ALGORITHM OF SEGMENTATION OF OCT MACULAR IMAGES TO ANALYZE THE RESULTS IN PATIENTS WITH AGE-RELATED MACULAR DEGENERATION

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Age-related macular degeneration (AMD) is one of the main causes of loss of sight and hypovision in people over working age. Results of optical coherence tomography (OCT) are essential for diagnostics of the disease. Developing the recommendation system to analyze OCT images will reduce the time to process visual data and decrease the probability of errors while working as a doctor. The purpose of the study was to develop an algorithm of segmentation to analyze the results of macular OCT in patients with AMD. It allows to provide a correct prediction of an AMD stage based on the form of discovered pathologies. A program has been developed in the Python programming language using the Pytorch and TensorFlow libraries. Its quality was estimated using OCT macular images of 51 patients with early, intermediate, late AMD. A segmentation algorithm of OCT images was developed based on convolutional neural network. UNet network was selected as architecture of high-accuracy neural net. The neural net is trained on macular OCT images of 125 patients (197 eyes). The author algorithm displayed 98.1% of properly segmented areas on OCT images, which are the most essential for diagnostics and determination of an AMD stage. Weighted sensitivity and specificity of AMD stage classifier amounted to 83.8% and 84.9% respectively. The developed algorithm is promising as a recommendation system that implements the AMD classification based on data that promote taking decisions regarding the treatment strategy.

Keywords: artificial intelligence, neural network, age-related macular degeneration, optical coherent tomography, machine learning algorithm

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Compliance with ethical standards: the study was performed in accordance with the principles of Declaration of Helsinki; all patients signed voluntary informed consent to OCT.

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АЛГОРИТМ СЕГМЕНТАЦИИ ОКТ-ИЗОБРАЖЕНИЙ МАКУЛЫ ДЛЯ АНАЛИЗА ПАЦИЕНТОВ С ВОЗРАСТНОЙ МАКУЛЯРНОЙ ДЕГЕНЕРАЦИЕЙ

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Одной из основных причин слепоты и слабовидения у лиц старшего трудоспособного возраста является возрастная макулярная дегенерация (ВМД), для диагностики которой крайне важны результаты оптической когерентной томографии (ОКТ). Создание рекомендательной системы для анализа ОКТ-снимков позволит сократить время на обработку визуальной информации и снизить вероятность ошибок в процессе работы врача. Целью исследования было разработать алгоритм сегментации для анализа данных ОКТ макулы пациентов с ВМД, позволяющий, основываясь на форме выделенных патологий, корректно предсказывать стадию развития ВМД. Разработана программа на языке программирования Python с использованием библиотеки PyTorch и TensorFlow. Качество работы программы оценили на ОКТ-изображениях макулы 51 пациента с ВМД ранней, промежуточной и поздней стадией. Разработан алгоритм сегментации ОКТ-снимков, основанный на сверточной нейронной сети. В качестве архитектуры сверточной нейронной сети была выбрана сеть UNet. Нейронная сеть обучена на ОКТ-снимках макулы 125 пациентов (197 глаз). Авторский алгоритм продемонстрировал 98,1% верно сегментированных областей на ОКТ-снимках, наиболее важных для диагностики и определения стадии ВМД. Взвешенная чувствительность и специфичность классификатора стадий ВМД составили соответственно 83,8% и 84,9%. Разработанный алгоритм перспективен в качестве рекомендательной системы, реализующей классификацию ВМД на основе данных, способствующей принятию решений о тактике лечения пациентов.

Ключевые слова: искусственный интеллект, нейронная сеть, возрастная макулярная дегенерация, оптическая когерентная томография, алгоритм машинного обучения

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Соблюдение этических стандартов: исследование проведено в соответствии с принципами Хельсинкской декларации; все пациенты подписали добровольное информированное согласие на проведение ОКТ.

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Age-related macular degeneration (AMD) is one of the main causes of loss of sight and hypovision in people aged 50 and over [1–3]. An annual growth of patients with this pathology is noted due to an increased expectation of life and upgrading the methods of diagnostics [4, 5]. Thus, based on prognosis of the World Health Organization, a number of people with AMD will be increased by 1.2 times from 2020 to 2030 (from 195.6 to 243.3 million of people) [6].

There exist various classifications of AMD: we differentiate between dry (non-exudative and atrophic in the late stage) and wet (exudative or neovascular) forms of AMD [7, 8]. According to the Age-Related Eye Disease Study (AREDS), an early, intermediate and late stages of age-related macular degeneration have been identified [9]. Based on literature data, in 10–20% of cases the non-exudative form of disease is transformed into the exudative one; in other cases, the course is slowly progressing and results in a geographic atrophy [10–12]. Specific treatment of dry AMD is currently lacking, and the emphasis is on prevention measures [13]. Wet AMD leads to rapid and irreversible loss of central vision. Intravitreal injections of vascular endothelial growth factor (VEGF) inhibitors improve vision and reduce the possibility of blindness in wet AMD [14]. However, treatment success depends on many factors, one of which being modern diagnostics of the disease [3]. Optical coherence tomography (OCT) acquired the most widespread use both in clinical trials, and in real practice as a means of diagnostics and monitoring of patients with AMD [15–16]. It is highly informative, contactless and allows to estimate the architecture of eye structures and retina, in particular, in real time [17]. A growing number of patients with this pathology is accompanied by an increased need in OCT studies, improved capacity of medical institutions and improved quality of the method.

