ResNet-50 based Method for Cholangiocarcinoma Identification from Microscopic Hyperspectral Pathology Images

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Abstract. As the second most common primary liver tumour, the early detection of cholangiocarcinoma is very important. Computer-aided diagnosis based on deep learning using pathological tissue images is often used in cancer diagnosis. Compared with traditional RGB pathological images, hyperspectral image has more advantages in deep learning based automatic pathological diagnosis because it contains spectral dimension information. In this paper, a ResNet-50 based method is used to identify cholangiocarcinoma from microscopy hyperspectral images. The microscope hyperspectral choledoch tissue images are captured by our microscopy hyperspectral imaging system (MHIS) and annotated by experienced pathologists manually. After pre-processing and data argumentation, we split them into training set (6800 images) and testing set (210 images) and choose ResNet-50 structure to train the classification model. The classification model can automatically classify the choledich tissue images into cancerous and non-cancerous regions. Our experimental results show that the accuracy of proposed method is 82.4% in case of ResNet-50 structure.

1. Introduction
Cholangiocarcinoma is the second most frequent type of primary liver cancer [1] and the incidence of this fatal disease is increasing worldwide especially in Northeast Thailand. Due to its client clinical character, cholangiocarcinoma is difficult to diagnose and the majority of patients develop symptoms only at an advanced stage [2]. The 5-year survival rate for cholangiocarcinoma is only 35%. As a consequence, cholangiocarcinoma is challenging to prevent and diagnosis. Medical imaging technology plays an important role in the diagnostic method of cholangiocarcinoma. Computerized tomography (CT) [3] and magnetic resonance imaging (MRI) [1] are both commonly used to detect the primary tumour. However, these non-invasive imaging methods sometimes are limited in the early detection. For more accurate evaluation, pathological examination is required [2].
Histopathological examination is regarded as the ‘gold standard’ for tumour diagnosis and therapy. It is performed by pathologist with light microscope acquiring professional knowledge and plenty of time in tradition. With the fast development of computer-aided diagnosis (CAD) and artificial intelligence, automatic classification of histopathological images has become more and more significant. Some studies on pathological images have got high accuracy. [4] [5] These studies utilize 2D images has limitation to some extent. In order to acquire more information of the histopathological slide image, hyperspectral image is considered.

Hyperspectral Imaging (HSI), integrated conventional imaging and spectroscopy, is a new type of medical image processing technology. Hyperspectral imaging technology develops from remote sensing imaging and has made important application in precision agriculture [6] and food industry [7], as well as in medical. HSI contains two dimensions of spatial information and hundreds of contiguous spectral bands which can discriminate subtle spectral characteristics. Different components and structures are diversified in absorption and reflection spectral [8]. Therefore, the advantages of HSI make it possible to be applied in medical field, especially the cancer related analysis.

In this paper, a method of cholangiocarcinoma classification is proposed based on deep learning using hyperspectral pathological choledoch tissue images. We use a microscopy hyperspectral imaging system to capture hyperspectral images of choledoch tissues stained with HE (hematoxylin and eosin), which would be labelled by experienced pathologists and pre-processed before classification. ResNet-50 model is then used to automatically classify the images into benign (non-cancerous) and malignant (cancerous) and well experiments results of cholangiocarcinoma classification are achieved.

2. Material and Method
In this section, we will introduce our proposed classification method for cholangiocarcinoma which can be illustrated in figure 1 and the method is described in detail in the following sections.

![Figure 1. Classification Method Architecture.](image)

2.1. Hyperspectral Images Acquisition
To acquire the hyperspectral images of choledoth tissue, a microscopy hyperspectral imaging system (MHIS) is used. The MHIS consists of six parts, including a microscope, a radiofrequency driver model AOFT controller, an AOTF adapter, a CCD camera, a data collection and control module, and personal computer software and hardware. [9, 10] With the wavelength switching from 550nm to 1000nm by AOTF, CCD captures different single band images, which includes two dimensions of spatial information and one dimension of spectral information. The hyperspectral image data is stored in the stored in band sequential file format (BSQ) and can be visualized as a data cube shown in figure 2(a). Each hyperspectral image consists of 60 bands with each wavelength band 1024*1280 pixels.
Figure 2(b) is the spectral curve of one sample point. It indicates that different components of the tissue have different reflectance and transmittance.

