

Spaceflight Associated Neuro-ocular Syndrome (SANS)

Tyson Brunstetter, MBA, OD, PhD, FAAO, FAsMA

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1600 – 1700 (ET)



“Medically Ready Force...Ready Medical Force”

Tyson Brunstetter, MBA, OD, PhD, FAAO, FAsMA



- Recently-retired USN Aerospace Optometrist
 - ❑ Served primarily in Research, Development, Test, and Evaluation (RDT&E) roles in USN & DHA commands – LEP, refractive surgery, deployable battlefield medical devices
 - ❑ Deployed to Expeditionary Medical Facility (EMF) Kuwait – 2010
- Now serving at NASA Johnson Space Center (JSC) Space Medicine Operations Division; Houston, TX
 - ❑ SANS Clinical Lead (Eyes & Vision)

Disclosures



- Dr. Brunstetter has no relevant financial or non-financial relationships to disclose relating to the content of this activity
- The views expressed in this presentation are those of the presenter and do not necessarily reflect the official policy or position of NASA, Department of Defense, nor the U.S. Government
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- DHA J-7 CEPO staff, as well as activity planners and reviewers have no relevant financial or non-financial interest to disclose
- Commercial support was not received for this activity

Learning Objectives



At the conclusion of this activity, participants will be able to:

1. Analyze the primary known ocular and brain anatomical changes associated with short- and long-duration spaceflight.
2. Describe why SANS presents a risk to astronauts, especially for extended-duration spaceflight (e.g., a Mars mission).
3. List the ocular/vision tests performed onboard the International Space Station (ISS) and their purposes.



Astronaut Case Report



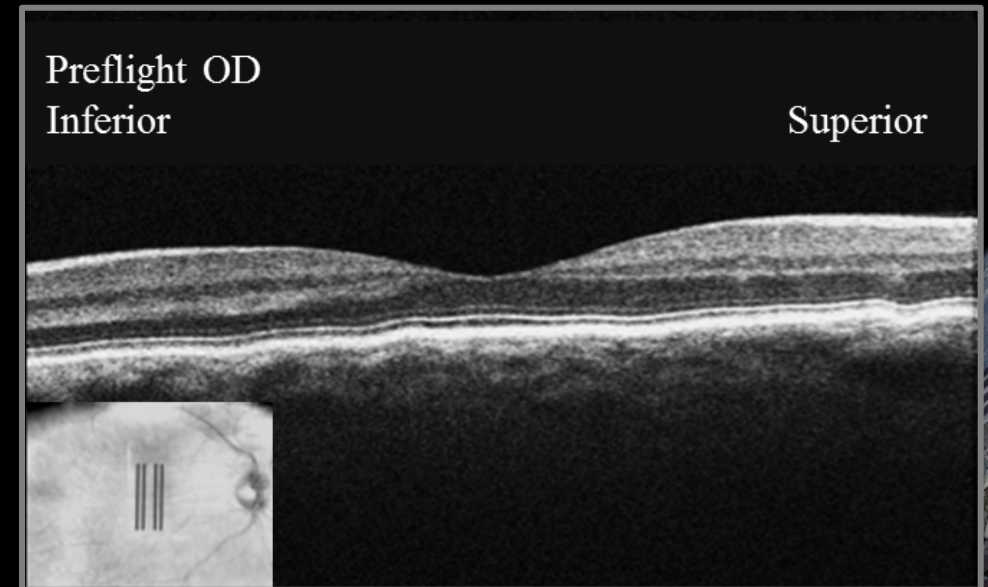


Astronaut Case: Pre-ISS Flight



- Space shuttle (short-duration) spaceflight veteran
 - Flight occurred before special astronaut ocular test battery initiated
 - Pre-flight ocular data limited: Comprehensive eye exam & visual fields; all normal
 - No imagery (MRI, OCT, or ultrasound)
 - Experienced **+0.75D refractive error (RE) shift** (pre-to-post-flight)
- Years later, prior to ISS (long-duration) flight:
 - 3T MRI & ultrasound: **Mild globe flattening OU***
 - OCT: **Mild choroidal folds OU***

** Both presumed consequences of short-duration spaceflight*

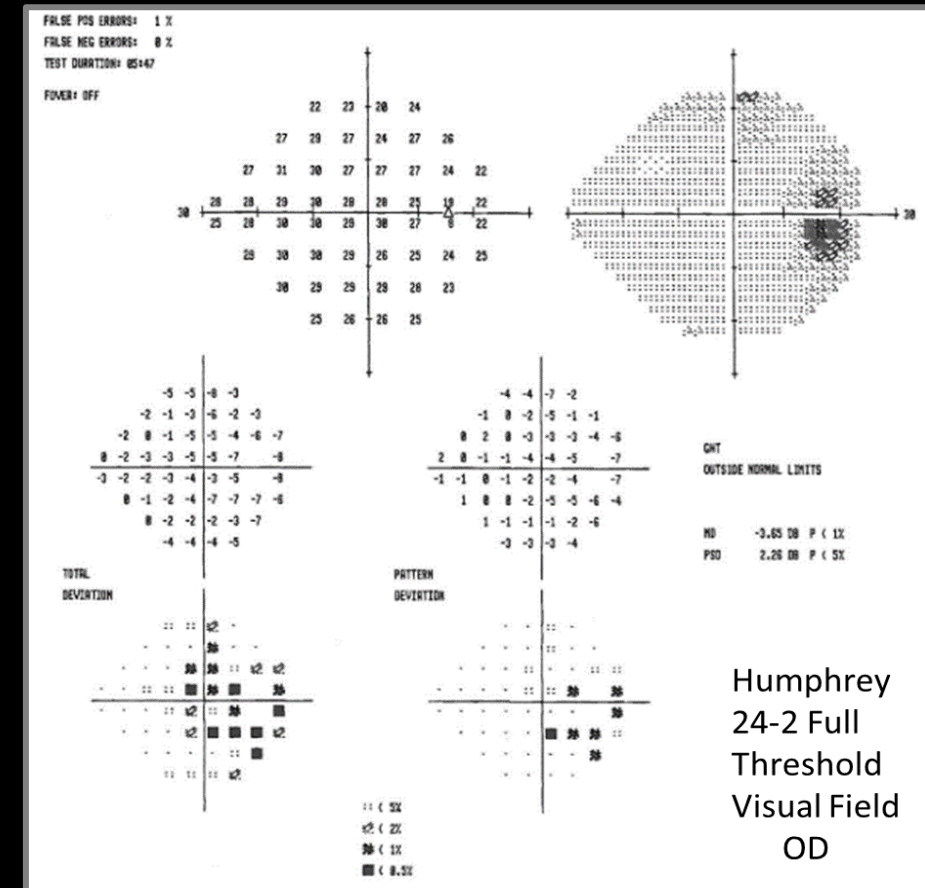




Astronaut Case: Post-ISS Flight



- In-Flight: ISS (long-duration)
 - Subjective decrease in VA OU (dist & near); Otherwise completely asymptomatic
 - Mild disc edema OS
- Post-Flight Diagnoses
 - Grade I 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, but recovered approx. -0.25D to -0.50 OU
 - No loss in best-corrected VA (i.e., 20/20)

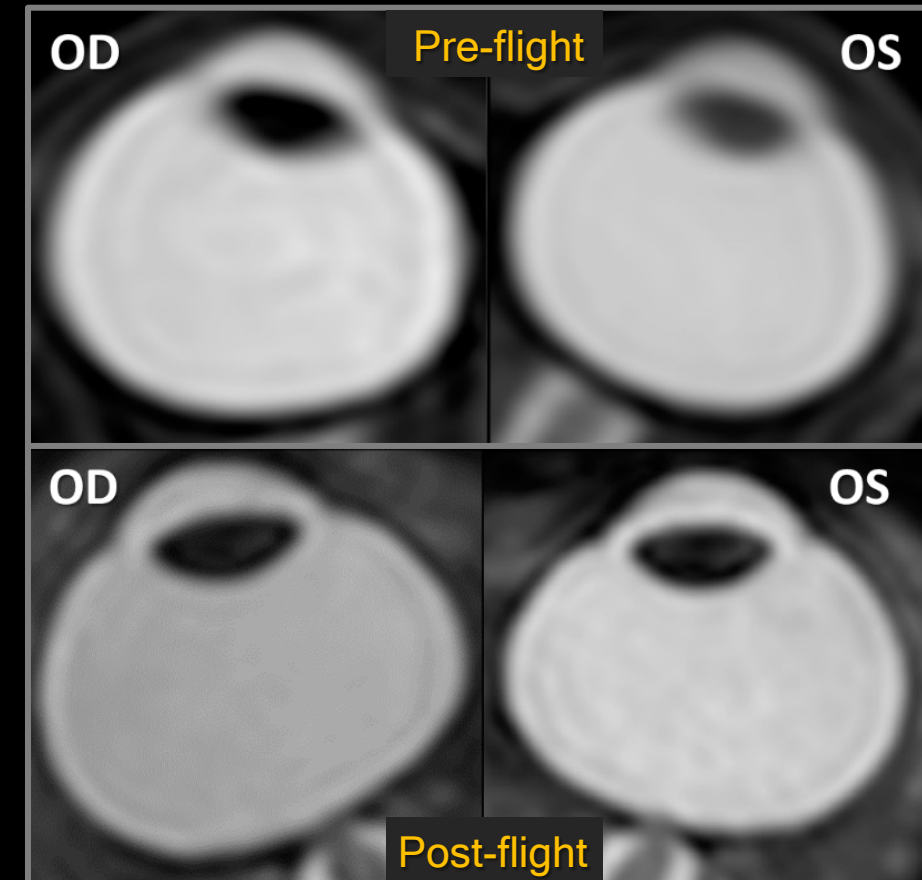




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Astronaut Case: Post-ISS Flight