Analysis and interpretation of large amounts of data is one of the issues [18, 19]. It can be solved using artificial intelligence (AI). AI intelligence becomes a perspective trend in diagnostics of ophthalmological diseases [20]. Thus, machine learning can be used to detect peculiarities of retinal tissue structure to evaluate the changes in it [21], detect vascular plexuses [22] and such retinal lesions as intraretinal cysts or subretinal fluid [23]. Methods of deep learning have recently become popular in the sphere of computer vision and are now included into the area of retinal image analysis. The methods of detecting retinal disease based on isolated biomarkers have gained special recognition; it enables close imitation of visual analysis by an expert and makes verification of a classifier easier [24–30]. Latest studies in the area of integration of recommendation systems in ophthalmology reveal brilliant results regarding less time spent on diagnostics and influence of a human factor on the process of doctors' working [31, 32]. These systems were operated based on the intellectual algorithms similar to previously available ones, which proves relevance of the search and development of new algorithms that could be used to determine the signs of AMD of various stages on OCT images with high sensitivity and specificity.

The purpose of the research is to develop an algorithm of segmentation to analyze macular OCT data in patients with AMD, that enables proper prediction of an AMD stage based on the form of extracted pathologies.

METHODS

To solve the set task, supervised learning was used. During this training, the intellectual algorithm compares incoming and expert-labeled data increasing the generalization ability for unknown examples. At the stage of formation of three samples (training, validation and test ones), it was decided to use the database obtained during a standard ophthalmological examination and macular OCT using Avanti XR (Optovue; USA) and REVO NX (Optopol; Poland) at Optimed Center for Laser Eye Surgery (Ufa, Russia). Direct formation of a data set made it possible to regulate the parameters of the ratio of classes (stages) of the disease, gender and age-related distribution of patients and concomitant diseases, and a number of produced biomarkers, resulting in analysis of working algorithm outcomes in the presence of formerly known peculiarities of a set of OCT images. Incoming data included OCT macular images of 125 patients (197 eyes) with 89 women and 36 men having a mean age of 74.88 years (40–97). Inclusion criteria: patients with early (32%), intermediate (26%) and late (42%) stages AMD with sufficient transparency of optical media. Exclusion criteria: presence of diabetic retinopathy, retinal vessel occlusion; pachichoroid diseases; pathology of vitreomacular interface; and myopic choroidal neovascularization. The obtained set of OCT images consisted of training, validation and testing samples that account for 80, 10 and 10% respectively. Python programming language was a tool to develop an algorithm of image classification and formatting using TensorFlow and Pytorch libraries. Predictors of AMD stages were searched using the convolutional neural network segmenting the eye pathology. The operation principle of this neural networks was based on multi-layered successive convolution of an image with filters, whereas weight coefficients are selected while training an algorithm. These filters are intended to mark various image-located forms and textures in accordance with the principle of cerebral cortex operation having small parts of cells sensitive to certain areas of the field of vision. UNet initially created for segmentation of biomedical images was selected as architecture of a convolutional neural network. This architecture implements not only a slow increase of numerous signs (a tensor) that characterize the incoming image using four layers of convolution with filters and compression in encoder. It also preserves data related to their localization on the image by adhesion to parallel layers of convolution and use of operations reverse to file compression in a decoder.

ReLu was used as a function of activation. It provided qualitative training of a model using a relatively low amount of incoming data. OpenCV library was selected to ensure the best indicators of image processing and noise clearance.

To solve the issue of overfitting, several approaches were reviewed. Transfer learning, when the applied network is previously educated using a large set of data, is a popular method in this context [33–35]. However, it should be taken into account that the biomarkers marked on an OCT image will have little correlation with entities produced by networks trained using common databases such as ImageNet. This can make the method less effective [36, 37]. Using methods of attention concentration is another approach that reduces the probability of network overfitting. For this, a block of attention was added to the neural network structure following every convolution layer. This block included searching of key points of the outcome of the layer process and increase of nearby values of network-processed tensor elements, on one hand, and a method of searching the adaptive limit value of tensor elements, on the other hand.

Classification based on segmented data was done by calculating the area of the largest pathologies of the same nature. The limit values were determined taking into consideration clinical signs of AMD by the size of concomitant pathologies [9].

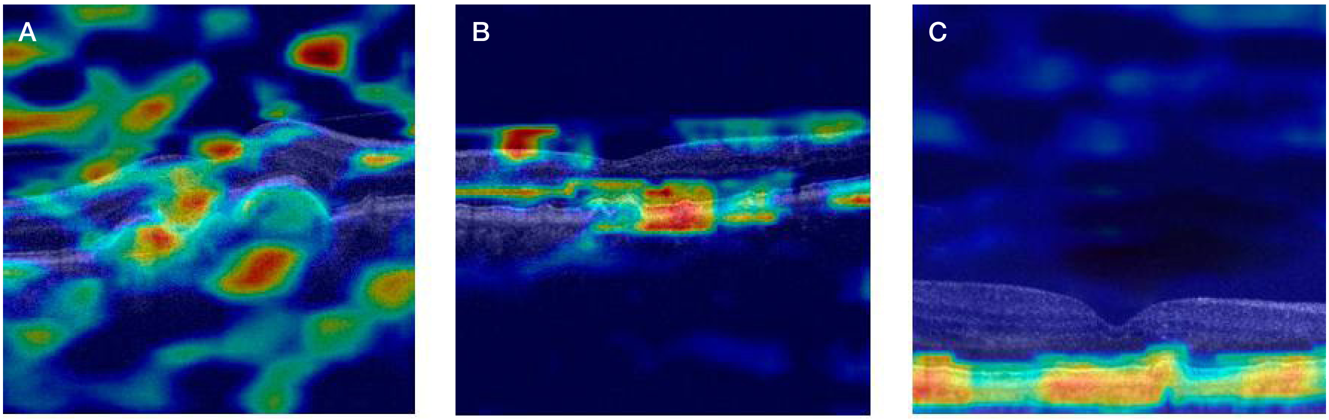


Fig. 1. Class activation cards: with no use of attention concentration module (**A**); while using the SIFT method (**B**); while using the SALV method (**C**)

