Decision-making support system for the personalization of retinal laser treatment in diabetic retinopathy

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Abstract

In this work, we propose a decision-making support system for automatically mapping an effective photocoagulation pattern for the laser treatment of diabetic retinopathy.

The purpose of research to create automated personalization of diabetic macular edema laser treatment. The results are based on analysis of large semi-structured data, methods and algorithms for fundus image processing. The technology improves the quality of retina laser coagulation in the treatment of diabetic macular edema, which is one of the main reasons for pronounced vision decrease. The proposed technology includes original solutions to establish an optimal localization of multitude burns by determining zones exposed to laser. It also includes the recognition of large amount of unstructured data on the anatomical and pathological locations' structures in the area of edema and data optical coherent tomography. As a result, a uniform laser application on the pigment epithelium of the affected retina is ensured. It will increase the treatment safety and its effectiveness, thus avoiding the use of more expensive treatment methods. Assessment of retinal lesions volume and quality will allow predicting the laser photocoagulation results and will contribute to the improvement of laser surgeon's skills. The architecture of a software complex comprises a number of modules, including image processing methods, algorithms for photocoagulation pattern mapping, and intelligent analysis methods.

Keywords: fundus, laser coagulation, diabetic retinopathy, image processing; segmentation; classification.

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Introduction

Artificial intelligence technologies are penetrating all spheres of human activity. The modern medicine is one of the most high-tech industries. Recently the introduction of artificial intelligence and digital medicine technologies into healthcare practice is rapidly changing the methods of diagnosis and treatment [1, 2]. Increasingly, robotic systems are being used to support the diagnosis and treatment of diseases [3]. 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 [4]. 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 [5 – 7]. If timely treatment, vision loss can be prevented in more than 50 % of cases [8 – 12]. 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 [13 – 16]. Modern systems mainly rely on the use of a preset pattern for generating a photocoagulation map [14 – 16]. However, due to highly variable shapes of the macular edema and vascular system, a uniform photocoagulation map cannot be realized using a standard pattern [14 – 15]. The state-of-the-art system NAVINAS provides an option of manually mapping a coagulation plan, which is then used for automatically guiding the laser [17 – 21]. 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). The proposed technology is fundamentally new, since the procedure for optimizing laser coagulation based on intelligent analysis of fundus images and optical coherence tomography (OCT) of the retina has not been previously considered in the literature. 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.

In this work, we propose architecture of the software for automatically mapping an effective photocoagulation pattern for the laser treatment of DR. The architecture comprises a number of modules, including image processing methods, algorithms for photocoagulation pattern mapping, and intelligent analysis methods.

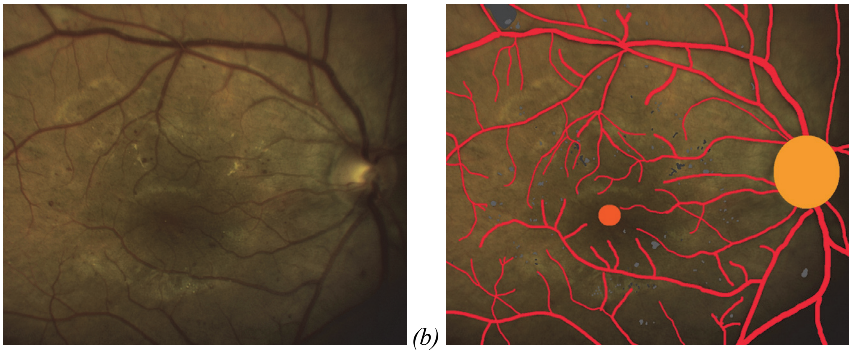
1. Technology of mapping a laser photocoagulation plan

In the first stage of the proposed information technology for mapping a photocoagulation pattern, a laser photocoagulation region of interest (ROI) is extracted, for which the result of the retinal image segmentation needs to be known. Methods for the retinal image segmentation work by extracting different classes of objects in the image. In the retinal image, one may observe areas prohibited for the laser light expo-sure. The prohibited areas, firstly, include the disk of optic nerve, the fovea, and blood vessels. The retinal image may also contain pathological formations, like edema and exudates, which should not be exposed to the laser light to avoid negative effects.