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

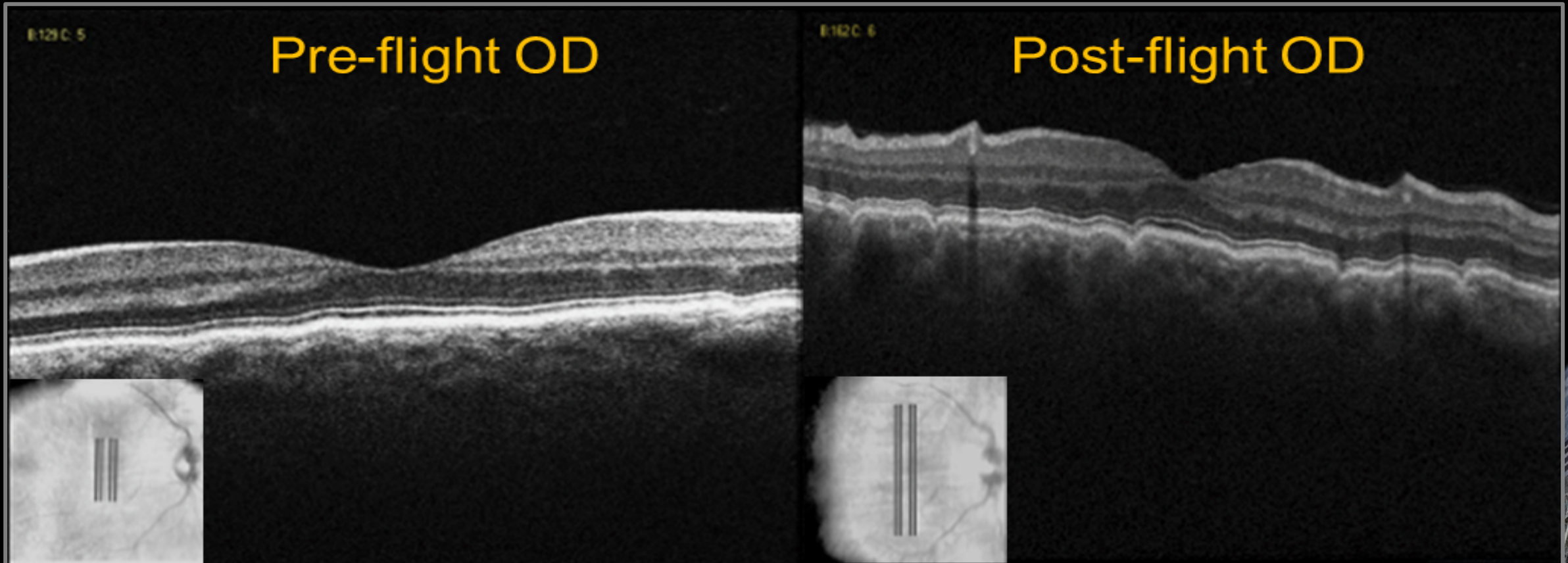




Astronaut Case: Post-ISS Flight



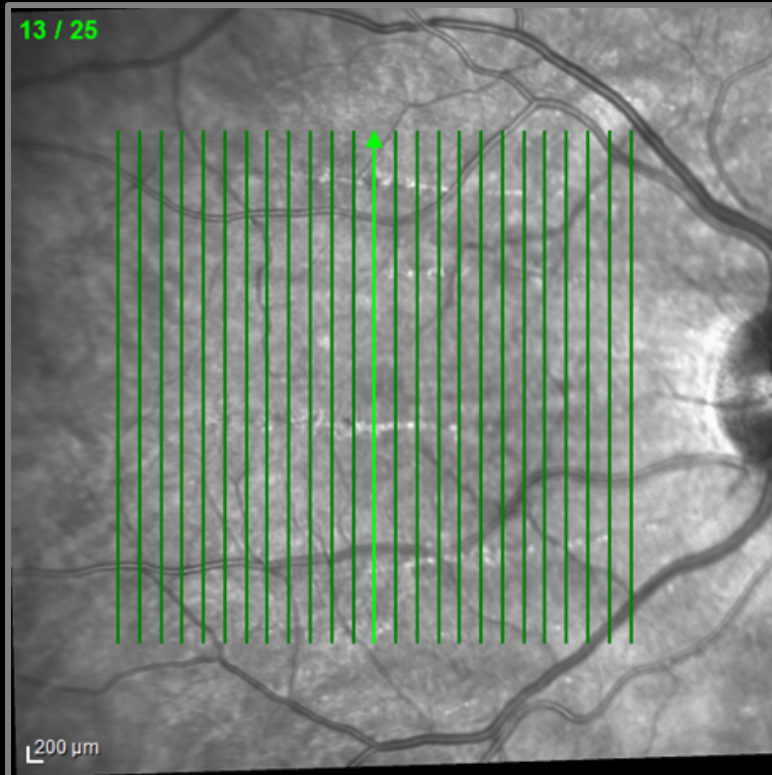
- Post-Flight Diagnoses
 - **Chorioretinal folds (OD>OS)** – No metamorphopsia OD/OS. No reduction in BCVA



Astronaut Case: Post-ISS Flight

- Post-Flight Diagnoses

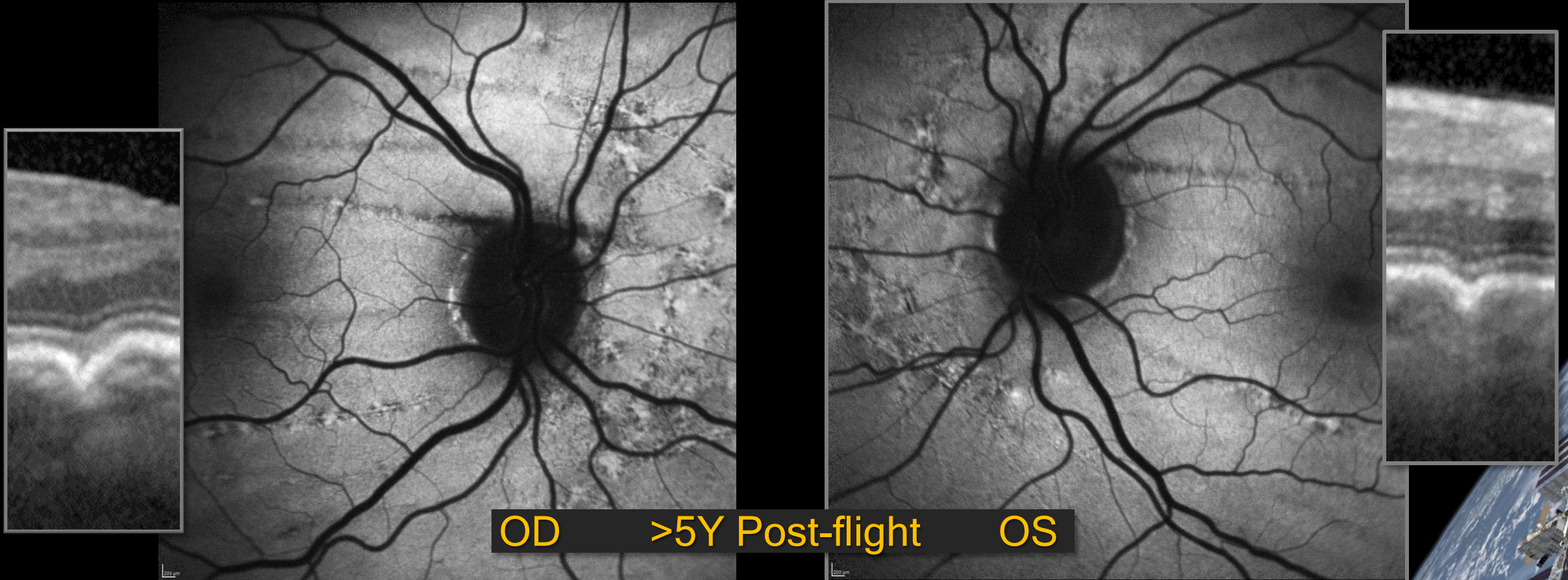
- **Chorioretinal folds (OD>OS)** – Improvement over time, but choroidal folds *still persist today*



Astronaut Case: Post-ISS Flight

- Post-Flight Diagnoses

- **Disrupted RPE (OD>OS)** – Discovered recently w/ **AutoFL** & MultiColor Imaging





Astronaut Case: Summary

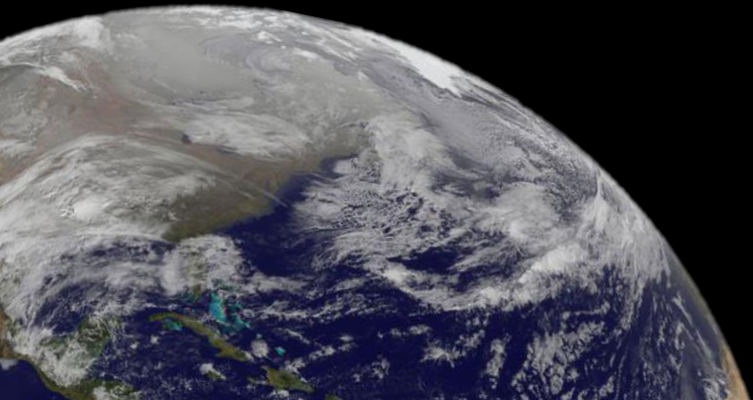


- Terrestrially, chorioretinal folds are an infrequent finding
- >20% of ISS astronauts have been diagnosed w/ chorioretinal folds
 - Due to spaceflight-associated choroidal engorgement or globe flattening (or both)?
- Astronaut Case: Current State
 - Asymptomatic
 - No reduction in best-corrected VA or visual performance
 - Moderate-severe globe flattening + hyperopic RE shift persist OU
 - Choroidal folds OU persist; have induced RPE disruption
 - No retinal/photoreceptor damage detected
 - Being monitored annually



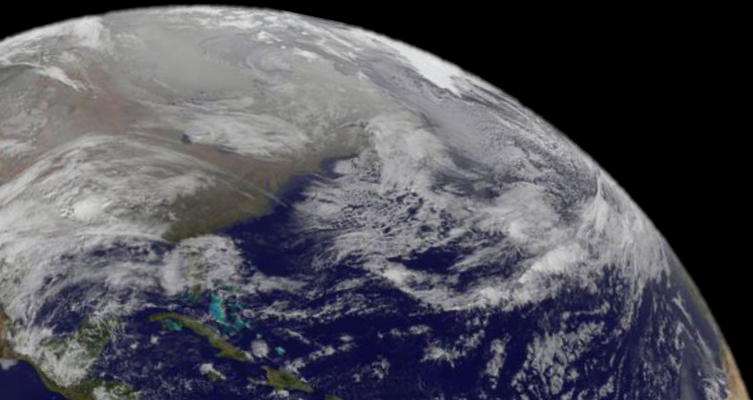


What *in the world* is going on?





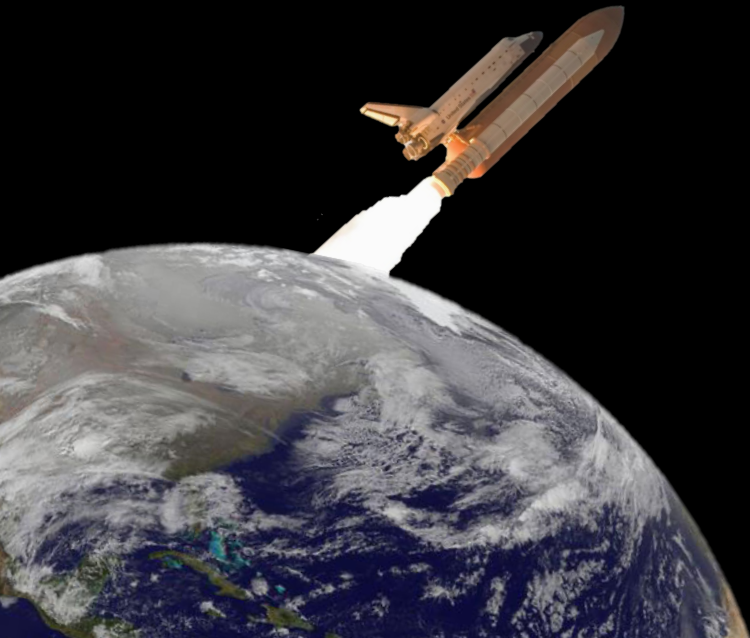
Mission Duration: *Short* (<30 days)





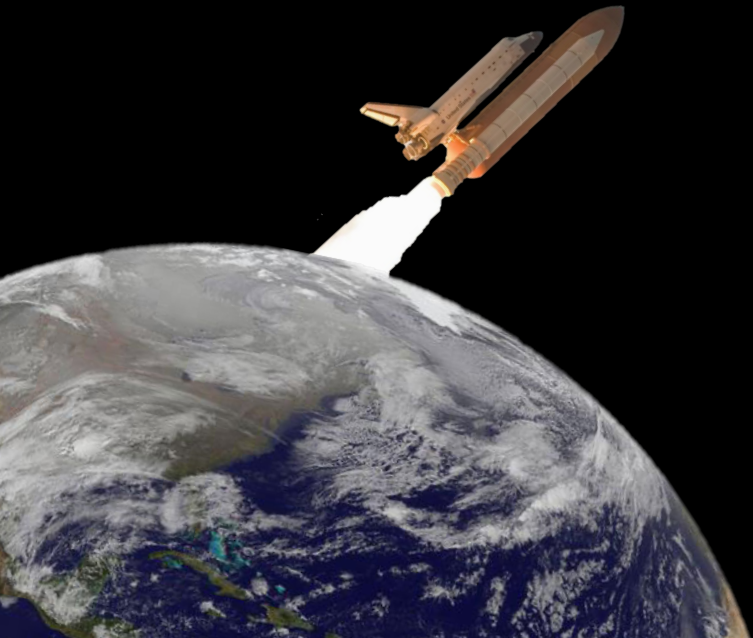
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Micro-
gravity





