

Ministry of Education and Science of the Republic of Kazakhstan
Suleyman Demirel University

UDC.....

On manuscript rights



Sherkhan Bertailak

A handwritten signature in blue ink, appearing to read 'Sherkhan', is positioned to the right of the author's name.

**Development of Computer Research Methods for
Diagnosis Based on Blood Vessels of a Human
Face**

THESIS

Presented in Partial Fulfillment for the
Degree of Master of Science in Computing Systems and Software
(degree code: 6M070400)

Department of Computer Sciences
Faculty of Engineering and Natural Sciences

Supervisor: **Prof. Yedilkhan Amirgaliyev**

Kaskelen, 2020

Аңдатпа

Сонғы жылдары суреттерді компьютерлік анализ жасау қарқынды дамып келе жатыр. Медицина саласында диагноз қою жүйесі үшін көптеген көмегін тигізу арқылы жаңа деңгейге шығарды. Қазіргі таңда офтальмология және кардиология саласында ақпараттық жүйелер көптеп кездеседі. Дамыған технологиялар дәрігерлердің жұмыстарын тездетіп қана қоймай ауру жағдайын ерте анықтап, ем тағайындауға көмектеседі. Бұл ғылыми мақалада көз жүйесіндегі қан тамырларының томографиялық суреттерің дерекқорын қолдана отырып машиналық оқытудың алгоритмдерінің анализі жасалынды. Белгілі бір модельді таңдаудың бірнеше себептерін, оның қасиеттерін, кейбір артықшылықтарын және маңыздылығын есептеу үшін қолданылатын әдістерді зерттелді. Бұл зерттеу жұмыстарының басты мақсаты дәрігерлер өздерінің емделушінің көзінің қазіргі жағдайын тексеріп қана қоймай, диабет және анемия сияқты белгілі бір ауру жүйелеріне диагноз қоя алуы.

Аннотация

В последние годы компьютерный анализ изображений развивается быстрыми темпами. В области медицины был выявлен на новый уровень оказав большую помощь для диагностической системы. На сегодняшний день существует множество информационных систем в области офтальмологии и кардиологии. Передовые технологии не только ускоряют работу врачей, но и помогают своевременно диагностировать заболевание и назначать лечение. В данной научной статье был выполнен анализ алгоритма машинного обучения с использованием базы данных томографических изображений кровеносных сосудов в глазной системе. Были изучены используемые методы для расчета нескольких причин в целях выбора конкретной модели а также методы для расчета его свойств и методы для расчета некоторых преимуществ и значимости. Основная цель этого исследования состоит в том, что врачи могут не только проверить текущее состояние глаза пациента, но и диагностировать определенные заболевания, такие как диабет и анемия.

Acknowledgements

I would like to express my sincerest gratitude to my supervisor, Prof. Yedilkhan Amirgaliyev, for his guidance and support throughout my course work and my research. You have been a solid ground with your guidance, infinite knowledge and positive attitude, for being helpful and willing to listen when problems arise. This dissertation would not be possible without his help. Thanks to my family, who had always stood by me through thick and thin. Also, I would like to acknowledge the study grant from Ministry of Science of Republic of Kazakhstan.

Contents

1	Introduction	7
1.1	Motivation	7
1.2	Aims and Objectives	10
1.3	Thesis Outline	12
2	Preliminaries	17
3	Methodology	19
3.1	Pre-processing	19
3.2	Processing	25
3.3	Fisher Linear Discriminant	29
3.4	Experiments	33
4	Results	39
5	Discussion	42
5.1	Benefits	42
5.2	Limitations	50
6	Conclusion	58
	References	59

Nomenclature

CFL Courant Friedrichs Lewy

KNN K-Nearest Neighbor Classifier

KNN K-Nearest Neighbor Classifier

LDA Linear Discriminant Analysis

NRD Neurosensory Retinal Detachment

OCT Optical Coherence Tomography

PCA Principal Component Analysis

SVM Support Vector Machine

1. Introduction

1.1 Motivation

In recent years, computer image analysis has been developing rapidly. In the field of medicine has been identified to a new level that has greatly helped for the diagnostic system. There are many information systems in the field of ophthalmology and cardiology. Advanced technologies not only accelerate the work of doctors but also help to diagnose the disease in a timely manner and prescribe the treatment. In this research paper was carried out an analysis of the machine learning algorithm using a database of tomographic images of blood vessels in the eye system. Were studied the used methods for calculating several reasons in order to select a specific model, methods for calculating its properties and advantages. The main goal of this research is that doctors can not only check the current condition of the patient's eye but also diagnose certain diseases, such as diabetes and anemia.

The use of optoacoustics is a relatively young method of medical imaging, which is used to diagnose blood vessels, brain activity, skin lesions and breast cancer. However, the quality of the images largely depends on the number and distribution of sensors used by the device: the more of them, the better the image quality. A new approach developed in Zurich can significantly reduce the number of sensors without giving up the specified image quality. This allows you to reduce the cost of the device, increase the speed of image processing or improve diagnostics.

After discarding most of the sensors, the team of researchers obtained images with artifacts-missing bands. Previously trained neural network was able to restore image quality to a large extent, close to what it was originally.

The developed machine learning algorithm has also been successful in improving the quality of images that were recorded using just a narrowly defined sector.

This is especially important for clinical use, since laser pulses cannot penetrate the entire human body, therefore, the displayed area is usually available in only one direction.

A feature vector was calculated for each pixel, consisting of the pixel intensity and the response of the 2D wavelet transform calculated for different scales. A classifier based on a model from a combination of Gauss functions was applied to each of the pixels to determine the probability of belonging to a vessel. The algorithm takes into account local information obtained during the filtering process, but ignores very important information about the shapes and structures represented in the image. The method does not work well on images with uneven illumination due to false alarms at the edge of the optical disk, hemorrhage, and other abnormalities that have a high contrast with the background. A bandpass filter is widely used in image processing due to the ability to adjust its spatial orientation, the ability to allocate frequencies in two-dimensional space with good indicators in the spatial and frequency regions.

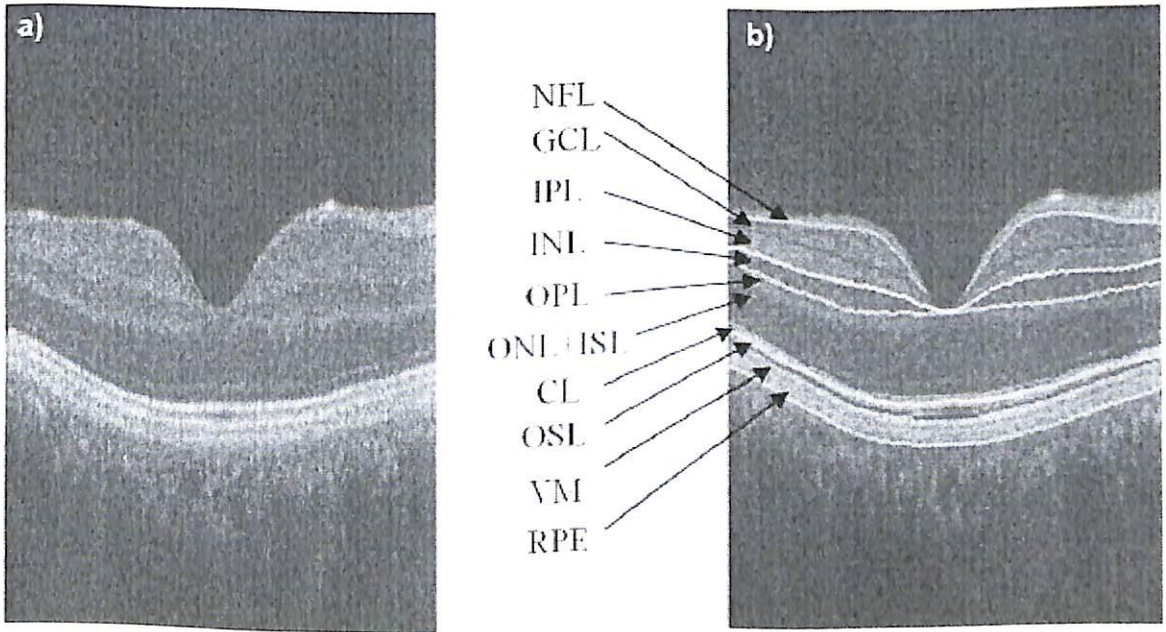


Figure 1.1: Optical coherence tomography B-scan image of normal eye

There are two main approaches to selecting vessels – vessel segmentation, which allows you to select the entire vessel tree in one iteration, and vessel tracking (tracing). In relation to the development of vascular segmentation algorithms, according to the literature, the following approaches can be distinguished: - clas-

sification of image samples(without training, with training); - consistent filtering;
- mathematical morphology; - multi-scale approaches; - model-based approaches.

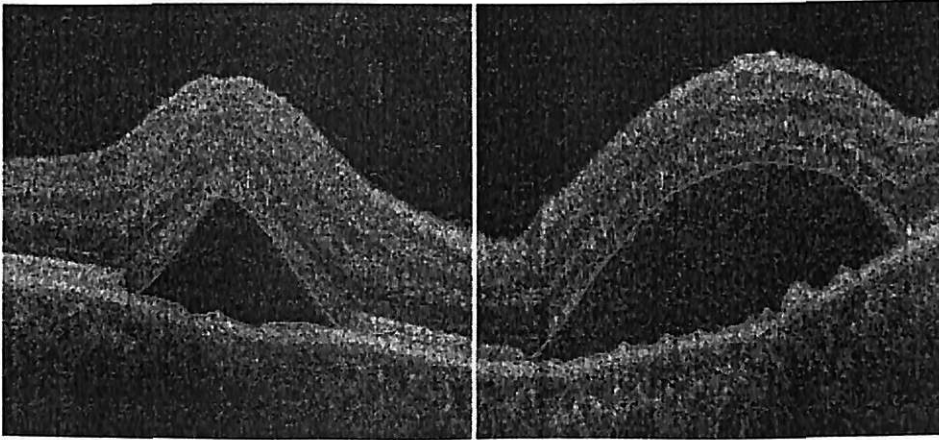


Figure 1.2: B scan with neurosensory retinal detachment associated subretinal fluid

The use of linear operators as a feature vector and the use of *SVM* to classify pixels are proposed in the works. A simple detector based on an estimate of the average brightness level along lines of a fixed length passing through the pixel in question was applied to the green channel of color images. Then the response of the detector was subjected to threshold processing. A detector based on two orthogonal lines was also used to create the feature vector, and the classification was carried out using the *SVM* classifier. Compared to other approaches, the algorithm required fewer features for classification, features are very simple to calculate, less images were needed for training. The algorithm showed good reliability when working on images with uneven illumination and contrast. The algorithm also showed acceptable results on images containing vessels with a central reflex. It used a filter obtained from the Gabor filter by rotation in a certain number of directions. In order to highlight lines of different widths, it is necessary to apply a filter with a different scale. Since these methods are based on already classified images, they are usually more effective than other methods.

In the works, pre-trained neural networks were used to classify vessels. The *KNN* classifier is presented, where each pixel was assigned the probability of its belonging to the vessel. Artificial neural networks use weights to determine the correspondence between input and output data. They can be configured using a

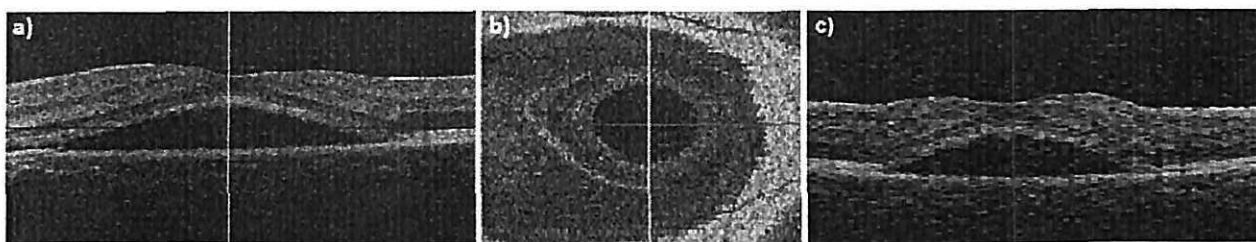


Figure 1.3: Optical coherence tomography cube scan of the macula acquired with the device

training set based on backpropagation networks. The pixels of the window sliding across the image were used as input to the network. For each pixel, a feature vector was generated based on the pixel intensity values from a window centered relative to the classified pixel. To train the network, labeled angiograms were used.

The use of the principal component analysis method of principal component analysis to localize the anatomical parts of the retina was demonstrated in the work. The method showed good agreement with the marking of an experienced ophthalmologist made on the images.

1.2 Aims and Objectives

The classifier was applied to images processed by a multi-scale filter to select candidates for belonging to the vessel among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on pixel classification without the use of training search for patterns specific to blood vessels in retinal images. These algorithms do not require direct use of the training sample. In this paper, we have proposed a method for expanding regions based on the analysis of information about the gradient and curvature of the field.

An analysis of the relationships between changes in vascular characteristics and various diseases contributes to the timely detection and treatment of diseases at an early stage. Automated analysis also finds application in computer laser surgery and biometric identification.

