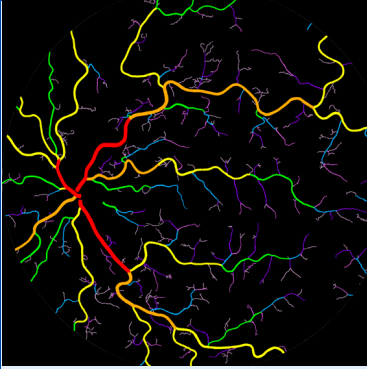
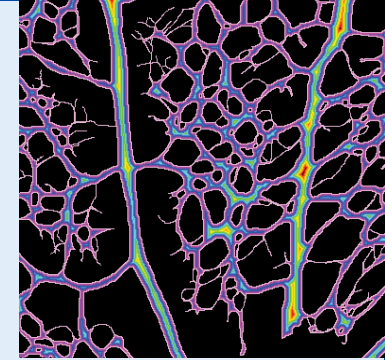


# NASA's VESsel GENeration Analysis (VESGEN) Software



Human Retina



Mouse Retina

## Mapping by VESGEN of Blood Vessels in Astronaut Retinas Pre- and Post-Flight to the ISS

P. Parsons-Wingerter<sup>1</sup>, R. J. Vyas<sup>1</sup>, M. C. Murray<sup>1</sup>, M. Predovic<sup>1</sup>, S. Lim<sup>1</sup>,  
G. Vizzeri<sup>2</sup>, G. Taibbi<sup>2</sup>, S. S. Mason<sup>3</sup>, S. B. Zanello<sup>4</sup>, M. Young<sup>5</sup>

<sup>1</sup>NASA Ames Research Center, NASA, Mountain View CA,

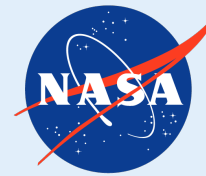
<sup>2</sup>Department of Ophthalmology and Visual Sciences, University of Texas Medical Branch,  
Galveston TX, <sup>3</sup>MEI Technologies, <sup>4</sup>Universities Space Research Association and <sup>5</sup>Human Health  
and Countermeasures, NASA Johnson Space Center, Houston TX

Supported by NRA from NASA's Human Health & Countermeasures

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A photograph of an astronaut in a white spacesuit floating in space. The astronaut's helmet and visor are visible on the left. In the background, the Earth's blue and white horizon is visible, and a bright sun with a starburst effect is in the upper right. The text is overlaid on this image.

Primary Risk Spaceflight-Induced Intracranial Hypertension/Vision Alterations

Primary Gap VIIP1 We do not know the etiological mechanisms and contributing risk factors

VESGEN Hypothesis & Background

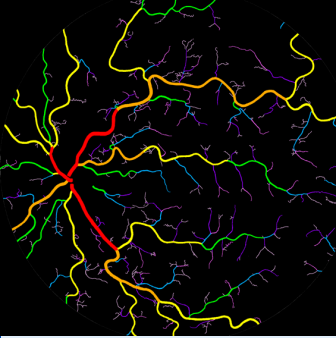
VIIP VESGEN Studies for 2 NRA Awards

Preliminary Results for Crew Members

Study Completion April 2017

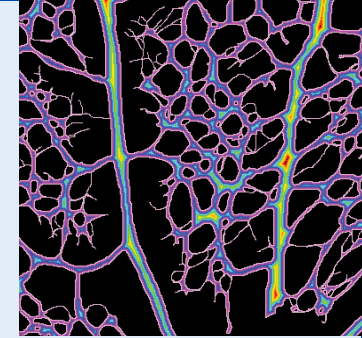
### Hypothesis

The retinal microvasculature within necessarily remodels during long-duration microgravity to accommodate ocular fluid shifts



# VESGEN

## Translational Mapping and Quantification of Fractal-Based Vascular Branching Patterns From Physiological Rules



Human Retina

Mouse Retina

### Vascular Trees

Retinal Vascular Disease, Mouse/Avian Coronary Vessels, CAM, Yolksac

### Vascular Networks

Mouse Intestinal Inflammation, CAM Lymphatic Vessels, Abnormal Mouse Corneal Angiogenesis, Drosophila (Fruitfly) Wing

### Vascular Tree-Network Composites

Mouse Postnatal Retina, Early Embryonic Coronary Vessels, Juvenile and Adult Leaf Venation

### Mapping and Quantification by Multiparametric Weighted Analysis

Fractal Dimension,  $D_f$

Vessel Number Density,  $N_v$

Vessel Length Density,  $L_v$

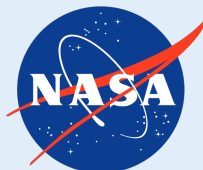
Vessel Diameter,  $D_v$

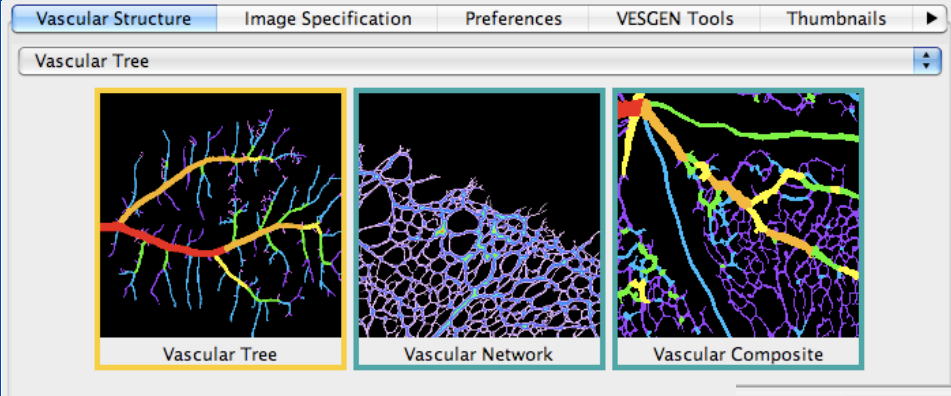
Branchpoint + Endpoint Densities,  $Br_v + E_v$

