

Automatic system to determine indications for 2RT treatment

Ionov Artem¹[0009-0001-2319-3015], Ilyasova Natalia^{1, 2}[0000-0003-3027-1963], Zolotarev Andrey³[0000-0002-9107-5221], Dotsenko Kamila³[0009-0002-2578-2646], Demin Nikita^{1, 2}[0000-0002-8707-770X]

¹ Samara National Research University, Moskovskoye Shosse 34, 443086 Samara, Russia

² Image Processing Systems Institute, NRC "Kurchatov Institute", Molodogvardeyskaya Street 151, 443001 Samara, Russia

³ Samara State Medical University, Chapayevskaya Street 89, 443079 Samara, Russia
artem.ionov.96@mail.ru

Abstract. Age-related macular degeneration (AMD) is a leading cause of irreversible vision loss in individuals over 50 years of age. Nanosecond retinoreparative laser therapy (2RT) is an innovative treatment for early and intermediate forms of AMD. However, the efficacy and safety of this method critically depend on proper patient selection, which requires accurate identification of a number of biomarkers – indications and contraindications – on optical coherence tomography (OCT). This paper presents an automated decision support system for physicians designed to determine indications for 2RT treatment. The system includes sequential processing of OCT images: segmentation of retinal layers and soft drusen using a modified Attention U-Net convolutional neural network (0.92 accuracy), an algorithm for detecting reticular pseudodrusen based on the classification of regions of interest (SVM model, 0.72 accuracy), and detection and classification of atrophy (Random Forest model, 0.88 accuracy). Additionally, calculation of the geometric parameters of soft drusen and drusenoid detachments has been implemented. A graphical interface has been developed that allows for the loading of OCT scan series, visualization of results, and tools for manual analysis. The proposed system reduces the workload of the diagnostician, improves the reproducibility of assessments, and expedites the selection of patients for 2RT therapy.

Keywords: Age-Related Macular Degeneration, Optical Coherence Tomography, Nanosecond Laser Therapy, Image Segmentation, Convolutional Neural Networks, Reticular Pseudodrusen, Atrophy, Soft Drusen.

1 Introduction

Age-related macular degeneration is one of the leading causes of blindness worldwide, especially among people over 50 years of age [1, 2]. A novel treatment for early and intermediate forms of AMD is the nanosecond laser 2RT (Nano Second Retinal Therapy), which stimulates reparative processes in the retina [3]. 2RT's mechanism of action involves selectively targeting the retinal pigment epithelium with nanosecond laser

pulses, triggering a cascade of reparative processes: activation of growth factors, reduction of drusenous load, and restoration of the barrier function of the pigment epithelium [4, 5]. Unlike macropulse lasers, 2RT does not cause thermal damage to the neurosensory network, as confirmed by histological studies [6, 7].

However, the efficacy and safety of this method critically depend on proper patient selection: therapy is indicated for soft drusen or drusenoid detachments less than 1000 μm wide, but is contraindicated in the presence of reticular pseudodrusen (RPD) or atrophy of the outer retinal layers [8, 9]. The therapy includes specific circumstances and abnormalities associated with specific types of changes observed on optical coherence tomography.

Fig. 1a shows an example of soft drusen indicated for 2RT treatment (in the absence of other abnormalities). Fig. 1b shows RPD one of the main abnormalities. Another contraindication is atrophy of the retinal pigment epithelium and retinal layers (Fig. 1c) [10].

