Development of a deep learning based pathological aid using weakly annotated data for the colonoscopy surgery

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Abstract

Collateral cancer is one of the fatal malignancies. During the surgical procedure, the confirmation of the total removal of cancer tissue can reduce the risk of re-development of the cancer cell. But the practice of manual pathology is not feasible to adapt during the surgical procedure because screening for the diagnostically relevant region of interest (ROIs) is time-consuming and exhausting on high-resolution images. The cognitive workload can be minimized by leveraging a visual aid to narrow down the visual search area highlighting only the cancer probable regions. This research presents a deep learning framework for colonoscopy pathology whole slide image (WSI) analysis. Our framework contains a pretrained resnet152 as a fixed feature extractor with a custom head as the final classifier. For training the network, we use a weighted cross-entropy loss function to overcome the class imbalance problem of the dataset. The dataset we are using is weakly annotated provided by our collaborator from Asan Medical Center. We introduce a specific sliding overlapped window-based patch generation algorithm for model training dataset preparation and testing. The dataset preparation algorithm minimizes the mixing of normal tissue and colon cancer patches. We have 15 WSIs so far, and initially, we have used 3 WSIs to train the model. In the transfer learning approach of model training, the feature extractor is pretrained on the ImageNet dataset. The custom final layers are trained with randomly initialized weights. On the prepared dataset, the achieved model accuracy is 0.95. The result of cancer tissue detection on WSIs is evaluated by expert pathologists. We use cancer prediction probability maps for result visualization. Our method can generalize to other datasets without retraining.

1. Background

For colorectal cancer detection, pathology examination is considered as gold standard. Because of advancements in digital pathology, WSIs are being used for pathological analysis. But a manual examination of WSI is a tedious task, and it is not suitable for making a quick decision surgical procedure. Pathologists need to go through carefully to detect the minor tissue of the remaining tumor. Recently deep learning methods are being leveraged in pathological data analysis. Cancer tissue and lesion segmentation, classification, and grading tasks have recently been gaining attention in cancer diagnosis because of the improvement of deep learning models. The approaches are different based on the study and organs – Unet[1] is a widely used segmentation model consisting of skip connections from down-sampling to up-sampling layer for preserving the information for high-resolution images. In recent years, HistoCAE[2] has been implemented for tumor region segmentation on WSI, which integrates convolutional autoencoder (CAE) and convolution neural network (CNN) for incorporating supervised and unsupervised learning approaches. Computer-aided diagnosis (CAD) is for bladder cancer diagnosis[3], which consists of s-net (resemble of Unet), d-net (combination of inceptionV3 CNN and Language model) for pixel-wise classification for getting pixel-wise segmentation, visual information learning, and diagnosis generation. CNNs are also implemented widely for breast cancer segmentation from histopathology images[4] and classification of renal cell carcinoma[5] on the WSI level. Colon cancer diagnosis is also being performed using CNN- an improved Unet has been implemented for colon cancer segmentation and classification using VGG19 as a backbone network [6].

In this research work, rather than a fully automated diagnosis purpose, we have proposed a pathological aid to remove most of the false positive part of the WSI and suggest the probable cancerous region on WSI for colon cancer detection using the transfer learning method.

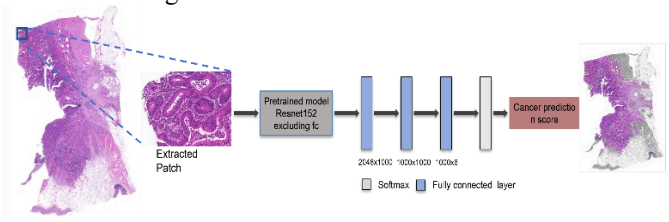

Fig 1: system architecture

2. Method

We have used a patch-based classifier network to segment the cancer tissue on the WSI. The algorithm developed here for the dataset preparation follows segmenting out the tissue area from the WSI, reading the annotations from the ground truth, and labeling different annotated regions (cancer, normal mucosa, and other normal tissue areas) with different pixel markers (fig.2). If at least one pixel is cancer annotated, then the patch is considered a cancer tissue patch, and other patches are separated as normal tissue areas based on the label. We have used 25% overlapped, random initializations, and random step size sizes to extract the patches using a sliding window-based patch extractor algorithm. Since histological images are highly diverse, we have applied rotation, flipping, and color jitter to the dataset for data augmentation. The patch size is 1024 x 1024 px.

Table 1: dataset description

Tissue region	Patches	Tissue region	Patches
Cancer	4626	Submucosa	94
Mucosa	392	Muscularis propria	183
Subserosa	215		

The final extracted patches dataset size is 200k from 4 WSIs, which will be used for later model training.

The proposed model consists of a feature extractor and classifier layers as the final head (fig.1). The final classifier layers are a sequence of 4 fully connected layers and a relu activation layer with a dropout layer and a softmax layer. During the dataset preparation for the classifier, we have separated the WSI into 6 regions to make the model learn specific features of – mucosa, submucosa, muscularis propria, subserosa, cancer tissue, and background regions. The data size in each class is not similar (table 1); therefore, we have used a weighted cross-entropy loss function for training the network to overcome the class imbalance problem.

