

# DETECTION AND CLASSIFICATION OF BREAST CANCER METASTASES IN HISTOPATHOLOGY IMAGES

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## ABSTRACT

The detection and classification of breast cancer metastases in lymph nodes are of great importance to breast cancer diagnosis and prediction. Challenge CAMELYON17 focus on the pathologic N-stage according to TNM classification. In this paper, we propose a fine detection and boosting classification (FDBC) framework to predict pathologic Np-stage. In fine detection section, we detect the regions of breast cancer and obtain annotated slides by a path-segmentation network. In boosting classification section, we fusion multiple classifiers do lymph node classifier on the base of predicted annotated slides. Experiment results on Camelyon17 dataset show the effectiveness of our proposed framework.

**Index Terms**— CAMELYON17, Lymph Node Classifier, Fine Detection, Boosting Classification

## 1. INTRODUCTION

Considering the situation of metastatic involvement of lymph nodes is of great importance for breast cancer diagnosis, surgery planing and prediction of patient outcome. We can use the TNM system to finish the histological assessment of lymph node metastases, which classify the states of cancer spread into account the size of the tumour (T-stage), whether the cancer has spread to the regional lymph nodes (N-stage), and whether the tumour has metastasised to other parts of the body (M-stage). Among the above states, the automated prediction of N-stage (also called pN-state) is greatly essential for reducing the workload of pathologists, while at the same time, reducing the subjectivity in diagnosis.

The CAMELYON 17 challenge focusing on the pathologic pN-stage aims to automatically detect and classify of breast cancer metastases in whole-slide images of histological lymph node sections. That is to say, the task consists of 1) detection of the region that breast cancer metastasizes to in multiple lymph node slides and 2) classification of pathologic lymph node metastasis and determination for per patient which of the following pN-stages applies. First, the whole-slide images (WSI) of histological slides offer available material to detect the regions of breast cancer. Then according to the detection results of 5 slides every patient, there are three

categories of lymph node metastasis each identity including macro-metastases (Macro), micro-metastases(Micro), isolated tumour cells (ITC). Further, based on categories of each patient, pathologic lymph node classification (pN-stage) are divided into the following conditions, namely, no micro-metastases or macro-metastases or ITCs found (pN0), only ITCs found(pN0(i+)), micro-metastases found but no macro-metastases found(pN1mi), metastases found in 1C3 lymph nodes(pN1), metastases found in 4C9 lymph nodes(pN2).

Several part works have been used CNN network to detect lymph node breast tumor and achieved great performances in CAMELYON 16 challenge focused on the detection of lymph node metastases. In this paper, we propose a fine detection and boosting classification (FDBC) framework to predict pathologic Np-stage of each patient. The FDBC framework consists of three sections: detection of cancer regions, pathology feature extraction and lymph node classifier. First, differed from typical detection work, in this paper we use a fully convolutional segmentation network to obtain the regions of breast tumor so that we can get pixel level breast cancer distribution. Second, we extract digital and pathology features from the mask of breast cancer distribution, which offer different kinds of information to the classification of lymph node metastases stage. Finally, Multi-classifier fusion is used to classify of lymph node metastases stage after feature extraction.

The rest of the paper would detailed introduce the methodology in Section 2 and the experiment results in Section 3.