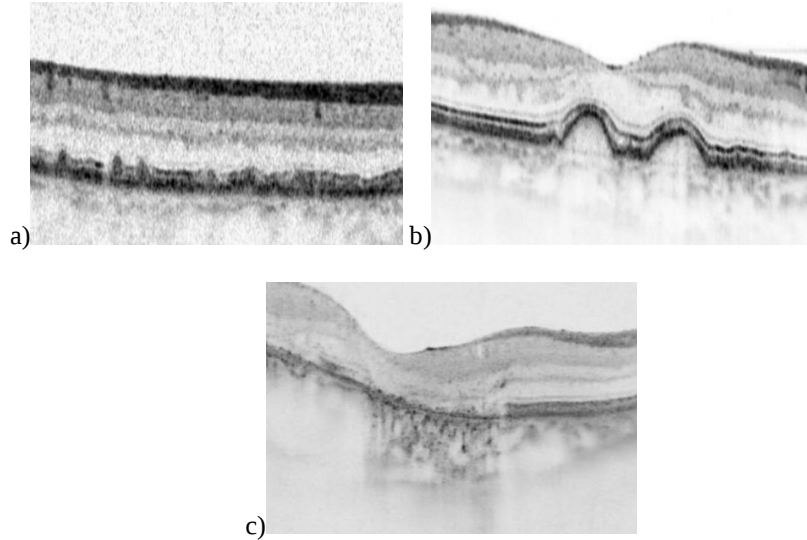


Fig. 1. Biomarkers of age-related macular degeneration on optical coherence tomography images. (a) Soft drusen, which are an indication for 2RT laser therapy. (b) Reticular pseudodrusen, which are a contraindication to treatment. (c) Atrophy of the retinal pigment epithelium and outer retinal layers, also classified as a contraindication.

Differentiation of these structures on OCT is difficult due to the small size of reticular drusen, low contrast and variety of atrophy types [11, 12]. Diagnostic errors lead to unjustified refusal of treatment or to therapy in the presence of contraindications, which accelerates disease progression [13, 14]. In this regard, the development of an automatic system capable of analyzing OCT images and forming a conclusion on the possibility of 2RT laser therapy is relevant [15, 16]. Such a system can be based on a strict diagnostic algorithm regulating the sequence of biomarker detection, the scheme of which is shown in Fig. 2. To solve image segmentation problems in such systems, convolutional neural network architectures such as U-Net [17] and Attention U-Net

[18] are used, and the support vector machine [19] and random forest [20] are used for classification.

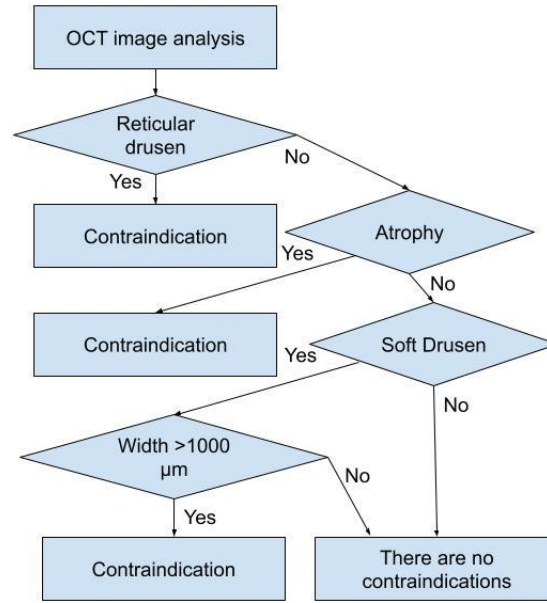


Fig. 2. Algorithm for determining indications for 2RT laser treatment based on OCT data

The hypothetical system must strictly follow the algorithm shown in Fig. 2. The first step involves preprocessing and segmenting the OCT image to identify retinal layers and soft drusen. Then, the presence of contraindications is sequentially checked: RPD are detected first. If they are detected, the system issues a "Contraindicated" verdict without further analysis. If no RPD is present, the algorithm proceeds to a search for atrophy. If any type of atrophy is detected (complete, outer layers, or lower layers), a contraindication is also issued. Only in the absence of both contraindications does the system evaluate the indications: the presence of soft drusen and measurement of the drusenoid detachment width. If the width does not exceed 1000 μm , a "Indicated" verdict is issued; otherwise, a "Contraindicated" verdict is issued. This strict sequence eliminates the possibility of erroneous prescription of 2RT therapy in the presence of any absolute contraindication.

2 Structure and components of the automatic system

The developed system is a sequential OCT image processing technology. A retinal B-scan is input. The output is a visualized report with highlighted biomarkers and a textual summary regarding the feasibility of 2RT. The overall system flowchart is shown in Fig. 3.