It was estimated whether an AMD stage was classified properly based on the automatic recognition of OCT images and analysis of the nine-field coupling matrix, which is a matrix that provides correspondence between the actual and predicted AMD stages (early, intermediate, late). Three four-field coupling matrices developed using the principle of prediction of one AMD stages only were obtained. Thus, values of specificity and sensitivity for every AMD stages were calculated for every matrix. Sensitivity means a percentage of properly predicted cases of a certain stages of AMD, whereas specificity is a percentage of properly predicted cases not related to the AMD stages.

Weighted sensitivity (Se_w) and specificity (Sp_w) of the entire classification algorithm were calculated using definite values

$$Se_w = \frac{Se_1 n_1 + Se_2 n_2 + Se_3 n_3}{n};$$

$$Sp_w = \frac{Sp_1 n_1 + Sp_2 n_2 + Sp_3 n_3}{n};$$

where Se_1, Sp_1 mean sensitivity and specificity of early AMD recognition; Se_2, Sp_2 denote sensitivity and specificity of late AMD recognition; Se_3, Sp_3 mean sensitivity and specificity of intermediate AMD recognition; n_1 means a number of cases with early AMD; n_2 means a number of cases with late AMD; n_3 means a number of cases with intermediate AMD, where $n = n_1 + n_2 + n_3$.

RESULTS

To develop a recommendation system determining AMD stages, an approach imitating a visual analysis made by an expert was selected. When it is used, position and form of disease pathologies can be found on an OCT image and they can be compared with a previous diagnostic experience. At the stage of detecting pathologies, the key issue consists in transfer of an expert's experience in its differentiation with an intellectual algorithm. As use of methods of deep learning displays its effectiveness and immunity to the variety of incoming information only in the presence of a sufficient scope of the training samples, which is proportional to the algorithm complexity [38], a set of marked OCT images is required. Its generation is a resource-intensive task.

To avoid the limitation in the structure of UNet segmenting neural network, it was decided to include a block of additional treatment of a set of signs from an output of the convolution layer. This is how data about pathology contours were preserved, which could be reduced to the neural network attention concentration. The presented approach enables to decrease the complexity of the applied neural network algorithm by reducing a number of educated values while preserving exactness in a training sample. Effectiveness of the attention concentration approach was estimated by comparing the exact determination of segmented abnormal area borders using test data and analysis of class activation maps of abnormal retinal parts of UNet coder that visualizes the key areas of the images used for segmentation of this predictor.

During training of the neural network with a set of data formed by the authors with no involvement of the attention concentration block into UNet, the segmentation results amounted to 58.7% of properly segmented abnormal areas. The class activation maps presented in Fig. 1A, display little concentration of attention on AMD signs. This is how low accuracy of pathology borderlines can be explained.

When selecting an algorithm of the attention concentration block it has been taken into account that retinal layers on OCT images have a properly marked difference in shades of gray. Deformation of pigmented epithelium and neuroepithelial edema are clearly seen. These shades, considering their difference in size during different stages of the disease, can be revealed by finding scale-invariant key points with Scale-Invariant Feature Transform (SIFT) [39]. They denote edges and angles and deformity margins on the image using the method of searching the adaptive limit value (SALV). The method proved to be effective while detecting pathologies [40].

The SIFT approach with a fixed lower threshold of key point scope, equal to the minimal sizes of drusen found in early stages of AMD [9] enabled to improve exactness of abnormal

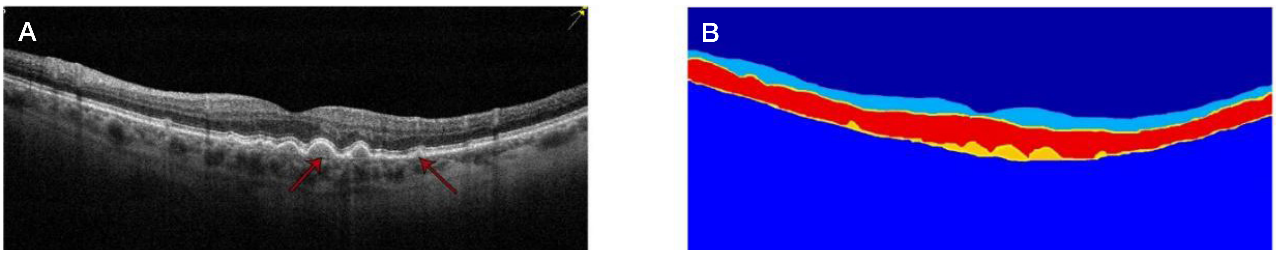
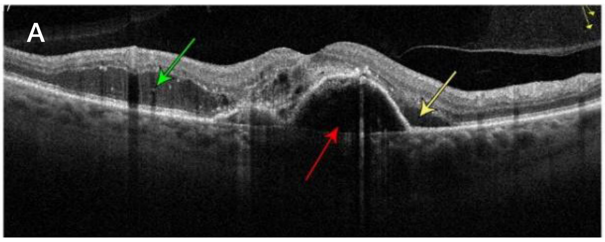


Fig. 2. OCT macular images in early and intermediate AMD. **A**. Hard and soft Bruch's membrane drusen (*red arrows*) marked by the doctor. **B**. Algorithm segmented image



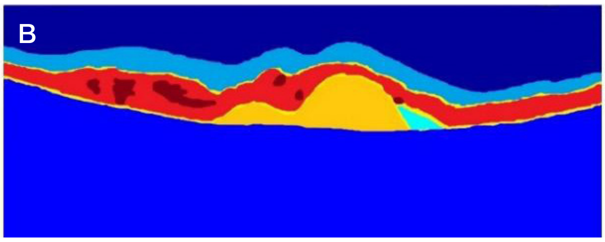


Fig. 3. OCT image late macular OCT image in AMD. **A**. Signs of AMD recorded by the physician (described in the text). **B**. Algorithm segmented data

segmentation to 76.7%. However, the attention concentration block helps find key areas not related to pathologies (Fig. 1B), decreasing the concentration of the neural network.

