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Effect of amplitude-envelope statistics of each region of interest on CNN classification of liver fibrosis stages of ultrasonic B-mode images

超音波画像の CNN による肝線維化ステージの分類における各解析領域の振幅統計量の影響

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1. Introduction

The progression and therapeutic effect of diffuse liver disease can be evaluated by the quantitative estimation of liver fibrosis. However, there are some problems in diagnostic methods; the invasiveness of liver biopsy, the effect of statistical fluctuations on statistical analysis of ultrasound echo envelope amplitude[1], and the effect of steatosis and inflammation on ultrasound elastography[2]. Therefore, a method for the quantitative estimation of liver fibrosis with non-invasive and high accuracy is desired.

In this study, the classification of liver fibrosis stages using a convolutional neural network (CNN) has been studied. In the CNN, position information and brightness (amplitude) information in each pixel can be concurrently used for analysis. Moreover, diagnostic accuracy and robustness can be potentially improved by learning a large number of images. However, ultrasound B-mode images contains also pixel information such as speckles, artifacts, and gradients of brightness due to beamforming and attenuation, other than pixel information directly related to the acoustic characteristics of the fibrous tissue. In this report, a basic study on the relationship between the statistic of echo envelope amplitude, which is known to change with the progress of liver fibrosis, and the accuracy of CNN classification of liver fibrosis stages is described.

2. CNN image classification

The CNN is a deep learning algorithm, consists of a number of convolutional layers, pooling layers and fully connected layers. In this study, the CNN for classification of liver fibrosis stages is created by the transfer learning of VGG-16, which is a pretrained CNN, in MATLAB Deep Learning Toolbox. For the transfer learning, the last fully connected layer of VGG-16 was replaced for classification of the Metavir score F0 to F4, as illustrated in **Fig. 1**. Weights of the replaced layer were initialized with random numbers. In the transfer learning, only 3 fully connected layers were trained by using the stochastic gradient descent.

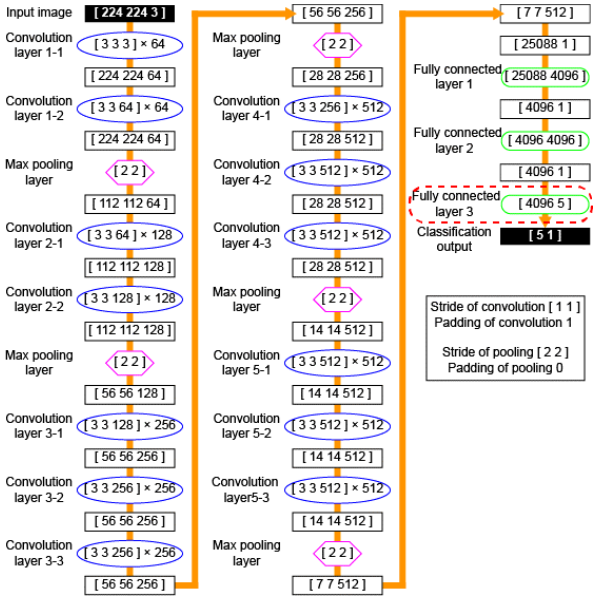

Fig. 1 Architecture of the pre-trained CNN model VGG-16 for transfer learning.

3. Dataset of clinical ultrasound images

A total of 101 ultrasound images with hepatitis B virus and hepatitis C virus infections is acquired at Chang Gung Memorial Hospital, Taiwan. The clinical ultrasound scanner (Model3000, Terason) equipped with the convex array probe (Model5C2A, Terason) was used to acquire raw echo data. The center frequency of the transmitted ultrasound and the sampling frequency of the echo data are 3.5 and 30 MHz, respectively. The liver fibrosis stage is assessed by liver biopsy; normal (F0), early to severe fibrosis (F1-F3), and cirrhosis (F4).

4. Creation of region of interest

To create the region of interest (ROI) as the input image for CNN, raw echo data after the manual segmentation of the liver were normalized. For the normalization of the pixel, the root mean square (RMS) in the region that is centering on the pixel and

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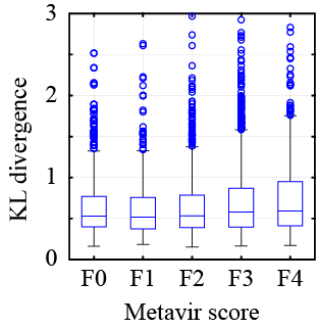

Fig. 2 KLD of PDFs of all ROIs between the Rayleigh distribution.

