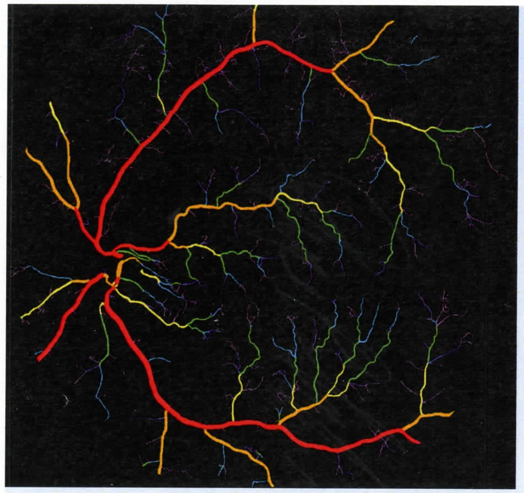
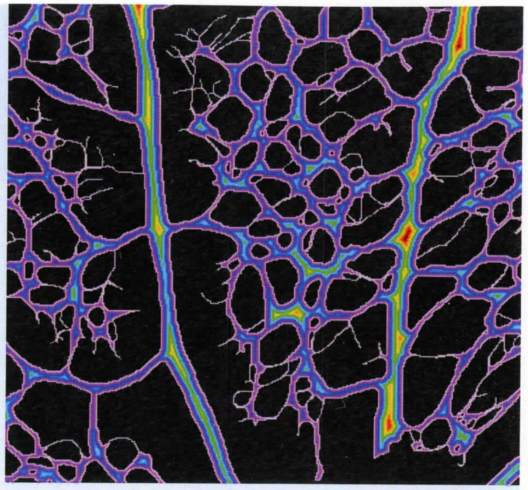
Mapping and Quantification of Vascular Branching in Plants, Animals and Humans by VESGEN Software

Humans face daunting challenges in the successful exploration and colonization of space, including adverse alterations in gravity and radiation. The Earth-determined biology of plants, animals and humans is significantly modified in such extraterrestrial environments. One physiological requirement shared by larger plants and animals with humans is a complex, highly branching vascular system that is dynamically responsive to cellular metabolism, immunological protection and specialized cellular/tissue function. VESsel GENeration (VESGEN) Analysis has been developed as a mature beta version, pre-release research software for mapping and quantification of the fractal-based complexity of vascular branching. Alterations in vascular branching pattern can provide informative read-outs of altered vascular regulation. Originally developed for biomedical applications in angiogenesis, VESGEN 2D has provided novel insights into the cytokine, transgenic and therapeutic regulation of angiogenesis, lymphangiogenesis and other microvascular remodeling phenomena. Vascular trees, networks and tree-network composites are mapped and quantified. Applications include disease progression from clinical ophthalmic images of the human retina; experimental regulation of vascular remodeling in the mouse retina; avian and mouse coronary vasculature, and other experimental models *in vivo*. We envision that altered branching in the leaves of plants studied on ISS such as *Arabidopsis thaliana* cans also be analyzed.
(Supported by NASA GRC IR&D04-54 and 2010 TTP Fund,
NIH EY-01759 & NSF Center of Excellence UWEB, University of Washington Engineered Biomaterials)



VESGEN



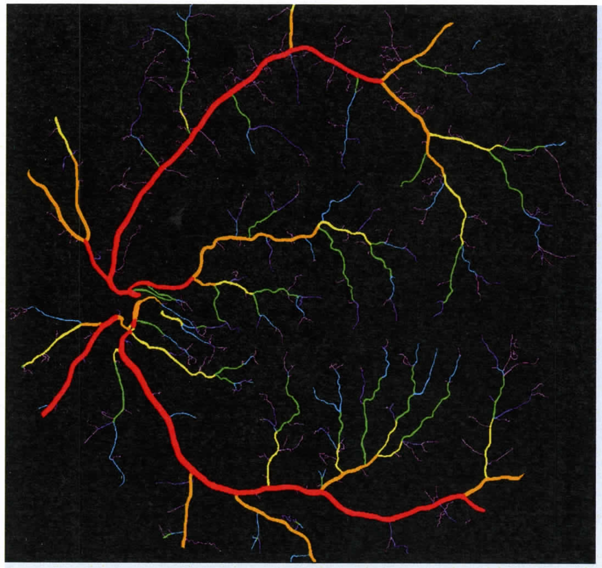
Innovative
Research Discovery Tool

Mapping and Quantification of Vascular Branching in Plants, Animals and Humans by VESGEN Software

Patricia A. Parsons-Wingerter, Mary B. Vickerman and Patricia A. Keith

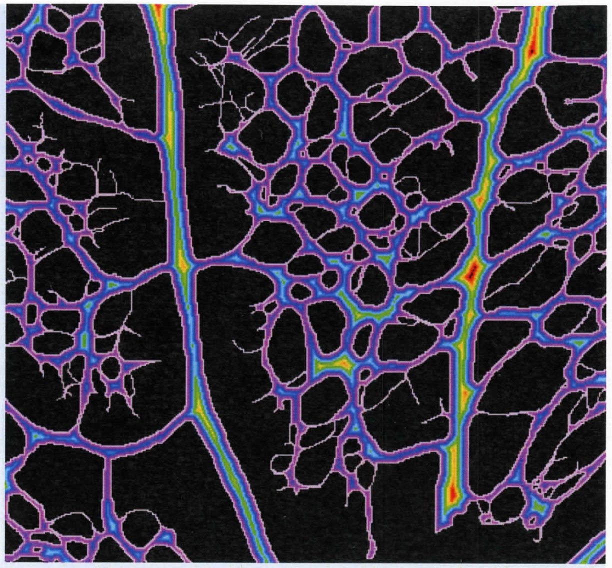
Point of Contact: Patricia Parsons-Wingerter PhD
Biomedical Research Engineer, patricia.a.parsons-wingerter@nasa.gov
216-433-8796


Vascular Alterations, Immunosuppression & Bone Loss:
NASA-defined risk categories for human space exploration
2



VESGEN 2D

APPLICATIONS



Vascular Trees

Human Retina

Avian CAM, Yolksac and Murine/Avian Coronary Vessels

Plant Leaf Venation such as in Arabidopsis thaliana?

