Ocular Impacts of Prolonged Space Flight

Tyson Brunstetter, OD, PhD, MBA, FAAO, FAsMA, CAsP
Captain, Medical Service Corps, U.S. Navy

Navy Aerospace/Research Optometrist
Space and Occupational Medicine Branch
NASA Johnson Space Center

Aerospace Physiology Society Luncheon
Aerospace Medical Association – 89th Annual Scientific Meeting – 09 May 2018

Background: *My Assignment*

- Detailed via DoD Executive Secretary, Office of Secretary of Defense (OSD)
  - 3-year tour (PRD: Oct19)
  - Occupying 9999 billet (“General Group”)
  - Stationed at NASA Johnson Space Center (Houston, TX), w/in Space Medicine Operations Division
- Interact routinely with…
  - Clinicians (i.e., flight surgeons, optometrists, etc.)
  - Scientists
  - Trainers
  - Astronauts/cosmonauts – Terrestrial & on-orbit
  - External Subject Matter Experts (SMEs)
- Primary duty: Support efforts associated w/ Spaceflight Associated Neuro-ocular Syndrome (SANS)

Background: *Johnson Space Center*

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Background: *ISS*

- International Space Station (ISS)
  - In use since 2000
    - 54 expeditions completed
  - U.S. n* = 61 (as of Dec17)
  - Duration: ~0.5 to 1y
  - International partners
    - United States
    - Russia
    - European Union
    - Canada
    - Japan
  - Crew: Typically 5-6
  - “Low Earth orbit”

* Person flights; may include multiple-time flyers w/in program

Background: *The Future…*

- The space environment: *Not human friendly*
- NASA plans to send astronauts outside of Earth's magnetic & gravitational fields in 2020s
  - Moon return?
  - Mars missions in 2030s. Duration: 2.25 to ~3 yrs
    - Unprecedented challenges to health & performance
    - Top NASA human research priorities for expeditionary missions
      - Radiation risks
      - Spaceflight Associated Neuro-ocular Syndrome (SANS)
      - Behavioral health
      - Food & pharmaceutical stability
      - In-flight medical conditions

Recent SANS Headlines

Speaking of Science

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

Health & Science

The mysterious syndrome impairing astronauts' sight

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

Astronauts Returning to Earth With Vision Problems

Video Channels

The Washington Post

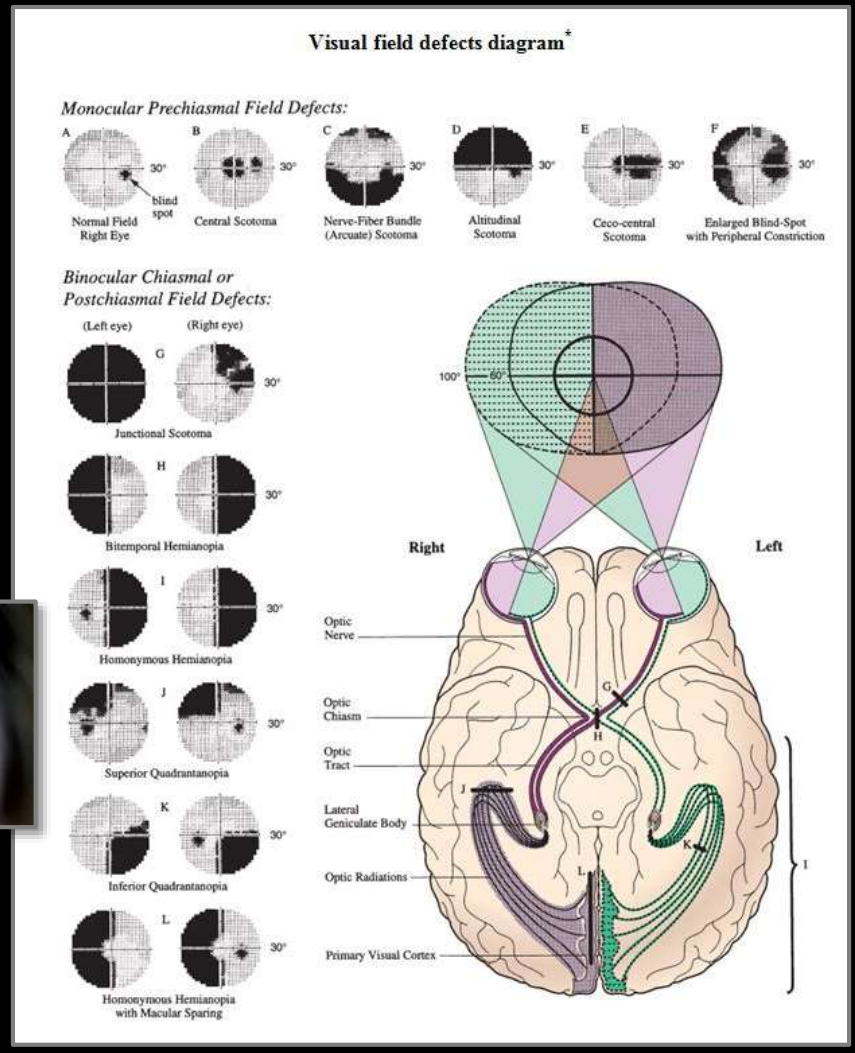
POST ORIGINALS

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

What's So Special About the Eye?

What's So Special About the Eye?

- Only about 1" in diameter, but…
  - Provides ~80% of our sensory input
    - Medical Emergency: "Life, limb, or eyesight"
  - Presents tremendous amount of health information
    - Neurological state (4-of-12 cranial nerves): via eye position, lid position, pupil size & reaction, visual performance
      - Tumor, aneurysm, stroke, etc.



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    - Presence/severity of systemic disease
      - High blood pressure; diabetes; impending stroke; high intracranial pressure; hyperthyroidism; etc.

Normal view of eye's posterior pole: Retina; optic nerve head (optic disc); retinal blood vessels; macula