Retinal image segmentation was done by calculating texture features in the image neighborhoods, followed by the feature-based classification. Out of the large set of features, most informative ones were chosen to simplify the classification process.

In biomedical image recognition and analysis, the majority of tasks are solved using texture features [22–24], which are abundant. Studies looked into calculating the following groups of features: (a) histogram features; (b) gradient features; and (c) Haralik features. Texture features have been utilized for extracting vessels, exudates, and other elements in the retinal image. Some elements are better extracted using geometric parameters. For instance, a method for extracting the disk of optic nerve (DON) by means of a local fan transform and evaluating the vessel direction at the DON edge has been reported [25]. The texture features are mainly utilized for extracting freeform objects that can be located everywhere across the image. The main drawback of the texture-feature-based segmentation is its high computational complexity. An alternative approach is based on the use of a convolutional neural net-work U-Net, whose key drawback is the need to have a fairly large sampling with the ROIs marked off by a doctor-expert [26].

Fig. 1 illustrates segmentation examples for various areas in the retinal image. Provided an accurate extraction of prohibited areas, the system will provide a safe exposure of the retina to the laser light as it will avoid the prohibited retina areas. In this respect, segmentation plays a key role in providing safe DR treatment.



(a) *(b)*

Fig. 1. An example of fundus image segmentation: original image (a); segmented image: the optic disc, fovea, exudates and vessels are highlighted (b)

The method of extracting the ROI for laser treatment presupposes that prohibited areas are excluded from the pathological zone, with the latter being outlined based on optical coherence tomography (OCT) date. Using OCT images, it is possible to recon-struct a map of thickness deviations of a given retina from the healthy one, with high deviations indicating that the given region needs to be photocoagulated.

The deviation map is built by evaluating the difference between the OCT-aided retinal thick-ness map and that of a healthy retina. As a result, a map of the regions to be photo-coagulated is created [27, 28].

The algorithms for creating a photocoagulation plan operate by marking future photocoagulation spots in the ROI while aiming to attain optimal parameters or a suitable photocoagulation pattern [28, 29]. Most importantly, the plan needs to pro-vide safe photocoagulation, meaning that the inter-coagulate distance should not be smaller than the present one. What is equally important is that the pattern-based treatment should produce a therapeutic effect. The effectiveness of a photocoagulation pattern can be estimated by calculating a number of features relating to the mutual position of coagulates. The majority of the features can be best described in terms of the inter-coagulate distance. The sampling of distances can be formed in a variety of ways, for instance, by conducting a Delaunay triangulation relative to marked points. In [28], seven algorithms for mapping a photocoagulation pattern were proposed. Each of the proposed algorithms offers its own photocoagulation plan, for which characteristics such as variance, a median, and the number of coagulates need primarily to be analyzed (Tab. 1).

Table 1. Feature values for various algorithms for mapping a coagulation plan

Algorithm	Variance	Median	Number
Random map	6.32	31.62	223
Square map	6.09	30.00	220
Hexagonal map	7.68	30.00	248
Wave map	0.95	30.08	311
Boundary map	0.90	30.08	305
Boundary-adaptive map	0.70	30.07	315
Ordered map	0.19	30.08	312

The proposed techniques were used as a basis for a technology of mapping a photocoagulation pattern, allowing the efficacy of DR treatment to be enhanced (fig. 2). The technology is aimed at mapping an effective photocoagulation pattern [27]. The ophthalmologist will be able to correct the processing result for any block in the diagram in fig. 2. For instance, the ophthalmological surgeon can correct the outline of the ROIs for laser treatment if in their opinion the ROIs have not all been automatically marked off.

Among the above-described stages, the data matching stage presupposes that key points can be marked off both manually and using automatic algorithms. The experience of practical eye surgeons suggests that marking off the key points is not a problem. What presents the problem is the need to perform the manual segmentation of retinal images and laying-out of the coagulation pattern as both procedures are cumbersome and subjective. Because of this, automatization of these procedures is key in developing the technology.