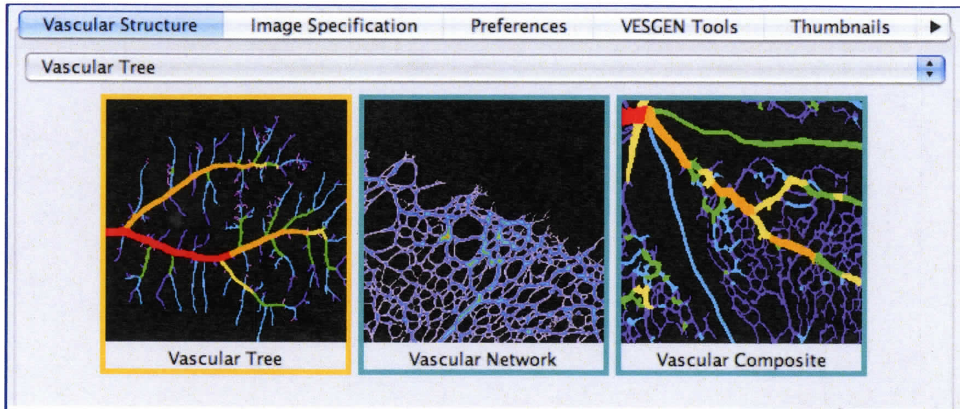
Vascular Networks

Mouse Postnatal Retina and Intestinal Inflammation

CAM Lymphatic Vessels

Vascular Tree-Network Composites

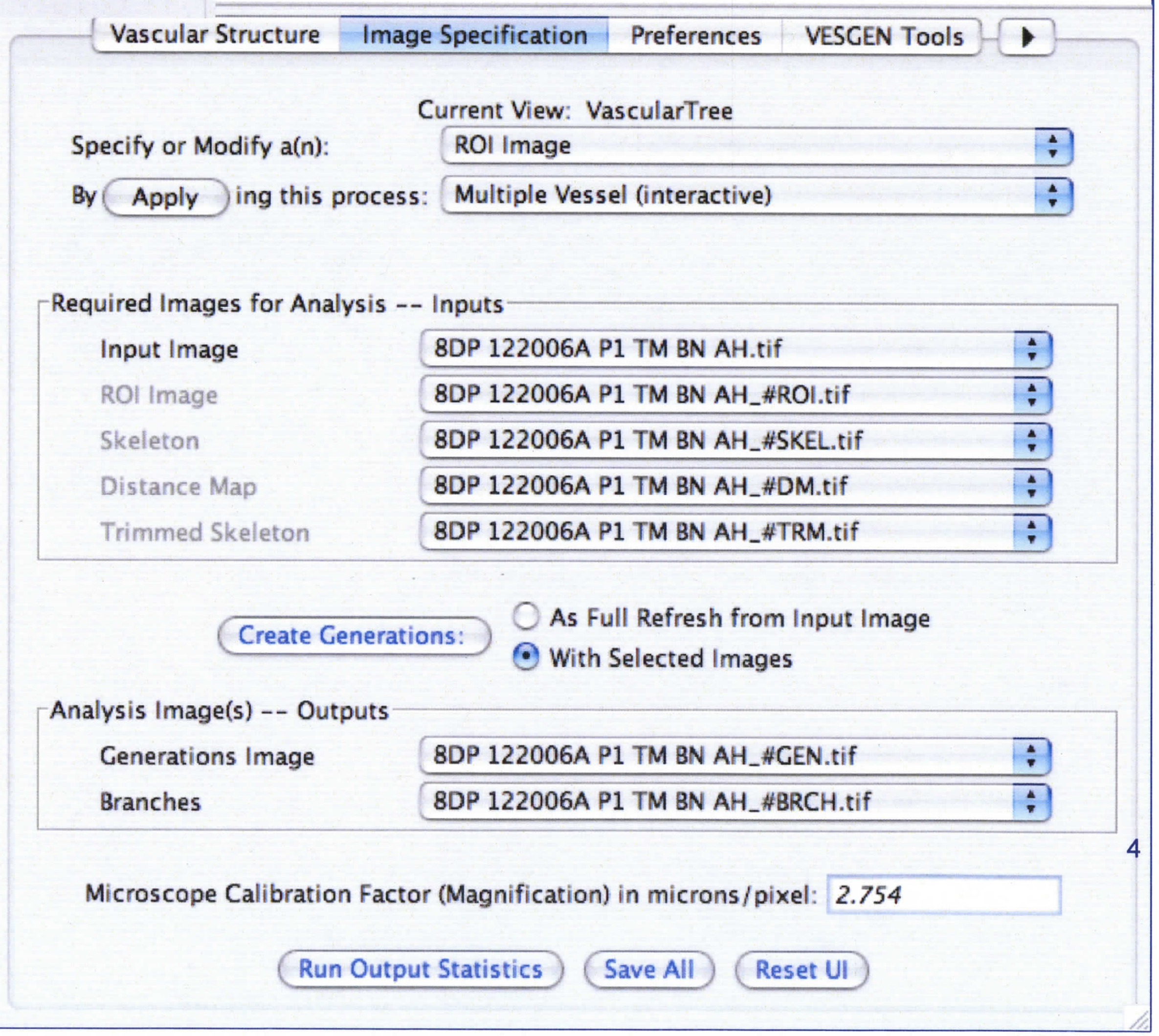
Normal and Abnormal Embryonic Coronary Vessels



Panel to specify vessel type

Main panel

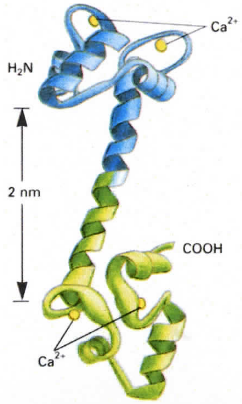
- **Image specification**
- **Algorithm selection**
- **Process initiation**



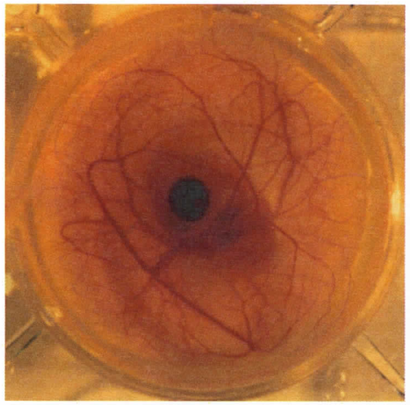
VESGEN Patent Pending

Mapping and Quantification of Microvascular Remodeling and Angiogenesis by VESGEN

