PREDICTION OF PATIENT-LEVEL BREAST CANCER METASTASES BASED ON CONVOLUTIONAL NEURAL NETWORK

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ABSTRACT

Cancer diagnosis by pathologists is costly, and the results of diagnosis may differ a lot depending on pathologists. The automated cancer diagnosis may provide a solution to these problems. In this paper, we present a machine learning-based classifier for the diagnosis of breast cancer metastases in lymph nodes. First, a CNN-based classifier is trained with small patches extracted from whole slide images(WSIs). Then, based on the result of patch classification, WSIs are used to generate heatmaps from which we extract handcrafted features. The slide-level classifier is trained using these features and predict lymph node metastasis categories for the test dataset. Finally, synthesizing the metastasis categories, the model predicts each patient's pN-stage by rule-based criteria.

Index Term – Breast cancer metastases, Lymph nodes, pN-stage, Machine learning, Convolutional neural network.

1. METHODS

We automatically diagnose breast cancer metastasis of lymph nodes via two-level classification.

Patch-level classification
- Split WSIs into small patches and train a patch-level classifier using a convolutional neural network.

Slide-level classification
- Extract handcrafted features from heatmaps and train a slide-level classifier using random forests.

1.1 Dataset

We use both Camelyon 16[1] and Camelyon 17 datasets[2] (abbreviated to the ‘16 dataset and the ‘17 dataset, respectively) for training the patch classifier. To exclude incorrectly labeled data, only slides that were fully annotated in each dataset(50 slides from the ‘17 dataset and 81 slides from the ‘16 dataset) were used for training the model. A total of 131 annotated slides are split into small patches. We reserve 20% of the patches for validation. We generate 500 heatmaps from the ‘17 dataset for slide classification. Slide classification proceeds with 5-fold cross-validation to fully utilize a limited dataset.

1.2 Data augmentation

We split the tissue region of WSIs into small patches to train the patch-level classifier. Otsu thresholding[3] is used to find the tissue region. Patches are resized to a size of 224 x 224 to mitigate the micron per pixel(mpp) problem. Images are randomly flipped and rotated 90 degrees for robust prediction. Color jittering, whose parameters are brightness, contrast, saturation, and hue, is randomly applied to handle color variation. Patches are labeled depending on the proportion of the image that is comprised of tumor cells.

1.3 Patch-level Classification

We use DenseNet-201[4] for the patch-level classifier. The model is pre-trained on the ImageNet dataset to more easily learn low-level features of cells. The learning rate for Adam optimizer is 0.0001, and no weight scheduling is applied. We train models for 50 epochs and take the parameters with the highest validation accuracy.

1.4 Feature Extraction

We extract handcrafted features from generated heatmaps. Twenty morphological features, such as the size of the main tumor cluster and the length of the major axis of the cluster, are used for classifying tumor clusters. Five stochastic features, including average probability and variance of probability, are used as context information.

1.5 Slide-level Classification

Lymph node slides are classified by a random forest using the extracted features. The slide-level classifier is validated with 5-fold cross-validation. Finally, we predict pN-stages of patients using the given rules.

2. RESULTS

The accuracy of the patch-level classifier is 0.997 on the validation dataset. We test the model 1000 times for the 100 randomly sampled test slides and take the average result. The mean slide-level accuracy is 0.862, and the mean kappa score is 0.86.

3. CONCLUSION

We predict breast cancer metastases in lymph nodes by two-level classification based on machine learning. On the patch-level, the patch classifier distinguishes tumor cells and benign cells well. But on the slide-level, the slide classifier has difficulty distinguishing negative and isolated tumor cell (ITC) images. Even minor errors in the output of the patch classifier cause misclassification of metastasis due to the small size of isolated tumor cells.

In future work, we will experiment with images at higher magnification to better distinguish isolated tumor cells than the original model.

4. REFERENCE

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