

KAUNAS UNIVERSITY OF TECHNOLOGY

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**AUTOMATED ANALYSIS OF EYE FUNDUS IMAGES**

Summary of Doctoral Dissertation  
Technological Sciences, Informatics Engineering (07T)

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KAUNO TECHNOLOGIJOS UNIVERSITETAS

MARTYNAS PATAŠIUS

**AKIES DUGNO VAIZDŲ AUTOMATINĖ ANALIZĖ**

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## **INTRODUCTION**

### **Relevance of the research**

Eye fundus is the part of an eye that can be seen through the pupil. It can be observed and photographed easily, cheaply and noninvasively. The eye fundus images are used to diagnose and monitor various eye and systemic diseases. The importance of non-invasiveness is emphasised in, for example, EU Seventh Framework program.

Eye fundus is the main part of a human body where microvasculature can be observed directly. Thus eye fundus images are used to diagnose and monitor the systemic diseases that damage the blood vessels (for example, arterial hypertension, diabetes, atherosclerosis, and their complications). For example, blood vessel tortuosity is used to diagnose such diseases as hypertensive retinopathy, diabetic retinopathy or retinopathy of prematurity

The changes of optic nerve disc (the place through which the optic nerve enters the eye) also help to diagnose not only the eye diseases (for example, glaucoma that, according to the data of the World Health Organisation, is the second main cause of blindness in the world and in most of the regions), but also some changes of brain and the whole nervous system (for example, increases of intracranial pressure).

Some other eye diseases are also diagnosed using eye fundus images. They include the age-related macular degeneration that, according to the World Health Organisation, is the most common cause of blindness in the developed countries and the third most common in the world.

In most cases screenings are used in order to achieve early diagnosis of those diseases. However, such screenings often require highly qualified ophthalmologists who are then unavailable for their normal duties. Thus lots of attention is paid to the automated analysis of eye fundus images that would make it possible to perform the screenings while leaving the ophthalmologists available for their normal duties.

This work discusses the blood vessel detection, especially with objective to evaluate blood vessel tortuosity using the estimates, the interpretation of which is made easier using blood vessel models. This work also discusses the methods of evaluating the clarity of optic nerve disc margin (which allows noninvasive estimating of the intracranial pressure) and detection of drusen – the main symptom of age-related macular degeneration.

### **Aim of the research**

The aim of the research is to develop algorithms that would help with parameterisation of the eye fundus images, thus improving the diagnostics.

## **Tasks of the research**

The following tasks were formulated in order to achieve the aim:

1. To create a biomechanical finite element model of a blood vessel, to validate it experimentally and to use it to find the relationships between blood pressure and various tortuosity estimates.
2. To find the colour combinations that would emphasise the blood vessels in eye fundus images.
3. To create a blood vessel tracking algorithm that would start the tracking from a single automatically located point and to evaluate the possibility to achieve the performance of blood vessel detection achieved using other existing algorithms.
4. To create a method to evaluate the clarity of optic disc margin.
5. To create a drusen detection algorithm.

## **Scientific novelty**

Using a created and experimentally validated biomechanical blood vessel, it has been found that the tortuosity estimate based on the integral of module of curvature tends to increase linearly as the pressure rises, while the arc-chord ratio, hysteresis-based estimate and the estimate based on the integral of square of derivative of curvature tend to increase quadratically.

The colour combinations optimised for detection of blood vessel pixels were found. It has been found that in the eye fundus images filtered by averaging filter the pixels with the maximal values of the difference between the values of red and green channels belong to the blood vessels with a high probability. A blood vessel tracking algorithm has been created that achieves the blood vessel detection quality superior to the one of the other methods even while excluding the blood vessel bifurcations from the detected blood vessel mask (they are ignored during tortuosity estimation).

Two methods of evaluation of optic disc margin clarity have been created.

An alternative blob detection method usable for drusen detection has been created.

## **Research object**

Models of anatomical structures of eye fundus and algorithms of detection and parameterisation of those structures.

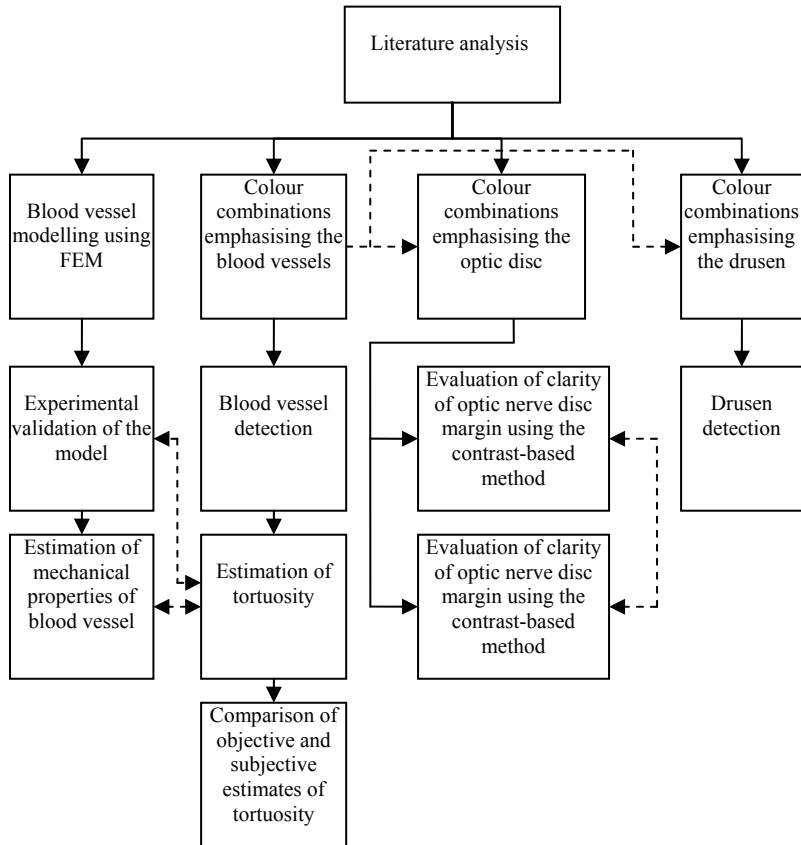
## **Practical significance**

The results of this work are used to process the results of the screening performed at Kaunas University of Medicine. The results of this work are

also being used in the ophthalmological image processing software developed for project E!4297 NICDIT under EUROSTARS programme.

## Structure of the dissertation

The dissertation consists of introduction, five main parts, conclusions, list of references and appendix (Fig. 1).



**Fig. 1.** Structure of the dissertation

The first part of the dissertation presents the analysis of scientific literature related to the topic being explored.