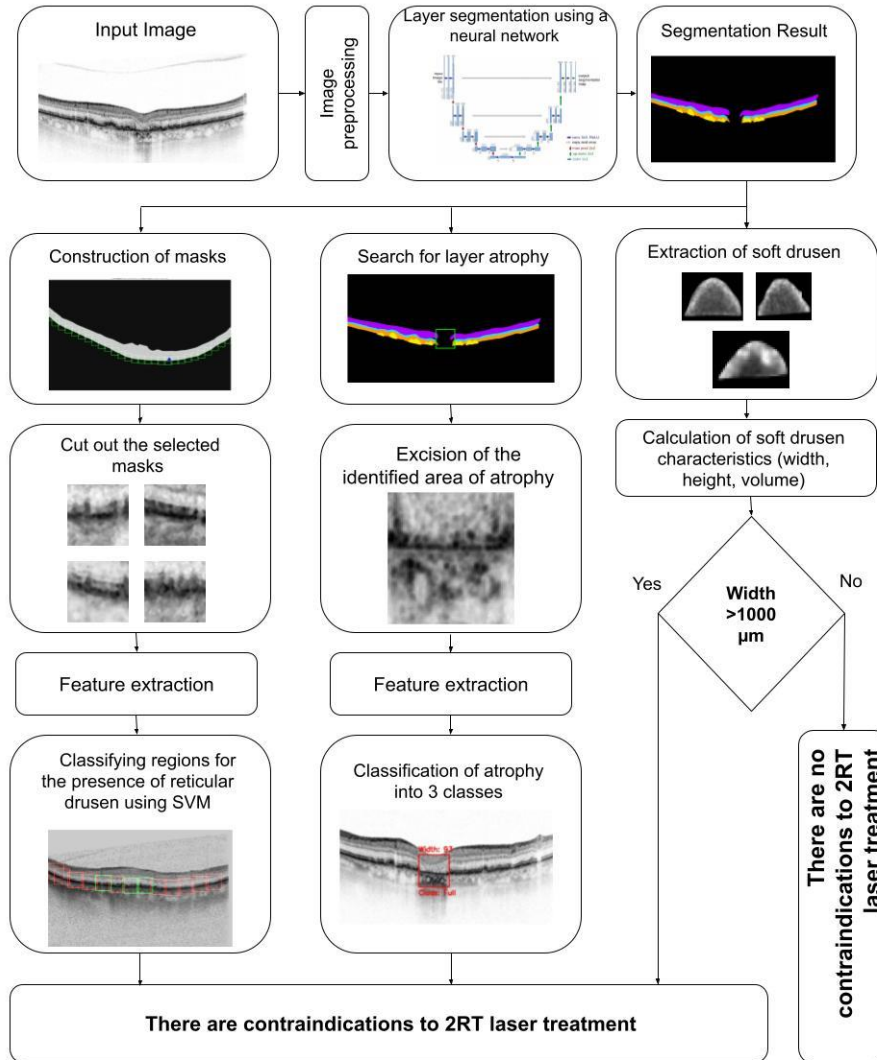


Fig. 3. Flowchart of the technology for automatic determination of indications for 2RT laser treatment

The system includes the following sequential stages: pre-processing of the original OCT image, segmentation of layers and soft drusen using the Attention U-Net neural network, searching for RPD based on the classification of areas of interest (SVM), detection and classification of atrophy (Random Forest), calculation of the geometric parameters of soft drusen, and the formation of the final conclusion.

2.1 Data preprocessing

All source OCT images obtained from four types of scanners (HUVITZ, Optopol, Optovue, Heidelberg) are median filtered (3x3 kernel), normalized, and resized to a standard size of 256x256 pixels. To improve the generalization ability of the models, augmentation (rotations) is applied. To increase the diversity of the training set and improve the generalization ability of the model, data augmentation was performed, specifically image rotation (Fig. 4).

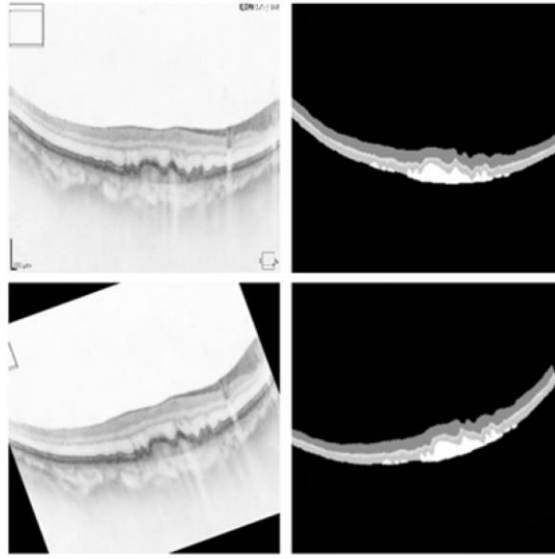


Fig. 4. Augmented data: original image and its corresponding mask

2.2 Segmentation of retinal layers and soft drusen

The first key step of the technology is semantic segmentation, which identifies pigment epithelium, the ellipsoid zone of photoreceptors, the external limiting membrane, and soft drusen. A comparative experiment evaluated the U-Net, Attention U-Net, and U-Net++ architectures. The Attention U-Net model demonstrated the best results, achieving 0.91 accuracy on the validation set and 0.92 on the test set. The average IoU (Intersection over Union) across all classes was 0.83.