Not surprisingly, with the increasing number of patients and the need to find

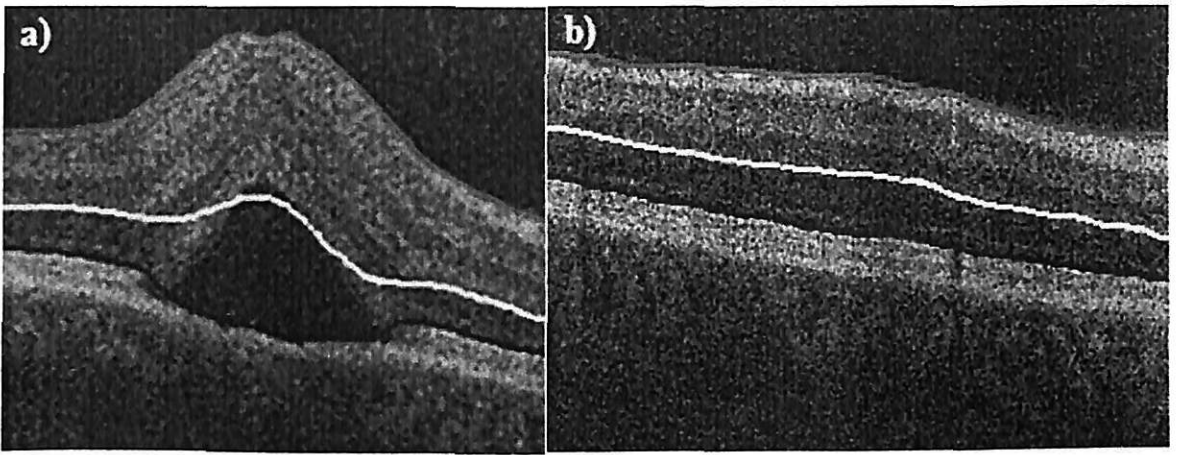


Figure 1.4: Retinal layer segmentation result of the Optical coherence tomography B-scan

ways to improve the quality of monitoring of vascular systems over the past 20 years, significant efforts have been made to develop computer technologies that can detect changes in vascular systems. The medical community agrees that automatic quantification of vascular systems is the first step in the development of computer-based disease diagnosis systems.

Creating a methodology for digital analysis of vascular systems is impossible without solving a number of problems: recognition of vessels in digital images, selection of a vascular analysis methodology. Pre-trained neural networks were used to classify vessels. The *KNN* classifier is presented, where each pixel was assigned the probability of its belonging to a vessel.

Artificial neural networks use weight coefficients to determine the correspondence between input and output data. They can be configured using a training sample based on error back propagation networks. Pixels of the window sliding over the image were used as input data for the network. For each pixel, a feature vector was generated based on pixel intensity values from a window centered relative to the classified pixel. Marked angiograms were used to train the network.

The use of the principal component analysis method for localization of anatomical parts of the retina was demonstrated in the work. The method showed a good match with the markings of an experienced ophthalmologist made on the images.

A diagnostic images analysis is a long and tedious task sinuosity of blood vessels, which also requires preparation and skill. Specialists learn to distinguish damage to vascular systems from the appearance of vascular systems without pathologies. In addition, with this kind of analysis, there is always a subjective

factor, which often leads to differences in the diagnoses made by doctors.

1.3 Thesis Outline

The thesis provides an overview of the main approaches to digital image analysis of human vessels. The algorithm proposed using a two-dimensional filter core based on the Gauss function or its derivative for segmentation of vessels. The filter profile is designed to best fit the vessel profile, which is usually in the form of a Gauss function or its derivative. The filter core rotates in 15 increments to match vessels with different spatial orientations. To get a binary image of vessels, the best response of the filter is determined for each pixel, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels. The approach proved that the width of the vessels can be measured based on the amplitude parameters of the filter that gives the best response. Measuring the width of vessels allows you not only to estimate the size of the vessel, but can also be useful for optimizing the parameters of a matched filter.

Applied a consistent filter, used, improved with an optimizing search procedure. The optimization procedure was applied on 20 retinal images to determine the best parameters of the matched filter, such as the filter size, the standard deviation of the Gauss function used to design the filter, and the threshold value. The improved filter is more efficient than the standard filter. In this paper, the classical matched filter was refined by using the first derivative of the Gauss function. This modification was made based on the symmetry of the Gauss-shaped section of the vessel relative to its peak, while the boundaries in pathology are not symmetrical. The method used two filters: a filter based on the Gauss function and a filter based on the first derivative of the Gauss function. In the area of maximum vessel intensity, the filter gave a strong response, while the filter gave a zero response. In contrast, structures other than vessels, for example, have sharp borders. The technique allowed to significantly reduce the number of false positives and determine a larger number of thin vessels compared to a conventional filter. Mathematical morphology is used as a tool for extracting parts of an image that are useful for describing various shapes, such as the borders and skeleton of a vessel. Mathematical morphology offers a powerful tool for solving many

image processing problems. Morphological operators were used for localization of microaneurysms, as well as for vascular segmentation.

A method based on spatial-scale analysis for estimating the width, size, and spatial orientation of blood vessels using two geometric features based on the first and second intensity derivatives is presented. This approach provides information about the image topology. The boundary points of the vessel are characterized by the gradient magnitude in the image, the greatest value change which is observed in the direction of the corresponding intensity maximum in the region of the ridges of the image of greatest field curvature. The maximum gradient value and maximum curvature at various image scales were then used in the area expansion algorithm. The algorithm was tested on images without a red component and fluorescent retinal angiograms and showed, according to the authors, promising results. A modification of this spatial-scale algorithm is made based on the observation that the image intensity is proportional to the amount of blood in the vessel. Therefore, a diameter-dependent equalization factor was applied to multi-scale information.

The thesis provides an overview of the main approaches of digital analysis of images of human blood vessels. The main stages of processing diagnostic images are identified, an analysis of various approaches to the isolation and quantification of morphological signs of blood vessels is carried out. The collected statistics allows you to show which of the approaches was used most often within each of the stages.

A large number of algorithms and methods for digital analysis of human vascular systems have been published. Image analysis of vascular systems for the detection of pathologies comes down to the task of pattern recognition. The process of detecting multiple images and their relationships in vascular images involves a number of operations or steps, using low-quality image processing methods that allow you to move on to more complex analysis. Digital images of vessels are processed using a sequence of algorithms, which may consist of one or more pre-processing steps preceding the steps of image segmentation, feature evaluation, and classification. Pre-processing can be used to even out the brightness of the image, correct inhomogeneities, suppress noise or eliminate distortion. Segmentation splits the image into fragments containing individual objects, for example, blood vessels, the optic nerve root, or malignant lesions. In the process of cal-

culating attributes, numerical information about individual objects obtained by segmentation is evaluated. The calculated features can be used to classify objects according to predetermined criteria, such as size, structure or color.

Health Technology Assessment has published a review of digital imaging technologies in the field of diabetic retinopathy. Their initial goal was to conduct a numerical analysis of various technologies for working with digital diagnostic images. The paper notes that they were not able to do this, since digital technologies were only at an early stage of their development in this area. The chart shows that quite a large number of articles dedicated to evidence-based medicine, well-researched medical problem, identified the necessary requirements to tasks analysis of digital vessels and conducted numerous studies in this field to link the change of morphology of blood vessels major diseases. The diagram also shows that most of the researchers' efforts are devoted to solving problems of vascular system isolation.

This analysis presents the classification of the main stages of digital analysis of vascular systems in the problems of diagnostics of vascular pathology and classification. For statistical analysis, the literature list of the found articles was used as a secondary source. When analyzing the articles, they were categorized according to their belonging to different stages of processing diagnostic images of vascular systems. In the review articles was reviewed and included the analysis of secondary sources. The main stages of the analysis of key features of vessels were identified: evidence-based medicine, pre-treatment; localization and segmentation of the optic nerve disk; segmentation of vessels; tracing of vessels, evaluation of diameters, evaluation of diagnostic signs. The table shows a list of articles related to the stages presented in the review in whole or in part. The number of articles related to each step in the sequence.

One of the main issues of modern medicine is to determine the boundaries of the normal human phenotype, its variability, and the individual risk threshold for disease. This question is particularly relevant when determining the norm in children and adolescents. The environment changes rapidly, and the development of the child's body in these conditions can be characterized from the point of view of a set of adaptive variants of this human phenotype. Currently, children and adolescents with asthenic physique, with impaired posture, increased flexibility of the joints are more common.

Thus, in the modern population there is an increasing proportion of children and young people with undifferentiated connective tissue dysplasia – according to statistics, this figure is from 10 to 80 percent. Increased elasticity of connective tissue is useful for " push-button " civilization, but can be dangerous with significant physical exertion.

It should be noted that most adolescents with undifferentiated connective tissue dysplasia are workaholics. They study well, attend a lot of additional educational programs, and as a result, they work from dawn to dawn. It is known that famous representatives with undifferentiated connective tissue dysplasia, such as Paganini, who had Marfan syndrome – a disease with pronounced connective tissue dysplasia, were distinguished by tremendous performance. It should also be noted that undifferentiated connective tissue dysplasia is not a disease, but can be a predictor of a number of diseases, including heart rhythm disorders, emotional disorders – asthenia, phobias, agitation, mitral valve prolapse, and many others. Often, medical measures are not timely. It is necessary to predict life-threatening complications and early detect the presence of connective tissue dysplasia. If dysplasia is not detected in time, it may one day lead to collapsoid complications during physical activity, for example, during a physical education lesson.

The first reviews of algorithms for selecting vascular structures in medical images can be seen in the works. Recent studies have discussed algorithms for automatically diagnosing diabetic retinopathy in retinal images. The review is unique in that it presented an analysis and categorization of literature related to digital image processing technologies in the field of diabetic retinopathy, and focused on algorithms and segmentation methods on two-dimensional color images of the retina obtained using fundus cameras. This review is still the best known on diabetic retinopathy. The system made it possible to evaluate the width, contrast, and direction of blood vessels at each point in the image. The algorithm also used the additive noise model, which, together with the assessment of the parameters of the vessel, made it possible to determine the position of the center line of the vessel. At first, consistent filtering was used to improve the contrast of the vessels, and then a matrix was calculated on the basis of which statistical values were determined for the subsequent threshold processing. Threshold processing based on local entropy was then applied to segment the vascular system. The algorithm used a filter with a different scale based on the second derivative of the

Gauss function to the image, and the filter response was used to detect vessels and evaluate their signs. A Gaussian noise model was also used to suppress it. Vascular profile and noise distribution models were used together for the probabilistic assessment of vascular parameters.

One of the main issues of modern medicine is determining the boundaries of the normal human phenotype, its variability, and the individual threshold for the risk of disease. This issue is especially relevant when determining the norm in children and adolescents.

The environment is rapidly changing, and the development of the child's body in these conditions can be characterized from the perspective of a set of adaptive variants of this human phenotype. Currently, children and adolescents of asthenic physique are more common, with impaired posture and increased joint flexibility.

Thus, in the modern population, an increasing proportion of children and young people with undifferentiated connective tissue dysplasia is noted - according to statistics, this indicator is from 10 to 80 percent. The increased elasticity of the connective tissue is useful for the "push-button" civilization, but can be dangerous with significant physical exertion.

It should be noted that most adolescents with undifferentiated connective tissue dysplasia are workaholics. They study well, attend a lot of additional educational programs, and as a result work from dawn to dawn. It is known that famous representatives with undifferentiated connective tissue dysplasia, such as Paganini, who had Marfan syndrome, a disease with pronounced connective tissue dysplasia, were distinguished by tremendous performance. It should also be noted that undifferentiated dysplasia of connective tissue is not a disease, but it can be a predictor of a number of diseases, including cardiac arrhythmias, emotional disturbances - asthenia, phobias, agitation, mitral valve prolapse, and many others. Often, treatment is not timely. It is necessary to predict life-threatening complications and to detect the presence of connective tissue dysplasia in the early stages. Timely undetected dysplasia can one day lead to collapsoid complications during physical activity, for example, at a physical education lesson.

2. Preliminaries

This thesis presents a classification of the main stages of the digital analysis of vascular systems in the diagnosis of vascular pathology and classification. The algorithm proposed using a two-dimensional filter core based on the Gauss function or its derivative for segmentation of vessels. The filter profile is designed to best fit the vessel profile, which is usually in the form of a Gauss function or its derivative. The filter core rotates in 15 increments to match vessels with different spatial orientations. To get a binary image of vessels, the best response of the filter is determined for each pixel, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels.

For statistical analysis, as a secondary source, a list of references of found articles was used. When analyzing the articles, they were categorized in accordance with their belonging to various stages of processing the diagnostic image of vascular systems. The review examined articles and included analysis of secondary sources. The main stages of the analysis of the key features of the vessels were identified: evidence-based medicine, pre-treatment; localization and segmentation of the optic disc; vascular segmentation; vascular tracing, assessment of diameters, assessment of diagnostic features. The table contains a list of articles related to the stages presented in the review in whole or in part. The number of articles per step in the sequence.

The thesis focuses only on diabetic retinopathy and includes the analysis of such signs of diabetic retinopathy as microaneurysms, small point hemorrhages, blood spots, lipid exudates and cotton-like spots, which are essentially microinfarctions of the nerve fiber.

A review of algorithms that mainly focus on vascular extraction in two-dimensional, color images of the retina obtained using fundus cameras or fluorescence angiog-

raphy is presented, and the emphasis is only on studies related to retinal vascular segmentation[1].

3. Methodology

3.1 Pre-processing

Two main approaches are used to isolate blood vessels - vascular segmentation, which allows you to select the entire vessel tree in one processing step, and vessel tracking - step-by-step vessel tracing. Segmentation of blood vessels has a further division into subcategories. In the literature, the algorithms for distinguishing vascular-like objects in medical images are usually divided into the following classes: algorithms based on the allocation of the boundaries of the object; area growth algorithms; pattern recognition methods; model-based methods; using neural networks; object tracking algorithms. The set of vascular extraction algorithms is represented by the following six categories: - classification of image samples (without training, with training); - consistent filtering; - mathematical morphology; - multiscale approaches; - model-based approaches; - tracking and tracing of blood vessels. Some of these categories have been further divided into subcategories.

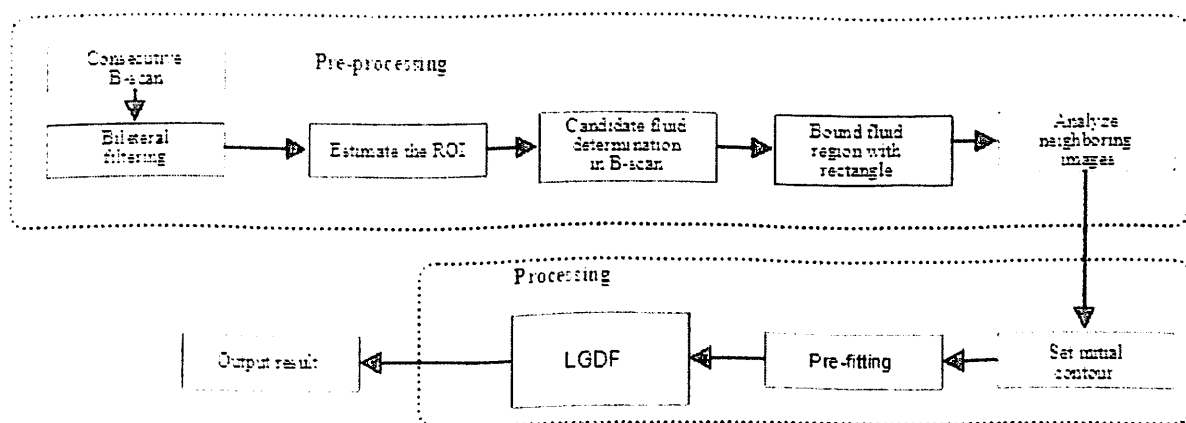


Figure 3.1: Overview of proposed framework

It is shown that automated selection and digital analysis of vascular systems can help in the implementation of monitoring systems for diabetic retinopathy and senile retinopathy.