For the pathological zone to be extracted, one needs to have information on deviations of the retina thickness from the normal values, which can be derived using the medical software SOCT [30]. For the pathological zone to be extracted, one needs to have information on deviations of the retina thickness from the normal values, which can be derived using the medical software SOCT [30]. By performing preprocessing, the software builds a map of deviations of a particular retina from the norm. Enhanced deviations indicate that the given zone has a pathology.

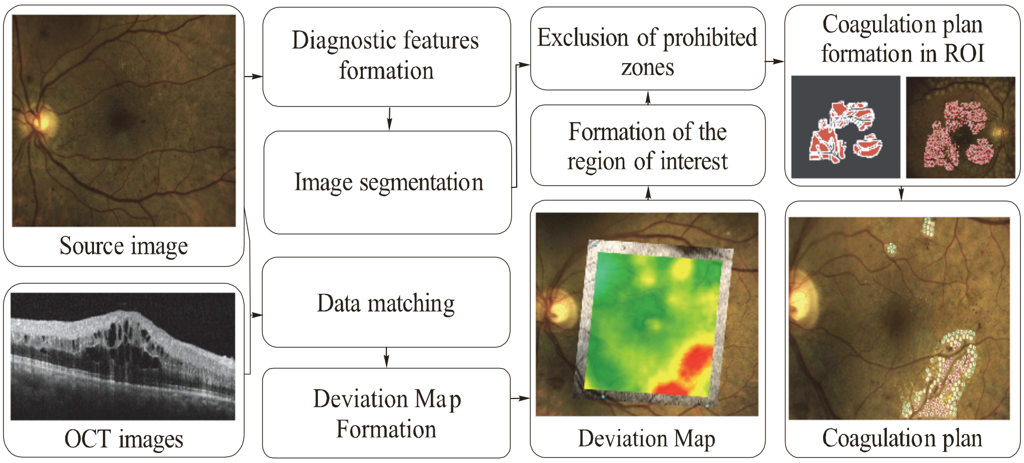


Fig. 2. Technology of mapping a photocoagulation plan of laser coagulation

A fundus image reconstructed from OCT data needs to be aligned with a fundus-camera-aided retinal image. The technology proposed herein suggests that key points should be marked in the reconstructed retinal image and fundus image, followed by marking off a pathological zone, which is then aligned with the fundus image. The zone of laser exposure, which is generated automatically based on the segmentation result and the pathological zone, can be corrected manually if necessary. At the final step, a photocoagulation pattern is mapped, for which quality characteristics are calculated and the probability of the successful outcome of laser treatment is evaluated.

2. Technology of the intelligent analysis of a preliminary photocoagulation pattern

As far as a minimal inter-coagulate distance is observed, mapping a photocoagulation pattern within a pathological zone guarantees safe photocoagulation because such an approach enables one to exclude two possible problems: exposure of prohibited areas to the laser light and excessive retina damage due to a very small distance between neighboring coagulates. Nonetheless, even if the laser parameters are chosen correctly, minor damage to the retina due to micro burns cannot be ruled out. Although the damage is usually insignificant but it should be possibly avoided.

An important problem is analyzing the mutual arrangement of photocoagulates as a result of planning. Characteristics of the photocoagulation plan are able to provide a prognosis of the laser coagulation outcome. In any case, to be able to estimate its various properties, the preliminary plan needs to be described quantitatively. We note that the preliminary plan can be mapped using an arbitrary technique, including a manual one. A photocoagulation plan comprises an array of points each of which is characterized by certain parameters. The parameters affect the degree of burn at the exposed points and can be evaluated using a technique described in [31, 32]. The laser treatment parameters can be fitted in an optimal way at any layout of points given that the minimal distance is observed. With all the points known to be located in the ROI that needs to be exposed to laser treatment, inter-point distances come to the forefront.