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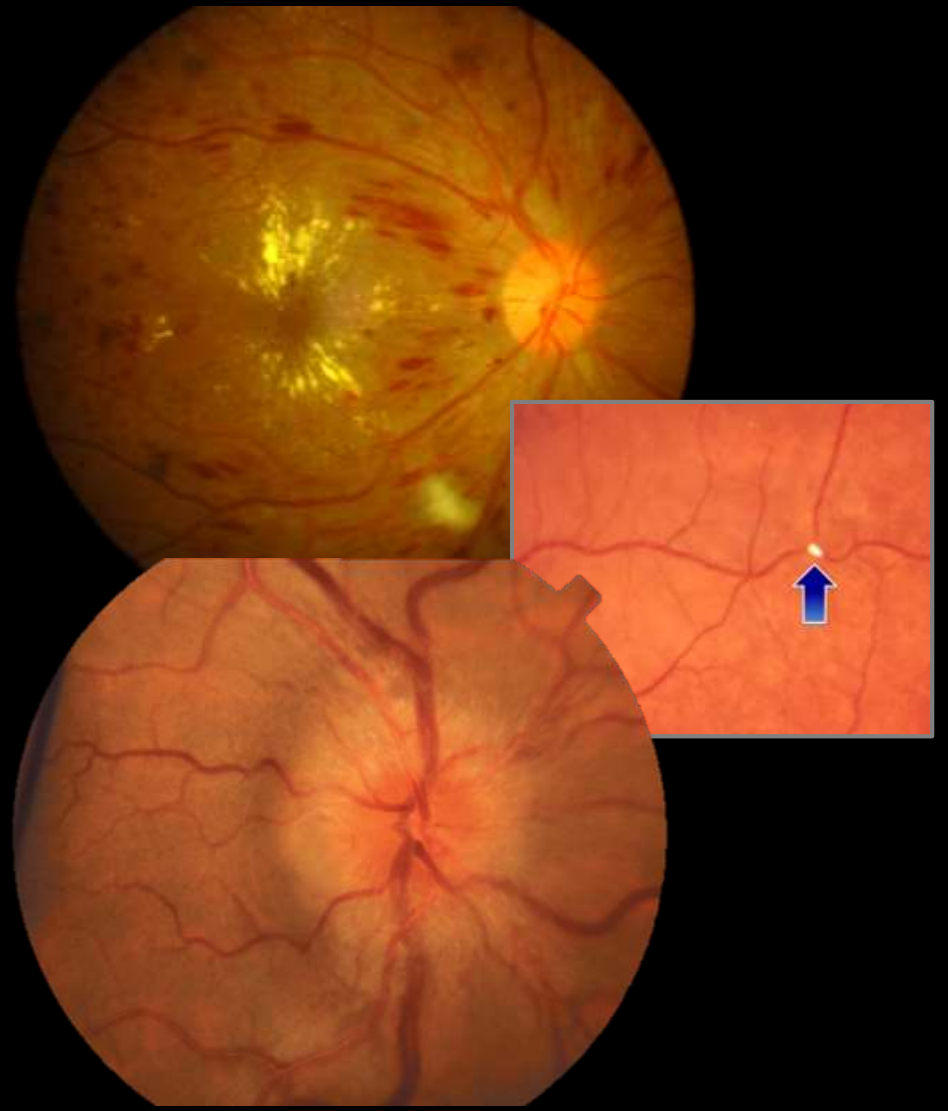
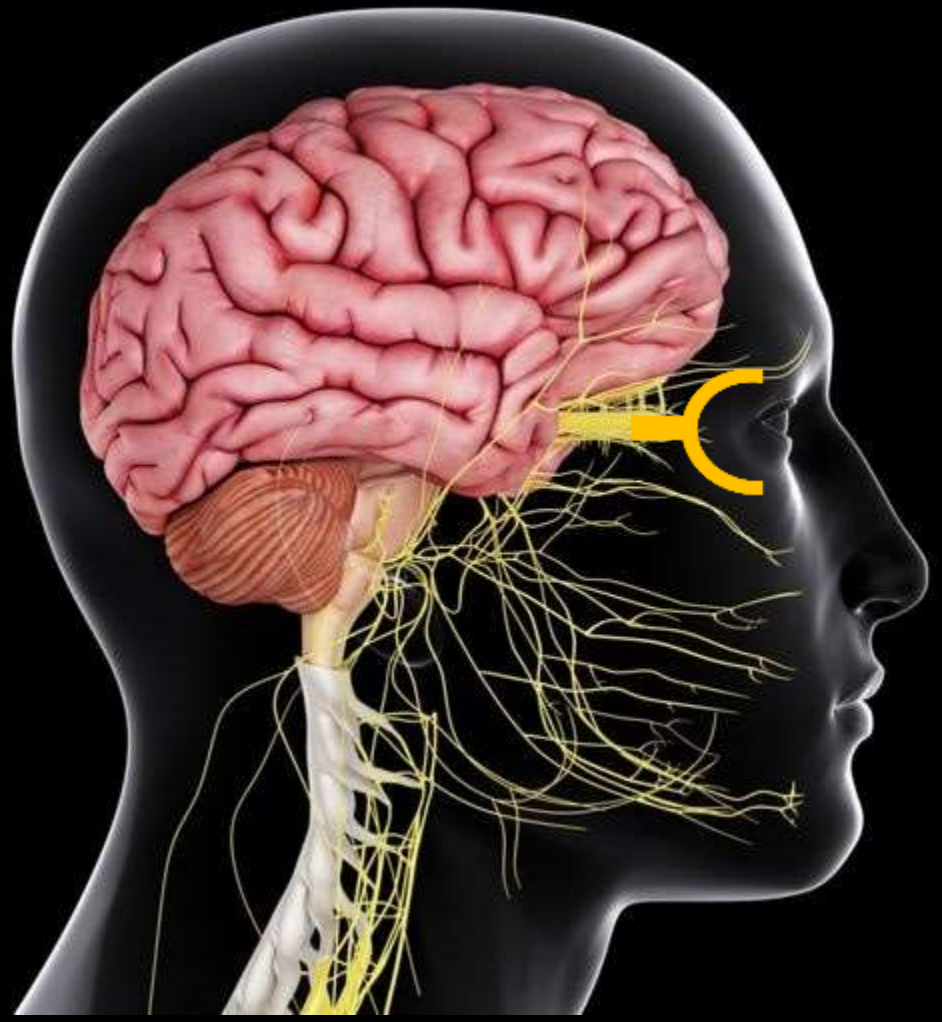
  - "Window to the soul": ∴ Astronaut eyes have always been eval'd pre/post-flight by NASA



What's So Special About the Eye?

- Optic nerve, optic nerve head, and retina…
  - *Central nervous system*
    - Behind blood-brain barrier
    - Susceptible to permanent loss



