

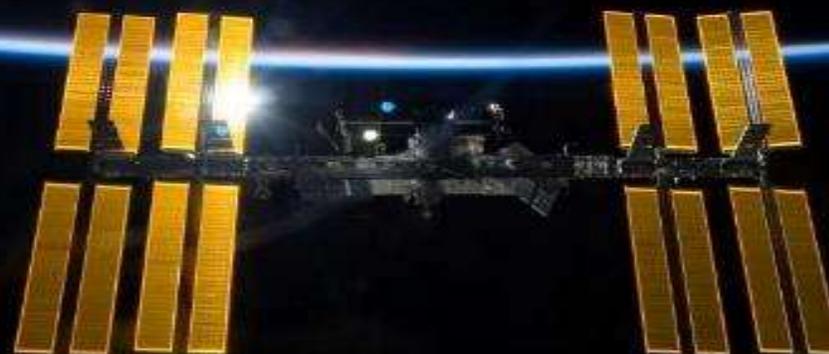


# **Part I: An Introduction to Spaceflight Associated Neuro-ocular Syndrome (SANS)**



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Space and Occupational Medicine Branch (SD3)  
NASA Johnson Space Center



*Introduction to Telehealth* – University of Missouri–St Louis

09 December 2022



# Background: *ISS*

## ■ International Space Station (ISS)

- In use since 2000
- Crew: Typically, 5-7
- Mission duration: ~0.5 to 1y
- International partners
  - United States / NASA
  - Russia / Roscosmos
  - European Union / ESA
  - Canada / CSA
  - Japan / JAXA
- “Low Earth orbit”
- In constant free-fall



Image credit: NASA





# Background: *The Future...*



- Astronauts will soon venture outside of Earth's magnetic & gravitational fields, starting in 2020s
  - Return to the Moon
  - **Mars missions. Duration: 2.25 to ~3 yrs (w/out option of early return)**
    - Unprecedented challenges to health & human performance
      - Psychological
      - Environmental
      - Physiological
    - Top human research priorities for exploration missions
      - Radiation risks
      - Behavioral health
      - Food & pharmaceutical stability
      - In-flight medical conditions
      - **Spaceflight Associated Neuro-ocular Syndrome (SANS)**



<https://mars.nasa.gov/>



# Recent Headlines



Too much space travel is hazardous for your eyeballs

### Spaceflight Bad for Astronauts' Vision, Study Suggests

By SPACE.com Staff | March 13, 2012 12:00am ET

### Possible Mars Mission 'Showstopper': Vision Risks for Astronauts

By Mike Wall, Senior Writer | April 8, 2014 07:00am ET

The mysterious syndrome impairing astronauts' sight

Spacemen on the way to Mars will have to wear swimming goggles to save their sight say NASA experts

### How An Astronaut's Eyes Are Damaged By A Year In Space

JV Chamary Contributor @ Science  
I cover science and technology in popular culture

Houston, We Have an Eye Problem

### Astronauts Returning to Earth With Vision Problems

Astronauts' eyes are at risk after too much time in space

Space travel is causing visual impairment for some astronauts. Will this prevent travel to Mars?

NASA's new sleeping bags could prevent eyeball 'squashing' on the ISS  
It sucks fluid out of astronaut's heads and toward their feet.



# What's So Special About the Eye?



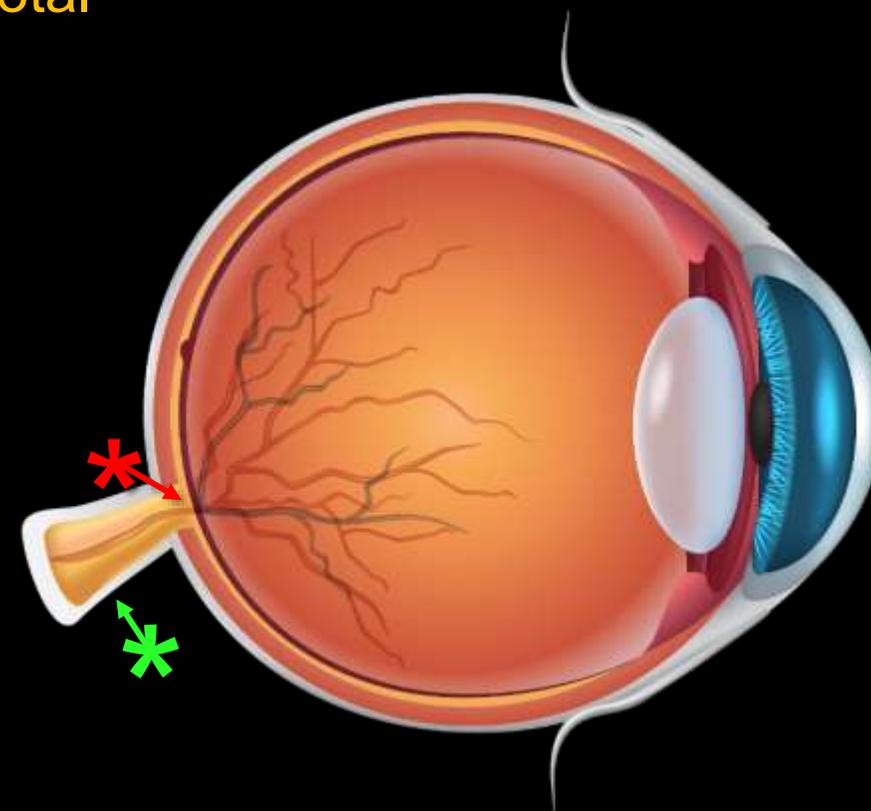
Image credit: NASA



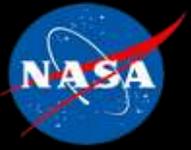
# What's So Special About the Eye?



- Only about 1" in diameter, but provides ~80% of our total sensory input
- Optic nerve, optic nerve head, and retina...
  - *Central nervous system*
    - Behind blood-brain barrier
    - Susceptible to permanent loss
  - Optic nerve
    - Connects eye to brain
    - Bathed in cerebrospinal fluid (CSF)
  - Optic nerve head (ONH) / "Optic disc"
    - Where optic nerve meets eye
    - Has *intracranial pressure (ICP)* posteriorly, *intraocular pressure* anteriorly



<https://similarpng.com/eye-anatomy-details-clipart-png-2/>



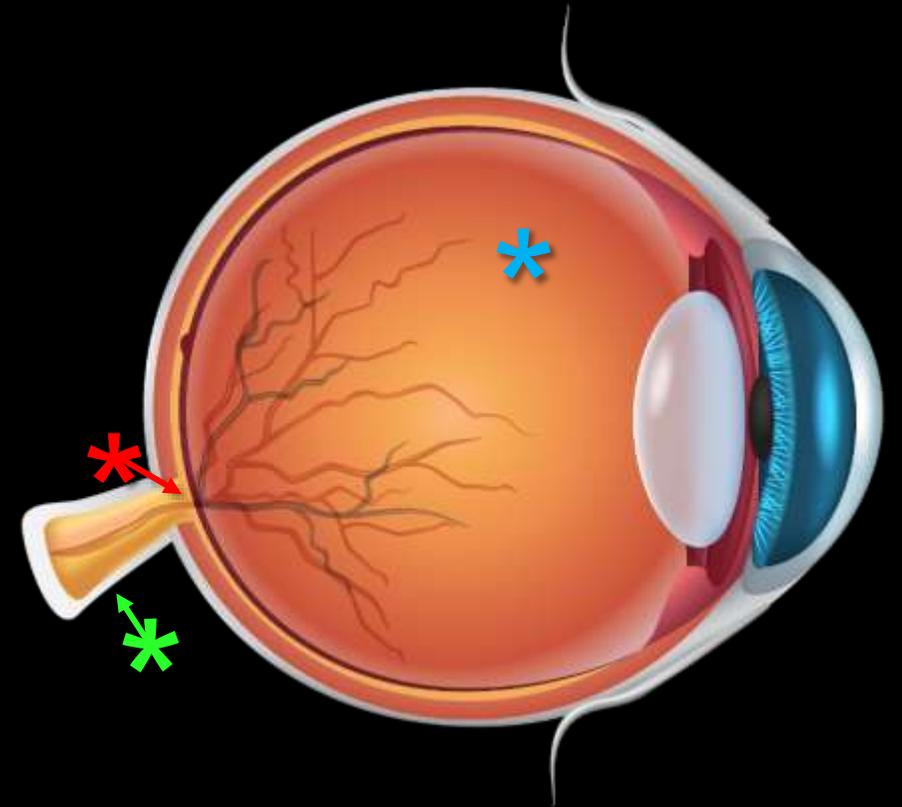
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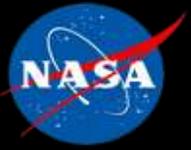
## ■ Optic nerve, optic nerve head, and retina...(cont.)

### • Retina

- Converts light energy into neural signals
  - Sent through nerve fibers (via **optic disc** & **optic nerve**)  
→ brain → “vision”
- Extremely high metabolism: *High demands, low reserves*
  - Photoreceptor mitochondria operate at ~70-80% capacity
  - Retinal nerve fiber axons: Non-myelinated w/in eye
  - **Requires reliable, sustained blood supply**



<https://similarpng.com/eye-anatomy-details-clipart-png-2/>



# What's So Special About the Eye?



- SANS-relevant ocular anatomy:





# What's So Special About the Eye?



- SANS-relevant ocular anatomy:
  - Retina
  - Fovea - Central vision
  - Optic nerve head (optic disc)
- Optical coherence tomography (OCT)
  - Onboard the ISS since 2013
  - Our most critical tool to detect and monitor SANS
  - Provides non-invasive, high resolution, cross-sectional images

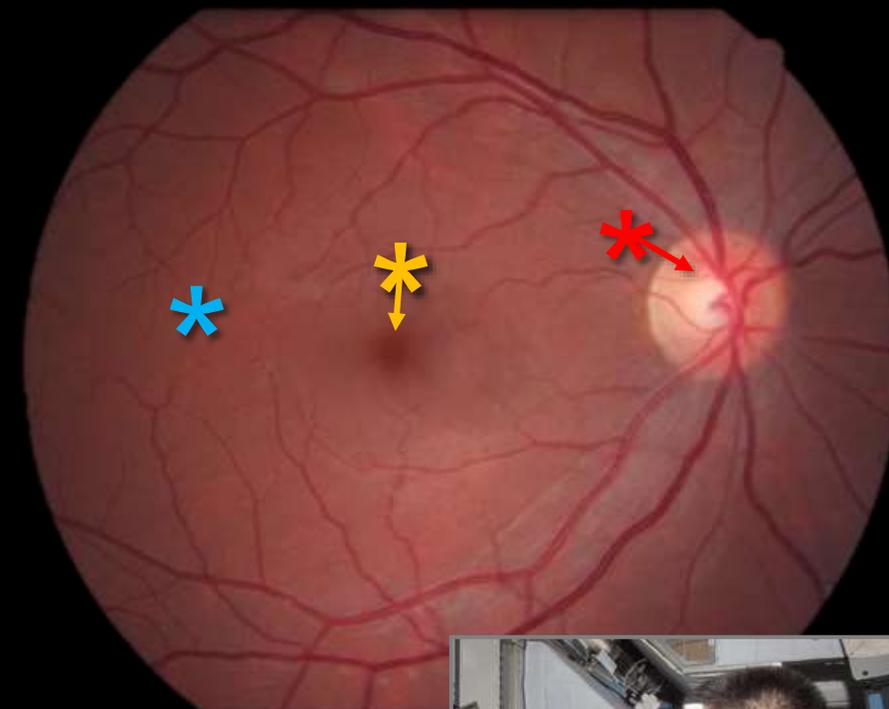


Image credit: NASA



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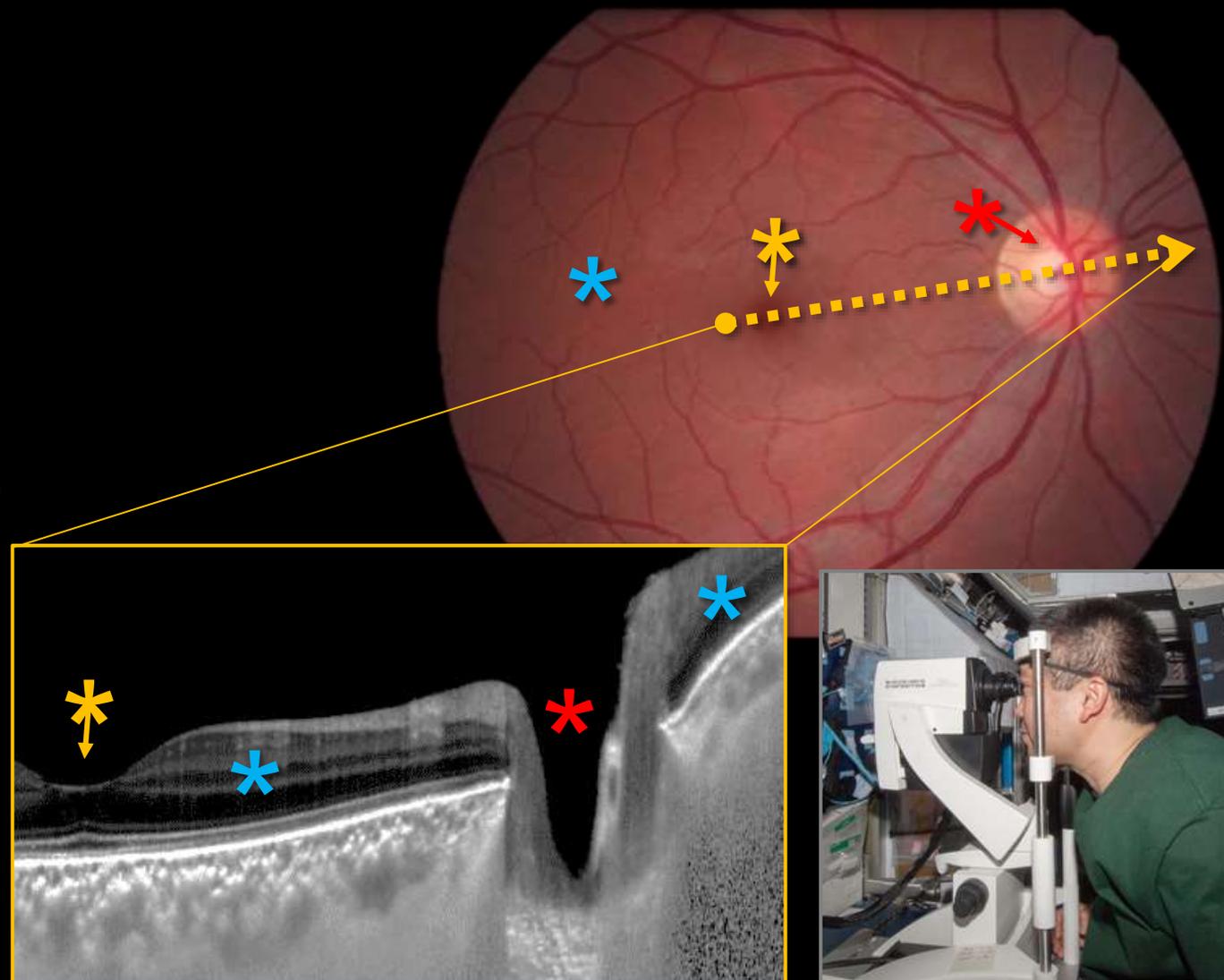