For a distance sampling to be generated, a point-connecting technique needs to be chosen based on some rule. Next, using a standard Euclidean measure, values of the distances are calculated and written into a general sampling. Noise distances are then excluded and statistical characteristics are calculated, before being written in the general set of features. Such an approach is schematically depicted in fig. 3. Based on their expertise, ophthalmologists [14, 15] suggest using statistical characteristics such as the variance of mutual distances, the mathematical mean, and so on.

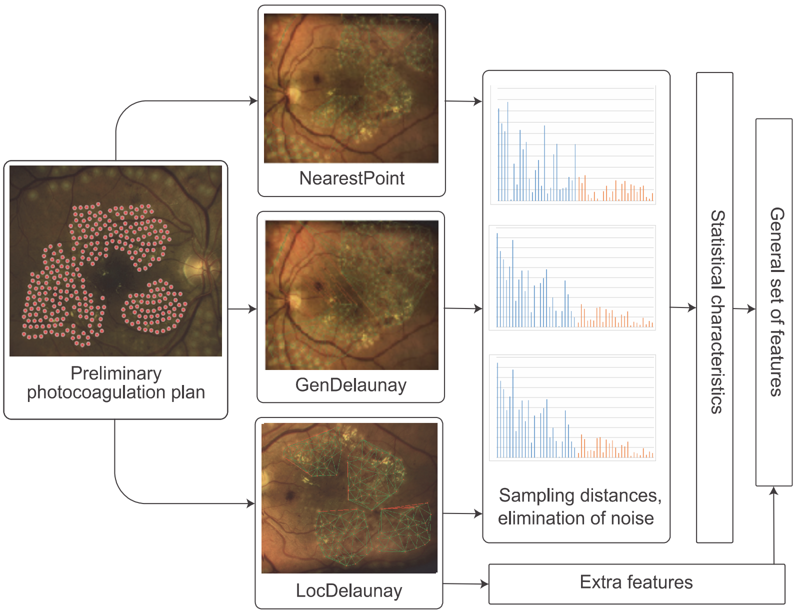


Fig. 3. Flowchart of feature calculation based on a preliminary photocoagulation pattern

Medical doctors used to analyze the uniformity of the photocoagulation pattern primarily based on the variance. The features used include various statistical characteristics of the inter-coagulate distance (a mutual location feature) and features corresponding to the coagulation pattern volume and the area covered (general features). Fig. 4 illustrates a Delaunay triangulation performed with respect to the coagulate center points. The triangulation distances are written into the general sampling, from which distances disobeying a three-sigma rule are then excluded. Such distances are marked red in fig. 4. Among statistical characteristics, the following were chosen: a mean arithmetic, variance, a root-mean-square deviation, median, asymmetry, kurtosis, a minimal value, and a maximal value [33]. These characteristics form a basis for evaluating the uniformity and balance of the photocoagulation pattern. Alongside statistical characteristics, an important feature is the number of points in the photocoagulation plan. As an extra feature, the number of local regions in the coagulation pattern may be used.

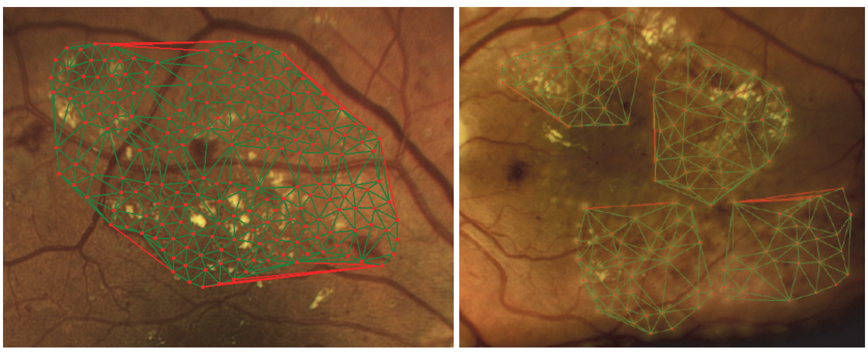


Fig. 4. Examples of the Delaunay triangulation using the present points corresponding to coagulate centers (left and right)

Techniques proposed for finding matching points include the following algorithms: an algorithm for nearest point searching (Nearest Point algorithm), Delaunay triangulation (GenDelaunay algorithm), and an algorithm for extracting local regions, followed by the Delaunay triangulation in each region (LocDelaunay algorithm). The LocDelaunay algorithm is a generalization of the GenDelaunay algorithm. If the photocoagulation plan contains a single region, results of both algorithms will be identical. If there are several local regions in the plan, the GenDelaunay algorithm will connect even distant points (fig. 3). However, as a rule, the distances for such points are excluded as noise. Tab. 2 shows the number of features for each group.