VESGEN Patents Pending

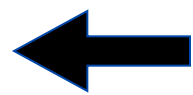


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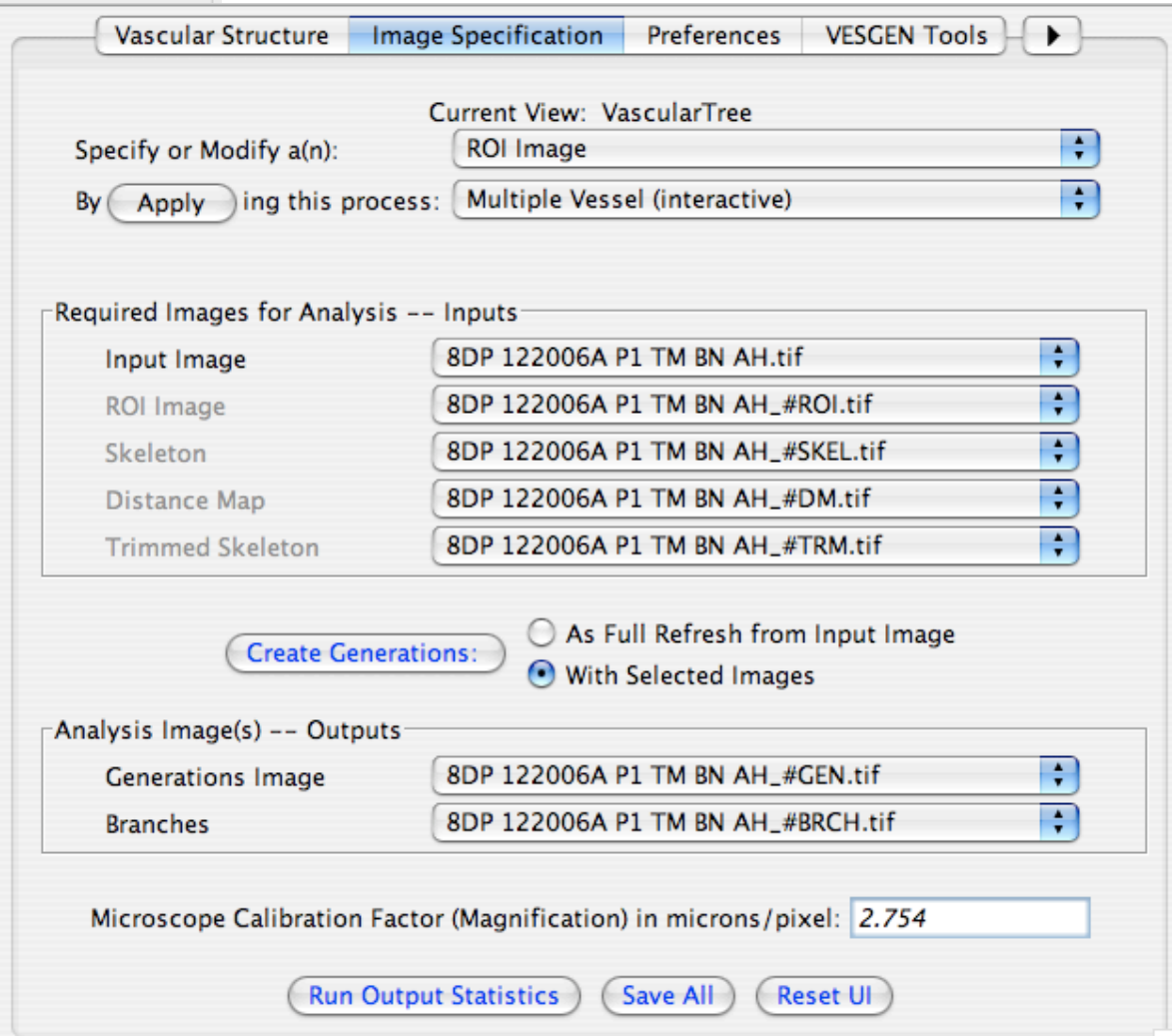
# Mature, Beta-Level VESGEN



Panel to specify vessel type

Main panel

- Image specification
- Algorithm selection
- Process initiation



# Common VESGEN Study Design for ISS Crew Members, 70-Day HDT Bed Rest, and 90-Day HS Rodents

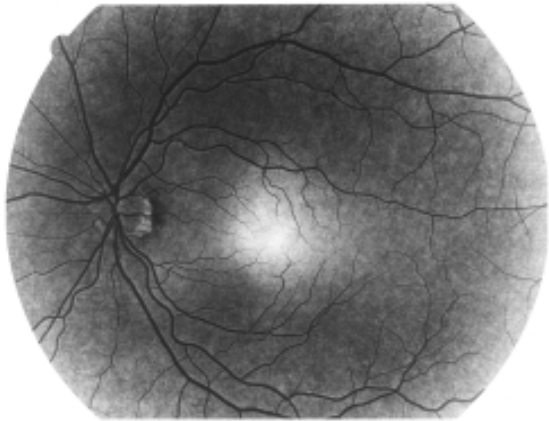
- Retrospective Human Subject Studies approved by NASA's HHC, LSAH and IRB
- **Phase 1** Masked VESGEN analysis of retinal images
- **Phase 2** Unmasking of subject status and correlation with other ocular, vision and cardiovascular parameters
- **Crew Members and Bed Rest** Retinal imaging by Heidelberg Spectralis 30° Infrared (IR)
- 8 Crew Members by 32 Spectralis IR images



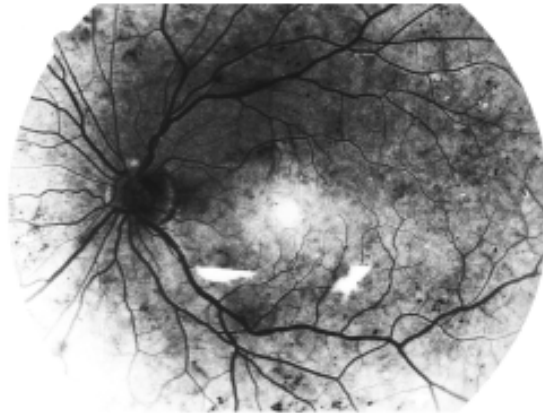
# Diabetic Retinopathy

Previous grading by secondary, indirect consequences,  
not primary, indirect vascular changes