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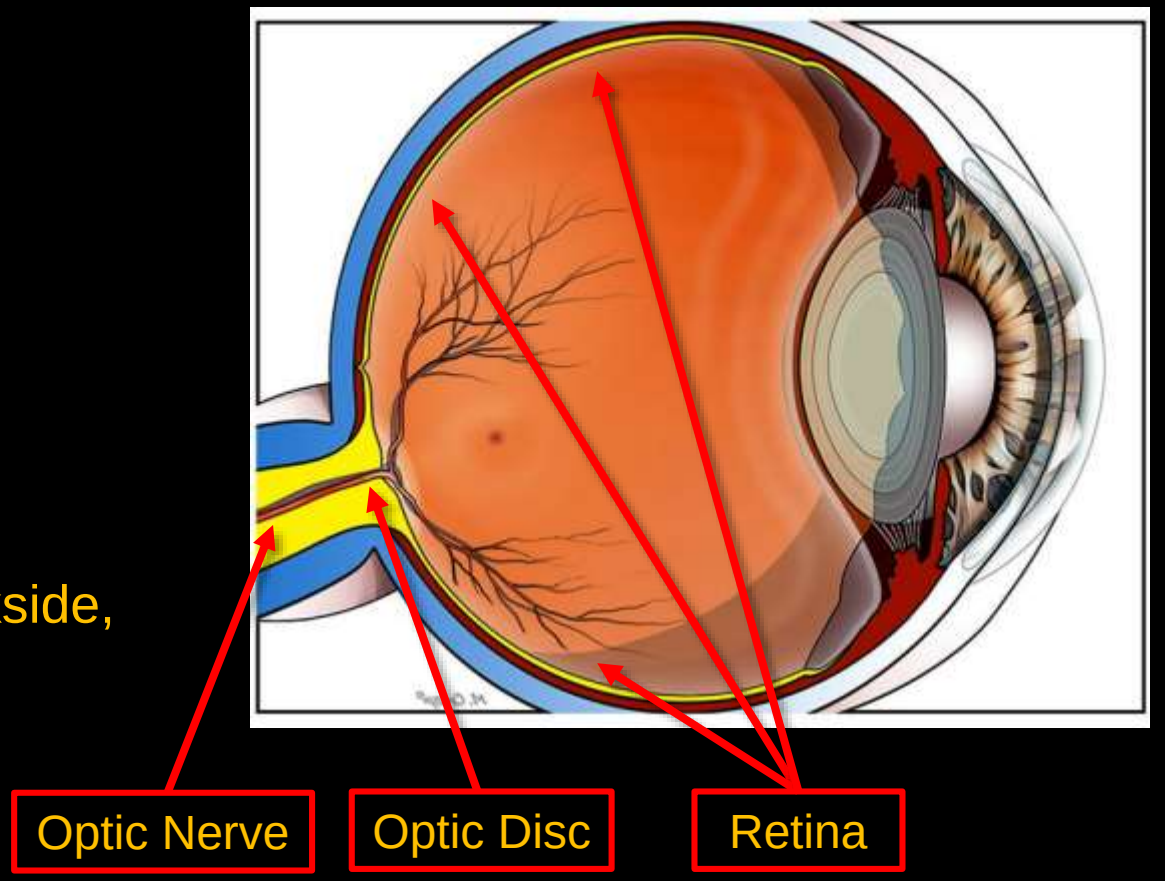
  - *Central nervous system*
    - Behind blood-brain barrier
    - Susceptible to permanent loss
  - Optic nerve
    - Connects eye to brain
    - Bathed in cerebrospinal fluid (CSF)
  - Optic nerve head (ONH) / "Optic disc"
    - Where optic nerve meets eye
    - Has *intracranial* pressure (ICP) on backside, *intraocular* pressure on frontside



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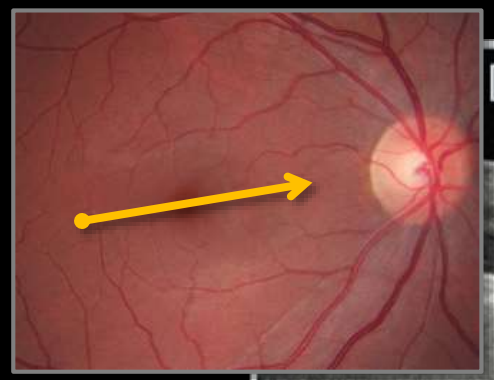
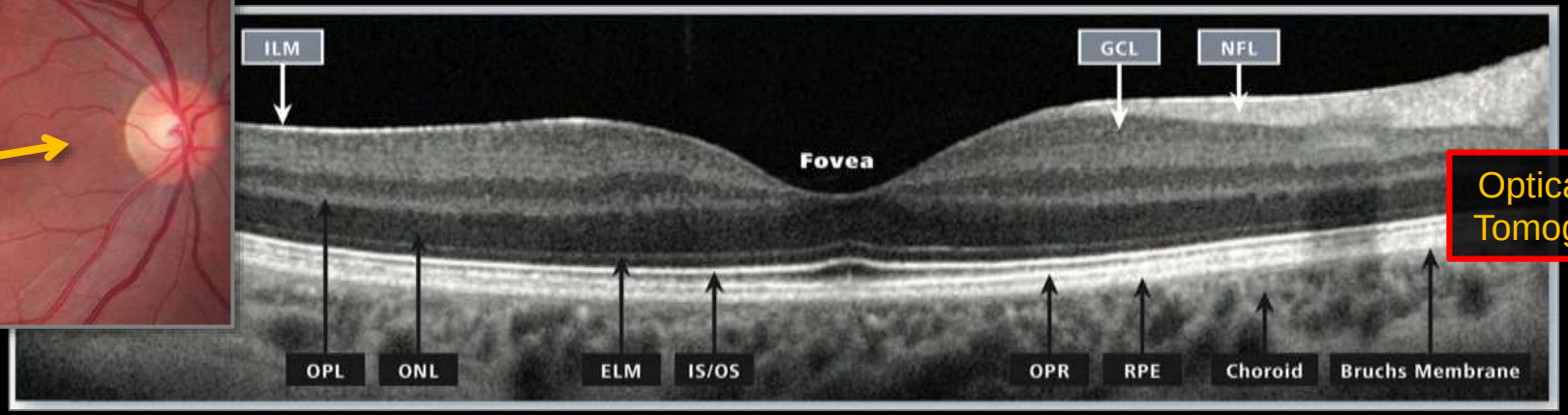
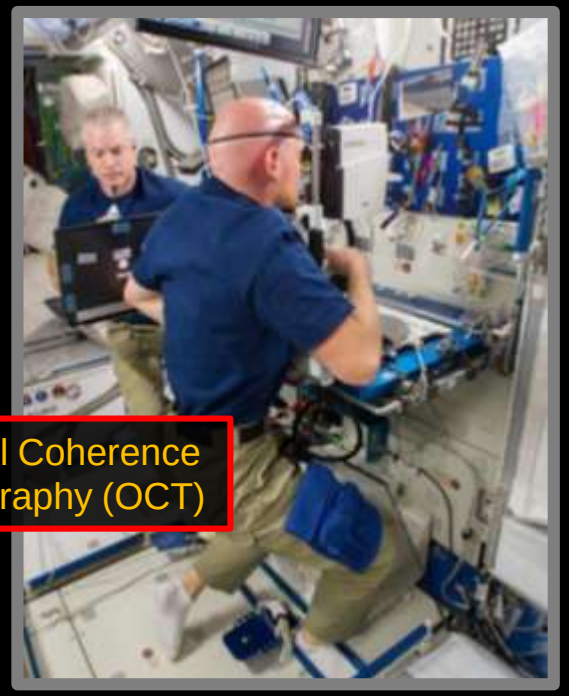
- Optic nerve, optic nerve head, and retina…
  - Retina
    - Converts light energy into neural signals
      - Sends signals through nerve fibers (via disc & optic nerve) → brain → "vision"
    - Extremely high metabolism: *High demands, low reserves*
      - Photorecepter mitochondria operate at ~70-80% capacity
      - Requires reliable, sustained blood supply (O_2, glucose, etc.)