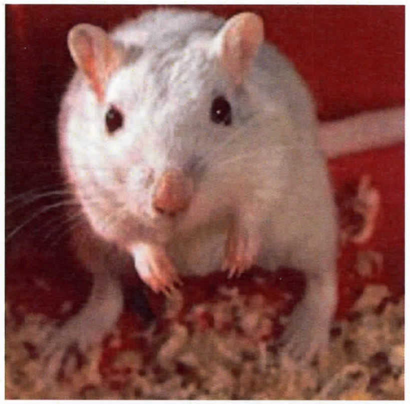
Molecular Regulation

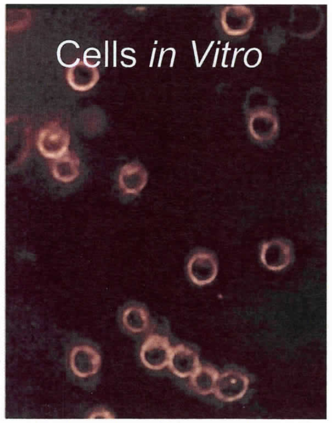


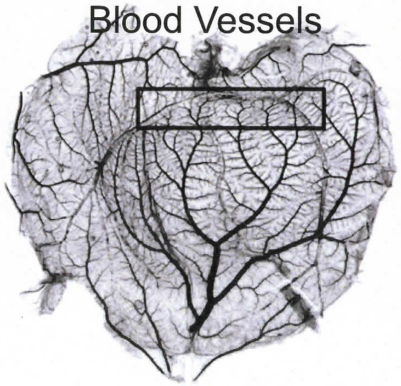
Avian CAM

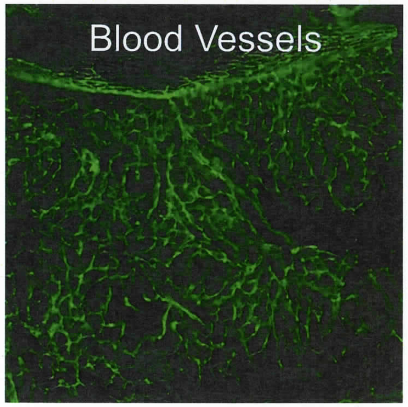


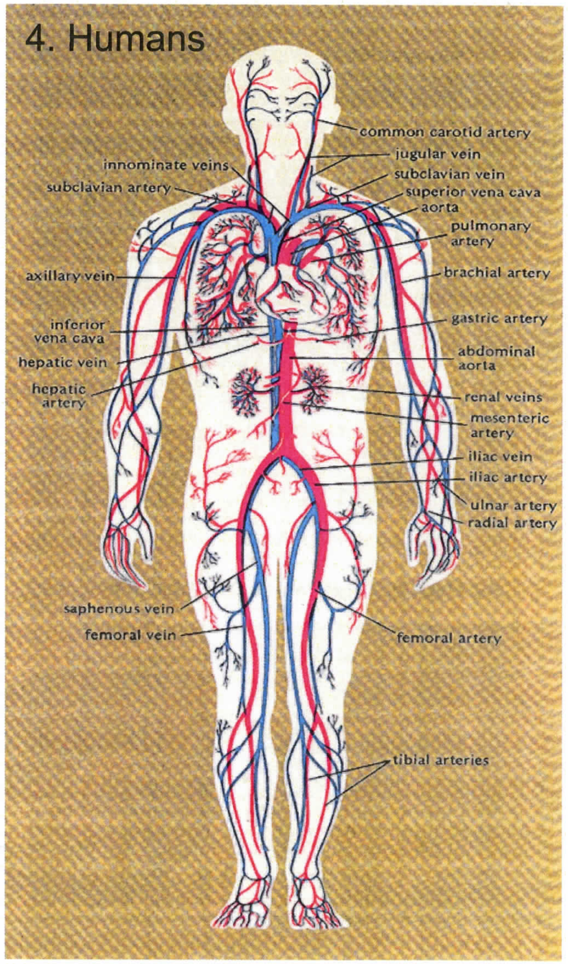
Transgenic Mouse



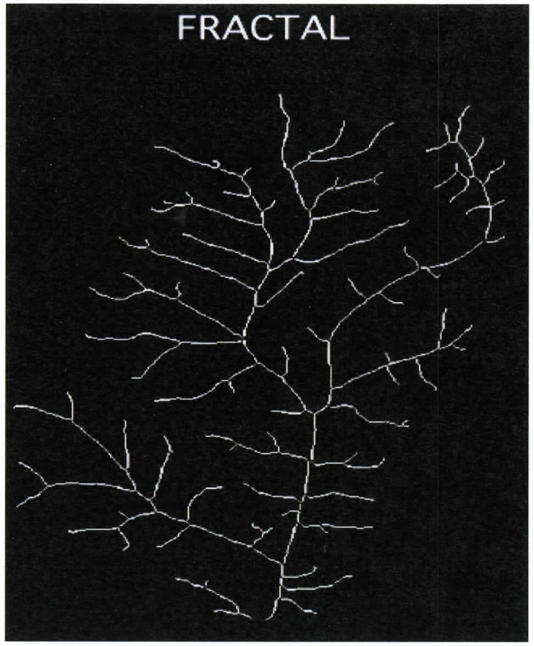




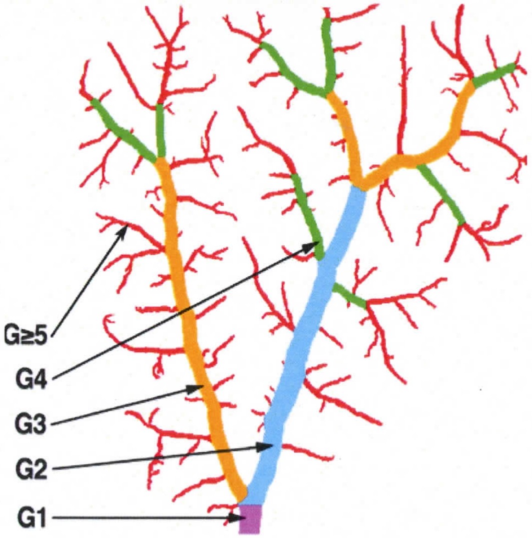




VESGEN Hypothesis: *'Signature'* Vascular Patterns



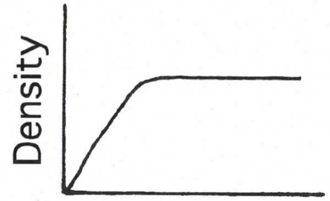
VESGEN



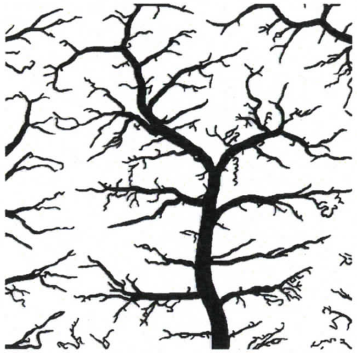
The form of an object is a 'diagram of forces'

- D'Arcy Thompson

FGF-2 as a Simple Stimulator
(Fibroblast Growth Factor-2)

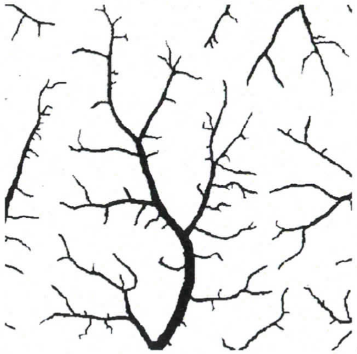


Arterio Scler Thromb Vasc Biol 20 2000

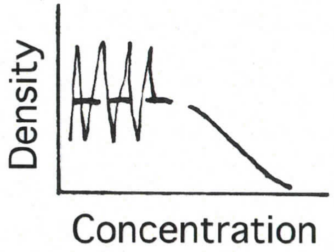


VEGF as a Complexity Factor
(Vascular Endothelial Growth Factor-2)

