Multi-class analysis of urinary particles based on deep learning

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Abstract

Abstract Aim: Traditional artificial microscopic technologies cannot meet the current demands of automated urine detection. Furthermore, the number of cell types detected in previous studies was relatively limited; therefore, previous studies are considered to be insufficient. Methods: The present study proposes a multi-class detection method of urinary particles based on deep learning. First, we obtained an image database containing 15 types of cellular components, i.e., normal, shrinking, glomerular, and abnormal erythrocytes; leukocytes; calcium oxalate, uric acid, other types of crystals; particle and transparent casts; epithelial cells; low-transitional epithelium; Candida; Bacillus; and abnormal epithelium. The image data was then input into Resnet50 basic network and feature pyramid network (FPN) to obtain a multi-layer feature map. Thereafter, the classification sub-networks and regression sub-networks were used to classify and locate the cellular components. The network detection model was obtained after training was completed. Results: The experimental data showed that for the test set, the mean average precision (mAP) of the network model reached 82.86%, and the time required to process a single image sample was 195 ms. Therefore, we were able to perform multi-class analysis and detect urine cells with good results in terms of detection speed. Conclusion: This study applies the deep learning network model for the multi-category detection of urine cells. The method can be used to analyze and detect urinary particles in actual clinical practice and has great reference significance for the detection of other cells in the clinic.

1. Introduction

The incidence of kidney diseases has recently undergone considerable changes worldwide. Among these diseases, chronic kidney disease needs to be particularly researched[1]. It is noteworthy that most patients with kidney disease are early patients, having more treatment opportunities than those with advanced renal insufficiency. Regular screening allows patients to receive treatment in a timely manner to prevent and control kidney damage. The analysis and diagnosis of clinical urinary particles are important for screening and preventing kidney as well as related diseases[2,3], because it can provide information about the type and quantities of cells in the urine, which, in turn, can provide a scientific basis for diagnosis by doctors. Therefore, it is crucial to accurately analyze and detect the types and quantities of cells in urinary particles.

Urinary particles are formed from the urinary tract and refer to substances formed by exudation, discharge, shedding, and concentration of crystals in visible form[4]. Common urine cells include erythrocytes, leukocytes, epithelial, casts, crystals, bacteria, fungi, etc.[5,6]. Among them, erythrocytes, casts, and crystals can be subdivided into several types. Depending on the type and number of cells, each component has a clear pathological significance. For example, erythrocytes in normal urine are invisible; however, when they appear in urine, it may indicate pathological bleeding in the urinary system. Common examination methods for urinary particles are microscopy[7], SM staining[8] and morphological examination. Among them, microscopy is the "gold standard" for urine analysis[9] and can accurately detect cells in urine. The SM staining method requires staining of a urine smear, and the detection accuracy is further improved by using microscopy in combination with SM staining. However, the first two methods require manual operation, which is time consuming and labor intensive, and cannot meet the actual needs of clinical tests and the detection of automated urinary particles.

Urine morphological examination detects different cellular components by examining the size and shape of the cells under a microscope. According to different detection algorithms, the method can be roughly divided into two categories: traditional and new object detection algorithms based on artificial neural network. A typical object detection algorithm includes a detection algorithm based on decision tree classifier[10], a support vector machine and template matching (SVM) [11], and an adaptive discrete wavelet entropy energy algorithm[12]. Traditional detection algorithms require the use of steps, such as object segmentation and manual design of feature extractors, and the speed and accuracy of detection need to be improved. With the rise and development of deep learning[13], the object detection algorithm based on artificial neural network has achieved great success. It mainly includes a one-stage target detection algorithm represented by Yolo[14,15] and SSD[16], a two-stage target detection algorithm represented by Faster-RCNN[17,18,19], and various variants derived from these algorithms[20,21]. Compared with traditional recognition algorithms, these algorithms have considerably improved the speed and accuracy of detection.

The object detection algorithm based on deep learning has been applied for the detection of urinary particles; however, the accuracy of detection needs to be further improved. In terms of the speed of detection[22], the author pointed out that the slow detection speed was due to a class imbalance between the object class and the background class. In the online hard example mining algorithm[23], the author increased the weight of the misclassified sample but ignored the easily categorized samples. Therefore, these algorithms have room for improvement in terms of detection speed. Most importantly, fewer cell types have been detected in previous studies due to three main reasons: the detection of multi-class cells is difficult, and it is a huge challenge for network design and parameter adjustment; as the number of categories increases, the confusion between cell categories increases, ultimately affecting the performance of the model; owing to the small size of cells and the large differences in the cell characteristics, character-stabilized, easily identifiable cells have been studied. However, the clinical significance of other categories is also huge and should be considered.