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



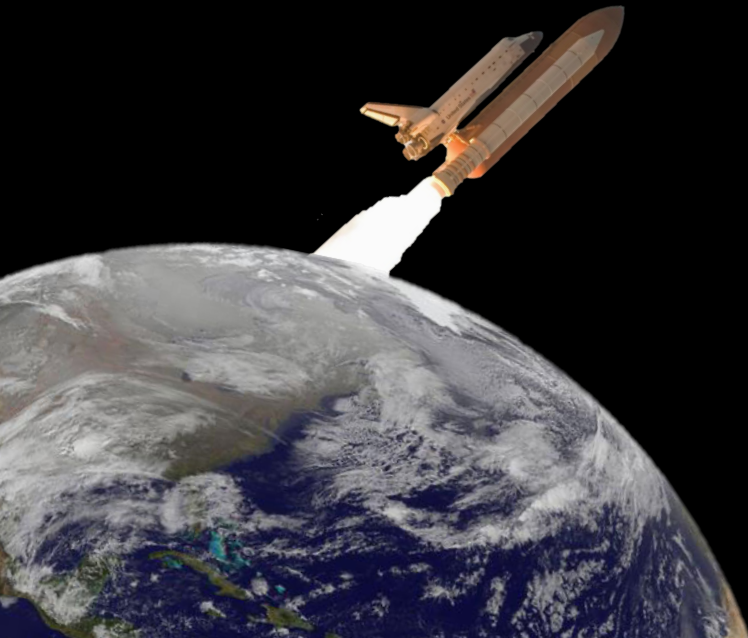


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Micro-
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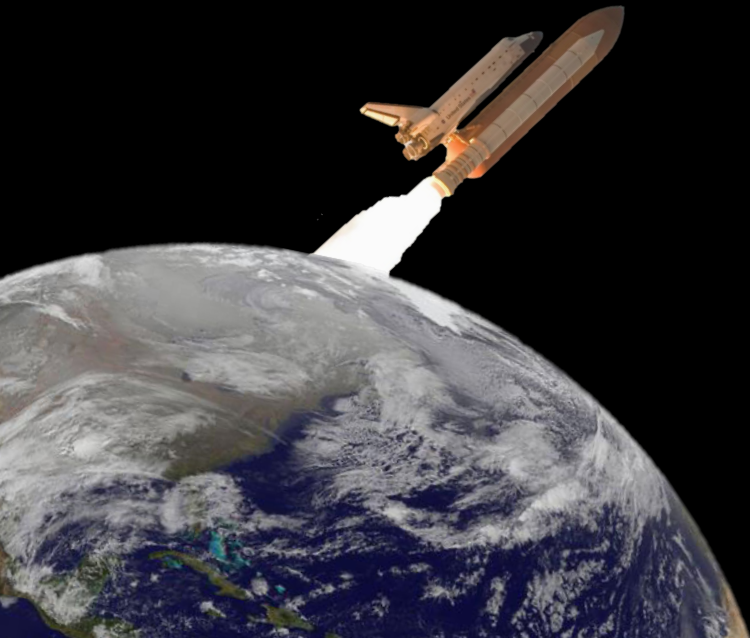
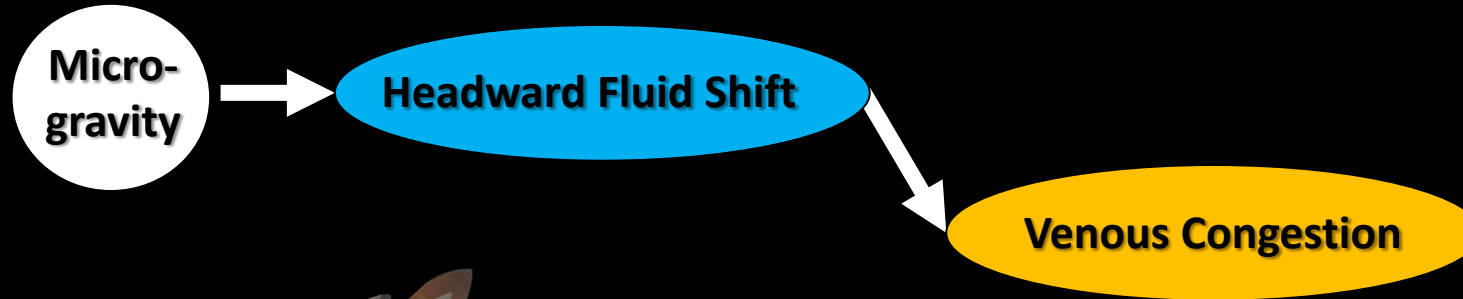
Headward Fluid Shift



“Puffy Face Syndrome”

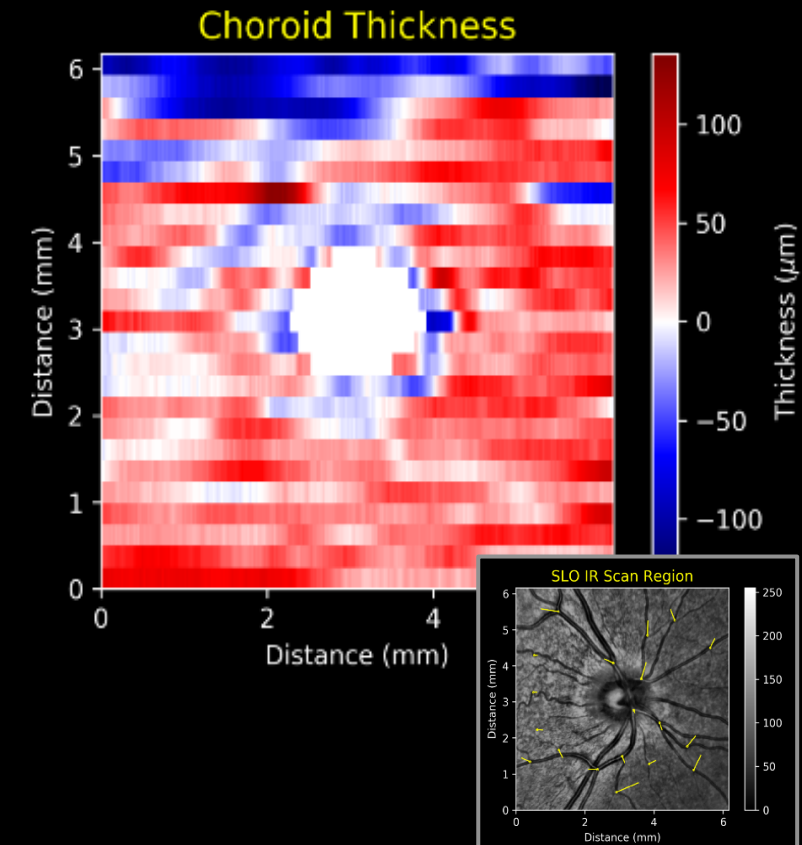
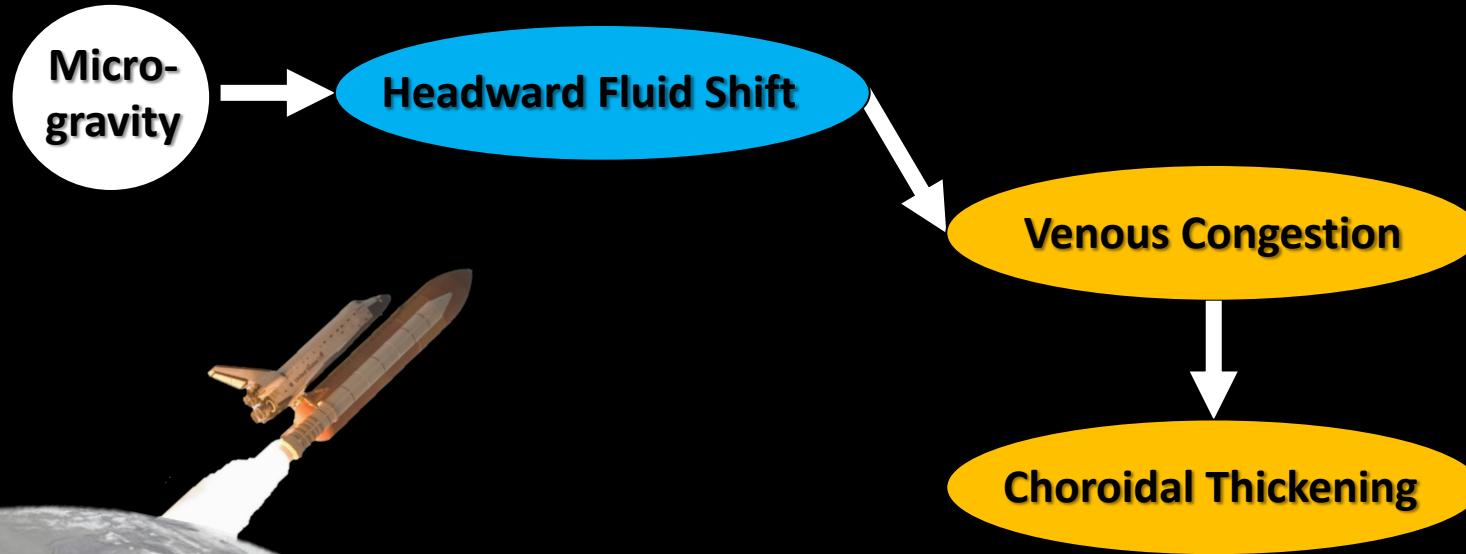


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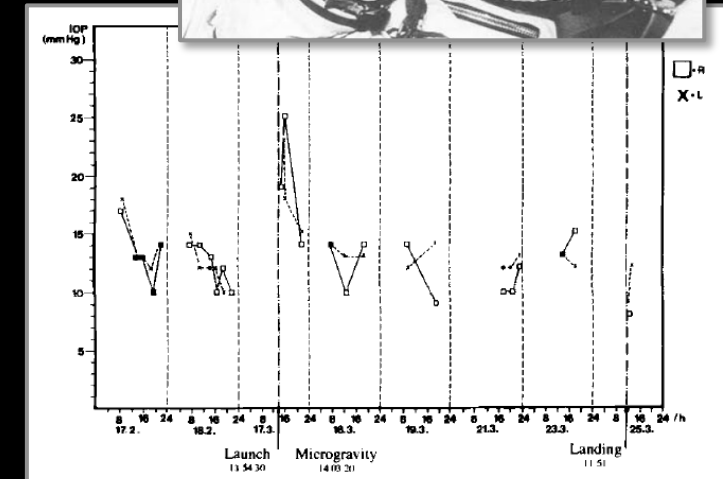
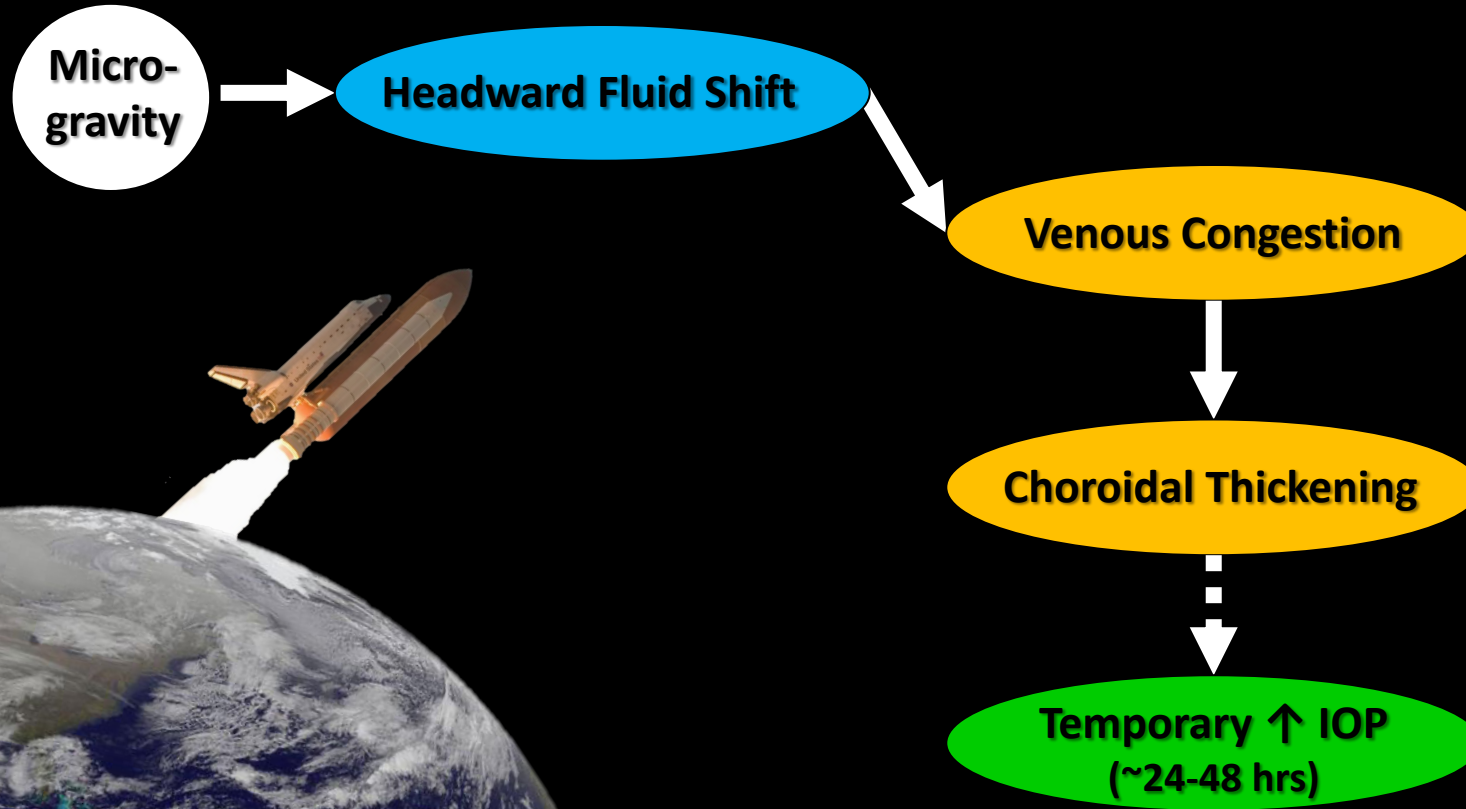


Source: Mayra Nelman & Simon Clemett (NASA)



