Application of Artificial Intelligence in Ophthalmology for the Diagnosis and Treatment of Eye Diseases

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Abstract—In this paper, we present the main aspects of artificial intelligence application in ophthalmology for the diagnosis and treatment of eye diseases on the example of developing a computer system for personalizing retinal laser photocoagulation. Approaches to the automation of eye disease prediction and treatment based on fundus images are described. Four problems of applying the neural network approach are highlighted. Decision support information technology for personalizing laser treatment of diabetic macular edema and identifying prognostic factors of surgical outcome using methods of intellectual analysis of large unstructured data is described. The system allows the doctor to form a plan of optimal coagulation arrangement for retinal laser coagulation for each case, to predict the quality of laser coagulation depending on the initial data on the localization and severity of edema and to improve his skills by comparing the result of coagulation performed and the coagulation plan proposed by the system.

1. INTRODUCTION

Recently the introduction of artificial intelligence and digital medicine technologies into healthcare practice is rapidly changing the methods of diagnosis and treatment [8, 15]. Increasingly, robotic systems are being used to support the diagnosis and treatment of diseases [9]. According to the Forecast of Scientific and Technological Development of the Russian Federation for the period until 2030, the promising areas of scientific research include the design of intelligent systems to support medical decisions, as well as the provision of services for the analysis of medical data. Ophthalmology is in dire need of a transition to personalized medicine, which would make it possible to make a qualitative leap in the treatment of eye diseases [18]. However, this transition is impossible without the development and implementation of fundamentally new intelligent methods for analyzing patients' biomedical data.

Diabetic retinopathy (DR) is often found in diabetes patients, triggering severe complications [6, 17, 19]. If timely treated, vision loss can be prevented in more than 50% of cases [1, 2, 4, 7, 20]. A key instrument for treatment of diabetic retinitis is laser photocoagulation, in which a series of well-measured photocoagulates are inflicted on retina areas with pathology [3, 11, 21, 22]. Modern systems mainly rely on the use of a preset pattern for generating a photocoagulation map [11, 21, 22]. Due to highly variable shapes of the macular edema and vascular system, a uniform photocoagulation map cannot be realized using a standard pattern [21, 22]. However, the ophthalmologist first needs to analyze the retina and eye fundus condition to ensure that the photocoagulates be inflicted in admissible areas. On the one hand, this method provides a more effective laser photocoagulation given a correctly mapped pattern, but on the other hand, it takes the surgeon an extra time to analyze the retina condition.

The aim of the research is to increase the efficiency of retinal laser coagulation by developing information technology that allows implementing a personalized approach to the treatment of diabetic macular edema (DME). To do it, a new technique for applying coagulates was used, which takes into account the various properties of the coagulates totality location. The method of preliminary planning of the coagulates location takes into account the individual features of the anatomical structures location in the area of edema and its shape. To obtain optimal results of laser treatment of DME, a method was used with personalized placement of coagulates at equal distances from each other, taking into account the individual characteristics of anatomical structures and edema boundaries in a particular patient.

2. METHODS FOR AUTOMATED DECISION MAKING IN THE TREATMENT OF DIABETIC RETINOPATHY

Our research focuses on the development of decision automation techniques for the treatment of diabetic retinopathy based on the intelligent analysis of large amounts of unstructured data, including digital biomedical images. Through collaboration with various experts in medical institutions, we are developing new digital technologies for the diagnosis and treatment of eye diseases. On the basis of Samara University, Image Processing Systems Institute, a Branch of the Federal Scientific Research Centre "Crystallography and Photonics" of the Russian Academy of Sciences and Samara State Medical University, as well as the Eroshevsky Ophthalmology Hospital, we are working on the development of new technologies for the diagnosis and treatment of eye diseases. The research is carried out jointly to identify effective ways to diagnose and treat eye diseases. Through collaboration with physicians, work is being done to collect and interpret patient data, for which effective digital methods for diagnosing diseases and supporting decision-making in the treatment process are subsequently determined. Since 2017, research has begun on the treatment of diabetic macular edema using digital image processing, machine learning, and mathematical modeling of biophysical processes.