Based on the above discussion, we propose a method for analyzing and detecting urinary particles using multi-class fine classification based on deep learning. Compared with the previous urine object detection method, we have added many other rare but important categories of clinical significance that will not affect the accuracy and speed of detection, allowing quick and easy detection of multiple categories of urine cells and providing doctors with more abundant disease information, which can be of great significance for the clinical examination of urinary particles.

2. Materials and Methods

2.1. Data set and preprocessing. The image data of urinary particles were obtained from the urine samples of 384 patients at the Shenzhen Sixth People's Hospital of Guangdong Province. Before the picture was collected, informed consent was obtained from each patient. The study was approved by the Ethics Review Committee of Shenzhen University. The method of database establishment was simple. An appropriate amount of urine sample was taken into the U-shaped area of the urine smear device (Figure 1a). Then, the U-shaped area with the urine sample was placed into the microscopic imaging system (Figure 1b) for data acquisition. When the magnification of the microscope was too low, the size of the cells in the image was very small, and thus, not conducive to network training and object detection. When the magnification of the microscope was too high, the number of cells in a single image was small and was, thus, again not conducive to the establishment of database. Therefore, we choose a 40× objective lens for data collection. The acquired images (Figure 1c) had a resolution of 1536 × 1024, which are all RGB three-channel color images, in which each sample randomly acquires 20-cell morphology images under a 40-fold objective lens.

We invited three clinically experienced experts to label the cells in the morphological images using the commonly used labeling software LabeImg for deep learning, as shown in Figure 1d. Fifteen different cell types of image data were obtained. We randomly divided the data into training and test sets. The ratio of the number of images in the training and test sets was 7:3. To enhance the robustness of the network model and make it highly generalizable for different test images, we had to enhance the image data. The data enhancement methods used were geometric transformation, adding noise, and changing contrast and brightness. After data enhancement, we could train the data on the network.

2.2. Network model. The RetinaNet network[22]includes one backbone network and two sub-networks. The structure diagram of the network model is shown in Figure 2. The backbone network comprises the resnet and FPN modules[24] that are responsible for feature extraction of the cells and generate many different sizes of the feature maps. On the other hand, the sub-network comprises a classification sub-network and a regression sub-network for the classification and location of objects, respectively.

The FPN network is the core module of the network, and its structure is shown in Figure 3. It mainly comprises two processes: top-up and top-down. In the top-up process, as the network deepens, the spatial dimension is gradually halved, whereas in the top-down path, the corresponding convolutional module layer is output through a 1 × 1 convolution filter and is then added to the upper-level up-sampling (top level exception). Finally, the feature map of each layer is obtained by the convolution of 3 × 3. The FPN network combines multiple layers of feature information to enable the network to better handle small objects like cells.

In the classification sub-network, for each layer of the feature pyramid output in the FPN, a 4-layer 3 × 3 convolution is used, followed by a ReLU activation function, which is then input into a 1-layer 3 × 3 convolution, and the number of convolution kernels is KA(K represents the number of categories. In the experiment, we take K=15, A=9). Finally, the sigmoid activation function is used for category output. The regression sub-network has the same structure as the classification sub-network; however, each uses different parameters.

It is noteworthy that to solve the problem of imbalance between the background class (no object) and the foreground class (including the object) in the one-stage target detection algorithm, the network introduces an optimized loss function, as shown in Equation 1. This loss function adjusts the weight of the easily categorized sample (background class), thus improving the detection speed of the model.

$$\mathrm{FL}\,(\mathrm{Pt}) = -\alpha_t\,(1-\mathrm{Pt})^{\gamma}\log(Pt) \quad (1)$$

Where Pt represents the probability that the category is predicted, αt is a weighting factor between 0 and 1, and γ is a modulation factor that can control the weighting rate of the easily categorized samples. In the experiment, αt was 0.25 and γ was 2.0.

2.3. Model training. After network construction was completed, we normalized the image data of the training set containing 15 types of urine cells and then input them into the network model for training in batches. In the initialization of the network parameters, we use the Gaussian weight initialization method with a standard deviation of 0.01 and bias of 0. In the training parameter setting, we set the momentum to 0.9, weight attenuation to 0.0005, learning rate to 1e-4, and input eight images each time for network training. The model optimization method used was Adam[25]. In the experiment, we used the Keras deep learning model framework to perform network training on a 64-bit Ubuntu 16.04.5 system. The computer had the following configurations: Nvidia 1080 GPU, i7-6600 CPU, and 16G memory deep learning server. We used the training set to iterate the entire model, and after one epoch, we tested the model parameters using the validation set and then saved the best model parameters.