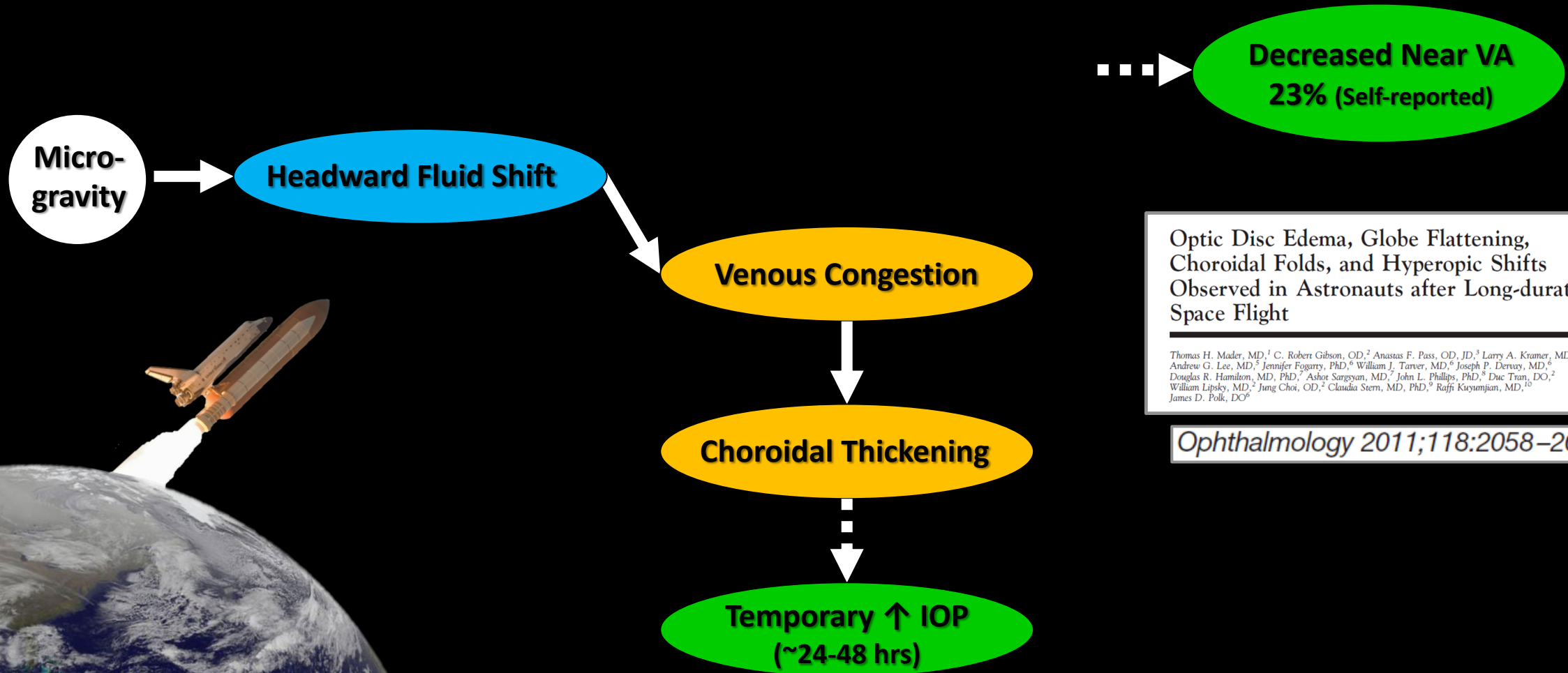
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DRAEGER J, SCHWARTZ R, GROENHOFF S, STERN C. *Self-tonometry under microgravity conditions. Aviat Space Environ Med* 1995; 66:568-70.





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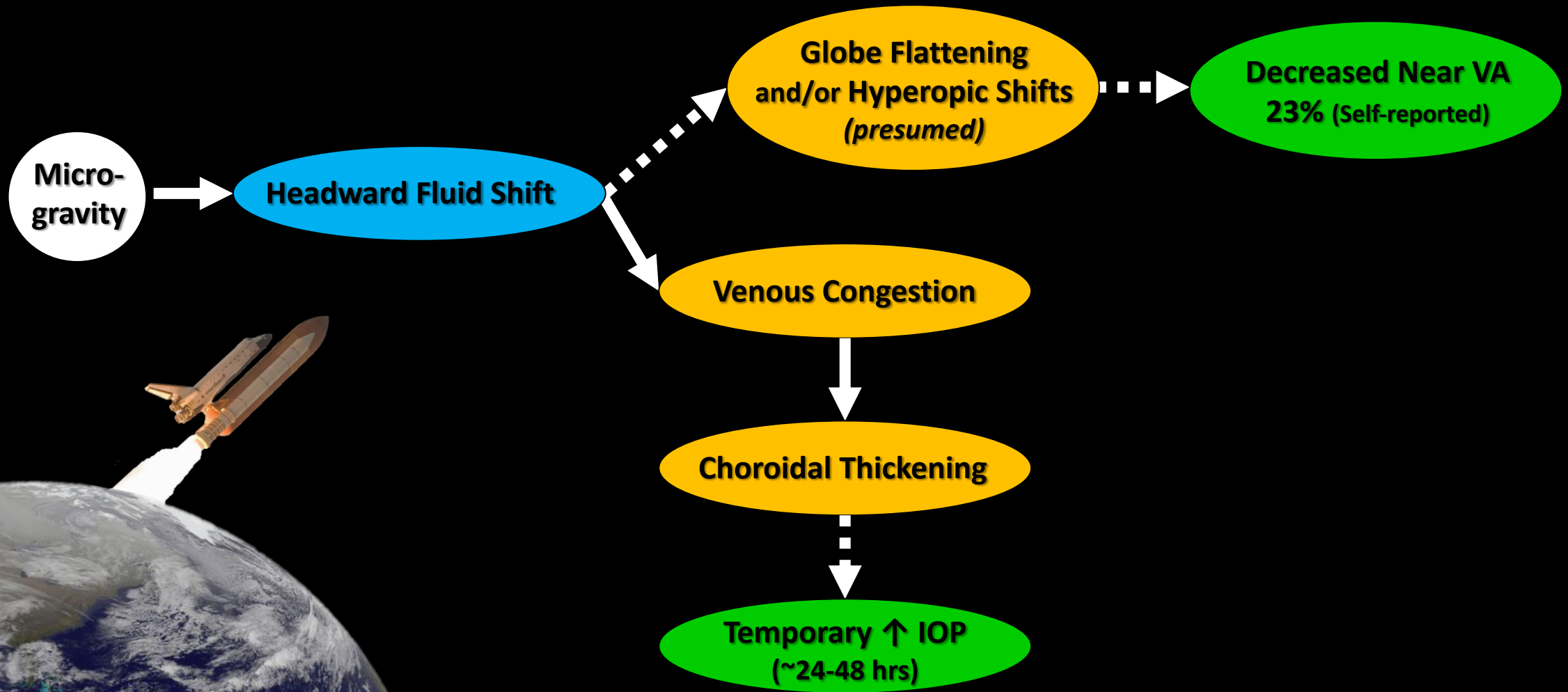
Optic Disc Edema, Globe Flattening, Choroidal Folds, and Hyperopic Shifts Observed in Astronauts after Long-duration Space Flight

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Ophthalmology 2011;118:2058–2069

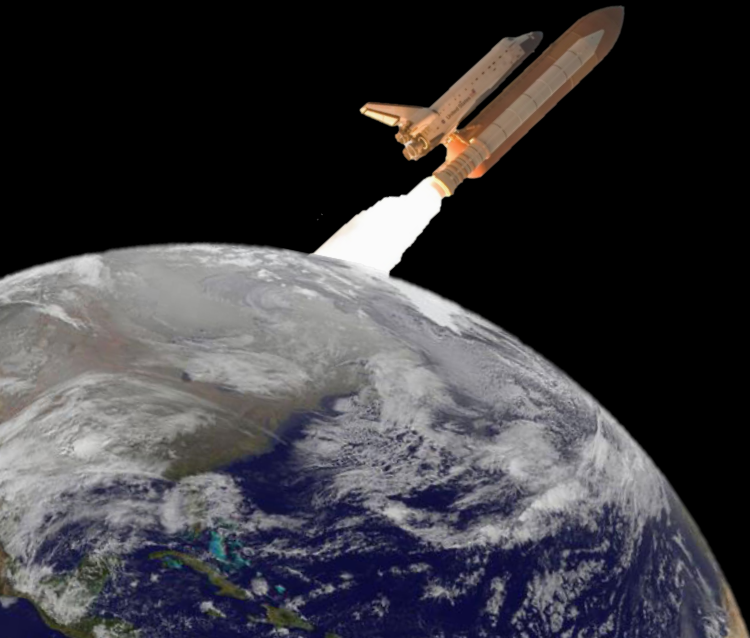


Mission Duration: **Short** (<30 days)





Mission Duration: *Sbngt* (<60 days)



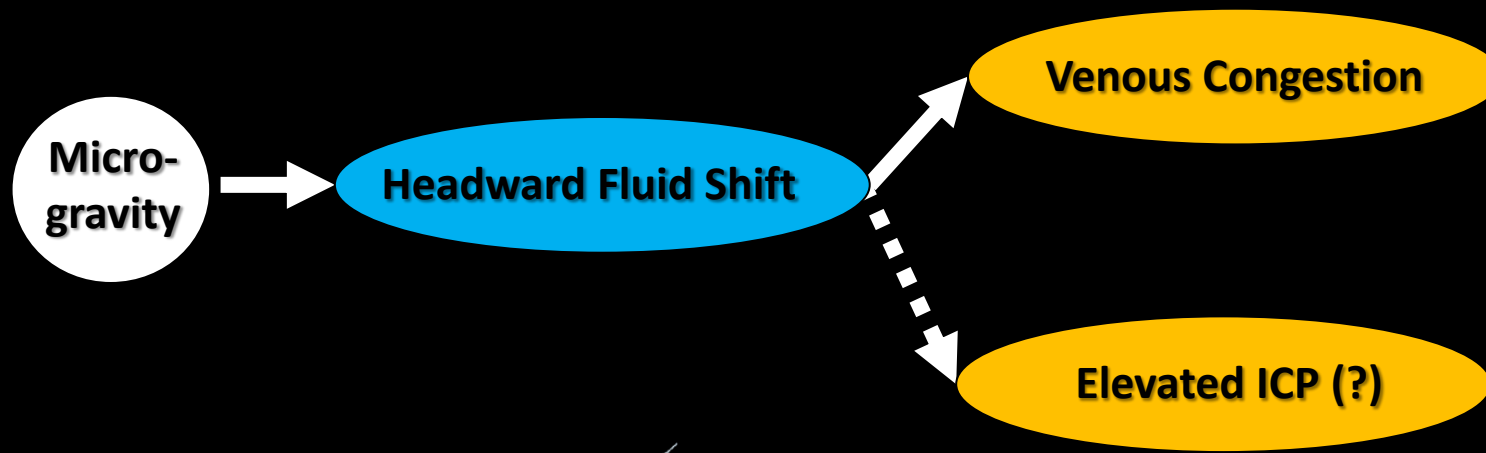


Mission Duration: *Long* (~6-12 mo)