The second part discusses the blood vessel models created with the objective to find the relationships between blood vessel tortuosity and blood flow parameters. It describes the finite element models of blood vessels and the experimental validation of conclusions found using those models.

The third part discusses blood vessel detection and parameterisation. It describes the method that was used to find the optimised colour combinations that emphasise the blood vessels in eye fundus images and the blood vessel detection method utilising those optimised colour combinations. The automatically calculated tortuosity estimates are also compared with the estimates provided by the ophthalmologists.

The fourth part describes and compares two proposed methods to evaluate the clarity of optic nerve disc margin. It also gives the optimised colour combinations that emphasise optic nerve disc, found according to the method described in the third part and being used in some variants of methods evaluating the clarity of optic nerve disc margin.

The fifth part describes the proposed drusen detection method. It also gives the optimised colour combinations that emphasise drusen, found according to the method described in the third part and being used in the drusen detection method.

The volume of dissertation is 109 pages. There are 48 figures and 16 tables in the text.

## **1. OVERVIEW OF MODELLING, LOCATING AND ANALYSIS OF ANATOMICAL STRUCTURES OF EYE FUNDUS**

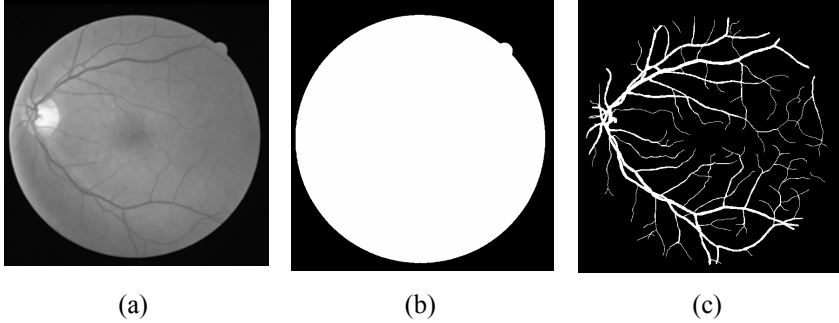
Eye fundus is the part of an eye that can be seen through the pupil. Non-invasively produced eye fundus images can show the signs of numerous ophthalmic and systemic diseases or their complications: arterial hypertension, diabetes, atherosclerosis, intracranial hypertension, etc.

As it is often impractical to investigate the properties of human anatomical structures *in vitro* or *in vivo*, models of such structures are used instead. The review of relevant literature has shown the dominance of finite element method and finite difference method for biomechanical and some other (for example, thermal) models. However, other methods (for example, electrical models of blood vessels) are also used.

The anatomical and pathological structures of eye fundus that are being analysed in the eye fundus images generally include blood vessels, optic disc and excavation, macula and fovea, and various eye fundus defects (haemorrhages, exudates, drusen, cotton wool spots etc.). In most cases various digital filters and machine learning methods are used to detect those objects.

There are several databases of eye fundus images. Probably the most popular of them is the DRIVE database, which includes 40 eye fundus images with blood vessels marked manually. A sample record from this database is shown in Fig. 2.





**Fig. 2.** Sample record from DRIVE database: eye fundus image (a), eye fundus mask (b), blood vessel mask (c)

Tortuosity of retinal blood vessels is one of the most commonly used parameters describing eye fundus objects. However, there are many different estimates of tortuosity, including arc-chord ratio, estimate based on the integral of module of curvature, hysteresis-based estimate, estimate based on the integral of the square of the derivative of curvature, etc.

## 2. BIOMECHANICAL MODELLING OF BLOOD VESSELS

Dependencies between blood pressure and the tortuosity of blood vessel have been investigated using a finite element model.

Several models have been tried. In one case, the blood vessel was modelled by a cylinder in a rectangular box. The modelled vessel was made asymmetric by adding a round defect. Blood pressure was modelled by pressuring the inside surface of the cylinder. The central line of the deformed blood vessel was generated by dividing the outer surface of blood vessel into 50 slices, approximating each of them by circles and taking the line connecting their centres. The diameter of the blood vessel was approximated by the diameters of those circles.

Four of the tortuosity estimates were compared. It has been found that all of them tend to increase as the pressure increases. The estimate based on the integral of module of curvature tends to increase linearly while the arc-chord ratio, hysteresis-based estimate and estimate based on the integral of square of derivative of curvature tend to increase quadratically. It has also been observed that the estimate based on the integral of module of curvature tends to be inversely proportional to the Young's modulus of the blood vessel while the other estimates tend to be inversely proportional to the square of the Young's modulus.

Another finite element model was created with intent of validating the results experimentally. In this case the blood vessel was modelled by a

cylinder made asymmetric by having one side thicker than the other. The central line and diameters were extracted as in the previously described model.

At first this model was validated using a symmetrical silicone tube. It has been confirmed that, as predicted by the finite element model, the diameter of the tube tended to increase linearly as the pressure increases. Thus an asymmetrical latex tube has been manufactured. The experiment using the latex tube has confirmed that the estimate based on the integral of module of curvature tends to increase linearly with increase of the pressure while the other estimates tend to increase quadratically, meaning that it is not necessary to take account of the hyper-elasticity of the blood vessel wall or latex to find the dependencies between mechanical parameters and tortuosity estimates.

Further, it has been checked if it is possible to utilise the dependencies between mechanical parameters and tortuosity to estimate the mechanical parameters from the shape of the deformed blood vessel in simplified conditions. It has been found that it is possible to estimate the ratio between pressure and Young's modulus as long as other parameters stay constant and no non-mechanical changes of the blood vessel shape occur.

### **3. DETECTION AND PARAMETERISATION OF BLOOD VESSELS**

Most existing blood vessel detection methods only utilise green component of RGB, with some utilising luminance, although research to support this preference was never exhaustive. Thus it has been decided to investigate the suitability of other colour space components and their linear combinations.

At first components of commonly used colour spaces (RGB, YIQ, HSV, HSL and XYZ) were investigated. Colour space components were compared according to the area under the ROC curve using different thresholds on the image (images from the training set of the DRIVE database were used) in the given colour space component to classify the pixels. The images of the training set of the DRIVE database were used for this comparison.

It has been confirmed that green component of RGB is one of the most suitable for blood vessel detection, but some of other colour space components (for example, H of HSV or difference between G and B of RGB) should also be considered.

It has also been found that the pixels with the highest difference between R and G components of RGB in an image, filtered with an averaging filter (window size 3x3 px), belong to the blood vessels with a very high probability (every single of such pixels for all but two images of training set

of the DRIVE database belonged to a blood vessel, while at least one half of such pixels in each of the remaining images also belonged to a blood vessel).