![Figure 2](image.png)

**Figure 2.** (a) Hyperspectral image cube module with 60 bands. (b) The spectral curve of a point.

### 2.2. Preprocessing

Because of the existing constraints in data acquisition, including the emission spectral caused by illumination sources, the microscope optics’ transmission and the CCD’s detection sensitivity, the original images have noise and cannot be used for classification. Normalization in spectral domain need to be performed on the raw data.

Spectral-domain normalization can realize the spectral response calibration and obtain relative transmittance. In order to implement the spectral normalization, a blank reference region is also collected when collecting each slide region. The process is defined in equation (1):

\[
H_{n}^{\text{out}} = \frac{\text{float}(I_{n}^{\text{sample}})}{\text{float}(I_{n}^{\text{blank}})}
\]

where \(n\) indicates the \(n\)’s wavelength of the HSI and \(H_{n}^{\text{out}}\) is the spectral value of the \(n\)th wavelength output image after normalization. \(I_{n}^{\text{sample}}\) and \(I_{n}^{\text{blank}}\) are respectively the value of original image data and its corresponding blank region data. Figure 3(b) is the spectral normalization image of figure 3(a).

![Figure 3](image.png)

**Figure 3.** (a) Original image. (b) The result of spectral normalization.

Data augmentation is usually required to achieve high results in medical image process. As a consequence, we crop the original images. At the same time, we and choose the first 30 bands data because the poor quality of the last 30 bands affected by noise may cause drawbacks. To yield better performance, we split the dataset into training dataset and testing dataset with no overlap.

### 2.3. Data Classification Module

Nowadays, with the improvement of computer hardware, deep learning has progressed rapidly and producing efficient result in handing mass data such as sound and images. For image classification tasks, the advance in deep learning is inspiring.

Convolutional Neural Network (CNN), one of the representative algorithms in deep learning, is a feedforward neural network to learn different image features in both low level and high level. Based on CNN, different types of network has been proposed, such as AlexNet, VGG and U-net. By increasing the depth of the neural network, CNN are able to learn more features. However, increasing the depth of the network will lead to the disappearance and degradation of the gradient. In order to solve this problem and simplify the training network, deep residual learning was proposed by Kaiming
He et al. in 2016 [11]. Although the depth of ResNet is up to 152 layers, the complexity is still lower than VGG nets and the accuracy of ResNet increases considerably.

By introducing a ‘Residual block’ shown in figure 4, ResNet adds the output data from previous layer to the next making the gradient propagate lossless. In the basic block of ResNet, when the dimension of x is different from F(x) the size of x will be adjusted by padding of max-polling. Compared with the traditional CNN, ResNet can still maintain stability with more layers [11].

In this paper, we utilize ResNet-50 model to extract the feature of hyperspectral choledoch tissue images. The module of ResNet-50 is shown in figure 5 and the parameter of ResNet 50 is shown in table 1. Entire ResNet-50 module consists of 5 stages, including 49 convolution layers and one fully connected layer. Before the final output of the module, a linear layer called Softmax layer [12] is used to map the 1000 dimension vectors to a length 2 vector of values. The output classification result depends on the higher probability value.