Image credit: NASA



# What's So Special About the Eye?



- SANS-relevant ocular anatomy:
  - Retina
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  - Optic nerve head (optic disc)
  - **Choroid** - Dense vascular bed; serves back half of retina
  - **Retinal pigment epithelium (RPE)** - Blood-brain barrier
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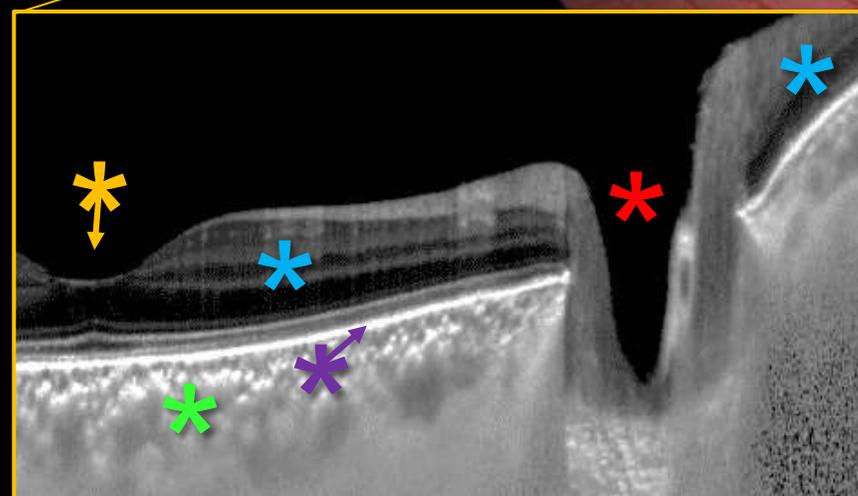
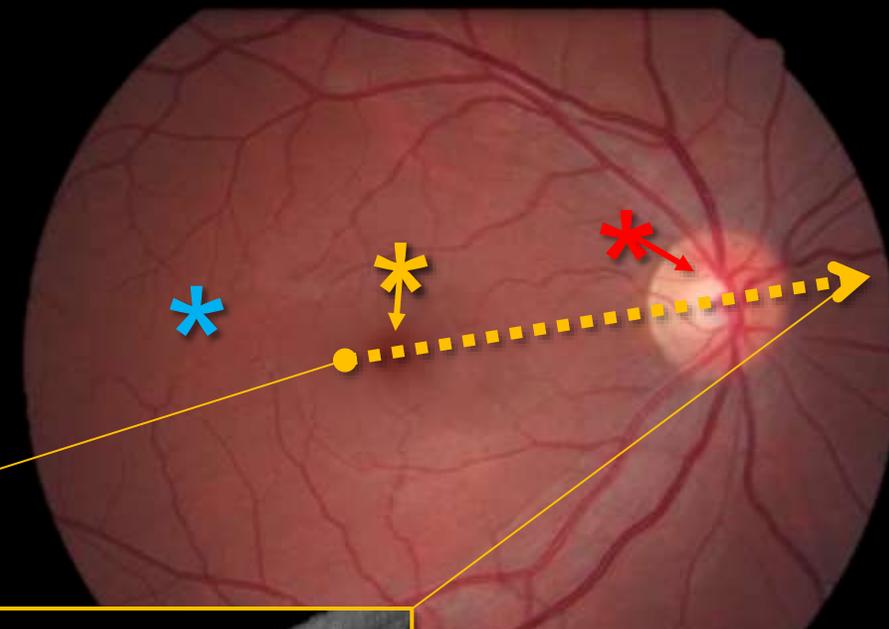


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## ■ Optical coherence tomography (OCT)

- Onboard the ISS since 2013
  - Our most critical tool to detect and monitor SANS
  - Provides non-invasive, high resolution, cross-sectional images
- OD = Right eye; OS = Left eye
  - OU = Both eyes

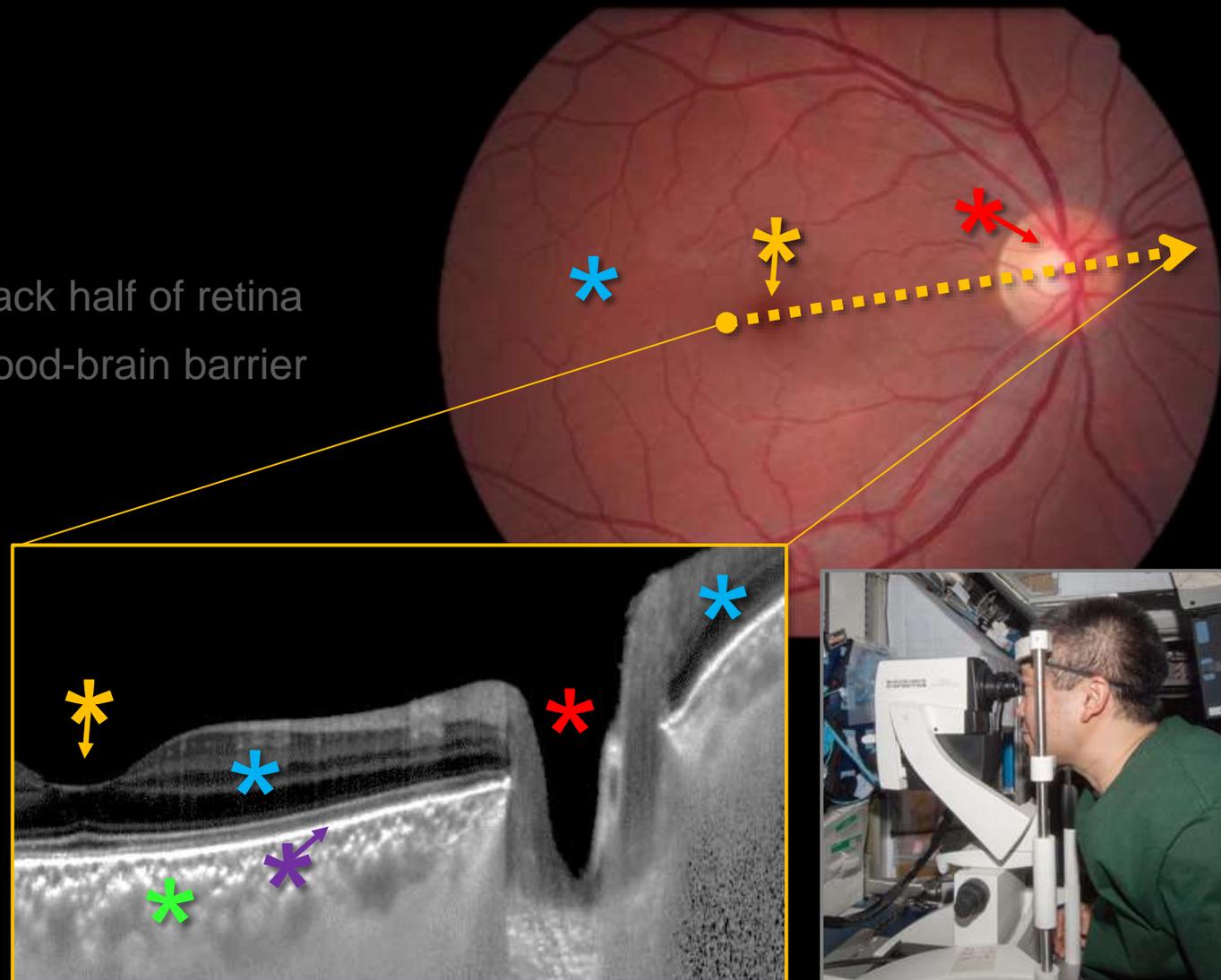


Image credit: NASA



# Astronaut Case Report



Image credit: NASA



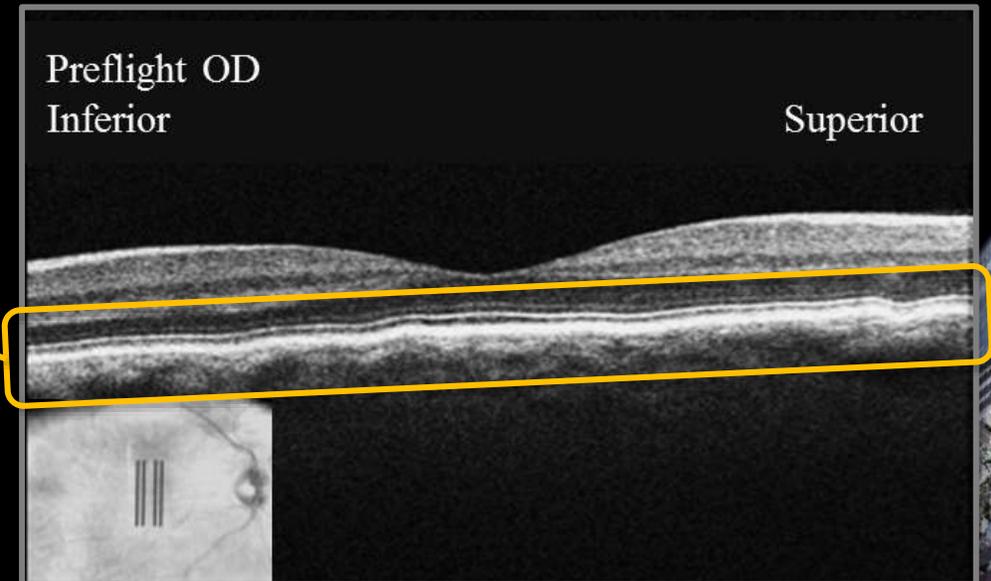
# Astronaut Case: Pre-ISS Flight

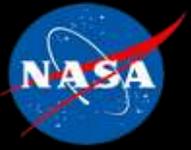


- First spaceflight: Space shuttle mission (short duration)
  - Flight occurred before special ocular test battery introduced
    - Pre-flight ocular data limited: Comprehensive eye exam & visual fields; all normal
  - **+0.75D refractive error (RE) shift** (pre-to-post-flight)

- Years later, prior to ISS flight:
  - MRI & ultrasound: **Mild globe flattening OU\***
  - OCT: **Mild choroidal folds OU\***

\* *Presumed consequences of short-duration spaceflight*

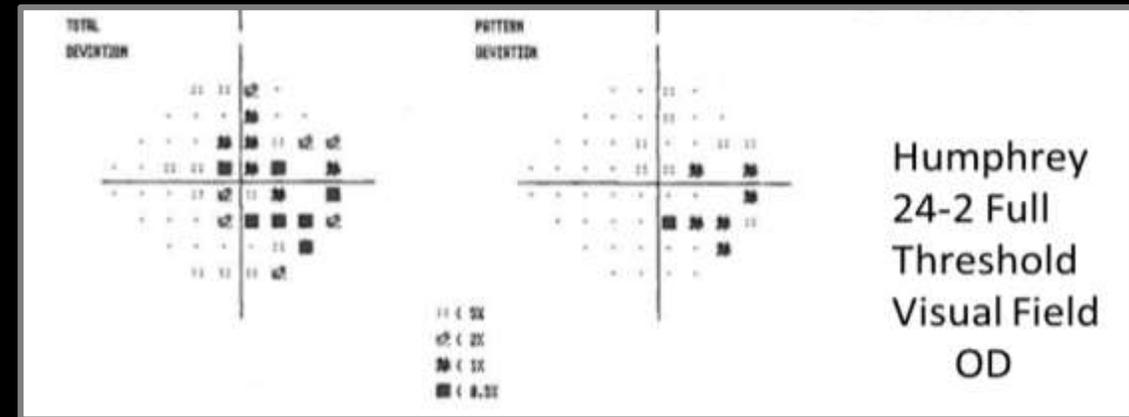




# Astronaut Case: In- & Post-ISS Flight



- In-Flight: ISS (long-duration)
  - Subjective decrease in VA OU (dist & near); Otherwise, asymptomatic
  - Mild optic disc edema OS
- Post-Flight Diagnoses
  - Mild optic disc edema OU
    - Resolved by 6M post-flight
  - Enlarged blind spots OU: Resolved →
  - Moderate-to-severe globe flattening OU
    - Persists, years post-flight
  - +1.50D shift OU (vs. pre-ISS);  
+2.25D shift OU (vs. pre-Shuttle)
    - Persists, years post-flight
    - No loss in best-corrected VA (i.e., 20/20 or better)

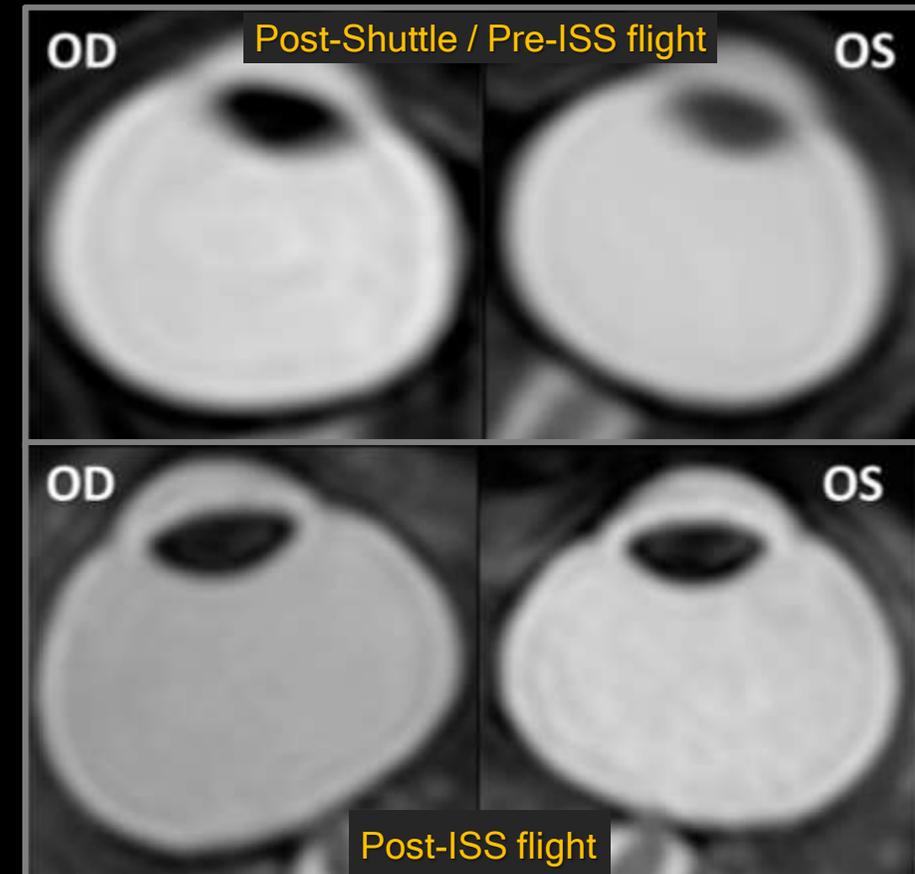


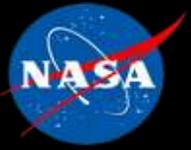


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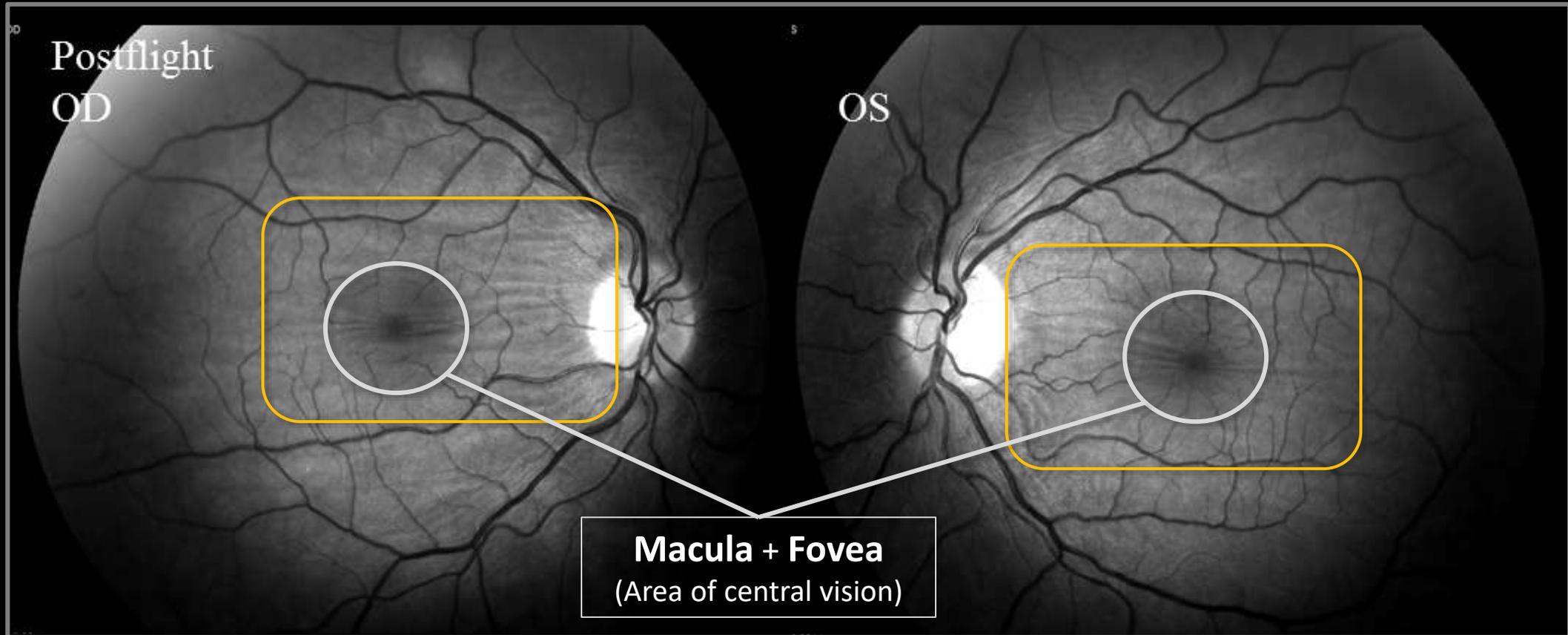