While using the attention concentration block based on the SALV method, accuracy of properly segmented abnormal areas was achieved in 98.1% of cases. Owing to the method, the entire attention of the neural network was concentrated on drusen (Fig. 1C). When the rate of occurred pathologies was changed from equally likely to statistical [10, 11], exact detection of neuroepithelial edema was reduced by 15%. Thus, to increase effectiveness, a conclusion was made that distribution of all pathologies on the training sample should be regular.

Segmentation results for predictors of dry intermediate AMD using the latest version of attention concentration block are well shown on Fig. 2. Hard and soft drusen of Bruch's membrane that deform the pigmented epithelium (displayed in arrows) are visualized on OCT macular images (Fig. 2A). The layers that correspond to structural elements of photoreceptors are above the drusen. The internal layers of neuroepithelium are clear and not deformed. Foveolar deepening has a proper configuration. In Fig. 2B these areas are segmented using the algorithm where the deformed pigmented epithelium is shown in yellow, just like the orange layers above the drusen.

Retinal thickness is increased due to cystic edema of neuroepithelium (*green* arrow), local elevation of pigmented epithelium probably occurring due to the hidden neovascular membrane (*red* arrow) with accumulation of hyporeflective content found under the neuroepithelium (*yellow* arrow). The fovea is concave. On Fig. 3B neuroepithelial edema is highlighted in dark red, elevation of pigmented epithelium in orange, and fluid accumulation under the neuroepithelium in blue. Predictors of late AMD are shown on Fig. 3A.

Automatic classification of AMD stages was done based on the obtained results, and values of specificity and sensitivity for each stage were calculated as well (Table). Based on the acquired values, the weighted values of sensitivity and specificity of a stage classifier (Se_w = 0.838 and Sp_w = 0.849) were calculated.

DISCUSSION

The presented results were obtained while using OCT images from tomography scanners of several manufacturers. This produced a significant effect on accurate operation of segmentation algorithm due to differences in data visualization. Owing to specific block attention concentration methods when various labeling of OCT images is provided along with predictors, it is necessary to implement additional training of the recommendation system using new examples or remove the mentioned data. In this case, preliminary treatment of images can be required.

It should also be noted that the obtained forms of segmented areas will differ depending on the disease presence and stage. The data contain predictors needed for detection and determination of an AMD stage by the recommendation system. However, in some cases the limits of the ratio of abnormal area shape and proper diagnosis in an expert opinion can be rather blurred due to individual features of the disease course in a patient and in a different selection of eye radial scanning images.

Thus, a fully connected layer, which is the most frequently applied in computer vision tasks with neural networks, as a classifier of AMD stages will also require an extensive training sample to provide the indistinct borders. Considering statistics about an irregular frequency of AMD stage determination [10, 11], the task can't be solved easily. Same conclusions will be just for the limit values of AMD stage determination by the area of pathologies. It means that their hard task can involve additional errors. It is advisable to use methods of imprecise logics that effectively display a doctor's heuristic experience to analyze the signs resulting from the segmentation algorithm.

The obtained composite indices of specificity and sensitivity of the classification algorithm display proper quality of recognition of AMD stages (> 83%). Their values were mainly determined by a classification of OCT images from several tomography scanners with various imaging techniques. This occurs due to a wish to improve the generalizing capability of the algorithm for appliances from different manufacturers. It should also be noted that the average result of sensitivity is obtained for the intermediate AMD (58% only). It occurs because the stage of AMD is the most complicated one for recognition due to very similar forms of pathologies. It is suggested that methods of fuzzy logic should be applied to improve sensitivity while determining the stage of AMD during subsequent studies.

CONCLUSIONS

The machine learning algorithm was developed to segment the AMD pathologies based on OCT-images with attention concentration. A physician can apply the obtained results to focus on the most important for diagnostics areas or as part of the recommendation system of detection and determination of an AMD stage that has to be developed in subsequent studies. The algorithm displayed its perspectives regarding organizational issues associated with AMD diagnostics, less load on ophthalmologists, and effective recognition of AMD on OCT images with 98.1% of properly segmented abnormal areas.

