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Towards Recognition of Pleural Effusion Images

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***Abstract* — early diagnosis of patients' diseases allows to prescribe effective treatment in a timely manner. This article presents the results of research related to the recognition of images of pleural effusions. The purpose of the research is the recognition of images characteristic of pathologies associated with oncological diseases. When recognizing images, convolutional neural networks were used. When developing software, the authors used the TenzorFlow and OpenCV libraries. Image recognition accuracy is 95%. The studies are incomplete; the authors are trying to improve the results of research by replenishing the training sample with new copies of images of pleural effusions and using combinations of pattern recognition methods.**

***Index Terms* — pleural effusion, convolution neural networks, segmentation, classification**

I. Introduction

Currently the efforts of physicians and other scientists are aimed at research that allows to diagnose cancer in the early stages of it development. Early diagnosis allows physicians to increase the number of patients for whom treatment will help to prolong life and, in some cases, significantly. Perhaps some patients may be completely treated.

It is known that statistics shows a significant increasing of patients diagnosed with cancer. So we may conclude that this paper is relevant.

The syndrome of pleural effusion (PE) refers to a clinical complex of symptoms characterized by fluid accumulation in the pleural cavity in excess of the norm [1]. PV syndrome occurs most often when the pleura itself is involved in the pathological process. This may be the pathology of the chest, lungs, diaphragm, kidney, cardiovascular system, etc. The occurrence of PV is always a sign of an unfavorable course of the disease [10].

In addition, PE is a sign of a large part of each type of pathology separately. For example, the syndrome is diagnosed in 10% of patients with diseases of the pulmonary system.

Diagnosing the disease is a time-consuming process and very often it may not be named successful, in 20% of cases the cause of PE cannot be established [2].

Thus, PE can be a sign of a large range of oncological diseases, therefore, the urgency of the problem of establishing the cause of a pleural effusion in a malignant neoplasm is beyond doubt [1, 3, 4].

It is worth noting that the examination of a patient with PE is a complex and lengthy process and it includes a large number of procedures and tests.

Doctors have proposed a large number of different algorithms to study the causes of pathology, but none of them is optimal due to complexity, resource-intensiveness and a large number of different tests [5].

The most common procedures are: definition of patient history, analysis of effusion dynamics, blood analysis, pleural fluid analysis (PF), analysis using radiation diagnostic methods (X-ray, ultrasound), bronchoscopy, pleural biopsy, etc. [1].

The authors of this paper suggested analyzing cellular images of pleural fluid obtained during pleural puncture. It is assumed that the analysis will speed up the process of identifying the tumor process, but it will also relieve the patient from the often traumatic and painful procedure / operation.

Unfortunately, often the presence of tumor pleurisy in a patient implies that the cancer process has already developed. But early diagnosis, even in this case, can help improve patient survival rates due to an earlier start of treatment.

It should be noted that analyses is carried out by specialists manually, which does not exclude subjectivity and makes it impossible to mass and rapid study of samples.

Thus it is necessary to automate this process.

II. Related Works

The process of image analysis can be performed by various methods, which in turn may include the use of expert opinions. Often the process of image analyses involves several steps: segmentation, selection of markers or features, and classification.

Often an image includes not only one cell, it is necessary to select boundaries of one or several cells. Counting the number of cells has important diagnostic value for many studies in the field of cancer pathologies [6].

Depending on the number and position of the cells, the type and quality of the image, as well as the possibility of post-processing, different segmentation methods can be applied, for example, threshold segmentation ("Thresholding") or fuzzy segmentation algorithm ("Fuzzy c-means").

In addition to the above methods, others can be used: methods of graph theory, methods that use the sign of movement, etc. Often, algorithms containing different segmentation methods are included in various program libraries. For example, the popular Python library, Pillow, implements the threshold segmentation method, thresholding [7].

In order to highlight markers, features one may use such image characteristics as color, texture, size.

