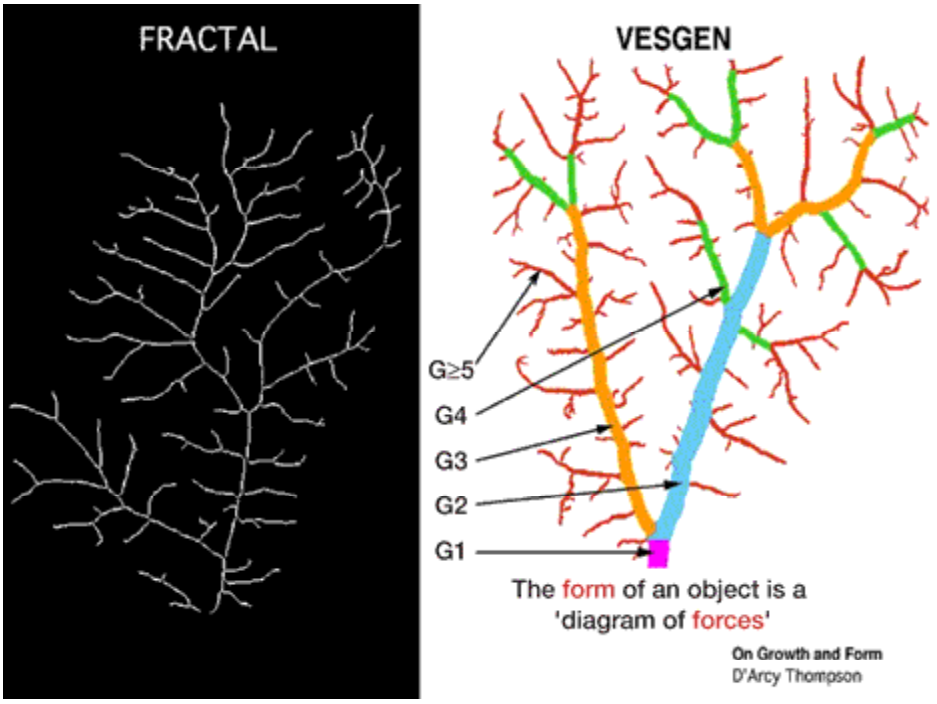
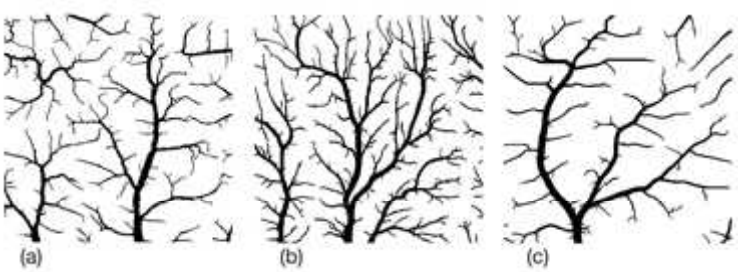
Growth and Remodeling in Blood Vessels Studied In Vivo With Fractal Analysis

Every cell in the human body must reside in close proximity to a blood vessel (within approximately 200 μm) because blood vessels provide the oxygen, metabolite, and fluid exchanges required for cellular existence. The growth and remodeling of blood vessels are required to support the normal physiology of embryonic development, reproductive biology, wound healing and adaptive remodeling to exercise, as well as abnormal tissue change in diseases such as cancer, diabetes, and coronary heart disease. Cardiovascular and hemodynamic (blood flow dynamics) alterations experienced by astronauts during long-term spaceflight, including orthostatic intolerance, fluid shifts in the body, and reduced numbers of red (erythrocyte) and white (immune) blood cells, are identified as risk factors of very high priority in the NASA task force report on risk reduction for human spaceflight, the "Critical Path Roadmap."



Growth and remodeling of blood vessels are measured with a fractal-based analysis of parameterized images, including skeletonized images (left) that also incorporates the branching generation of blood vessels (right) via the computer code VESGEN.