As the investigation has shown significant differences between components of different colour combinations, an effort was made to find a linear combination of RGB components that would be ideal for blood vessel detection.

As previously, the ROC curves for classification of pixels of training set of the DRIVE database were used to compare the colour combinations. Three different variants of combining those classifications were used. In one case areas under the ROC curve were calculated for each image and the average area was taken as the goal function (“global” classification). In the second case the images were divided into square regions (40x40 px), the areas under the ROC curves calculated for the regions including at least five blood vessel pixels and at least five pixels that do not belong to the blood vessels (“local” classification). In the third case all images were combined (“super-global” classification). The colour combinations found in each case are given in Table 1).

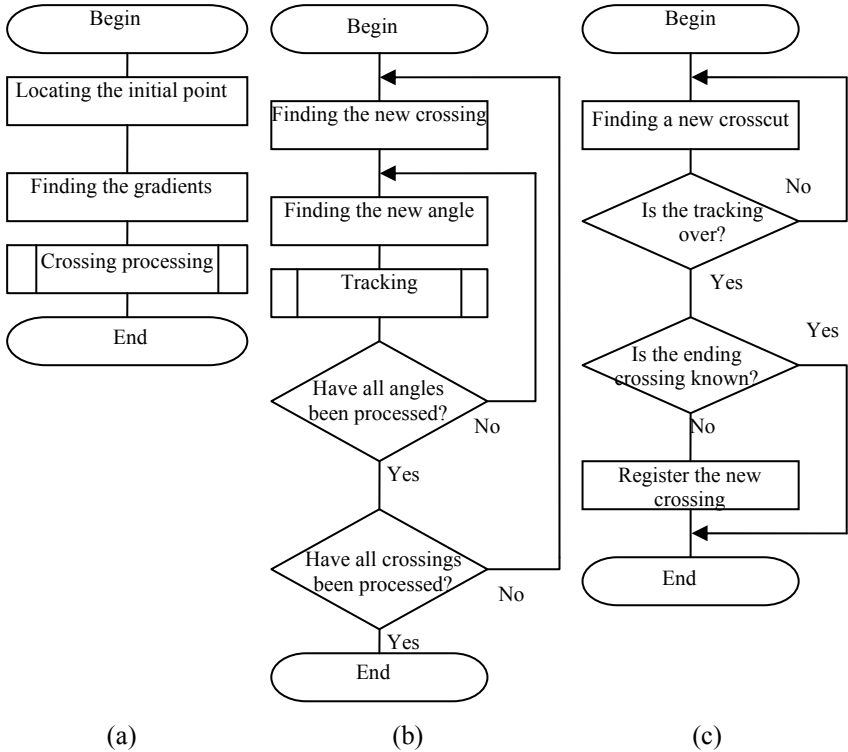
**Table 1.** Colour combinations optimised for blood vessel detection

Colour combination	Coefficients for colour intensities			Average area under the ROC curve
	Red	Green	Blue	
„Global“	-0.1053	0.5265	-0.3682	0,7503
„Local“	-0.0512	0.7565	-0.1923	0,8375
„Super-global“	-0.0085	0.4685	-0.4458	0,6606

It can be seen that the green component of RGB dominates in all the colour combinations, while the “super-global” combination is very similar to the difference between green and blue components of RGB.

The optimised colour combinations were tested with two existing blood vessel detection methods that used the green component of RGB. The green channel of the images of the testing set of the DRIVE database were replaced with the optimised colour combinations and then the blood vessels were detected in the images. It has been found that the use of optimised colour combinations improved the results of one method while worsening the results of another one. Thus it seems worthwhile to create a blood vessel detection method that could take advantage of the optimised colour combinations.

In order to increase blood vessel detection performance further a new blood vessel tracking method has been developed. The initial point can be located by exploiting the fact that the pixels with the highest difference between R and G channels belong to a blood vessel with a high probability. Then the blood vessels are tracked in each direction from this point (Fig. 3). If the tracking fails, it is repeated with a higher initial step.



**Fig. 3.** Simplified flowchart of iterative blood vessel detection algorithm: main algorithm (a), crossing processing (b) and tracking (c)

During the tracking the crosscut of the blood vessel is primarily described by two edge points and a central point, while a previous crosscut is described by a central point and direction. The initial central point of the new crosscut is found by moving the previous central point to the direction associated with the previous crosscut by the expected step. The edge points are found by requiring the initial new crosscut to be perpendicular to the previous direction. The width of the crosscut is set to the expected width. The coordinates of the edge points are then rounded and the new central point is found.

The initial edge points are then moved while maximising a goal function: a new position for each edge point is found by direct search of the neighbouring pixels while assuming the position of the other edge point to be constant. The position of the other point is found afterwards. The process is stopped when direct search fails to find a new position for both points.

The goal function consists of seven multipliers, depending on the dot products of gradients and the vectors pointing towards the centre of the crosscut, difference between real step and expected step, width of the new crosscut etc.

**Table 2.** Comparison of results (sensitivity, specificity and Matthews correlation coefficient) of different blood vessel detection methods

Method	Sensitivity	Specificity	MCC
Chanwimaluang et al.	63.26%	97.20%	63.14%
Sofka and Stewart	69.77%	95.21%	60.14%
Developed method (basic variant)	63.19%	96.74%	60.76%
Chanwimaluang et al. (with blackening of eye fundus edge)	88.40%	81.99%	47.90%
Sofka and Stewart (with blackening of eye fundus edge)	66.79%	96.11%	60.95%
Developed method – basic variant (with blackening of eye fundus edge)	61.53%	97.84%	64.38%
Developed method – variant with filtering (with blackening of eye fundus edge)	57.96%	98.62%	65.64%

The blood vessel detection performance was compared using three estimates: sensitivity (number of correctly recognised “positive” cases – blood vessel pixels), specificity (number of correctly recognised “negative” cases) and Matthews correlation coefficient:

$$MCC = \frac{TP \cdot TN - FP \cdot FN}{\sqrt{(TP + FP) \cdot (TP + FN) \cdot (TN + FP) \cdot (TN + FN)}}; \quad (1)$$

here  $TP$  is number of true positives,  $TN$  – number of true negatives,  $FP$  – number of false positives,  $FN$  – number of false negatives.