Injuries are manifested in hypertension in elderly people, as well as in people who were underweight at birth. According to research, both of these factors are associated with frequent morbidity and even death from cardiovascular diseases. The paper shows the relationship between changes in the vascular system and cardiovascular diseases.

The system presented the following diagnosis algorithm: 1) Localization of the most important areas, such as vessels, optical disc, using segmentation methods. 2) Search for signs of pathologies, such as venous expansion, excessive vascular curvature, etc., using classification. 3) Diagnosis based on identified signs of pathology. The system also published its research in the field of medicine, which served as a theoretical basis for automatic diagnosis. They noted that retina can tell hundreds of diseases, and their system could do 13 different diagnostics based on 39 signs of vascular changes. Despite the fact that this system was significantly inferior to an expert doctor on diagnostics, at that time it already showed rather good results.

The problem of digital analysis of the vessels of the optic nerve head is addressed in publications. The largest number of articles is devoted to the problem of localization of the optic nerve head disk and the lesser - to algorithms for assessing the signs of the optic nerve head for the diagnosis of pathologies.

In total, out of all the articles examined, 218 are devoted to the problems of vascular isolation, which include segmentation and tracing methods.

118 articles devoted to evidence-based medicine were reviewed, which is 21 percent of the total number of articles devoted to the analysis of images of vascular systems, and shows a great interest of doctors in this field of research. The articles in this category prove that the selection of vessels and the assessment of their morphological features, such as length, width, tortuosity, branching angles, etc., can be used for the diagnosis, monitoring, treatment and evaluation of various cardiovascular and ophthalmological diseases, such as diabetes, hypertension, arteriosclerosis and neovascularization of the vascular membrane. A variety of research in this area is also demonstrated. The authors actively use numerical measurements of vascular systems as auxiliary tools to study the relationship

between changes in vascular structure and various diseases.

Numerous studies in the field of vascular pathology diagnostics are focused on the recognition of retinal images as the first step in the construction of automated vascular diagnostic systems. The most significant areas of the retina are the optical disc, fovea and the vascular system of the retina. Identification of these areas will help specialists in identifying diseases that affect these areas in the first place. This is glaucoma, which causes the expansion of the optic disc, hypertension, which makes the vessels more convoluted, diabetic retinopathy, which can cause the growth of new vessels, which have a characteristic sinuous shape.

An optical disk can also serve as a guide or starting point for vascular extraction algorithms. The authors also noted that despite the existence of many diseases that cause retinopathy, most researchers focused on diabetic retinopathy for the following reasons: 1) diabetic retinopathy is a serious disease that causes blindness. It can even cause death; 2) this disease affects a huge number of people, and there is the possibility of its early detection and successful treatment; 3) for the detection of diabetic retinopathy, localization of the optic disc, vascular excretion is necessary, and considerable experience has already been accumulated in this area.

Studies have shown that an analysis of vascular changes can help identify the disease at an early stage, and timely treatment can save the baby's eye. The authors developed a new tool for evaluating premature retinopathy based on a quantitative assessment of sinuosity and dilatation of blood vessels. The authors in the work proved that tortuosity turned out to be a more reliable and promising parameter than the width of the vessel for the detection of retinopathy of premature infants. The doctors examined the relationship between the rate of change in the diameter of the vessels of the retina and the high risk of severe retinopathy in premature infants. The authors presented methods for tracking and evaluating vascular tortuosity to analyze the progression and severity of premature retinopathy, investigated the correlation of the severity of premature retinopathy with vascular width and sinuosity.

An important characteristic of the image of blood vessels is its quality, which is affected by factors such as clouding, defocusing, the presence of a noise component or uneven illumination, and the main goal of pre-processing methods is to improve

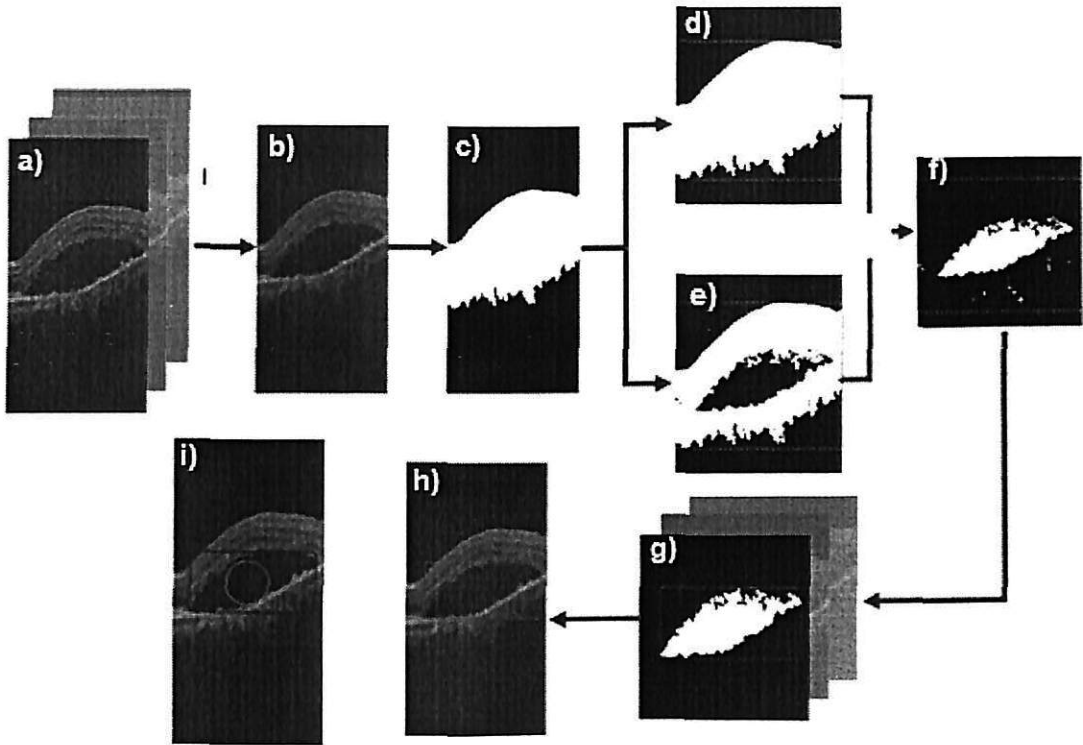


Figure 3.2: Flowchart of processing

the quality of the diagnostic image for its subsequent analysis.

Distortions appear on single images due to differences in light scattering in different parts of the photographed object, changes in its thickness. Differences between images of the same object appear due to camera differences, differences in lighting, differences in shooting angles and pigmentation. Pre-processing of both grayscale and color images of vessels can be broken down to eliminate uneven lighting, improve contrast and color alignment. The problems of this stage of the processing of vascular systems are described in detail in the work.

Isolation and quantification of blood vessels are of primary interest in the problems of diagnosis and treatment of a number of diseases. As noted above, the accurate allocation of vascular systems is often an important step in the tasks of localizing various anatomical parts of an organ, as well as localizing signs of pathologies. Difficulties in accurate vascular isolation are associated with the fact that 1) the width of the vessels can vary within wide limits; the retinal vascular system is a tree structure, and the closer the vessels to the base of the tree, the thicker they are; depending on the location of the vessel and image resolution, the thickness can vary from 1 to 20 pixels, 2) the intensity of the vessel may slightly differ from the intensity of the background, 3) various damage to the retina can

cause false triggering of segmentation algorithms.

There are two main approaches for vascular extraction: vascular segmentation, which allows you to select the entire vascular tree in one iteration, and vascular tracking (tracing). In relation to the development of vascular segmentation algorithms, according to the literature, the following approaches can be distinguished: - classification of image samples (without training, with training); - consistent filtering; - mathematical morphology; - multiscale approaches; - Model-based approaches.

For each pixel, a feature vector was calculated, consisting of the pixel intensity and the response of the Gabor 2D wavelet transform calculated for various scales. A classifier based on a model from a combination of Gaussian functions was applied to each of the pixels to determine the likelihood of a vessel. The algorithm takes into account local information obtained during the filtering process, but ignores very important information about the forms and structures shown in the image. The method does not work well on images with uneven illumination due to a false response at the edge of the optical disc, hemorrhage and other pathology, which has a high contrast with the background. Gabor's band-pass filter is widely used in image processing due to the possibility of adjusting its spatial orientation, the ability to select frequencies in two-dimensional space with good performance in spatial and frequency domains.

The use of linear operators as a feature vector and the use of *SVM* for pixel classification is suggested in the works. A simple detector based on an estimate of the average brightness level along fixed-length lines passing through the pixel in question was applied to the green channel of color images. Then the detector response was subjected to threshold processing. To create a feature vector, a detector based on two orthogonal lines was also used, and classification was performed using an SVM classifier. Compared to other approaches, the algorithm required fewer features to classify, the features were very easy to calculate, and fewer images were required for training. The algorithm showed good reliability when working on images with uneven illumination and contrast. The algorithm also showed acceptable results on images containing vessels with a Central reflex. It used a filter obtained from the Gabor filter by rotating in a certain number of directions. In order to select lines of different widths, you must apply a filter with different scales.

In the works, a classifier was applied to images processed by a multiscale Gabor filter to select candidates for vessel membership among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on the classification of pixels without using training search for patterns specific to blood vessels in retinal images. These algorithms do not require the direct use of a training set. In the works, a method for growing regions based on the analysis of information about the gradient and curvature of the field was proposed.

The paper presents an algorithm for fuzzy clustering, which uses the separation of pixels by vessel affiliation for tracing on angiographic images. Their algorithm uses only information about the intensity of the image and does not make any assumptions about the shape of the vessel. The fuzzy grouping algorithm is applied to each probable vessel. Each image area that contains more than 3 points belonging to the vessels is considered as a candidate for the position of the starting point of the iterative fuzzy tracing algorithm. False candidates are discarded by the algorithm for 2 or 3 iterations. An amazing feature of the algorithm is that it does not use any information about the boundaries to determine the position of the vessels, which reduces the sensitivity to noise, nor does it make any assumptions about the model of the profile of the vessel. Moreover, the algorithm does not require tuning and any initialization actions. The algorithm copes well with the task of tracing clearly defined vessels, but it does not take into account vessels of small diameter and low contrast [2].

A clustering algorithm is proposed that uses distances based on the principle of displaying the distribution of image pixels. The algorithm used the green color channel of the image, local gradient maxima and local maxima of the eigenvalues of the Hessian matrix. The algorithm was compared in efficiency with the algorithm and showed the best results in detecting small vessels. The method of fuzzy segmentation, used information about the intensity of the red and green color channels of the image to correct uneven illumination. Consistent filtering was used to improve the contrast of the vessels relative to the background [3].

The system allowed evaluating the width, contrast, and direction of blood vessels at each point in the image. The algorithm also used an additive noise model, which together with the estimation of vessel parameters allowed determining the

position of the vessel's center line. First, consistent filtering was used to improve vascular contrast, and then a matrix was calculated, based on which statistical values were determined for subsequent threshold processing. Then, threshold processing based on local entropy was applied for segmentation of the vascular system. The algorithm applied a filter with a different scale based on the second derivative of the Gauss function to the image, and the response of the filter was used to detect vessels and evaluate their features. A Gaussian noise model was also used to suppress it. Vessel profile and noise distribution models were used together for probabilistic estimation of vessel parameters.

A consistent filter was applied, used, improved using an optimizing search procedure. The optimization procedure was applied on 20 images of the retina to determine the best parameters of the matched filter, such as the filter size, the standard deviation of the Gaussian function used to design the filter and the threshold value. The improved filter has outperformed the standard filter. In the work, the classical matched filter was refined using the first derivative of the Gauss function. This modification was made based on the symmetry of the gaussian-shaped section of the vessel relative to its peak, while the borders are not symmetrical in pathology. The technique used two filters: a filter based on the Gaussian function and a filter based on the first derivative of the Gauss function. In the region of maximum vessel intensity, the filter gave a strong response, while the filter gave a zero response. In contrast, structures other than blood vessels, for example, having sharp boundaries. The technique allowed to significantly reduce the number of false positives and determine a larger number of thin vessels compared to a conventional filter. Mathematical morphology is used as a tool to extract portions of an image that are useful for describing various shapes, such as the borders and skeleton of a vessel. Mathematical morphology offers a powerful tool for solving many image processing problems. Morphological operators were used to localize microaneurysms, as well as for vascular segmentation.

3.2 Processing

Three methods prevail among approaches to vascular extraction: 25 percent of the articles examined used vascular tracing techniques, the other 22.9 percent and 23.4 percent use approaches based on consistent filtering and methods for classify-

ing pixels with user participation (with training), of which using neural networks account for 32 percent. Approximately 17 percent of articles use multiscale approaches, morphological analysis - 15 percent, methods based on models - 17 percent and 6.4 percent use automated recognition algorithms without training.