Diabetes mellitus is recognized as one of the global medical and social problems of modern society. Among its most severe and widespread complications is diabetic retinopathy. This disease has become one of the main causes of visual impairment up to irreversible blindness. As mentioned above, one of the effective treatments for diabetic retinopathy is focal laser surgery—applying multiple dosed microscopic burns (coagulates) in the area of macular edema caused by lesions of the small blood vessels of the retina. The efficiency of this procedure depends on the experience and qualification of the particular ophthalmic surgeon and the accuracy of the placement of the coagulants. In preparation for surgery, the specialist combines data from optical coherence tomography (OCT) and the patient's fundus and uses it to develop a plan for laser photocoagulation of the affected regions of the retina. However, manual placement is not always optimal and accurate enough. Standard templates are used for planning which do not correspond to a variety of edema forms and vessel locations. Uneven placement of cauterization points either creates a risk of increased trauma in areas of excessive coagulation or reduces the effectiveness of treatment in areas where exposure was insufficient. In addition, it takes a long time to plan such an operation.

The use of artificial intelligence makes it possible to accurately segment the retina of a particular patient, ensure uniform planning of coagulates exclusively in the area of the affected area of the eye, and most importantly, dose the power of laser exposure for each cauterization point. Doctors estimate that this will result in a ninefold decrease in the probability of laser burns beyond the borders of the edema, shorten the time needed to prepare the patient for surgery, and reduce the risk of postoperative complications.

Only one facility in the world uses digital techniques to support laser photocoagulation, the NAVILAS facility [5, 10, 12, 14, 16]. We are developing a more advanced technology that will help physicians plan retinal surgeries to prevent blindness in diabetic patients. According to the Chief Physician of the Eroshevsky Samara Regional Clinical Ophthalmologic Hospital Andrei Zolotarev, no laser in the world today is capable of analyzing video data in such a mode, so the doctors suggested creating an intelligent laser coagulation support system that would significantly improve the effectiveness of diabetic macular edema treatment and prevent severe complications after treatment, and, most importantly, that would also individually dose the laser power.

Currently, we are conducting research on semantic segmentation of fundus images to highlight anatomical and pathological zones, separation of retinal layers on optical coherence tomography (OCT) images, mathematical modeling of laser exposure, and developing methods of automatic formation of an effective laser coagulation plan to improve the effectiveness of treatment of diabetic retinopathy.

To solve the problem of semantic segmentation of fundus images we investigated and compared 2 approaches: neural network and texture analysis. The first approach is based on machine learning of deep neural networks to improve the accuracy of detection of pathological and anatomical structures in the edema area.

Recently, most of the data mining tasks are solved by neural network algorithms. The emergence of neural networks has revolutionized image processing tasks. In biomedicine, neural networks have found their frequent application in solving semantic segmentation problems, e.g., to determine the area of lung lesions of the SARS-CoV-2 virus, to find human brain tumors, etc.

3. PROBLEMS OF APPLYING A NEURAL NETWORK APPROACH TO THE TASK OF AUTOMATING THE ANALYSIS OF FUNDUS IMAGES

The application of the neural network approach for solving the problem of semantic segmentation of ocular fundus images is due to a number of reasons. Neural network algorithms have a good generalizing ability; are more accurate (surpassed any other approaches) in many tasks of data mining; are able to take into account the whole context of the image. However, their applicability is limited by the charac-

teristics of the training dataset. It was found that the application of neural networks in biomedicine involves a number of problems specific to this field.

(1) More often than not, due to privacy policies and the laborious nature of the markup procedure, which requires a highly skilled professional, it is extremely difficult to create a sufficiently large set of data of the required quality. The impact of the problem of insufficient data volume can be mitigated through the use of various data augmentation techniques. For example, in tasks related to the processing of biomedical images, especially effective is elastic augmentation of data: random angle rotation, reflections, elastic deformation.

(2) Another problem peculiar to biomedical data is the problem of pronounced class imbalance, which is a distinctive feature of our data. The sample contains classes that do not occur in almost all retinal images, and the relative power of these classes is extremely low. This peculiarity should be taken into account when developing a neural network-based segmentation algorithm. The solution of the problem when many classes are unbalanced is non-trivial, but there are algorithms that neutralize this problem [13].

(3) The most complex problem is the poor quality of data labeling, which is the most difficult to identify and eliminate at the training stage of the algorithm.

During the development of the intelligent system we solved the following tasks.

(1) The applicability of different neural networks for solving the problem of semantic segmentation of eye fundus images was investigated.