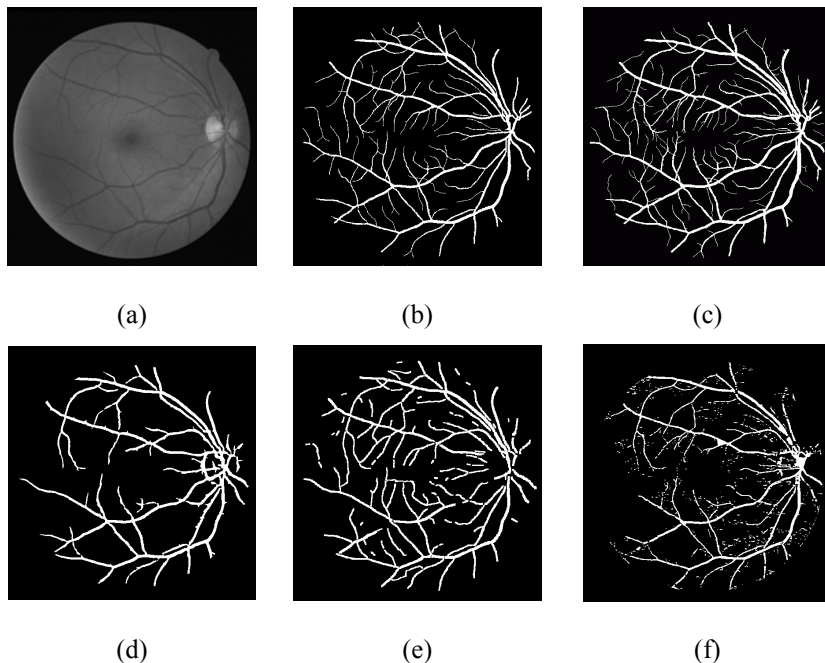
The blood vessel detection performance achieved by this method has been found to be similar or better than the performance achieved by other existing methods (Table 2). The difference of average Matthews correlation coefficient between the best variant of the developed method and the best tried alternative method was found to be statistically significant (using t-test  $p < 0.01$ ).

The sample image processed using those methods is shown in Fig. 4.

Finally, the automatic (objective) tortuosity estimates were compared with subjective estimates by ophthalmologists. A set of 61 eye fundus images was created and three blood vessels were chosen in each image. Three ophthalmologists evaluated the tortuosity of those blood vessels for two times: without any aids and using optometric grading scale. Those estimates were compared with automatic estimates by the Spearman correlation coefficient.

It has been found that, although correlation between subjective and objective estimates tends to be lower than correlation between subjective

estimates themselves, the correlation between different subjective estimates themselves is relatively low (in two cases the Spearman correlation coefficient has been found to be lower than 0.6), while in one case the correlation between automatic estimate (based on the integral of square of derivative of curvature) and subjective estimate given by one of ophthalmologists was higher than correlation between that subjective estimate and the estimate of another ophthalmologist.



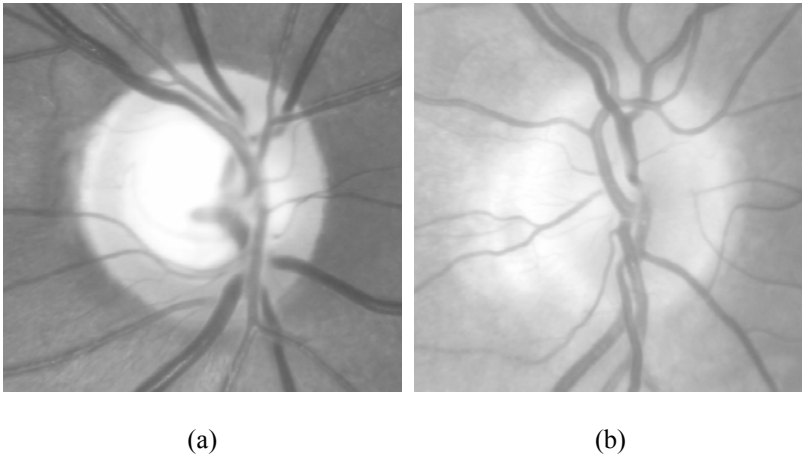
**Fig. 4.** Results of blood vessel detection using different algorithms: nineteenth eye fundus image from DRIVE database test set (a), blood vessels marked by the first expert (b), blood vessels marked by the second expert (c), blood vessels detected using the method developed by Chanwimaluang et al. (d), blood vessels detected using the method developed by Sofka and Stewart (e), blood vessels detected using the developed method (f)

Thus it can be considered that the level of agreement between objective and subjective estimates is acceptable. It also means that the proposed blood vessel tracking method can track the blood vessels sufficiently well to evaluate their tortuosity using the automatic estimates.

#### 4. EVALUATION OF CLARITY OF OPTIC DISC MARGINS

Optic disc margins are known to become blurred when intracranial pressure increases (for example, in papilledema and neuritis). Thus two estimates optic disc margin clarity were developed.

The set consisting of 128 eye fundus images with ellipses approximating boundary of optic disc marked by an ophthalmologist was used to evaluate the estimates. Two ophthalmologists classified those images into two groups – “clear margin” (50 images) and “blurred margin” (45 images). 33 images (about 26%) were judged to be of bad quality, or the experts could not agree on the estimate. Two examples of such images are shown in Fig. 5.



**Fig. 5.** A fragment of an image with a druse (a), the same fragment after the preprocessing (b), the relationship  $S=S(V)$  (c) and the detected area of a druse (d)

The first automatic estimate was contrast-based. It was considered that one possible description of “local” clarity can be described by the directional derivative of colour intensity. In such case the clarity of margin on the ray  $L$  can be considered to be

$$B = \int_L I'(x, y) dl = \int_a^b I'(r) dr = I(b) - I(a); \quad (2)$$

here  $I(x, y)$  is the colour intensity at point  $(x; y)$ . However, such an estimate would have very low resistance to noise. Thus the single intensities  $I(a)$  and  $I(b)$  were replaced by average intensities along the segments of the ray. The clarity of the whole margin would be described by average of such clarity estimates along the different rays.

To make comparisons between different images possible, the clarity estimate had to be normalised. It is possible to use normalisation analogous to the one used in Michelson contrast

$$B_{Mich} = \frac{I(b) - I(a)}{I(b) + I(a)}, \quad (3)$$

or the one analogous to the one used in the Weber contrast – either

$$B_{Web} = \frac{I(b) - I(a)}{I(a)}, \quad (4)$$

or

$$B_{Web} = \frac{I(b) - I(a)}{I(b)}. \quad (5)$$

Different lengths and positions of the segments of the rays that describe the inside and outside areas were compared, as well as different RGB components. The largest area under the ROC curve (0.6773) resulted from the use of red component of RGB with the segments of rays with one end being 15 px away from the margin itself and with another one being 25 px away from the margin.