The quality of soft drusen segmentation proved particularly high (F1 score of 0.90 on the test data). This model formed the basis for all subsequent algorithms. Fig. 5 below shows a comparison of the predicted and true masks from the test set.

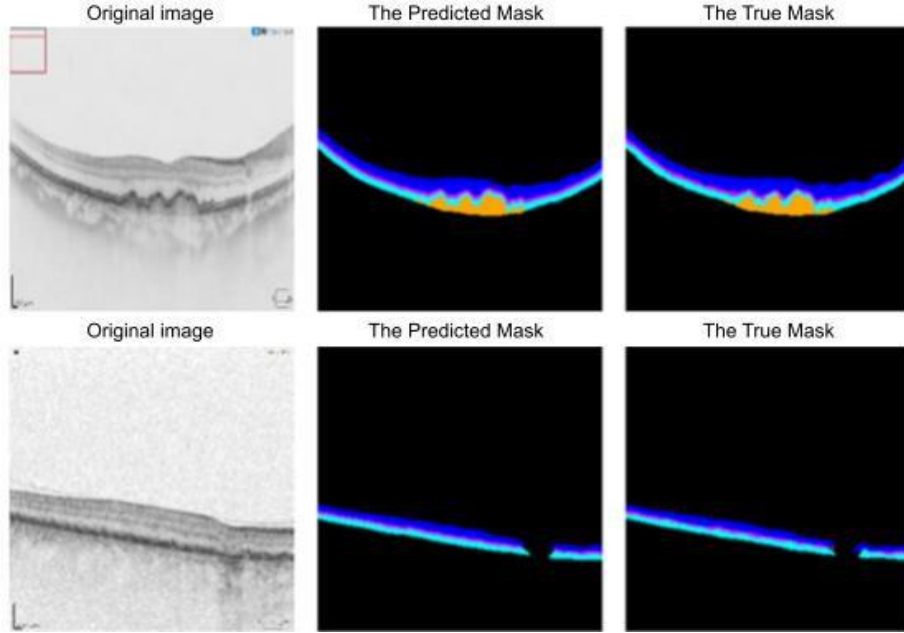


Fig. 5. Predicted and true mask from the test sample

2.3 Detection of reticular pseudodrusen

The second stage of the technology is the detection of RPD. Since RPDs are small and have low contrast, directly adding a separate class to the segmentation network yielded unsatisfactory results (recognition accuracy of approximately 0.35). Therefore, a two-stage algorithm was developed. First, the pigment epithelium zone is identified using the trained Attention U-Net model. Along the lower boundary of this layer, 64x64 pixel windows are formed (Fig. 6), each of which is classified as the presence or absence of RPDs. Features are extracted from each window: intensity histogram, HOG descriptors, Haralick texture features, and local binary patterns (LBP). After feature selection, classification is performed using a support vector machine (SVM). In a cross-validation experiment with five classifiers, SVM demonstrated maximum accuracy of 0.72 on the test set. The system combines adjacent positive windows into rectangular regions, visually indicating the location of RPDs.

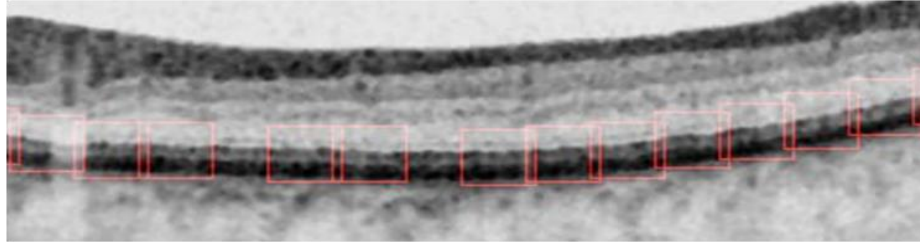


Fig. 6. Construction of masks along the pigment epithelium

2.4 Detection and classification of atrophy

The third stage of the technology is the identification of atrophy as a strict contraindication to 2RT. The algorithm analyzes the contours of segmented layers. If a gap is detected in any layer (pigment epithelium, ellipsoid zone, or external limiting membrane) – that is, two separate contours instead of one – the gap area is localized and cropped from the original image. To improve the information content, a classification into three types was introduced: complete atrophy of the pigment epithelium and outer layers; atrophy of the outer layers with a preserved pigment layer; atrophy of the lower layers with preservation of the upper layers. The Random Forest ensemble method is used for classification. Due to the limited number of training samples for rare classes, augmentation was applied. Random Forest outperformed other models (quadratic discriminant analysis, KNN, logistic regression), achieving an overall accuracy of 0.88 on the test set. The result of the algorithm is displayed as a rectangular area around the atrophy zone with a text label of the type (Full, Up, Down) and the measured width, as shown in Fig. 7.