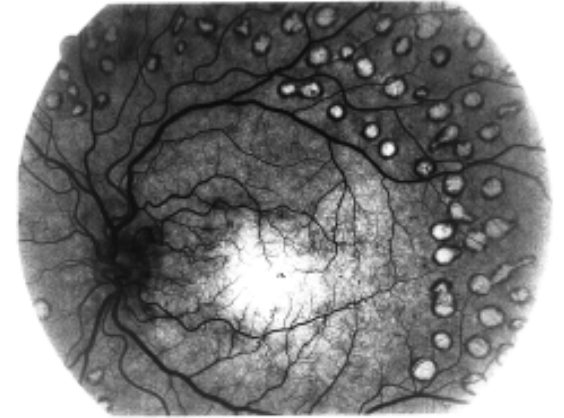
Normal



NPDR



after Laser Ablation



**EARLY** *Vascular* Nonproliferative DR (NPDR)  
**LATE** *Vascular* Proliferative DR (PDR)

# Mapping of Progressive Diabetic Retinopathy by VESGEN

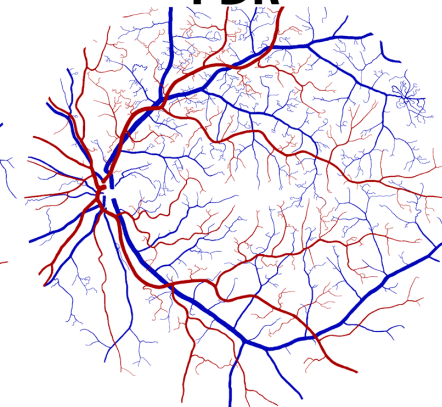
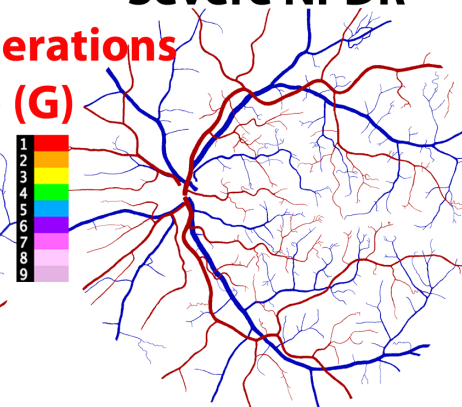
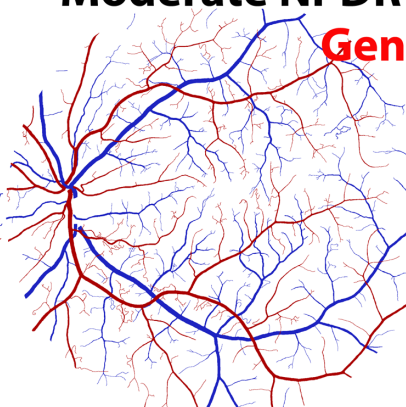
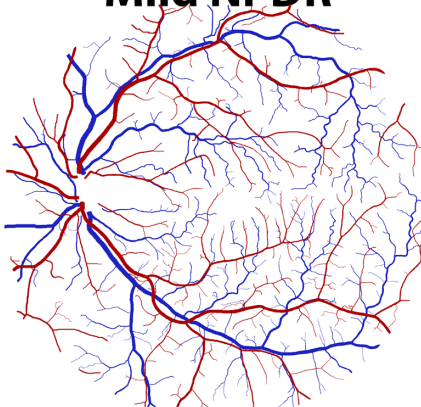
Mild NPDR

Moderate NPDR

Severe NPDR

PDR

Vascular Trees

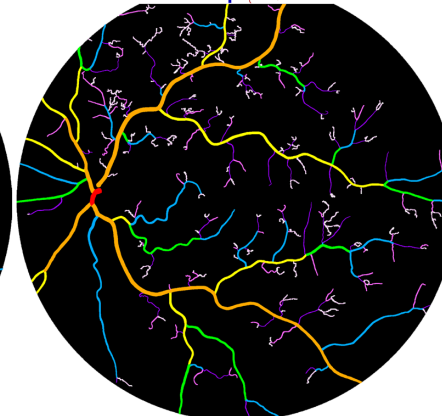
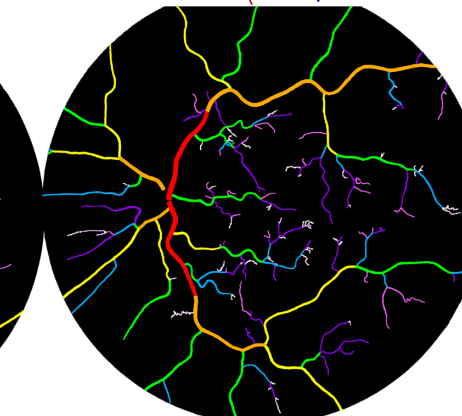
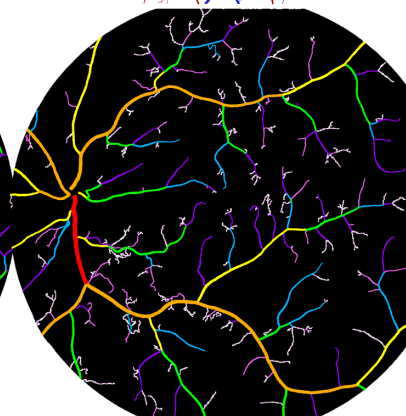
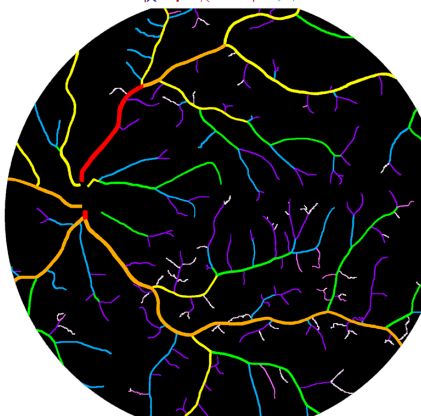