The second automatic estimate was expected to take advantage of the fact that the filtered (de-noised) image is blurred. Thus, in case of clear margins the filtered image can be expected to be more different from the original one than in case of blurred margins. So, the estimate of blurriness can be calculated as an average squared difference between filtered and original pixels in the zone near the optic disc margin:

$$B = \frac{1}{|M|} \sum_{(i,j) \in M} (I(i,j) - I_F(i,j))^2; \quad (6)$$

here  $I$  is the original image,  $I_F$  – the filtered image and  $M$  – the zone near the optic disc margin.

The best results (area under the ROC curve – 0.7316) have been achieved using averaging filter (window size 20x20) to filter R component of RGB in the ring that is 31 px wide.

## 5. DRUSEN DETECTION IN EYE FUNDUS IMAGES

A set of 20 eye fundus images (size of each image – 3072x2048 px) was used for drusen detection research. For each image drusen have been marked by an expert ophthalmologist.

At first, optimised colour combinations (“global” and “local”) were found using the method analogous to the one used for blood vessel detection.

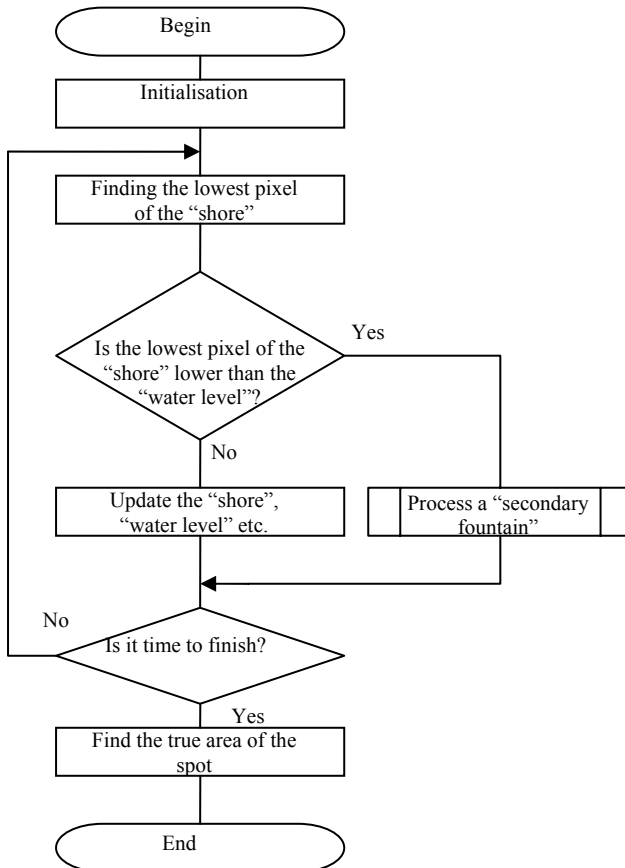


Then the drusen detection method utilising those colour combinations was created.

Drusen detection method consisted of three parts:

1. Starting point generation.
2. Druse area detection around each starting point.
3. Rejection of obvious false positives.

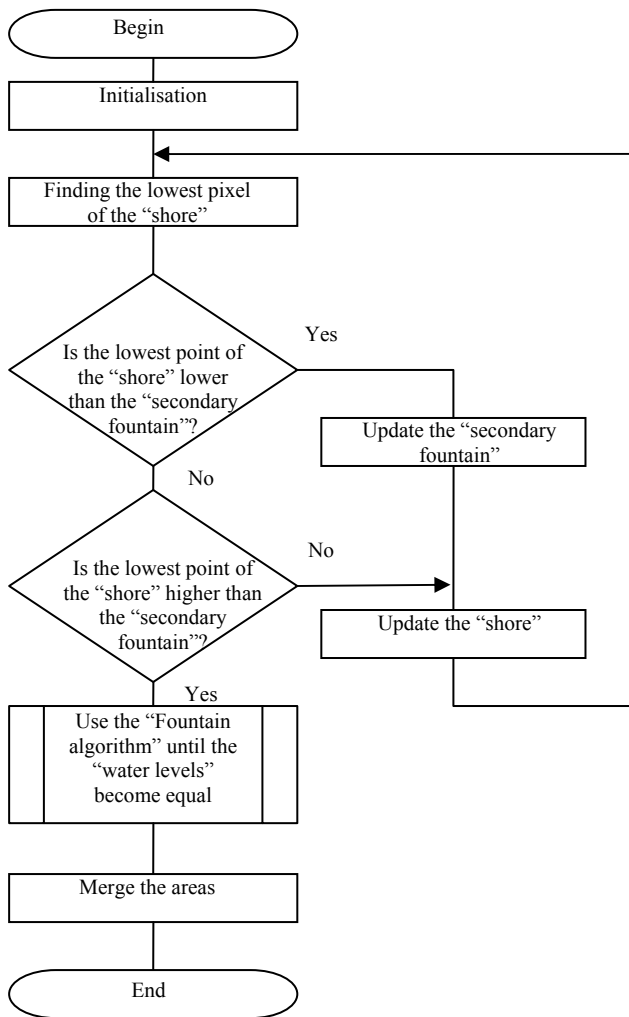
Starting points can be generated by finding local maximums of Laplacian of “global” colour combination.



**Fig. 6.** Simplified flowchart of “Fountain” algorithm

Druse area was found using “Fountain” algorithm (Fig. 6). The image is filtered using Wiener filter with 5x5 window. At first, a rectangular area around the starting point is cut. Then the potential area of the druse is found

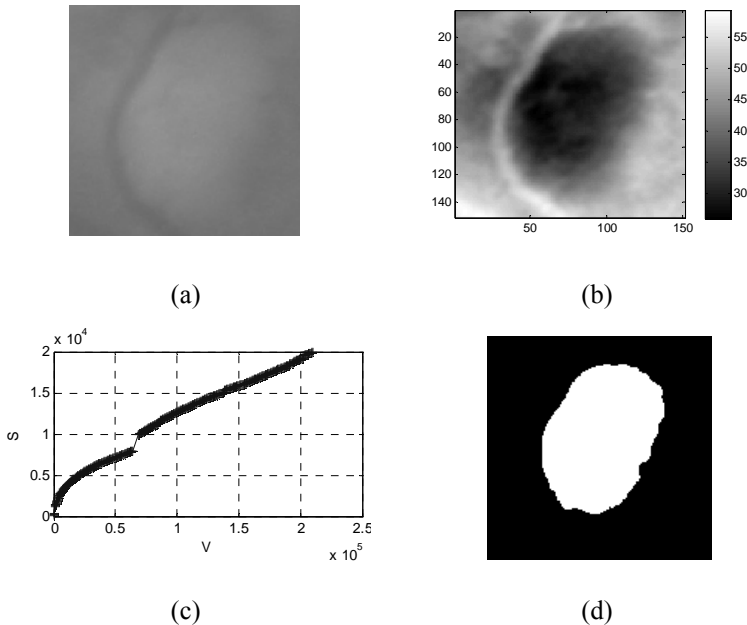
using the “Fountain algorithm”. This algorithm simulates the flooding of an area with uneven terrain (in our case – inverted image in the “local” colour combination). It seems reasonable to use such an analogy, as the profile of a druse looks like a hill, or an inverted pit.