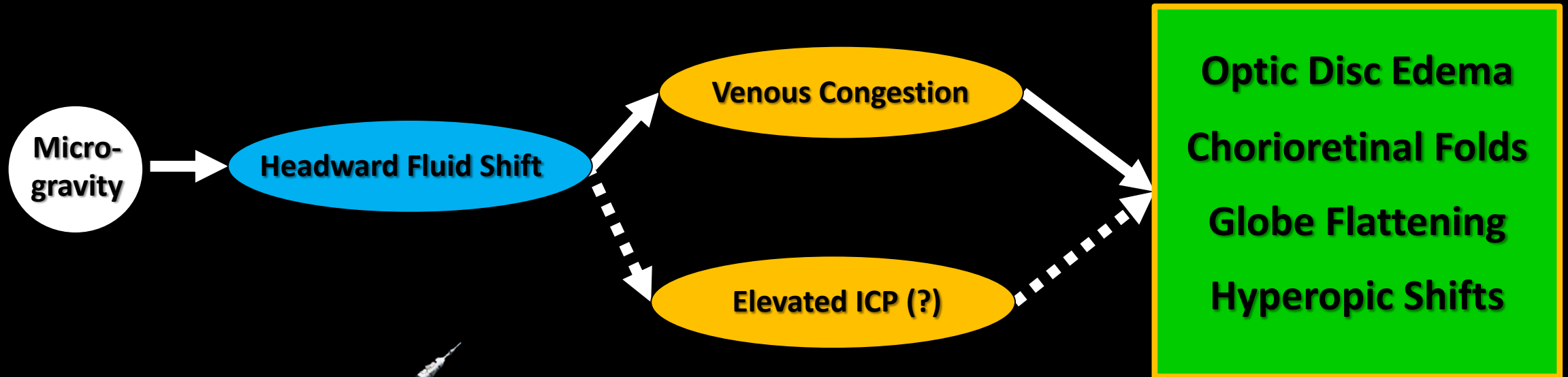


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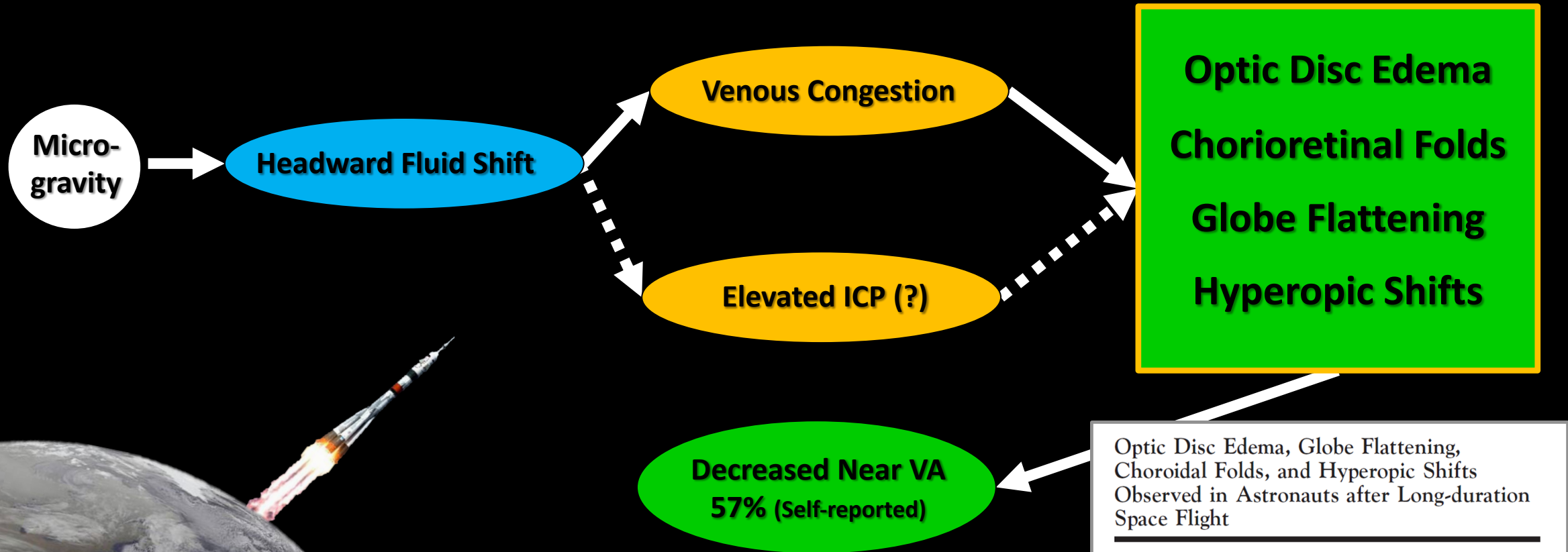
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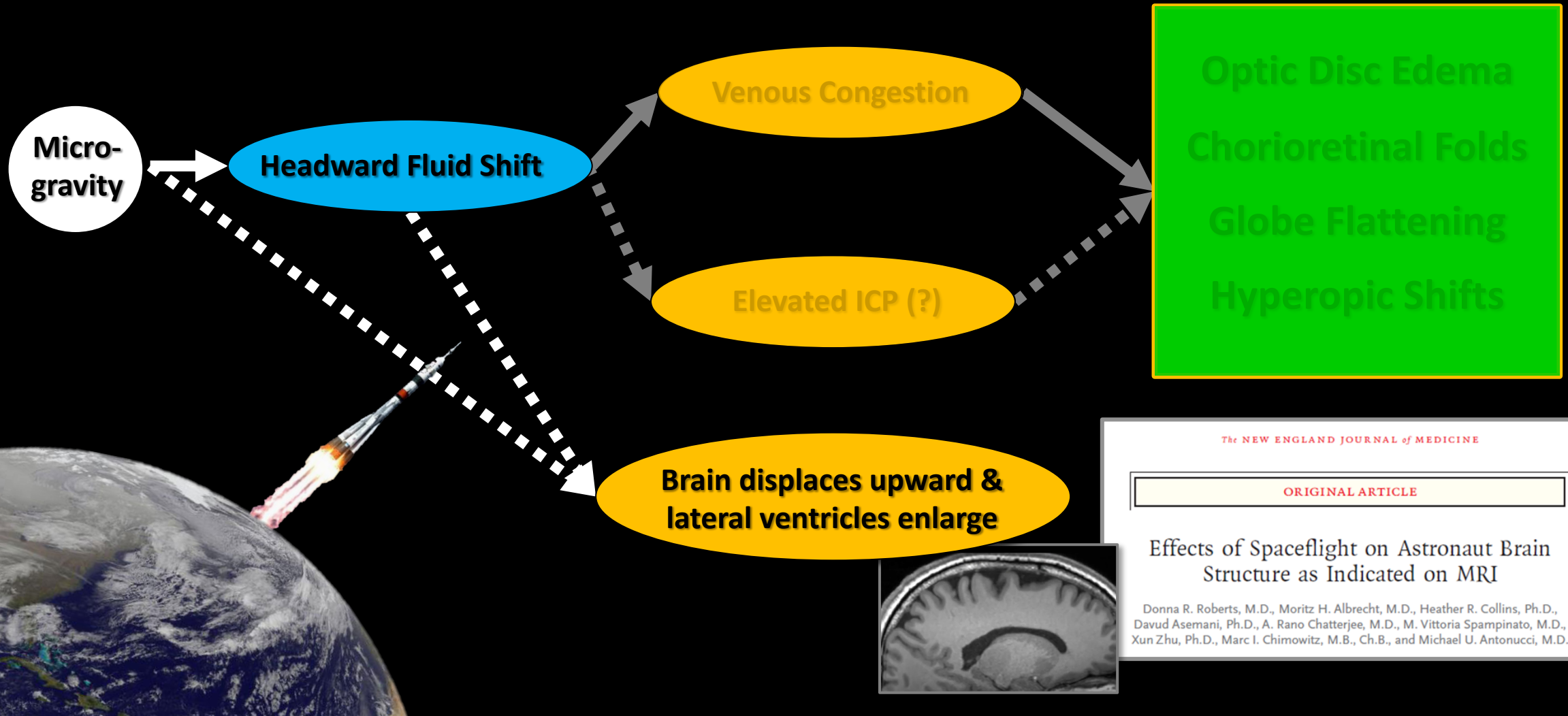
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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

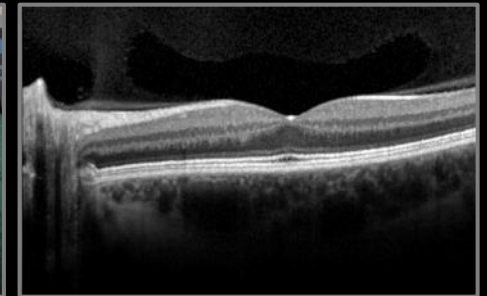
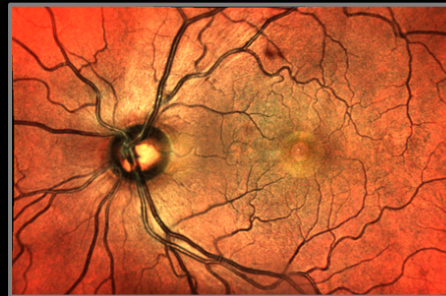
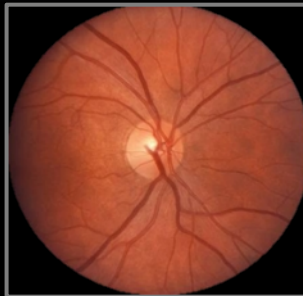
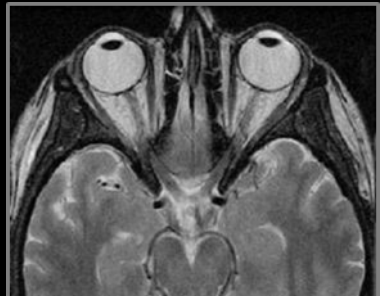
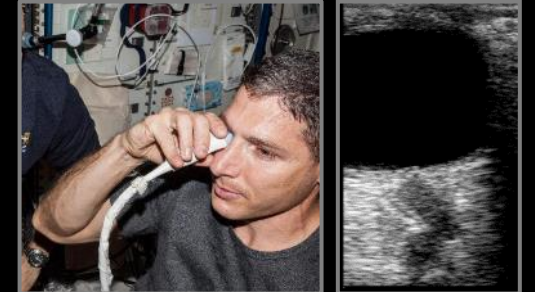
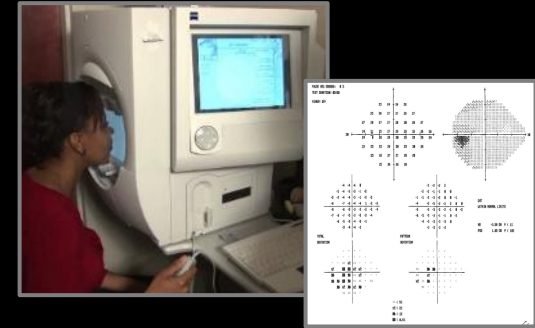
Effects of Spaceflight on Astronaut Brain Structure as Indicated on MRI

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)

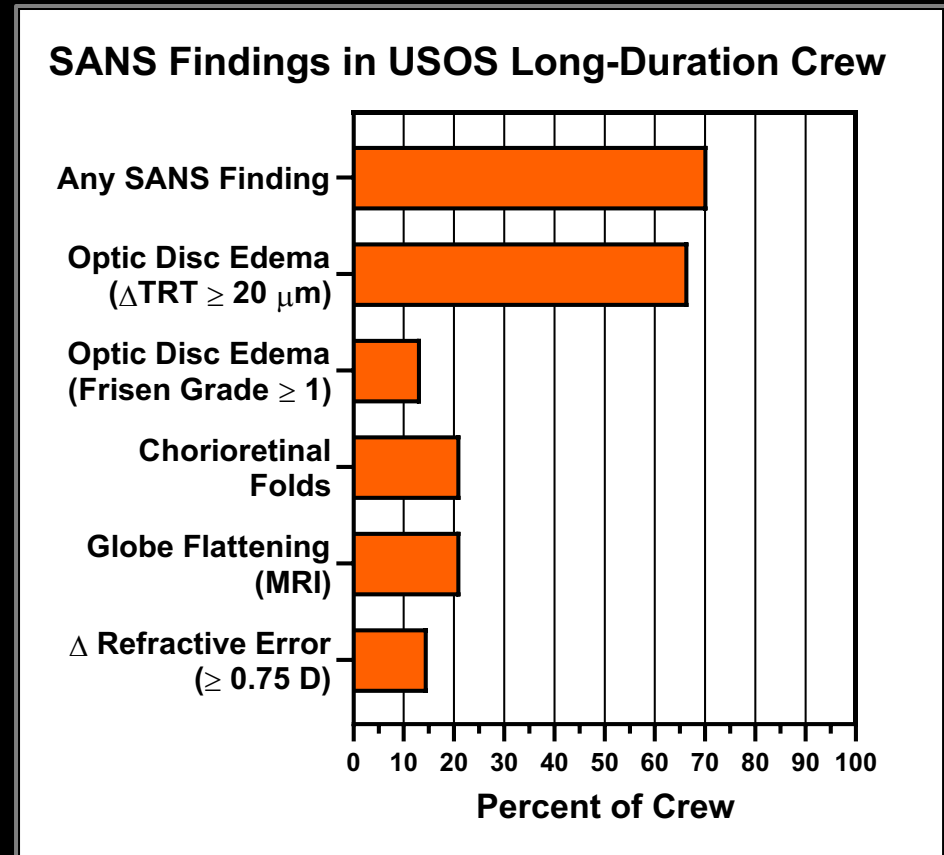
Primary SANS Tests	Pre-flight	On-orbit			Post-flight
		FD30	FD90	R-30	
3T MRI – <i>Head & Orbits</i>	X	-	-	-	X
Vision Screening – <i>VA, Amsler grid, Questionnaire</i>	X	X	X	X	X
Retinal Photography – <i>Fundoscopy / MCI</i>	X	X	X	X	X
Optical Coherence Tomography	X	X	X	X	X
Ocular Ultrasound	X	X	X	X	X
Visual Field – <i>24-2 SITA Standard</i>	X	Deploying 2022			X