Generations

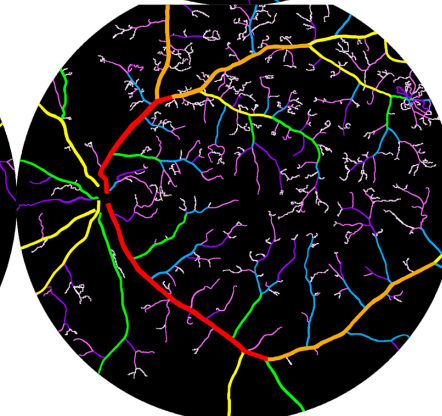
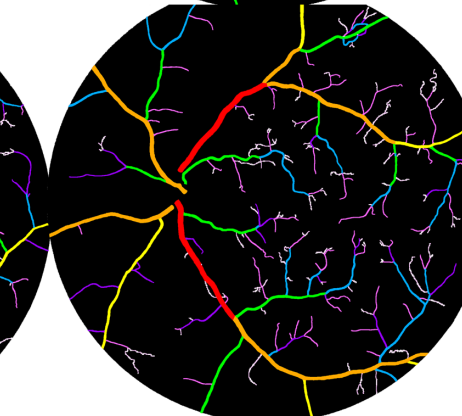
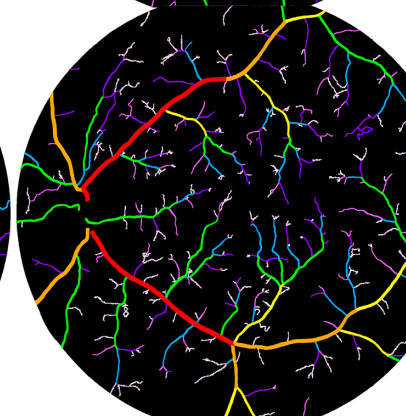
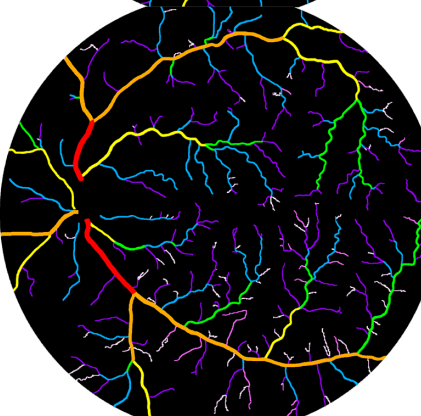
(G)