Table 2. The number of features for each group

Name of feature group	Feature group NearestPoint	Feature group GenDelaunay	Feature group LocDelaunay	Extra features
Number of features	8	8	8	2

In total, 26 features were selected and then analyzed using an in-house technology of intelligent data analysis (fig. 5). The technology allows analyzing the classification quality of both initial features and features selected based on discriminant analysis, which relies on evaluating the linear separability of classes. Discriminant analysis aims to transform the initial features so as to maximize the separability criterion [33].

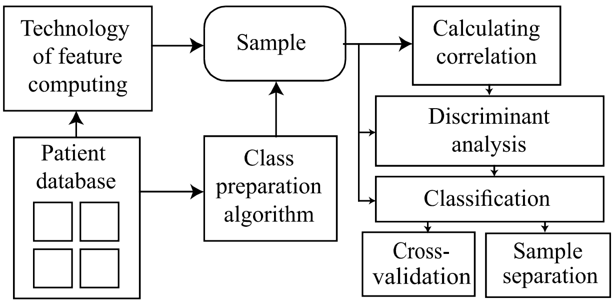


Fig. 5. Technology of the intelligent analysis of the photocoagulation plan

The ophthalmology surgeons argue that laser treatment is most effective when the photocoagulation pattern is laid out in the most uniform way. The efficacy may be based on the use of intelligent analysis methods for a sampling containing information on the photocoagulation pattern and the outcome of DR treatment. These methods allow one to construct a high efficiency classifier for prognosticating the surgery outcome.

3. Computer-aided system for mapping and analyzing a preliminary photocoagulation pattern

The above-described technology has formed the basis of a computerized system for mapping and analyzing a preliminary photocoagulation pattern for DR laser treatment.

System functionality:

1. The possibility of forming a coagulation plan during one visit of the patient.
2. Availability of mechanisms for saving and loading the results of the intellectual analysis of the preliminary coagulation plan with the coagulation plan itself, as well as the patient database;
3. Implementation of methods for selecting the zone of laser exposure and the formation of a coagulation plan;
4. Possibility of manual arrangement of key points on the OCT image and the image of the fundus for alignment;
5. Providing visualization of intermediate stages of processing by a software system;
6. Ability to adjust the main stages of data processing, if necessary;
7. Providing visualization of the final coagulation plan with the values of the signs characterizing the effectiveness of the coagulation plan;
8. Providing prompts for the user and messages about valid input parameters.

Recommended system requirements for the operation of the software package: RAM: 4 GB; external memory: 100 GB, processor frequency: 2.50 GHz, video card: NVidia GeForce 1050.

The architecture of the system shown in Fig. 6 comprises several modules, which realize the proposed methods and algorithms. The software complex was realized on the platform Microsoft.Net Framework 4.5.2, with C# used as a basic language and C++ for realizing high-speed algorithms, and Microsoft Visual Studio serving as the tool development framework.

The software developed is intended for the use of high-performance algorithms that can be parallelized using either a processor or a graphics processing unit. Parallelization using CUDA technology is used to quickly calculate texture features. The sequential algorithm for calculating features is implemented in C++. The architecture allows data exchange through the network if one needs to connect to an external algorithm, say, an algorithm for retinal image segmentation based on neural networks. External algorithms work as RESTful web services with data exchange in JSON.