Table. Values of specificity and sensitivity for every stage

Quality metrics	Late	Early	Intermediate
Sensitivity *Se*	0.929	0.921	0.58
Specificity *Sp*	0.823	0.769	0.993

References

1. Zapata MA, Royo-Fibla D, Font O, Vela JI, Marcantonio I, Moya-Sánchez EU, et al. Artificial intelligence to identify retinal fundus images, quality validation, laterality evaluation, macular degeneration, and suspected glaucoma. Clinical Ophthalmology (Auckland, NZ). 2020; 14: 419. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7025650/.
2. Stark K, Olden M, Brandl C, Dietl A, Zimmermann M E, Schelter SC, et al. The German AugUR study: study protocol of a prospective study to investigate chronic diseases in the elderly. BMC geriatrics. 2015; 15 (1): 1–8. Available from: https://link.springer.com/article/10.1186/s12877-015-0122-0.
3. Mehta S. Age-related macular degeneration. Primary Care: Clinics in Office Practice. 2015; 42 (3): 377–91. Available from: https://www.primarycare.theclinics.com/article/S0095-4543(15)00042-1/fulltext.
4. Lawrenson JG, Evans JR, Downie LE. A critical appraisal of national and international clinical practice guidelines reporting nutritional recommendations for age-related macular degeneration: are recommendations evidence-based? Nutrients. 2019; 11 (4): 823. Available from: https://www.mdpi.com/2072-6643/11/4/823.
5. Li JQ, Welchowski T, Schmid M, Mauschitz M M, Holz FG, Finger RP. Prevalence and incidence of age-related macular degeneration in Europe: a systematic review and meta-analysis. British Journal of Ophthalmology. 2020; 104 (8): 1077–84. Available from: https://bjo.bmj.com/content/104/8/1077.abstract.
6. Vsemirnyj doklad o problemax zreniya [World report on vision]. Zheneva: Vsemirnaya organizaciya zdravooxraneniya, 2020. Licenziya: CC BY-NC-SA 3.0 IGO.
7. Balashevich LI, Izmajlov AS, Ulitina AYu. Modificirovannaya klinicheskaya klassifikaciya vozrastnoj makulyarnoj degeneracii. Oftal'mologicheskie vedomosti. 2011; 4 (4): 41–47. Available from: https://cyberleninka.ru/article/n/modifitsirovannaya-klinicheskaya-klassifikatsiya-vozrastnoy-makulyarnoy-degeneratsii. Russian.
8. Avdeeva ON, Avetisov SEh, Aklaeva NA, Akopov EL, Alekseev VN, Astaxov SYu, i dr. redaktory. Oftal'mologiya: nacional'noe rukovodstvo. M.: GEhOTAR-Media, 2018; 625 s. Russian.
9. Ferris III FL, Wilkinson CP, Bird A, Chakravarthy U, Chew E, Csaky K, et al. Beckman Initiative for Macular Research Classification Committee. Clinical classification of age-related macular degeneration. Ophthalmology. 2013; 120 (4): 844–51. Available from: https://www.sciencedirect.com/science/article/abs/pii/S016164201201055X.
10. Hyttinen JM, Kannan R, Felszeghy S, Niittykoski M, Salminen A, Kaarniranta K. The regulation of NFE2L2 (NRF2) signalling and epithelial-to-mesenchymal transition in age-related macular degeneration pathology. International journal of molecular sciences. 2019; 20 (22): 5800. Available from: https://www.mdpi.com/1422-0067/20/22/5800.
11. Friedman DS, O'Colmain BJ, Munoz B, Tomany SC, McCarty C, De Jong Pt, et al. Prevalence of age-related macular degeneration in the United States. Arch ophthalmol. 2004; 122 (4): 564–72. Available from: https://jamanetwork.com/journals/jamaophthalmology/article-abstract/416232.
12. Schultz NM, Bhardwaj S, Barclay C, Gaspar L, Schwartz J. Global Burden of Dry Age-Related Macular Degeneration: A Targeted Literature Review. Clin Ther. 2021; 43 (10): 1792–818. DOI: 10.1016/J.CLINTHERA.2021.08.011.
13. The Age-Related Eye Disease Study Research Group. A randomized, placebocontrolled, clinical trial of supplementation with vitamins C and E and beta-carotene for age related cataract and vision loss: AREDS report number 9. Arch. Ophthalmol. 2001; 119: 1439–52.
14. Varma R, Bressler NM, Doan QV, Danese M, Dolan CM, Lee A, et al. Visual impairment and blindness avoided with ranibizumab in Hispanic and non-Hispanic whites with diabetic macular edema in the United States. Ophthalmology. 2015; 122 (5): 982–89. Available from: https://www.sciencedirect.com/science/article/pii/S0161642014011476.
15. Aznabaev BM, Muxamadeev TR, Dibaev TI. Opticheskaya kogerentnaya tomografiya + angiografiya glaza v diagnostike, terapii i xirurgii glaznyx boleznej. M.: Avgust Borg, 2019; 57 s. Russian.
16. Drexler W, Fujimoto JG, editors. Optical coherence tomography: technology and applications. Berlin: Springer, 2015; 2.
17. Victor AA. The Role of Imaging in Age-Related Macular Degeneration. In Visual Impairment and Blindness-What We Know and What We Have to Know. London, UK: IntechOpen, 2019.
18. Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Progress in retinal and eye research. 2018; 67: 1–29. Available from: https://www.sciencedirect.com/science/article/pii/S1350946218300119.
19. Venhuizen FG, van Ginneken B, van Asten F, van Grinsven MJ, Fauser S, Hoyng CB, et al. Automated staging of age-related macular degeneration using optical coherence tomography. Investigative ophthalmology & visual science. 2017; 58 (4): 2318–28. Available from: https://iovs.arvojournals.org/article.aspx?articleid=2623584.
20. Shlyapnikova OA, Kamenskix TG, Roshhepkin VV, Reshnikova LB. Perspektivnye napravleniya razvitiya oftal'mologii (obzor). Saratovskij nauchno-medicinskij zhurnal. 2021; 17 (3): 675–8. Available from: https://cyberleninka.ru/article/n/perspektivnye-napravleniya-razvitiya-oftalmologii-obzor. Russian.
21. Quellec G, Lee K, Dolejsi M, Garvin MK, Abramoff MD, Sonka M. Three-dimensional analysis of retinal layer texture: identification of fluid-filled regions in SD-OCT of the macula. IEEE transactions on medical imaging. 2010; 29 (6): 1321–30. Available from: https://ieeexplore.ieee.org/abstract/document/5440910.
22. Hu Z, Niemeijer M, Abramoff MD, Garvin MK. Multimodal retinal vessel segmentation from spectral-domain optical coherence tomography and fundus photography. IEEE transactions on medical imaging. 2012; 31 (10): 1900–11. Available from: https://ieeexplore.ieee.org/abstract/document/6228540.
23. Esmaeili M, Dehnavi AM, Rabbani H, Hajizadeh F. Three-dimensional segmentation of retinal cysts from spectral-domain optical coherence tomography images by the use of three-dimensional curvelet based K-SVD. Journal of medical signals and sensors. 2016; 6 (3): 166. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4973460/.
24. Chakravarty A, Sivaswamy J. A supervised joint multi-layer segmentation framework for retinal optical coherence tomography images using conditional random field. Comput. Methods Programs Biomed. 2018; 165: 235–50. DOI: 10.1016/J.CMPB.2018.09.004.
25. Bogunović H, et al. Machine Learning of the Progression of Intermediate Age-Related Macular Degeneration Based on OCT Imaging. Investigative ophthalmology & visual science. 2017; 58 (6): BIO141–BIO150.
26. Tvenning AO, Hanssen SR, Austeng D, Morken TS. Deep learning identify retinal nerve fibre and choroid layers as markers of age-related macular degeneration in the classification of macular spectral-domain optical coherence tomography volumes. Acta Ophthalmologica. 2022. DOI: 10.1111/AOS.15126.
27. Rim TH, et al. Detection of features associated with neovascular age-related macular degeneration in ethnically distinct data sets by an optical coherence tomography: trained deep learning algorithm. British Journal of Ophthalmology. 2020; 105 (8): 1133–9. DOI: 10.1136/BJOPHTHALMOL-2020-316984.
28. Zhang G, et al. Clinically relevant deep learning for detection and quantification of geographic atrophy from optical coherence tomography: a model development and external validation study. Lancet Digit Heal. 2021; 3 (10): e665–e675. DOI: 10.1016/S2589-7500(21)00134-5.
29. Sousa JA, Paiva A, Silva A, Almeida JD, Braz Junior G, Diniz JO, et al. Automatic segmentation of retinal layers in OCT images with intermediate age-related macular degeneration using U-Net and DexiNed. Plos one. 2021; 16 (5): e0251591.
30. Alsaih Khaled, et al. Deep learning architectures analysis for age-related macular degeneration segmentation on optical coherence tomography scans. Computer methods and programs