(2) Factors that must be taken into account to obtain a qualitative segmentation of fundus images were determined.

(3) The optimal neural network architecture and hyperparameters were determined.

(4) The peculiarities of the data set to be taken into account when developing neural network algorithms were identified.

The peculiarities of our problem are the fact that the original data are unbalanced, the number of images is small, and the labelling does not exactly match the actual location of the objects.

Therefore, for the application of neural network algorithms, the first priority is to prepare the data and level out the problems of unbalanced data and small sample size. The combined use of different data augmentation techniques allowed us to significantly expand the set of available images, bringing the number of images to more than 6000. The images were divided into three sets: training, test, and validation in the ratio of 80, 10, and 10%, respectively.

During the research several different neural network architectures were adapted for the task of semantic segmentation. As a result, such architectures as U-NetMobileNetV2, U-NetResNet, U-NetXception were developed and investigated, using pretrained MobileNetV2, ResNet, and Xception networks as a feature extractor, respectively. The average value of the Dice coefficient that was achieved during the experiments was found to be 0.5542. This value was obtained using the U-NetXception architecture, with the error function—FocalLoss with gamma parameter = 2. In this research U-Net and ResNet were combined; thus, a new architecture for semantic segmentation tasks, U-NetResNet, was obtained. Its advantage over U-Net is that there are weights for ResNet in free access, so we could engage in transfer learning. The decoder structure on U-NetResNet is a mirror image of the encoder. Significant influence on the result had the data balancing algorithm and use of optimization routines, which allowed the neural network based on U-NetXception architecture significantly outperformed the others. In this experiment, class balancing was performed using oversampling and undersampling techniques to obtain a higher frequency of rare classes. The weights of the pretrained networks were used to initialize the encoder and were fixed for the training time. Neural networks were constructed and trained using the TensorFlow library. The use of pretrained encoders allows the training of neural networks much faster.

The second approach we use to solve the problem of segmentation of fundus images is texture analysis. This is one of the classical methods based on the use of texture features. Studies in which texture features are used for image segmentation are still relevant. Segmentation of images using texture features is performed in several steps: (1) image fragmentation, (2) calculation of texture features for each fragment (this stage is the longest, so the calculation of a small set of a couple of tens of features for one image of 1024 × 1024 pixels size can take several hours when using calculations on the central processor of a modern multicore computer), (3) classification of fragments based on the calculated values of texture features (at this stage the classification of one pixel of an image fragment by a vector of calculated. Using the full set of texture features for image segmentation is inefficient, so we made a selection of features according to the individual criterion of informativeness of the discriminant analysis. The selection of features according to this criterion is a classical way to find informative features. The choice of this method of feature selection is also due to the properties of the discriminant analysis. Its criteria allow choosing such features that best partition the space of objects. The following metrics have been used to estimate the quality of image segmentation: precision, recall, f1-score. The reliability of the results of the experiment was ensured by the use of k-fold cross-validation. For neural networks the data set was divided into three parts ($k = 3$), and for texture features it was divided into five parts ($k = 5$). The metric values obtained for all parts were averaged.
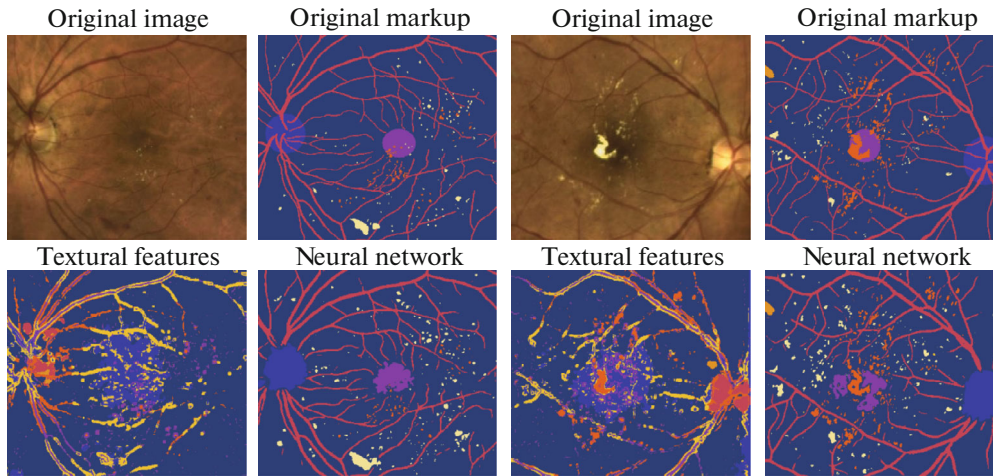
Fig. 1. Examples of fundus image segmentation obtained as a result of the experiment.
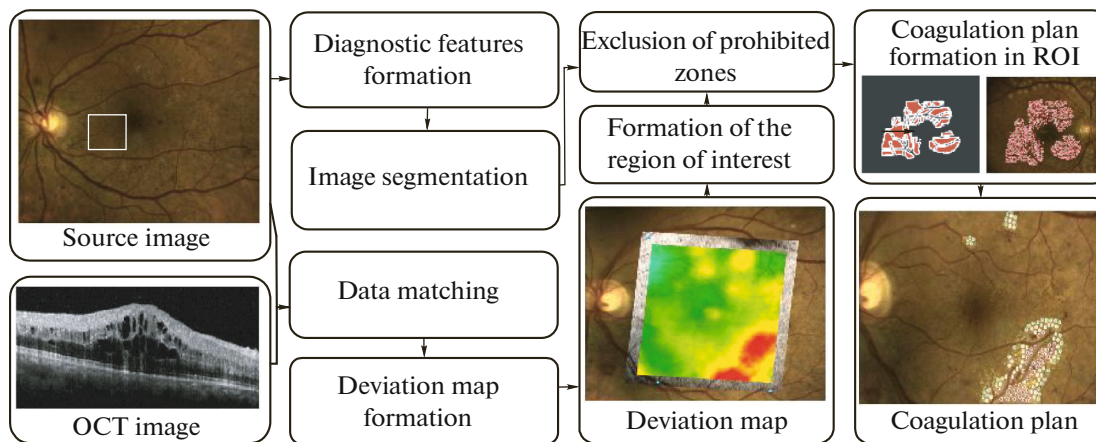