# Astronaut Case: Post-ISS Flight



- Post-Flight Diagnoses
  - Chorioretinal folds (OD>OS)

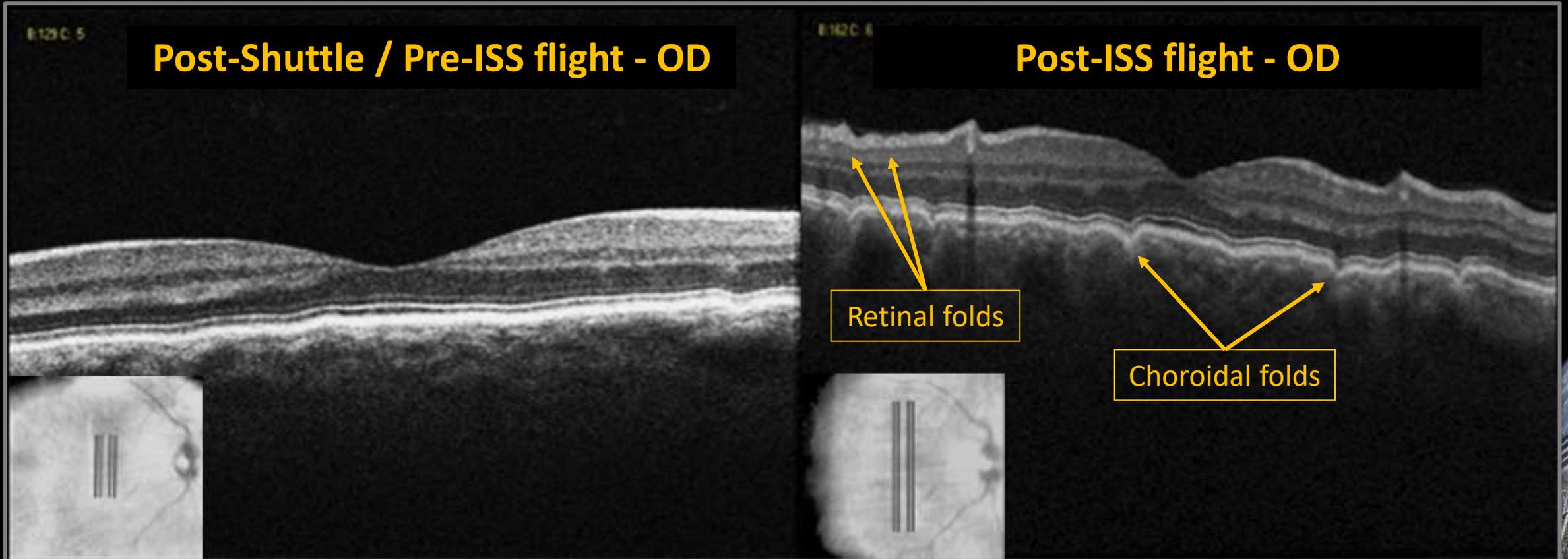


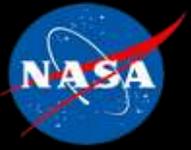


# Astronaut Case: Post-ISS Flight



- Post-Flight Diagnoses
  - **Chorioretinal folds (OD>OS)** – No distorted vision OD/OS. No loss in best-corrected VA

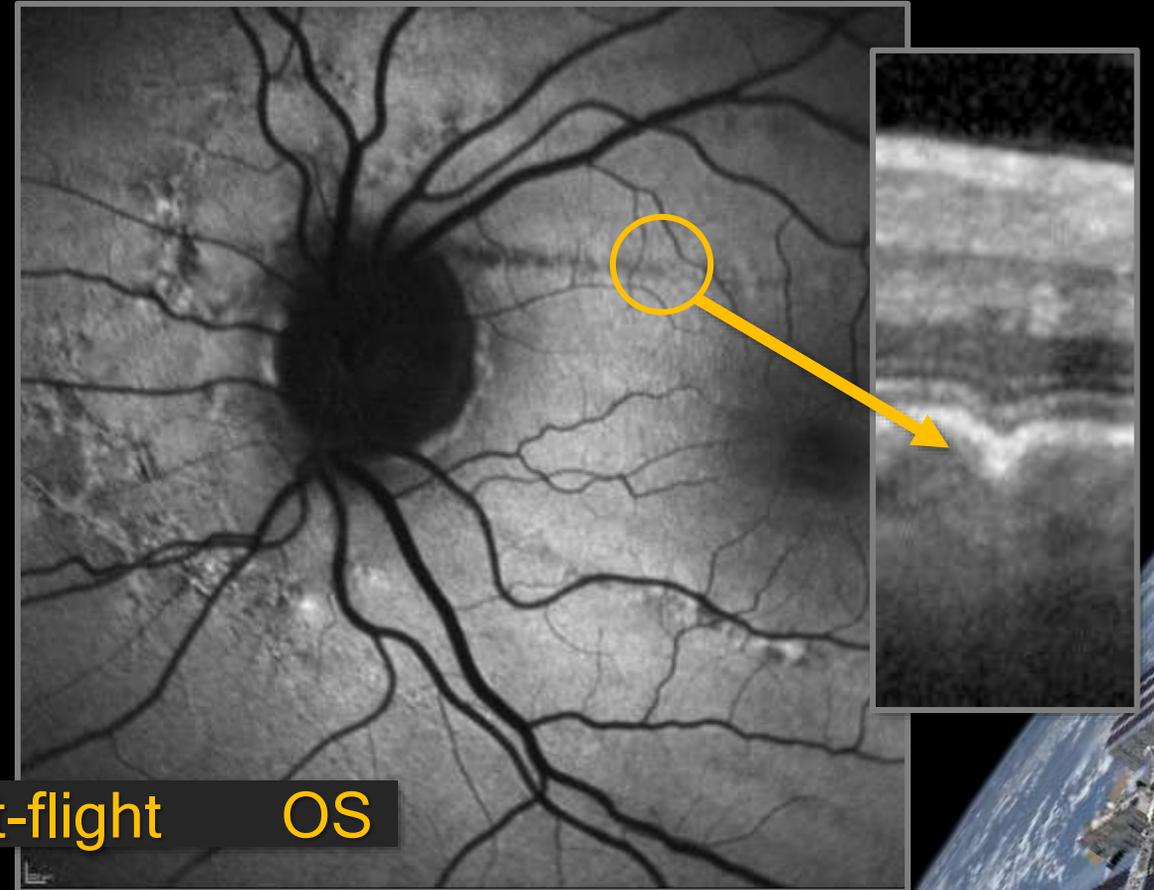
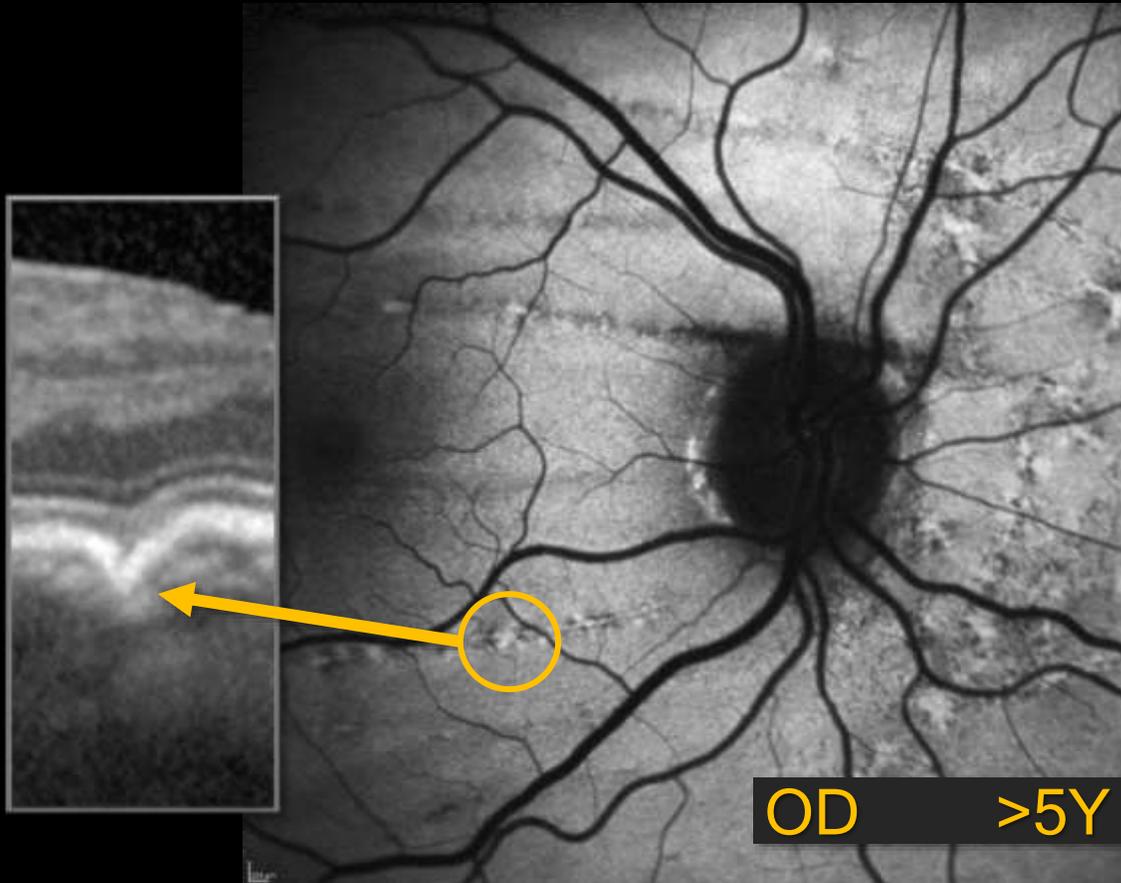


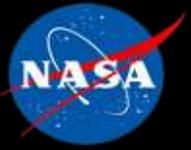


# Astronaut Case: Post-ISS Flight



- Post-Flight Diagnoses
  - **Disrupted RPE (OD>OS)** – Discovered >5 years post-flight





# Astronaut Case: Summary



## ■ Current State

- **Asymptomatic. No reduction in visual performance detected**
- **Moderate-severe globe flattening + hyperopic RE shift: Persist OU**
- **Choroidal folds: Improved, but persist OU; RPE disruption: Persist OU**
  - No retinal damage detected
  - Being monitored annually

## ■ Highlights the “Big Four” signs of SANS:

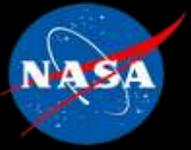
- **Optic disc edema**
- **Chorioretinal folds**
- **Globe flattening**
- **Shifts in refractive error**





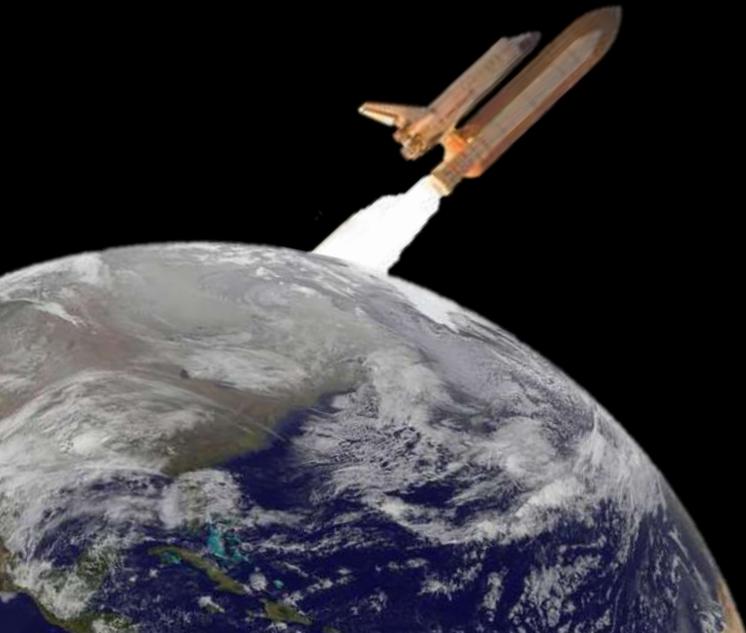
What *in the world* is going on?