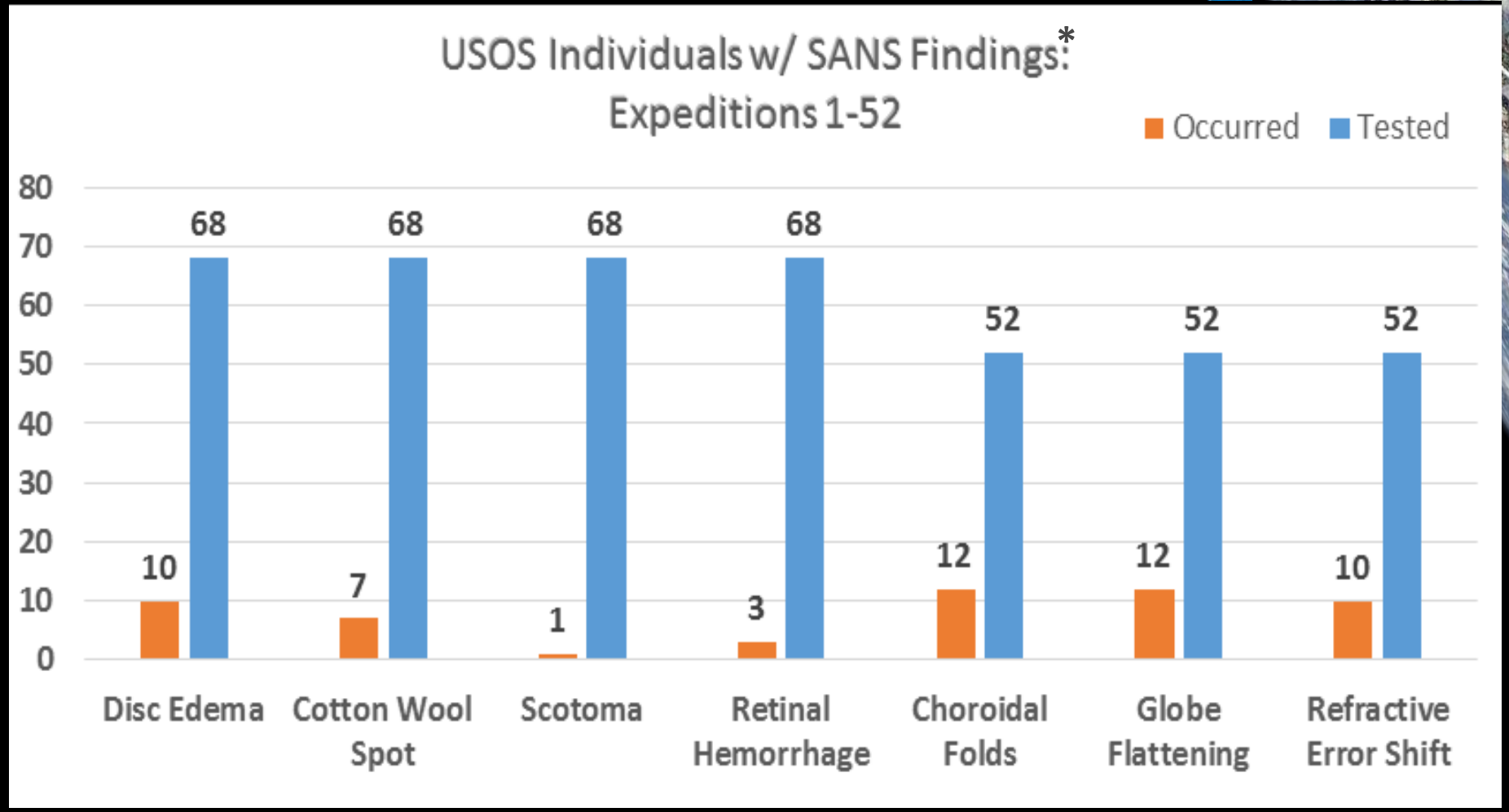






Optical Coherence Tomography (OCT)

SANS: Clinical Findings



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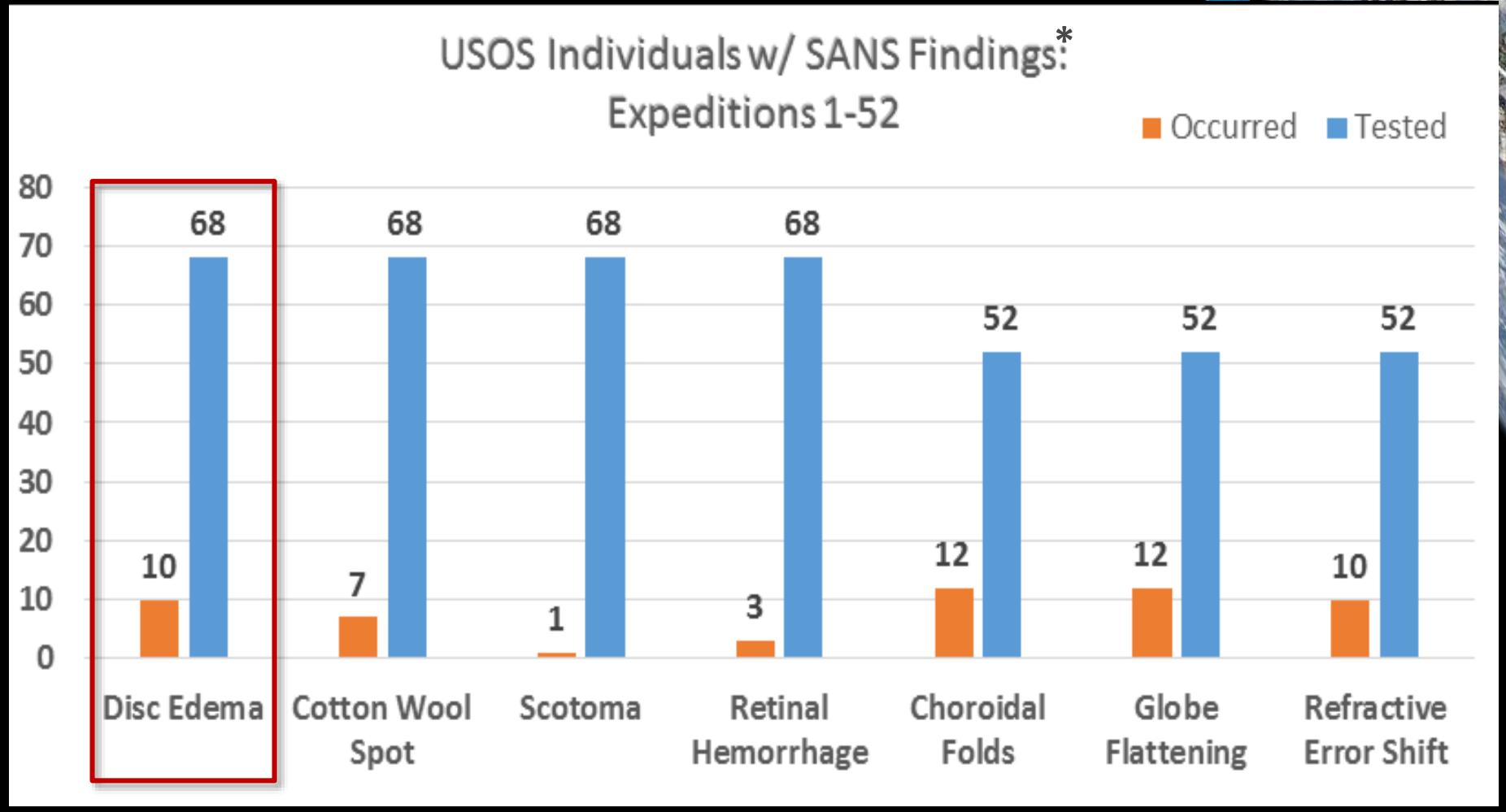
Pre-flight - OD