![Figure 4. The Basic Block of Resnet.](image)

![Figure 5. The block diagram of ResNet-50.](image)

### Table 1. Network parameters

| Layer Name | Output Size | Net Size |
|------------|-------------|----------|
| Stage 1    | 112×112     | 7×7, 64, stride 2, 3×3, Max Pool, stride 2 |
| Stage 2    | 56×56       | [1×1, 64] 3×3, stride 3, [1×1, 256] 1×1, 256 |
|            |             | [3×3, 128] 1×1, 512 |
| Stage 3    | 28×28       | [1×1, 256] 3×3, 256, stride 4, 1×1, 1024 |
| Stage 4    | 14×14       | [1×1, 512] 3×3, 512, stride 6, 1×1, 2048 |
| Stage 5    | 7×7         | Average Pool, 1000-d FC |

### 2.4. Evaluation

To evaluate the performance of the classification method, confusion matrix is used. In binary classification, there are only two categories represent as positive (cancerous) and negative (non-cancerous) and the confusion matrix is defined in table 2.

### Table 2. Confusion matrix of binary classification.

| Label/Predict | Positive | Negative |
|---------------|----------|----------|
| Positive      |          |          |
| Negative      |          |          |
Positive True Positive (TP) False Negative (FN)
Negative False Positive (FP) True Negative (TN)

Accuracy, recall and precision are defined in the following equations:

\[
\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN}
\]

(2)

\[
\text{Recall} = \frac{TP}{TP + FP}
\]

(3)

\[
\text{Precision} = \frac{TP}{TP + FN}
\]

(4)

In this classification task, we tend to improve recall first because it is far more serious to missing cancerous areas than mistaking non-cancerous areas as cancerous areas. Receive operating characteristic curve (ROC) is used to measure the trade-off between recall and false positive rate. Area Under Curve (AUC) is defined as the area enclosed by coordinate axis under ROC curve and the closer the AUC is to 1.0, the higher accuracy of the model is.

3. Experiments and results

3.1. Experiments

The method of cholangiocarcinoma classification is divided into four steps: collecting hyperspectral microscope images of choledoch tissue slide, image pre-processing, ResNet module training and module evaluation.

Step1: Collecting HSI images of pathology choledoch tissue stained with H&E by HSMI system. As the base of our task, these hyperspectral data play an important role to our method. We collected hyperspectral images under 20x magnification choosing 60 bands of wavelength from 5500 to 1000nm with resolution of 6nm on average. The size of the images is 1024*1280*60.

Step2: Pre-processing the hyperspectral images by spectral normalization and data augmentation. We extended our dataset to 6000 images by cropping and the size of images in our dataset is 512*640*30 now. Then we split the dataset into training set (3350 images labelled as ‘negative ‘and 3492 images labelled as ‘positive’) and testing set (100 images labelled as ‘negative ‘and 110 images labelled as ‘positive’) without overlap.

Step3: Setting up deep learning module by ResNet-50 architecture and training the module for classification of cholangiocarcinoma. The module used open source library named PyTorch developed by Python programming language and run on Graphical Processing Unit (GPU). The number of epochs, batch size and learning rate were set to be 100, 4 and 0.001 respectively.

Step4: Classification on Testing set. To evaluate the final result of our method, we put the testing dataset into the model for classification.

3.2. Classification Results

The classification result on the test dataset is shown below. Table 3 illustrates the confusion matrix of the test dataset and table 4 shows the performance of positive and negative samples respectively. The accuracy of our method achieves 82.4%.

| Label/Predict | Positive | Negative |
|---------------|----------|----------|
| Positive      | 106      | 4        |
| Negative      | 33       | 67       |

| Label/Performance | Recall | Precision | Accuracy |
|------------------|--------|-----------|----------|
| Negative         | 0.670  | 0.944     | 0.824    |
| Positive         | 0.964  | 0.763     |          |

The ROC curves of the method illustrated in figure 6 and the AUC reached up to 0.9222.
4. Conclusions

In this study, we demonstrated a classification method of cholangiocarcinoma based on the hyperspectral pathology choledoch images with accuracy more than 82%. Hyperspectral images provide more information of the pathology tissue than normal images for our method. Benefit from the residual block with shortcut, the deep learning module could have more layers without gradient degradation.