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

- No permanent loss of visual or cognitive function yet detected in long-duration crew
- 69% of long-duration crewmembers present w/ earliest signs of SANS
 - Diagnosed in males *and* females
 - *Can't yet predict* who will develop SANS
 - Severity thought *related to mission duration*
 - *Optic disc edema and choroidal folds do not typically plateau during a 6-mo mission*
 - Some changes can become *permanent* (i.e., globe flattening, hyperopic shifts, choroidal folds)



NASA Data



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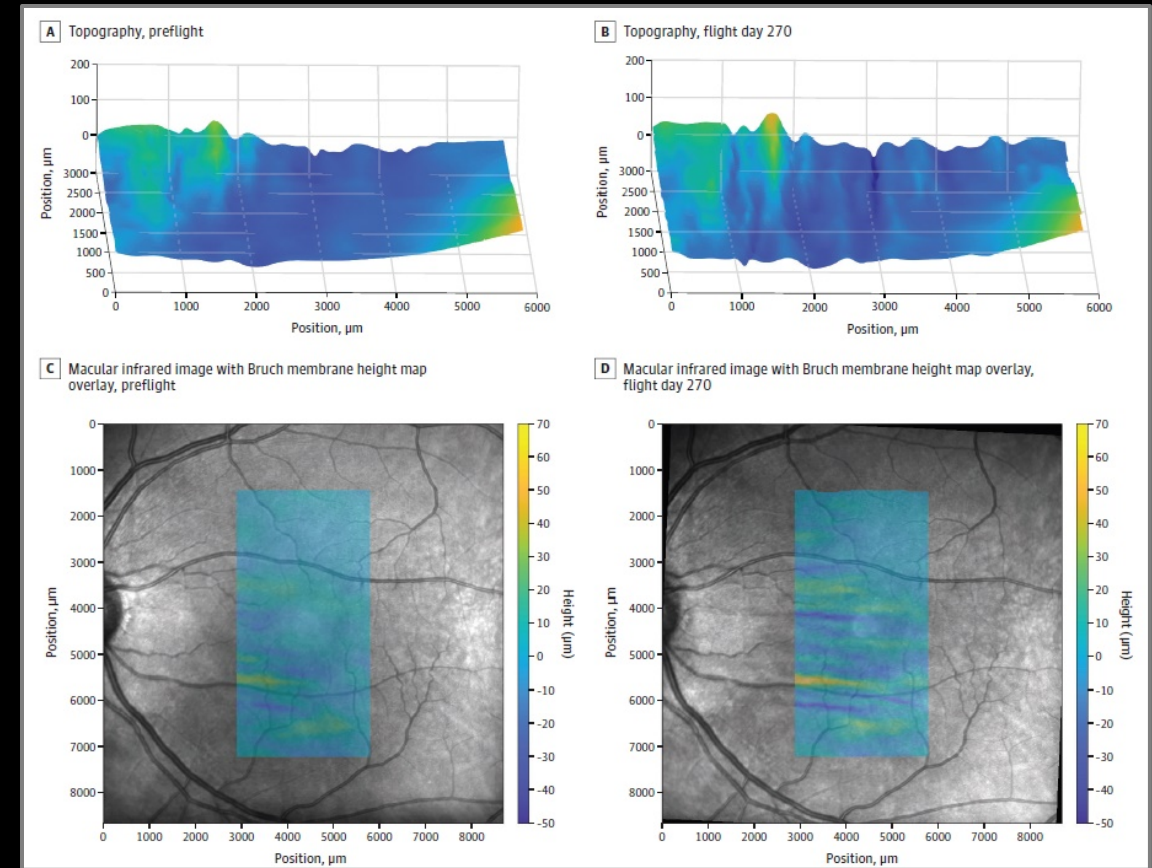


Macias BR, et al. Changes in the Optic Nerve Head and Choroid Over 1 Year of Spaceflight. JAMA Ophthalmol. 2021 Apr 29



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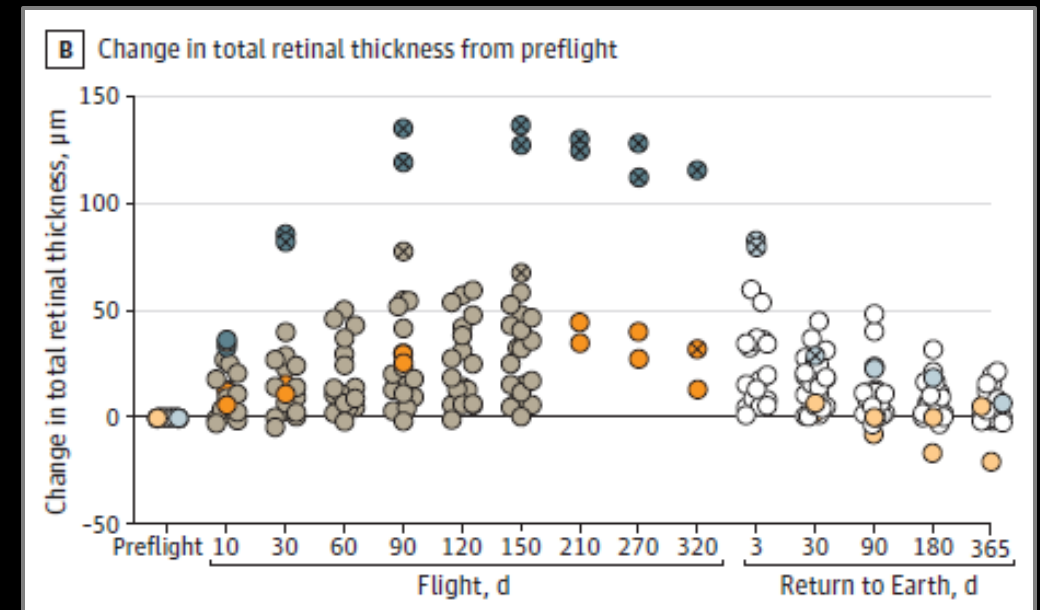


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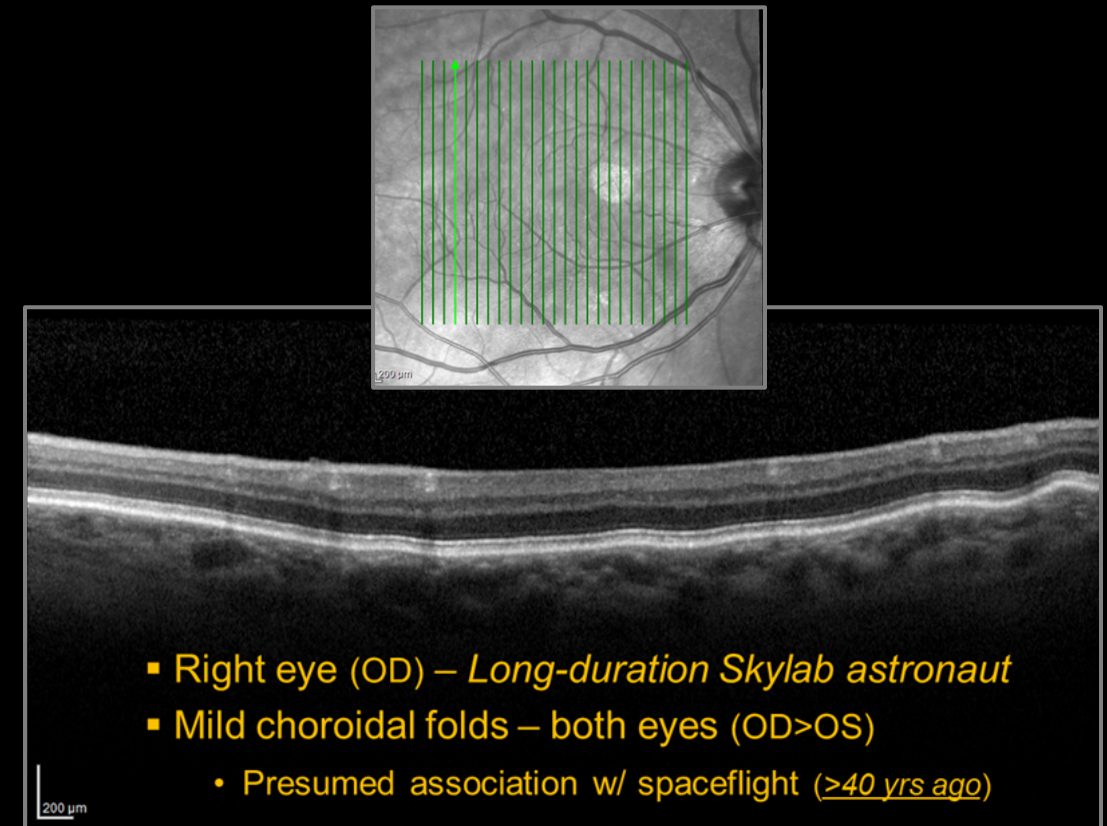


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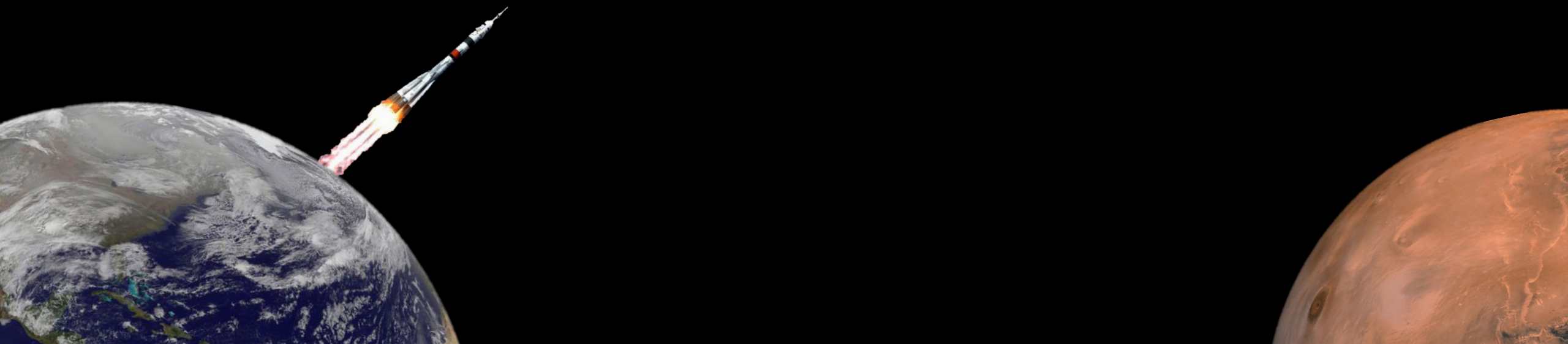
- Tempting to compare SANS to idiopathic intracranial hypertension (IIH)
 - *Different* demographics, symptoms, anatomical Δ s
 - No evidence of *pathologically elevated* ICP in SANS

	IIH	SANS
ONH/Disc Edema	<i>YES</i>	<i>YES</i>
Intracranial Pressure	Increased	<u>TBD</u> ; inconclusive evidence
Female : Male	9 : 1	<u>TBD</u> ; “changes” seen in <u>both</u> sexes
BMI	Obese (>90%)	Normal to highly athletic
Symptoms	Chronic headaches (94%); Transient vision obscuration (68%)	None besides near vision complaints
ONH Displacement	Gross movement forward	Expands forward & backward
Side Bias	< 4% unilateral	<u>TBD</u> ; but gross signs have been right-biased
Retinal : Choroidal Folds	5 : 1; <i>Retinal</i> folds occur first	1 : 3; <i>Choroidal</i> folds occur first
Fold Pattern	Typically concentric around ONH	Typically linear
Post-flight MRI	Brains displaces <u>downward</u> ; no change in size of lateral ventricles	Brain displaces <u>upward</u> ; lateral ventricles enlarge*

* Associated w/ long-duration spaceflight; *no official association w/ SANS has been established*