## 2. METHODOLOGY

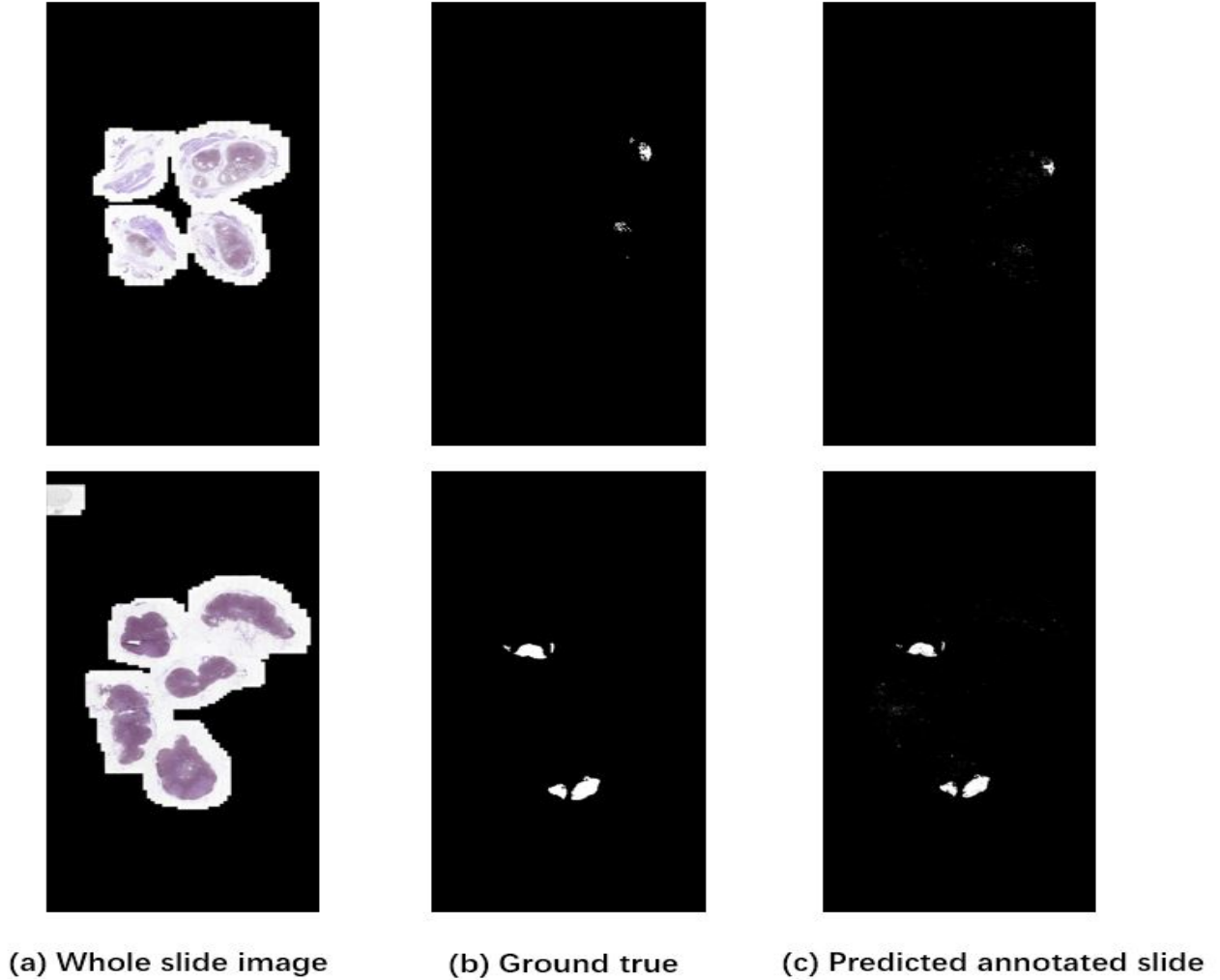
In this section, we introduce fine detection and boosting classification (FDBC) framework as the following components: 1) a path-segmentation method for detecting regions of breast cancer, 2) pathology feature extraction for obtaining reliable and availed features from annotated slides, 3) boosting classification to classify pN-stage by fusing multi classifiers. The specific introduction please see the following chapter.

### 2.1. Detection of Cancer Regions

We detect the cancer regions from a typical whole-slide image which is approximately 200000 x 100000 pixels. In contrast,

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**Fig. 1.** Examples of (a) whole slide image, (b) ground true which is given as annotated slide, (c) predicted annotated slide which is given by the path-segmentation method.

the regions of breast tumor are small and irregular pathes, so there would be misleading judgments for breast tumor regions if we use a typical detection network with bounding boxes. To detect the edge region more finely, we use the pixel-level segmentation method to obtain the tumor region with incomplete edge. However, since the whole-slide images are too large to be put into the training network directly, we propose a path-segmentation network to train for the model. For each slide image, we first random crop a path with  $256 \times 256$  and crop the corresponding mask. We then determine the mask path whether includes labels of positive examples (stand for breast tumor) and regard the pathes meeting the above conditions as training samples. Through training by the pathes, we get the model which is able to achieve the classification of non-tumor/tumor at the pixel level.

For training, we propose a path-segmentation method which can select pathes with tumor regions by modifying a

fully convolutional network and then we can obtain the model which can classify non-tumor/tumor at the pixel level. For testing, we use the model to take the segmentation for pathes with sliding window and finally connect all the predicted masks into the final result. In the detection stage, we can get 5 mask for each patient (See Fig. 1).

## 2.2. Pathology Feature Extraction

Feature extraction is an important process for lymph node classifier. According to medical judgment of pathologic lymph node classification, we extract pathology feature such size, coverage and so on of each mask. There are four categories of lymph node metastasis. Macro-metastases is that metastases greater than 2.0 mm. Micro-metastases is that metastases greater than 0.2 mm or more than 200 cells, but smaller than 2.0 mm. ITC is defined as single tumour cells or a cluster of tumour cells smaller than 0.2 mm or less than 200

cells. Negative means mask without any metastases.

