5 plasma cells (10 HPF). For interobserver reproducibility, we used Cohen's kappa evaluation (for each pair of pathologists) and Fleiss' kappa evaluation for all three pathologists (both for h/e and IHC slides).

Then we digitized the slides and used NN EndoNet created on the basis of CenterNet (backbone UNet++ ResNet50). It was trained for stromal and glandular cells detection on the open dataset EndoNuke and fine-tuned on the dataset "Endometrium" (54 tiles, 200x200 mkm, and 790x790 pxl) that we made and labeled from our slides. After that we defined and applied HSV color cut-off that plasmatic cells have to cells that NN EndoNet classified as stromal. Then we modified our NN EndoNet for only plasmatic cells detection and trained it on the train/val part of the dataset “Plasmatic” (373 tiles 200x200 mkm and 790x790 pxl) that we made and labeled from our slides. Precision, recall, and F1-score were assessed for quality evaluation.

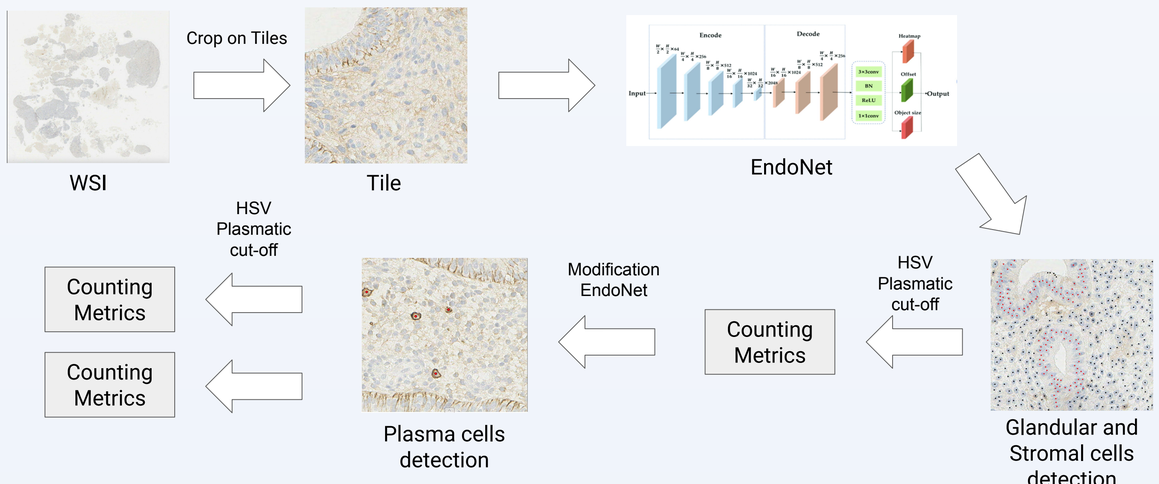

Figure 2. Pipeline of plasma cells search solution

RESULTS

At first, we assessed the interobserver reproducibility of plasma cells counting on h/e stained slides and in IHC slides with CD138-positive cells between 3 gynecologic pathologists. We revealed then the reproducibility was minimal (0.25-0.39) for h/e stained slides and was moderate to perfect for IHC slides (0.67-0.84) for pairwise comparison and moderate (0,40) for he to good (0.73) for ICH according to Fleiss’ kappa results (table 1).

Cohen’s kappa h/e		P-value	Cohen’s kappa IHC		P-value
Pathologists 1-2	0.25	0.068	Pathologists 1-2	0.67	<0.001
Pathologists 1-3	0.56	<0.001	Pathologists 1-3	0.77	<0.001
Pathologists 2-3	0.39	0.005	Pathologists 2-3	0.84	<0.001

RESULTS (continue)

When NN EndoNet was applied on the dataset ‘Endometrium’ the accuracy of stromal and glandular cells detection was mAP = 0.72. After that we defined the HSV color threshold bounds that plasma cells have (fig. 3).

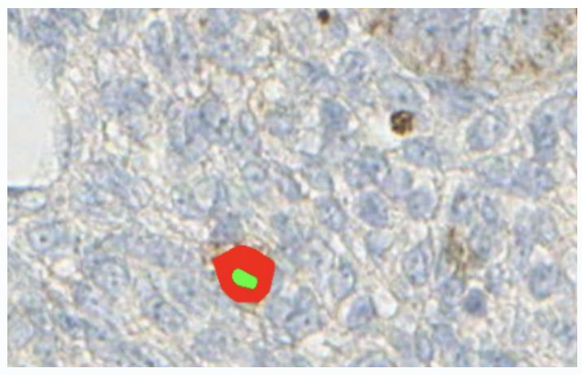

Figure 3. HSV counting for plasma cell (marked be red)