Nevertheless, there still remains many limitations in our study. The classification of cholangiocarcinoma subtype and the detection of the precision positions of tumour region need to be realized in the further research to help doctors automatically diagnose cholangiocarcinoma. The rich information of hyperspectral image is conducive to the feature extract of pathology tissue, but there are still many researches needed to be done for hyperspectral images used in clinic diagnosis.

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References

[1] A. Forner, G. Vidili, M. Rengo, L. Bujanda, M. Ponz-Sarvise, and A. Lamarca, "Clinical presentation, diagnosis and staging of cholangiocarcinoma," (in English), Liver Int., Review vol. 39, pp. 98-107, May 2019, doi: 10.1111/liv.14086.

[2] B. Blechacz, M. Komuta, T. Roskams, and G. J. Gores, "Clinical diagnosis and staging of cholangiocarcinoma," Nat Rev Gastroenterol Hepatol, vol. 8, no. 9, pp. 512-22, Aug 2 2011, doi: 10.1038/nrgastro.2011.131.

[3] A. D. Baheti et al., "Correlation of CT patterns of primary intrahepatic cholangiocarcinoma at the time of presentation with the metastatic spread and clinical outcomes: retrospective study of 92 patients," Abdom Imaging, vol. 39, no. 6, pp. 1193-201, Dec 2014, doi: 10.1007/s00261-014-0167-0.

[4] P. J. Sudharshan, C. Petitjean, F. Spanhol, L. E. Oliveira, L. Heutte, and P. Honeine, "Multiple instance learning for histopathological breast cancer image classification," Expert Systems with Applications, vol. 117, pp. 103-111, 2019, doi: 10.1016/j.eswa.2018.09.049.

[5] J. N. Kather et al., "Deep learning can predict microsatellite instability directly from histology in gastrointestinal cancer," Nat Med, vol. 25, no. 7, pp. 1054-1056, Jul 2019, doi: 10.1038/s41591-019-0462-y.

[6] M. Zovko, U. Žibrat, M. Knapič, M. B. Kovačić, and D. Romić, "Hyperspectral remote sensing of grapevine drought stress," Precision Agriculture, vol. 20, no. 2, pp. 335-347, 2019, doi: 10.1007/s11119-019-09640-2.

[7] H. Jiang, W. Wang, H. Zhuang, S.-C. Yoon, Y. Yang, and X. Zhao, "Hyperspectral imaging for a rapid detection and visualization of duck meat adulteration in beef," Food Analytical Methods, vol. 12, no. 10, pp. 2205-2215, Oct 2019, doi: 10.1007/s12161-019-01577-6.
[8] M. Zhang, W. Li, and Q. Du, "Diverse Region-Based CNN for Hyperspectral Image Classification," *IEEE Trans Image Process*, vol. 27, no. 6, pp. 2623-2634, Jun 2018, doi: 10.1109/TIP.2018.2809606.

[9] Q. Li, X. He, Y. Wang, H. Liu, D. Xu, and F. Guo, "Review of spectral imaging technology in biomedical engineering: achievements and challenges," *J Biomed Opt*, vol. 18, no. 10, p. 100901, Oct 2013, doi: 10.1117/1.JBO.18.10.100901.

[10] G. Yunfeng, Z. Mei, L. Qingli, L. Hongying, and Z. Yang, *AOTF based molecular hyperspectral imaging system and its image pre-processing method* (2015 8th International Conference on Biomedical Engineering and Informatics). 2015, pp. 14-18.

[11] K. He, X. Zhang, S. Ren, and J. Sun, "Deep Residual Learning for Image Recognition," in *IEEE Conference on Computer Vision & Pattern Recognition*, 2016.

[12] W. Liu, Y. Wen, Z. Yu, and M. Yang, "Large-margin softmax loss for convolutional neural networks," presented at the Proceedings of the 33rd International Conference on International Conference on Machine Learning - Volume 48, New York, NY, USA, 2016.