Mission Duration: **Short** (<30 days)

Micro-gravity





# Mission Duration: **Short** (<30 days)

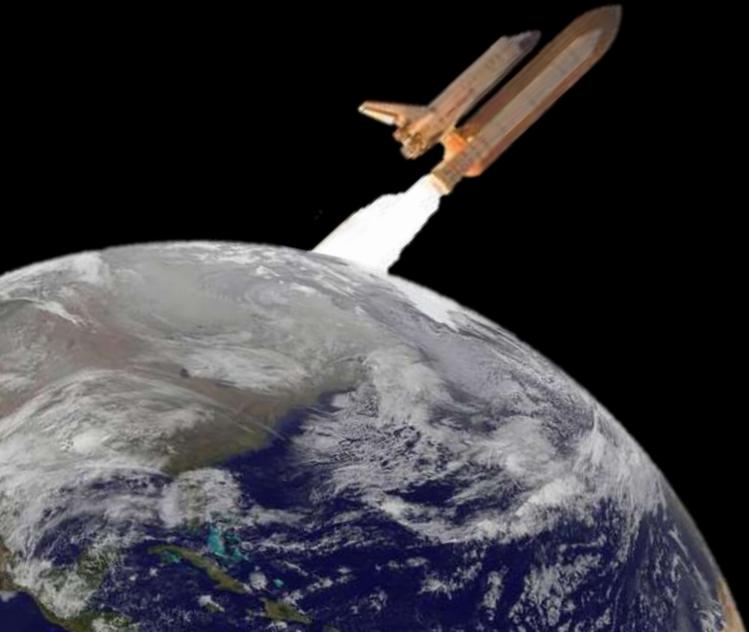
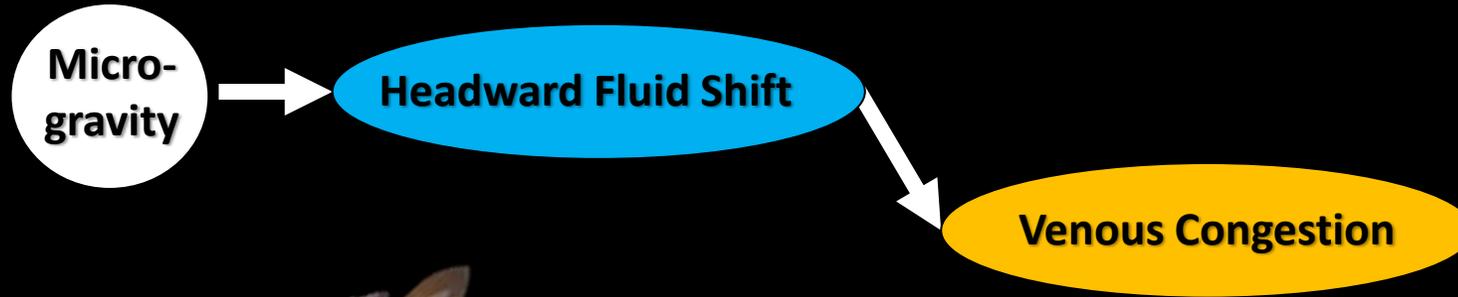


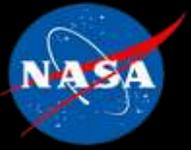
Image credits: NASA

**“Puffy Face Syndrome”**

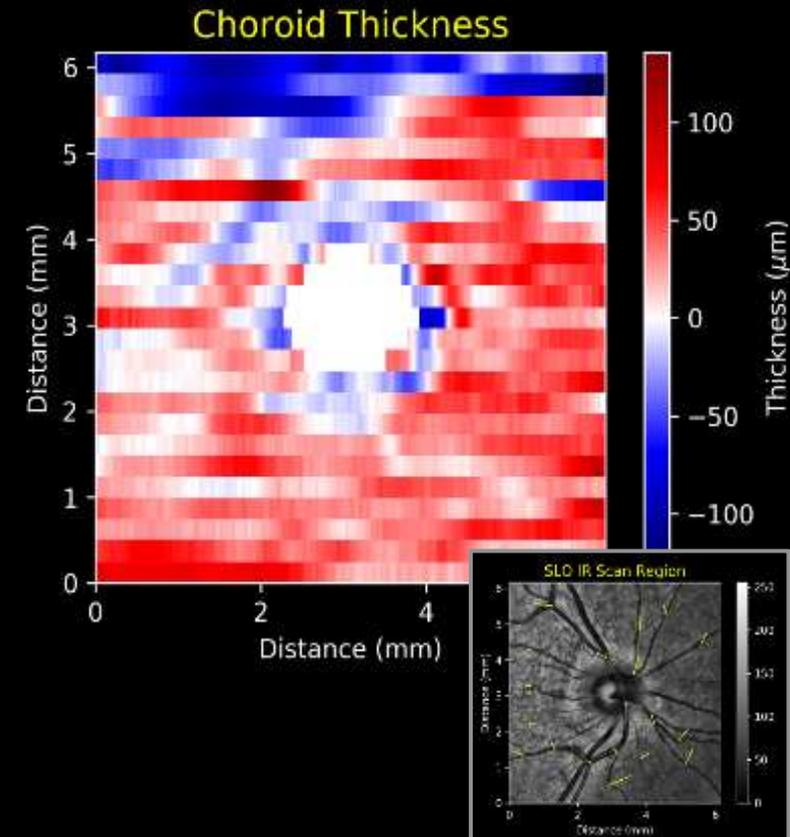
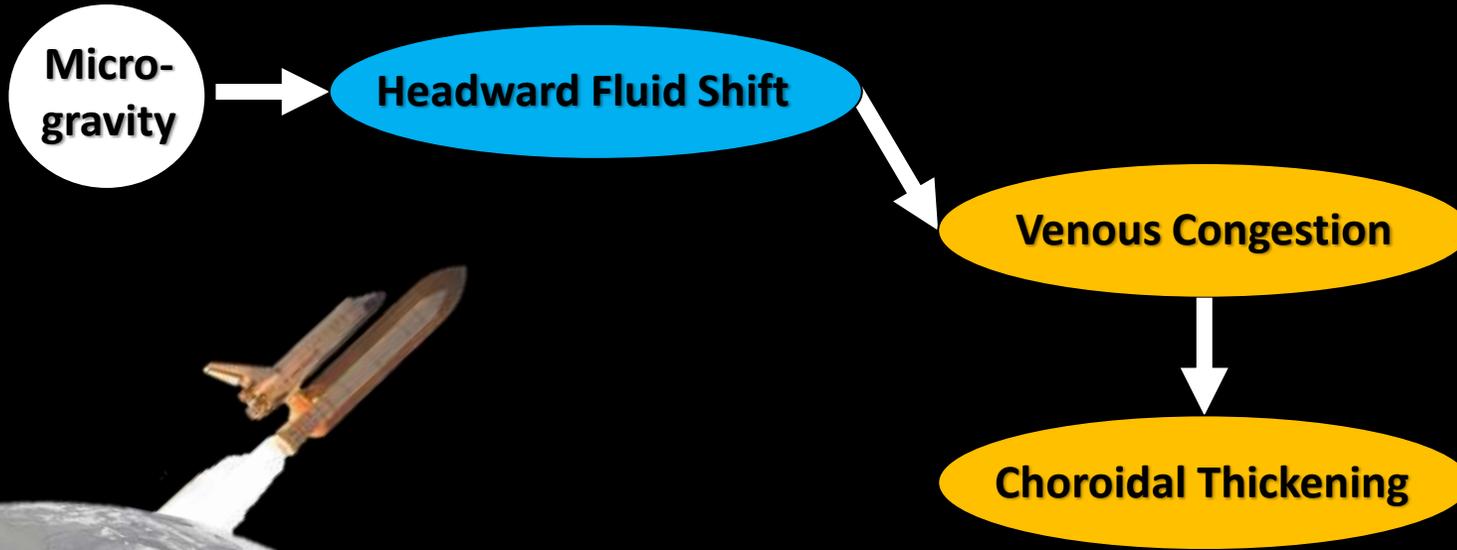


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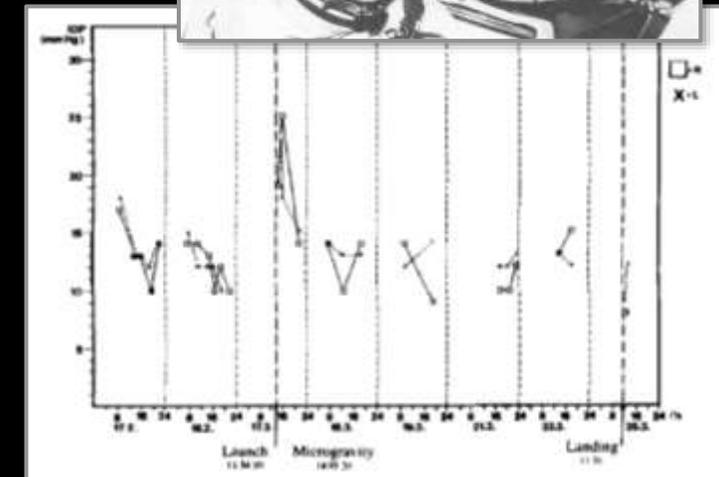
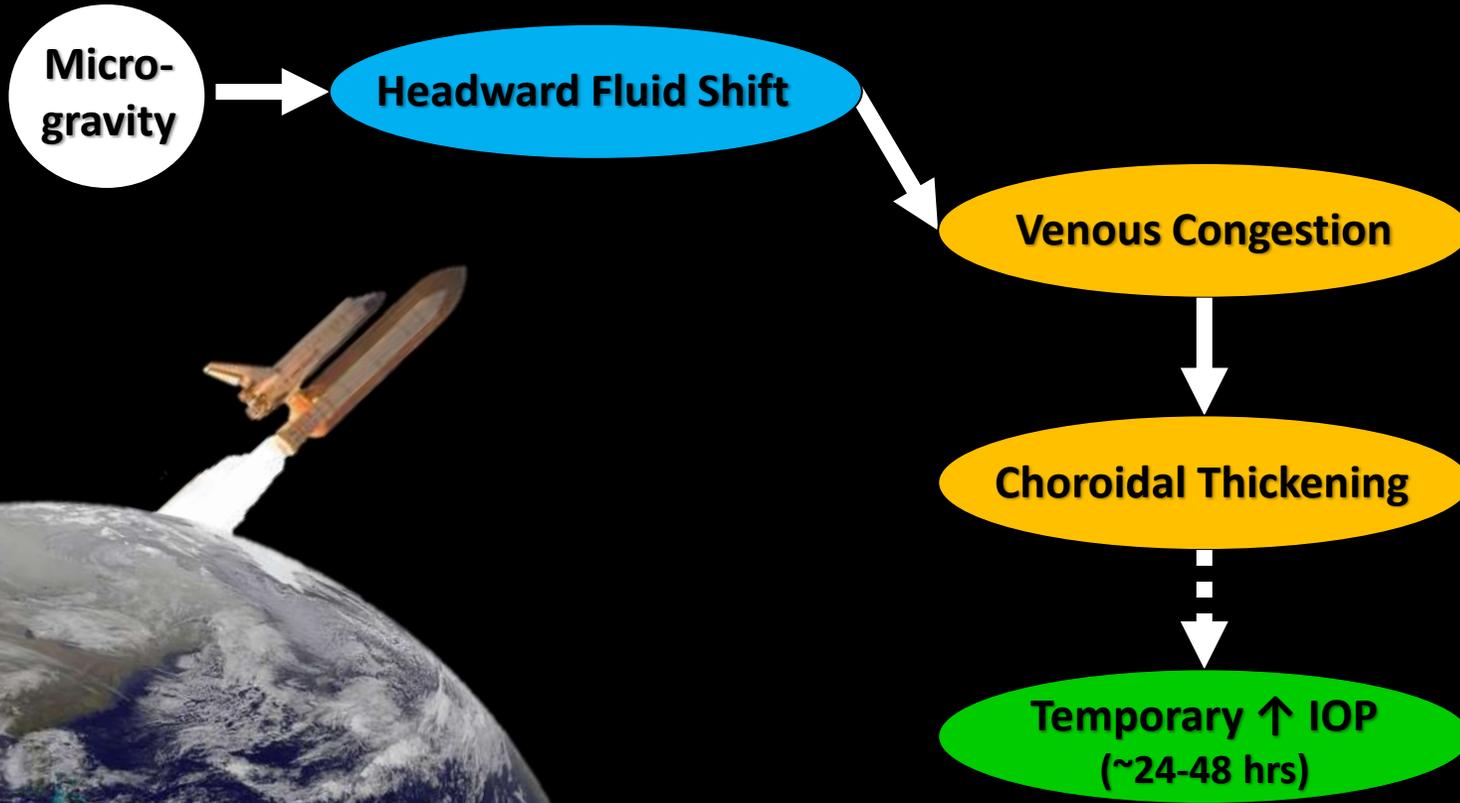


Source: Mayra Nelman & Simon Clemett (NASA)



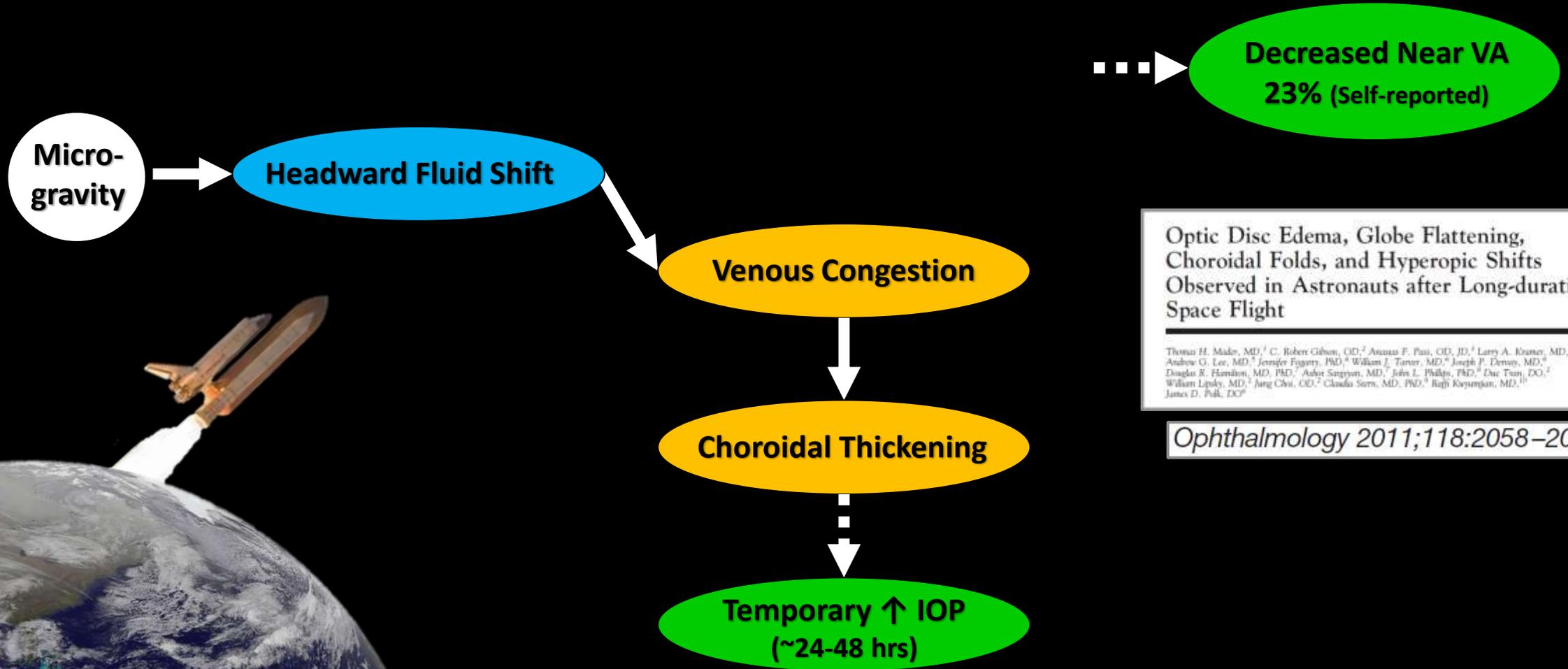
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DRAEGER J, SCHWARTZ R, GROENHOFF S, STERN C. *Self-tonometry under microgravity conditions*. Aviat Space Environ Med 1995; 66:568-70.





