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Artificial Intelligence

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[AP2-E2-4-04] Clinical Assessment of Artificial Intelligence Model for Leukocyte Classification in Peripheral Blood Smear Screening

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Keywords: Artificial Intelligence, Convolutional Neural Network, Hematological Morphology, Leukocyte Classification

Medical Artificial Intelligence (AI) is a next-generation medical technology that presents a diagnosis based on EBM regardless of the experience of clinical laboratory technologists. The technology is characterized by learning large amounts of patient data diagnosed by experts based on years of experience. In this study, we examined the clinical usefulness of screening technology with AI for peripheral leukocyte classification. The subjects were 57 healthy person's peripheral blood smears performed MG staining. The first convolutional neural network (CNN) model performed transfer learning with background trimmed training images of mature leukocyte cells that show typical morphology, and parameter tuning for optimization was performed. Then, we performed additional learning and fine-tuning on first CNN model with leukocyte images which include background cells, and the second CNN model was created. As a result of clinical data evaluation, the accuracy of five classification showed 0.990 and six classification showed 0.822 respectively in the first CNN model with background-less images. Contrast, the accuracy of five classification showed 0.992 and six classification showed 0.879 respectively in the second CNN model with leukocyte images which include background cells. It was cleared that the mature leukocyte cell morphology screening with CNN was highly accurate and useful. However, it is necessary to examine further the cutoff value and the judgement pending condition for the boundary area cells in the clinical application.

Clinical Assessment of Artificial Intelligence Model for Leukocyte Classification in Peripheral Blood Smear Screening

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Abstract

Medical Artificial Intelligence (AI) is a next-generation medical technology that presents a diagnosis based on EBM regardless of the experience of clinical laboratory technologists. The technology is characterized by learning large amounts of patient data diagnosed by experts based on years of experience. In this study, we examined the clinical usefulness of screening technology with AI for peripheral leukocyte classification. The subjects were 57 healthy person's peripheral blood smears performed MG staining. The first convolution neural network (CNN) model was performed transfer learning with training data set which is composed of original mature leukocyte images that show typical morphology, and parameter tuning for optimization was also performed. The second CNN model was performed transfer learning with training data set which is composed of mature leukocyte images trimmed from the original images, furthermore additional learning and fine-tuning with original mature leukocyte images not deleted background cells. As a result of clinical data evaluation, the accuracy of five classification showed 0.990 and six classification showed 0.822 respectively in the first CNN model. Contrast, the accuracy of five classification showed 0.992 and six classification showed 0.879 respectively in the second CNN model. It was cleared that the mature leukocyte cell morphology screening with CNN model was highly accurate and useful in hematological CBC test. However, it is necessary to examine further the cutoff value and the judgement pending condition for the boundary area cells in the clinical application.

Keywords:

Artificial Intelligence, Convolutional Neural Network, Hematological Morphology, Leukocyte Classification

Introduction

AI is rapidly developing as an automation technology based on human thought process. AI is a technology in which a computer performs intellectual actions such as language understanding, reasoning, and problem solving. In the medical field, AI technology research is underway to assist diagnostic specialists in fields such as radiological image diagnosis, pathological image diagnosis, and endoscopic image diagnosis. While many efforts have been started in medical image diagnosis, there are few research reports using AI technology in blood morphological diagnosis which also requires morphological analysis. Even today, abnormal leukocytes and immature cells are detected by performing leukocyte classification under a microscope on peripheral blood smears and bone marrow smear smears in blood morphology examination. Then, hematologists have diagnosed leukemia, lymphoma, and myelodysplastic syndrome based on the results of white blood cell classification. However, hematologists or clinical laboratory technologists require a long training period for the skill of white blood cell classification technology. Therefore, the practical application of automatic diagnosis technology is strongly desired. New morphological analysis technologies with AI are also expected in the diagnosis of blood diseases. Therefore, in this study, we studied peripheral blood leukocyte classification screening technology with CNN as blood cell morphology analysis technology.

Materials and Methods

Materials

1. Training Images

The subjects were 40 healthy adults. A thin-layer blood smear was prepared from peripheral blood supplemented with EDTA-2Na and stained with May-Grünwald-Giemsa (MG). The MG-stained specimen was observed under a microscope using an objective 100x oil immersion lens, and typical normal leukocyte images were photographed with a microscope color camera (Axiocam ERc5s, Carl Zeiss). A database of 1335 typical normal leukocyte images was created.

2. Test Images

The subjects were 57 adults. A thin-layer blood smear was prepared from peripheral blood supplemented with EDTA-2Na and stained with MG. The MG-stained specimen was observed under a micro-scope using an objective 100x oil immersion lens, and leukocyte color images (200 cells each) were photographed with a microscope camera (Axiocam ERc5s, Carl Zeiss).

Training Dataset for CNN model creation

Leukocyte images were classified into six categories: rod-shaped neutrophils (Band), segmental nucleus neutrophils (Segment), eosinophils (Eosino), basophils (Baso), monocytes (Mono), and lymphocytes (Lymph). The image of each cell group was trimmed at 750×750 pixels. Two types of dataset were created, one is image dataset “DB1” in which background cells such as erythrocytes and platelets were deleted and only leukocytes were trimmed, and the other is original

image dataset "DB2" with leukocytes and background cells. Augmentation processing was performed to increase the number of original data. Total of 2982 images were created in each data set (500 images for Band, 500 images for Segment, 462 images for Eosino, 520 images for Baso, 500 images for Mono, and 500 images for Lymph).