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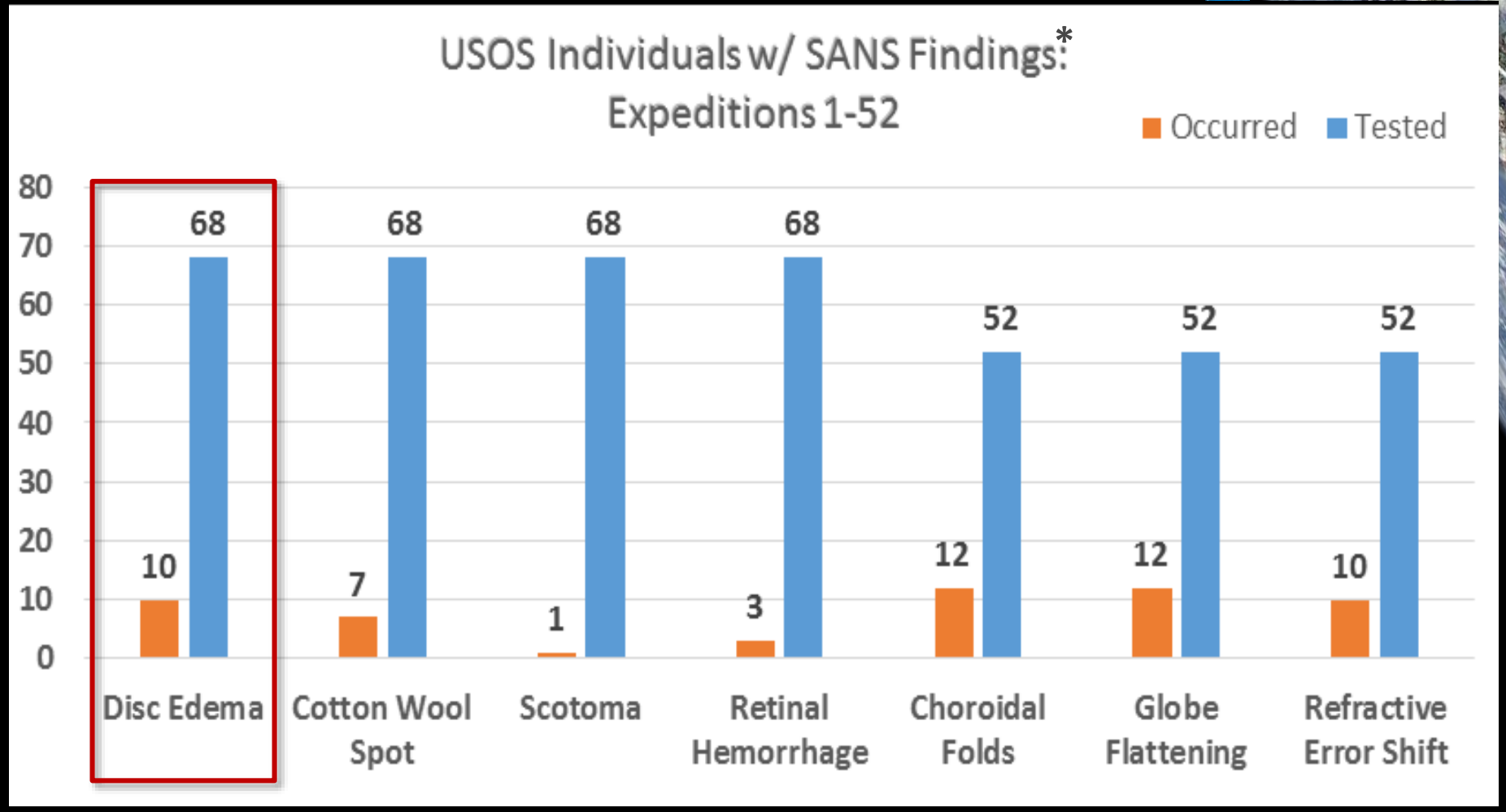
Post-flight - OD



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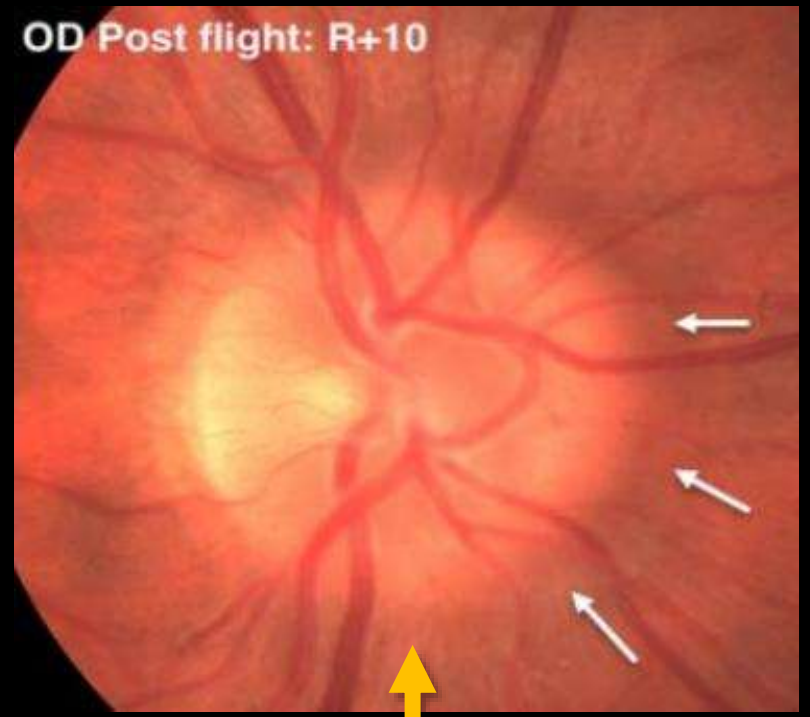
Clinical Findings: *Optic Disc Edema*

- *Edema: "Accumulation of excess fluid; swelling." Indicates an underlying abnormal condition (pathology)*
- *Terrestrially* -- Disc edema typically associated w/:
  - Unilateral: Optic neuritis/neuropathy, retinal artery occlusion, extreme hypertension
  - Bilateral: *Increase in ICP…*
    - e.g., Idiopathic intracranial hypertension (IIH)
  - Typically causes *symptoms* (e.g., for IIH: severe headaches, transient vision loss, double vision, enlarged blind spot, color vision impairment)
  - Edematous CNS neurons can atrophy, lost permanently, depending on *severity & duration*
    - Good News: So far, no obvious loss of ocular nerve tissue detected in astronauts