Microvascular Research 72(3) 2006



TGF-β1 as a Simple Inhibitor
But Complex Potentiator
(Transforming Growth Factor-β1)



Microvascular Research 59(2) 2000

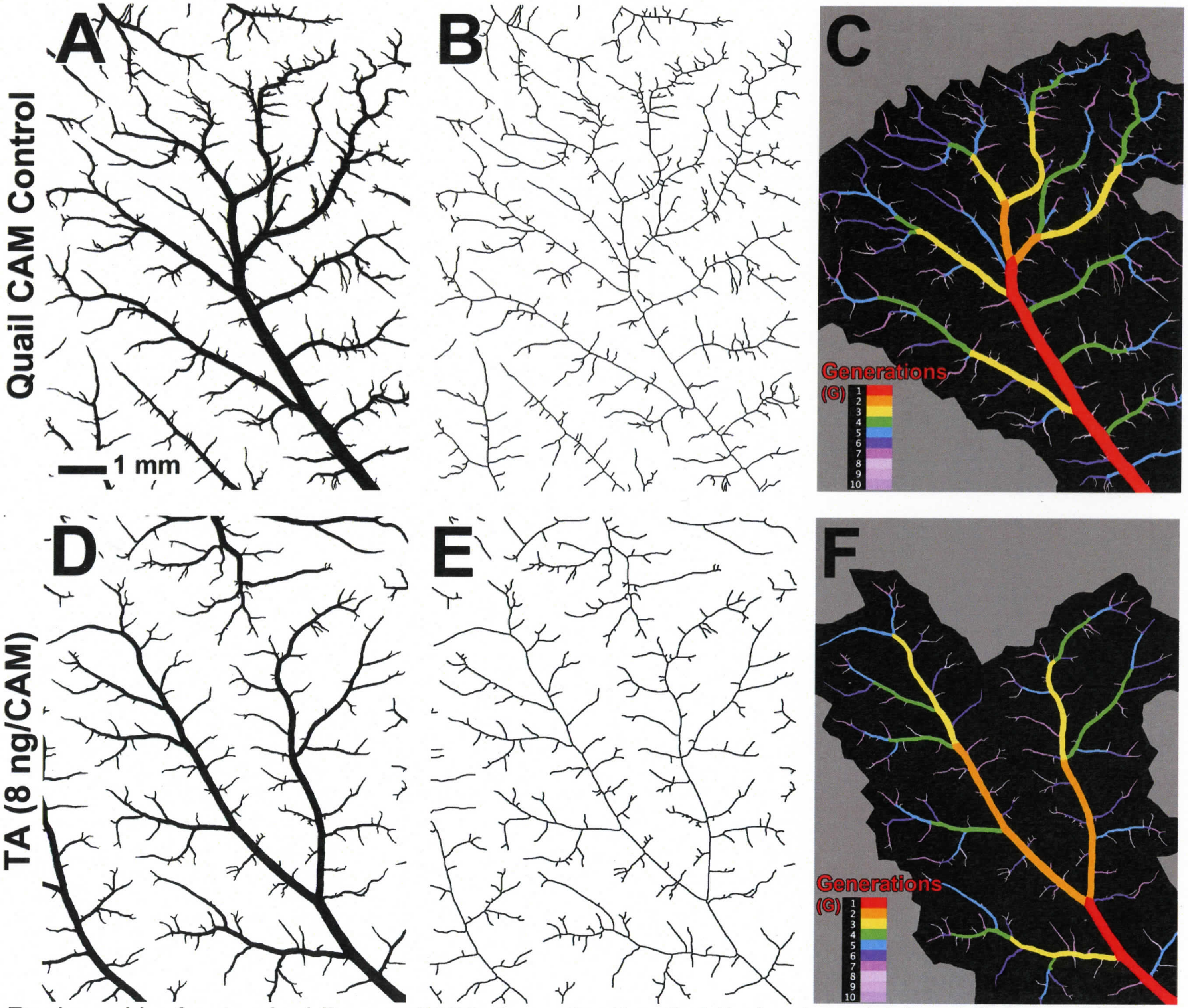
Long-Term Hypothesis

Vascular pattern provides an integrative read-out of dominant molecular regulators in complex signaling pathways of angiogenesis and microvascular remodeling

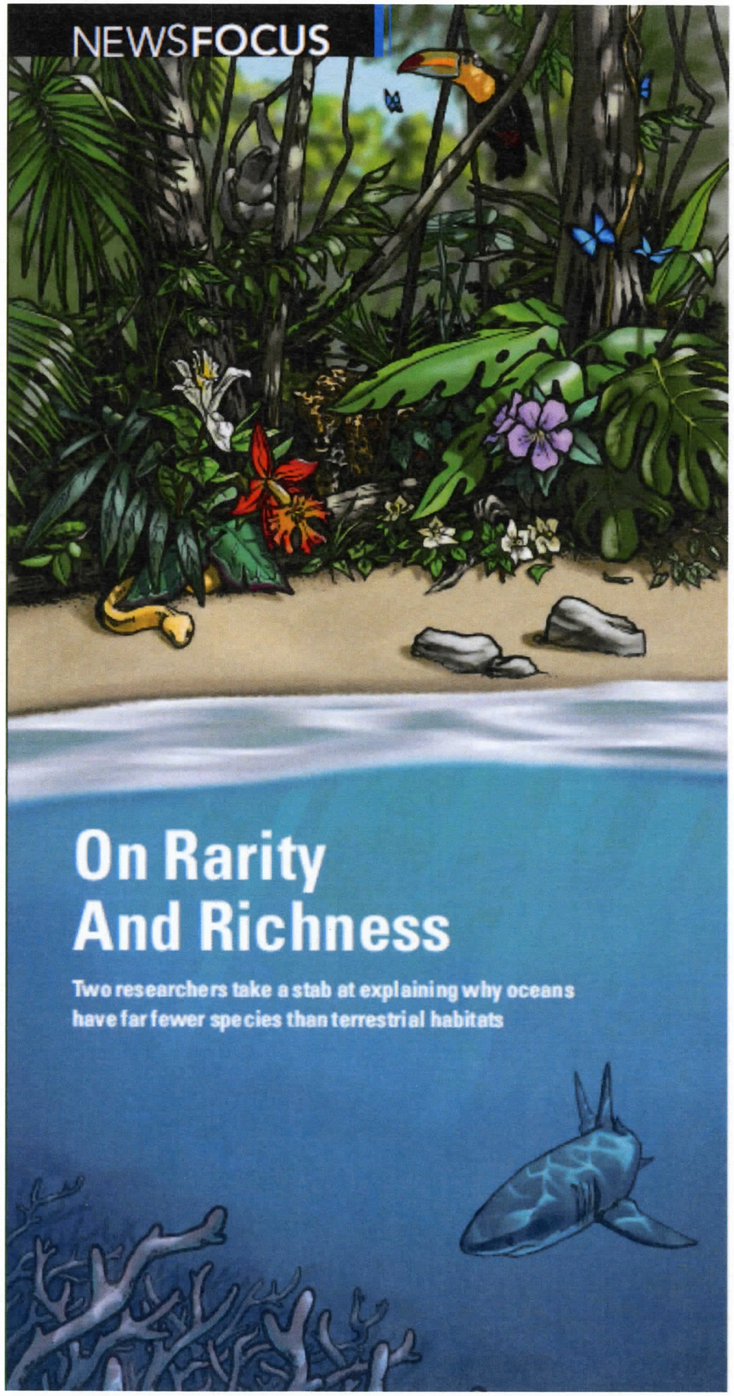
VESsel GENeration (VESGEN) Analysis Software