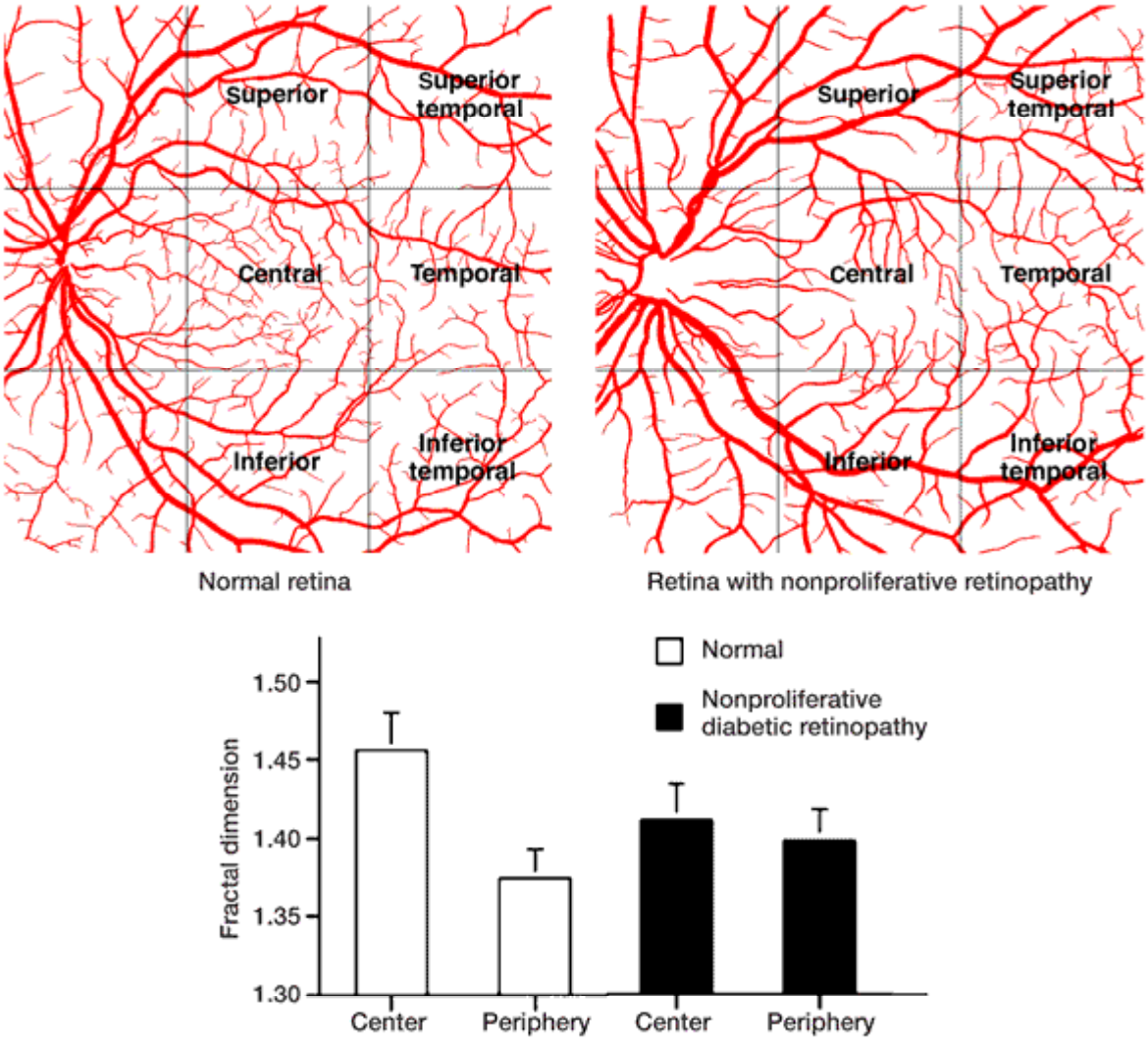


Compared with untreated blood vessels (left) in fertilized quail eggs, blood vessels were stimulated to grow (center) and inhibited from growing (right) by molecular regulators. Quail eggs are being flown as space biology experiments on the International Space Station and were orignially flown on Mir.

