Endometrial cancer is the most common cancer of the female reproductive system, with approximately 66,500 patients diagnosed per year in the US, resulting in 12,900 deaths. Cancer is confirmed via pathological analysis of a whole slide H&E image. However, whole slide images are often too large to be processed by pathologists in a timely manner. An AI system that can classify images of endometrial biopsy samples can aid in the diagnosis and treatment of endometrial cancer.

**HYPOTHESIS**

An artificial intelligence (AI) system to predict benign, type 1, and type 2 endometrial cancer from images of endometrial biopsies stained with H&E could serve as a decision support tool for pathologists. Such an AI system is needed as approximately 66,500 patients are diagnosed with endometrial cancer every year in the US.

**AI CHALLENGES**

Recent advances in deep learning have led to breakthroughs in medical image analysis. However, deep neural networks: 1) cannot directly process H&E images as a whole, 2) require large training image sets, whereas a few existing public datasets of H&E images of endometrial biopsies are very small, including ours consisting of only 245 images.

**KEY ASPECTS OF OUR APPROACH**

- Use ResNet18 for feature extraction from images, since it performs well when trained on small training datasets [1].
- Sample a number of smaller tiles from the large H&E image for multi-instance learning (MIL) [2].
- Annotate tissue regions in H&E images to train a tissue classifier as: 1) good quality tissue, 2) unusable folded or damaged tissue, 3) blood, and 4) background and debris.
- Ensure that the tile sampling comes only from the good-quality tissue regions.
- Annotate tissue regions in H&E images to train a tissue classifier as: 1) good quality tissue, 2) unusable folded or damaged tissue, 3) blood, and 4) background and debris.
- Ensure that the tile sampling comes only from the good-quality tissue regions.

**METHODS**

H&E-stained slides of endometrial biopsy samples from 245 patients were collected at ProPath and scanned on the Holologic Genius platform. Attention-based multi-instance learning (MIL) [2] was used to predict "benign", "type 1", or "type 2" cancer as follows:

1. Tile sampling: ResNet18 [1] was trained to select 128 tiles with size 256x256 pixels from good-quality tissue using manual annotations of image regions as: 1) good-quality tissue, 2) unusable folded or damaged tissue, 3) blood, and 4) background and debris.
2. Tile attention: A fully-connected network was used to estimate importance of each tile for cancer prediction.
3. Tile fusion: A weighted sum of the tile features was passed to a multilayer perceptron to classify the H&E image as "benign", "type 1", or "type 2" cancer, where the weights in the sum were set to the tile attentions.

**RESULTS**

Our MIL model estimates relative importance of H&E image tiles for cancer type recognition, and achieves the 3-class and 2-class classification accuracies of 95.9% and 100%, respectively, averaged over 10 random training-testing splits of 245 H&E slides of endometrial cancer biopsies. Our results suggest that a reliable prediction of endometrial cancer type from H&E images is possible, given slide-level annotations of the cancer type and tile-level annotations of the tissue-region quality in training.

**REFERENCES**