Vessel Number Density, N_v
Vessel Length Density, L_v
Vessel Diameter, D_v
Fractal Dimension, D_f
Branchpoint + Endpoint Densities, Br_v+E_v

Clinical Steroid (TA) Treatment in CAM Vascular Tree



Reviewed in *Anatomical Record* 2009; *Investigative Ophthalmology & Visual Science* 2008



On Rarity And Richness

Two researchers take a stab at explaining why oceans have far fewer species than terrestrial habitats

IF BIODIVERSITY WERE AN OLYMPIC SPORT, life on land would take home the gold and the sea might not even enter a team. Given the vastness of the oceans and the length of time life has thrived there, you might expect marine species to outnumber terrestrial ones. Yet, microbes aside, upward of nine in 10 species crowd into the 30% of Earth's surface that's dry.

It wasn't always that way, say Richard Grosberg and Geerat Vermeij. These researchers from the University of California (UC), Davis, have been studying land and ocean features to understand how evolution proceeds in these two realms. At a recent meeting,* they argued that the difference in diversity is a recent phenomenon.

Back in the Devonian period, 400 million years ago, the seas were home to an abundance of species, perhaps even more than on land. But about 110 million years ago, land plants went through a burst of speciation; so did the pollinators, fungi, and herbivores associated with them. These relationships made "rare" species possible, as plants acquired help in dispersing their pollen and seeds, resulting in relatively low population densities for individual species. Quickly, their numbers left marine biodiversity behind. The trigger for this terrestrial explosion, Grosberg and Vermeij say, was the evolution of a more efficient way in which land plants use water.

"This is an excellent and thoughtful paper addressing an issue in biodiversity that has rarely been tackled," says Michael Benton, a paleontologist at the University of Bristol in the United Kingdom. Jeremy Jackson, a marine ecologist at the Scripps Institution of Oceanography in San Diego, California, calls it "a very big-picture paper. … It's the kind of paper that you think about forever."

A physical phenomenon?

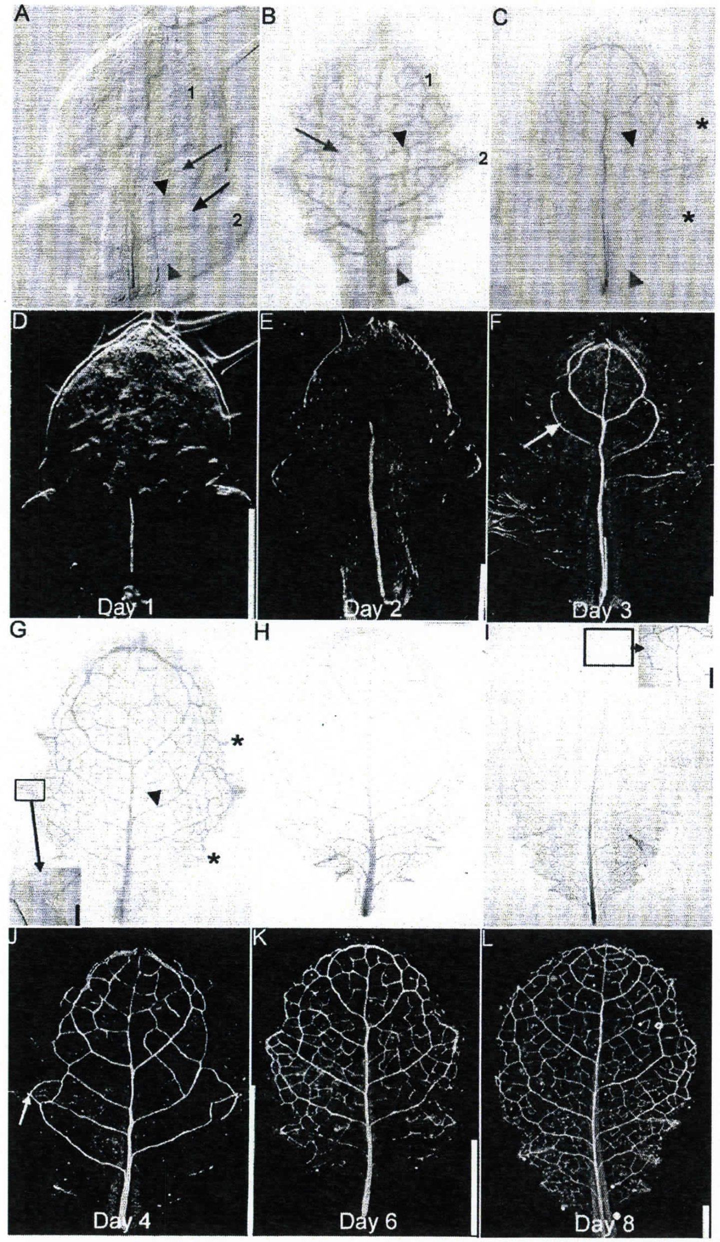
Grosberg started thinking about these issues when he was preparing a series of talks for the 200th anniversary of Charles Darwin's birth. "To me, the interesting question is why are there so many fewer species in the sea than on the land," says Grosberg.

The difference is striking. In 1994, Robert May of the University of Oxford in the United Kingdom concluded that 85% of the world's macroscopic species lived on land, based on the existing record of species across the globe. A 2009 study by Benton found landlubbers to be even more common, accounting for 95% to 98% of the world's multicelled species. "Both recognized that the estimates were ballparks, simply because we don't actually know how

*The Society for Integrative and Comparative Biology meeting was held 3 to 7 January in Seattle, Washington.