Among the classical methods of classification the authors distinguish: discriminant, the support vector machine (SVM) method and the k-nearest neighbor method. In addition, they use boosting algorithms, neural networks, a decision tree, and fuzzy logic methods. In addition, in some cases it is correct to use a multiple classifier that uses different methods [8].

Let us consider methods more precisely.

Because of that fact that an analysis of publications shows that neural networks are most preferable we will consider neural networks. Let us discuss convolutional neural network (CNN) [8].

CNN have a specific architecture and consists of several convolution layers and sub-sampling layers. These layers alternate.

The convolutional neural network has several critical advantages:

- With the architecture of convolutional neural networks it is possible to parallelize computational processes using graphics processors.
- Compared to a fully connected neural network (perceptron), a convolutional neural network has a much smaller number of adjustable weights. This makes it possible to recognize images with a large number of features with weak requirements for technical means.
- The convolutional neural network is sufficiently invariant to a rotations and shifts of the image being recognized.

But it is difficult to choose and adjust parameters of CNN (a number of layers, implementation of each of layer). When developing a network architecture, it is worth considering the specifics of the application area and the requirements put forward to the network[8].

A convolutional neural network, as described earlier, is usually an alternation of convolutional layers, subsampling layers and fully connected layers at the output. All kinds of layers can be included in CNN in random order [9]. Each neuron performs a convolution of a certain area of the previous layer when computing a network.

III. Analysis of Cellular Images of Pleural Fluid

Nowadays despite the continuing growth of interest in medicine to study pleural liquid [10], not many systems have been developed for analyzing pleural effusion. As stated earlier, all the recognition systems that use classical methods of classification are often based on expert opinions of the people in this specific domain of study. However, in contrast to this approach, machine learning methods that do not require prior identification of key features, such as neural networks, can be used. Let us consider one of the most successful systems of recognition of oncological pathologies among cellular images.

In 2016 year a group of scientists from Iran proposed a method for recognizing melanoma cells using the "bottleneck" algorithm, the "watershed" method and the support vector machine method (SVM) [11]. The proposed algorithm is shown below.

The algorithm includes preprocessing steps, image clustering (using the k-means algorithm), image processing algorithms with subsequent selection of marker attributes, and the final classification.

The final step, the classification, is based on signs that have been highlighted with regard to the current knowledge of medicine about cells and oncological cell manifestations.

The best results of the algorithm were the recognition accuracy of cancer pathology equal to 95.28%. Despite the high percentage of classification, the part of the general algorithm responsible for segmentation did not show good results. The reason for this was the fact that the data for analysis were taken by different people in different conditions, the data were not homogeneous. Another disadvantage of this algorithm is its dependence on expert data, which makes it (the algorithm) less adaptable to changes in the nature of the disease.

Another successful example of recognition of oncological diseases in cells is the work of a group of scientists (P. Buissen, A. Elmoataz and O. L-Ezorai) on the use of convolutional neural networks in the process of analyzing cellular images of oncological diseases [12].

We will consider this work in more detail, since the authors analyzed cellular images of pleural fluid.

39000 cell images taken with a Leica SCN400 scanner with a magnification of 40 times were used as a training sample. Images were classified into 6 categories (by the nature of the disease).

At the preprocessing stage, manual cell segmentation was performed, as well as data transformation. Image resolution has changed from 80,000 × 90000 to 80 × 80. Scientists have proposed for classification to use the results of several convolutional neural networks - namely, a multiscale system of convolutional neural networks (multiscale CNN). As internal neural systems, systems of various architectures were used to recognize images with different resolutions.

The best results were achieved when training networks for about 50 epochs and comprised from 80.22% to 99.14% recognition accuracy in each of the 6 categories.

Despite the obvious advantages of the system, namely, high recognition accuracy and complexity of the task, the system is not without flaws. Among them it is possible to single out a high resource cost due to the training of several neural networks and a large number of samples for training.