**Fig. 7.** Simplified flowchart of “Fountain” algorithm: processing of the “secondary fountain”

The algorithm initialises with the starting point (“a fountain”), the value of a pixel at the starting point (“water level”), the starting pixel (“flooded area”) and its 8-neighborhood (“shore”). Then at each iteration the algorithm finds the “shore” pixel with the minimal value and checks if this value is lower than the current “water level”. If this value is not lower, the “water level” is increased to the value of that pixel, the pixels of “shore” with values equal to the new “water level” are added to the “flooded area” and the “shore” is updated. If the minimal value is lower than the “water level”, a new (secondary) “fountain” is initiated (Fig. 7).

The 8-neighbourhood of that pixel is searched for the pixel with the lowest value (that becomes the candidate for “secondary fountain”). If this value is lower or equal than the one of original pixel, the new pixel is added to the “local flooded area” and if it is lower, it becomes the new candidate “secondary fountain”. The process is repeated until all pixels in the 8-neighbourhood of the “local flooded area” have values higher than the candidate “secondary fountain”. The candidate “secondary fountain” then becomes the “secondary fountain” and is processed like the original “fountain” until the associated “water level” becomes equal to the one of the original “flooded area”. The “flooded areas” are then merged.



**Fig. 8.** A fragment of an image with a druse (a), the same fragment after the preprocessing (b), the relationship  $S=S(V)$  (c) and the detected area of a druse (d)

This process results in a series of “flooded areas”, each corresponding to some “water level” ( $h$ ). Thus it is necessary to find out which of them corresponds to the correct area of the druse. Analysis of the relationship between area ( $S$ ) and volume ( $V$ ) has shown that at the point of “overflow” a small increase of the “volume” results in a high increase of “flooded area”. An example of a processed druse can be seen in Fig. 8.

Finally, some of the areas that are unlikely to be drusen are found. Areas, the convex hull of which includes more than one percent of pixels that do not belong to the area, are rejected.

Subsequently the developed druse detection method was combined with watershed transform based method. The druse area is estimated using both methods and the larger area is chosen (exploiting the fact that the watershed transform tends to underestimate the blob area). In this case average sensitivity of 43.69%, specificity of 99.70% and the Matthews correlation coefficient of 45.73% has been achieved. The average of the Matthews correlation coefficient has been found to be statistically significantly higher than the corresponding average for other evaluated methods.

## CONCLUSIONS

1. A biomechanical finite element model of a blood vessel has been developed and experimentally validated. It has been used to find the relationships between blood pressure and various blood vessel tortuosity estimates. It has been found that the estimate based on the integral of module of curvature tends to increase linearly as blood pressure increases, while arc-chord ratio, estimate proposed by the scientists of Padua and estimates based on the integral of square of curvature and the integral of square of derivative of curvature tend to increase quadratically. That suggests a conjecture that analogous trends can be expected to hold in case of actual retinal blood vessels (especially venules). Such conjecture is supported by structure of retinal blood vessels (retinal venules have no or a very limited amount of muscles) and the view (dominating in medicine) that the increase of blood vessel tortuosity (especially the tortuosity of venules) is related to increase of blood pressure (this view is also supported by results of experiments similar to the one used in this work). However, those trends should be checked additionally in a longitudinal clinical trial.
2. Colour combinations emphasising the blood vessels in eye fundus images have been found. It was found that those pixels of eye fundus images filtered by averaging filter that have maximal difference between red and green RGB component belong to a blood vessel with a high probability: in 90% of images of the DRIVE base training set all

such pixels belonged to the blood vessels while in the testing set and STARE base that was the case with 85% of images.

3. A blood vessel tracking algorithm that starts the tracking from a single automatically located point has been created. It has been found that it can achieve the quality of blood vessel detection (the average Matthews correlation coefficient – 65.64%) statistically significantly (using t-test  $p < 0.01$ ) superior to the one achieved using other existing algorithms. It has also been found that the estimates given by automated tortuosity evaluation method based on the integral of derivative of curvature are sufficiently similar to the estimates given by the ophthalmologists: in one case correlation between two estimates given by ophthalmologists was lower than between an automated and ophthalmologist's estimates. In turn, that indicates that the developed blood vessel detection method is sufficiently suitable for blood vessel tortuosity estimation.
4. Two methods to evaluate the clarity of optic disc margin (one contrast based method and one filtering based method) have been created. It has been found that the filtering-based method can achieve results that are closer to the ophthalmologist estimates (area under the ROC curve – 0.7316) than the results by contrast-based method (area under the ROC curve – 0.6773). R of RGB was found to be the most suitable for the optic disc clarity estimation of all tried colour space components. The reliability of the results could be improved by performing analogous trial with a larger data set. It also seems to be worth to investigate the relationships between those estimates and intracranial pressure.
5. Optimised colour combinations emphasising the drusen have been found. It has been found that the green component of RGB has the highest weight in them.
6. A new drusen detection algorithm has been proposed. It has been found that the quality achieved by this algorithm (the average Matthews correlation coefficient 0.4573) is statistically significantly (using t-test  $p < 0.02$ ) higher than the quality achieved by other existing algorithms. It is recommended to use this method semi-automatically to increase the accuracy of estimates of area of the drusen (used to estimate the level of age-related macular degeneration).

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Martynas Patašius was born in 1982.

In 2000 he graduated from the Kaunas “Dainava” secondary school.

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Since September of 2010 he works as a lecturer in Department of system analysis of Faculty of Informatics of Kaunas University of Technology.

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## **REZIUMĖ**

### **Darbo aktualumas**

Akies dugnas – akies dalis, matoma per vyzdį. Ji gali būti nesudėtingai, pigiai ir neinvaziškai stebima ir fotografuojama. Gauti akies dugno vaizdai naudojami įvairių akies ir sisteminių ligų diagnostikai. Neinvaziškumo svarba yra pabrėžiama, pavyzdžiui, Europos Sąjungos Framework 7 programoje.