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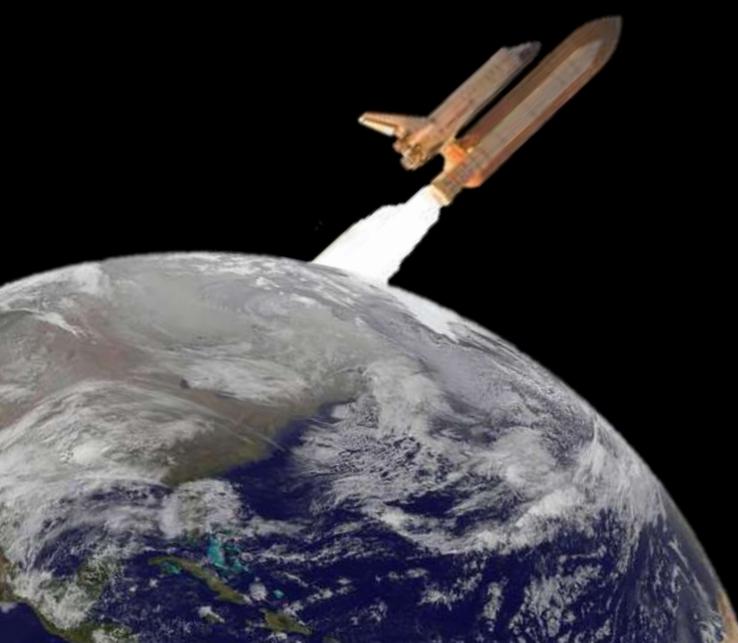
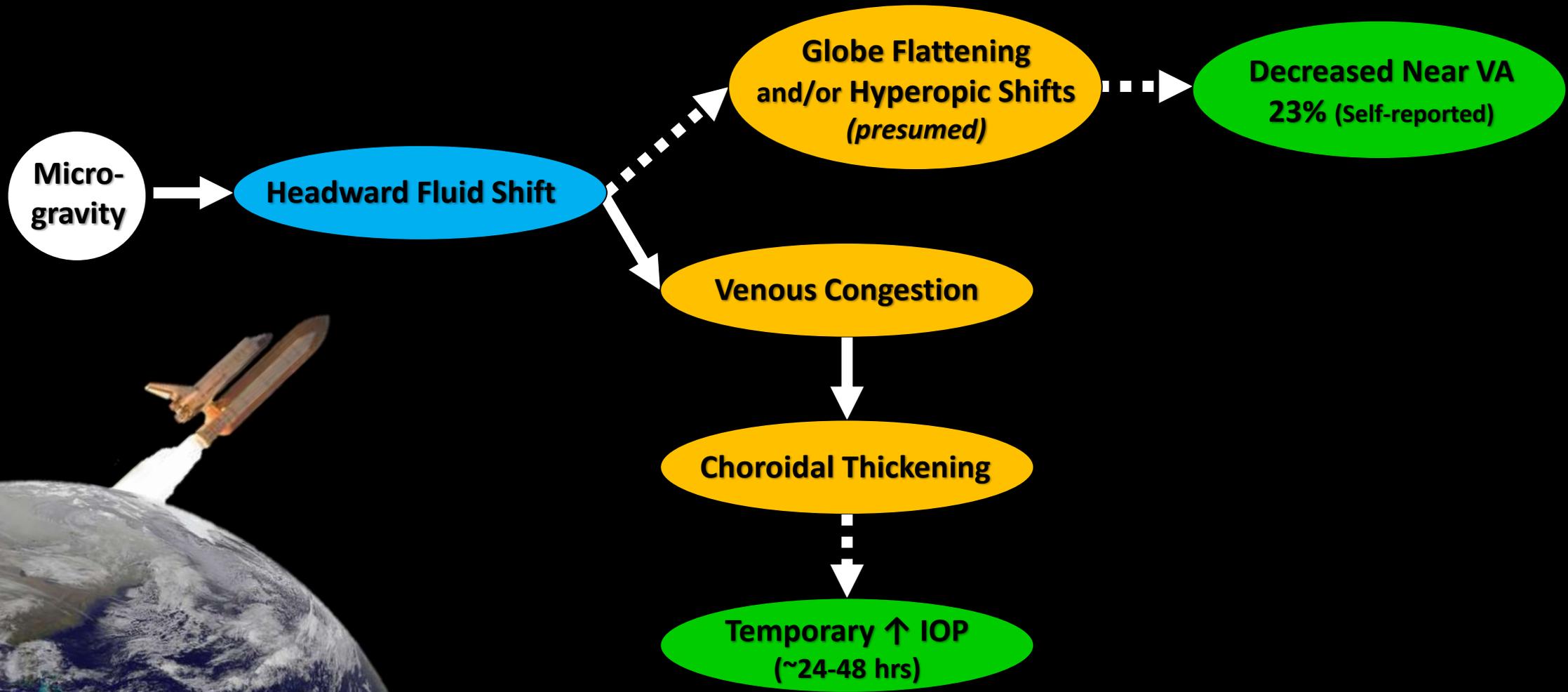
Optic Disc Edema, Globe Flattening, Choroidal Folds, and Hyperopic Shifts Observed in Astronauts after Long-duration Space Flight

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*Ophthalmology* 2011;118:2058–2069



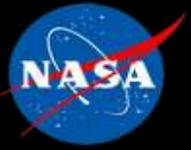
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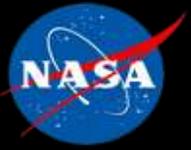
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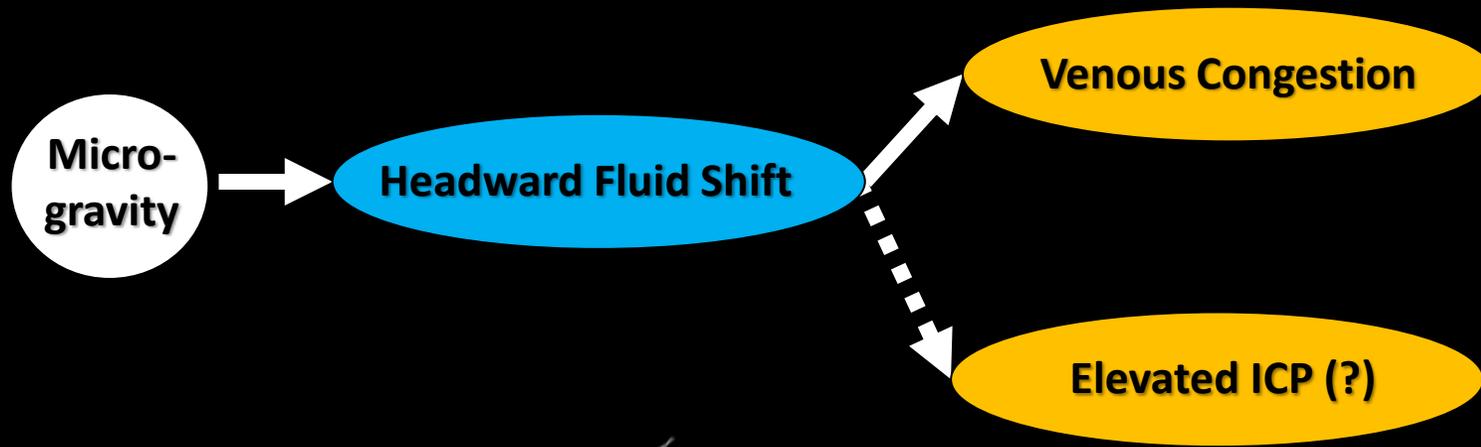


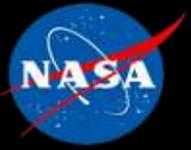
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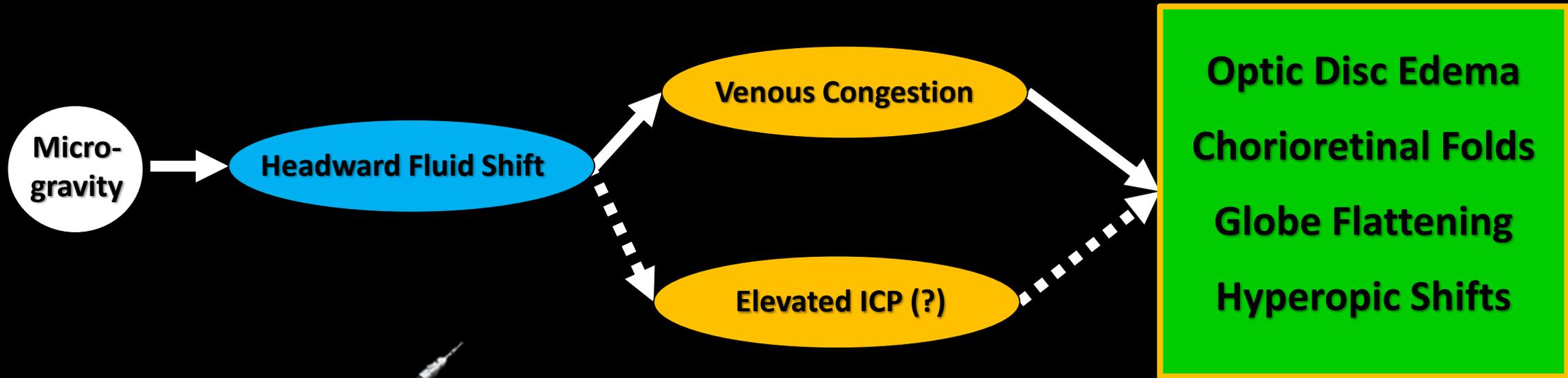


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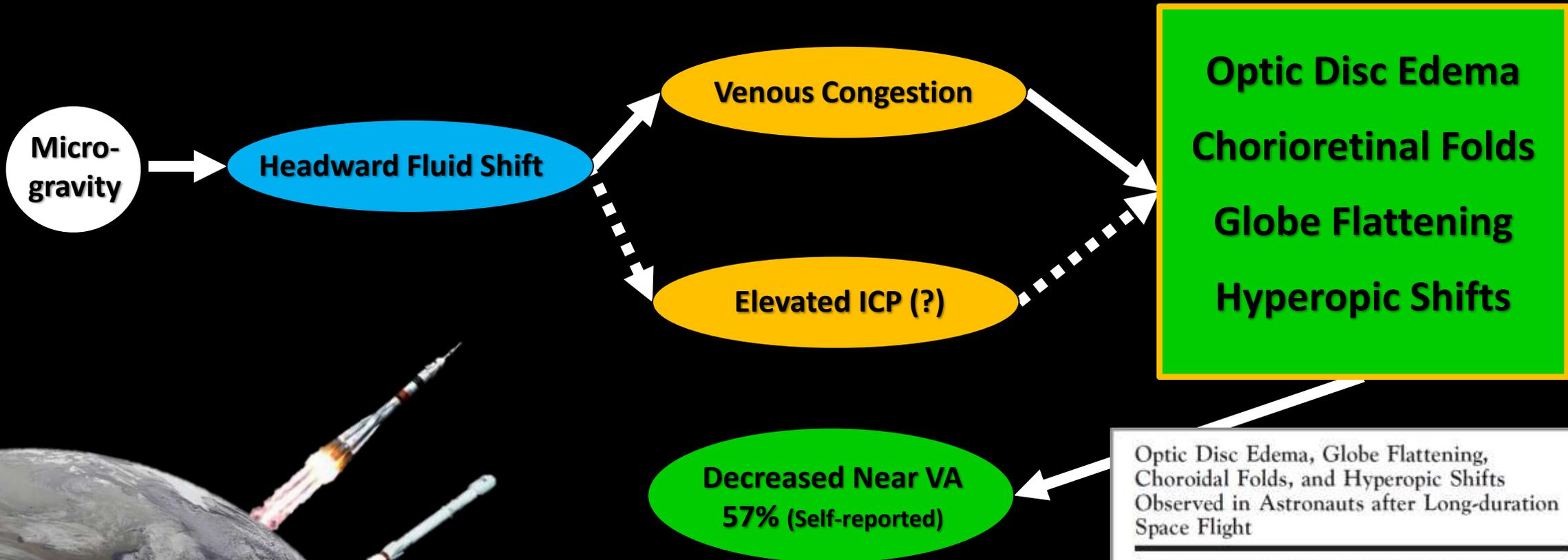


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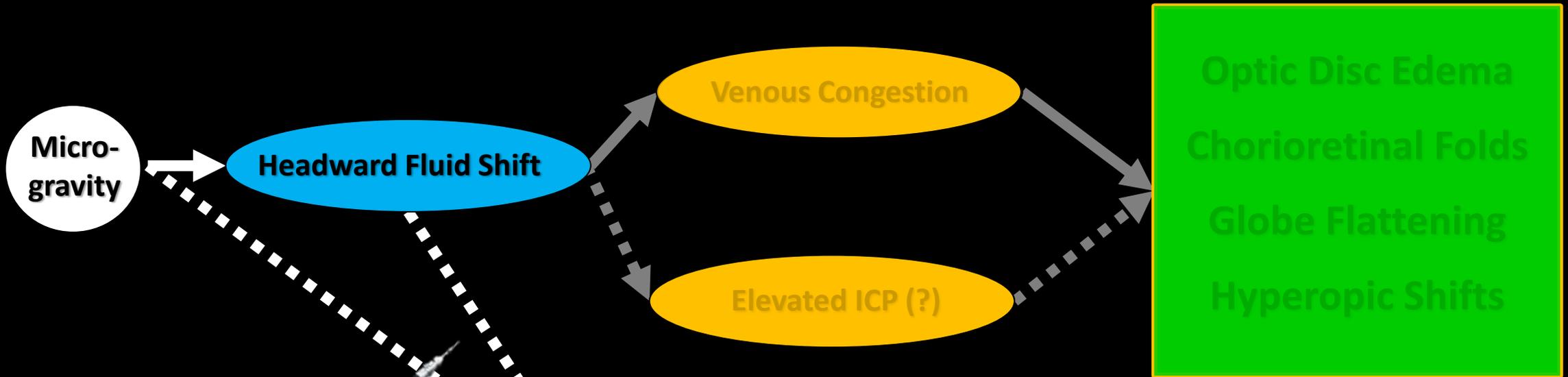


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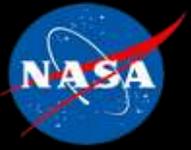


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ORIGINAL ARTICLE

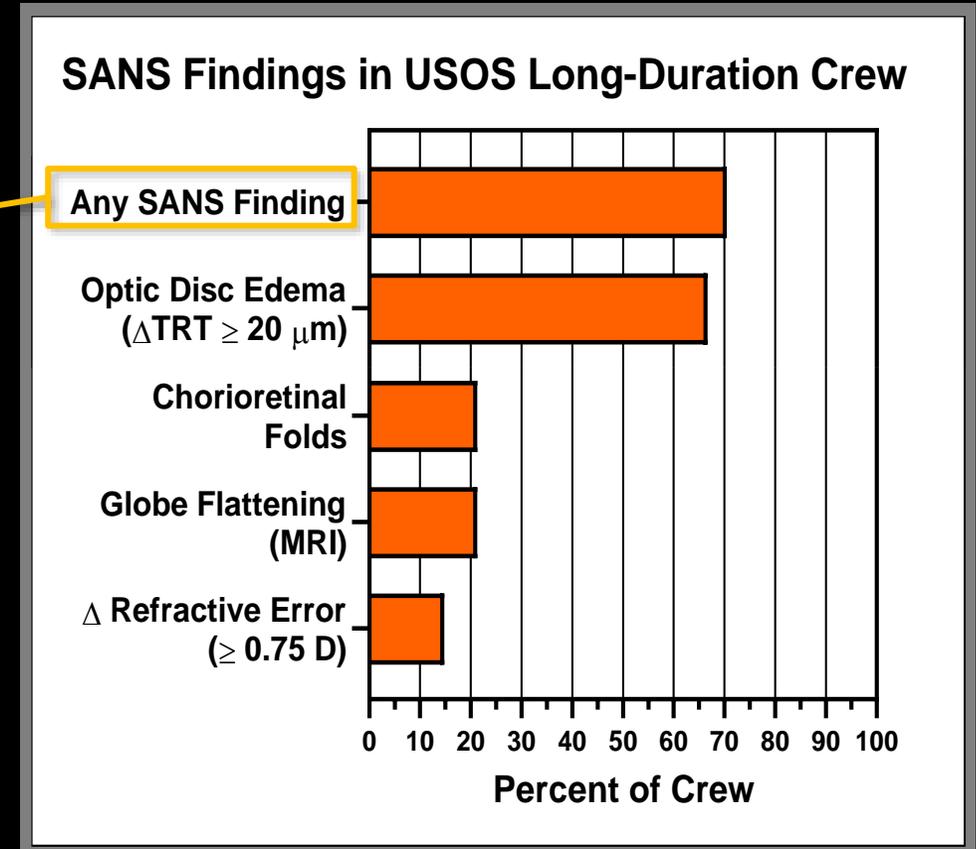
Effects of Spaceflight on Astronaut Brain Structure as Indicated on MRI

Donna R. Roberts, M.D., Moritz H. Albrecht, M.D., Heather R. Collins, Ph.D., Davud Asemani, Ph.D., A. Rano Chatterjee, M.D., M. Vittoria Spampinato, M.D., Xun Zhu, Ph.D., Marc I. Chimowitz, M.B., Ch.B., and Michael U. Antonucci, M.D.