IV. THE RECOGNTION SYSTEM DESIGN AND IMPLEMENTATION

The data of the recognition system were provided by the Perm State Medical Academy named after Academician Ye.A. Wagner. Data were collected with the consent of patients in the laboratory using a Levenhuk Rainbow 2L microscope. The initial set of data provided consisted of 143 color images in JPG format. All images were divided into 9 categories, each of which was a specific type of pathology:

- Nephrogenic.
- Oncological.
- Pancreatogenic.
- Hepathogenic.
- “After removing the lung”.
- Postpneumonic.
- Posttraumatic.
- Heart failure.
- Tuberculosis

Examples of “healthy” cells of the pleurel liquid (PL) were not used, since the PL sampling should be carried out only with PE, which always indicates pathology. An example of an image with oncological pathology is located below (Fig.1).

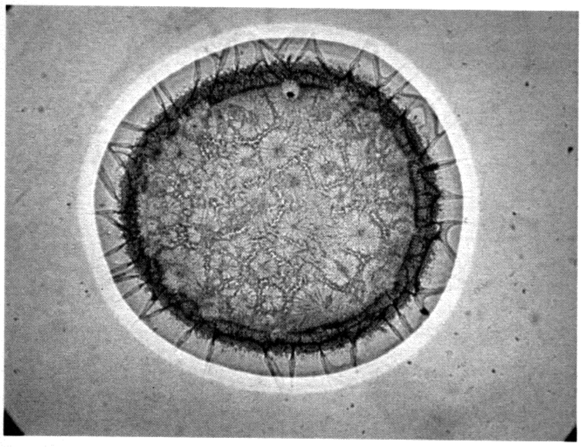

Fig.1. The image of pleural liquid cell with oncology pathology

As a method of recognition, it was decided to use a convolutional neural network. Neural networks in general do not have any limitations to the data when it comes to images. However, it is worth noting that when working with neural networks, special attention should be paid to input data, since this directly affects the learning process and result [8].

The data preprocessing process for recognizing cells of PL includes:

- Manual selection of photos without obvious defects.
- Image conversion to black and white (gray-scale).
- Cleaning images from noise.
- Croping each image along the border of the cell.
- Increasing the number of samples through hard conversion.

The initial set of images contained images of different color scales and images with obvious distortions. Below is an example of a fuzzy image (Fig.2.).

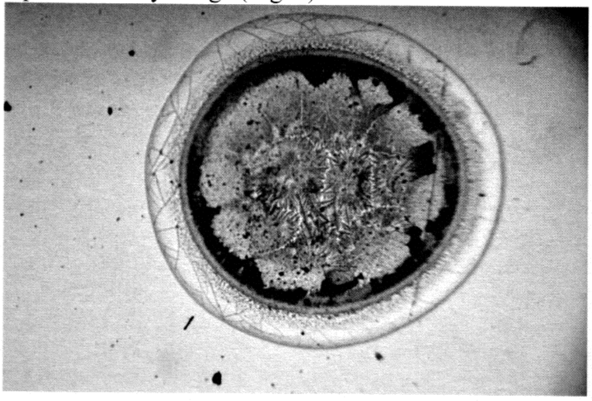

Fig.2. An example of fuzzy image of pleural liquid cell

Images with other defects that may adversely affect the learning process were discovered at the stage of converting images to black and white. Below is an illustration of the transfer to a black and white photo format without defects except for minor noises on the background (Fig. 3):

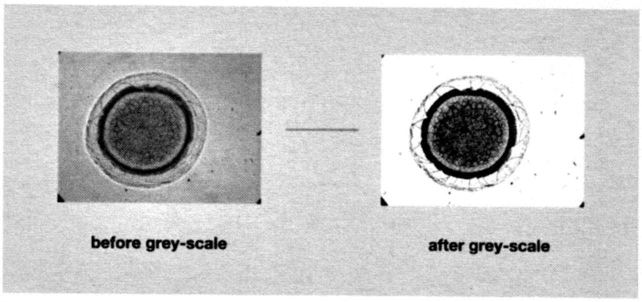

Fig.3. An example of pleural liquid cell image after preprocessing (without defects)

During converting images with defects into black and white format some photos are not suitable for further recognition process (Fig. 4).

