

## Algorithm of Improving Image Quality, Diagnosis and Morphometry at Retinopathy of Prematurity

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**Received:** February 26, 2019; **Published:** May 23, 2019

### Abstract

**Objective:** 100000 premature infants are born per year, 70% of them are at risk, and in 37% cases is developed retinopathy of prematurity (ROP) in Russian Federation. All of them are examined in 98 perinatal centers and ophthalmological medical institutions.

**Materials and Methods:** 272 Infants examined at the department of ophthalmology at the VSMU aged 37 to 62 post-conceptual weeks, with a birthweight 500g to 2980g. The new 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, the zone and extension, the measurement of the number of bifurcations and fractal analysis of the vasculature, complexity of vascular systems from stage A (creation of a preliminary capillary plexus), B (normal vascularization) to C (pathological vasculogenesis).

**Results and Discussion:** The incidence of ROP was I stage 55.9%, II stage 16.5%, III stage 3%, plus-disease 2.6%, immaturity of the retina 22%. The worst screening quality was at the lower temporal zone in 65%. I zone is visualized fully, II zone is visible partially, III zone is not available for screening. Mean index of traction was 1.3 at I stage, 1.46 at II stage, 1.77 at III stage. The significant changes were identified 10% 12:00 - 12:10 and 6:30 - 7:00 hours, in 20% - 40% 12:10 - 1:00 and 4:30 - 6:30, in 50% - 60% 1:00 - 2:00 and 4:00 - 4:30, 70% - 90% 2:00 - 2:45 and 3:15 - 4:00, practically in 100% 2:45 - 3:15. The I zone is affected at IV and V, II zone at I, II and III stages. Fractal dimension increases from 1.4 in I stage with extension 2-3 hours to 1.67 in plus-decease and 1.78 1800 in III stage.

**Conclusion:** Developed algorithm allows to obtain new ROP screening and treatment control criteria.

**Keywords:** Retinopathy of Prematurity; Retina Images; Fractal Analysis; Fractal Dimension; Complexity of Vascular System

### Abbreviations

Df: Fractal Dimension; ROP: Retinopathy of Prematurity; Tm: The Index of Traction; FAG: Fluorescein Angiography

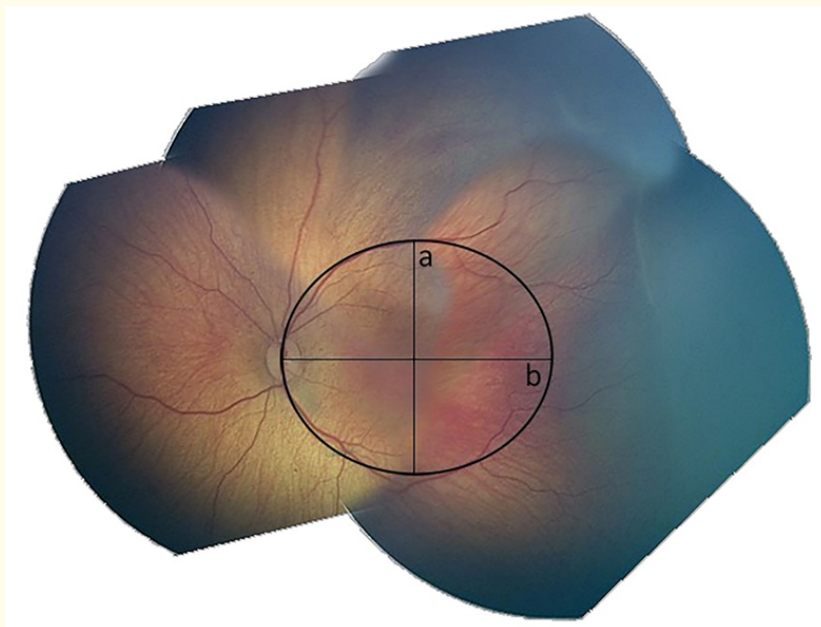
### Introduction

The deep structure of the hierarchy of blood vessels has not yet been revealed in retinal pathology. In biometric studies of plant morphology, Df has been used as an attribute to characterize the complexity of a structure by quantifying irregular and ramified processes [1]. The study of the vascular net of chicken embryos demonstrated that fractal geometry is the most appropriate method to characterize the evolution of this vascular system [2]. According to FAG Df of retinal vascular system in adults is 1.7. Mechanism of lesion of retinal vessels geometry are endothelial cell dysfunction, hypoxia and neovascularization [3]. ROP is prototype of retinal disorders involving vascular