Arteries

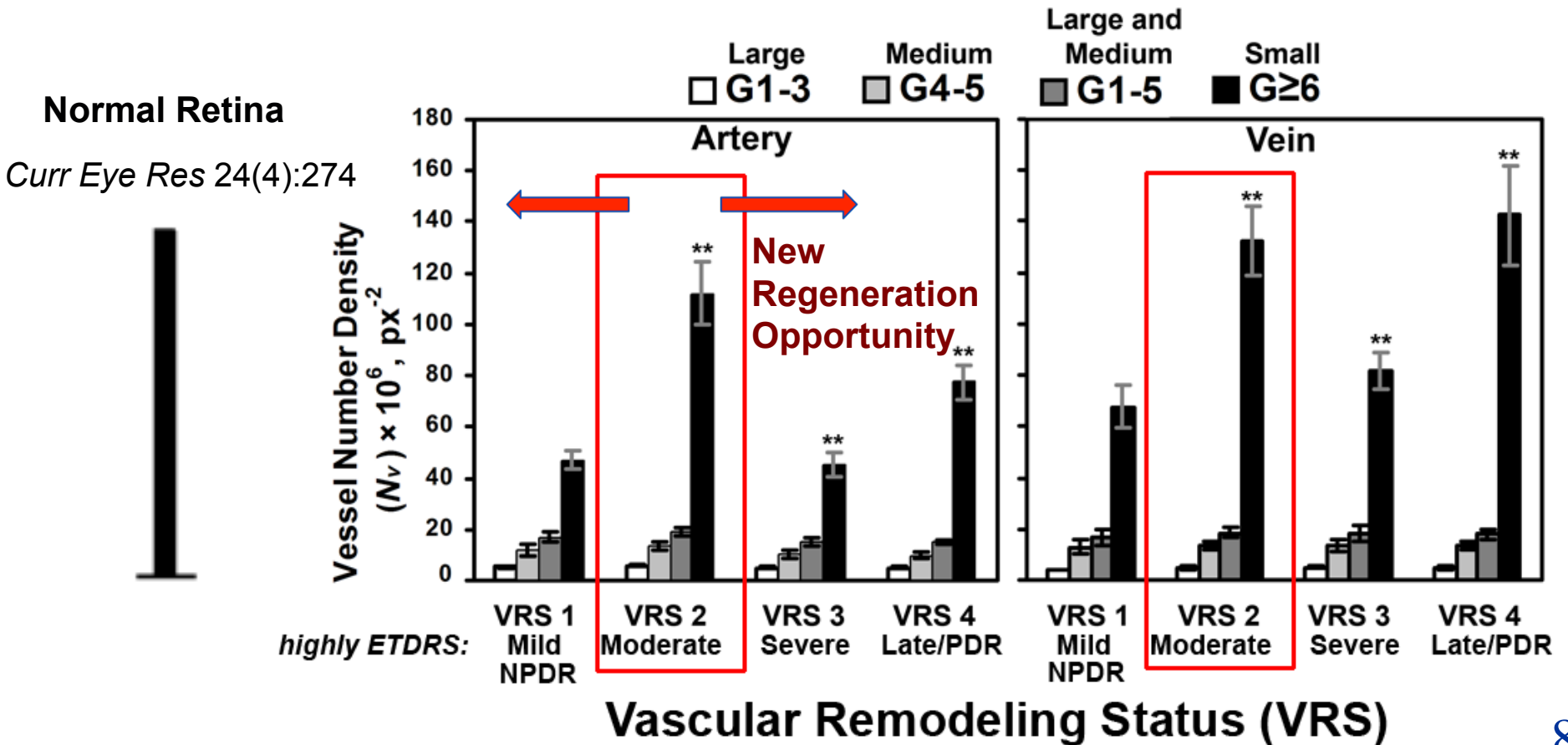


Veins



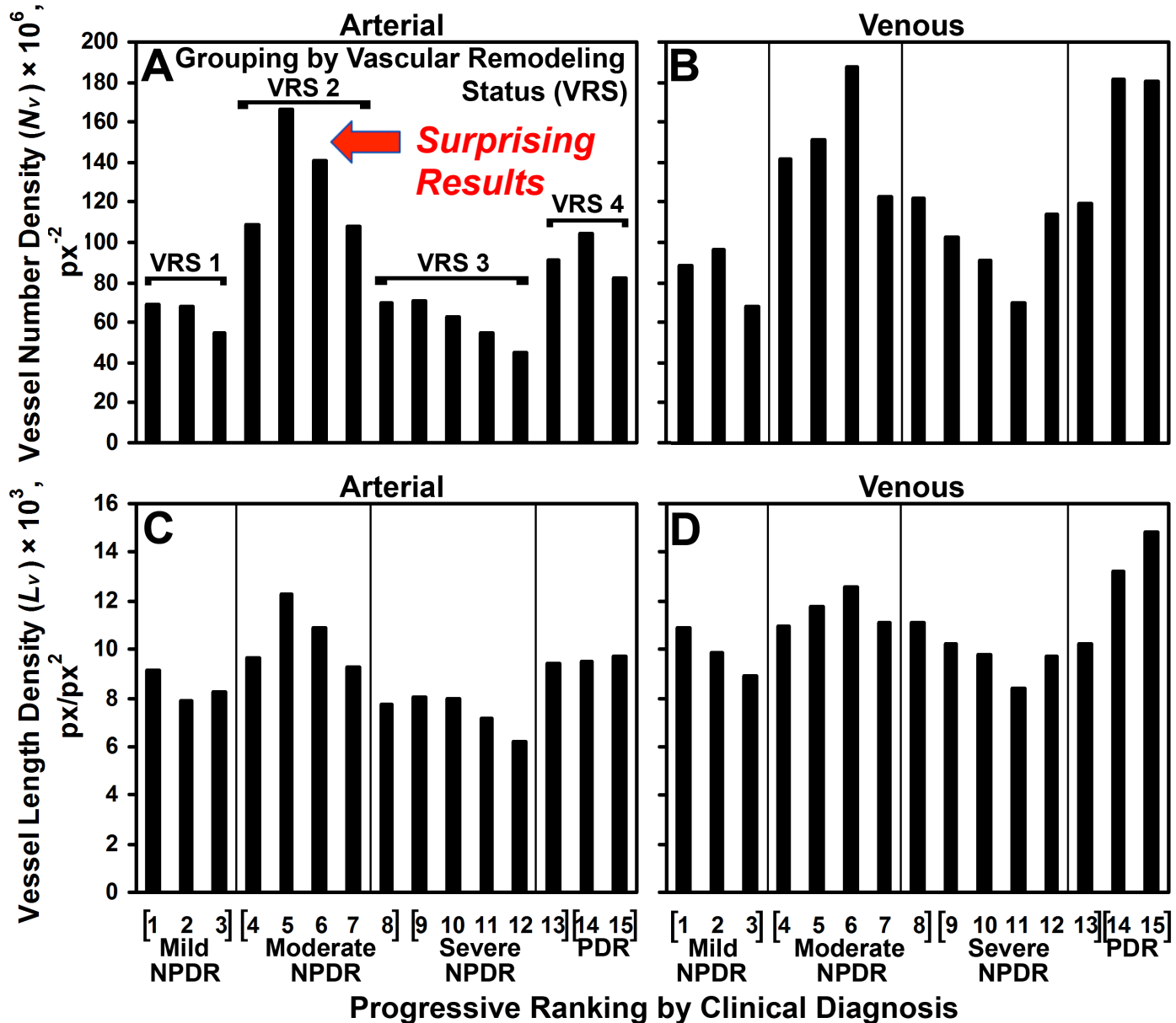
# Surprising, Innovative Paradigm Shift by VESGEN

Alternation of Vascular Dropout with Vascular Growth (Angiogenesis) during Progression of Diabetic Retinopathy