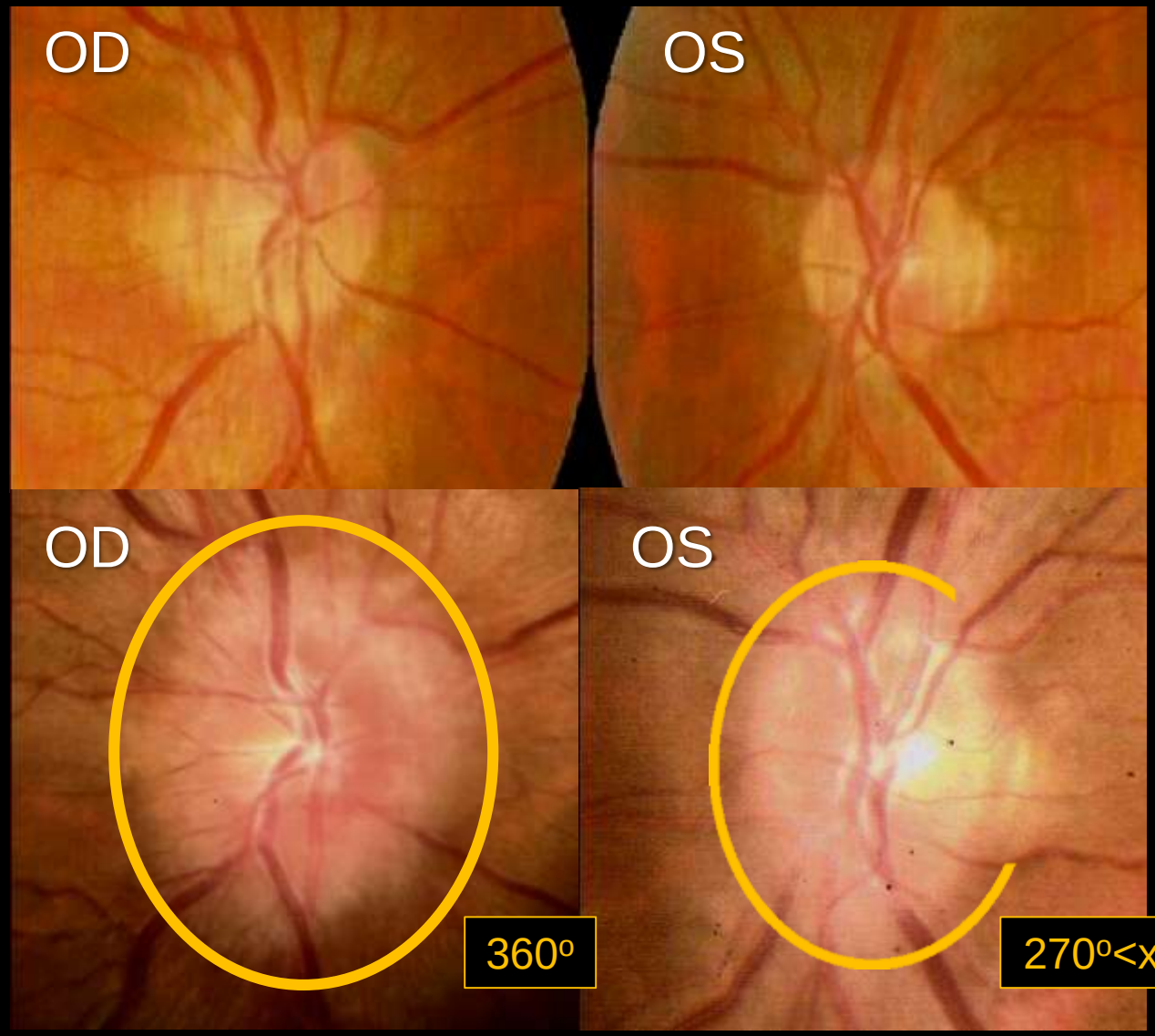


Fundoscopic image of optic disc OD, R+10 days. Arrows indicate "C" shaped halo of edema

Clinical Findings: *Optic Disc Edema*

Pre-flight fundoscopic images of the optic discs

Post-flight images of optic discs, showing: *Grade 3 edema OD*
Grade 1 edema OS

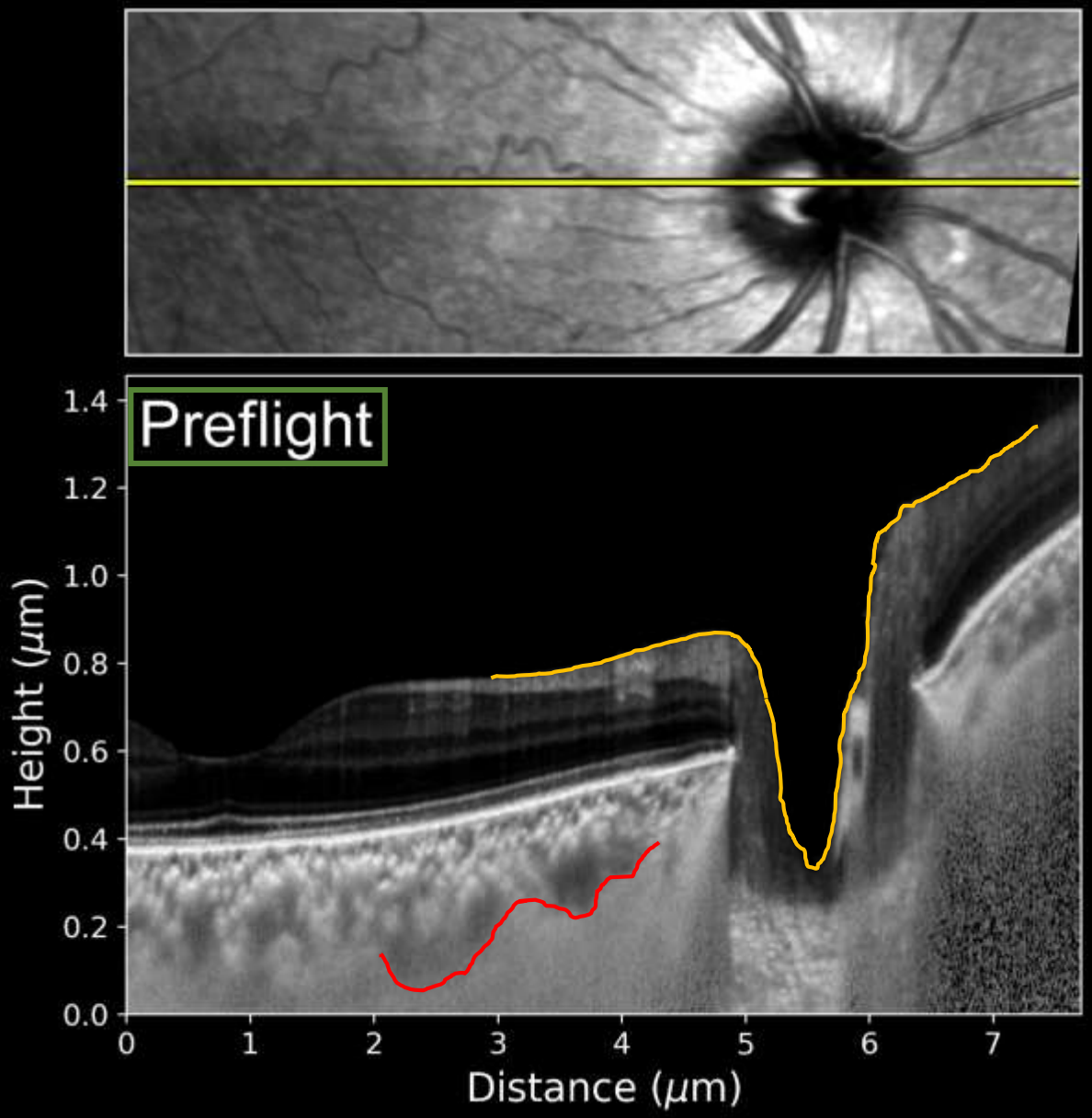


Clinical Findings: *Optic Disc Edema*

Recent Findings

- "Optic disc changes" w/ long-duration spaceflight
  - David Brown, MD – Retinal specialist; SANS Research & Clinical Advisory Panel
    - Analyzed 14 crewmembers having complete pre-flight & on-orbit OCT data, *ALL* showed signs of:
      - Choroidal thickening
      - Venous engorgement
      - *Optic disc edema*
      - And…optic discs tend to expand forward *and backward* (opposite to IIH)
  - Nimesh Patel, OD, PhD – OCT scientist/SME; analyzes all crewmember OCT data
    - Also described these edema & disc expansion findings