CREDIT: M. TWOMBLY/SCIENCE

Vein pattern development in adult leaves of *Arabidopsis thaliana*



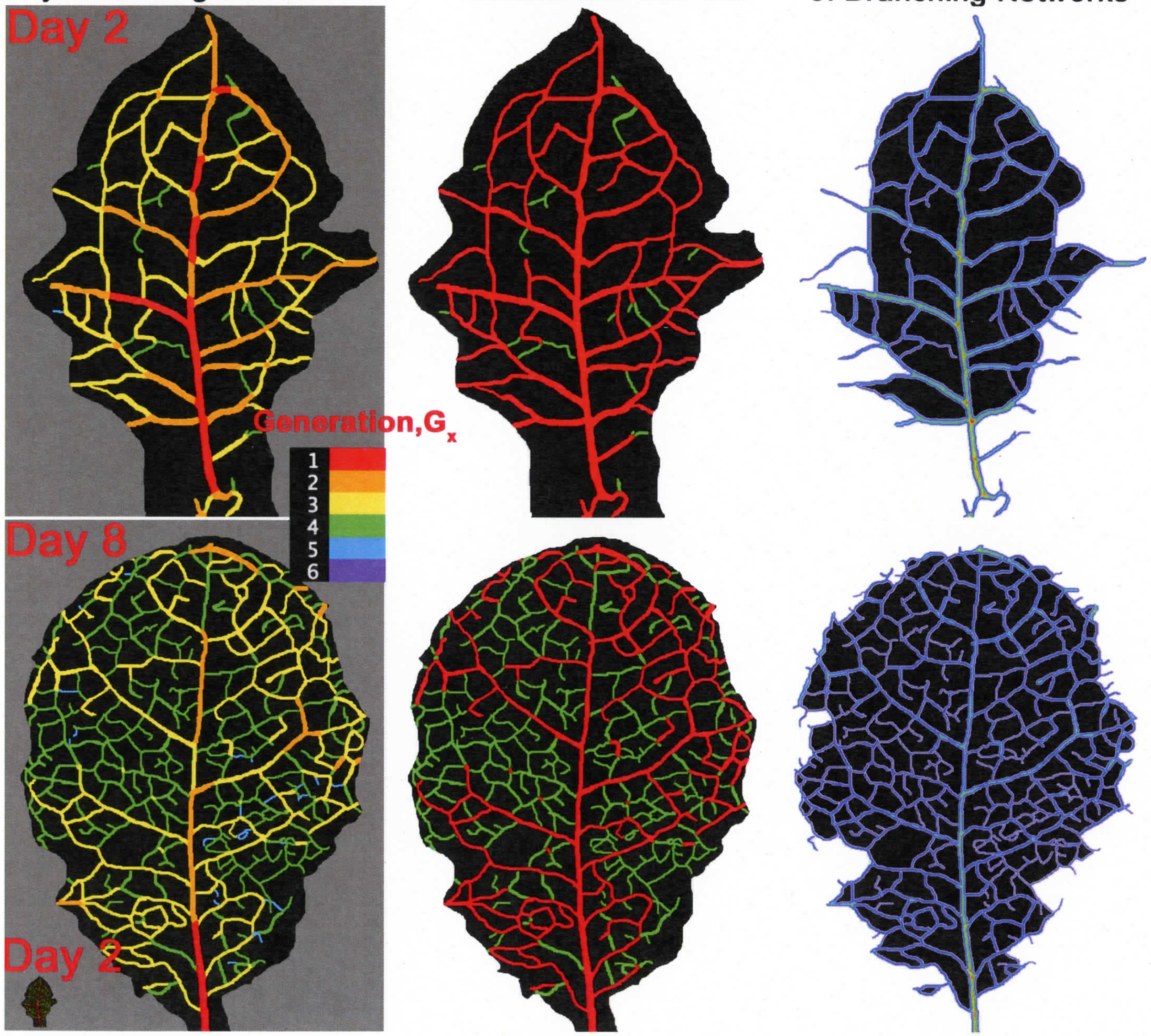
Kang J & Dengler N, Int J Plant Sci 165:231(2004)

See also Candela H et al, 'Venation Pattern Formation in *Arabidopsis thaliana* Vegetative Leaves', Developmental Biology 205:205(1999)

VESGEN

Research Tool for Mapping and Quantification of Vascular Branching Pattern in Genetically Engineered *A. thalia* on ISS

Vascular Pattern by Branching Generation | Grouping of Generations: LARGE and SMALL | Avascular Spaces of Branching Networks



Results

Day 2

Fractal Dimension
D_f = 1.32

Area, Length, Branchpoint Densities
A_V(LARGE) = 0.195
A_V(SMALL) = 0.013

Average Vessel Diameter (μm)
D_V(LARGE) = 11.8 μm
D_V(SMALL) = 7.0 μm

Day 8

D_f = 1.47

A_V(LARGE) = 0.159
A_V(SMALL) = 0.276

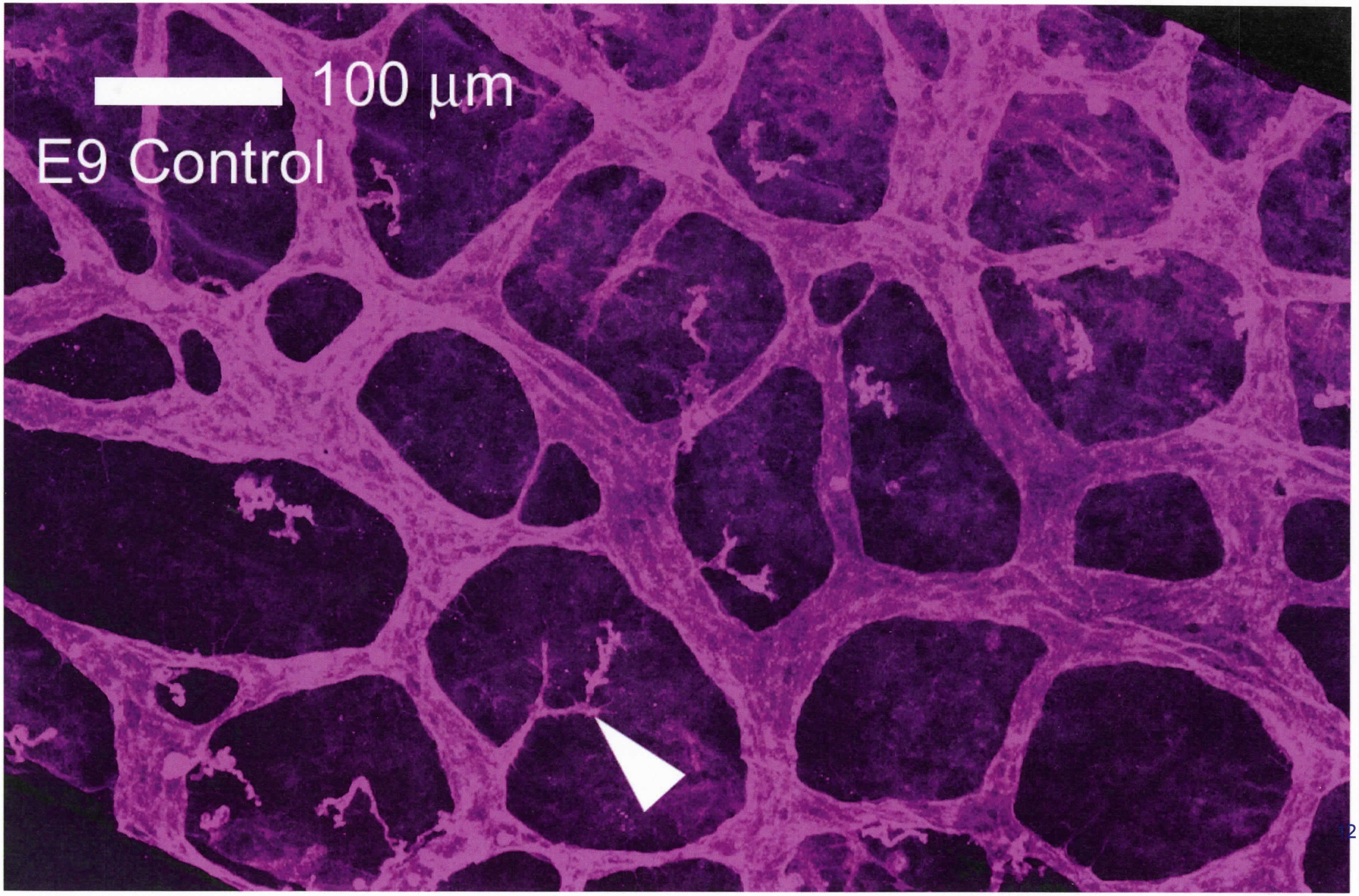
D_V(LARGE) = 93.1 μm
D_V(SMALL) = 66.8 μm