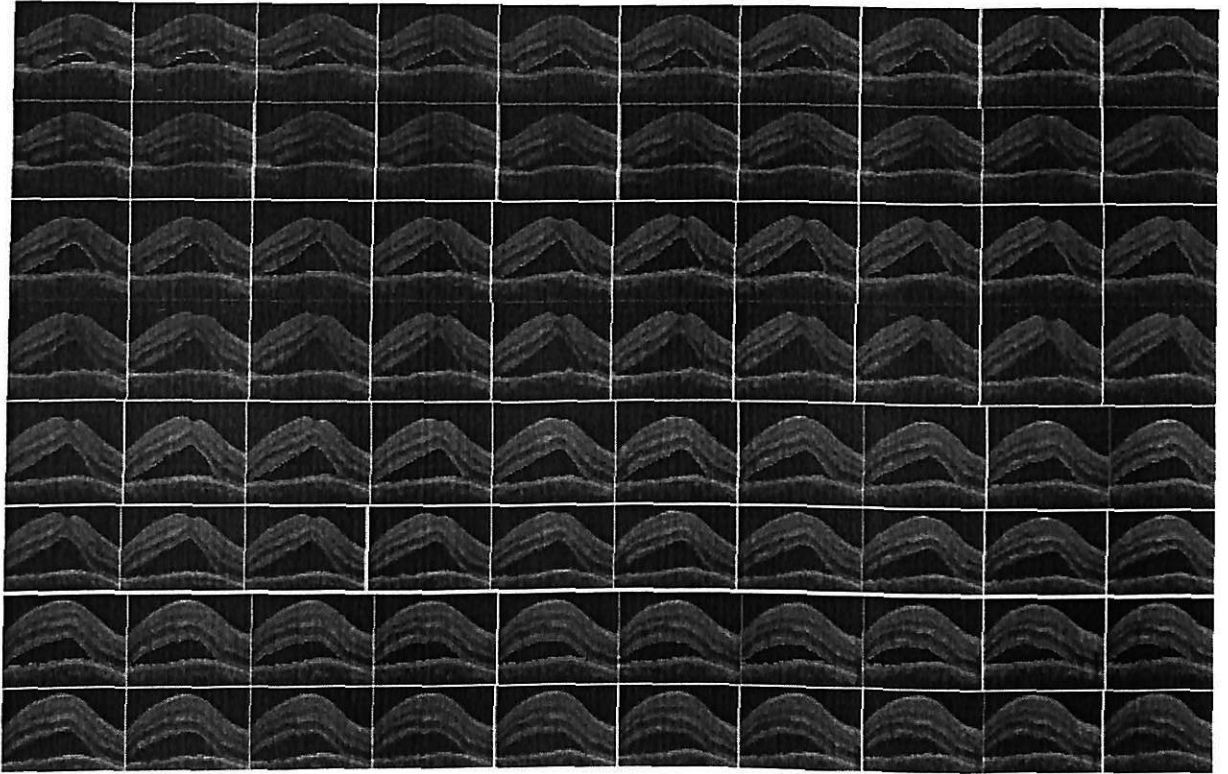


Figure 3.3: Segmentation result of proposed method

Thus, the techniques described in the articles were divided into categories according to their belonging to one of the stages of image analysis: - Evidence-based medicine. -Preliminary processing. - Elimination of uneven lighting. - Alignment of color. -Increase the contrast. -Processing images of the optic disc. -Localization of the optical disk. - Segmentation of an optical disk. -Evaluation of the parameters of the optical disk. Segmentation of the vascular system. - Classification of image samples (without training, with training). - Consistent filtering. -Mathematical morphology. -Multi-scale approaches. -Model-based approaches. -Vascular tracking and tracing. -Assessment of diameters. -Evaluation of diagnostic features.

The system provides the following algorithm for making a diagnosis: 1) Localization of the most important areas, such as vessels, optical disk, using segmentation methods. 2) Search for signs of pathologies, such as venous dilation, excessive

curvature of blood vessels, etc., using classification. 3) making a diagnosis based on the detected signs of pathologies. The system also published its research in the field of medicine, which served as the theoretical basis for automatic diagnostics. They noted that the retina can tell you about hundreds of diseases, and their system could make 13 different diagnoses based on 39 signs of vascular changes. Despite the fact that this system was significantly inferior to the expert doctor on diagnostics, at that time it already showed quite good results.

The algorithm suggested using a two-dimensional filter core for the segmentation of blood vessels based on the Gaussian function or its derivative. The filter profile is designed in such a way as to best fit the profile of the vessel, which usually takes the form of a Gaussian function or its derivative. The filter core rotates in increments of 15 to match vessels with different spatial orientations. To obtain a binary image of vessels for each pixel, the best filter response is determined, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels. The approach proved that the width of the vessels can be measured based on the amplitude parameters of the filter giving the best response. Measuring the width of the vessels allows not only to estimate the size of the vessel, but can also be useful for optimizing the parameters of the matched filter.

A consistent filter was applied, used, improved using an optimizing search procedure. The optimization procedure was applied on 20 images of the retina to determine the best parameters of the matched filter, such as the filter size, the standard deviation of the Gaussian function used to design the filter and the threshold value. The improved filter has outperformed the standard filter. In the work, the classical matched filter was refined using the first derivative of the Gauss function. This modification was made based on the symmetry of the gaussian-shaped section of the vessel relative to its peak, while the borders are not symmetrical in pathology. The technique used two filters: a filter based on the Gaussian function and a filter based on the first derivative of the Gauss function. In the region of maximum vessel intensity, the filter gave a strong response, while the filter gave a zero response. In contrast, structures other than blood vessels, for example, having sharp boundaries. The technique allowed to significantly reduce the number of false positives and determine a larger number of thin vessels compared to a conventional filter. Mathematical morphology is used as a tool to

extract portions of an image that are useful for describing various shapes, such as the borders and skeleton of a vessel. Mathematical morphology offers a powerful tool for solving many image processing problems. Morphological operators were used to localize microaneurysms, as well as for vascular segmentation.

The use of linear operators as a feature vector and the use of *SVM* for pixel classification is suggested in the works. A simple detector based on an estimate of the average brightness level along fixed-length lines passing through the pixel in question was applied to the green channel of color images. Then the detector response was subjected to threshold processing. To create a feature vector, a detector based on two orthogonal lines was also used, and classification was performed using an SVM classifier. Compared to other approaches, the algorithm required fewer features to classify, the features were very easy to calculate, and fewer images were required for training. The algorithm showed good reliability when working on images with uneven illumination and contrast. The algorithm also showed acceptable results on images containing vessels with a Central reflex. It used a filter obtained from the Gabor filter by rotating in a certain number of directions. In order to select lines of different widths, you must apply a filter with different scales.

In the works, a classifier was applied to images processed by a multiscale Gabor filter to select candidates for vessel membership among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on the classification of pixels without using training search for patterns specific to blood vessels in retinal images. These algorithms do not require the direct use of a training set. In the works, a method for growing regions based on the analysis of information about the gradient and curvature of the field was proposed [4].

The paper presents an algorithm for fuzzy clustering, which uses the separation of pixels by vessel affiliation for tracing on angiographic images. Their algorithm uses only information about the intensity of the image and does not make any assumptions about the shape of the vessel. The fuzzy grouping algorithm is applied to each probable vessel. Each image area that contains more than 3 points belonging to the vessels is considered as a candidate for the position of the starting point of the iterative fuzzy tracing algorithm. False candidates are discarded by

the algorithm for 2 or 3 iterations. An amazing feature of the algorithm is that it does not use any information about the boundaries to determine the position of the vessels, which reduces the sensitivity to noise, nor does it make any assumptions about the model of the profile of the vessel. Moreover, the algorithm does not require tuning and any initialization actions. The algorithm copes well with the task of tracing clearly defined vessels, but it does not take into account vessels of small diameter and low contrast [5].

3.3 Fisher Linear Discriminant

Linear Discriminant Analysis (*LDA*) are methods used in statistics, pattern recognition and machine learning to find a linear combination of characteristics which describes or splits two or more classes of objects. The resulting combination may be used as a linear classifier. *LDA* is closely related to Principal Component Analysis (*PCA*) for both of them are based on linear and matrix multiplication, transformations. In case of *PCA*, the transformation is based on minimizing mean square error between original data vectors and data vectors that can be estimated for the reduced dimensionality data vectors and the *PCA* does not considers any difference in class. However, for *LDA* the transformation is based on maximizing a ratio of “between-class variance” to “within-class variance” to lower data variability in the same class and increasing the separation between classes.



Figure 3.4: Segmentation results of proposed method overlaid on 3-D

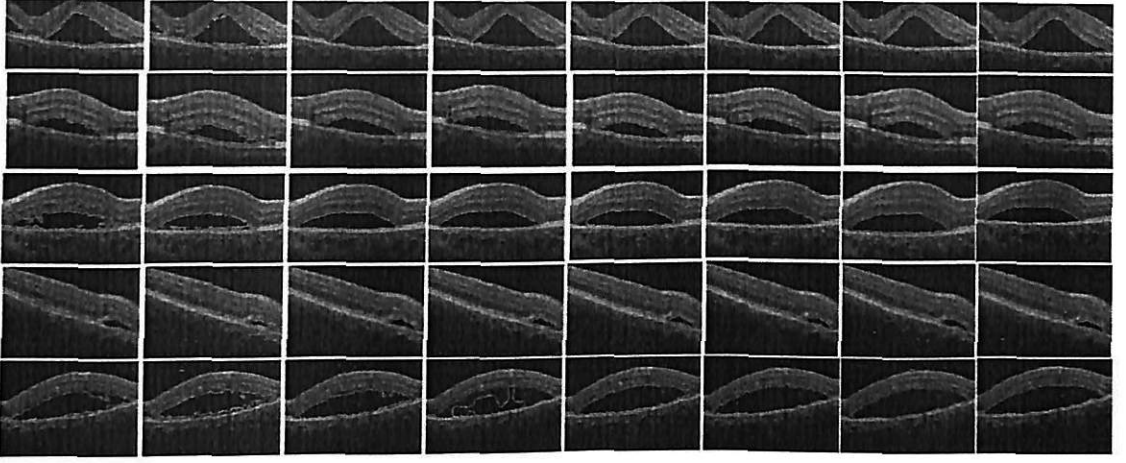


Figure 3.5: Examples of subretinal fluid segmentation

To find out LDA, we need to aware what is the “between-class variance” and “within-class variance” [6]. Then we have to maximize the ratio between these two. Assume we have a set of D -dimensional samples $X = \{x_1, x_2, \dots, x_m\}$, N_1 of which belong to class C_1 and N_2 belong to class C_2 . In our case, class C_1 is fluid associated region, and class C_2 is outer region, respectively. For this case we also assume the mean vector of two classes in X space:

$$u_k = \frac{1}{N_k} \sum_{i=1}^{\infty} x^i, \quad (3.1)$$

where $k=1,2$, and in y space:

$$u'_k = \frac{1}{N_k} \sum_{i=1}^{\infty} y^i = \frac{1}{N_k} \sum_{i=1}^{\infty} \Theta^T x^i = \Theta^T u_k, \quad (3.2)$$

where $k=1,2$. One of the ways to define a measure of separation between two classes is to choose the distance between the projected means, which is in y space [7], so the between-class variance is:

$$u'_2 - u'_1 = \Theta^T (u'_2 - u'_1), \quad (3.3)$$

and within-class variance for each class C_k is:

$$s_k^2 = \sum_{i=1}^{\infty} (y^i - u_k)^2, \quad (3.4)$$

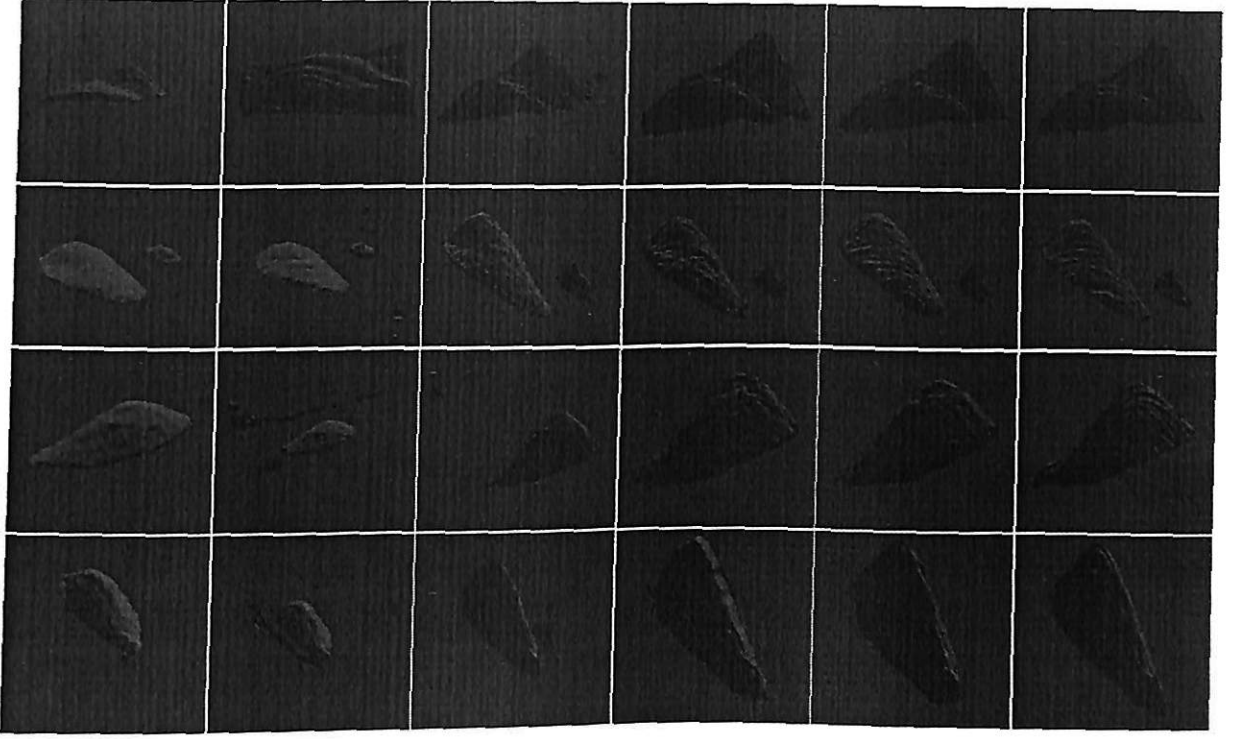


Figure 3.6: Comparison of segmentation results overlaid on 3-D

Final Fisher criterion in terms of some measure scatters as following:

$$J(\Theta) = \frac{\Theta^T S_B \Theta}{\Theta^T S_W \Theta}, \quad (3.5)$$

where

$$S_B = (u_2 - u_1)(u_2 - u_1)^T, \quad (3.6)$$

$$S_W = \sum_{k=1}^{\infty} \sum_{i=1}^k (x^i - u_k)(x^i - u_k)^T, \quad (3.7)$$

The easiest way to maximize the object function J is to derive it and set it to zero[8].