(*Patel N, Pass A, Mason S, Gibson CR, Otto C. Optical coherence tomography analysis of the optic nerve head and surrounding structures in long-duration International Space Station astronauts. JAMA Ophthalmol 2018 Feb 1;136(2):193-200*)



Source:
Mayra Nelman &
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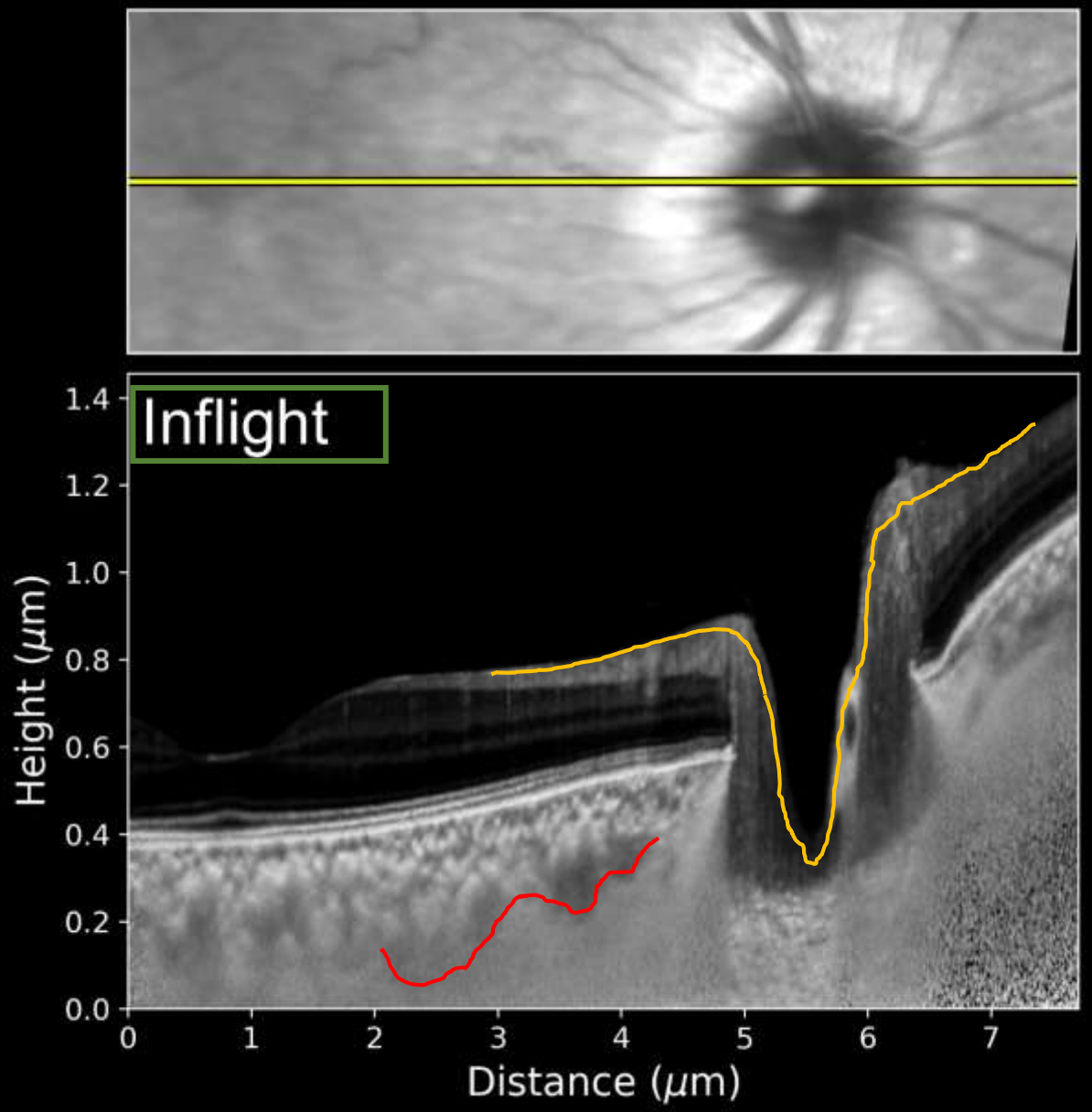

Non-Case w/ “subclinical edema”

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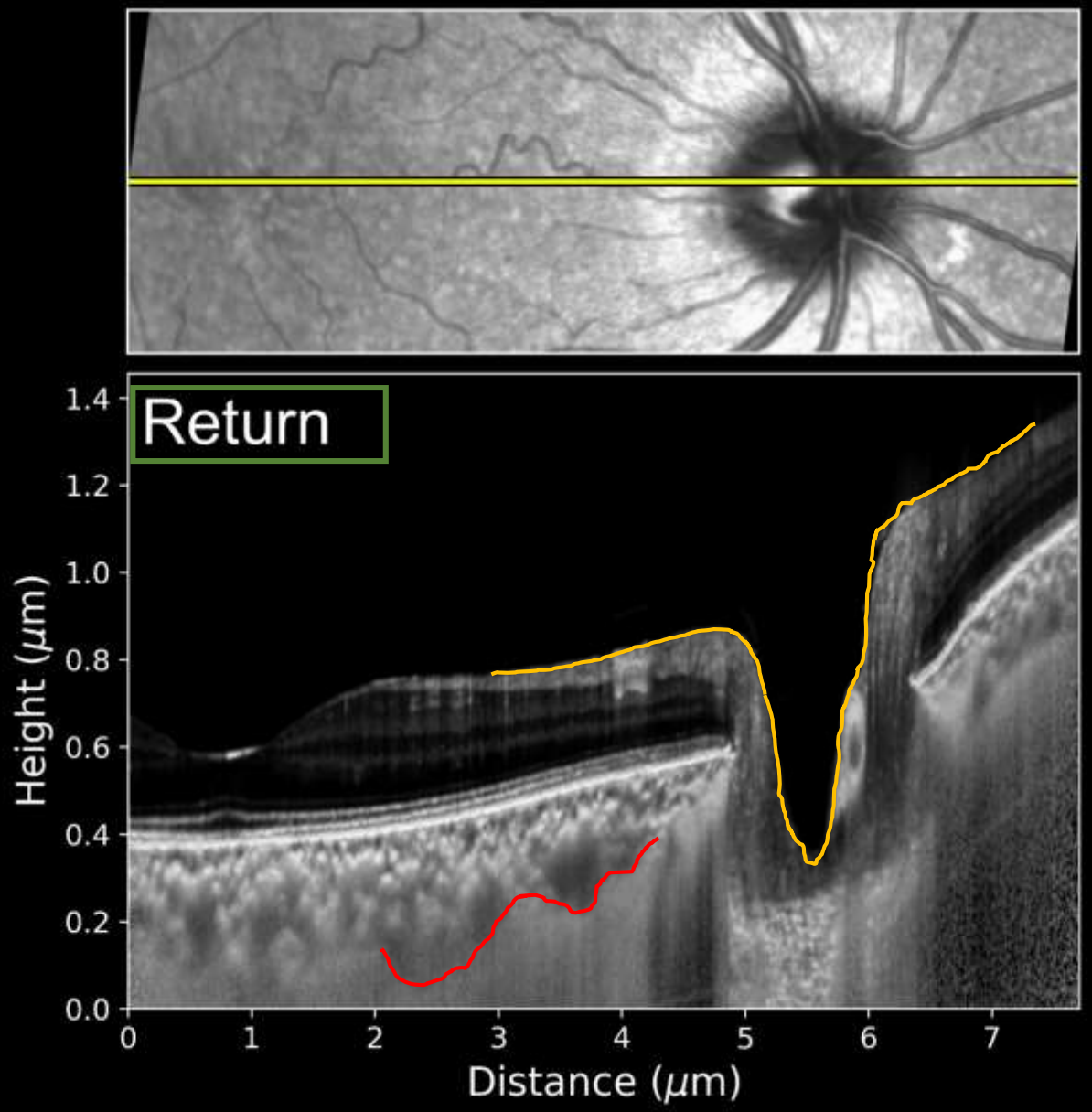