2.4. Model evaluation method. We used mAP, which is commonly used in deep learning, to evaluate the performance of the model. In addition, the time taken by the computer to process a single image was also considered to be an indicator of the evaluation. For a certain type of cells in an image (for example, crystals, replaced by the letter C below), the model could correctly detect the number of C as x and the total number of C as y; the accuracy of category C in this image can be expressed as P, and the average accuracy of n pictures as AP. Using this method, we could calculate the accuracy rates of the 15 types of urine cells (AP1, AP2, ... AP15). mAP is the average of the accuracy rates of all 15 types. It is calculated as follows.

$$p = x/y \quad (2)$$

$$AP = \left(\sum_{t=1}^{n} \mathrm{Pt}\right)/n \quad (3)$$

$$mAP = \left(\sum_{t=1}^{m} \mathrm{APt}\right)/m \quad (4)$$

3. Results

After 50 epoch trainings and a total of 62 hours, we developed a fine classification model having an accuracy of 86.67% on the training set. The accuracy of the test set reached 82.86%, and a good prediction result was obtained. Figure 4a, Figure 4b shows the recognition effect of the image of the urinary particle after the model test. Table 1 lists the average accuracy results for each category of the model. Among them, the crystals class had the highest accuracy of 92.26%, whereas those of abnormal erythrocytes, abnormal epithelial cells, and calcium oxalate crystals were not ideal. We discuss the specific reasons behind this result in the next section.

4. Discussion

Based on the RetinaNet model technology of deep learning, we established a multi-class classification method for the detection of urinary particles. The average accuracy of recognition was 82.86%, and the detection accuracy of a single category was also high. Compared with other methods, our method was able to perform multi-class analysis and detect urine cells. The experimental results showed that the accuracy of recognition is relatively high, with some categories showing better accuracy than others; good results were also achieved in terms of speed performance. However, using experimental data, we found that the recognition effect of some categories was unsatisfactory. Therefore, we discuss the specific factors that affect the accuracy of recognition result through both internal factors and external interference.

In the early stage of model design, the network structure and network parameters are often determined using empirical values. Different network parameter configurations will have different effects on the network model. As shown in Table 2, we discussed the impact of the following four conditions on accuracy: weight initialization method, feature extractor selection, anchor size, and loss function parameter configuration.

The experimental results demonstrated that the accuracy of the model was higher in the COCO weight initialization mode. The experimental results of Resnet50 and Resnet101 basic networks were very close; however, considering the Resnet101 network model is deep and more complex, we chose the Resnet50 basic network. In addition, anchors with a smaller size can help in improving the accuracy of the method. In the parameter selection of loss function, we observed that when αt was 0.25 and γ was 2.0, the effect was better.

Based on the above discussion, we chose a satisfactory model parameter configuration. In addition, medical images are expensive to label, and a lack of pathological samples could result in a lack of sample data in certain categories. However, deep learning is based on multi-dimensional data extraction and analysis of big data. The lack of data could fundamentally affect the accuracy of model testing. In this study, due to insufficient data regarding uric acid crystals, low-transitional epithelium, and abnormal erythrocyte, the recognition accuracies of these types are low, thus affecting the accuracy of the method.

In order to compare with other methods, we compare the optimized model results with two other typical methods. The comparison results are shown in Table 3. The results show that our accuracy rate is higher than the other two methods. This method also has advantages in processing a single image. Therefore, this method is very helpful for the clinical diagnosis and automated detection of urinary particles.

When the focus of the objective lens is not clear, poor image quality could lead to recognition errors or missing recognition. In order to explore this influencing factor, we artificially changed the focus of the objective lens and photographed four sets of images using different sharpness in the same field of view. The acquired image was input into the model for object detection. The detection effect diagram is shown in Figure 5a, Figure 5b, Figure 5c and Figure 5d. As observed in the figure, as the degree of blurring of the image deepens, the situation regarding the leak recognition becomes more serious. Compared with Figure 5a, there is a significant difference in the sharpness of the image, and many category recognition errors appear in Figure 5d. Therefore, beyond a certain range, the quality of the image can also affect the accuracy of recognition.

Similar to focus blur, when the shape of the cell changes (during cell degradation) the data characteristics of the cell change, affecting the accuracy of identification. Therefore, we should conduct timely processing of the

detected sample or perform human interference (such as refrigeration of the sample) to prevent degradation.