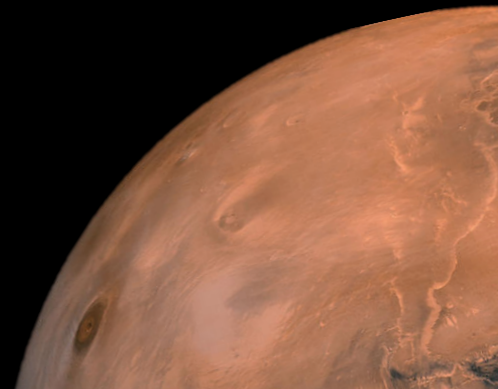
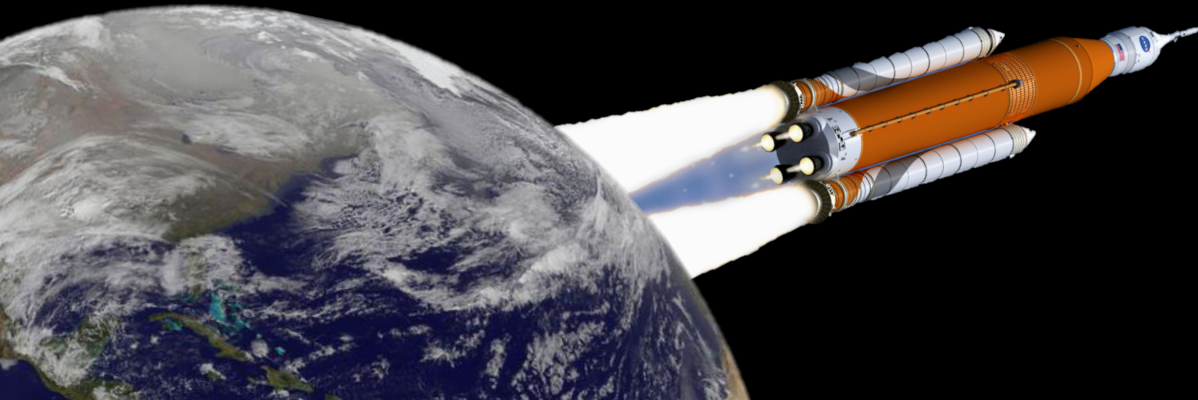
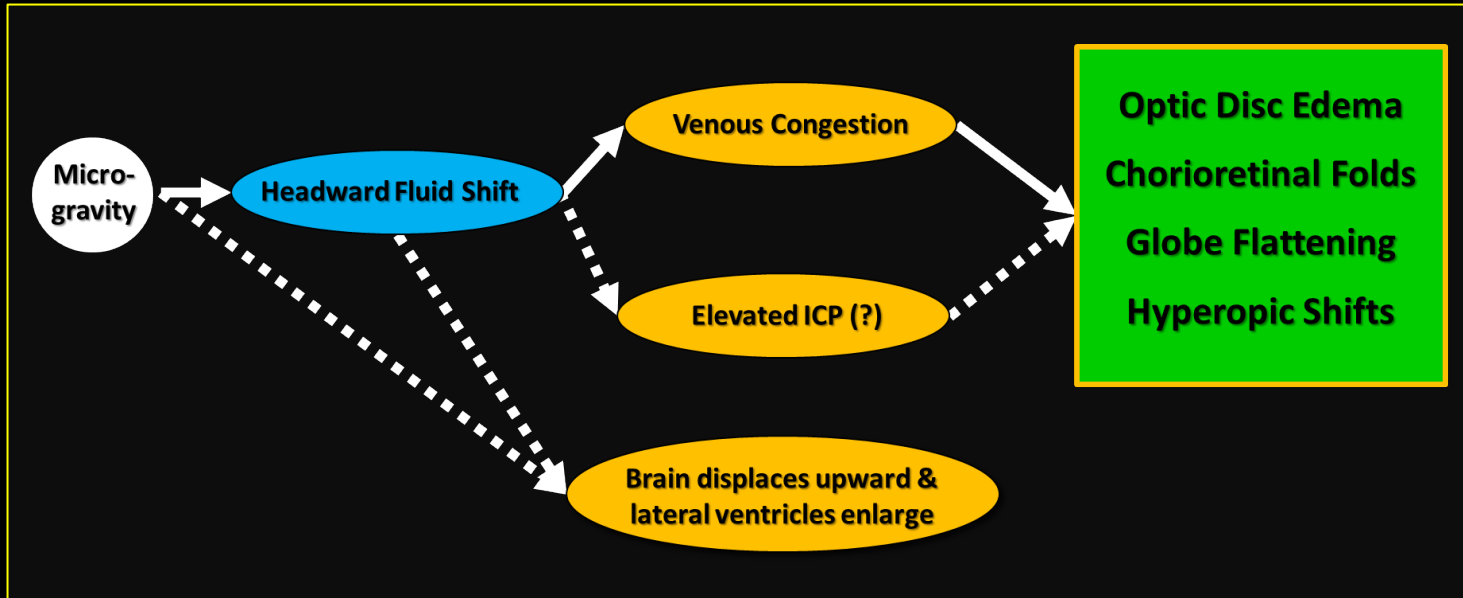


Missions Duration Expeditionary (~6-12 months)



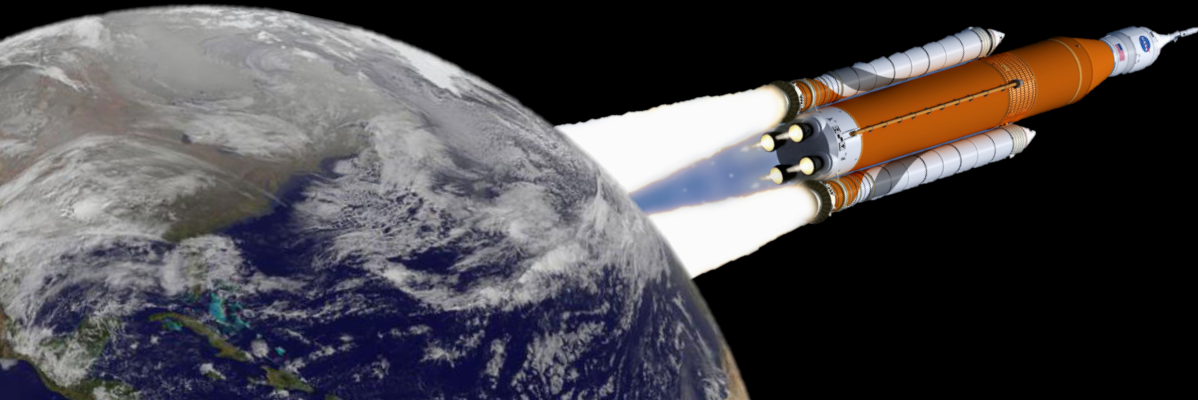
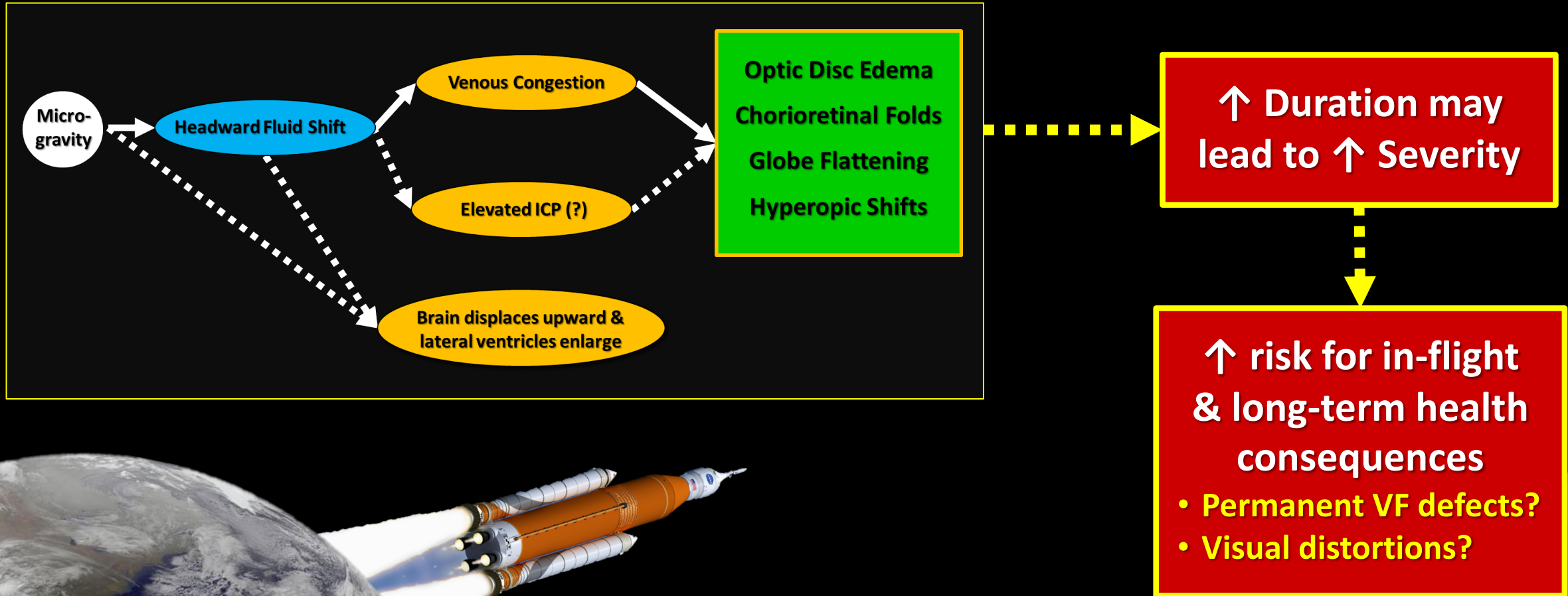


Mission Duration: *Expeditionary* (~3 years)





Mission Duration: *Expeditionary* (~3 years)



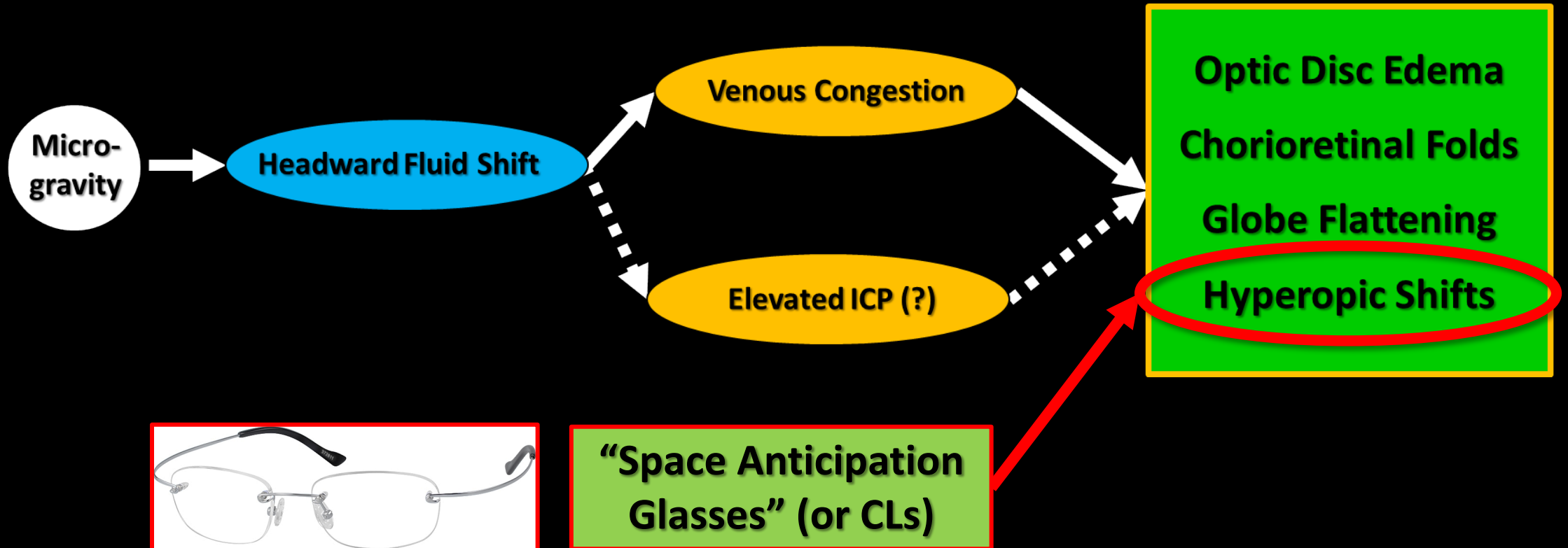


Mitigation Strategies





SANS Mitigation Strategies



SANS Mitigation Strategies

- Artificial Gravity
- Lower Body Negative Pressure (?)
- Thigh Cuffs (?)

