Method of recognition of the blasts nuclei structure by using light microscopy and computer data processing

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Abstract. Method for recognizing the structure of blood and bone marrow blast nuclei using light microscopy and computer data processing is proposed to improve the accuracy of diagnosis of acute leukemia, including reducing the subjectivity of microscopic analysis of blood and bone marrow preparations. The paper presents a model of automated recognition of blood cells during microscopic analysis based on objective criteria of classification of images of pathological cells, focused on the differential diagnosis of acute leukemia. The application of the proposed method allows to clarify the variant of the disease and reduce the time of the diagnostic process.

1. Introduction

The use of methods and means of digital image processing for the recognition of cell types for the diagnosis of acute leukemia is of considerable interest. This allows the analysis of images of blood cell nuclei to obtain data in the form of numerical indices. The latter is important because visual microscopy provides qualitative assessments based on the subjective analysis of a doctor conducting a microscopic analysis [1-4].

The developed methods and means of image processing and analysis for digital processing systems include different equipment, tested on different amounts of experimental material [1, 5-10]. In most cases, these parameters are not described in the publications, which in turn makes it difficult to reproduce the results of the study.

One of the problems in the development of such systems is a limited sample of initial data-images of blood cells (some developers use images of blood cells from Internet resources in their research) [10-13].

It should be noted that the development and development of methods and tools for automated recognition of blood cells for scientific and practical application requires a complex analysis and accounting of many parameters (system settings and shooting conditions), followed by experimental studies to assess their impact [14]. The result of the analysis, which leads to errors in leukocyte recognition, is influenced, in particular, by deviations from the technology of preparation of smears,
coloring of slides, the quality and type of slides [15-16]. In addition, it is necessary to consider a number of problems: significant variability of morphological parameters of biological micro-objects within one class, the lack of a formal approach to the assessment of the structure and shape of biological micro-objects, the difficulty of formalizing the rules used by the expert to interpret the results of microscopic analysis, etc.

The aim of the work is to develop a method for recognizing the structure of blood and bone marrow blast nuclei using light microscopy and computer data processing to improve the accuracy of diagnosis of acute leukemia, including reducing the subjectivity of the analysis.

2. Materials and methods.

Leukocytes on microscopic images of peripheral blood and bone marrow smears are the objects of measurements in the systems of automated recognition of blood cells.

The proposed method of image processing of leukocytes includes the following steps. At the first stage, the nucleus of the leukocyte cell is allotted. The second step is to convert the core image into color models. At the third stage, characteristics based on spatial adjacency matrices and series lengths are calculated for the obtained halftone images [9]. Thus, for each image of the blood cell nucleus, a set of quantitative characteristics of chromatin structure is formed. The set is formed for cells of each type and is represented by the following model: 

\[ C = \{Q_N\} \times \{P_k\} \]

where \( Q_N \) is a cell with number \( N \), \( P_k \) is a set of texture characteristics studied in our work \( P = \{P_k\} = W \times KCM \), \( W = \{w_1, ..., w_j\} \) – a set of characteristic values calculated by the formulas presented above, \( KCM = \{R, ..., Y\} \) – a set of color components. At the fourth stage, a set of characteristics for the sample of blasts and lymphocytes (Cb and Cl) is calculated. Features from the set \( \{P_k\} \) for which the error of the separation of cell types is minimal is searched at the fifth stage.

A model of research to improve the accuracy of automated recognition of blood cells during microscopic analysis is shown in Fig.1.

For experimental studies, a sample of images of blood cells and bone marrow was formed: 1029 images from donors, 3004 images from patients with B- acute lymphoblastic leukemia (B-ALL), 2415 images from patients with T- acute lymphoblastic leukemia (T-ALL), 1495 images from patients with follicular lymphoma.

Imaging of lymphocytes and blasts was performed on stained preparations in the computer microscopy system (robotic microscope Olympus BX43 with camera Imperx IPX-4M15T-GCFB). The images were saved in BMP format, color-coded RGB24 (more than 16 million colors per pixel) [17-20].

3. Analysis of results

The proposed method of recognition of the structure of blood and bone marrow blast nuclei, based on the measurement of morphological, texture and wavelet characteristics, allows us to determine the quantitative criterion for the separation of leukemic blasts by type in T and B variants of acute lymphoblastic leukemia. The use of the system based on light microscopy and computer data processing made it possible to identify the correlation between the structure of blasts and their immunophenotypic status. Identification of correlation is the basis for the application of the method of calculating the atypical index of cells in the differential diagnosis of acute leukemia, allowing to evaluate the sub-variant of acute leukemia at the stage of microscopic analysis.
Figure 1. Research model to improve the accuracy of automated recognition of blood cells in microscopic analysis.

Previously, the use of light microscopy in visual morphological examination did not allow doctors to distinguish between B - and T - linear acute lymphoblastic leukemia. The proposed methods and models of digital image processing of the structure of the nuclei of blood and bone marrow blasts allowed to distinguish between B - and T - linear acute lymphoblastic leukaemia. Experiment accuracy of the distinction between B - and T - linear acute lymphoblastic leukaemia is 95%.

It was shown that the use of the method of analysis of texture characteristics of images of the structure of the chromatin of the nuclei of the blood cells on microscopic examination of aspirates of bone marrow allows to distinguish between T-ALL and b-ALL variants of acute lymphoblastic leukemia. As a reference (reference) method, the data of morphocytochemical and immunophenotypic studies were used, on the basis of which the diagnosis was established. These studies were carried out in the laboratory of hematopoiesis immunology of N. N. Blokhin NMIC Oncology of Russian Federation Ministry of health (head of the laboratory doctor of medical Sciences, Professor N. N. Tupitsyn), digital data processing was carried out at the Department of computer medical systems of the National Research Nuclear University MEPhI (head of the Department, doctor of technical Sciences, Professor, laureate of the RF government prize in the field of education V. G. Nikitaev).

4. Conclusion
The paper presents a method of recognition of the structure of nuclei blasts of blood and bone marrow with the use of light microscopy and computer data processing to reduce the subjectivity of the results of the microscopic analysis and improving the accuracy of diagnosis of acute leukemia. The proposed approach makes it possible to clarify the variant of the disease at the stage of microscopic analysis and reduce the total time of the diagnostic study, including immunophenotypic analysis to determine the sub-variant of acute lymphoblastic leukemia, by a third. In the end, it increases the effectiveness of treatment of acute leukemia.
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