All images that could adversely affect the result of the study were excluded from the sample. Thus, after preliminary processing and selection of photographs, the sample size was 111 images.

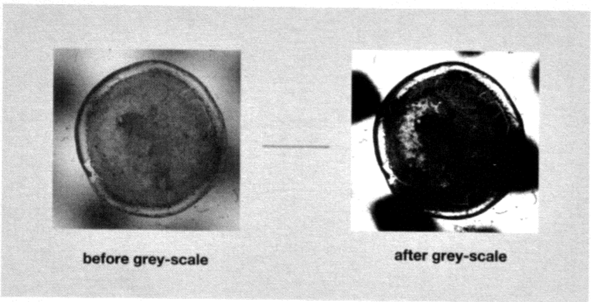

Fig.4. Image after preprocessing with defects

A small number of images does not correctly identify each of 9 classes presented above. Therefore, it was decided to divide the images into two categories: oncological (oncology) and others (others), which include pathologies: hepatogenic, nephrogenic, pancreatogenic, etc.

Thus, the final data set consists of 111 images (JPG format) with the following characteristics:

- The size of the original images range from 1200 × 1000 to 1600 × 1200 pixels.
- The background on the images is mostly homogeneous, however with the presence of defects and "noise".
- Images are divided into two categories: oncology (oncology) and others (others).

V. The Architecture of the Pattern Recognition System

Based on the results of the domain analysis, as well as the requirements for the related systems of pattern recognition, a system consisting of 5 modules was designed: (a) a preprocessing module, (b) a client-server interaction module, (c) a recognition and classification module, (d) a module for processing primary classification results, and (e) a client web module applications

Each module of the system is an independent part of it. It allows developers to improve and modify modules, as well as add new ones, which ensures the scalability of the system. This approach provides a flexible system for setting up and developing application functionality, as well as the possibility of unit testing the system. Let us consider below each module separately:

Client web application module. This is the application interaction module with the user and is a web application with the ability to upload images and display the classification results.

The ReactJS JavaScript library developed by Facebook [35] was chosen as the main technology for the development of this module. The ReactJS architecture has several key advantages:

ES6 was chosen as the standard of the JavaScript language, which is used in most modern projects. It is also supported by most browsers through the use of the Babel plugin, which compiles code to old standards (for example, ES5).

The server part of the system is written entirely in the Python programming language. It is rather popular, including among the scientific community, so there are a large number of libraries for various purposes. The TensorFlow library [14] is used to build the neural network. The computer vision library OpenCV[15] are used to write the auxiliary modules. The preprocessing uses the Pillow library[6].

(b) *Image pre-processing module*. This module is necessary because the input data can be presented with the help of different formats: size, shape, color, contrast, etc. In addition, this module helps to increase the amount of data by rotation of image. Pre-processing of images will be done in several steps, which are aimed at standardizing data, as well as increasing the number of data. In this step, we will use hard transformation methods (for example, rotation) (Fig.5).

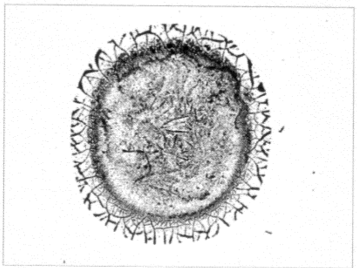

Fig.5. A result of preprocessing module

(c) *Recognition and classification module*. This module is the main one and is a convolutional neural network that classifies images into two classes: oncological pathology and another type of pathology. A pre-processed black and white photographic image with a size of 128 × 128 pixels is fed to the input of the neural network. As a result of the network at the output is obtained a vector of length 2, with the values of the probabilities of belonging to each of the classes.