in biomedicine. 2020; 195: 105566.

31. Lee B, D'Souza M, Singman EL, Wang J, Woreta FA, Boland MV, et al. Integration of a physician assistant into an ophthalmology consult service in an academic setting. American journal of ophthalmology. 2018; 190: 125–33. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0002939418301387.
32. Pandey SK, Sharma V. Robotics and ophthalmology: Are we there yet? Indian Journal of Ophthalmology. 2019; 67 (7): 988. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6611303/.
33. Yan Y, Jin K, Gao Z, Huang X, Wang F, Wang Y, et al. Attention — based deep learning system for automated diagnoses of age–related macular degeneration in optical coherence tomography images. Medical Physics. 2021; 48 (9): 4926–34. DOI: 10.1002/MP.15002.
34. Treder M, Lauermann JL, Eter N. Automated detection of exudative age-related macular degeneration in spectral domain optical coherence tomography using deep learning. Graefe's Archive for Clinical and Experimental Ophthalmology. 2017; 256 (2): 259–65. DOI: 10.1007/S00417-017-3850-3.
35. Bhatia KK, Graham MS, Terry L, Wood A, Tranos P, Trikha S, et al. Disease classification of macular optical coherence tomography scans using deep learning software: validation on independent, multicenter data. Retina. 2020; 40 (8): 1549–57. DOI: 10.1097/IAE.0000000000002640.
36. Tvenning AO, Hanssen SR, Austeng D, Morken TS. Deep learning identify retinal nerve fibre and choroid layers as markers of age–related macular degeneration in the classification of macular spectral–domain optical coherence tomography volumes. Acta Ophthalmologica. 2022. DOI: 10.1111/AOS.15126.
37. Sunija AP, Kar S, Gayathri S, Gopi VP, Palanisamy P. Octnet: A lightweight cnn for retinal disease classification from optical coherence tomography images. Computer methods and programs in biomedicine. 2021; 200: 105877. DOI: 10.1016/J.CMPB.2020.105877.
38. Juba B, Le HS. Precision-recall versus accuracy and the role of large data sets. In Proceedings of the AAAI conference on artificial intelligence. 2019; 33 (01): 4039–48. DOI: 10.1609/AAAI.V33I01.33014039.
39. Lowe DG. Distinctive image features from scale-invariant keypoints. International journal of computer vision. 2004; 60 (2): 91–110. Available from: https://link.springer.com/article/10.1023/B:VISI.0000029664.99615.94
40. Shahedi MB, Amirfattahi R, Azar FT, Sadri S. Accurate breast region detection in digital mammograms using a local adaptive thresholding method. In Eighth International Workshop on Image Analysis for Multimedia Interactive Services (WIAMIS'07). IEEE. 2007; 26–26. Available from: https://ieeexplore.ieee.org/abstract/document/4279134.