Conclusions

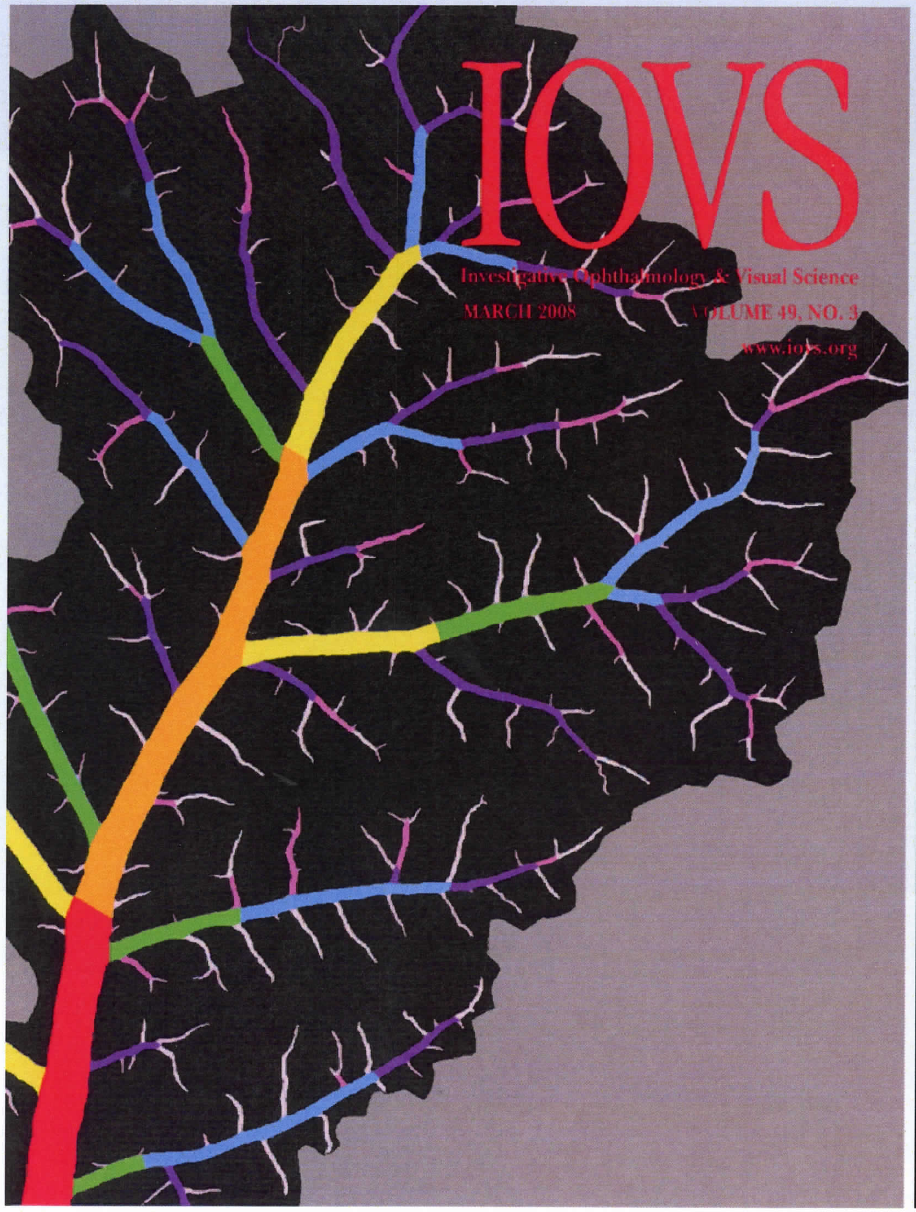
Less mature branching

Increased vascular complexity–

especially density of smaller vessels

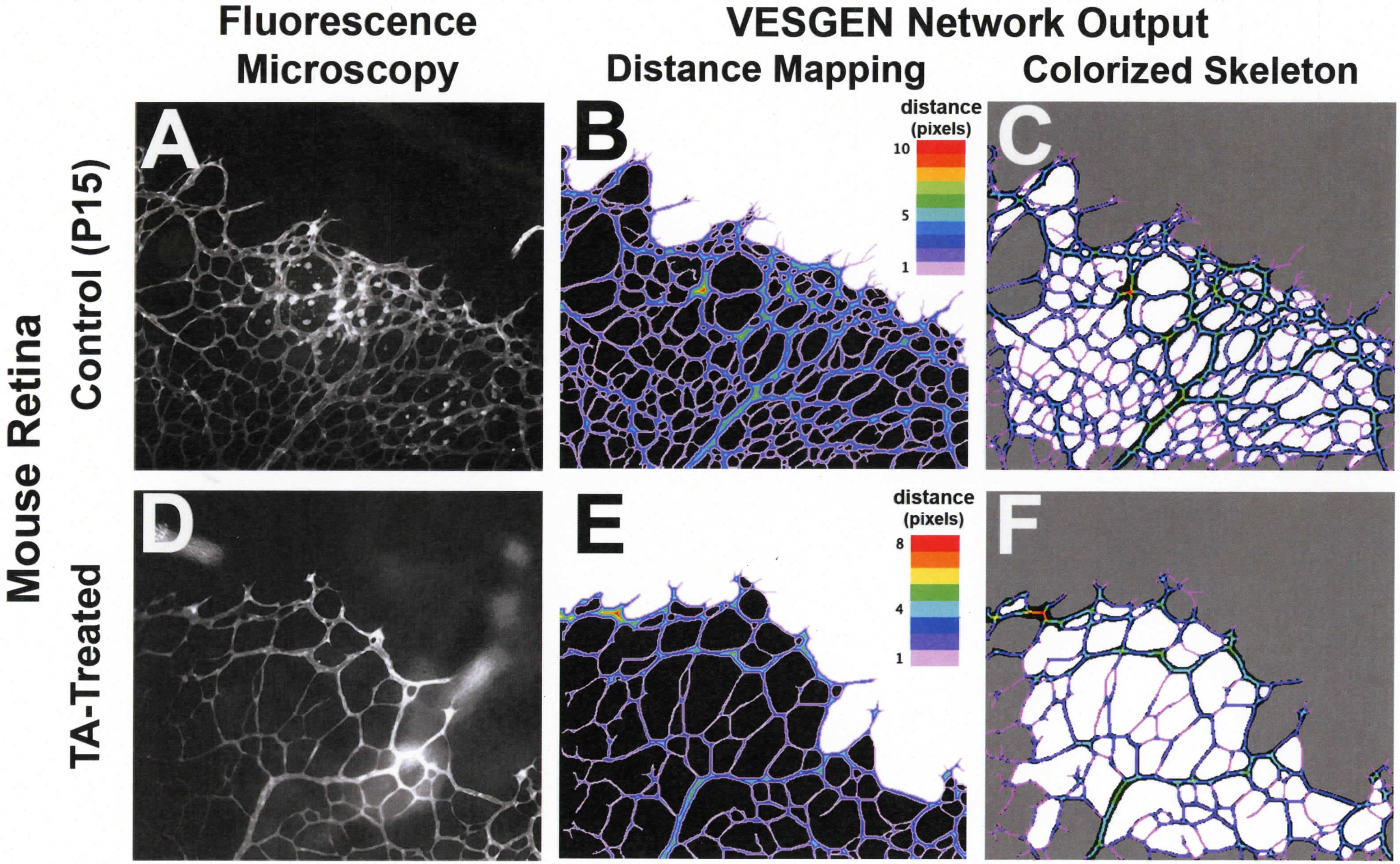


Parsons et al, *Microvascular Research* 167(1):193-211(2005)


IOVS
Investigative Ophthalmology & Visual Science
MARCH 2008
VOLUME 49, NO. 3
www.iovs.org


THE ANATOMICAL RECORD
KURT H. ALBERTINE • EDITOR-IN-CHIEF
MARCH 2009
AN OFFICIAL PUBLICATION OF THE AMERICAN ASSOCIATION OF ANATOMISTS
VOL. 292·NO. 3·PAGES 309-460
WILEY-BLACKWELL