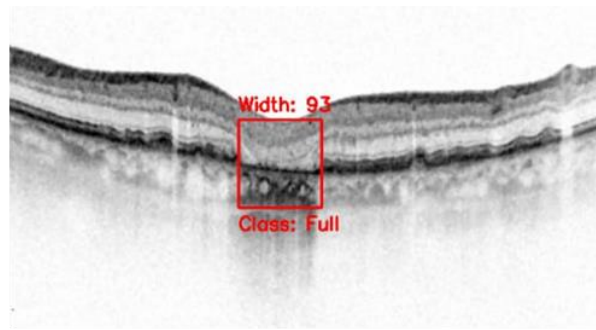


Fig. 7. An example of using the search and classification algorithm for atrophy

2.5 Calculation of parameters of soft drusen and drusenoid detachment

The fourth stage of the technology is the quantitative assessment of soft drusen. One of the main indications for 2RT is the presence of soft drusen or drusenoid detachment, but the detachment width should not exceed 1000 μm . The algorithm separates the objects identified by the U-Net into single soft drusen (one peak on the horizontal pixel

density plot) and confluent drusenoid detachments (two or more peaks). For each object, the area, width, and height are calculated and converted to microns (based on image calibration). If the threshold of 1000 μm is exceeded, the system identifies a contraindication.

3 Software implementation and user interface

The developed technology for automatically determining indications for 2RT laser treatment is implemented as a Python software tool. The PyQt5 module was used to create the graphical interface, OpenCV and NumPy libraries were used for image manipulation, and TensorFlow/Keras and joblib were used for the neural network and classifiers. All computations are performed on the central processor.

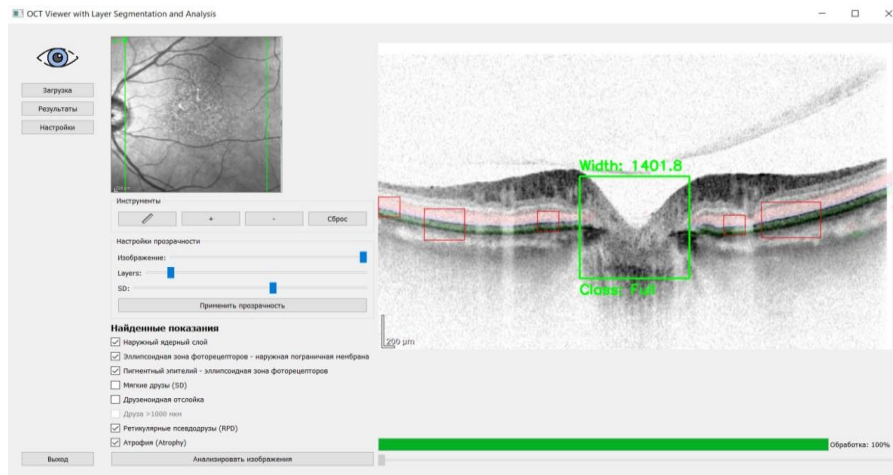


Fig. 8. Graphical interface of the system

The graphical interface (Fig. 8) allows the user to upload a single or a series of OCT images, set the zoom level, and launch automatic analysis. After processing, the system displays the original image and the resulting image with overlaid color masks: retinal layers, soft drusen, and rectangular areas around RPD and atrophic zones are highlighted. For each area of atrophy, its type is indicated (complete, atrophy of the outer layers, or atrophy of the lower layers). All identified indications and contraindications are displayed in the text panel.

4 Conclusion

In this study, we developed and implemented a system for automatically determining indications for 2RT laser treatment for age-related macular degeneration based on OCT image analysis. The relevance of this study is due to the high prevalence of AMD, one

of the leading causes of blindness worldwide, as well as the complexity and labor-intensive nature of diagnostic testing for contraindications to nanosecond retinal reparative therapy.

The technology developed for the system includes several sequential steps: preprocessing of the original OCT images; segmentation of retinal layers (pigment epithelium, ellipsoid zone of photoreceptors, external limiting membrane) and soft drusen using a convolutional neural network; detection of reticular pseudodrusen based on the classification of zones of interest; detection and classification of atrophic changes; and calculation of the geometric parameters of soft drusen and drusenoid detachment.