# Mission Duration: **Long** (~6-12 mo)

- No permanent loss of vision or cognitive function yet detected in long-duration crew
- About 69% of long-duration crewmembers present w/ signs of SANS
  - Diagnosed in males *and* females
  - *Can't yet predict* who will develop SANS
- Severity thought *related to mission duration*
- Some changes can become *permanent* (i.e., globe flattening, hyperopic shifts, choroidal folds)

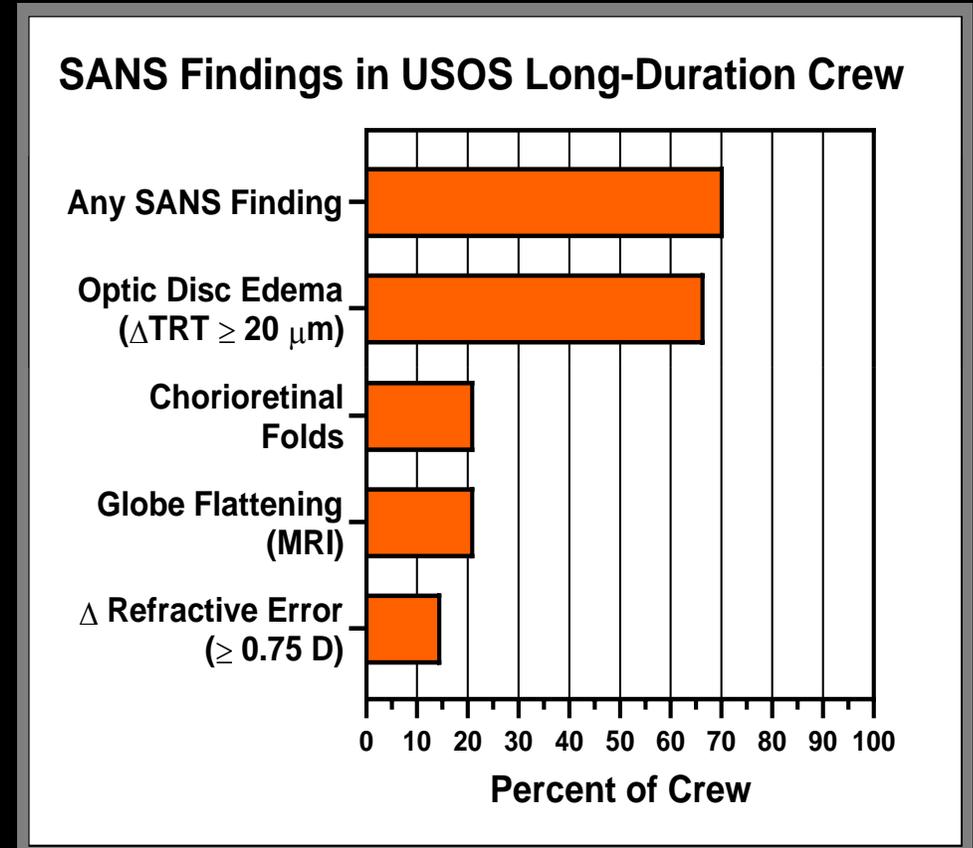


Data courtesy of NASA LSAH



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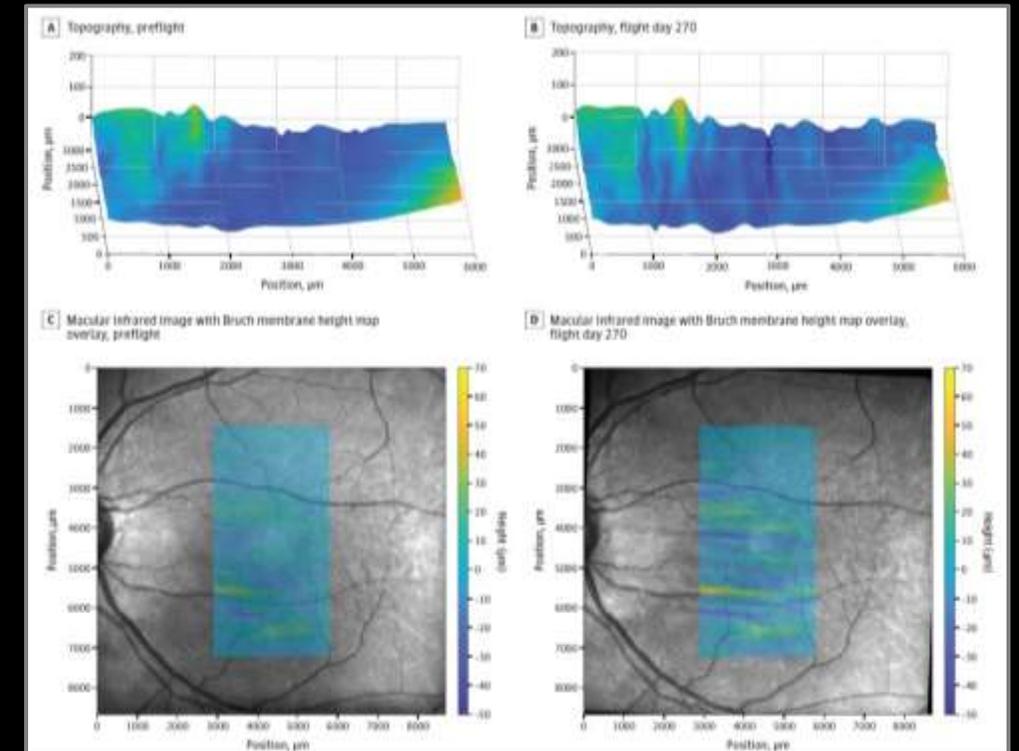


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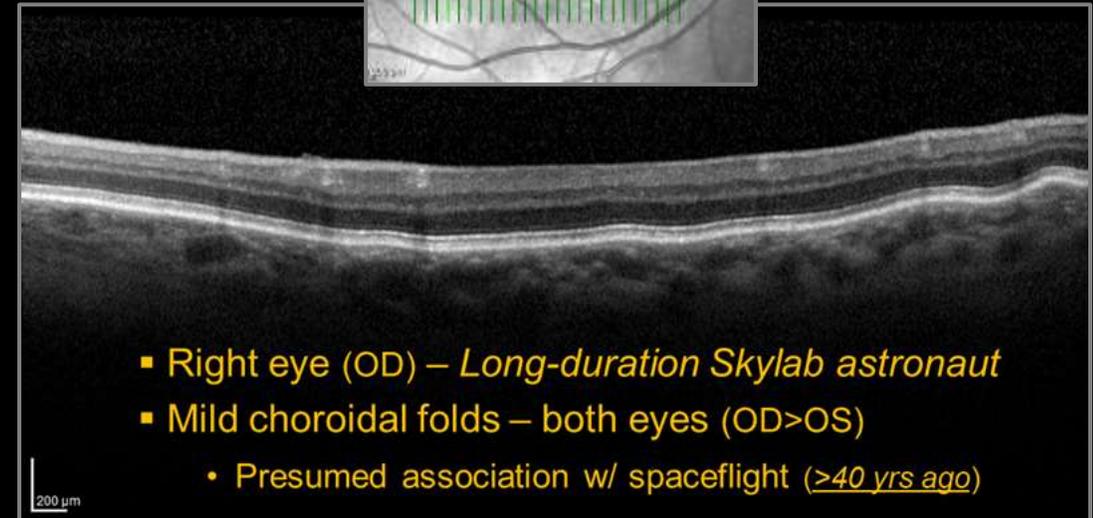
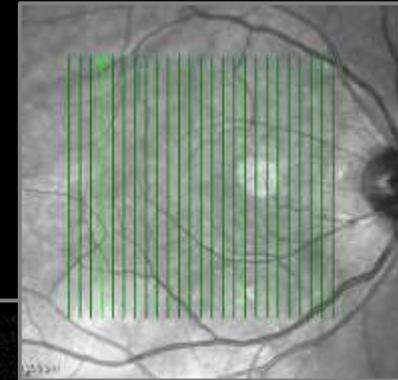


Macias BR, et al. Changes in the Optic Nerve Head and Choroid Over 1 Year of Spaceflight. JAMA Ophthalmol. 2021 Apr 29



## Mission Duration: **Long** (~6-12 mo)

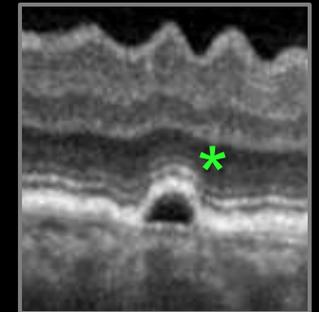
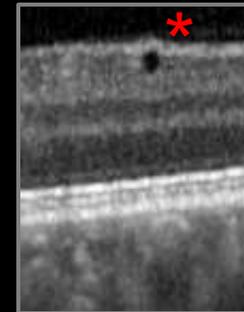
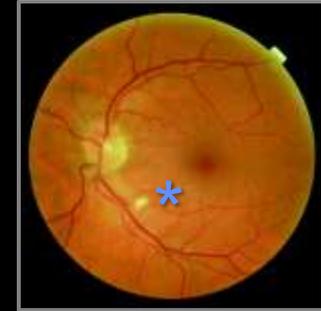
- No permanent loss of vision or cognitive function yet detected in long-duration crew
- About 69% of long-duration crewmembers present w/ signs of SANS
  - Diagnosed in males *and* females
  - *Can't yet predict* who will develop SANS
- Severity thought *related to mission duration*
- **Some changes can become permanent** (i.e., globe flattening, hyperopic shifts, choroidal folds)



## Mission Duration: **Long** (~6-12 mo)

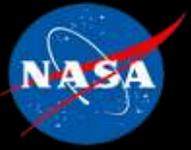
### Other neuro-ocular signs observed in crewmembers:

- Cotton wool spots\* (retinal ischemia)
- Retinal hemorrhages
- Retinal cysts\*
- Retinal pigment epithelial detachments (PEDs)\*
- Optic nerve sheath distention
- Brain changes (mentioned earlier)



However, these are not definitively associated w/ SANS or do not pose a significant risk to vision or missions



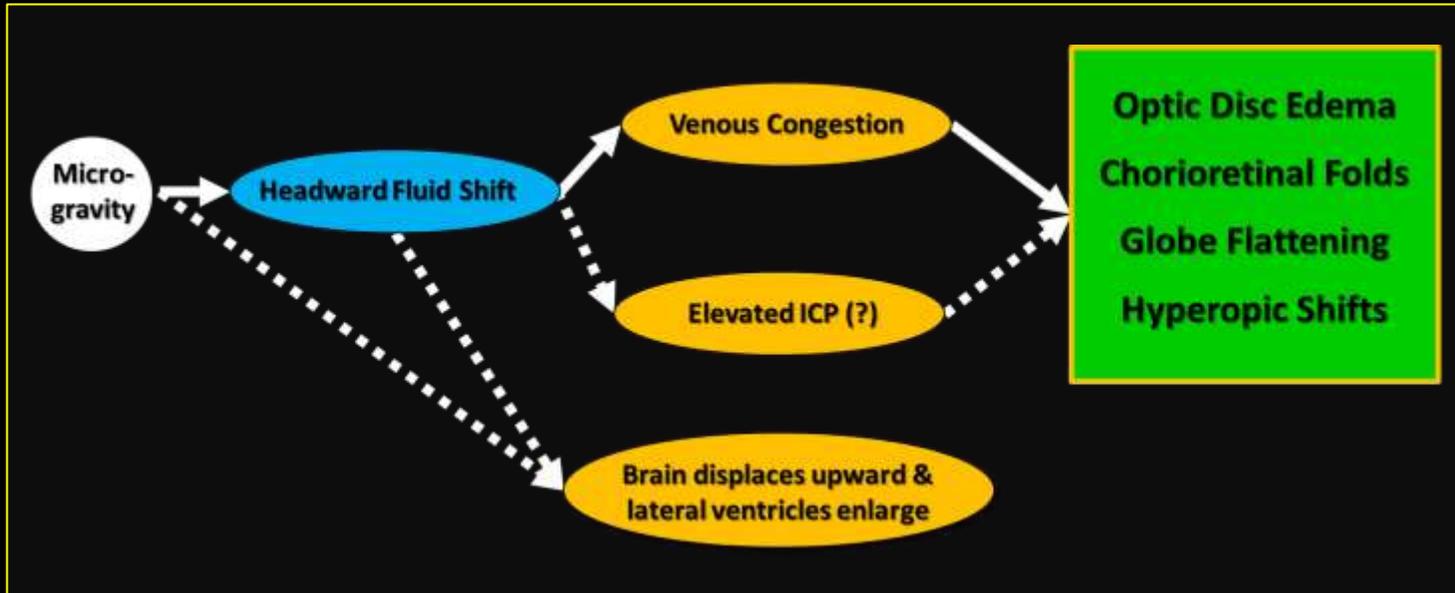


Mission Duration: *Deep Space Exploration* (~3 years)