VOL. 292 NO. 3 MARCH 2009
AR
The Anatomical Record
Advances in Integrative Anatomy and Evolutionary Biology
Celebrating
OVER
100 YEARS
of Excellence in
ANATOMICAL
PUBLICATION
Thematic Papers:
Imaging Living
Vasculature

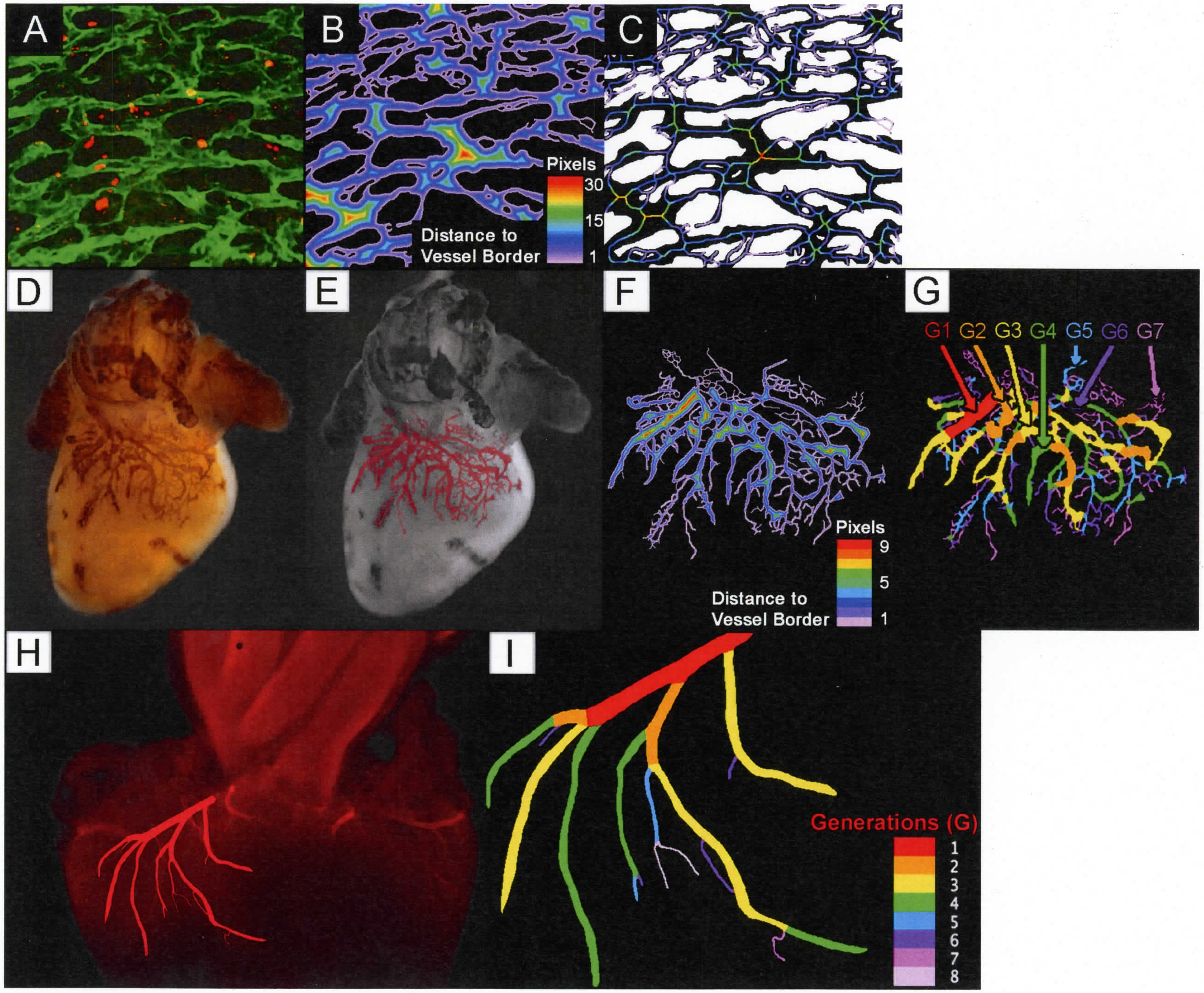
VASCULAR NETWORKS IN TRANSGENIC MOUSE RETINA



with J Sears & Q Ebrahem (Cole Eye Institute), from Vickerman et al, *Anatomical Record A* 292(3), 2009

VESGEN Patent Pending

CORONARY VESSEL NETWORK-TO-TREE TRANSITIONS



Vickerman et al, VESGEN Review, *Anatomical Record A* 292(3), 2009