Fig. 2. Technology of mapping a photocoagulation plan of laser coagulation.

Texture features are well studied and successfully applied to a variety of tasks. However, their use is time-consuming, which makes their implementation in medical practice difficult. In addition, texture features have insufficient generalizability to solve complex problems.

From the analysis of the research results, it was found that neural networks are superior to texture-based features in accuracy (Fig. 1).

Moreover, neural networks can be applied for segmentation of fundus images that were obtained under different imaging conditions, in contrast to texture features. The use of pretrained neural networks and their post-training on a small dataset together with the use of a balancing algorithm and augmentation techniques, allowed to develop sufficiently accurate algorithms for semantic segmentation of fundus images on a small dataset. The fundus image segmentation algo-rithm based on the use of a neural network with U-NetXception architecture can be used in decision support systems for diagnosticians when they need to work in real time through the use of a user-level graphics card.

All approaches presented above solve the problem of high-precision recognition of pathological and ana-tomical structures of the fundus in order to form laser exposure zones and personalized plan of optimal coagulation location in the DME area. This will increase the quality of laser treatment and objective assessment of the volume and localization of patho-logical structures, allowing predicting treatment results and timely changing the tactics of diabetic reti-nopathy treatment. Figure 2 shows a general scheme of technology of coagulation plan formation using the developed methods of fundus images segmentation and coagulation placement.

CONCLUSIONS

The paper considers the application of artificial intelligence methods in ophthalmology for the treatment of eye diseases on the example of a computer system for retinal laser photocoagulation personalization. The main problems of using the neural network approach in the tasks of biomedical image analysis are described. Decision support information technology for personalization of laser treatment of diabetic macular edema and identification of prognostic factors of surgical outcomes using methods of intellectual analysis of large unstructured data is presented. To solve the problem of semantic segmentation of images to highlight anatomical and pathological areas of the fundus two approaches were investigated and compared: neural network analysis and texture analysis. The disadvantages and advantages of each approach were highlighted. The studies showed that neural networks are superior to texture-based features in accuracy.

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This article is a completely original work of its authors; it has not been published before and will not be sent to other publications until the *PRIA* Editorial Board decides not to accept it for publication.

Conflict of Interest

The authors declare that they have no conflicts of interest.

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