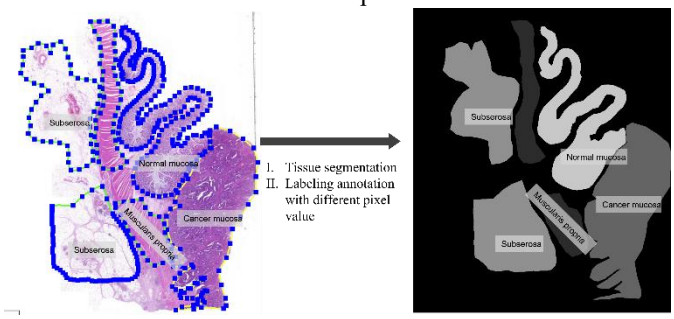

Fig 2: Dataset preparation approach

3. Result

We have used 80% of the patch dataset for training the model and 20% as the validation set. Model validation accuracy is 0.95 on the prepared dataset. The trained model is used for generating the prediction of cancer for each patch. The generated cancer probability map is used for result visualization on WSI. All patches from a WSI are extracted using a sliding window, and the prediction score is obtained. The cancer prediction score is used as a parameter to change the patch color intensity by multiplying the score to change the color intensity of the patch. After reassembling, the resultant patches are reassembled, and the result is visualized on WSI (fig.3). The result shows precise detection of cancer regions though the ground truths are weakly annotated.

4. Acknowledgements

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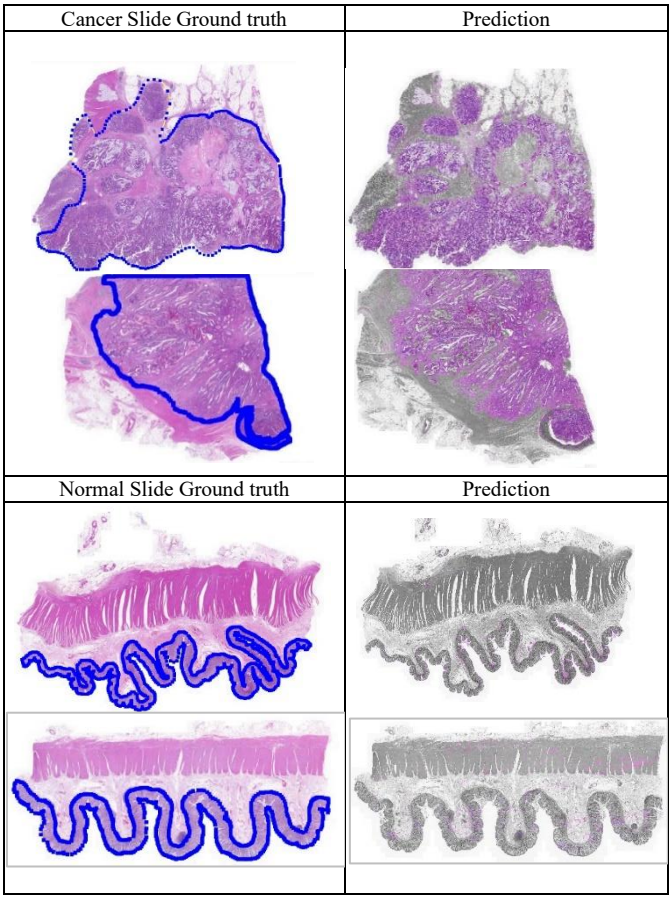

Fig 3: Result visualization

5. Reference

[1] O. Ronneberger, P. Fischer, and T. Brox, "U-net: Convolutional networks for biomedical image segmentation," in *International Conference on Medical image computing and computer-assisted intervention*, 2015, pp. 234–241.

[2] M. Roy *et al.*, "Convolutional autoencoder based model HistoCAE for segmentation of viable tumor regions in liver whole-slide images," *Sci. Rep.*, vol. 11, no. 1, pp. 1–10, 2021, doi: 10.1038/s41598-020-80610-9.

[3] Z. Zhang *et al.*, "Pathologist-level interpretable whole-slide cancer diagnosis with deep learning," *Nat. Mach. Intell.*, vol. 1, no. 5, pp. 236–245, 2019, doi: 10.1038/s42256-019-0052-1.

[4] B. M. Priego-Torres, D. Sanchez-Morillo, M. A. Fernandez-Granero, and M. Garcia-Rojo, "Automatic segmentation of whole-slide H&E stained breast histopathology images using a deep convolutional neural network architecture," *Expert Syst. Appl.*, vol. 151, p. 113387, 2020, doi: 10.1016/j.eswa.2020.113387.

[5] M. Zhu, B. Ren, R. Richards, M. Suriawinata, N. Tomita, and S. Hassanpour, "Development and evaluation of a deep neural network for histologic classification of renal cell carcinoma on biopsy and surgical resection slides," *Sci. Rep.*, vol. 11, no. 1, pp. 1–9, 2021, doi: 10.1038/s41598-021-86540-4.

[6] R. Feng, X. Liu, J. Chen, D. Z. Chen, H. Gao, and J. Wu, "A Deep Learning Approach for Colonoscopy Pathology WSI Analysis: Accurate Segmentation and Classification," *IEEE J. Biomed. Heal. Informatics*, vol. 25, no. 10, pp. 3700–3708, 2021, doi: 10.1109/JBHI.2020.3040269.