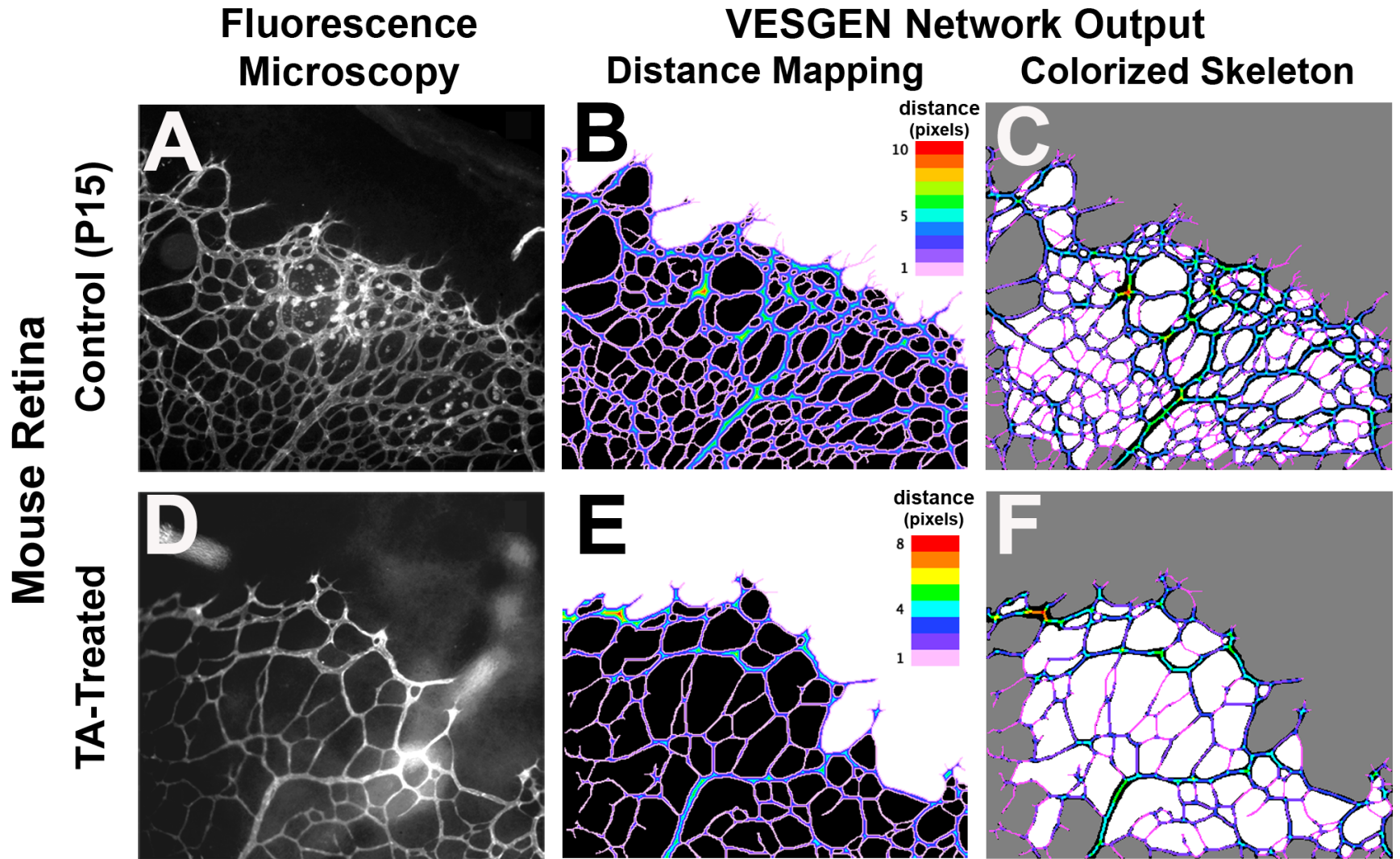




# Grouping by Vascular Remodeling Status (VRS)



# Vascular Networks in Transgenic Mouse Retina



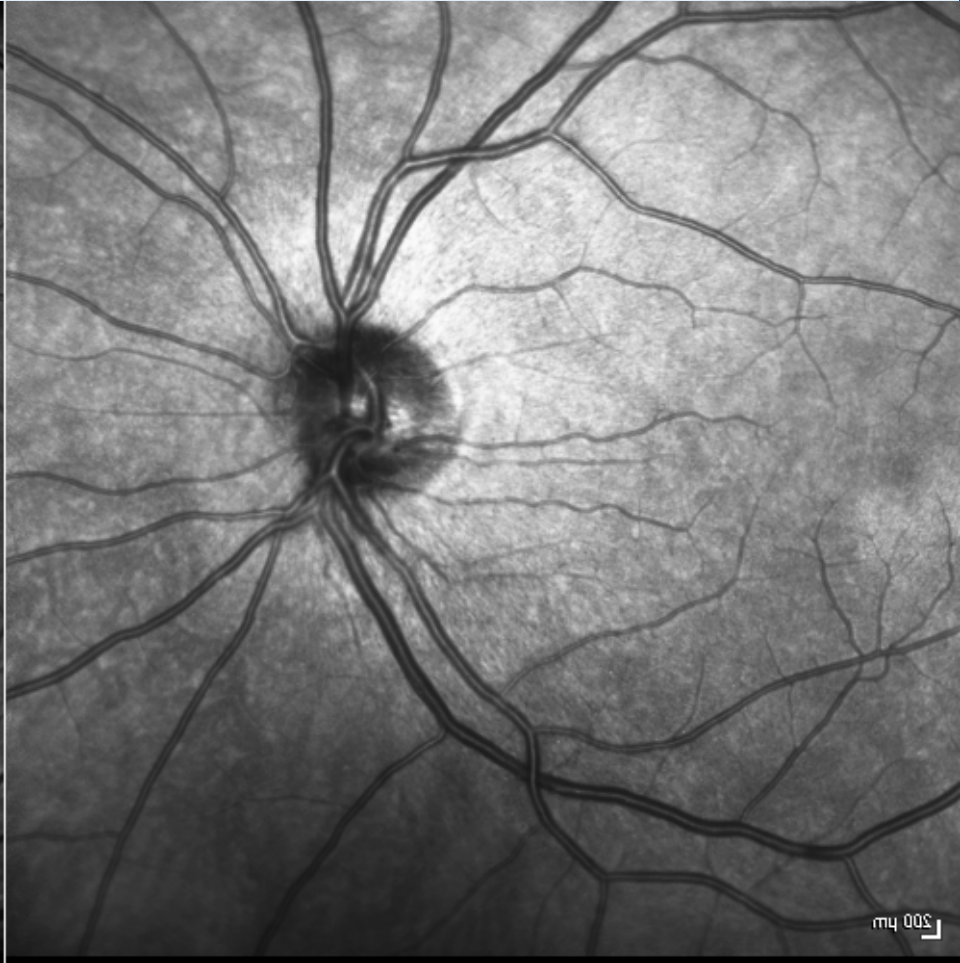
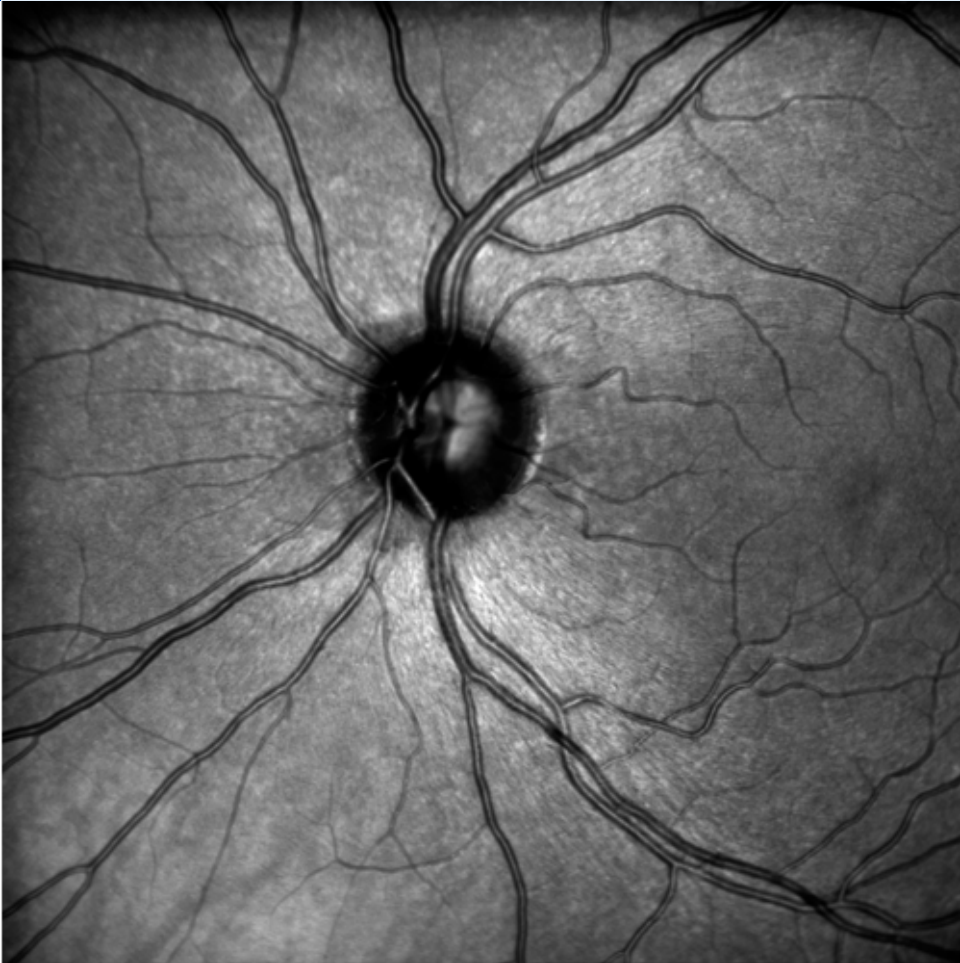
with J Sears & Q Ebrahim (Cole Eye Institute), from Vickerman et al, *Anatomical Record A* 292(3), 2009