Akies dugnas – kone vienintelė žmogaus organizmo vieta, kur galima tiesiogiai stebėti mažas kraujagysles. Dėl to akies dugno vaizdai naudojami kraujagysles pažeidžiančių sisteminių ligų (arterinės hipertenzijos, aterosklerozės, cukrinio diabeto, jų komplikacijų ir pan.) diagnozei ir sekimui.

Regos nervo disko (tai vieta, per kurią regos nervas patenka į akį) pakitimai taipogi padeda diagnozuoti ir sekti ne tik akių ligas (pavyzdžiui, glaukomą, kuri, Pasaulio sveikatos organizacijos duomenimis, yra antra pagrindinė aklumo priežastis pasaulio mastu ir daugelyje regionų), bet ir kai kuriuos galvos smegenų ir visos nervų sistemos pokyčius (pavyzdžiui, intrakranalinio slėgio padidėjimą).

Be to, pagal akies dugno pokyčius diagnozuojamos ir kitos akių ligos, pavyzdžiui, amžinė makulos degeneracija, kuri, Pasaulio sveikatos organizacijos duomenimis, yra pagrindinė aklumo priežastis išsivysčiusiose šalyse ir trečia pagrindinė visame pasaulyje.

Siekiant kuo anksčiau nustatyti šias ligas naudojami masiniai sveikatos patikrinimai. Tačiau tokie sveikatos patikrinimai neretai atitraukia nuo darbo daug aukštos kvalifikacijos oftalmologų. Dėl to didelis dėmesys skiriamas automatinei akies dugno vaizdų analizei, kuri leistų greitai atlikti masinius periodinius sveikatos patikrinimus neatitraukiant aukštos kvalifikacijos oftalmologų nuo darbo.

Šiame darbe nagrinėjamas kraujagyslių radimas akies dugno vaizduose, ypač su tikslu įvertinti kraujagyslių vingiuotumą (pagal kurį diagnozuojamos tokios ligos kaip hipertenzinė retinopatija, diabetinė retinopatija ar neišnešiojimo retinopatija) pagal įverčius, kurių interpretacijai palengvinti naudoti kraujagyslių modeliai. Taip pat nagrinėjamas regos nervo disko ribos aiškumo, pagal kurį galima neinvaziškai nustatyti intrakranalinio slėgio padidėjimą, įvertinimas ir drūzų – pagrindinio amžinės makulos degeneracijos simptomo – radimas.

### **Darbo objektas**

Akies dugno vaizdų anatominių struktūrų modeliai ir šių struktūrų radimo ir parametrizavimo algoritmai.

## **Darbo tikslas**

Darbo tikslas – sukurti vaizdų apdorojimo algoritmus, kuriuos būtų galima pritaikyti akies dugno vaizdų parametrizavimui palengvinant diagnostiką.

## **Darbo uždaviniai**

Darbo tikslui pasiekti buvo iškelti tokie uždaviniai:

1. Sukurti ir eksperimentiškai patikrinti biomechaninį kraujagyslės modelį baigtiniais elementais. Juo naudojantis rasti įvairių kraujagyslių vingiuotumo įverčių priklausomybes nuo kraujospūdžio.
2. Rasti spalvų rinkinius, išryškinančius kraujagysles akies dugno vaizduose.
3. Sukurti kraujagyslių radimo akies dugno vaizduose algoritmą, pradedantį trasavimą nuo vieno automatiškai rasto taško, ir patikrinti, ar jį naudojant galima pasiekti kraujagyslių radimo patikimumą, palyginamą su kitų esamų metodų pasiekiamu patikimumu.
4. Sukurti metodą, leidžiantį įvertinti regos nervo disko ribų aiškumą.
5. Sukurti metodą, leidžiantį rasti drūzas akies dugno vaizduose.

## **Mokslinis naujumas**

Naudojantis sukurtu ir eksperimentiškai patikrintu biomechaniniu kraujagyslės modeliu baigtiniais elementais, pritaikytu tirti vingiuotumo priklausomybėms nuo kraujagyslių ir kraujotakos parametrų, nustatyta, kad kreivumo modulio integralas didėja tiesiškai, didėjant slėgiui, tuo tarpu lanko-stygos santykis, kreivumo išvestinės kvadrato integralas ir Paduvos universiteto mokslininkų pasiūlytas įvertis tokiu atveju didėja kvadratiškai.

Rasti spalvų rinkiniai, išryškinantys kraujagysles akies dugno vaizduose. Nustatyta, kad filtruoto vidurkiniu filtru akies dugno vaizdo pikseliai su maksimalia raudono ir žalio RGB komponentų skirtumo reikšme priklauso kraujagyslėms su didele tikimybe. Sukurtas kraujagyslių atpažinimo akies dugno vaizduose algoritmas, pradedantis trasavimą nuo vieno automatiškai rasto taško. Įsitikinta, kad jį naudojant galima pasiekti kraujagyslių radimo patikimumą, palyginamą ir viršijantį pasiekiamą kitų išbandytų metodų.

Sukurti ir palyginti du regos nervo disko ribos aiškumo vertinimo metodai – vienas paremtas kontrastu ir, kitas – paremtas filtravimu.

Sukurtas eliptinių dėmių radimo algoritmas, kurį galima pritaikyti drūzoms rasti akies dugno vaizduose.

## **Darbo rezultatų vertė**

Darbo rezultatai pritaikyti Kauno medicinos universiteto klinikose vykdyto masinio sveikatos patikrinimo rezultatams apdoroti. Darbo rezultatai taip pat taikomi oftalmologinių vaizdų apdorojimo programinėje įrangoje, ruošiamoje pagal EUROSTARS programos projektą E!4297 NICDIT.

## **Darbo struktūra**

Disertacija susideda iš įvado, penkių pagrindinių dalių, išvadų ir literatūros sąrašo bei vieno priedo.

Pirmojoje dalyje analizuojama su disertacijos tema susijusi literatūra.

Antroje dalyje nagrinėjami kraujagyslės modeliai, sukurti siekiant nustatyti kraujagyslės vingiuotumo priklausomybes nuo kraujotakos parametrų. Joje aprašyti kraujagyslių modeliai baigtiniais elementais ir naudojantis šiais modeliais gautų išvadų eksperimentinis patikrinimas.

Trečioje dalyje nagrinėjamas kraujagyslių radimas ir parametrizavimas akies dugno vaizduose. Jame aprašyta metodika, pagal kurią rastos spalvų kombinacijos, išryškinančios kraujagysles akies dugno vaizduose, šias spalvų kombinacijas panaudojantis kraujagyslių atpažinimo metodas. Taip pat palyginti automatiškai apskaičiuoti ir gydytojų oftalmologų nustatyti vingiuotumo įverčiai.