Micro-gravity

Headward Fluid Shift

Ven

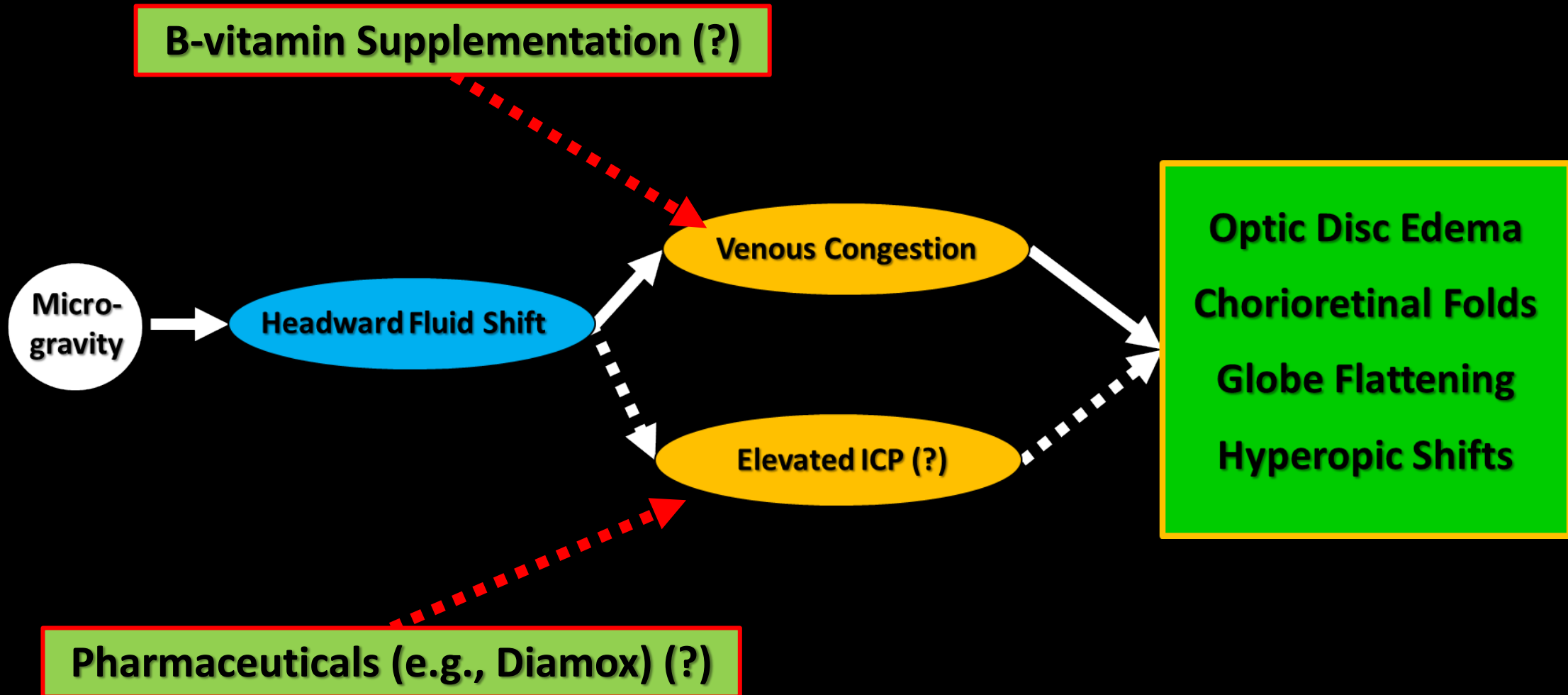
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SANS Mitigation Strategies





Take-Home Messages

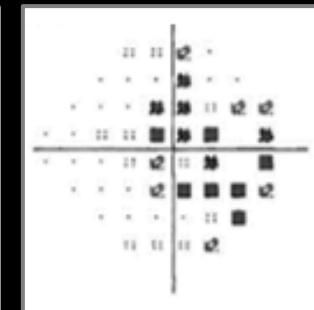
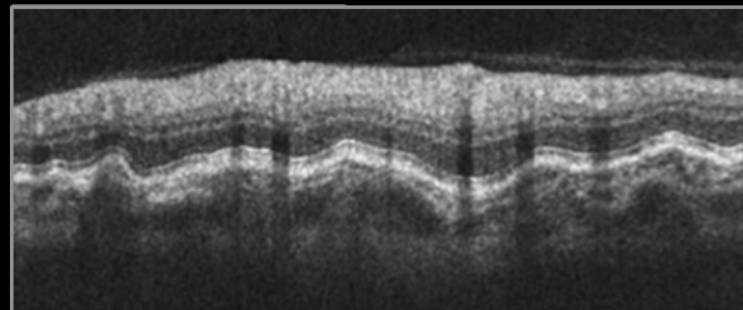
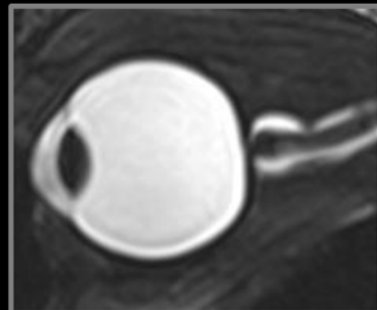




Take-Home Messages



- Currently, *no evidence* of true vision or cognitive impairment in long-duration astronauts; however, earliest signs of SANS are detected in 69% of ISS crew:
 - Δ total retinal thickness (TRT) $>20\ \mu\text{m}$ – First indication of **optic disc edema**
 - Development of **chorioretinal folds**
 - Change in **cycloplegic refraction** $\geq 0.75\ \text{D}$
 - and/or development of **globe flattening**
- SANS severity thought related to mission duration. SANS poses a significant risk to expeditionary spaceflight (e.g., a 3-yr Mars mission)

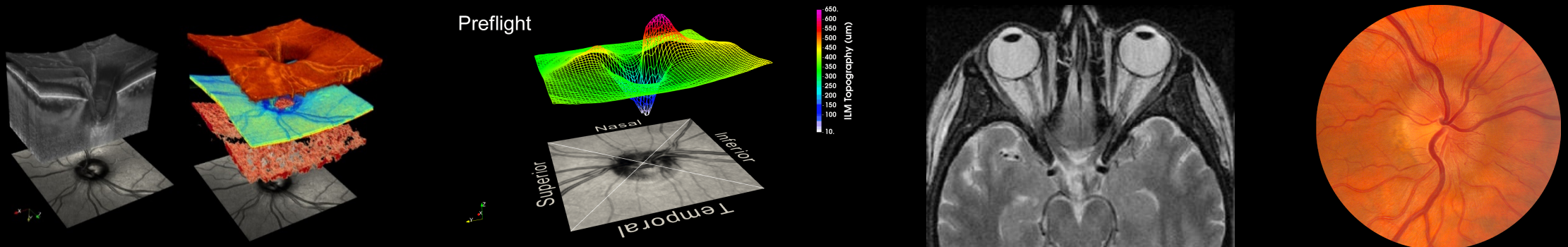




Take-Home Messages



- **SANS countermeasures are being aggressively pursued & studied**
- **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., CO₂ levels, NaCl intake, exercise type/levels, etc.)
 - Low sample sizes (especially females)
- **Efforts will benefit terrestrial medicine** (e.g., advanced & automated data analytics; miniaturized & semi-autonomous diagnostic devices; new objective-based definitions of ONH disease; etc.)

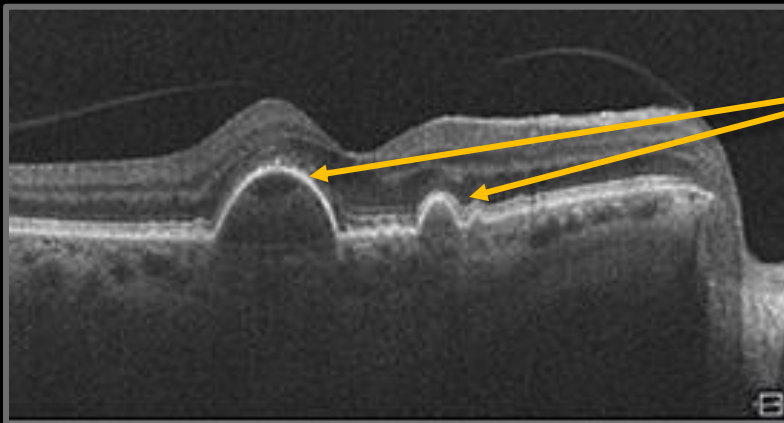




Newly-Discovered Ocular Changes



- **Retinal Pigment Epithelial Detachments (PEDs)**
 - Separations between retinal pigment epithelium (RPE) & Bruch's membrane
 - Terrestrially:
 - Associated w/ chorioretinal disease (e.g., central serous chorioretinopathy, age-related macular degeneration)
 - May blur or obscure vision, especially if located near fovea
 - **Small PEDs being detected more frequently on-orbit**
 - Due to use of higher density OCT scans since 2019 (??)



OCT scans of NON-astronaut showing *extreme PEDs* in age-related macular degeneration

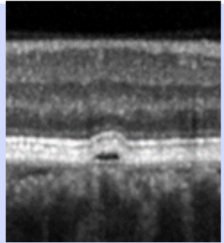
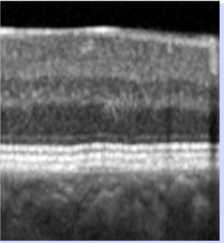
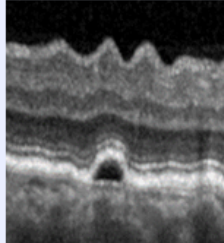
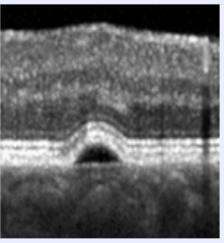
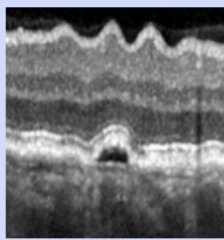
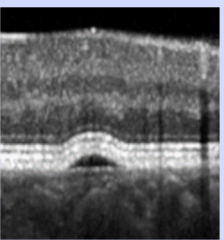
LL Zheng, et al., 2018, *Treatment of Pigment Epithelial Detachments in Age-Related Macular Degeneration*, Retinal Physician, accessed 22 Jan 2021, <<https://www.retinalphysician.com/issues/2018/nov-dec-2018/treatment-of-pigment-epithelial-detachments-in-age>>



Newly-Discovered Ocular Changes



- **Retinal Pigment Epithelial Detachments (PEDs)**
 - On-orbit PEDs tend to:
 - Occur in areas of “disrupted” RPE (pre-flight)
 - Sit above thickened choroid (i.e., pachychoroid)
 - Expand vertically, but not horizontally, during mission
 - Resolve quickly post-flight or--*in one case*--progress into serous chorioretinopathy (which later resolved)
 - To date, on-orbit PEDs *have not affected vision*
 - On-orbit PED questions:
 - Induced by pachychoroid ??
 - Precursor to pachychoroid-induced disease ??
 - Associated w/ SANS and/or do they provide insight into SANS pathogenesis ??

	Crewmember A	Crewmember B
Pre-Flight		
In-Flight		
Immediate Post-Flight		



Thoughts? Questions? Theories?



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References



- Draeger J, Schwartz R, Greonhoff S, Stern C. (1995). Self-tonometry under microgravity conditions. *Aviat Space Environ Med.* 66:568-70.
- Lee A, Mader T, Gibson C, Tarver W, Rabiei P, Riascos R, Galdamez L, Brunstetter T. (2020). Spaceflight Associated Neuro-ocular Syndrome (SANS) and the neuro ophthalmologic effects of microgravity: A review and an update. *npj Microgravity.* 2020. doi.org/10.1038/s41526-020-0097-9.
- Macias BR, Ferguson CR, Patel N, Gibson C, Samuels BC, Laurie SS, Lee SMC, Ploutz-Snyder R, Kramer L, Mader TH, Brunstetter T, Alferova IV, Hargens AR, Ebert DJ, Dulchavsky SA, Stenger MB. (2021) Changes in the Optic Nerve Head and Choroid Over 1 Year of Spaceflight. *JAMA Ophthalmol.* doi: 10.1001/jamaophthalmol.2021.0931
- Mader TH, Gibson CR, Barratt MR, Miller NR, Subramanian PS, Killer HE, Tarver WJ, Sargsyan AE, Garcia K, Hart SF, Kramer LA, Riascos R, Brunstetter TJ, Lipsky W, Wostyn P, Lee AG. (2020). Persistent globe flattening in astronauts following long-duration spaceflight. *Neuro-Ophthalmology.* 45(1): 29-35.

References



- Mader TH, Gibson CR, Pass AF, Kramer LA, Lee AG, Fogarty J, Tarver WJ, Dervay JP, Hamilton DR, Sargsyan A, Phillips JL, Tran D, Lipsky W, Choi J, Stern C, Kuyumjian R, Polk JD. (2011). Optic disc edema, globe flattening, choroidal folds, and hyperopic shifts observed in astronauts after long-duration space flight. *Ophthalmology*. 118(10):2058-69.
- Roberts DR, Albrecht MH, Collins HR, Asemani D, Chatterjee AR, Spampinato MV, Zhu X, Chimowitz MI, Antonucci MU. (2017). Effects of Spaceflight on Astronaut Brain Structure as Indicated on MRI. *N Engl J Med*. 377(18):1746-1753.
- Zheng LL, Tang PH, Todorich B, Mruthyunjaya P. Treatment of Pigment Epithelial Detachments in Age-Related Macular Degeneration, Retinal Physician, <https://www.retinalphysician.com/issues/2018/nov-dec-2018/treatment-of-pigment-epithelial-detachments-in-age>

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