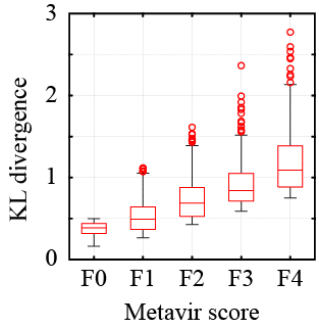

Fig. 3 KLD of PDFs of the ROIs, whose KLD increase with fibrosis, between the Rayleigh distribution.

9 (3×3) times as large as the spatial resolution (1.9 mm×2.4 mm) of the ultrasound image is estimated. Then, the pixel amplitude is divided by the RMS around the pixel. However, the pixel, whose amplitude is 3 times larger than the RMS, is removed from the normalized image and the estimation of other RMSs because the echo is regarded not to associate the normal tissue or the fibrous tissue. The region of 10 mm square where extrahepatic pixels or the removed pixels are less than 1 % is extracted as the ROI. The overlapping of the adjacent ROIs is permitted less than 50 %.

5. Statistics of region of interest

In the ultrasound image of a normal liver, the probability density distribution (PDF) of pixel amplitudes can be approximated by a Rayleigh distribution. Then, the PDF of a fibrotic liver deviates from the Rayleigh distribution with the progression of fibrosis. Therefore, Kullback-Leibler divergence (KLD) of PDFs of all ROIs between the Rayleigh distribution are estimated, as illustrated in **Fig. 2**. Averages of KLD in each stage and those in each ultrasound image obviously increase with the Metavir score. However, there are also the large-KLD ROIs of F0 and the small-KLD ROIs of F4.

In this report, the ROIs, whose KLD increase with fibrosis, are selected, as illustrated in **Fig. 3**. Then, CNN classification is conducted to study the relationship between KLD of ROIs and classification accuracy. For comparison, the ROIs, whose KLD are unchanged, are also selected, as illustrated in **Fig. 4**.

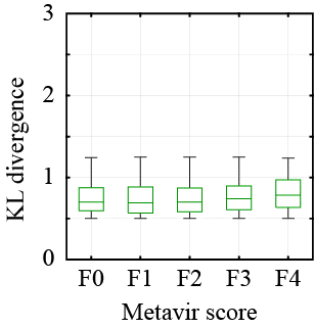

Fig. 4 KLD of PDFs of the ROIs, whose KLD are unchanged, between the Rayleigh distribution.

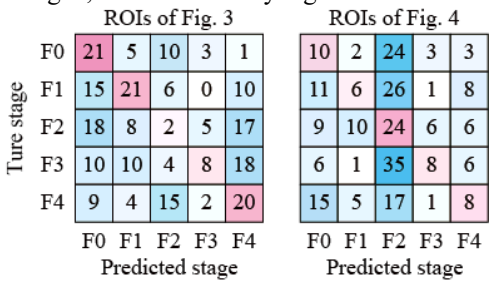

Fig. 5 Confusion matrix by CNN classification of liver fibrosis stages using the selected ROIs.

ROIs in **Figs 3, 4** are extracted from almost the same ultrasound images.

6. CNN classification

The transfer learning of VGG-16 using the KLD-increase ROIs and the unchanged ROIs were conducted. In the former case, numbers of training data and validation data were 1024 and 242. In the latter case, numbers of them were 1024 and 251. In both cases, the mini-batch size and the learning rate were 64 and 0.001, respectively. The training epochs of 6 and 10, ones just before overfitting, were used.

The confusion matrix by CNN classification of liver fibrosis stages is illustrated in **Fig. 5**. In the case of the KLD-increase ROIs, predictions of F2 and F3 are inaccurate. However, most low-KLD ROIs and high-KLD ROIs of F2 and F3 are predicted as F0 and F4, respectively. The total accuracy is 29.8%. In the case of the KLD-unchanged ROIs, the total accuracy is 22.3%. However, most ROIs are predicted as F2.

7. Conclusion

In this report, the effect of KLD of the ROIs on CNN classification of liver fibrosis stages is studied. In the case of the transfer learning of VGG-16 with a small amount of training data, liver fibrosis stages can be possibility classified by KLD.

Acknowledgment

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References

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