(d) Result processing module. After the classification process, the array of probabilities received from the neural network module will be converted into a more convenient format for presenting information to the user. JSON (JavaScript Object Notation) was chosen as such a format. It is a textual data format based on the programming language JavaScript.

(e) The module of interaction between the client and the server. This part of the application implements the interaction between the server modules of the system and the client part. It accepts requests from the client and returns the result. At the heart of the interaction of components is the REST architecture.

Advantage of REST: scalability, reliability, performance, simplicity, portability (modularity) of components, etc. REST is well suited for a wide range of tasks.

As a result of the recognition system, the user receives information about the class, the probability of a successful image classification.

VI. Neural Network Architecture Design

As mentioned earlier, the convolutional neural network was chosen as the main tool for recognizing and classifying photographic images of pleural fluid. This choice was made based on the requirements for the system being developed, the specifics of the subject area, and also on the results of data analysis:

When developing the system, it was decided not to rely on the expert opinions of medical experts due to the fact that today, in many cases, a person cannot, with a high degree of probability, identify the type of diseases from a photographic image of a pleural fluid cell.

- Modern convolutional neural networks show excellent results in the classification of raster images [12].
- Convolutional neural networks in the process of their learning themselves build a hierarchy of features ("feature map"), while filtering the least important details and highlighting the most important ones.
- Convolutional neural networks are best of all, in comparison, for example, with fully connected, suitable for classifying images with a large number of signs.

The choice of convolutional neural networks is also supported by the ability of the neural network to find for itself signs, previously unnoticed by humans, important for classification.

As previously described, a convolutional neural network is a special architecture consisting of alternating convolutional layers (convolution layers) and sub-sampling layers (pooling layers). There is a large amount of research on the best architectural solution for CNN, but there is definitely no right solution.

A large number of different architectures of convolutional neural networks are proposed. One of the most popular of convolution networks are, so-called, AlexNet [16]. This architecture was designed by a group of researchers (A. Krizhevsky, D. Hinton and I. Suckevere) and won the 2012 ImageNet international competition. The proposed architecture includes 5 convolutional layers, as well as 2 fully connected layers. Despite the seemingly small amount, the network contains 650 thousand neurons with 60 million parameters. It is necessary a very large sample for it training.

Despite this, the AlexNet network is a vivid example of the success of the application of convolutional neural networks in the classification process and uses architectural solutions that can be used to solve other problems.

In addition to the AlexNet network, networks VGG16 [17], Inception [18] and ResNet50 [19] are among the most recognized and popular. However, these networks are mainly aimed at training with the use of large computing powers, so they will not be considered in detail.

As the first (initial) network architecture, architecture was chosen that was inspired by the AlexNet network, but included several changes:

- The filter size has been reduced to 3 × 3, since the initial image will be limited to the size of 128 × 128 pixels (due to the low computing power).
- In addition, the configuration of the system will change, namely, the depth of convolutional layers and the number of neurons on fully connected layers.
- Added a flat layer (flattened). This layer is necessary to convert a multidimensional array (tensor) into a one-dimensional vector (the specificity of the software implementation).

Thus, the initial network consists of the following components:

- The input is 128 × 128 pixel images.
- The neural network contains 5 consecutive convolutional neural layers. All use filters of 3 × 3 each. In the first two layers, 64 filters are used in each, in the following - 32 filters. In each layer, except the last one, a down sampling layer is used, it carry out the max element selection (max pooling).
- Flattened layer.
- 2 fully connected layers (128 neurons) + RELU function.
- A fully connected output layer (128 neurons). The result is 2 classes.

We denote this architecture variant as "CNN_0".

Let us consider the result of investigations.

Several other architectures where designed. Let us discuss these architectures.

The next version of the architecture included some changes:

- The last layer of the convolution was removed with the assumption that it is possible that the image is rolled up to the size of complex to classification; possible signs are lost [20].
- After the last convolution layer, a sub-sampling layer (max pooling) is added.
- In addition, as variants of the network architecture, variants with different numbers of convolutional and fully connected layers were used.