$$\frac{\partial J(\Theta)}{\partial \Theta} = \frac{\partial}{\partial \Theta} \left(\frac{\Theta^T S_B \Theta}{\Theta^T S_W \Theta} \right), \quad (3.8)$$

By solving above equation we get the direction of the θ , which is the:

$$\theta^* \propto S_W^{-1}(u_2 - u_1), \quad (3.9)$$

Intensity inhomogeneity phenomenon presents a systematic change on intensities of both object and background and usually manifests itself as a smooth spatially

varying function across the image. A novel region based model is proposed to segment image with intensity inhomogeneity [9]. The model consists of three components: linear discriminant analysis, region scalable fitting energy and regularization term of the level set function. The local discriminant analysis is used to classify pixels to background and foreground, while energy functional and regularization term are used to differentiate the image differences between the foreground and the background of an object, and iteratively evolve the initial contours [10]. According to above analysis, new feature space obtained by linear discriminant analysis can be incorporated into the *LBF* energy functional to assist in image segmentation. So the final energy functional can be expressed as:

$$E^{RSFLDA} = \sum_{i=1}^2 \int \int K_{\sigma}(x, y) |I(y) - f_i(x)|^2 + \alpha |Y(y) - u_i(x)|^2 H_i(\phi(y)) dy dx, \quad (3.10)$$

where α is nonnegative constant and $Y(y)$ is a new feature space obtained from Eq.(3.1). α is a parameter of linear discriminant analysis (*LDA*) term, it used to balance the effects of *LDA* term. $f_i(x)$ and $u_i(x)$ denote the intensity means for the image $I(x)$ and $Y(x)$, accordingly. By combining the regularization term and energy functional, the final fitting energy functional is given by[11]:

$$E(\phi) = E^{RSFLDA} + \mu P(\phi), \quad (3.11)$$

$E(\phi)$ is minimized with respect to the functions $f_i(x)$ and $u_i(x)$ [9], which satisfy the following:

$$f_i(x) = \frac{\int K_{\sigma}(x, y) H_i(\phi(y)) I(y) dy}{\int K_{\sigma}(x, y) H_i(\phi(y)) dy}, \quad (3.12)$$

$$u_i(x) = \frac{\int K_{\sigma}(x, y) H_i(\phi(y)) Y(y) dy}{\int K_{\sigma}(x, y) H_i(\phi(y)) dy}, \quad (3.13)$$

Keeping $f_i(x)$ and $u_i(x)$ fixed, $E(\phi)$ is minimized with respect to ϕ , resulting in the evolution formula of the level set function ϕ :

$$\frac{\partial \phi}{\partial t} = -\delta(\phi) (e_1 - e_2 + v \operatorname{div}(\frac{\nabla \phi}{|\nabla \phi|})) + \mu (\nabla \phi - \operatorname{div}(\frac{\nabla \phi}{|\nabla \phi|})), \quad (3.14)$$

$$e_i = \int K_{\sigma}(x, y) (|I(y) - f_i(x)|^2 + \alpha |Y(y) - u_i(x)|^2) dy, i = 1, 2 \quad (3.15)$$

where $\delta(\phi)$ is the derivative of the function $H(\phi)$, $\text{div}(\cdot)$ denotes the divergence operator, and $e_i(x)$ simultaneously quantifies the image difference between foreground and background for the original image[12]. In contour evolution, the level set function ϕ was initially assigned to a positive constant 1 outside a region and -1 inside. σ was assigned to 25 to balance the convergence rate and computational efficiency. Δt and μ were related by $\Delta t * \mu = 0.1$ to satisfy the Courant Friedrichs Lewy (*CFL*) condition for numerical stability and they were set $\Delta t=0.1$, $\mu=1$, respectively. The parameter ν was set $\nu = 0.007 * 255 * 255$.

3.4 Experiments

Fig. 4.1 gives the preview of our system. Automated initialization stage targets to find candidate fluid zone by estimating region of interest. Then level set method with Linear Discriminant Analysis is applied to segment subretinal fluid [9][13].

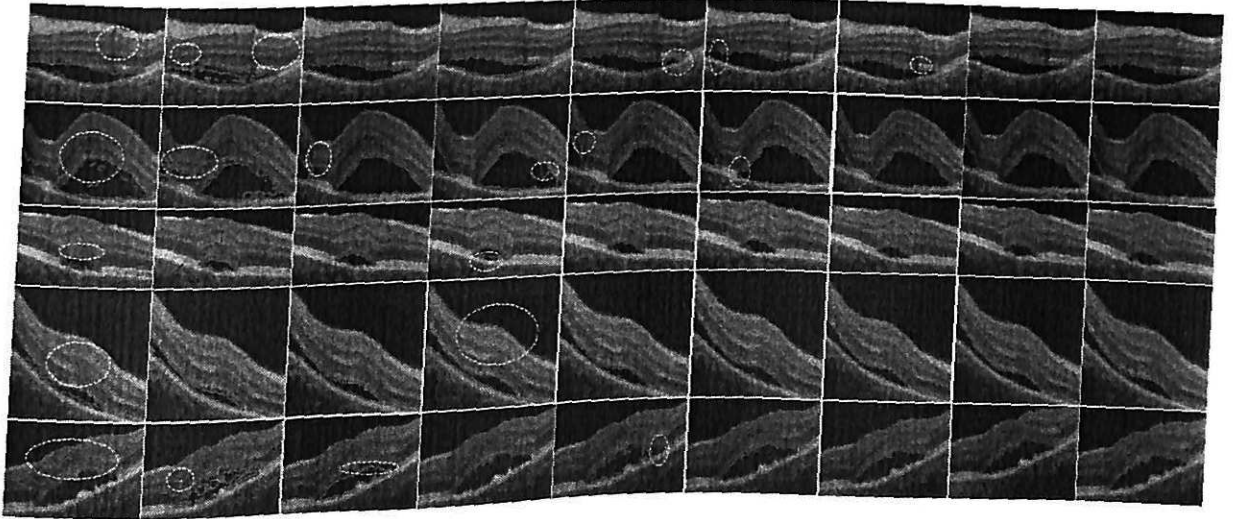


Figure 3.7: Segmentation result of proposed method

Two main approaches are used for vessel selection: vessel segmentation, which allows you to select the entire vessel tree in one processing step, and vessel tracking, which is a step – by – step tracing of vessels. Vessel segmentation is further divided into subcategories [14]. In the literature, algorithms for selecting vascular-like objects in medical images are usually divided into the following classes: algorithms based on the selection of object boundaries; algorithms for growing areas; methods for pattern recognition; methods based on models; using neural networks;

algorithms based on object tracking. The set of algorithms for selecting vessels is represented by the following six categories: - classification of image samples (without training, with training); - consistent filtering; - mathematical morphology; - multi-scale approaches; - model-based approaches; - tracing and tracing of vessels. Some of these categories were further divided into subcategories.

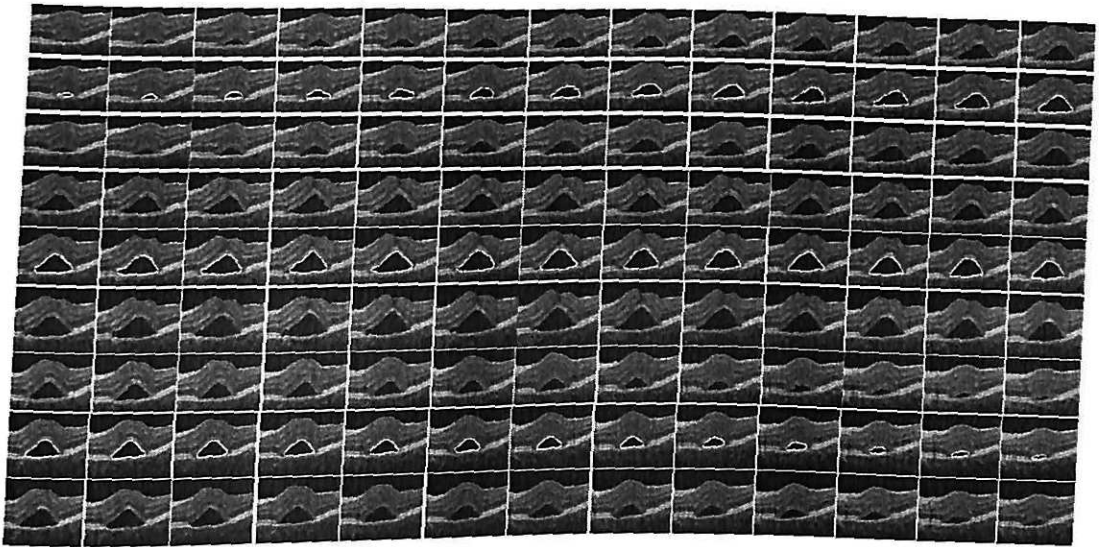


Figure 3.8: Subretinal fluid segmentation results examples

The problem of digital analysis of the vessels of the optic disc is addressed in 60 publications. The largest number of articles devoted to the problem of localization of the optic disc and less on the algorithms of estimation of characteristics of the optic nerve head for the diagnosis of pathologies.

In total, out of all the articles reviewed, 218 are devoted to the problems of vascular isolation, which include segmentation and tracing methods[15].

Three methods prevail among approaches to vessel identification: 25 percent of the articles reviewed used vessel tracing techniques, while the other 22.9 percent and 23.4 percent use approaches based on consistent filtering and pixel classification methods with user participation (with training), of which methods using neural networks make up 32 percent. Approximately 17 percent of the articles use multi-scale approaches, 15 percent use morphological analysis, 17 percent use model – based methods, and 6.4 percent use automated recognition algorithms without training.

Thus, the methods described in the articles were divided into categories according to their belonging to one of the stages of image analysis: -Demonstrative

medicine. -Pre-treatment. -The elimination of the uneven lighting. - Color alignment. -Contrast enhancement. -Image processing of the optic disc. - Localization of the optical disk. -Segmentation of the optical disc. -Estimation of parameters of an optical disk. - Segmentation of the vascular system. - Classification of image samples(without training, with training). - Consistent filtering. -Mathematical morphology. - Multi-scale approaches. - Model-based approaches. - Tracing and tracing of vessels. - Diameter estimation. - Assessment of diagnostic signs.

118 articles on evidence-based medicine were considered, which makes up 21 percent of the total number of articles devoted to the analysis of images of vascular systems and shows the great interest of doctors in this area of research. The articles in this category prove that the isolation of blood vessels and the assessment of their morphological features, such as length, width, tortuosity, branch angles, etc., can be used for the diagnosis, monitoring, treatment and evaluation of various cardiovascular, ophthalmic diseases, such as diabetes, hypertension, arteriosclerosis and neovascularization of the choroid. A variety of studies in this area are also demonstrated. The authors actively use numerical measurements of vascular systems as auxiliary tools to study the relationship between changes in the structure of blood vessels and various diseases [16].

It is shown in the works that automated isolation and digital analysis of vascular systems can help in the implementation of monitoring systems for diabetic retinopathy, senile retinopathy.

A clustering algorithm is proposed that uses distances based on the principle of displaying the distribution of image pixels. The algorithm used the green color channel of the image, local gradient maxima and local maxima of the eigenvalues of the Hessian matrix. The algorithm was compared in efficiency with the algorithm and showed the best results in detecting small vessels. The method of fuzzy segmentation, used information about the intensity of the red and green color channels of the image to correct uneven illumination. Consistent filtering was used to improve the contrast of the vessels relative to the background.

The system allowed evaluating the width, contrast, and direction of blood vessels at each point in the image. The algorithm also used an additive noise model, which together with the estimation of vessel parameters allowed determining the position of the vessel's center line. First, consistent filtering was used to improve vascular contrast, and then a matrix was calculated, based on which statistical

values were determined for subsequent threshold processing. Then, threshold processing based on local entropy was applied for segmentation of the vascular system. The algorithm applied a filter with a different scale based on the second derivative of the Gauss function to the image, and the response of the filter was used to detect vessels and evaluate their features. A Gaussian noise model was also used to suppress it. Vessel profile and noise distribution models were used together for probabilistic estimation of vessel parameters [17].

The transverse profile of the vessel can be approximated by the Gauss function; on a local scale, it is a rectilinear object with a gradually decreasing diameter. The idea behind the use of spatial-scale analysis to extract vessels is to determine the scale-independent information on the vessels. The authors considered multi-scale structures of the second order of the Hessian function in the context of the development of a filter for vascular isolation. The vessel search algorithm is based on an analysis of the eigenvectors of the Hessian matrix. It determines the main directions along which the local structure can be decomposed into components giving directions of the least field curvature along the channel of the vessel. The resulting assessment of the vessel was calculated using the geometric parameters of the vessel, as well as the eigenvalues and norms of the Frobenius matrix and was checked on images obtained using angiography and three-dimensional magnetic resonance imaging. The approach showed the ability to simultaneously suppress noise and background images. Many algorithms are based on this approach. The paper presents an algorithm for the selection of blood vessels, based on the use of the method of morphological amoeba. The application of the algorithm to the problem of the continuation of vessels from a set of points that are obviously points of vessels is considered [18].

A method based on spatial-scale analysis for estimating the width, size and spatial orientation of blood vessels using two geometric features based on the first and second derivatives of intensity is presented. This approach provides information on image topology. The boundary points of the vessel are characterized by the magnitude of the gradient in the image, the largest change in the value of which is observed in the direction of the corresponding maximum intensity in the area of the ridges of the image the greatest curvature of the field. The maximum gradient value and the maximum curvature at various image scales were further used in the region growth algorithm. The algorithm was tested on images without

a red component and fluorescence retinal angiograms and showed, according to the authors, promising results. A modification of this spatial-scale algorithm is made based on the observation that the image intensity is proportional to the amount of blood in the vessel. Therefore, a diameter-dependent equalization factor was applied to multiscale information [19].