Литература

1. Zapata MA, Royo-Fibla D, Font O, Vela JI, Marcantonio I, Moya-Sánchez EU, et al. Artificial intelligence to identify retinal fundus images, quality validation, laterality evaluation, macular degeneration, and suspected glaucoma. Clinical Ophthalmology (Auckland, NZ). 2020; 14: 419. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7025650/.
2. Stark K, Olden M, Brandl C, Dietl A, Zimmermann M E, Schelter SC, et al. The German AugUR study: study protocol of a prospective study to investigate chronic diseases in the elderly. BMC geriatrics. 2015; 15 (1): 1–8. Available from: https://link.springer.com/article/10.1186/s12877-015-0122-0.
3. Mehta S. Age-related macular degeneration. Primary Care: Clinics in Office Practice. 2015; 42 (3): 377–91. Available from: https://www.primarycare.theclinics.com/article/S0095-4543(15)00042-1/fulltext.
4. Lawrenson JG, Evans JR, Downie LE. A critical appraisal of national and international clinical practice guidelines reporting nutritional recommendations for age-related macular degeneration: are recommendations evidence-based? Nutrients. 2019; 11 (4): 823. Available from: https://www.mdpi.com/2072-6643/11/4/823.
5. Li JQ, Welchowski T, Schmid M, Mauschitz M M, Holz FG, Finger RP. Prevalence and incidence of age-related macular degeneration in Europe: a systematic review and meta-analysis. British Journal of Ophthalmology. 2020; 104 (8): 1077–84. Available from: https://bjo.bmj.com/content/104/8/1077.abstract.
6. Всемирный доклад о проблемах зрения [World report on vision]. Женева: Всемирная организация здравоохранения, 2020. Лицензия: CC BY-NC-SA 3.0 IGO.
7. Балашевич Л. И., Измайлов А. С., Улитина А. Ю. Модифицированная клиническая классификация возрастной макулярной дегенерации. Офтальмологические ведомости. 2011; 4 (4): 41–47. Available from: https://cyberleninka.ru/article/n/modifitsirovannaya-klinicheskaya-klassifikatsiya-vozrastnoy-makulyarnoy-degeneratsii.
8. Авдеева О. Н., Аветисов С. Э., Аклаева Н. А., Акопов Е. Л., Алексеев В. Н., Астахов С. Ю., и др. редакторы. Офтальмология: национальное руководство. М.: ГЭОТАР-Медиа, 2018; 625 с.
9. Ferris III FL, Wilkinson CP, Bird A, Chakravarthy U, Chew E, Csaky K, et al. Beckman Initiative for Macular Research Classification Committee. Clinical classification of age-related macular degeneration. Ophthalmology. 2013; 120 (4): 844–51. Available from: https://www.sciencedirect.com/science/article/abs/pii/S016164201201055X.
10. Hyttinen JM, Kannan R, Felszeghy S, Niittykoski M, Salminen A, Kaarniranta K. The regulation of NFE2L2 (NRF2) signalling and epithelial-to-mesenchymal transition in age-related macular degeneration pathology. International journal of molecular sciences. 2019; 20 (22): 5800. Available from: https://www.mdpi.com/1422-0067/20/22/5800.
11. Friedman DS, O'Colmain BJ, Munoz B, Tomany SC, McCarty C, De Jong Pt, et al. Prevalence of age-related macular degeneration in the United States. Arch ophthalmol. 2004; 122 (4): 564–72. Available from: https://jamanetwork.com/journals/jamaophthalmology/article-abstract/416232.
12. Schultz NM, Bhardwaj S, Barclay C, Gaspar L, Schwartz J. Global Burden of Dry Age-Related Macular Degeneration: A Targeted Literature Review. Clin Ther. 2021; 43 (10): 1792–818. DOI: 10.1016/J.CLINTHERA.2021.08.011.
13. The Age-Related Eye Disease Study Research Group. A randomized, placebocontrolled, clinical trial of supplementation with vitamins C and E and beta-carotene for age related cataract and vision loss: AREDS report number 9. Arch. Ophthalmol. 2001; 119: 1439–52.
14. Varma R, Bressler NM, Doan QV, Danese M, Dolan CM, Lee A, et al. Visual impairment and blindness avoided with ranibizumab in Hispanic and non-Hispanic whites with diabetic macular edema in the United States. Ophthalmology. 2015; 122 (5): 982–89. Available from: https://www.sciencedirect.com/science/article/pii/S0161642014011476.
15. Азнабаев Б. М., Мухамадеев Т. Р., Дибаев Т. И. Оптическая когерентная томография + ангиография глаза в диагностике, терапии и хирургии глазных болезней. М.: Август Борг, 2019; 57 с.
16. Drexler W, Fujimoto JG, editors. Optical coherence tomography: technology and applications. Berlin: Springer, 2015; 2.
17. Victor AA. The Role of Imaging in Age-Related Macular Degeneration. In Visual Impairment and Blindness-What We Know and What We Have to Know. London, UK: IntechOpen, 2019.
18. Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Progress in retinal and eye research. 2018; 67: 1–29. Available from: https://www.sciencedirect.com/science/article/pii/S1350946218300119.
19. Venhuizen FG, van Ginneken B, van Asten F, van Grinsven MJ, Fauser S, Hoyng CB, et al. Automated staging of age-related macular degeneration using optical coherence tomography. Investigative ophthalmology & visual science. 2017; 58 (4):