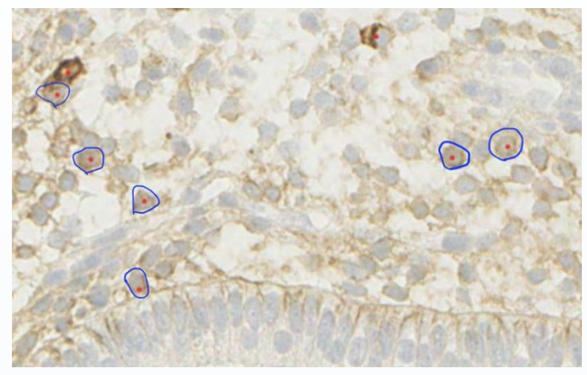

Figure 5. Not-stained stromal cells marked as plasma cells by NN

The threshold was counted for ten labeled plasma cells due to HSV color model (Hue, Saturation, Value): 5 <= hue <= 20. In plasma cells search algorithm we counted the cell as plasmatic If NN EndoNet classified the cell as stromal and the HSV color of the cell was inside the counted HSV plasmatic threshold bounds. The accuracy of this approach on the test dataset (90 tiles: 45 not-empty tiles with at least one plasma cell + 45 empty tiles without any plasma cells) is precision = 0.82, recall = 0.57 and f1-score = 0.67. Low recall resulted from NN could not classify plasma cells as stromal cells accurately enough (fig. 4).

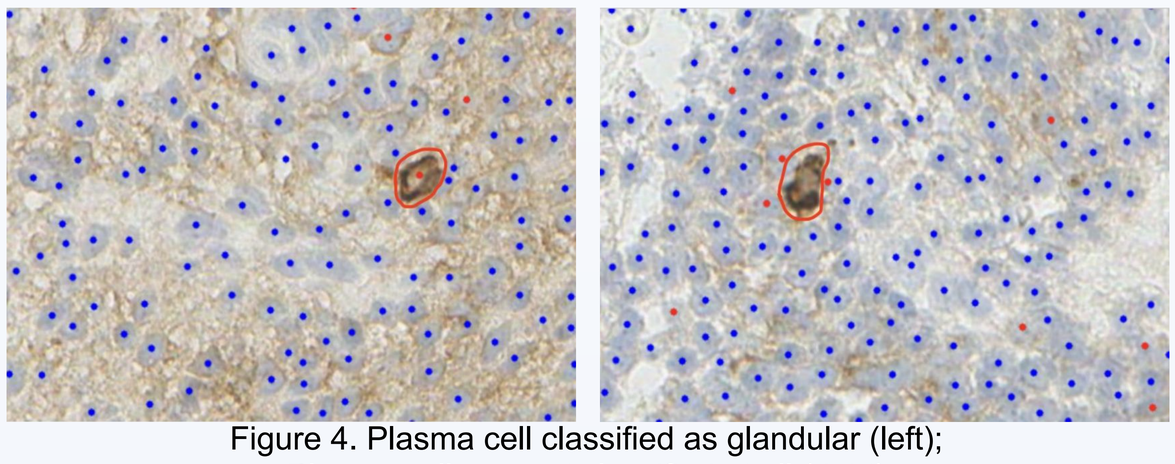

Figure 4. Plasma cell classified as glandular (left); Plasma cell was not classified at all (right)

Because of low recall with the EndoNet application and HSV color cut-off we decided to modify EndoNet for only plasma cells detection. Dataset ‘Plasmatic’ was labeled by 2 experts with high reproducibility (Cohen’s kappa was 0.89 on the basis of 65 matching tiles). In this dataset we collected 373 tiles with 826 labeled plasma cells. We modified NN EndoNet for only plasma cells detection. It was trained on the train/val part (132/56 tiles) of the dataset Plasmatic. The accuracy of EndoNet (modified for only plasma cells detection) on the test dataset (173 not-empty tiles with at least one plasma cell + 172 empty tiles without any plasma cells) is precision = 0.73, recall = 0.89 and f1-score = 0.80.

Analyzing the results we saw that modified EndoNet marks as plasma cells not-stained with CD138 stromal cells (fig. 5). To resolve this problem we decided to apply HSV color cut-off that plasma cells have the same as in the non-modified approach (fig 3.). After application of HSV color cut-off the accuracy of plasma cells detection on the test dataset (173 not-empty tiles with at least one plasma cell + 172 empty tiles without any plasma cells) is precision = 0.84, recall = 0.76 and f1-score = 0.80.

CONCLUSION

We concluded that plasma cells counting in IHC slides with CD138 expression can improve manual reproducibility of chronic endometritis in compare with h/e slides evaluation from moderate to good level according to Cohen’s kappa value. NN EndoNet trained for plasma cells detection with color cut-off can detect plasma cells with high accuracy and could be applied for routine practice in pathology department for chronic endometritis diagnosis.

CONTACTS

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