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Research Article

An Objective Approach in Diagnosis of Retinopathy of Prematurity Stages

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Abstract

Objective: To develop the concept of a universal diagnostic platform that will reduce the risk of subjectivity in diagnosis and treatment choice for ROP, DME, DARP, AMD, RVO and glaucoma and will allow to achieve objective nosology's data and targeted reasonable investment of health care resources.

Materials and Methods: 1278 retinal images and 77 OCT results of 412 patients were analyzed. 5 clinical group with subgroups were created: 1- ROP (n = 272), 2- Diabetic retinopathy (n = 120), 3- CRVO (n = 6), 4- AMD (n = 4), 5- Control (n = 10). A concept of an information platform was developed to exclude subjectivity in the interpretation and to automatize the multifactorial image analysis in the diagnosis of social valuable diseases of the retina and optic nerve. The platform works by analyzing 3D and 4D images, anamnesis data and laboratory tests by CNN.

Results and Discussion: Statistically valuable difference (Mann-Whitney U test) was indicated between Df in immature retina group (1,27 ± 0,01) and all stages of ROP (1 stage - 1,32 ± 0,02; 2 stage 1,4 ± 0,06; 3 stage 1,450 ± ,02; 4 stage 1,55 ± 0,01). In DARP groups $p < 0,05$ was only in groups with proliferate (1,52 ± 0,04) and terminal (1,43 ± 0,04) stages relatively to patients with normal retina (1,55 ± 0,04). A concept of an information platform was developed to exclude subjectivity in the interpretation and to automatize the multifactorial image analysis in the diagnosis of social valuable diseases of the retina and optic nerve. Platform modules for a wide-field fundus image modeling of infants, localization of the macula as a mark for morphometry and isolation of the vascular network using deep convolutional neural networks have been developed.

Keywords: Retina Images; Fractal Analysis; Complexity of Vascular System; Retinopathy of Prematurity; Diabetic Macular Edema; Diabetic Angioretinopathy; Retinal Vein Occlusion; Glaucoma

Abbreviations

Df: Fractal Dimension; OCT: Optical Coherence Tomography; FAG: Fluorescein Angiography; AMD: Age-Related Macular Degeneration; CRVO: Central Retinal Vein Occlusion; ROP: Retinopathy of Prematurity; Tm: The Index of Traction; CNNs: Convolutional Neural Networks; CNV: Choroidal Neovascularization; OCT-A: Optical Coherence Tomography-Angiography

Introduction

The 20th century is the age of ownership, the model of the 21st century is an access to information - the age of platforms. Medical imaging is a necessary component of the development of artificial intelligence in ophthalmology. In this area, convolutional neural networks (CNNs) are mainly used for three kinds of actions: classification, detection and segmentation [1]. They are suitable for solving problems which haven't got a specific mathematical solu-

tion, for example, identifying pathological changes in the retina. CNN has been already created to diagnose glaucoma by the ratio of excavation to area of the optic nerve head (optic nerve disc) and to determine a plus-disease stage in the diagnosis of retinopathy of prematurity (ROP) [2,3]. Despite the extensive capabilities of the CNN, there is a problem of detecting several objects as one, due to the size and shape similarity. This problem was solved by creating 3D images where objects have more spatial characteristics. Also, the 4D imaging technique has proven itself in cardiology. 4D flow data can provide visualization of complex hemodynamic patterns of blood flow [4]. A new direction in the diagnosis of age-related macular degeneration (AMD) is focused not on the analysis of retinal thickness, but on the activity of choroidal neovascularization (CNV), which fully corresponds to the complexity of the vascular system. This is the point for the appointment of anti-VEGF therapy [5]. In addition, the assessment of the parameters of the vascular network is used in the diagnosis of ROP, diabetic macular edema (DME), diabetic angioretinopathy (DARP), retinal vein occlusion (RVO), glaucoma. Now we have a lack of instruments to systematic analyzing of fundus images, optical coherence tomography - angiography (OCT-A) to reduce the risk of subjectivity in the diagnosis and choice of treatment tactics.

Materials and Methods

Clinical studies have been conducted at the Department of Ophthalmology of Voronezh N.N. Burdenko State Medical University, Voronezh, Russia. The study included 1278 retinal images and 77 OCT results. All images were divided into five groups. Group 1 - 272 (544 eyes) ROP patients divided into 5 subgroups: 1A - I stage ROP 152 (304 eyes) patients, 1B - II stage 45 (90 eyes) patients, 1C - III stage 8 (12 eyes) patients, 1D - posterior aggressive ROP 7 (14 eyes) patients, 1E - immature retina 60 (120 eyes) patients. Group 2 included 120 (148 eyes) patients with diabetic retinopathy. The patients of this group were divided into two subgroups: subgroup 2A - non-proliferative 13 (17 eyes) patients, 2B - pre-proliferative 47 (55 eyes) patients, 2C - proliferative 27 (33 eyes) patients, 2D - terminal 33 (37 eyes) patients. The third group included 6 patients with CRVO (1 retinal image, 24 OCT protocols). Group 4 consisted of 4 AMD (24 OCT protocols) patient. Group 5 included 10 healthy volunteers (16 eyes) as control.

In immature patients screening algorithm includes RetCam Shuttle video, the choosing the best pix, modeling wide-field image, which allows to identify missed the "mute" zones, the localization of the macula and to check the index of traction (Tm), the zone and extension, fractal analysis and complexity of vascular systems from stage A (creation of a preliminary capillary plexus), B (normal vascularization) to C (pathological vasculogenesis). Tm is the width-to-length attitude of ellipse which goes through center of optic nerve head and along temporal branches of a. centralis retinae.