The software complex is logically divided into the following systems: a system for retinal image data input, a system for aligning retinal images and OCT data, a system for extracting the ROI for laser treatment, a system for mapping a photocoagulation pattern, and a system for the intelligent analysis of the photocoagulation pattern. Data input involves uploading the retinal image and OCT data of a patient. Upon aligning the retinal image and OCT data, the key points are marked either manually or automatically, with a correction option available. When extracting a laser photocoagulation zone, the disk of optic nerve and fovea are extracted manually, with the subsequent stages of extracting the laser treatment zones being performed automatically.

The *system* for mapping the photocoagulation pattern automatically lays out photocoagulation points within the extracted zone, but if necessary, the surgeon can introduce corrections by shifting, removing or adding photocoagulation spots.

The coagulate placement module receives a binary image at the input, in which the white pixel corresponds to the laser impact zone, and the algorithm parameters: coagulate radius, minimum distance between coagulates, and placement method.

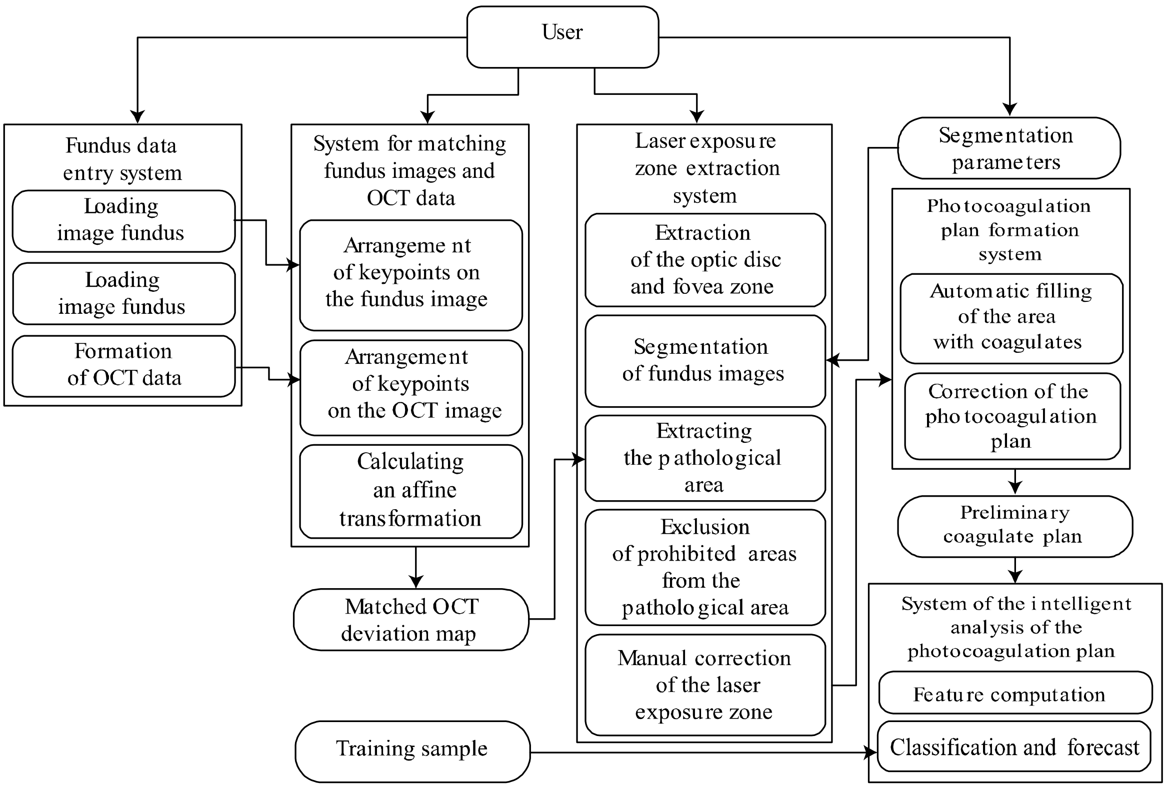


Fig. 6. Architecture of the software complex for DR laser treatment

The module is divided into 2 stages: the algorithm for identifying potential circle centers and the module for placing coagulates (fig. 7). The circle radius is used to highlight potential circle centers. And the minimum distance is used for the placement of coagulates by a given algorithm.

