CAMELYON17: AUTONATIC CLASSIFIER FOR PATHOLOGIC LYMPH NODE

Yuexiu Wang, Sheng Guo, Xiaojun Hu

Sun Yat-Sen University

ABSTRACT

Automatic detection of breast cancer from whole slide images is a challenge, due to the large-scale data with enormous resolutions and existence of hard mimics. In this paper, we describe a framework to automatically predict slide-level cancer metastasis with the Convolutional neural network(CNN). And we propose a novel framework by leveraging fully convolutional networks for efficient inference to meet the speed requirement for clinical practice. First, a whole slide image was split into a small patch as a detector for our special fully convolutional network. Next, the patch-level result is reconstructed to a confident map. After post-processed the image by simple morphology opening and morphology closing operation to remove the small outliers, the confident map is predicted by a slide-level lymph node classifier module.

Index Terms— Camelyon17, Metastasis detection, Deep learning, fully convolutional network [3]

1. INTRODUCTION

Breast cancer has been one of the leading cancer killers threatening women in the world. As one of the most important diagnostic criteria of breast cancer, detecting the metastases, especially in the sentinel lymph nodes, is a routine procedure for cancer staging performed by pathologists. According to the pathologic TNM breast cancer staging system [5], positive metastasis would lead to a higher staging of the patient, and afterwards necessary treatments would be accordingly arranged. However, as is widely known, the process of pathologic diagnosis is extremely time-consuming and laborious, which requires pathologists to fully focus themselves hour by hour on the samples under the microscope. Automated detection of lymph node metastasis and pN-stage prediction has a great potential to reduce their workload and help the pathologist.

The task in Camelyon17 challenge is to determine a pN-stage for every patient in the test dataset. To compose a Pathologic lymph node classification, the number of positive lymph nodes are counted. So, the pathologic lymph node classification is dependent on the slide-level lymph node classification, which is decided by the confident map from the Network. In the last few years, considerable improvements have been emerged in the computer vision task using convolutional neural network. In Camelyon16

challenge, CNN was used to predict lymph node breast tumor, which obtained the state-of-art result.

In this paper, we propose a fully convolutional network(FCN) to predict the confident map for a whole slide image. As the resolution of whole slide images is extremely huge, approximating to $200,000 \times 100,000$ pixels. How to efficiently process such a giga-pixel image further poses challenges for automatic detection methods. In order to consume less time on prediction, [4] propose a novel framework-ScanNet. Based on fully convolutional network (FCN), a bigger size of image can be processed during test, which can boost hundreds of times acceleration compare to traditional patch-based classification framework with the same stride in the training stage.

2. METHODS

2.1. Regions of Interests

The resolution of whole slide images is extremely huge, approximating to $200,000 \times 100,000$ pixels. It is observed that more than 70% area of a typical WSI is covered by the non-informative background that provides almost no information for cancer assessment. In order to select the regions of Interest to save computational cost, we employ the simple OTSU algorithm [8] to determine the regions of interests, as shown in Fig. 1(a). We notice that the whole slide image has different type in different centres. Centres_0, centres_1 and centres_3 have black background while centre_2 and centres_4 have white background. So we first jitter the background of all slide image into white, and then employ the simple OTSU algorithm to binary the image. In addition, to accelerate this operation, we conduct it using a multi-level mapping strategy. That is we process the down sample image (e.g., level-5) first and then map the binary image back into the original (level-0) image, which achieves dozen times of acceleration in the pre-processing step.