### 2.3. Lymph Node Classifier

There are two processes in lymph node classification. The first process is to predict the level of lymph node metastasis through counting the number of positive lymph nodes (i.e. nodes with a metastasis). We use multiple classifier fusion methods to make classification according to pathology features and multiple classifiers include random forest, logistic regression, neural networks, etc. After the first process, we can obtain 5 categories of lymph node metastasis of each patient. Furthermore, cascading decision tree is used to pathologic lymph node classification by determining different situations of 5 categories and we get the final pN-stage of each patient. In artificial neural networks, neuron processing units can represent different objects, such as features, letters, concepts, or some meaningful abstraction patterns. There are three types of processing units in the network: input units, output units, and hidden units. The input unit accepts the signals and data of the external world; the output unit implements the output of the system processing results; the hidden unit is a unit that is located between the input and output units and cannot be observed by the outside of the system. The connection weights between neurons reflect the strength of the connections between cells. The representation and processing of information is reflected in the connection relationships of the network processing units. Artificial neural network is an unprogrammed, adaptable and brain-style information processing. Its essence is to obtain a parallel and distributed information processing function through network transformation and dynamic behavior, and imitate people at different levels and levels. Information processing functions of the brain nervous system.

## 3. EXPERIMENTS

We evaluate our method on Camelyon17 dataset after the model fine-tune on Camelyon16 dataset. Accuracy and kappa of lymph node classifier are used to evaluate the performance. The result shows the effectiveness of our method.

### 3.1. Dataset

**Camelyon17 dataset** is the particular dataset including data on a lesion-level (with detailed annotations of metastases in WSI) and on a patient-level (with a pN-stage label per patient). There are 1000 whole-slide images (WSI) of hematoxylin and 500 patient identities. For data on a lesion-level, lesion-level annotations are also provided for 10 training slides from every medical centre within Camelyon17 (50 annotated slides total). For data on a patient-level, each patient has 5 WSIs with approximately 200000 x 100000 pixels, corresponding to 5 categories of lymph node, and 1 final label with a pN-stage. So we use 50 annotated slides for segmentation training and

**Table 1.** Detection precision of salient regions in saliency maps on Occluded-REID and Partial-REID

METHODS	Accuracy(%)
ResNet-101 + Random Forest	86.00%
ResNet-101 + Logistic regression	85.33%
ResNet-101 + Neural Networks	85.66%
ResNet-101 + Fusion	<b>83.48%</b>

features of 1000 whole-slide images for lymph node classifier.

**Camelyon16 dataset** includes 400 whole-slide images with annotated slides for all its metastasis slides. The WSIs are collected from five different medical centers. We used Camelyon16 dataset for fine-tuning.

### 3.2. Experiment Settings

**Methods for Comparison.** Accuracy and kappa of lymph node classifier are selected to evaluate the performance. Accuracy is described as:

Kappa is described as:

**Parameter Settings.** In the first step, called path-segmentation, we report the results trained on a baseline network, ResNet-101. The network randomly selects patches with  $224 \times 224$  as inputs, which is trained for 80k iterations on Camelyon16 dataset and then for 20k iterations on Camelyon16 dataset. Experiments are conducted with the initial learning rate of  $1e-4$ ,  $batch\ size = 20$ . In the second step, we threshold the confidence map with different thresholds such as 0.8 and 0.9 and extract features. In the final step, we used random forest with the number of trees = 500, support vector machines with kernel = rbf and K nearest neighbors with  $k = 5$  to classification fusion.

### 3.3. Experiment Results

In the experiment, we train ResNet-101 with initial parameters from ImageNet pre-trained model to speed up convergence. We evaluate our method on Camelyon17 validation set with 5-fold cross validation setting. Table shows the result that our method can effectively finish the detection and classification of breast cancer metastases in lymph nodes.

## 4. CONCLUSION

In this paper, we propose a fine detection and boosting classification (FDBC) framework for detection and classification of breast cancer metastases in lymph nodes. We first used a path-segmentation network to do fine detection so that we can get all the annotated slides of each one. Then we extract

pathology features and put them into multi classifiers to classify pN-stage. Experimental results on Camelyon17 validation set show the effectiveness and superiority of the proposed approach.

In the future, we would find more effective and more robust features to reach more outstanding classification.

## 5. REFERENCES

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