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# A system for the automatic segmentation of epithelium in cervical Whole Slide Images as a tool to assist diagnosis of Clinical Intraepithelial Neoplasia

**Problem**

Cervical Intraepithelial Neoplasia (CIN) is considered a potentially precancerous state of the cervix[1], and its treatment can prevent Cervical Cancer. Diagnosis of CIN Grade (severity) allows the estimation of cancer risk and determines patient treatment[2]. However, it involves a visual estimation of abnormal epithelial tissue width in biopsies, which results in high levels of inter-observer variability[3,4]. Deep Learning (DL) has been used for segmentation and quantification of digitalized biopsies[5], and could be used to support the diagnosis of CIN.

**Solution**

This work focuses on creating a system to support the diagnosis of CIN using Whole Slide Images (WSI) of cervical tissue samples. The system should identify epithelium automatically and display it as a marked region over the WSI using a visualization software. The user may annotate abnormal cell regions, and the system should calculate the *proportion* and *distribution* of epithelial width that is covered by abnormal cells. These are considered to be diagnostic indicators of CIN.

**Method**

DL models will be programmed and fine-tuned using the *Tensorflow*[6] library, and trained with 280 annotated cervical WSI. The best performing model will be incorporated to a visualization software. Diagnostic indicators will be calculated using manually annotated abnormal cell regions, and analyzed for each CIN Grade (CIN1, CIN2 and CIN3).

**Variables and metrics**

Resnet[7] and Inception[8] DL architectures will be evaluated. Measures of accuracy, precision, recall and processing time will be used to evaluate segmentation performance for each DL architecture and CIN Grade. An Analysis of Variance (ANOVA) test will be performed to evaluate statistical difference of diagnostic indicators for each CIN Grade.

**Hypothesis**

The DL model with the best performance will be capable of segmenting the epithelium automatically and in a reduced amount of time without statistically significant differences between CIN Grades, and diagnostic indicators will differ for each CIN Grade.

**Objectives**

1. Propose a set of parameters for the fine-tuning of DL models;
2. Evaluate segmentation performance of Resnet and Inception DL models;
3. Integrate the best performing model to a visualization software;
4. Calculate images' diagnostic indicators using manually annotated abnormal cell regions and analyze results for each CIN Grade.

**Expected Results**

Based on a preliminary single-WSI analysis, the best performing DL model should obtain precision and recall levels above 90%, and processing times averaging less than 30 seconds. Diagnostic indicators should be easily distinguishable for images diagnosed as CIN1 and CIN3, while CIN2 images should present a higher variance.

**Outlook**

In the future, a system to support the diagnosis of CIN may allow to standardize sample interpretation, reducing inter-observer variability and facilitating the quantification process for pathologists.

**References**


1. Schiffman, M., Castle, P. E., Jeronimo, J., Rodriguez, A. C. & Wacholder, S. Human papillomavirus and cervical cancer. *Lancet* **370,** 890–907 (2007).

2. Massad, L. S. *et al.* 2012 updated consensus guidelines for the management of abnormal cervical cancer screening tests and cancer precursors. *Obstetrics and Gynecology* **121,** 829–846 (2013).

3. Hopman, E. H., Voorhorst, F. J., Kenemans, P., Meyer, C. J. L. M. & Helmerhorst, T. J. M. Observer Agreement on Interpreting Colposcopic Images of CIN. *Gynecol. Oncol.* **58,** 206–209 (1995).

4. Stoler, M. H. *et al.* The interpretive variability of cervical biopsies and its relationship to HPV status. *Am. J. Surg. Pathol.* **39,** 729–736 (2015).

5. Litjens, G. *et al.* A survey on deep learning in medical image analysis. *Med. Image Anal.* **42,** 60–88 (2017).

6. Abadi, M. *et al.* TensorFlow: A system for large-scale machine learning. *12th {USENIX} Symp. Oper. Syst. Des. Implement. ({OSDI} 16)* 265–283 (2016).

7. He, K., Zhang, X., Ren, S. & Sun, J. Deep residual learning for image recognition. in *Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition* **2016–Decem,** 770–778 (2016).

8. Szegedy, C., Vanhoucke, V., Ioffe, S., Shlens, J. & Wojna, Z. Rethinking the Inception Architecture for Computer Vision. in *Proceedings of the IEEE Computer Society Conference on Computer Vision and Pattern Recognition* **2016–Decem,** 2818–2826 (2016).