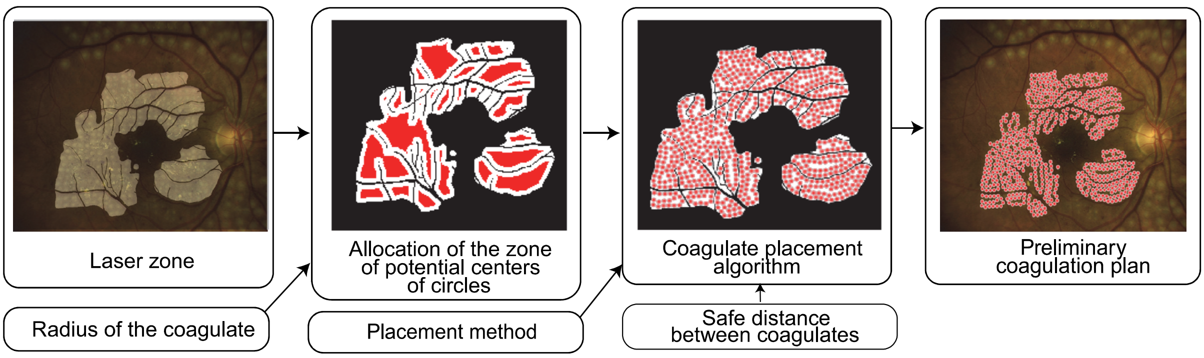


Fig. 7. Module for placement of coagulates in the area of laser exposure

The intelligent analysis system calculates features and displays the quantitative data using which the surgeon can analyze the photocoagulation plan.

The feature calculation module (fig. 8) was implemented as the AnCoLib library in C#. The library has a main function that calculates features from a set of points, and additional functions that allow you to visualize the results of the general Delaunay triangulation and Delaunay triangulation in local areas.

When a patient is admitted, the database stores information about this patient and his examination data: fundus image, OCT images, visual acuity, average retinal thickness and comments. After the formation of the coagulate plan, the doctor saves a report that is automatically saved to the database for the corresponding patient. According to this plan, the doctor performs an operation, and after the expiration of the rehabilitation period (a week or a month), at the next appointment, the patient is re-examined.

As a result of the examination, information about visual acuity and the average thickness of the retina is entered. The database then stores this information. The submodule for updating the database, shown in fig. 9, is responsible for such functionality.

Based on information about visual acuity and average retinal thickness before and after treatment, information is generated about the success of the operation. The database makes it possible to form a sample, according to which informative features can be selected, as well as predicting the success of laser coagulation when a new patient is admitted (fig. 10).

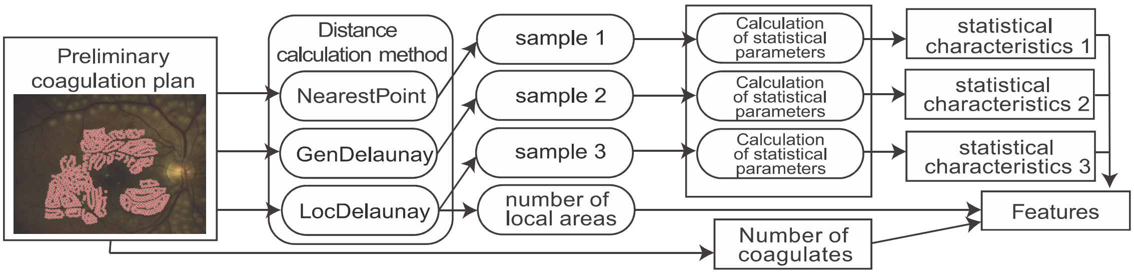


Fig. 8. Feature calculation submodule schema

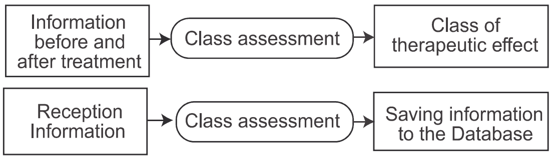


Fig.9. Database update submodule schema

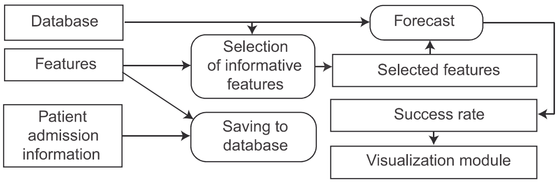


Fig.10. Technology of the intelligent analysis of the photocoagulation plan

Classification allows one to evaluate the probability of the successful laser treatment outcome.