Due to the characteristics of easy adhesion between cells, the phenomena of overlap, stacking, and even agglomeration occur, causing leakage recognition of the model and affecting the detection results of the model. As shown in Figure 6a, Figure 6b, due to the stacking of cells, the recognition algorithm treated it as a single cell, whereas others were not recognized. This is a flaw of the method. Thus, the algorithm has more room for improvement and research.

5. Conclusion

This paper proposes a multi-class analysis method for the detection of urinary particles based on deep learning. This method can simply and quickly detect and classify the cells in urine. Compared with other methods, our method can detect more cell types in the urine and provide more effective information for clinical diagnosis. Furthermore, compared with the artificial method, our method allows the automatic inspection of urinary particles, saving manpower, materials, and financial resources. However, in some aspects (such as cell stacking phenomenon), microscopy still has advantages. Therefore, the algorithm needs further improvement. In summary, we offer a new approach for the multi-class clinical examination of urinary particles, and this approach provides a new approach for other types of clinical cell testing.

Data Availability

The authors do not have permission to share data.

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CONFLICTS OF INTEREST

The authors have no relevant conflicts of interest to disclose.

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Tables

TABLE 1: Recognition accuracy of different cell types

Category of the cellular component	Accuracy
Normal erythrocytes	91.55%
Shrinking erythrocytes	82.46%
Glomerular erythrocytes	76.68%
Abnormal erythrocytes	75.32%
Leukocytes	90.13%
Calcium oxalate crystals	76.63%
Uric acid crystals	77.45%
Other types of crystals	92.26%
Particle casts	86.43%
Transparent casts	82.74%
Epithelial cells	90.27%
Low-transitional epithelium	88.17%
Candida	77.51%
Bacillus	78.66%

Category of the cellular component	Accuracy
Abnormal epithelial cells	76.67%

TABLE 2: Impact of different model configuration methods on network performance

Optimization method	Optimization method	mAP	Test time (ms/image)
Weight initialization	Gaussian distribution	0.8142	218
	Xavier	0.8023	209
	KaiMing	0.8169	211
	COCO	0.8248	205
Backbone	Resnet50	0.8275	195
	Resnet101	0.8313	205
	Resnetnet152	0.8166	210
Anchor scales	{642,1282,2562}	0.8014	199
	{1282,2562,5122}	0.7948	195
	{642,1282,2562,5122}	0.8189	210
	{322,642,1282,2562,5122}	0.8256	212
Loss function parameter	$\alpha t = 0.5$, $\lambda = 0.5$	0.7789	220
	$\alpha t = 0.25$, $\lambda = 1.0$	0.7856	212
	$\alpha t = 0.25$, $\lambda = 2.0$	0.8248	218
	$\alpha t = 0.25$, $\lambda = 5.0$	0.7985	210

TABLE 3: Compare results with two typical methods

Methods	mAP	Test time (ms/image)
Faster R-CNN	0.7254	245
YOLO	0.7863	196
Our method	0.8286	192

Legend

FIGURE 1a : The sample slide.

FIGURE 1b : Microscopic image acquisition system.

FIGURE 1c : The original image.

FIGURE 1d : Labeling work interface.

FIGURE 2 : The RetinaNet summarized into three parts: Resnet, FPN, and full convolutional neural (FCN) network. The FCN contains classification and regression subnets, as shown by the processes within the Class + box subnets.

FIGURE 3 : Feature pyramid network (FPN) includes bottom-up and top-down processes. C1–C5 represents convolution module, M2–M5 are the results of FPN up-sampling, and P2–P5 are feature map pyramids of object detection.

FIGURE 4a : Representative detection results of urinary particles using the detection models.

FIGURE 4b : Representative detection results of urinary particles using the detection models.

FIGURE 5a : The original image detection effect diagram.

FIGURE 5b : The image clarities of 6b is lower than 6a.The cell pointed by the red arrow represents leak recognition, and the cells indicated by the green arrows represent recognition errors.

FIGURE 5c : The image clarities of 6c is lower than 6b.The cell pointed by the red arrow represents leak recognition, and the cells indicated by the green arrows represent recognition errors.

FIGURE 5d : The image clarities of 6d is lower than 6c. The cell pointed by the red arrow represents leak recognition, and the cells indicated by the green arrows represent recognition errors.

FIGURE 6a : Cell stacking detection results. The red black arrows show the stacking of normal erythrocytes .

FIGURE 6b : Cell stacking test detection results. The black arrows show the stacking of oxalate crystals.