Image analysis with CNN

Nnabla (SONY) was used as the deep learning library, and Anaconda3.0 and Python3.5 were used as the development environment. The hardware used Intel(R) Core (TM) i7-8700 3.2GHz for CPU, NVIDIA GeForce GTX 1070 8GB for GPU, and Microsoft Windows 10 professional for OS. Low resolution images (3RGB, 480 × 480 pixels) as training image data set were generated from each training data set. The first CNN "Model A" was performed transfer learning with DB2. The second CNN "Model B" was performed additional learning and fine-tuning with DB2 to the pre-trained DB1 CNN model. These two types of CNN model were applied for clinical assessment.

Results

No divergence occurred both TRAINING ERROR curve and VALIDATION ERROR curve in each CNN model training, and both the VALIDATION ERROR curve and the COST function curve finally converged to less than 0.1.

Five Classification with CNN model

The accuracy of five classification showed 0.990 ± 0.011 (Mean $\pm$ SD) with Model A, and 0.992 ± 0.008 (Mean $\pm$ SD) with Model B (Figure 1).

Six Classification with CNN model

The accuracy of five classification showed 0.822 ± 0.062 (Mean $\pm$ SD) with Model A, and 0.879 ± 0.039(Mean $\pm$ SD) with Model B (Figure 1).

Statistical analysis

The evaluation results in all 57 cases improved accuracy 0.002 in the five classification and 0.057 in the six classification between the CNN model A and the CNN model B. As a result of statistical analysis, no significant difference was showed in the five classification ($p=0.473$), and a significant difference was showed in the six classification ($p<.001$) (Figure 1). The cell group with the highest improvement in accuracy was Segment, which improved accuracy 0.111 (Table 1). Figure 2 shows an example of misclassified leukocytes. No common morphological tendencies such as cytoplasmic shape and nuclear shape were recognized in the misclassified leukocytes.

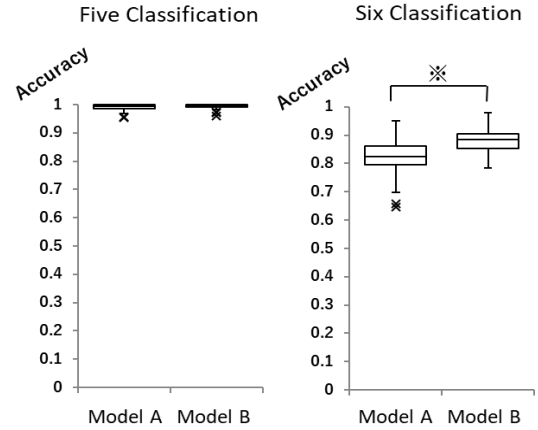

Figure 1- Accuracy of classification with CNN model analysis

Table 1- Classification accuracy rate of each cell group

Model A	Baso	Eosino	Lymph	Mono	Neutro (Band)	Neutro (Segment)	Accuracy
Baso	116						1.000
Eosino		246					1.000
Lymph			3179	34			0.989
Mono			61	579			0.905
Neutro (Band)	1		1		849	80	0.912
Neutro (Segment)	13		2		1812	4176	0.696
Total							0.822

Model B	Baso	Eosino	Lymph	Mono	Neutro (Band)	Neutro (Segment)	Accuracy
Baso	116						1.000
Eosino		246					1.000
Lymph			3184	29			0.991
Mono		1	43	596			0.931
Neutro (Band)	3				810	118	0.870
Neutro (Segment)	6	1		1	1152	4843	0.807
Total							0.879

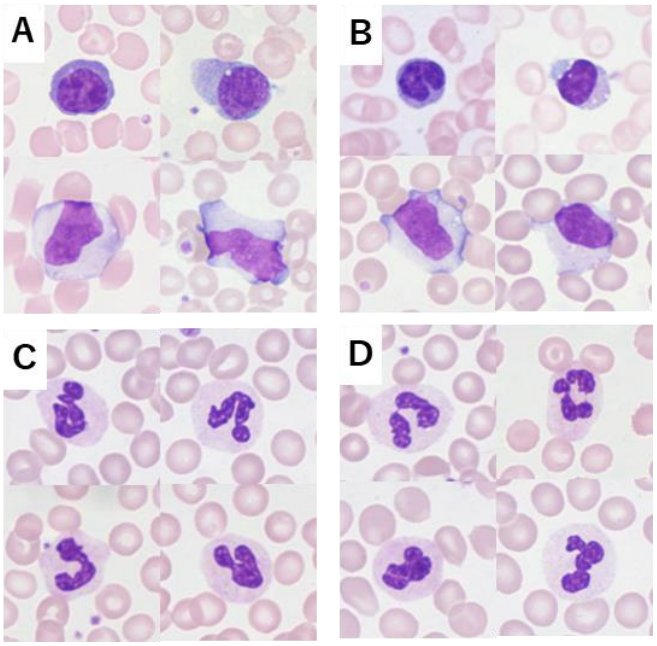

Figure 2. Misclassified cells
A: Lymph→Mono B: Mono→Lymph
C: Band→Segment D: Segment→Band

Conclusion

It was cleared that the mature leukocyte cell morphology screening with CNN model was highly accurate and useful in hematological CBC test. However, it is necessary to examine further the cutoff value and the judgement pending condition for the boundary area cells in the clinical application.

Acknowledgments

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