The use of linear operators as a feature vector and the use of *SVM* for pixel classification is suggested in the works. A simple detector based on an estimate of the average brightness level along fixed-length lines passing through the pixel in question was applied to the green channel of color images. Then the detector response was subjected to threshold processing. To create a feature vector, a detector based on two orthogonal lines was also used, and classification was performed using an *SVM* classifier. Compared to other approaches, the algorithm required fewer features to classify, the features were very easy to calculate, and fewer images were required for training. The algorithm showed good reliability when working on images with uneven illumination and contrast. The algorithm also showed acceptable results on images containing vessels with a Central reflex. It used a filter obtained from the Gabor filter by rotating in a certain number of directions. In order to select lines of different widths, you must apply a filter with different scales.

In the works, a classifier was applied to images processed by a multiscale Gabor filter to select candidates for vessel membership among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on the classification of pixels without using training search for patterns specific to blood vessels in retinal images. These algorithms do not require the direct use of a training set. In the works, a method for growing regions based on the analysis of information about the gradient and curvature of the field was proposed.

The paper presents an algorithm for fuzzy clustering, which uses the separation of pixels by vessel affiliation for tracing on angiographic images. Their algorithm uses only information about the intensity of the image and does not make any assumptions about the shape of the vessel. The fuzzy grouping algorithm is applied to each probable vessel. Each image area that contains more than 3 points belonging to the vessels is considered as a candidate for the position of the starting

point of the iterative fuzzy tracing algorithm. False candidates are discarded by the algorithm for 2 or 3 iterations. An amazing feature of the algorithm is that it does not use any information about the boundaries to determine the position of the vessels, which reduces the sensitivity to noise, nor does it make any assumptions about the model of the profile of the vessel. Moreover, the algorithm does not require tuning and any initialization actions. The algorithm copes well with the task of tracing clearly defined vessels, but it does not take into account vessels of small diameter and low contrast [3].

A clustering algorithm is proposed that uses distances based on the principle of displaying the distribution of image pixels. The algorithm used the green color channel of the image, local gradient maxima and local maxima of the eigenvalues of the Hessian matrix. The algorithm was compared in efficiency with the algorithm and showed the best results in detecting small vessels. The method of fuzzy segmentation, used information about the intensity of the red and green color channels of the image to correct uneven illumination [20].

4. Results

The developed linear discriminant analysis is used to construct the intensity fitting term $|Y(y) - u_i(x)|^2$. This causes that the proposed method has potential for handling intensity inhomogeneity and avoiding unnecessary contour evolution in segmentation by classifying image information to foreground and background, respectively. To demonstrate the performance of the proposed method, 23 longitudinal *SD-OCT* cube scans from 12 eyes of 12 patients acquired with the Cirrus *OCT* device were used in which all the subjects were diagnosed with *CSCR* with only *NRD*. Fig. 3.2 demonstrates the performance of proposed model to segment *NRD* associated subretinal fluid. In a qualitative comparison (Fig. 3.2),

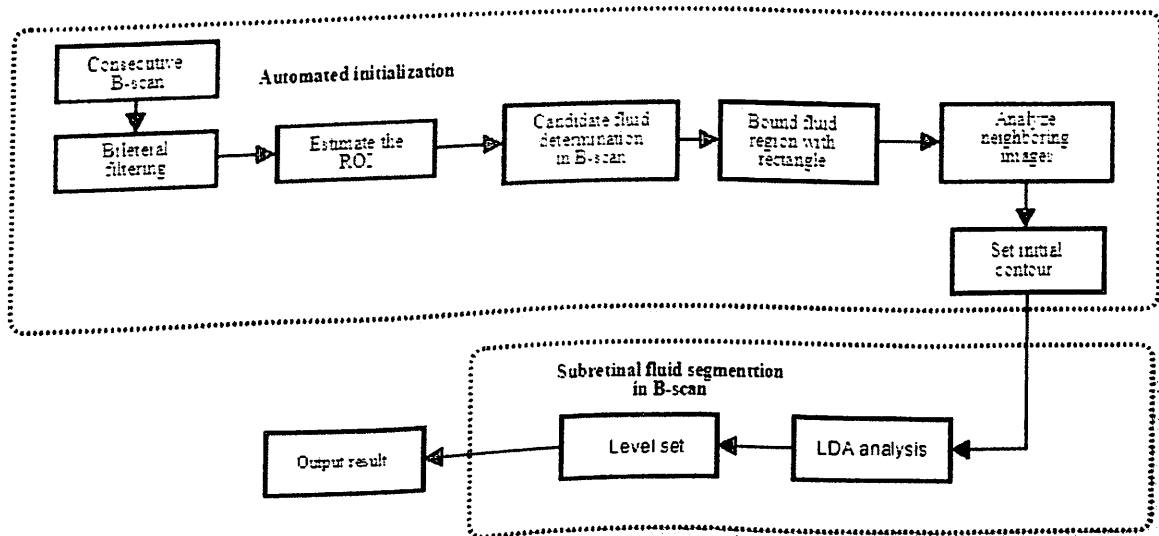


Figure 4.1: Overview of proposed method

the proposed method provided a smooth boundary of the fluid region, while the *LPHC* and *SS - KNN* method do not guarantee the smoothness of the contour [13]. The *LPHC* method suffers from a strong label propagation constraint. If the retinal structure changes dramatically, the regions might be segmented (de-

lineated by the dashed yellow ellipse). The automatic layer segmentation is not always correct, which may result in failure of layer segmentation method results, because of *NRD* which affects to retinal layer structure. Our model surpasses other state-of-art methods and generates the segmentation results similar to the ground truths. The results in Table 1 summarize the *PPV* and *DSC*. Overall, the proposed method is capable to produce a higher segmentation results without utilizing any layer segmentation results.

In the works, pre-trained neural networks were used to classify vessels. The *KNN* classifier is presented, where each pixel was assigned the probability of its belonging to the vessel. Artificial neural networks use weights to determine the correspondence between input and output data. They can be configured using a training set based on backpropagation networks. The pixels of the window sliding across the image were used as input to the network. For each pixel, a feature vector was generated based on the pixel intensity values from a window centered relative to the classified pixel. To train the network, labeled angiograms were used.

The use of the principal component analysis method of principal component analysis to localize the anatomical parts of the retina was demonstrated in the work. The method showed good agreement with the marking of an experienced ophthalmologist made on the images.

An analysis of the relationships between changes in vascular characteristics and various diseases contributes to the timely detection and treatment of diseases at an early stage. Automated analysis also finds application in computer laser surgery and biometric identification.

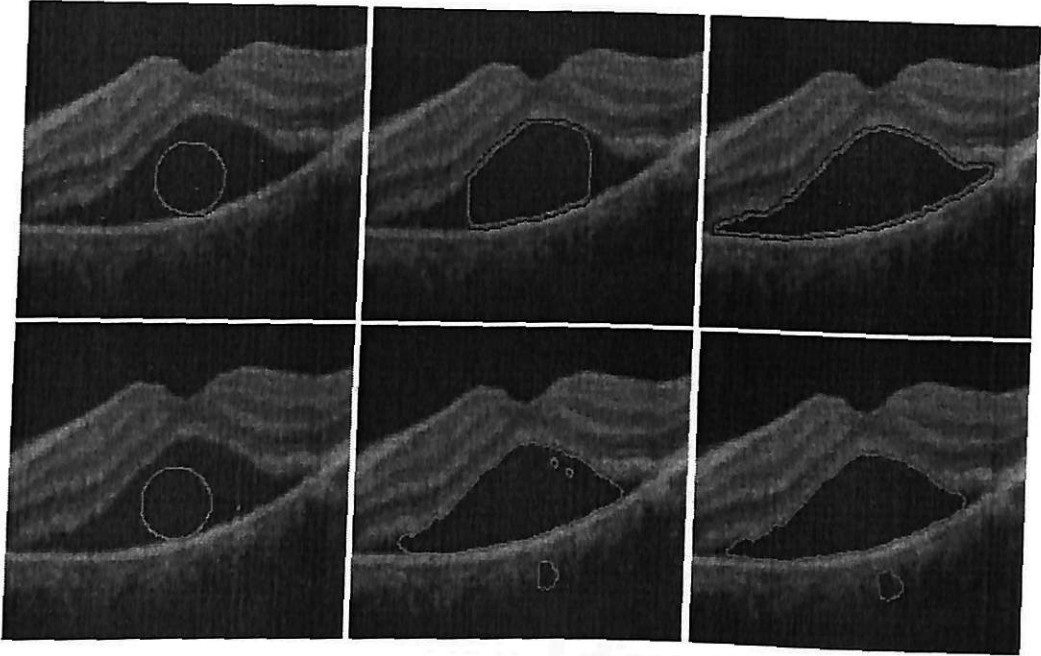


Figure 4.2: Segmentation of Neurosensory Retinal Detachment associated sub-retinal fluid using the proposed model

Methods	Expert 1		Expert 2	
	PPV	DSC	PPV	DSC
LPHC[9]	54.6 ± 12.3	64.3 ± 9.4	54.8 ± 11.8	64.7 ± 9.5
SS-KNN [22]	90.9 ± 3.8	85.1 ± 3.1	90.8 ± 2.8	84.9 ± 3.1
FLSCV [4]	85.2 ± 6.3	77.9 ± 20.7	85.8 ± 6.3	78.4 ± 1.2
CMF [23]	92.0 ± 2.4	92.9 ± 1.5	93.0 ± 2.5	93.3 ± 1.6
EFD [5]	92.0 ± 3.8	92.7 ± 3.0	93.1 ± 4.3	93.6 ± 3.1
Proposed	95.52 ± 0.013	93.79 ± 1.2	96.59 ± 0.1	94.4 ± 1.6

Table 4.1: To summarize the quantitative findings (mean \pm standard deviation) between the segmentations and the manual gold standards (segmentations of two individual experts).

5. Discussion

5.1 Benefits

One of the main issues of modern medicine is determining the boundaries of the normal human phenotype, its variability, and the individual threshold for the risk of disease. This issue is especially relevant when determining the norm in children and adolescents.

Optoacoustics is a relatively young medical imaging technique that is used to diagnose blood vessels, brain activity, skin lesions, and breast cancer. However, the image quality largely depends on the number and distribution of sensors used by the device: the more of them, the better the image quality. A new approach developed in Zurich allows you to significantly reduce the number of sensors without giving up the desired image quality. This allows you to reduce the cost of the device, increase the speed of image processing, or improve diagnostics.

Having discarded most of the sensors, the research team received images with artifacts - missing bands. A previously trained neural network was able to significantly restore image quality close to what was originally.

The developed machine learning algorithm was also successful in improving the quality of images that were recorded using just a narrowly defined sector. This is especially important for clinical applications, since laser pulses cannot penetrate the entire human body, hence the displayed area is usually only accessible in one direction.

Pre-trained neural networks were used to classify vessels. The *KNN* classifier is presented, where each pixel was assigned the probability of its belonging to a vessel.

Artificial neural networks use weight coefficients to determine the correspondence between input and output data. They can be configured using a training

sample based on error back propagation networks. Pixels of the window sliding over the image were used as input data for the network. For each pixel, a feature vector was generated based on pixel intensity values from a window centered relative to the classified pixel. Marked angiograms were used to train the network.

Specialists learn to distinguish damage to vascular systems from the appearance of vascular systems without pathologies. In addition, with this kind of analysis, there is always a subjective factor, which often leads to differences in the diagnoses made by doctors.

A large number of algorithms and methods for digital analysis of human vascular systems have been published. Image analysis of vascular systems for the detection of pathologies comes down to the task of pattern recognition. The process of detecting multiple images and their relationships in vascular images involves a number of operations or steps, using low-quality image processing methods that allow you to move on to more complex analysis.

To obtain a binary image of vessels for each pixel, the best filter response is determined, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels. The approach proved that the width of the vessels can be measured based on the amplitude parameters of the filter giving the best response. Measuring the width of the vessels allows not only to estimate the size of the vessel, but can also be useful for optimizing the parameters of the matched filter [21].

A consistent filter was applied, used, improved using an optimizing search procedure. The optimization procedure was applied on 20 images of the retina to determine the best parameters of the matched filter, such as the filter size, the standard deviation of the Gaussian function used to design the filter and the threshold value. The improved filter has outperformed the standard filter. In the work, the classical matched filter was refined using the first derivative of the Gauss function. This modification was made based on the symmetry of the gaussian-shaped section of the vessel relative to its peak, while the borders are not symmetrical in pathology. The technique used two filters: a filter based on the Gaussian function and a filter based on the first derivative of the Gauss function. In the region of maximum vessel intensity, the filter gave a strong response, while the filter gave a zero response. In contrast, structures other than blood vessels, for example, having sharp boundaries. The technique allowed to significantly

reduce the number of false positives and determine a larger number of thin vessels compared to a conventional filter. Mathematical morphology is used as a tool to extract portions of an image that are useful for describing various shapes, such as the borders and skeleton of a vessel. Mathematical morphology offers a powerful tool for solving many image processing problems. Morphological operators were used to localize microaneurysms, as well as for vascular segmentation.

Creating a technique for digital analysis of vascular systems is impossible without solving a number of problems: recognizing vessels in digital images, choosing a methodology for analyzing vessels and a mathematical model of the vascular bed for subsequent calculations, determining standard values for diagnostic parameters.

Recognition of vessels and determination of their morphological features are the key stages of automated methods of diagnostic analysis of vascular systems, since the accuracy of the selection and measurement of its elements depend on the results of diagnostics.

Specialists learn to distinguish damage to vascular systems from the appearance of vascular systems without pathologies. In addition, there is always a subjective factor in this type of analysis, which often leads to differences in the diagnoses made by doctors. One of the main issues of modern medicine is determining the boundaries of the normal human phenotype, its variability, and the individual threshold for the risk of disease. This issue is especially relevant when determining the norm in children and adolescents.

The environment is rapidly changing, and the development of the child's body in these conditions can be characterized from the perspective of a set of adaptive variants of this human phenotype. Currently, children and adolescents of asthenic physique are more common, with impaired posture and increased joint flexibility.

Thus, in the modern population, an increasing proportion of children and young people with undifferentiated connective tissue dysplasia is noted - according to statistics, this indicator is from 10 to 80 percent. The increased elasticity of the connective tissue is useful for the "push-button" civilization, but can be dangerous with significant physical exertion.