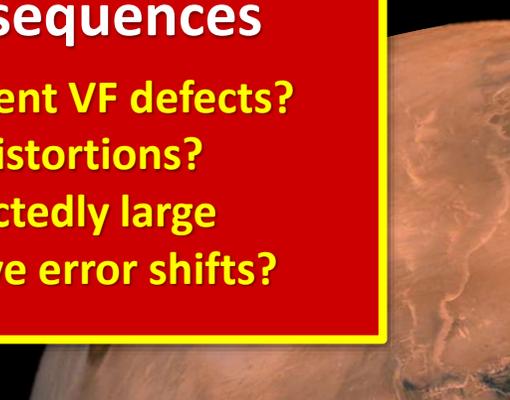
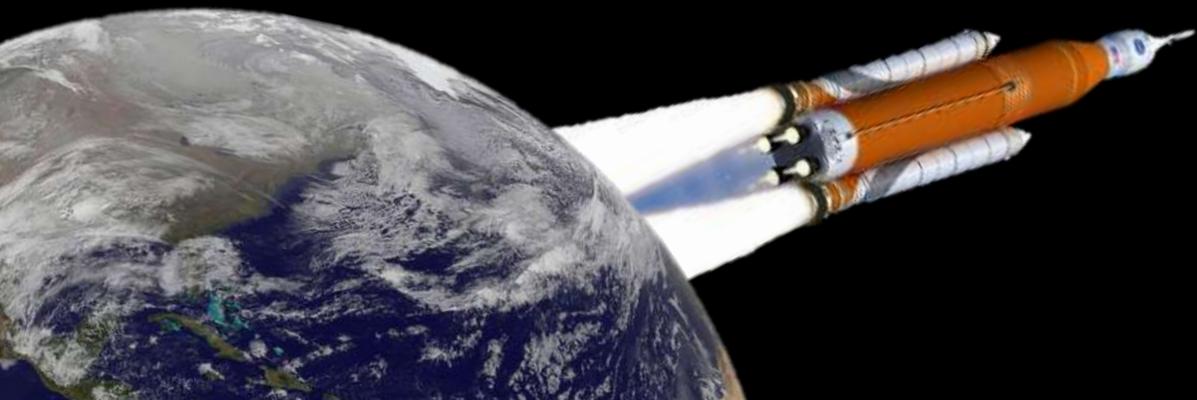
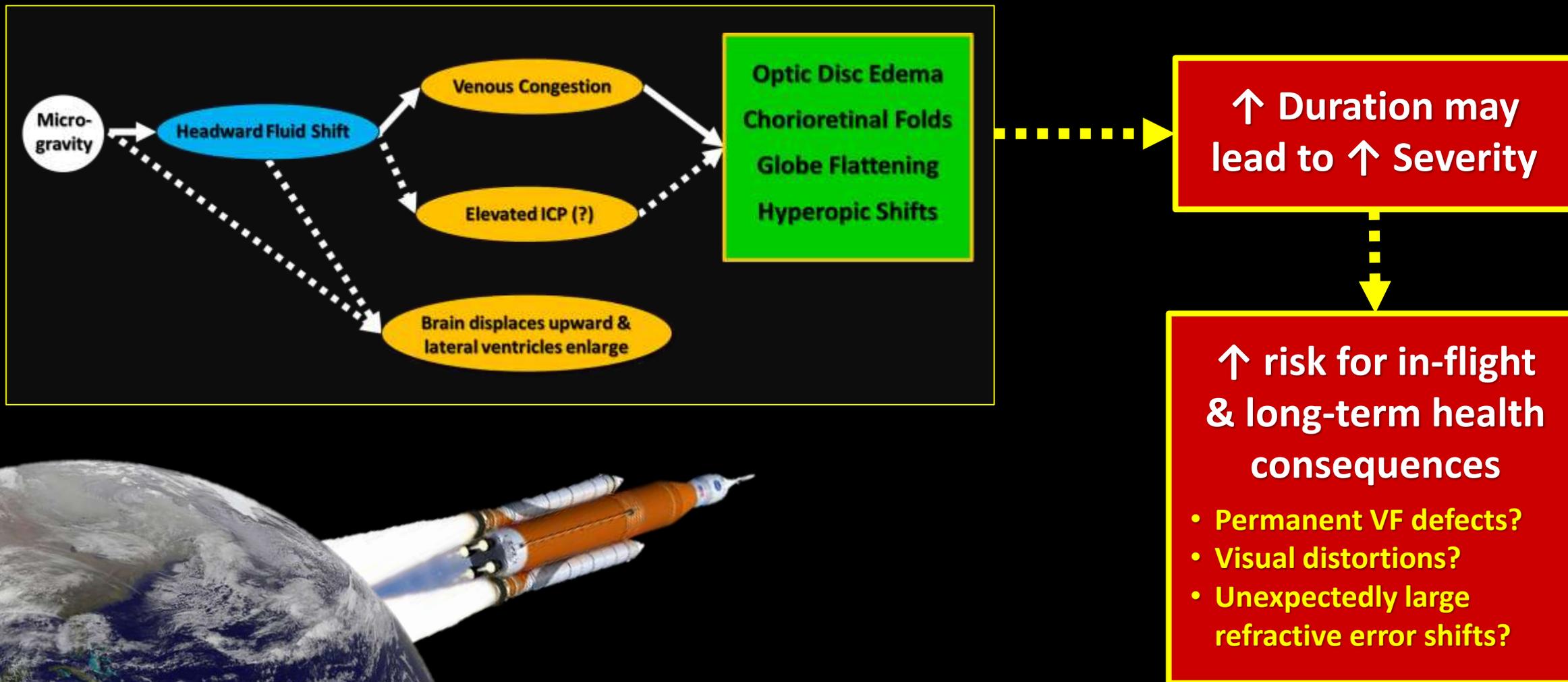


# Mission Duration: *Deep Space Exploration* (~3 years)





# Mission Duration: *Deep Space Exploration* (~3 years)





# Why is this Happening?



Image credit: NASA

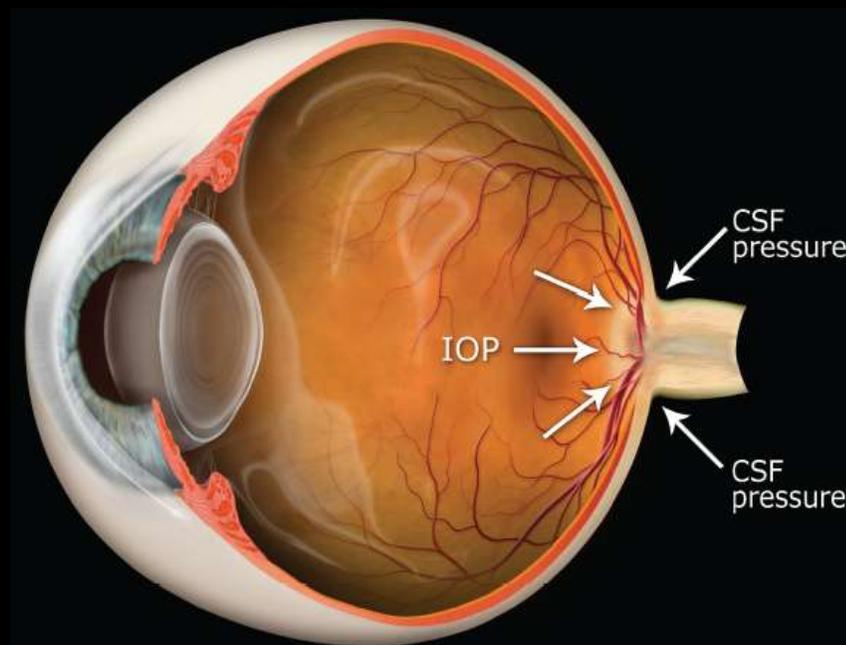


# Why is this Happening?



## Top SANS Pathogenesis Theories

- Hypothesis #1: *Increased optic nerve sheath pressure*
  - Due to an overall increase in ICP or localized to the perioptic subarachnoid space (e.g., due to compartmentalization)
  - Enough to cause an imbalance between ICP & intraocular pressure (i.e., a translaminar pressure gradient)
- Hypothesis #2: *Venous congestion* alters local physiology, reduces blood perfusion, and/or places direct pressure on retinal axons
- Hypothesis #3: *Individual anatomical/genetic factors*
  - e.g., Altered folate-dependent 1-carbon metabolism



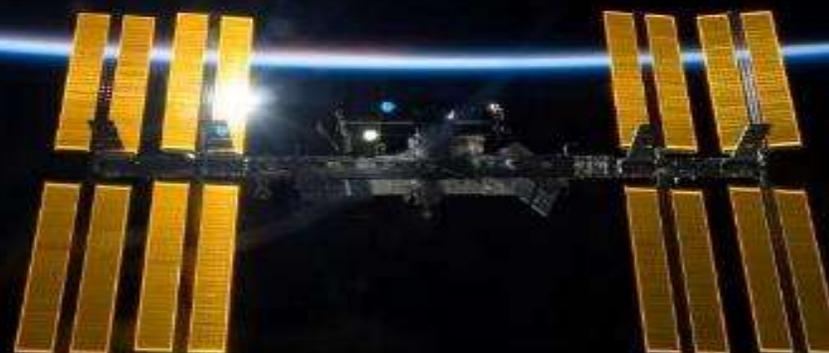


## **Part II: Challenges of Performing *Ocular Telemedicine* Onboard the International Space Station...and Beyond**



Tyson Brunstetter, MBA, OD, PhD, FAAO, FAsMA  
SANS Clinical Lead – Eyes/Vision

Space and Occupational Medicine Branch (SD3)  
NASA Johnson Space Center



*Introduction to Telehealth* – University of Missouri–St Louis

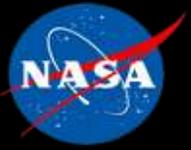
09 December 2022



# What ocular data are collected during ISS missions...and when?



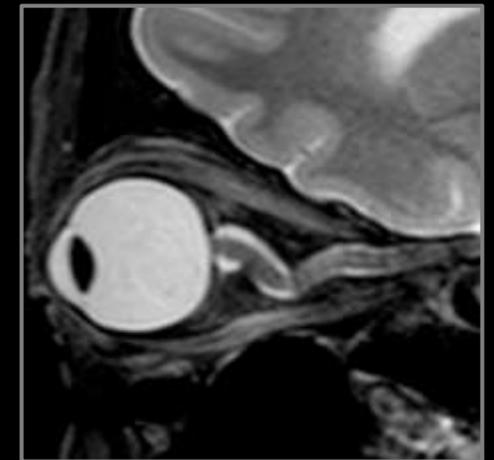
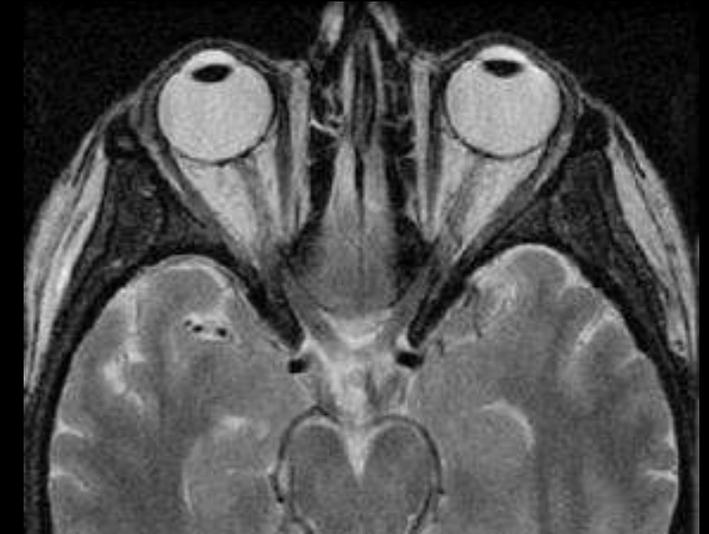
Image credit: NASA



# What On-orbit Ocular Data are Collected...and When?



Primary SANS/Ocular Tests	Pre-flight	On-orbit			Post-flight
		FD30	FD90	R-30	
<b>3T MRI</b> – Head & Orbits	X	--	--	--	X
<b>Comprehensive Eye Exam</b>	X	--	--	--	X
<b>Visual Field</b> – 24-2 SITA Standard	X	Not yet on-orbit			X
<b>Vision Screening</b> – VA, Amsler grid, Survey	X	X	X	X	X
<b>Retinal Photography</b> – Fundoscopy / MCI	X	X	X	X	X
<b>Optical Coherence Tomography</b>	X	X	X	X	X
<b>Ocular Ultrasound</b>	X	X	X	X	X
<b>Tonometry</b> – Intraocular Pressure	X	X	X	X	X
		<u>Note:</u> ESA only; ACI otherwise			





# What On-orbit Ocular Data are Collected...and When?

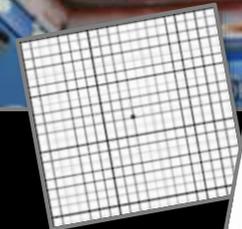


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Note: ESA only; ACI otherwise



Image credit: NASA



Christina H Koch  
@Astro\_Christina

“Float right there.” Words I never thought I’d hear my eye doctor say. Starting a week of baseline medical data collection to compare with later in flight. Long duration microgravity studies so we can set our sights on deep space!



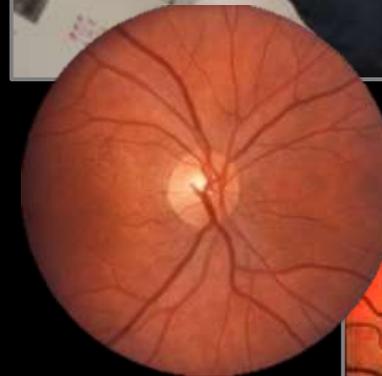
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Image credit: NASA





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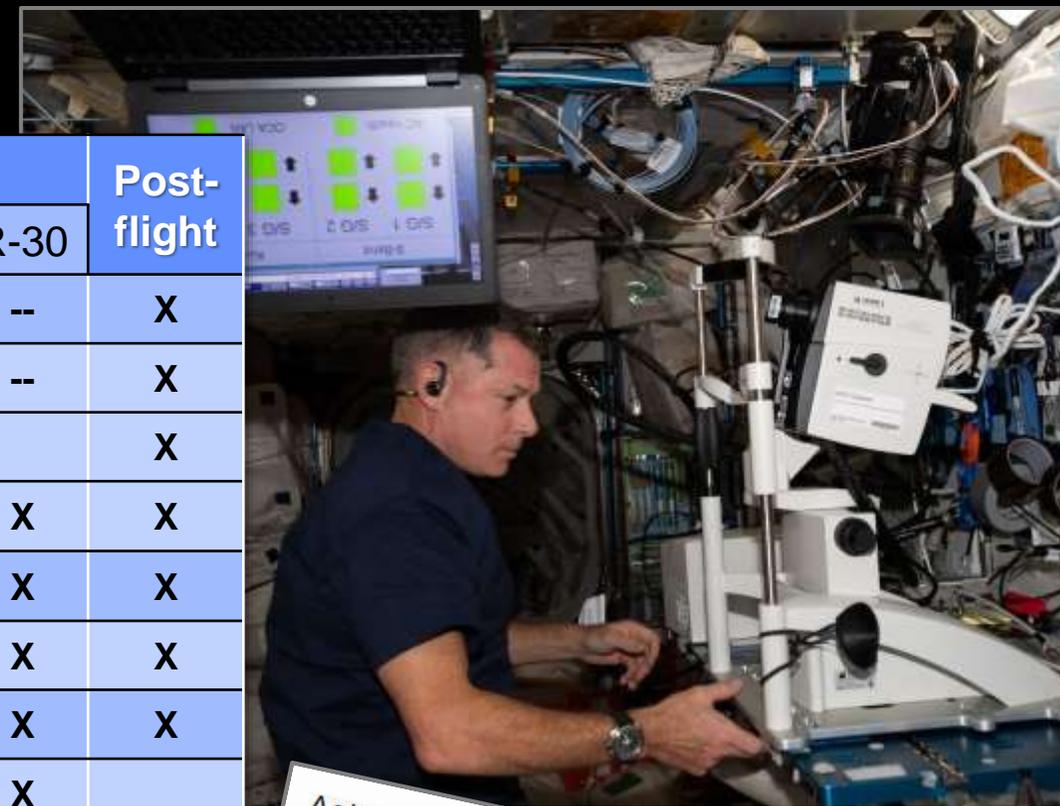


Image credit: NASA

Astronauts don't just conduct science experiments. They are often the test subjects! Here @Astro\_kimbrough sets up the near-infrared medical-imaging gear, also called optical coherence tomography, to capture detailed views of an astronaut's retina inside the @Space\_Station.



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Image credit: NASA



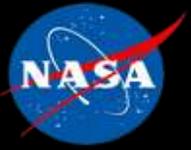
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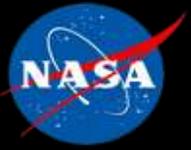
Image credit: NASA



# How are ocular data collected during ISS missions?



Image credit: NASA



# On-orbit Ocular Data Collections



- Pre-flight Preparation: *Training*
  - Crewmember “*subjects*”
    - Familiarization w/ equipment, data collection protocol, importance
  - Crewmember “*operators*”
    - Hands-on operation of equipment w/ test subjects
    - Tested on performance
    - Note: Crewmembers come from countless backgrounds, almost never w/ specialized ocular training

Occurs at **Johnson Space Center** in Houston, TX...