In a comparative experiment, the Attention U-Net architecture demonstrated the best results with an accuracy of 0.92 on the test set. An SVM model with an accuracy of 0.72 was selected for detecting RPD. A Random Forest model with an accuracy of 0.88 was selected for classifying atrophy into three types (complete atrophy, atrophy of the outer layers, and atrophy of the lower layers). An algorithm for calculating the width, height, and area of soft drusen was implemented, with a 1000 μm threshold for drusenoid detachment.

For practical use, a graphical user interface has been created that allows users to upload OCT image series, perform automatic analysis, view results with visualization of selected structures, and use tools for detailed image examination.

The developed system will reduce the workload of diagnosticians, minimize the risk of errors in identifying contraindications, accelerate the process of selecting patients for nanosecond retinoreparative therapy, and thereby improve the effectiveness of treatment for age-related macular degeneration.

Acknowledgment

The work was carried out within the state assignment of IPSI, NRC “Kurchatov institute”.

References

1. Fleckenstein, M., et al.: Age-related macular degeneration. *Nature Reviews Disease Primers* 7(1), 31 (2021)
2. Lim, L.S., et al.: Age-related macular degeneration. *The Lancet* 379(9827), 1728–1738 (2012)
3. Guymer, R.H., et al.: Subthreshold Nanosecond Laser Intervention in Age-Related Macular Degeneration: The LEAD Randomized Controlled Clinical Trial. *Ophthalmology* 126(6), 829–838 (2019)
4. Luttrull, J.K., et al.: Subthreshold diode micropulse laser photocoagulation. *Retina* 25(5), 567–573 (2005)
5. Lavinsky, D., et al.: Functional changes after subthreshold nanosecond laser in AMD. *Investigative Ophthalmology & Visual Science* 55(13), 3450 (2014)
6. Wood, J.P.M., et al.: Nanosecond laser therapy in AMD. *Clinical & Experimental Ophthalmology* 46(5), 512–520 (2018)
7. Sivaprasad, S., et al.: Subthreshold nanosecond laser in AMD. *Eye* 34(1), 137–144 (2020)

8. Khanifar, A.A., et al.: Drusen ultrastructure imaging with spectral domain optical coherence tomography in age-related macular degeneration. *Ophthalmology* 115(11), 1883–1890 (2008)
9. Spaide, R.F., et al.: Consensus nomenclature for reporting neovascular age-related macular degeneration data. *Ophthalmology* 127(5), 616–636 (2020)
10. Zweifel, S.A., et al.: Reticular pseudodrusen in age-related macular degeneration. *Retina* 31(8), 1498–1504 (2011)
11. Curcio, C.A., et al.: Reticular pseudodrusen in age-related macular degeneration. *Investigative Ophthalmology & Visual Science* 54(14), 2960 (2013)
12. Sadda, S.R., et al.: Consensus definition for atrophy in age-related macular degeneration. *Ophthalmology* 125(4), 537–548 (2018)
13. Holz, F.G., et al.: Progression of geographic atrophy in age-related macular degeneration. *Ophthalmology* 121(11), 2179–2186 (2014)
14. Wu, Z., et al.: Nanosecond laser therapy for age-related macular degeneration: systematic review. *Clinical & Experimental Ophthalmology* 49(4), 345–356 (2021)
15. Mares, V., et al.: AI-based support for optical coherence tomography in age-related macular degeneration. *International Journal of Retina and Vitreous* 10(1), 31 (2024)
16. Muntean, G.A., et al.: The Predictive Capabilities of Artificial Intelligence-Based OCT Analysis for Age-Related Macular Degeneration Progression – A Systematic Review. *Diagnostics* 13(14), 2464 (2023)
17. Ronneberger, O., et al.: U-Net: Convolutional networks for biomedical image segmentation. In: Navab, N., Hornegger, J., Wells, W.M., Frangi, A.F. (eds.) *Medical Image Computing and Computer-Assisted Intervention – MICCAI 2015*. LNCS, vol. 9351, pp. 234–241. Springer, Cham (2015)
18. Oktay, O., et al.: Attention U-Net: Learning where to look for the pancreas. *arXiv:1804.03999* (2018)
19. Cortes, C., Vapnik, V.: Support-vector networks. *Machine Learning* 20(3), 273–297 (1995)
20. Breiman, L.: Random forests. *Machine Learning* 45(1), 5–32 (2001)