2318–28. Available from: https://iovs.arvojournals.org/article.aspx?articleid=2623584.
20. Шляпникова О. А., Каменских Т. Г., Рощепкин В. В., Решникова Л. Б. Перспективные направления развития офтальмологии (обзор). Саратовский научно-медицинский журнал. 2021; 17 (3): 675–8. Available from: https://cyberleninka.ru/article/n/perspektivnye-napravleniya-razvitiya-oftalmologii-obzor.
21. Quellec G, Lee K, Dolejsi M, Garvin MK, Abramoff MD, Sonka M. Three-dimensional analysis of retinal layer texture: identification of fluid-filled regions in SD-OCT of the macula. IEEE transactions on medical imaging. 2010; 29 (6): 1321–30. Available from: https://ieeexplore.ieee.org/abstract/document/5440910.
22. Hu Z, Niemeijer M, Abramoff MD, Garvin MK. Multimodal retinal vessel segmentation from spectral-domain optical coherence tomography and fundus photography. IEEE transactions on medical imaging. 2012; 31 (10): 1900–11. Available from: https://ieeexplore.ieee.org/abstract/document/6228540.
23. Esmaeili M, Dehnavi AM, Rabbani H, Hajizadeh F. Three-dimensional segmentation of retinal cysts from spectral-domain optical coherence tomography images by the use of three-dimensional curvelet based K-SVD. Journal of medical signals and sensors. 2016; 6 (3): 166. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4973460/.
24. Chakravarty A, Sivaswamy J. A supervised joint multi-layer segmentation framework for retinal optical coherence tomography images using conditional random field. Comput. Methods Programs Biomed. 2018; 165: 235–50. DOI: 10.1016/J.CMPB.2018.09.004.
25. Bogunović H, et al. Machine Learning of the Progression of Intermediate Age-Related Macular Degeneration Based on OCT Imaging. Investigative ophthalmology & visual science. 2017; 58 (6): BIO141–BIO150.
26. Tvenning AO, Hanssen SR, Austeng D, Morken TS. Deep learning identify retinal nerve fibre and choroid layers as markers of age-related macular degeneration in the classification of macular spectral-domain optical coherence tomography volumes. Acta Ophthalmologica. 2022. DOI: 10.1111/AOS.15126.
27. Rim TH, et al. Detection of features associated with neovascular age-related macular degeneration in ethnically distinct data sets by an optical coherence tomography: trained deep learning algorithm. British Journal of Ophthalmology. 2020; 105 (8): 1133–9. DOI: 10.1136/BJOPHTHALMOL-2020-316984.
28. Zhang G, et al. Clinically relevant deep learning for detection and quantification of geographic atrophy from optical coherence tomography: a model development and external validation study. Lancet Digit Heal. 2021; 3 (10): e665–e675. DOI: 10.1016/S2589-7500(21)00134-5.
29. Sousa JA, Paiva A, Silva A, Almeida JD, Braz Junior G, Diniz JO, et al. Automatic segmentation of retinal layers in OCT images with intermediate age-related macular degeneration using U-Net and DexiNed. Plos one. 2021; 16 (5): e0251591.
30. Alsaih Khaled, et al. Deep learning architectures analysis for age-related macular degeneration segmentation on optical coherence tomography scans. Computer methods and programs in biomedicine. 2020; 195: 105566.
31. Lee B, D'Souza M, Singman EL, Wang J, Woreta FA, Boland MV, et al. Integration of a physician assistant into an ophthalmology consult service in an academic setting. American journal of ophthalmology. 2018; 190: 125–33. Available from: https://www.sciencedirect.com/science/article/abs/pii/S0002939418301387.
32. Pandey SK, Sharma V. Robotics and ophthalmology: Are we there yet? Indian Journal of Ophthalmology. 2019; 67 (7): 988. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6611303/.
33. Yan Y, Jin K, Gao Z, Huang X, Wang F, Wang Y, et al. Attention — based deep learning system for automated diagnoses of age–related macular degeneration in optical coherence tomography images. Medical Physics. 2021; 48 (9): 4926–34. DOI: 10.1002/MP.15002.
34. Treder M, Lauermann JL, Eter N. Automated detection of exudative age-related macular degeneration in spectral domain optical coherence tomography using deep learning. Graefe's Archive for Clinical and Experimental Ophthalmology. 2017; 256 (2): 259–65. DOI: 10.1007/S00417-017-3850-3.
35. Bhatia KK, Graham MS, Terry L, Wood A, Tranos P, Trikha S, et al. Disease classification of macular optical coherence tomography scans using deep learning software: validation on independent, multicenter data. Retina. 2020; 40 (8): 1549–57. DOI: 10.1097/IAE.0000000000002640.
36. Tvenning AO, Hanssen SR, Austeng D, Morken TS. Deep learning identify retinal nerve fibre and choroid layers as markers of age–related macular degeneration in the classification of macular spectral–domain optical coherence tomography volumes. Acta Ophthalmologica. 2022. DOI: 10.1111/AOS.15126.
37. Sunija AP, Kar S, Gayathri S, Gopi VP, Palanisamy P. Octnet: A lightweight cnn for retinal disease classification from optical coherence tomography images. Computer methods and programs in biomedicine. 2021; 200: 105877. DOI: 10.1016/J.CMPB.2020.105877.
38. Juba B, Le HS. Precision-recall versus accuracy and the role of large data sets. In Proceedings of the AAAI conference on artificial intelligence. 2019; 33 (01): 4039–48. DOI: 10.1609/AAAI.V33I01.33014039.
39. Lowe DG. Distinctive image features from scale-invariant keypoints. International journal of computer vision. 2004; 60 (2): 91–110. Available from: https://link.springer.com/article/10.1023/B:VISI.0000029664.99615.94
40. Shahedi MB, Amirfattahi R, Azar FT, Sadri S. Accurate breast region detection in digital mammograms using a local adaptive thresholding method. In Eighth International Workshop on Image Analysis for Multimedia Interactive Services (WIAMIS'07). IEEE. 2007; 26–26. Available from: https://ieeexplore.ieee.org/abstract/document/4279134.