system in adulthood with all aforementioned factors: hyperoxia leads to suppression of oxygen-regulated angiogenic growth factors, particularly erythropoietin and vascular endothelial growth factor (VEGF), which in turn causes both cessation of retinal vessel growth and loss of some existing retinal vessels, then the increasingly metabolically active yet poorly vascularized retina becomes hypoxic. Proliferation of blood vessels starts in response to hypoxia driven increases in VEGF and erythropoietin [4]. Multifactorial analysis of retinal vessels according to Df and complexity of vascular system can reduce risk of subjective evaluation of pathologic process stage.

### Materials and Methods

The clinical study included 272 (544 eyes) Infants examined at the department of ophthalmology at the Voronezh N.N. Burdenko State Medical University, Voronezh (Russia) aged 37 to 62 post-conceptual weeks, with a birthweight 500g to 2980g in period from 2013 to April 2017. 239 patients (548 eyes) were examined with time-lapse shooting, 33 patients (66 eyes) were video-recorded using the quality improvement algorithm and image analysis obtained with RetCam-Shuttle (USA). ROP patients were divided into 5 groups: 1 - I stage ROP 152 (304 eyes) patients, 2 - II stage 45 (90 eyes) patients, 3 - III stage 8 (12 eyes) patients, 4 - posterior aggressive ROP 7 (14 eyes) patients, 5 - immature retina 60 (120 eyes) patients. In patients screening algorithm includes RetCam Shuttle video, the choosing the best pix, modeling wide-field image (Adobe Photoshop) [5], which allows to identify missed the “mute” zones, the localization of the macula and to check the index of traction (Tm) [6], the zone and extension, fractal analysis of all vessels image and by zones (Figure 3) 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* (Figure 1) [7,8]. A computer program for automated RetCam images analysis by algorithm is being developed by “Altami” company (Saint-Petersburg, Russia).



**Figure 1:** The index of traction counting ( $Tm = a/b$ ).

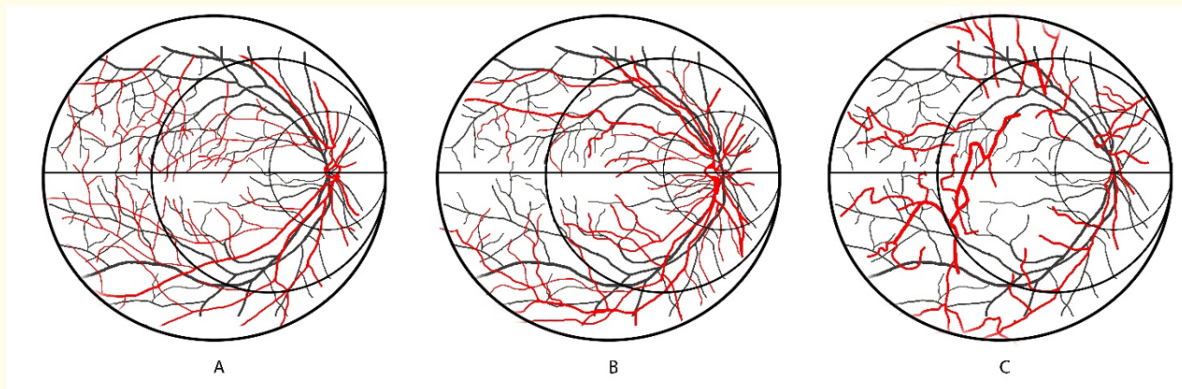


Figure 2: Types of complexity of vascular system in comparison with normal vascularization for adult patients.