# Differences in Spectralis IR Image Background between April 2014 Study and Current Crew Members, HDT

Dr N Patel March 2014

Crew Member



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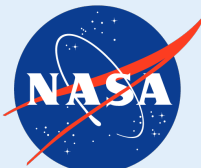
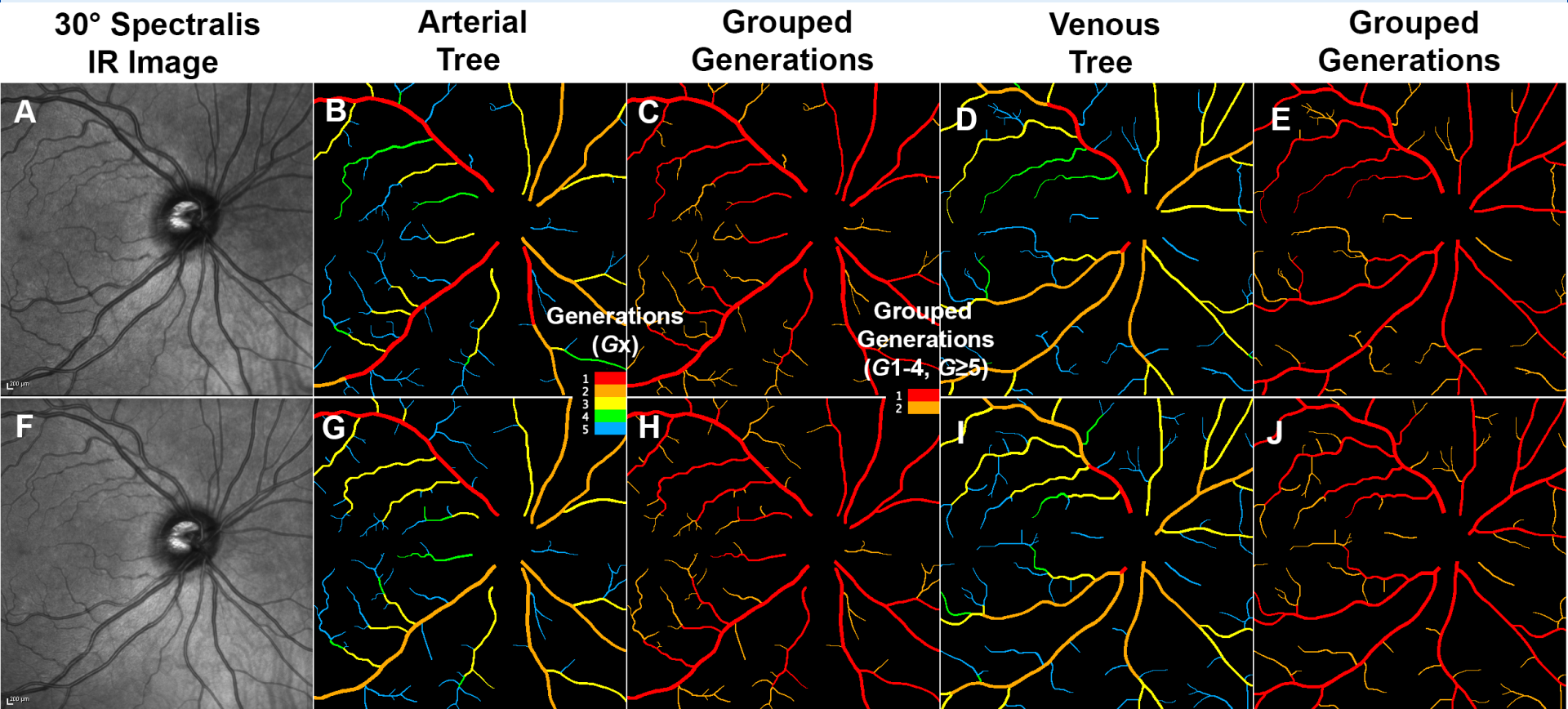