2.2. Metastasis Detection

We propose a modified fully convolutional network for fast prediction for large WSIs by taking its advantage of allowing us to take arbitrary sized images as input. We implement the FCN base on a modified VGG-16[2] by replacing the last three fully connected layers with fully convolutional layers $1024 \times 1024 \times 2$(kernel size 2×2). In
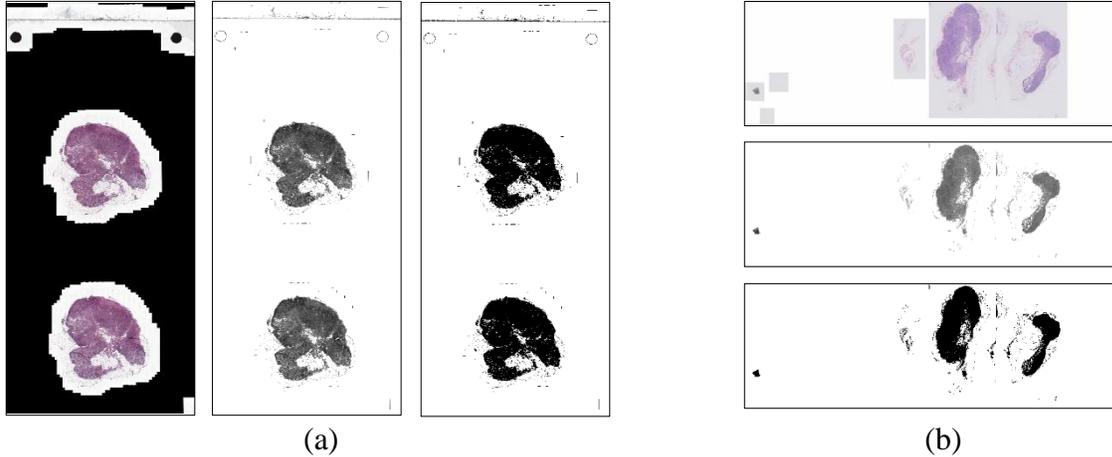
Fig.1. The illustration of Pre-processing. **(a)** is from centres_1, which has black background. **(b)** is from centres_4, which has white back ground. After the Pre-processing, we find the ROIs, which is black in the final image.

order to reduce the noise, we remove all the padding operations. Different from traditional FCNs that are commonly used for segmentation tasks, our FCN has no unsampled operation which is a must for segmentation but not necessary for our detection tasks. In this case, we employ the patch sample with size as 244×244 to train the network. In the train stage, After the ROIs are founded from WSIs, we sample the image patch with size as 244×244 randomly from the ROIs. We label a patch as tumor if over 50% pixels in the center 32×32 area are annotated as a tumor. To enrich the training samples, we augmented the training data with different transformations, such as randomly rotating over angles between 0 and 360 and flipping. Training FCN network for tumor and non-tumor detection is a challenge, because of the unbalance between the number of tumor and normal. During training, we sample tumor/normal patch at a rate of 0.1.

In the test stage, we take an image as large as 1204×1204 as input and output a confident map with size of 31×31. Thanks to the merit of the fully convolutional mechanism, the image size in detection stage is determined by the capacity of GPU memory. In our FCN, any image size as 212+32*n can be taken as input and output a confident map with size of n × n. The image patch input to network should be extracted under a certain stride to ensure that all of them are non-overlapped.

2.3. Slide-level Classifier

In the slide-level classify, we have to determine four classes (negative, itc, micro, macro). According to the classification criteria, the major axis length and the number of the tumor region are the condition of classification. In addition, we post-processed the confident map by morphology opening and closing operations to remove the small outliers.

3. EXPERIMENTS

3.1. Dataset

We evaluate our method on Camelyon17 dataset. In Camelyon17 dataset, there 1000 slides collected from five medical centres, 500 slides for train and another 500 slides for test. Since only 50 lesion-level annotations are provided, we select five slides from different medical centres as validation set. In the learning process of FCN, to save the memory space and augment the training samples flexibly, we generate the training samples on-the-fly. During the training stage, we train the FCN with initial parameters from VGG16 pretrained model to speed up convergence. The network was train for 20w iteration with a batch size of 20 per CPU. In detection, there is about 2500 image patch after filter by the pre-process operation in a slide, and it took less than 20 minutes to process one slide with size 200,000 × 100,000 on one NVIDIA GTX TITAN X GPU.