Patients with diabetic retinopathy, CRVO, AMD underwent standard ophthalmic research, OCT, FAG, retinal image analysis, which contains fractal dimension counting (box-counting method) and complexity of vascular system ranged from A - normal vessels or microaneurysms, B - vessel tortuosity and hemorrhage to C - neovascularization. Df and complexity of vascular system were counted by zones.

A concept of an information platform was developed to exclude subjectivity in the interpretation and to automatize the multifactorial image analysis in the diagnosis of social valuable diseases of the retina and optic nerve. The platform works by analyzing 3D and 4D images, anamnesis data and laboratory studies by CNN. Stereophotogrammetry is one of the simplest and most cost-effective methods of digital 3D reconstruction. To create a 3D model from photographs, images must be shot from different angles and have anchor points. This is accomplished by moving camera around or by eye rotating. To show the dynamics of pathological processes, we propose to use a 4D technology.

Results and Discussion

On previous stages of research, the correlation between Df, complexity of vascular systems and stages of ROP and DARP was revealed [6]. Statistically valuable difference (Mann-Whitney U test) was indicated between Df in immature retina group (1,27 ± 0,01) and all stages of ROP (1 stage - 1,32 ± 0,02; 2 stage 1,4 ± 0,06; 3 stage 1,45 0 ± ,02; 4 stage 1,55 ± 0,01). In DARP groups $p < 0,05$ was only in groups with proliferate (1,52 ± 0,04) and terminal (1,43 ± 0,04) stages relatively to patients with normal retina (1,55 ± 0,04).

Considering a low sensitivity of analyzing Df and complexity of vascular system of fundus images in early stages of DARP and AMD, we suggest new algorithms of multifactorial analysis of 3D and 4D fundus, OCT, OCT-A images and other clinical data depending on

pathology (ROP, DMO, DARP, AMD, CRO, glaucoma) using CNN. (patent application No. 2010116745 dated 05/10/2020).

For the ROP the algorithm includes the localization of the macula (Patent RU2017114873A), the Tm evaluation, using stereophotogrammetry, the construction of a 3D and 4D fundus model; determination of the zone (I, II or III), length (hours) and type of pathological changes; the Df (patent RU 2672924) and complexity of vascular system evaluation. For DARP, DMO, CRO it was modeling a wide-field image from 7 images obtained from the fundus camera and, separately, from the OCT-A images; the Tm evaluation, using stereophotogrammetry, construction of 3D and 4D fundus models; the localization and type of pathological changes in the fundus, OCT, OCT-A images; Df and complexity of vascular system evaluation for created images. For AMD - construction of 3D and 4D models of the fundus and vascular network; determination of the localization and type of pathological changes on fundus and OCT and OCT-A images; the Tm and CCC evaluation for fundus and OCT-A images, configuration of CNV, establishment of the probable stage. For glaucoma, on the basis of fundus images, OCT and OCT-A images of the macula and optic nerve disc, the gray scale of the computer static perimetry protocol, a 3D image is formed and analyzed, reflecting quantitative parameters: the size of the optic disc, the width and depth of excavation, the width of the neuroretinal rim, the thickness of the nerve fibers layer, the ratio of cup to the optic disc, as well as qualitative changes: decoloration of atrophic areas of the optic disc, hemorrhages on the optic disc surface, characteristics of peripapillary atrophy. The result of the platform's work is the marked pathological sings, the probable stage and prognosis of the disease.

Platform modules for a wide-field fundus image modeling of infants, localization of the macula as a mark for morphometry, and isolation of the vascular network using deep convolutional neural networks have been developed. Automatic wide-field fundus image algorithm was adaptive filtering, due to low contrast of images and outer contour, separation of the green channel, applying a Gaussian blur filter, adaptive local histogram equalization, building a general transformation map (Figure 1).

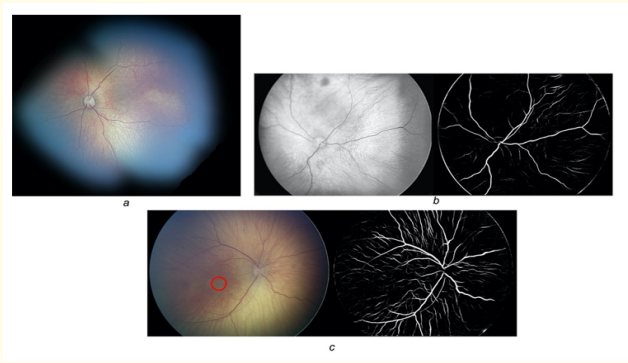

Figure 1: Diagnostic platform modules (a- wide-field fundus image modeling, b- isolation of the vascular network, c- localization of the macula).

Conclusion

The automated multifactorial analysis of 3D and 4D images will reduce the risk of subjectivity in diagnosis and choice of treatment tactics for ROP, DME, DARP, AMD, CRO and glaucoma. The use of the complexity of vascular system parameter, which was introduced for the ROP can be apply for observation of the CNV configuration in AMD in 4D model. It will allow to check the appearance of signs of its activity, and therefore accurately select the treatment plan.

Objects in 3D images, created using stereophotogrammetry, will have more distinctive characteristics for CNN recognizing. A creation of 4D images, as the reflection of changes in 3D images in time, will allow you to observe the dynamics of the pathological process.

Conflict of Interest

None.

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