

## Multilateral Analysis of Retinal Vascular System

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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.

**Introduction**

Chaotic systems have strange attractors and their structure can be characterized as fractal. Fractals are shapes that are self-similar, meaning they have the same structure at every scale. 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 vascularised retina becomes hypoxic. Proliferation of blood vessels starts in response to hypoxia driven increases in VEGF and erythropoietin [4]. J. Donald M. Gass defined a terminology for neovascularization in macular diseases that is based on the anatomical location of the neovessels: type 1 - subretinal pigment epithelium, type 2 - subsensory retina choroidal neovascularization and type 3 - intraretinal vascular complex emanating from the deep capillary plexus often associated

with adjoining telangiectatic vessels [5]. 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

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 four 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 ( $T_m$ ), 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).

$T_m$  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).

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

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 - vessels tortuosity and hemorrhage to C - neovascularization. (Figure 2) Df and complexity of vascular system were counted by zones (Figure 3).

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

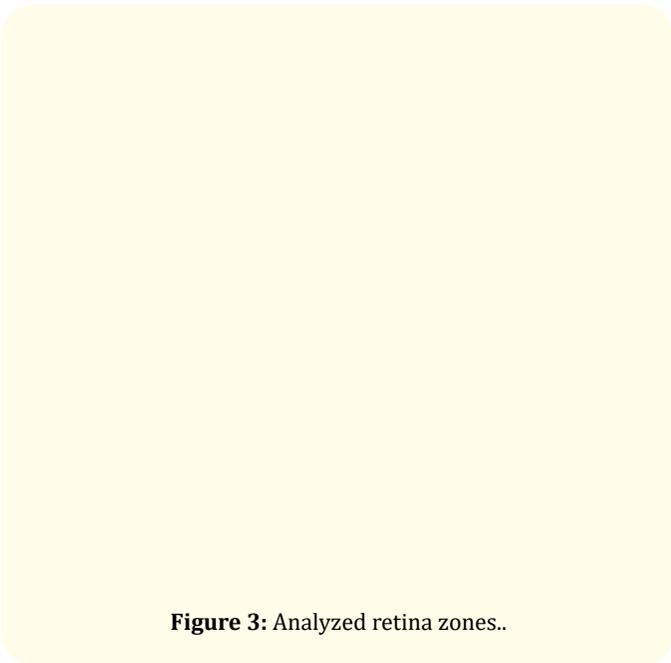


Figure 3: Analyzed retina zones..

Group	Number of patients (n=)	Average meaning of fractal dimension (Df)	Average meaning of complexity of vascular system
2.Diabetic retinopathy Subgroups:			
2A non-proliferative	13	1,57 ± 0,05*	1,2 ± 0,21**
2B pre-proliferative	47	1,54 ± 0,04	1,9 ± 0,28
2C proliferative	27	1,52 ± 0,05	1,8 ± 0,3
2D terminal	33	1,43 ± 0,03**	2,4 ± 0,24*
3. CRVO	6	1,57 ± 0,04	2,5 ± 0,11*
4. AMD	4	1,58 ± 0,05	1,1 ± 0,16**
5. Control	10	1,72 ± 0,03	1 ± 0,09

Table 1: Fractal dimension (Df) and complexity of vascular system in adults.

### Results and Discussion

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.

The study in the 4 clinical groups with a diabetic retinopathy, AMD, central retinal vein occlusion showed that Df decreased according to vessels geometry disorders, least Df values are in terminal stage of diabetic retinopathy (1,43 ± 0,03). The less irreversible changes in retina, the better vascular system organization, the higher Df values, as in non-proliferative diabetic retinopathy. The highest Df meanings in AMD (1,58 ± 0,05) can be explained by less area of vascular changes (Table 1).

The mean complexity of vascular system in CRVO was 2,5 ± 0,11. It was found to be higher than in the control group (1 ± 0,09), non-proliferative diabetic retinopathy (1,2 ± 0,21) and AMD (1,1 ± 0,16). (Table 1) Increasing values of complexity of vascular

system in late stages of diabetic retinopathy and CRVO associated with extension of impairments (hemorrhage, microaneurisms and neovascularization) (Table 1).

The results of our study revealed significant correlation between Df and stages of diabetic retinopathy (-0.6) and between complexity of vascular system and stages of diabetic retinopathy (0.6).

### Conclusion

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 and diabetic retinopathy and 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.

The irreversible impairments in retina in late stages of diabetic retinopathy and CRVO reflected in low Df values and high complexity of vascular system values. In the same time this value stays close to normal values in non-proliferative diabetic retinopathy and AMD because of smaller area of pathologic process.

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### Conflict of Interest

None.

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