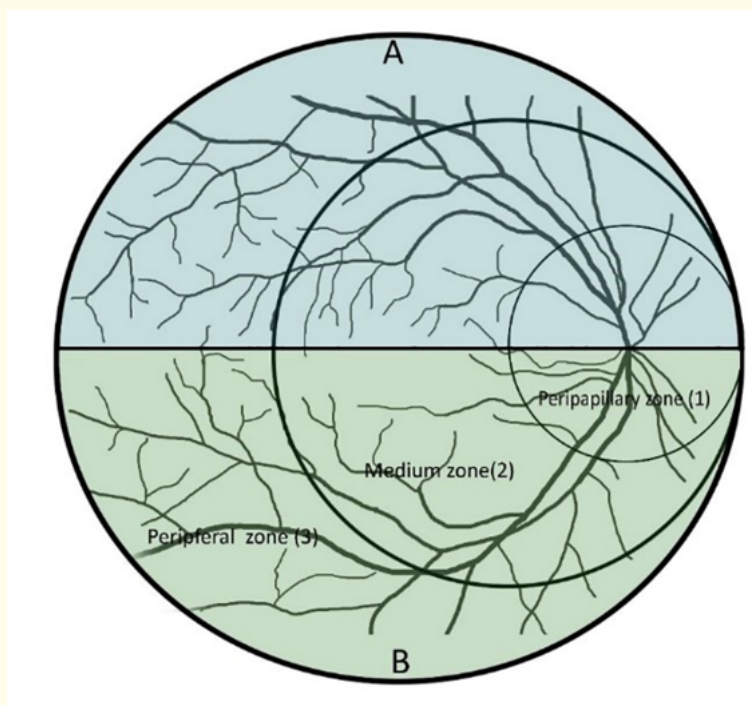


Figure 3: Analyzed retina zones.

**Results**

The study included the results of a survey of 272 children with ROP (544 eyes), average post-conceptual age at the time of the initial examination was 42,  $\sigma = \pm 4.133$  weeks, the average gestational weeks was 32,  $\sigma = \pm 2.96$  weeks, and the average body weight at birth - 1787g,  $\sigma = \pm 546.4$ g. The first clinical group contained 152 patients (304 eyes; 55,9%) - stage I ROP. In the second group there were 45 patients (90 eyes; 16,5%) with ROP II stage. The third group consisted of 8 (12 eyes, 3%) patients with ROP III. In the fourth group - 7 (14 eyes; 2,6%) patients with posterior aggressive ROP. The fifth group was 60 (120 eyes; 22%) patients with immature retina.

There are was revealed strong correlation between values of Df and stages of ROP (0,84). Df corresponds to 1.2 - 1.3 at I stage, 1.3 - 1.4 - II stage, 1.4 - 1.5 - III stage, 1.5 - 1.7 at posterior aggressive ROP. Mean Tm was from 0.95 at I stage to 0.52 at III stage. The significant changes were identified 10% 12:00 - 12:10 and 6:30 - 7:00 hours, in 20% - 40% 12:10 - 1:00 and 4:30 - 6:30, in 50% - 60% 1:00 - 2:00 and 4:00 - 4:30, 70% - 90% 2:00 - 2:45 and 3:15 - 4:00, practically in 100% 2:45 - 3:15. The I zone is affected at IV and V stages, II zone at I, II and III ROP stages. Complexity of the vascular system for I stage and immature retina was A, for II stage A-B, for III stage and posterior aggressive ROP B-C.

### Discussion

The video filming by RetCam Shuttle allowed to reduce the time of the survey and to get more informative images through self-selection, compared to time-lapse shooting. Video recording makes it possible to further model stop-frames from video by images overlaying, which allows to use a wide field images to obtain a three-dimensional view of retina.

Multifactorial analysis of vascular system allows to reduce risks of subjective evaluation of retinal changes. Has recorded significant correlation between Df or complexity of vascular system ROP stages. The Tm indicates traction process on the periphery of the retina in the temporal area even it is not registered on retinal images.

### Conclusion

The vitreoretinal pathology was studied in preterm children in the period from 2013 to April 2017. There was revealed the growth of patients with ROP in early periods of observation. The proportion of patients with ROP I was 55.9%, ROP II - 16.5%, ROP III - 3%, posterior aggressive ROP - 2.6%, and patients with immature retina - 22%.

The traction index of the macular region correlates with the intensity of fibrosis processes on the periphery of the retina in the temporal region and can be used as a marker of the severity of pathology.

According to the fractal analysis, the Df increases stage by stage from 1.3848 at stage I to 1.6622 with posterior aggressive ROP, regardless of the presence of "plus" disease, and the complexity of the vascular network. The number of bifurcations is significantly increased only with posterior aggressive ROP and "plus" disease in 1.5 - 2 times, in contrast to the typical ROP.

This study became the basis for the creation of an international unified image analysis platform "Children are waiting" funded by the Innovation Promotion Foundation (Russia). The IT platform can also be created in a laboratory, as small scale device by using the images from all perinatal centers.

### Conflict of Interest

None.

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**Volume 10 Issue 6 June 2019**

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