It should be noted that most adolescents with undifferentiated connective tissue dysplasia are workaholics. They study well, attend a lot of additional educational programs, and as a result work from dawn to dawn. It is known

that famous representatives with undifferentiated connective tissue dysplasia, such as Paganini, who had Marfan syndrome, a disease with pronounced connective tissue dysplasia, were distinguished by tremendous performance. It should also be noted that undifferentiated dysplasia of connective tissue is not a disease, but it can be a predictor of a number of diseases, including cardiac arrhythmias, emotional disturbances - asthenia, phobias, agitation, mitral valve prolapse, and many others. Often, treatment is not timely. It is necessary to predict life-threatening complications and to detect the presence of connective tissue dysplasia in the early stages. Timely undetected dysplasia can one day lead to collapsoid complications during physical activity, for example, at a physical education lesson.

It is not surprising that with the growing number of patients and the need to find ways to improve the quality of monitoring of vascular systems over the past 20 years, significant efforts have been made to develop computer technologies that can detect changes in vascular systems. The medical community agrees that automatic quantitative assessment of vascular systems is the first step in the development of computer-based disease diagnosis systems.

A feature vector was calculated for each pixel, consisting of the pixel intensity and the response of the 2D wavelet transform calculated for different scales. A classifier based on a model from a combination of Gauss functions was applied to each of the pixels to determine the probability of belonging to a vessel. The algorithm takes into account local information obtained during the filtering process, but ignores very important information about the shapes and structures represented in the image. The method does not work well on images with uneven illumination due to false alarms at the edge of the optical disk, hemorrhage, and other abnormalities that have a high contrast with the background. A bandpass filter is widely used in image processing due to the ability to adjust its spatial orientation, the ability to allocate frequencies in two-dimensional space with good indicators in the spatial and frequency regions.

The use of linear operators as a feature vector and the use of *SVM* to classify pixels are proposed in the works. A simple detector based on an estimate of the average brightness level along lines of a fixed length passing through the pixel in question was applied to the green channel of color images. Then the response of the detector was subjected to threshold processing. A detector based on two orthogonal lines was also used to create the feature vector, and the classifica-

tion was carried out using the SVM classifier. Compared to other approaches, the algorithm required fewer features for classification, features are very simple to calculate, less images were needed for training. The algorithm showed good reliability when working on images with uneven illumination and contrast. The algorithm also showed acceptable results on images containing vessels with a central reflex. It used a filter obtained from the Gabor filter by rotation in a certain number of directions. In order to highlight lines of different widths, it is necessary to apply a filter with a different scale.

Pre-processing of both grayscale and color images of vessels can be broken down to eliminate uneven lighting, improve contrast and color alignment. The problems of this stage of the processing of vascular systems are described in detail in the work. Three methods prevail among approaches to vascular extraction: 25 percent of the articles examined used vascular tracing techniques, the other 22.9 percent and 23.4 percent use approaches based on consistent filtering and methods for classifying pixels with user participation (with training), of which using neural networks account for 32 percent. Approximately 17 percent of articles use multiscale approaches, morphological analysis - 15 percent, methods based on models - 17 percent and 6.4 percent use automated recognition algorithms without training. There is always a subjective factor in this type of analysis, which often leads to differences in the diagnoses made by doctors.

There are two main approaches to selecting vessels – vessel segmentation, which allows you to select the entire vessel tree in one iteration, and vessel tracking (tracing). In relation to the development of vascular segmentation algorithms, according to the literature, the following approaches can be distinguished: - classification of image samples (without training, with training); - consistent filtering; - mathematical morphology; - multi-scale approaches; - model-based approaches.

The classifier was applied to images processed by a multi-scale filter to select candidates for belonging to the vessel among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on pixel classification without the use of training search for patterns specific to blood vessels in retinal images. These algorithms do not require direct use of the training sample. In this paper, we have proposed a method for expanding regions based on the analysis of information about the gradient and

curvature of the field.

A feature vector was calculated for each pixel, consisting of the pixel intensity and the response of the 2D wavelet transform calculated for different scales. A classifier based on a model from a combination of Gauss functions was applied to each of the pixels to determine the probability of belonging to a vessel. The algorithm takes into account local information obtained during the filtering process, but ignores very important information about the shapes and structures represented in the image. The method does not work well on images with uneven illumination due to false alarms at the edge of the optical disk, hemorrhage, and other abnormalities that have a high contrast with the background. A bandpass filter is widely used in image processing due to the ability to adjust its spatial orientation, the ability to allocate frequencies in two-dimensional space with good indicators in the spatial and frequency regions.

The use of linear operators as a feature vector and the use of *SVM* to classify pixels are proposed in the works. A simple detector based on an estimate of the average brightness level along lines of a fixed length passing through the pixel in question was applied to the green channel of color images. Then the response of the detector was subjected to threshold processing. A detector based on two orthogonal lines was also used to create the feature vector, and the classification was carried out using the *SVM* classifier. Compared to other approaches, the algorithm required fewer features for classification, features are very simple to calculate, less images were needed for training. The algorithm showed good reliability when working on images with uneven illumination and contrast. The algorithm also showed acceptable results on images containing vessels with a central reflex. It used a filter obtained from the Gabor filter by rotation in a certain number of directions. In order to highlight lines of different widths, it is necessary to apply a filter with a different scale.

The classifier was applied to images processed by a multi-scale filter to select candidates for belonging to the vessel among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on pixel classification without the use of training search for patterns specific to blood vessels in retinal images. These algorithms do not require direct use of the training sample. In this paper, we have proposed a method

for expanding regions based on the analysis of information about the gradient and curvature of the field.

The paper presents a fuzzy clustering algorithm that uses pixel separation by vessel membership to trace on angiographic images. Their algorithm uses only information about the intensity of the image and does not make any assumptions about the shape of the vessel. The fuzzy grouping algorithm is applied to each probable vessel. Each area of the image that contains more than 3 points belonging to vessels is considered as a candidate for the starting point of the iterative fuzzy tracing algorithm. False candidates are discarded by the algorithm within 2 or 3 iterations. The surprising feature of the algorithm is that it does not use any boundary information to determine the position of vessels, which reduces sensitivity to noise, nor does it make any assumptions about the vessel profile model. Moreover, the algorithm does not require any configuration or initialization actions. The algorithm does a good job of tracing clearly defined vessels, but does not take into account small-diameter vessels and low contrast.

A clustering algorithm is proposed that uses distances based on the principle of displaying the distribution of image pixels. The algorithm uses the green color channel of the image, local maxima of the gradient, and local maxima of the eigenvalues of the Hessian matrix. The algorithm was compared in efficiency with the algorithm and showed better results when detecting small vessels. The fuzzy segmentation method used information about the intensity of the red and green color channels of the image to correct uneven illumination. Consistent filtering was used to improve the contrast of blood vessels relative to the background.

The system made it possible to evaluate the width, contrast, and direction of blood vessels at each point in the image. The algorithm also used the additive noise model, which, together with the assessment of the parameters of the vessel, made it possible to determine the position of the center line of the vessel. At first, consistent filtering was used to improve the contrast of the vessels, and then a matrix was calculated on the basis of which statistical values were determined for the subsequent threshold processing. Threshold processing based on local entropy was then applied to segment the vascular system. The algorithm used a filter with a different scale based on the second derivative of the Gauss function to the image, and the filter response was used to detect vessels and evaluate their signs. A Gaussian noise model was also used to suppress it. Vascular profile and

noise distribution models were used together for the probabilistic assessment of vascular parameters.

A method based on spatial-scale analysis for estimating the width, size, and spatial orientation of blood vessels using two geometric features based on the first and second intensity derivatives is presented. This approach provides information about the image topology. The boundary points of the vessel are characterized by the gradient magnitude in the image, the greatest value change which is observed in the direction of the corresponding intensity maximum in the region of the ridges of the image of greatest field curvature. The maximum gradient value and maximum curvature at various image scales were then used in the area expansion algorithm. The algorithm was tested on images without a red component and fluorescent retinal angiograms and showed, according to the authors, promising results. A modification of this spatial-scale algorithm is made based on the observation that the image intensity is proportional to the amount of blood in the vessel. Therefore, a diameter-dependent equalization factor was applied to multi-scale information.

The algorithm proposed using a two-dimensional filter core based on the Gauss function or its derivative for segmentation of vessels. The filter profile is designed to best fit the vessel profile, which is usually in the form of a Gauss function or its derivative. The filter core rotates in 15 increments to match vessels with different spatial orientations. To get a binary image of vessels, the best response of the filter is determined for each pixel, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels. The approach proved that the width of the vessels can be measured based on the amplitude parameters of the filter that gives the best response. Measuring the width of vessels allows you not only to estimate the size of the vessel, but can also be useful for optimizing the parameters of a matched filter.

Applied a consistent filter, used, improved with an optimizing search procedure. The optimization procedure was applied on 20 retinal images to determine the best parameters of the matched filter, such as the filter size, the standard deviation of the Gauss function used to design the filter, and the threshold value. The improved filter is more efficient than the standard filter. In this paper, the classical matched filter was refined by using the first derivative of the Gauss function. This modification was made based on the symmetry of the Gauss-shaped

section of the vessel relative to its peak, while the boundaries in pathology are not symmetrical. The method used two filters: a filter based on the Gauss function and a filter based on the first derivative of the Gauss function. In the area of maximum vessel intensity, the filter gave a strong response, while the filter gave a zero response. In contrast, structures other than vessels, for example, have sharp borders. The technique allowed to significantly reduce the number of false positives and determine a larger number of thin vessels compared to a conventional filter. Mathematical morphology is used as a tool for extracting parts of an image that are useful for describing various shapes, such as the borders and skeleton of a vessel. Mathematical morphology offers a powerful tool for solving many image processing problems. Morphological operators were used for localization of microaneurysms, as well as for vascular segmentation.

5.2 Limitations

The thesis provides an overview of the main approaches of digital analysis of images of human blood vessels. The main stages of processing diagnostic images are identified, an analysis of various approaches to the isolation and quantification of morphological signs of blood vessels is carried out. The system made it possible to evaluate the width, contrast, and direction of blood vessels at each point in the image. The algorithm also used the additive noise model, which, together with the assessment of the parameters of the vessel, made it possible to determine the position of the center line of the vessel. At first, consistent filtering was used to improve the contrast of the vessels, and then a matrix was calculated on the basis of which statistical values were determined for the subsequent threshold processing. Threshold processing based on local entropy was then applied to segment the vascular system. The algorithm used a filter with a different scale based on the second derivative of the Gauss function to the image, and the filter response was used to detect vessels and evaluate their signs. A Gaussian noise model was also used to suppress it. Vascular profile and noise distribution models were used together for the probabilistic assessment of vascular parameters.

The algorithm proposed using a two-dimensional filter core based on the Gauss function or its derivative for segmentation of vessels. The filter profile is designed to best fit the vessel profile, which is usually in the form of a Gauss function or its

derivative. The filter core rotates in 15 increments to match vessels with different spatial orientations. To get a binary image of vessels, the best response of the filter is determined for each pixel, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels. The approach proved that the width of the vessels can be measured based on the amplitude parameters of the filter that gives the best response. Measuring the width of vessels allows you not only to estimate the size of the vessel, but can also be useful for optimizing the parameters of a matched filter.

Applied a consistent filter, used, improved with an optimizing search procedure. The optimization procedure was applied on 20 retinal images to determine the best parameters of the matched filter, such as the filter size, the standard deviation of the Gauss function used to design the filter, and the threshold value. The improved filter is more efficient than the standard filter. In this paper, the classical matched filter was refined by using the first derivative of the Gauss function. This modification was made based on the symmetry of the Gauss-shaped section of the vessel relative to its peak, while the boundaries in pathology are not symmetrical. The method used two filters: a filter based on the Gauss function and a filter based on the first derivative of the Gauss function. In the area of maximum vessel intensity, the filter gave a strong response, while the filter gave a zero response. In contrast, structures other than vessels, for example, have sharp borders. The technique allowed to significantly reduce the number of false positives and determine a larger number of thin vessels compared to a conventional filter. Mathematical morphology is used as a tool for extracting parts of an image that are useful for describing various shapes, such as the borders and skeleton of a vessel. Mathematical morphology offers a powerful tool for solving many image processing problems. Morphological operators were used for localization of microaneurysms, as well as for vascular segmentation.

A method based on spatial-scale analysis for estimating the width, size, and spatial orientation of blood vessels using two geometric features based on the first and second intensity derivatives is presented. This approach provides information about the image topology. The boundary points of the vessel are characterized by the gradient magnitude in the image, the greatest value change which is observed in the direction of the corresponding intensity maximum in the region of the ridges of the image of greatest field curvature. The maximum gradient value

and maximum curvature at various image scales were then used in the area expansion algorithm. The algorithm was tested on images without a red component and fluorescent retinal angiograms and showed, according to the authors, promising results. A modification of this spatial-scale algorithm is made based on the observation that the image intensity is proportional to the amount of blood in the vessel. Therefore, a diameter-dependent equalization factor was applied to multi-scale information.

A large number of algorithms and methods for digital analysis of human vascular systems have been published. Analysis of images of vascular systems for the detection of pathologies is reduced to the task of pattern recognition. The process of detecting multiple images and their relationships in vessel images involves a number of operations or stages.

A feature vector was calculated for each pixel, consisting of the pixel intensity and the response of the 2D wavelet transform calculated for different scales. A classifier based on a model from a combination of Gauss functions was applied to each of the pixels to determine the probability of belonging to a vessel. The algorithm takes into account local information obtained during the filtering process, but ignores very important information about the shapes and structures represented in the image. The method does not work well on images with uneven illumination due to false alarms at the edge of the optical disk, hemorrhage, and other abnormalities that have a high contrast with the background. A bandpass filter is widely used in image processing due to the ability to adjust its spatial orientation, the ability to allocate frequencies in two-dimensional space with good indicators in the spatial and frequency regions.

The use of linear operators as a feature vector and the use of *SVM* to classify pixels are proposed in the works. A simple detector based on an estimate of the average brightness level along lines of a fixed length passing through the pixel in question was applied to the green channel of color images. Then the response of the detector was subjected to threshold processing. A detector based on two orthogonal lines was also used to create the feature vector, and the classification was carried out using the *SVM* classifier. Compared to other approaches, the algorithm required fewer features for classification, features are very simple to calculate, less images were needed for training. The algorithm showed good reliability when working on images with uneven illumination and contrast. The

algorithm also showed acceptable results on images containing vessels with a central reflex. It used a filter obtained from the Gabor filter by rotation in a certain number of directions. In order to highlight lines of different widths, it is necessary to apply a filter with a different scale.