In the post-processing, the network output a confident map (32-times down-sampled), which has many small regions. In order to remove the small outliers, we threshold the confident map with a threshold 0.9, and process it by morphology opening and closing operations as shown Fig 2. Given the confident map, the major axis length and the number of the tumor region can be counted. According to those condition, the slide can be classified (i.e. Len>200 is classified as macro). Finally, the pN-stage can be determined by the prediction result of the given five slide image.
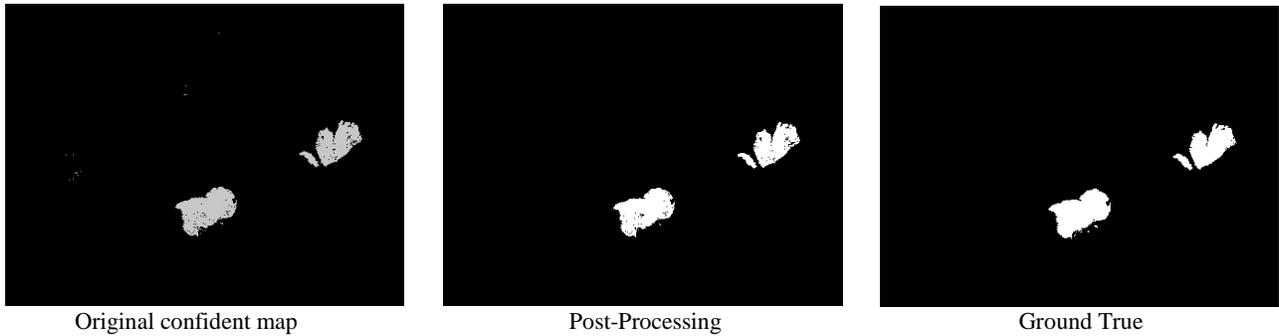
| Original confident map | Post-Processing | Ground True |

Fig.2. Pro-Processing of the confident map

3.2. Result

We evaluate our method on Camelyon17 validation set. And the patient-level quadratic weighted kappa score is 0.827

4. DISCUSSION

In this paper, we propose a framework to predict a whole slide image mask by patch-level classification. During the process image patch to train the network, we roughly crop it from the whole slide image, which is too small than the original image to learn the complete information. This is because the whole slide image is too big for network to train. In this case, the network can only learn little information from the image patch, resulting the limitation of accuracy.

Furthermore, the similarity of itc, micro and macro metastases increase the difficult of slide level classification. We only choose major axis length and the number of the tumor region as the condition of slide level classification. But in this way, it is hard to resolve isolated tumor cells(itc) and micro metastases, as well as isolated tumor cells and noise (False negative patch).

5. CONCLUSION

In this paper, we propose a simple and fast framework to patient-level classification for metastatic breast cancer detection. Base on CNN, we pretrain a patch-level classifier, but predict a slide-level approach. Therefore, there still remain some limitations.

In the future work, we would like to add the false positive samples, i.e., hard negative mining(HNM) example to retrain the network to enhance the discrimination capability of our FCN. And build a more effective framework for slide-level classification.

6. REFERENCES

[1] Oscar Geessink, Peter Bandi, Geert Litjens, and Jeroen van der Laak, "Camelyon17: Grand challenge on cancer metastasis detection and classification in lymph nodes," 2017.

[2] Simonyan, K., Zisserman, A.: Very deep convolutional networks for large-scale image recognition. arXiv preprint arXiv:1409.1556 (2014)

[3] J. Long, E. Shelhamer, and T. Darrell, "Fully convolutional networks for semantic segmentation," in CVPR, 2015.

[4] Chen, H., Qi, X., Yu, L., Dou, Q., Qin, J., Heng, P.A.: ScanNet: A Fast and Dense Scanning Framework for Metastatic Breast Cancer Detection from Whole-Slide Images. Medical Image Analysis 36, 135–146 (2017)

[5] Edge, S.B., Compton, C.C.: The american joint committee on cancer: the 7th edition of the ajcc cancer staging manual and the future of tnm. Annals of surgical oncology 17(6), 1471–1474 (2010)

[6] Wang, D., Khosla, A., Gargeya, R., Irshad, H., Beck, A.H.: Deep learning for identifying metastatic breast cancer. arXiv preprint arXiv:1606.05718 (2016)

[7] Kaiming He, Xiangyu Zhang, Shaoqing Ren, and Jian Sun, "Deep residual learning for image recognition," in Proceedings of the IEEE conference on computer vision and pattern recognition, 2016, pp. 770–778
.
[8] Nobuyuki Otsu, "A threshold selection method from gray-level histograms," IEEE transactions on systems, man, and cybernetics, vol. 9, no. 1, pp. 62–66, 1979.

[9] Gao Huang, Zhuang Liu, Laurens van der Maaten, and Kilian Q Weinberger, "Densely connected convolutional networks," in Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition, 2017.