In the version of the architecture "CNN_2" it was decided to try using 2 fully connected layers.

VII. The Review of Results

According to the results of testing, the best results were achieved using the architecture - "CNN_1. Let us conider this architecture more precisely:

1. So, the network includes several convolutional layers. In addition, each convolutional layer usually includes another down sampling layer or layer of subsampling (pooling), which provides optimization of the network by sifting out the least significant elements. In this layer, the function "max pooling" is used, in which

the maximum cells by value are selected from the feature map. This function was chosen due to the small size of the processed image. As the activation function, the RELU (Rectified Linear Unit) function was used. It is the most popular for use in the framework of convolutional neural networks and has the following advantages:

- Unlike the sigmoid function or the hyperbolic tangent, the RELU function is simple, which accordingly increases the speed of calculations.
- It was found that the RELU function significantly speeds up the convergence of gradient descent (in some cases up to 6 times).

2. Flattened layer. This layer is needed to convert a multidimensional array (tensor) into a one-dimensional vector.
3. Full-connected layer. The layer responsible for the classification of images receives a description of the markers at the input.
4. Output layer. Usually is a full layer layer. An array of values is supplied to the output of a neural network: the probability that an image belongs to a particular class.

The AdamOptimizer function is used as an optimization function (for calculating the gradient and optimizing weights). AdamOptimizer shows some of the best results among optimization features.

Moreover, third (CNN2) and fourth(CNN3) architecture were designed. Neural networks of each of architecture were tested. Let us describe the conditions of testing:

A personal computer MacBook Pro 13 2017 with the configuration: 2.3 GHz Intel Core i5, 8 GB 2133 MHz LPDDR3, Intel Iris Plus Graphics 640 1536 MB was used for testing.

As a training sample, 80% of the images of the initial sample were used.

As a variation sample, 20% of the images of the initial sample were used.

We present the results of investigations below:

Table 1. The results of testing

Architecture	The number of epochs (training)	Precision	Precision
CNN_0	25	87.5%	87.5%
CNN_1	20	95.6%	90%
CNN_2	25	83%	87%
CNN_3	26	82%	94.75%

So we may see, that neural network with the architecture CNN_1 has a best results.

VIII. Conclusion

The result is a designed prototype developed a system for classifying cells of pleural fluid into cells with oncological pathologies and pathologies of another type, Two major problems were identified while developing the system:

First problem is a problem of small amount of data and data quality. Problems related to the quality and amount of data for the samples are common, especially, in such specific areas as medicine. Often it may be decided by increasing the amount of data thanks to transformation of the original data through rigid and non-rigid methods of transformation, as well as data standardization.

The second problem is the difficulty of diagnosing the cause of pleural effusion. The difficulty lies in the fact that the cancer cells are unevenly distributed throughout the pleural liquid and the probability of collection pleural liquid without cells with cancer is very high. In addition, this system requires images of cells of the pancreas, which is often impossible within the technical capabilities of hospitals.

Despite of these problems authors received good results:

The scope of recognition of the type of pathology can be increased by collecting a larger number of images for each class of pathology. The recognition algorithm has shown itself well with small amount of data and can be used to classify other classes of diseases. In this case, this system can be fully applied in the process of diagnosing the cause of pleural effusion.

The disadvantage of this system is the absence, as such, of a cell recognition and segmentation module. Although segmentation is not the key goal of this type of research but this process can be useful both in the classification process (since the accuracy of the neural network can increase) and in the process of automating the process of cause of pleural effusion definition.

The achieved accuracy of the results: 95.6% for the class of oncological pathologies and 90% for the class of pathologies of other types is a good result in this work, since the system is only a prototype.

Future research may include the following developments:

- The development of a module for image segmentation for different types of images of pleural liquid.
- Development of a multiscale system of convolutional neural networks of similar architecture for input images of different sizes.

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