The classifier was applied to images processed by a multi-scale filter to select candidates for belonging to the vessel among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on pixel classification without the use of training search for patterns specific to blood vessels in retinal images. These algorithms do not require direct use of the training sample. In this paper, we have proposed a method for expanding regions based on the analysis of information about the gradient and curvature of the field.

This paper provides an overview of algorithms that focus primarily on vascular isolation in two-dimensional, color images of the retina obtained using fundus cameras or fluorescent angiography, and focuses only on studies related to retinal vascular segmentation.

This analysis presents the classification of the main stages of digital analysis of vascular systems in the problems of diagnostics of vascular pathology and classification. For statistical analysis, the literature list of the found articles was used as a secondary source. When analyzing the articles, they were categorized according to their belonging to different stages of processing diagnostic images of vascular systems. In the review articles was reviewed and included the analysis of secondary sources. The main stages of the analysis of key features of vessels were identified: evidence-based medicine, pre-treatment; localization and segmentation of the optic nerve disk; segmentation of vessels; tracing of vessels, evaluation of diameters, evaluation of diagnostic signs. The table shows a list of articles related to the stages presented in the review in whole or in part. The number of articles related to each step in the sequence.

One of the main issues of modern medicine is to determine the boundaries of the normal human phenotype, its variability, and the individual risk threshold for disease. This question is particularly relevant when determining the norm in children and adolescents. The environment changes rapidly, and the development of the child's body in these conditions can be characterized from the point of view

of a set of adaptive variants of this human phenotype. Currently, children and adolescents with asthenic physique, with impaired posture, increased flexibility of the joints are more common.

Thus, in the modern population there is an increasing proportion of children and young people with undifferentiated connective tissue dysplasia – according to statistics, this figure is from 10 to 80 percent. Increased elasticity of connective tissue is useful for "push-button" civilization, but can be dangerous with significant physical exertion.

It should be noted that most adolescents with undifferentiated connective tissue dysplasia are workaholics. They study well, attend a lot of additional educational programs, and as a result, they work from dawn to dawn. It is known that famous representatives with undifferentiated connective tissue dysplasia, such as Paganini, who had Marfan syndrome – a disease with pronounced connective tissue dysplasia, were distinguished by tremendous performance. It should also be noted that undifferentiated connective tissue dysplasia is not a disease, but can be a predictor of a number of diseases, including heart rhythm disorders, emotional disorders – asthenia, phobias, agitation, mitral valve prolapse, and many others. Often, medical measures are not timely. It is necessary to predict life-threatening complications and early detect the presence of connective tissue dysplasia. If dysplasia is not detected in time, it may one day lead to collapsoid complications during physical activity, for example, during a physical education lesson.

The system made it possible to evaluate the width, contrast, and direction of blood vessels at each point in the image. The algorithm also used the additive noise model, which, together with the assessment of the parameters of the vessel, made it possible to determine the position of the center line of the vessel. At first, consistent filtering was used to improve the contrast of the vessels, and then a matrix was calculated on the basis of which statistical values were determined for the subsequent threshold processing. Threshold processing based on local entropy was then applied to segment the vascular system. The algorithm used a filter with a different scale based on the second derivative of the Gauss function to the image, and the filter response was used to detect vessels and evaluate their signs. A Gaussian noise model was also used to suppress it. Vascular profile and noise distribution models were used together for the probabilistic assessment of vascular parameters.

The algorithm proposed using a two-dimensional filter core based on the Gauss function or its derivative for segmentation of vessels. The filter profile is designed to best fit the vessel profile. To get a binary image of vessels, the best response of the filter is determined for each pixel, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels. The approach proved that the width of the vessels can be measured based on the amplitude parameters of the filter that gives the best response. Measuring the width of vessels allows you not only to estimate the size of the vessel, but can also be useful for optimizing the parameters of a matched filter.

Applied a consistent filter, used, improved with an optimizing search procedure. The optimization procedure was applied on 20 retinal images to determine the best parameters of the matched filter, such as the filter size, the standard deviation of the Gauss function used to design the filter, and the threshold value. The improved filter is more efficient than the standard filter. In this paper, the classical matched filter was refined by using the first derivative of the Gauss function. This modification was made based on the symmetry of the Gauss-shaped section of the vessel relative to its peak, while the boundaries in pathology are not symmetrical. In the area of maximum vessel intensity, the filter gave a strong response, while the filter gave a zero response. In contrast, structures other than vessels, for example, have sharp borders. The technique allowed to significantly reduce the number of false positives and determine a larger number of thin vessels compared to a conventional filter. The authors considered multi-scale structures of the second order of the Hessian function in the context of developing a filter for vessel isolation. The vessel search algorithm is based on the analysis of eigenvectors of the Hessian matrix. It defines the main directions in which the local structure can be decomposed into components that give directions of the smallest curvature of the field along the vessel bed. The resulting vessel score was calculated using the vessel's geometric parameters, as well as the eigenvalues and norms of the Frobenius matrix, and was checked on images obtained using angiography and three-dimensional magnetic resonance imaging. The approach showed the ability to simultaneously suppress noise and background images. Many algorithms are based on this approach. Multistructure mathematical morphology the transformation was used to increase contrast, and vessel boundaries were detected

using morphological multistructure transformation. Falsely defined borders were removed using a morphological opening operation. The paper presents an algorithm for selecting blood vessels based on the method of morphological amoebae. The application of the algorithm to the problem of continuation of vessels from a set of points that are known to be points of vessels is considered.

A method based on spatial-scale analysis for estimating the width, size, and spatial orientation of blood vessels using two geometric features based on the first and second intensity derivatives is presented. This approach provides information about the image topology. The boundary points of the vessel are characterized by the gradient magnitude in the image, the greatest value change which is observed in the direction of the corresponding intensity maximum in the region of the ridges of the image of greatest field curvature. The maximum gradient value and maximum curvature at various image scales were then used in the area expansion algorithm. The algorithm was tested on images without a red component and fluorescent retinal angiograms and showed, according to the authors, promising results. A modification of this spatial-scale algorithm is made based on the observation that the image intensity is proportional to the amount of blood in the vessel. Therefore, a diameter-dependent equalization factor was applied to multi-scale information.

A method has been developed for extracting the Central line of the vessel, which finds the path with the lowest cost using a vector multi-scale representation of the image. To obtain a binary image of vessels for each pixel, the best filter response is determined, which is then subjected to threshold processing. Further, other image processing methods are used to obtain segments containing vessels. The approach proved that the width of the vessels can be measured based on the amplitude parameters of the filter giving the best response. Measuring the width of the vessels allows not only to estimate the size of the vessel, but can also be useful for optimizing the parameters of the matched filter [22].

The classifier was applied to images processed by a multi-scale filter to select candidates for belonging to the vessel among pixels. The classifier is essentially a Bayesian network in which the distribution function for each of the classification parameters is represented as a linear combination of Gaussian functions. Approaches based on pixel classification without the use of training search for patterns specific to blood vessels in retinal images. These algorithms do not re-

quire direct use of the training sample. In this paper, we have proposed a method for expanding regions based on the analysis of information about the gradient and curvature of the field.

The paper presents a fuzzy clustering algorithm that uses pixel separation by vessel membership to trace on angiographic images. Their algorithm uses only information about the intensity of the image and does not make any assumptions about the shape of the vessel. The fuzzy grouping algorithm is applied to each probable vessel. Each area of the image that contains more than 3 points belonging to vessels is considered as a candidate for the starting point of the iterative fuzzy tracing algorithm. False candidates are discarded by the algorithm within 2 or 3 iterations. The surprising feature of the algorithm is that it does not use any boundary information to determine the position of vessels, which reduces sensitivity to noise, nor does it make any assumptions about the vessel profile model. Moreover, the algorithm does not require any configuration or initialization actions. The algorithm does a good job of tracing clearly defined vessels, but does not take into account small-diameter vessels and low contrast.

A clustering algorithm is proposed that uses distances based on the principle of displaying the distribution of image pixels. The algorithm uses the green color channel of the image, local maxima of the gradient, and local maxima of the eigenvalues of the Hessian matrix. The algorithm was compared in efficiency with the algorithm and showed better results when detecting small vessels. The fuzzy segmentation method used information about the intensity of the red and green color channels of the image to correct uneven illumination.

6. Conclusion

In summary, we report a fully automatic method for the segmentation of subretinal fluid. Our framework can handle intensity inhomogeneity which can be seen in B-scan images. Compared with the other existing methods, the advantage of our method as follows: firstly, this method limits the spatial extent of the fluid region in B-scans by incorporating region of interest and thus improves the segmentation performance. Second, the experimental results reveal that two-stage automatic framework is robust to possible errors of automatic layer segmentation compared with SS-KNN method. Furthermore, linear discriminant analysis based level set segmentation can provide a smooth boundary of the subretinal fluid.

References

- [1] A. Nedzved, N. Olga, G. Alexey, K. Gregory, G. Igor, and Y. Vera, “Detection of dynamical properties of flow in an eye vessels by video sequences analysis”, *2017 International Conference on Information and Digital Technologies (IDT)*, 2017.
- [2] M. Fraz, P. Remagnino, A. Hoppe, B. Uyyanonvara, A. Rudnicka, C. Owen, and S. Barman, “Blood vessel segmentation methodologies in retinal images – a survey”, *Computer Methods and Programs in Biomedicine*, vol. 108, pp. 407–433, 2012.
- [3] D. Chernomorets, V. Mikhelev, and A. Chernomorets, “Multiscale approach of retinal blood vessels segmentation based on vessels segmentation with different scales”, *2018 3rd Russian-Pacific Conference on Computer Technology and Applications (RPC)*, 2018.
- [4] H. Guopeng, J. Hongbing, Z. Wenbo, and Z. Zhigang, “Adaptive multilayer level set method for segmenting images with intensity inhomogeneity”, *IET Image Processing*, vol. 13, 2019.
- [5] F. Alejandro, S. Julia, D. Christos, A.-L. Carlos, and F. Gabor, “Medical image computing and computer assisted intervention – miccai 2018”, *21st International Conference, Granada, Spain, September 16-20*, 2018.
- [6] A. Vinay, V. R. Kamath, M. Varun, Nidheesh, S. Natarajan, and K. Murthy, “Aggregation of lark vectors for facial image classification”, *ICMMSC 2018: Mathematical Modelling and Scientific Computing with Applications*, 2018.
- [7] M. Santanu, D. BiswaNath, and A. Safique, “Mathematical modelling and scientific computing with applications”, *ICMMSC: International Conference on Mathematical Modelling and Scientific Computation*, 2018.

- [8] L. Armin, W. Supriyadi La, and M. Salama, "Identifying irregularity electricity usage of customer behaviors using logistic regression and linear discriminant analysis", *2017 3rd International Conference on Science in Information Technology (ICSITech)*, 2017.
- [9] L. Wang, C. Guangqiang, S. Dai, Y. Chang, C. Sixian, P. Jiantao, and Y. Xiaodong, "Active contours driven by edge entropy fitting energy for image segmentation", *Signal Processing*, 2018.
- [10] N. Taubaldy and J. Zcxuan, "Beyond retinal layers: An automatic active contour model with pre-fitting energy for subretinal fluid segmentation in sd-oct images", *2018 IEEE 3rd International Conference on Image, Vision and Computing (ICIVC)*, 2018.
- [11] L. Wang, Z. Jianbing, M. Sheng, C. Adriana, Z. Shaocheng, and P. Jiantao, "Simultaneous segmentation and bias field estimation using local fitted images", *Pattern Recognition*, 2018.
- [12] W. Xiao-Feng, M. Hai, Z. Le, and Z. Yi-Gang, "A novel level set method for image segmentation by incorporating local statistical analysis and global similarity measurement", *Pattern Recognition*, vol. 48, pp. 189–204, 2015.
- [13] W. Menglin, C. Qiang, H. XiaoJun, L. Ping, F. Wen, Y. SongTao, and P. Hyunjin, "Automatic subretinal fluid segmentation of retinal sd-oct images with neurosensory retinal detachment guided by enface fundus imaging", *IEEE Transactions on Biomedical Engineering*, 2018.
- [14] P. Hamid, H. Alinejad-Rokny, B. Minaei-Bidgoli, and P. Sajad, "A new classifier ensemble methodology based on subspace learning", *Journal of Experimental & Theoretical Artificial Intelligence*, vol. 25, pp. 227–250, 2013.
- [15] A. Hadi-Vencheh, "A new nonlinear model for multiple criteria supplier-selection problem", *International Journal of Computer Integrated Manufacturing*, vol. 24, pp. 32–39, 2011.
- [16] K. Derdour and H. Mouss, "Digit recognition using multiple classifiers", *2015 12th International Symposium on Programming and Systems (ISPS)*, 2015.
- [17] Z. Stephen and H. Hongbing, "Nonlinear dimensionality reduction methods for use with automatic speech recognition", *Speech Technologies*, 2011.

- [18] J. Zexuan, X. Yong, S. Quansen, C. Guo, and C. Qiang, "Active contours driven by local likelihood image fitting energy for image segmentation", *Information Sciences*, 2015.
- [19] L. Lin, C. Dansong, T. Feng, S. Daming, and W. Rui, "Active contour driven by multi-scale local binary fitting and kullback-leibler divergence for image segmentation", *Multimedia Tools and Applications*, 2016.
- [20] W. Yue-Bin, Z. Cheng-Zhang, Y. Quan-Feng, and L. Li-Qiang, "A novel vessel segmentation in fundus images based on svm", *2016 International Conference on Information System and Artificial Intelligence (ISAI)*, 2016.
- [21] M. Natarajan, N. Dhinakaran, and C. Nabendu, "Advances in computing and information technology", *Proceedings of the Second International Conference on Advances in Computing and Information Technology (ACITY)*, vol. 2, 2012.
- [22] L. Jian-Huang, L. Cheng-Lin, C. Xilin, Z. Jie, T. Tieniu, Z. Nanning, and Z. Hongbin, "Pattern recognition and computer vision", *Chinese Conference on Pattern Recognition and Computer Vision (PRCV)*, 2018.