Mike Bronczek is imaging blood vessels in quail eggs intravitally prior to fractal-based quantification of blood vessel growth after culturing the eggs (shown on the white tray) in the new Vertebrate Cell Culture Facility at Glenn.

Blood vessels are difficult to study in the human body because the vasculature is a complex, highly branched, treelike structure embedded within three-dimensional opaque tissue. At the NASA Glenn Research Center, Patricia Parsons is using a novel in vivo model system to study vessel growth in the chorioallantoic membrane (CAM) of quail eggs (see the preceding figure and the following photograph), because the vascular tree of the CAM is two-dimensional and embedded within thin, transparent tissue (refs. 1 to 3). Modern fractal mathematics is used to measure and model the morphological stimulation

and inhibition of blood vessel growth by molecular regulators of angiogenesis (the growth of new blood vessels). In collaboration with ophthalmologists at the invitation of Carl Kupfer, M.D., former Director of the National Eye Institute at the National Institutes of Health, the fractal-based methodology for measuring blood vessel growth and remodeling was extended successfully from the quail CAM to clinical photographs of human eyes for measurement of early-stage diabetic retinopathy (see the final figure and ref. 4). Late-stage diabetic retinopathy results in blindness; eye researchers are currently searching for early-stage therapeutic and diagnostic interventions to avoid the relatively unsuccessful intervention of late-stage laser surgery. In collaboration with researchers at Glenn, the Institute for Computational Mechanics in Propulsion (ICOMP)/Ohio Aerospace Institute (OAI), the Cleveland Clinic Foundation, and elsewhere, we are currently extending these techniques to the gene-targeted expression of specific molecular regulators of vascular growth and form, and the intravital study of hemodynamics as a critical component of vascular growth and remodeling.



In clinical photographs of the human eye, fractal analysis measured the decrease of blood vessels in early-stage (nonproliferative) diabetic retinopathy (top right) compared with healthy blood vessels in the normal retina (top left).
Long description of figure 4 Two blood vessel images, showing superior, superior temporal, central, temporal, inferior, and inferior temporal locations, and a bar chart of fractal dimension of center and periphery of normal and nonproliferative diabetic retinopathy eye

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References

1. Parsons-Wingerter, P., et al.: Fibroblast Growth Factor-2 Selectively Stimulates Angiogenesis of Small Vessels in Arterial Tree. Arterioscler. Thromb. Vasc. Biol., vol. 20, no. 5, 2000, pp. 1250-1256.

2. Parsons-Wingerter P., et al.: Generational Analysis Reveals that TGF-β1 Inhibits the Rate of Angiogenesis In Vivo by Selective Decrease in the Number of New Vessels. Microvasc. Res., vol. 59, no. 2, 2000, pp. 221-232.

3. Parsons-Wingerter P., et al.: A Novel Assay of Angiogenesis in the Quail Chorioallantoic Membrane: Stimulation by bFGF and Inhibition by Angiostatin According to Fractal Dimension and Grid Intersection. Microvasc. Res., vol. 55, no. 3, 1998, pp. 201-214.

4. Avakian, Arpenik, et al.: Fractal Analysis of Region-Based Vascular Change in the Normal and Non-Proliferative Diabetic Retina. Curr. Eye Res., vol. 24, no. 4, 2002, pp. 274-280.

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Special recognition: Under P. Parsons' mentorship, NASA LERCIP undergraduate scholars Samille Jackson and Jalaine Johnson won the Best Student Team award for their research on a novel molecular regulator of angiogenesis in the quail CAM in July 2002. Ophthalmology Resident Fellow, Arpenik Avakian, M.D., Ph.D., received a Leslie W. Nesmith Lectureship Award for "Quantification of the Change in Vascular Pattern in Nonproliferative Diabetic Retinopathy," by A. Avakian, R.E. Kalina, and P. Parsons-Wingerter, at The Schepens International Society Meeting, Jackson Hole, Wyoming, June 6-9, 1999.