# Preliminary Phase 1 VESGEN Results for Crew Members Pre- and Post-Flight to the ISS

- 8 Crew Members by 32 Spectralis IR images
- Phase 1, Phase 2, Final Report complete by mid April 2017
- **Phase 1** Masked VESGEN analysis of retinal images
- **Phase 2** Unmasking of subject status and correlation with other ocular, vision and cardiovascular parameters
- **Crew Members and Bed Rest** Retinal imaging by Heidelberg Spectralis 30° Infrared (IR)



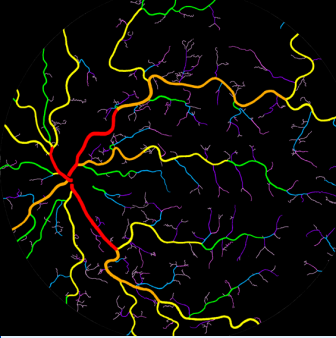
# Comparison of VESGEN Analysis for Arterial and Venous Trees In the Retina of ISS Crew Member Pre- and Post-Flight to ISS



# VESGEN Example Companion images of identical Crew Member retina 30° IR image resolution of vessels matched by vessel diameter

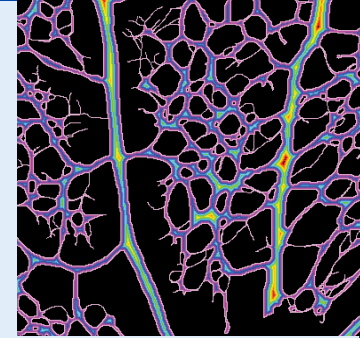
## Grouped by Branching Generation ( $G_x$ ) Large Vessels ( $G_{1-4}$ ), Small Vessels ( $G_{\geq 5}$ )

Crew Member	Vessel Number		Vessel Length Density (E+3, $\mu\text{m}/\mu\text{m}^2$ )		Fractal Dimension $D_f$	Vessel Diameter ( $\mu\text{m}$ )	
	$N_{1-4}$	$N_{\geq 5}$	$L_{v1-4}$	$L_{v\geq 5}$		$D_{v1-4}$	$D_{v\geq 5}$
Arteries	31	48	2.65	1.26	1.35	25	12
	<b>37</b>	<b>64</b>	<b>2.74</b>	<b>1.71</b>		<b>1.38</b>	26
Veins	29	63	2.35	1.48	1.35	28	12
	<b>32</b>	<b>69</b>	<b>2.52</b>	1.49		1.36	27



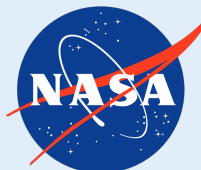
Human Retina

# Conclusions

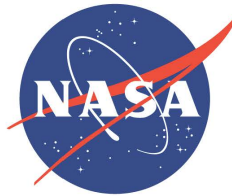


Mouse Retina

- Phase 1 nearing completion: VESGEN analysis of vascular patterning in the retinas of 8 Crew Members by 32 Spectralis IR images
- Phase 1, Phase 2, Final Report complete by mid April 2017
- VESGEN Results for Crew Members will be compared with 70-Day HDT Bed Rest study and 90-Day Rodent Hindlimb Suspension (in progress)
- Definitive testing of our hypothesis requires more advanced imaging of blood vessels in the retina and choroid by newer technologies such as OCT-A and AOSLO







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### Purpose

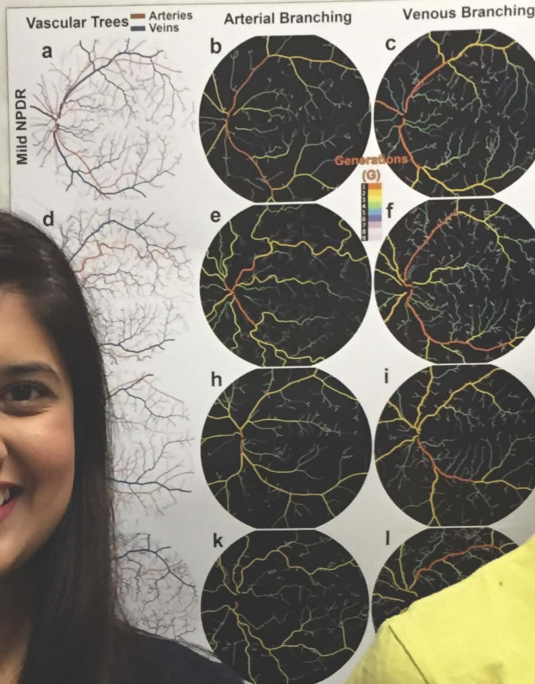
To examine changes in retinal vasculature with progression of diabetic retinopathy (DR) by Vessel GENERation (VESGEN) Analysis. VESGEN provides an innovative mapping of vessel branching generation for the informative quantification of vascular pattern and space-filling capacity.<sup>1,2</sup> In our previous study,<sup>3</sup> vessel density decreased in mild nonproliferative DR (NPDR) compared to the normal human retina.

### Method

In a study of 30 eyes diagnosed with mild NPDR, moderate NPDR, severe NPDR or very severe NPDR, 50° fluorescein angiography (FA) images were obtained by semi-automatic image processing. The 30 images were segmented into successively smaller branching generations (G-1 to G-30) based on the location of branchpoint and endpoint densities ( $Br+E$ ). The density of each generation was more accurately predictive of vascular density than total vessel density. Once established, secondary vascular characteristics were determined. Nonetheless, VRS correlation with clinical diagnosis of retinal remodeling.

strongly with vascular dropout during DR progression. VRS decreased from VRS 2 to VRS 3, and retinal remodeling was dominated first by arterial remodeling. Previously we showed in *in vivo* that retinal remodeling was associated with a trend toward increased vessel density (but no angiogenesis) at high VRS. With increased DR in the human retina, we used a *in vitro* manner to stimulate angiogenesis and enlarged.

with vascular dropout in DR. Oscillatory remodeling and treatments of early DR. Angiogenesis is indicated for the retinal remodeling.



Estimated from Normal Retina, Fractal Analysis



dropout oscillate with DR progression. VRS 1-VRS 4, which is highly correlated with VRS 3 and VRS 4, respectively, for confidence estimates.