# Johnson Space Center – Hub of Human Spaceflight



Image credits: NASA



# Johnson Space Center – Hub of Human Spaceflight





# Johnson Space Center – Hub of Human Spaceflight



Image credit: NASA

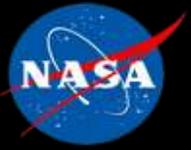


# Johnson Space Center – Hub of Human Spaceflight



Image credit: NASA

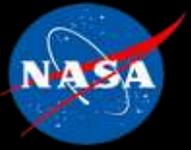




# On-orbit Ocular Data Collections



- In-flight Preparation: Scheduling
  - “Eye Week” sessions placed on OPTIMIS timeline
    - Secures crewmember(s): Subject & operator (if required)
    - Secures tasks (e.g., equipment setup, dilation drops, data collection, equipment stow)
  - Key ground support
    - Remote Guider
    - Subject Matter Expert (SME), if required
    - Biomedical Engineer (BME)
    - Interpreter, if required
    - Crew Surgeon (optional, always welcome)



# On-orbit Ocular Data Collections



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    - Subject Matter Expert (SME), if required
    - Biomedical Engineer (BME)
    - Interpreter, if required
    - Crew Surgeon (optional, always welcome)
  - **Mission Control room** secured



# On-orbit Ocular Data Collections

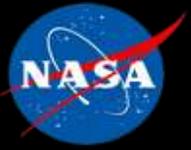


Image credit: NASA



# On-orbit Ocular Data Collections



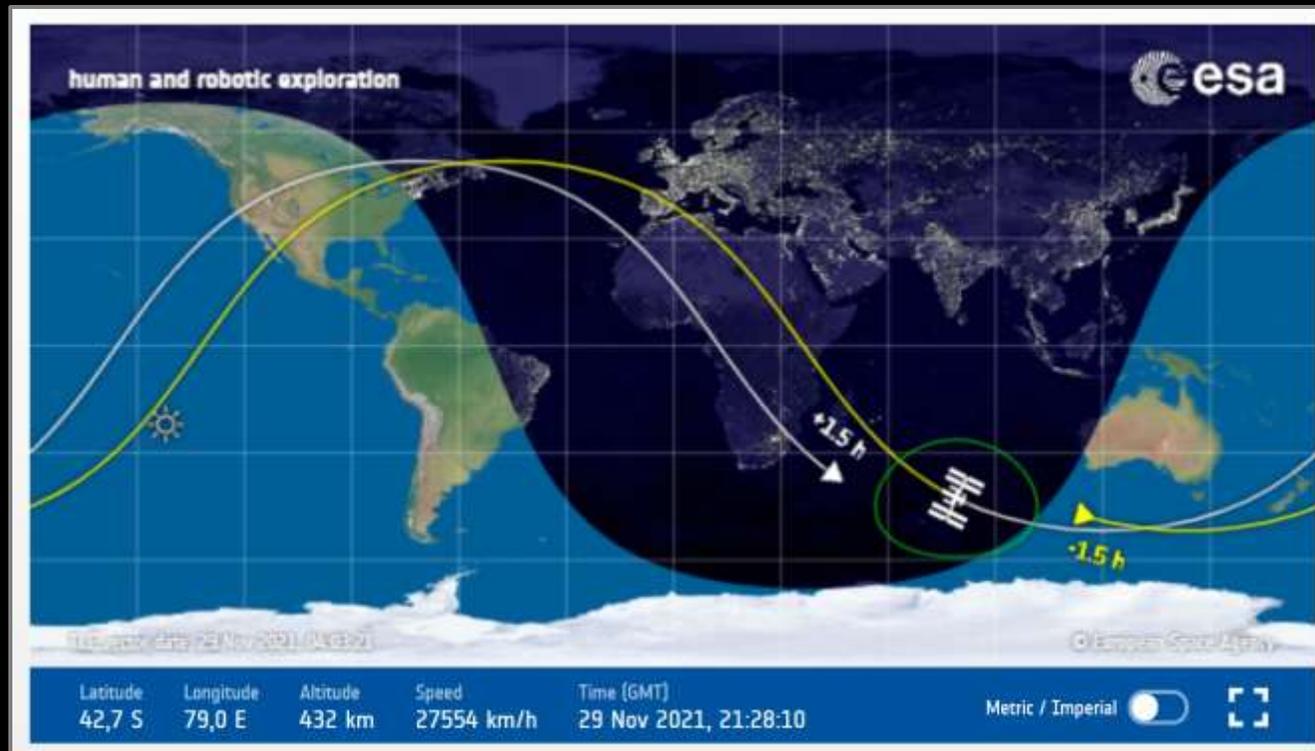


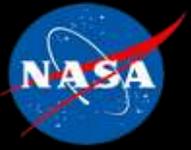
# On-orbit Ocular Data Collections



- In-flight Session:

- *Privatized* communication established
  - ISS is a moving target @ ~250 mi altitude; ~17,500 mph velocity; orbits Earth q93min



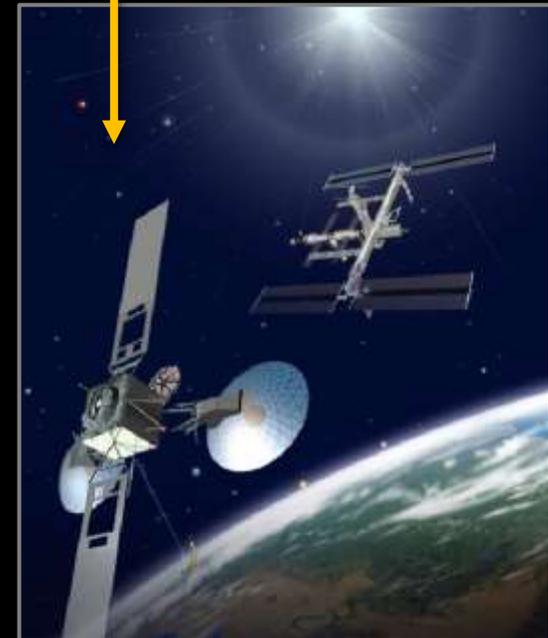


# On-orbit Ocular Data Collections



## ■ In-flight Session:

- *Privatized* communication established
  - ISS is a moving target @ ~250 mi altitude; ~17,500 mph velocity; orbits Earth q93min
  - COM primarily via **Tracking and Data Relay Satellites (TDRS)**
    - In geosynchronous orbit
    - Relay data to ground antennas at **White Sands Complex, NM** & **Guam Remote Ground Terminal**
    - Speed: **600 megabits/second**
    - **COM delay: ~1 sec (roundtrip)**



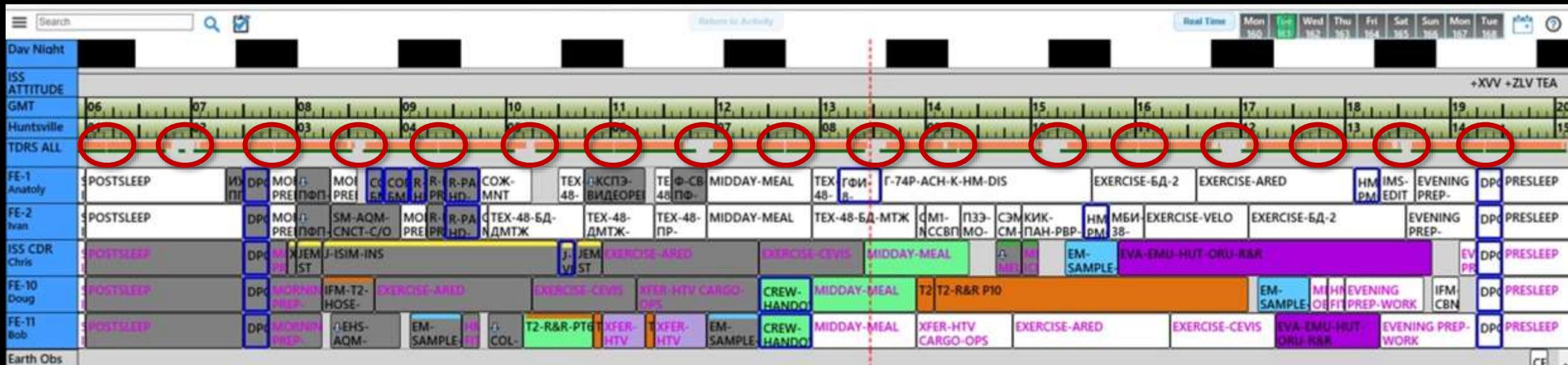


# On-orbit Ocular Data Collections



- In-flight Session:

- Privatized communication established (cont.)
  - **Loss of signal (LOS)** experienced whenever a satellite “hand-over” occurs
    - Occurs frequently, lasts seconds to >15 min
    - Disruptive, but can be accurately predicted & anticipated





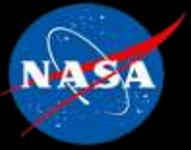
# On-orbit Ocular Data Collections



- In-flight Session:
  - Data collected via careful choreography between crewmember(s) and ground personnel (e.g., Remote Guider, SME, interpreter, BME)
  - Session duration: 15-60 min, including LOS
  - Data saved onto ISS laptop (OCT, U/S, funduscopy) or recorded by RG (vision, tonometry)



Image credits: NASA



# On-orbit Ocular Data Collections



## ■ In-flight Session:

- Data collected via careful choreography between crewmember(s) and ground personnel (e.g., Remote Guider, SME, interpreter, BME)
- Session duration: 15-60 min, including LOS
- Data saved onto ISS laptop (OCT, U/S, funduscopy) or recorded by RG (vision, tonometry)



Image credits: NASA



# On-orbit Ocular Data Collections



- Post-Session:
  - **Data downlinked** from ISS laptop by Data BME
  - Data migrated to ground-based diagnostic devices & **SMEs for analysis**
  - **Reports:** Generated; entered into EMR; communicated to crew surgeons
  - **Follow-on tasks coordinated**, if necessary
  - Timeline of events...

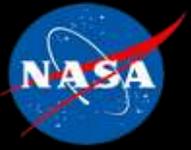




# Future Challenges to SANS Telemedicine...



Image credit: NASA



# Future Challenges to SANS Telemedicine...



- Outside of low Earth orbit (LEO):
  - *Space will be extremely limited*
    - **Less equipment** (medical or otherwise) will be deployed, w/ selections based on **priority**
    - Currently, most SANS diagnostic devices are **too large**. Can they be miniaturized?
  - *COM delay will increase*
    - **~5 seconds** for signal to travel roundtrip between **Moon & Earth**
    - **~10-40 minutes** for radio signal to travel roundtrip between **Mars & Earth**
      - **Will require increased crewmember autonomy, device automation**
  - *SANS severity may increase* during long-duration Mars mission (vs. 6-mo ISS mission)

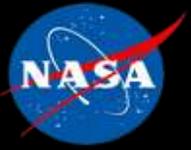




# Take-Home Messages



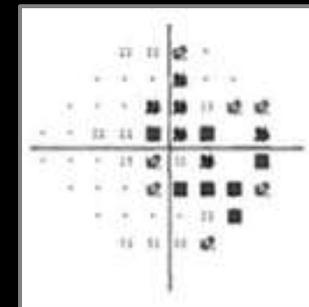
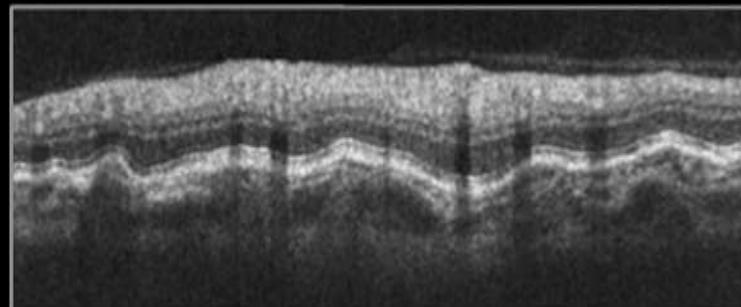
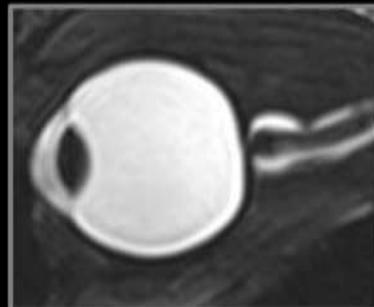
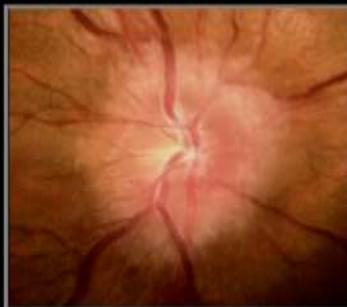
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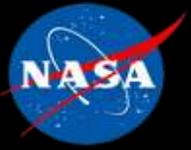


# Take-Home Messages



- Currently, no evidence of true vision or cognitive impairment in any astronauts
- SANS affects ~69% of long-duration crewmembers. Severity is thought related to mission duration; poses a significant risk to expeditionary spaceflight (e.g., 3-yr Mars mission)
- Challenges to clinical decision-making, research, and long-term surveillance:
  - SANS pathogenesis & pathophysiology remain unclear
  - SANS is unique to spaceflight, with no perfect terrestrial equivalent
  - Medications can have different pharmacokinetics in space
  - Confounding variables (e.g., CO<sub>2</sub> levels, NaCl intake, exercise type/levels, etc.)
  - Low sample sizes (especially females)

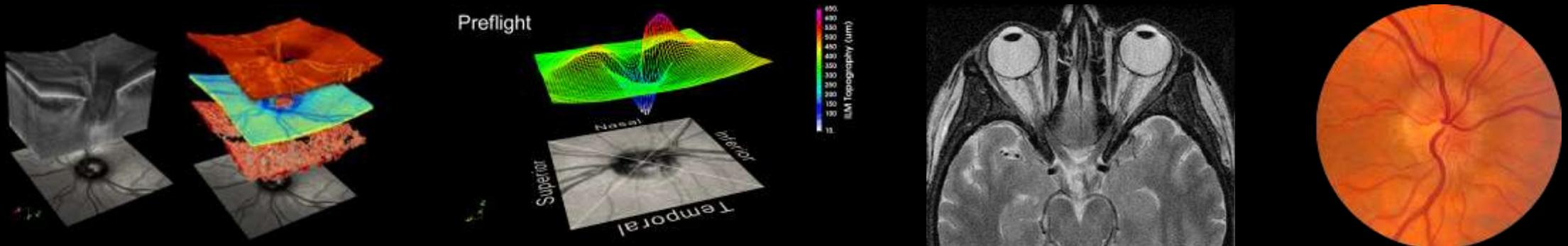


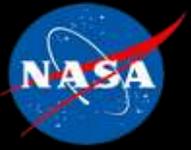


# Take-Home Messages



- **Telemedicine functions well in LEO, but several challenges must be overcome prior to Mars missions, especially...**
  - Shrinking & automating SANS diagnostic devices
  - Training crewmembers to collect ocular data autonomously
  - Access to SANS countermeasures
- **SANS efforts will benefit terrestrial medicine** (e.g., advanced data analytics; miniaturized & semi-autonomous diagnostic devices; new objective-based definitions of ONH disease; telemedicine technology & techniques; etc.)





# Thoughts? Questions?



## Acknowledgements

Tyson Brunstetter, OD, PhD<sup>1</sup>  
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- William J. Tarver, MD, MPH<sup>1</sup> — SANS Clinical Lead (CNS)
- Ann H. Tsung, MD, MPH<sup>2</sup> — SANS Deputy Clinical Lead
- Steven S. Laurie, PhD<sup>2</sup> — SANS Research Lead
- Brandon R. Macias, PhD<sup>1</sup> — SANS Deputy Research Lead

- David M. Brown, MD<sup>3</sup>
- Simon J. Clemett, PhD<sup>4</sup>
- Jane Gensler<sup>1</sup>
- C. Robert Gibson, OD<sup>2,5</sup>
- Stephen F. Hart, MD<sup>1</sup>
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- Thomas Mader, MD<sup>2</sup>
- Daniel A. Marburgh<sup>2</sup>
- Sara S. Mason<sup>7</sup>
- Amirah M. Mathin, MS<sup>2</sup>
- Anna M. Mendiola<sup>2</sup>
- William T. Misek<sup>2</sup>
- Mayra Nelman-Gonzalez<sup>2</sup>
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- Wafa F. Taiym, MS<sup>2</sup>
- Elizabeth Talburt<sup>2</sup>
- Mary Van Baalen, PhD<sup>1</sup>
- Julia A. Wells, BSN, RN<sup>2</sup>

1. NASA Johnson Space Center, Houston, TX
2. KBR, Houston, TX
3. Retina Consultants of Houston, Houston, TX
4. Jacobs Technology, Inc., Houston, TX
5. Coastal Eye Associates, Webster, TX
6. Blanton Eye Institute, Houston, TX
7. Aegis Aerospace, Inc., Houston, TX





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