Ketvirtoje dalyje aprašyti ir palyginti du sukurti regos nervo disko ribos aiškumo įvertinimo metodai. Taip pat pateiktos pagal trečiame skyriuje pateiktą metodiką gautos regos nervo diską išryškinančios optimizuotos spalvų kombinacijos, naudotos kai kuriuose regos nervo disko ribos aiškumo įvertinimo metodų variantuose.

Penktoje dalyje aprašytas sukurtas drūzų radimo metodas. Taip pat pateiktos pagal trečiame skyriuje pateiktą metodiką gautos drūzas išryškinančios optimizuotos spalvų kombinacijos, naudotos šiame metode.

Disertacijos apimtis – 109 puslapiai, tekste pateikti 48 paveikslai ir 16 lentelių.

## **Gynimui teikiami teiginiai**

1. Filtruoto vidurkiniu filtru akies dugno vaizdo pikseliai su maksimalia raudono ir žalio RGB komponentų skirtumo reikšme priklauso kraujagyslėms su didele tikimybe ir gali būti panaudoti kaip pradiniai taškai kraujagyslių trasavimui.
2. Naudojant kraujagyslių radimo algoritmą, pradedantį trasavimą nuo vieno automatiškai rasto taško, priklausančio kraujagyslei su didele tikimybe, galima pasiekti kraujagyslių radimo patikimumą, palyginamą su kitų esamų metodų pasiekiamu patikimumu.

3. Pasiūlytu algoritmu, randančiu drūzas akies dugno vaizduose, pasiekiamų rezultatų patikimumas viršija kitų išbandytų metodų pasiekiamą patikimumą.

## Išvados

1. Sukurtas ir eksperimentiškai patikrintas biomechaninis kraujagyslės modelis baigtiniais elementais. Juo naudojantis rastos įvairių kraujagyslių vingiuotumo įverčių priklausomybės nuo kraujospūdžio: kitoms sąlygoms nekintant, kreivumo modulio integralu pagrįstas įvertis, kylant kraujospūdžiui didėja tiesiškai, tuo tarpu lanko-stygos santykis, Paduvos universiteto mokslininkų pasiūlytas įvertis, kreivumo kvadrato integralu bei kreivumo išvestinės kvadrato integralu pagrįsti įverčiai didėja kvadratiškai. Remiantis tuo keliami hipotezė, kad analogiškai dėsningumai turėtų galioti ir akies dugno kraujagyslėms (ypač venulėms). Tokios hipotezės teisingumas laikytinas tikėtiniu atsižvelgiant į šių kraujagyslių struktūrą (akies dugno venulės iš esmės neturi raumeninio audinio) ir medicinoje dominuojantį požiūrį, pagal kurį kraujagyslių (ypač venulių) vingiuotumo padidėjimas sietinas su kraujospūdžio padidėjimu (šis požiūris remiasi ir rezultatais eksperimentų, panašių į panaudotąjį šiame darbe). Tačiau nustatytus dėsningumus tikslinga papildomai patikrinti atliekant longitudinalinį klinikinį tyrimą.
2. Rasti spalvų rinkiniai, išryškinantys kraujagysles akies dugno vaizduose. Nustatyta, kad filtruoto akies dugno vaizdo pikseliai su maksimalia raudono ir žalio RGB komponentų skirtumo reikšme priklauso kraujagyslėms su didele tikimybe: devyniasdešimtyje procentų DRIVE bazės apmokymo imties vaizdų visi tokie pikseliai priklausė kraujagyslėms; iš DRIVE bazės testavimo imties bei STARE bazės tokių vaizdų buvo 85%. Dėl to nuo šių pikselių tikslinga pradėti trasuoti kraujagysles.
3. Sukurtas kraujagyslių radimo akies dugno vaizduose algoritmas, pradedantis trasavimą nuo vieno automatiškai rasto taško. Įsitikinta, kad jį naudojant galima pasiekti kraujagyslių radimo patikimumą (vidutinis Metjuzo koreliacijos koeficientas 65,64%), statistiškai reikšmingai (naudojant t-kriterijų  $p < 0,01$ ) viršijantį kitų esamų metodų pasiekiamą patikimumą. Be to, nustatyta, kad įverčiai, gauti naudojant automatinį vingiuotumo įvertinimo metodą, paremtą kreivumo išvestinės kvadrato integralu, yra pakankamai panašūs į oftalmologų pateikiamus įverčius: vienu atveju koreliacija tarp dviejų oftalmologų įverčių buvo silpnesnė negu tarp oftalmologo įverčio ir automatinio įverčio. Savo ruožtu, tai reiškia, kad sukurtasis

- kraujagyslių radimo metodas pakankamai gerai išskiria kraujagysles, kad jų vingiuotumą būtų galima įvertinti automatiniais įverčiais.
4. Sukurti du regos nervo disko ribų aiškumą vertinantys metodai – vienas paremtas kontrastu ir vienas paremtas filtravimu. Nustatyta, kad filtravimu paremtu metodu galima gauti rezultatus, kurie labiau atitinka gydytojų pateiktus įverčius (plotas po ROC kreive – 0,73), negu gauti kontrastu paremtu metodu (plotas po ROC kreive – 0,68). Iš išbandytų spalvų erdvių komponentų ir jų kombinacijų regos nervo disko ribos aiškumui vertinti labiausiai tinka R komponentas iš RGB spalvų erdvės. Regos nervo diską išryškinančios spalvų kombinacijos nepagerino regos nervo disko ribos aiškumo nustatymo rezultatų. Siekiant padidinti rezultatų patikimumą, prieš klinikinius taikymus analogiškus tyrimus gali būti tikslinga atlikti su didesniu duomenų kiekiu. Taip pat tikslinga panagrinėti šių įverčių ryšį su intrakranaliniu slėgiu.
  5. Rastos drūzas išryškinančios spalvų kombinacijos. Nustatyta, kad didžiausią svorį jose turi žalias RGB komponentas.
  6. Sukurtas naujas algoritmas, atpažįstantis drūzas akies dugno vaizduose, kurio rezultatai yra statistiškai reikšmingai (naudojant t-kriterijų  $p < 0,02$ ) artimesni gydytojų pateiktiems (vidutinis Metjuzo koreliacijos koeficientas 45,73%) nei gauti kitais išbandytais metodais. Tokį metodą tikslinga naudoti kaip pusiau automatinį, siekiant padidinti drūzų ploto įverčių (naudojamų amžinės makulos degeneracijos progresavimo įvertinimui) tikslumą.

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