This module is taught, meaning that after inputting corresponding data, it can be taught to recognize new data of the system, expanding the learning sampling. Fig. 6 shows a flowchart of submodule for features intelligent analysis, which allows the information on the laser treatment outcome to be output. Fig. 11 shows a graphic interface of the system.

To ensure the safety of the operation, the interface of the software package allows you to monitor each individual stage of processing and edit it if necessary. Fig. 11 on the left shows interactive repositioning of key points in the fundus image. The physician can visually control the degree of image alignment. The result of coagulate placement can be corrected by moving coagulates, adding new coagulates and removing unwanted coagulates. Editing at this stage is usually required when the clinician visually notices insufficiently dense coagulate filling of some area as a result of a simple coagulate placement algorithm with low computational complexity.

Summing up, in this work we have proposed a software complex allowing the surgeon to map a preliminary laser photocoagulation plan and analyze its efficacy on the basis of quantitative data. The system allows to correct interim stages of the procedure.

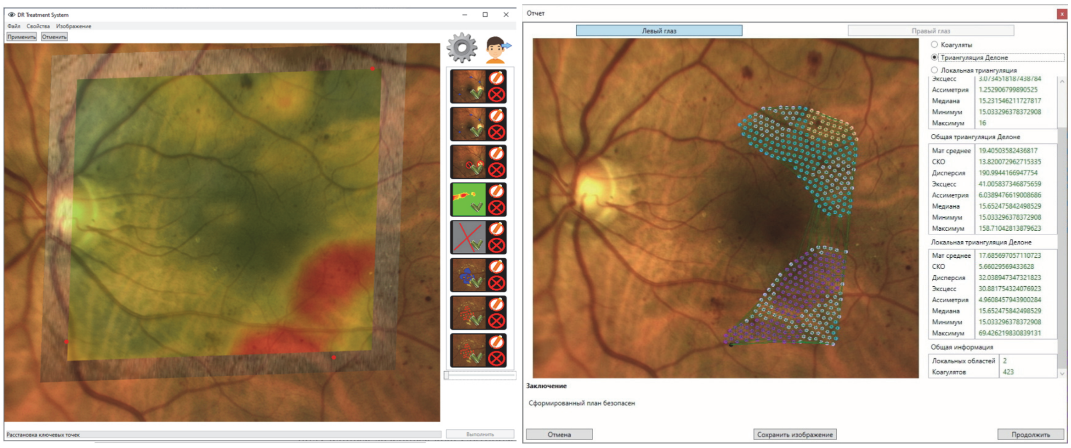


Fig. 11. Illustration of the graphical interface of the system

Conclusion

We have proposed a software complex for mapping and analyzing a preliminary photocoagulation plan for laser treatment of diabetic retinopathy. The software is aimed at automatically mapping a recommended photocoagulation plan and pro-vides for the correction of interim results. The feasibility of introducing corrections at any interim stage of data processing in the computerized system makes for a safe treatment. A key module of the proposed software architecture is the system for the intelligent analysis of the photocoagulation pattern, allowing the proposed plan to be analyzed and the treatment outcome to be prognosticated.

Working with the proposed system, the surgeon is able to input patient's data and map an effective photocoagulation pattern, which is aimed at providing a higher-quality DR laser treatment when compared with the current approaches. In the future, we plan to adapt the system to novel techniques of interim data processing.

A prototype of an intelligent system was created that allows automatic planning of operations on the retina. Its clinical trials are being conducted at the Eroshevsky Ophthalmological Hospital.

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