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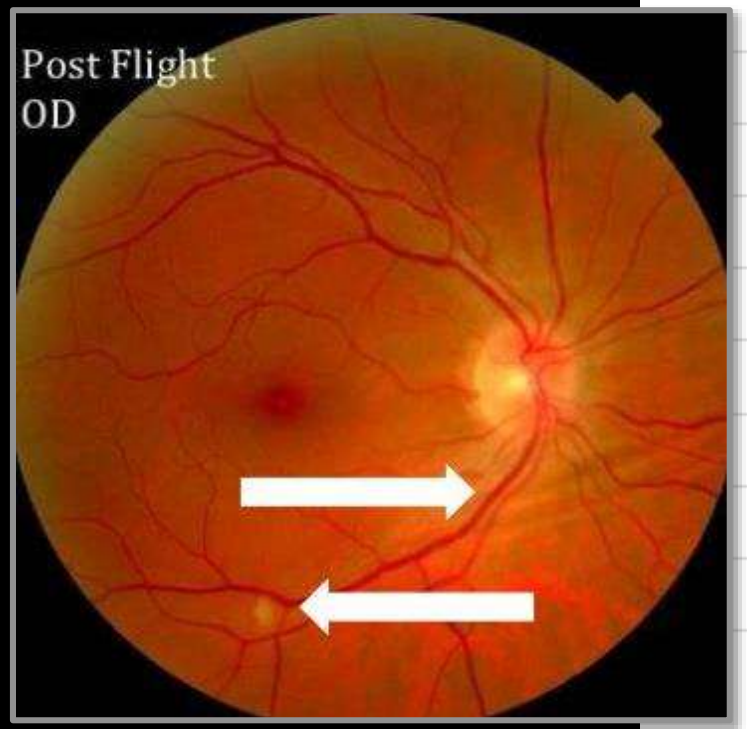

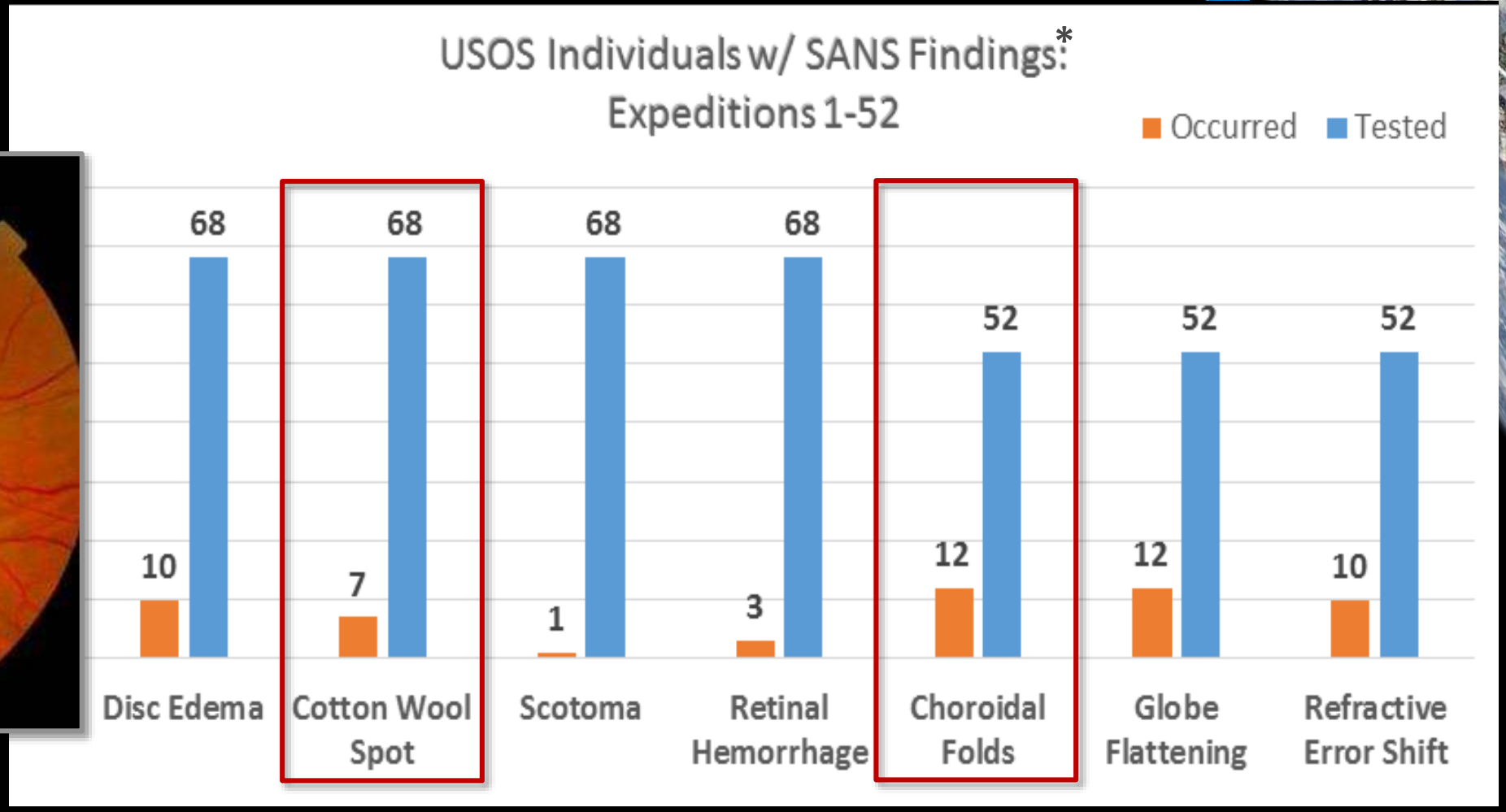

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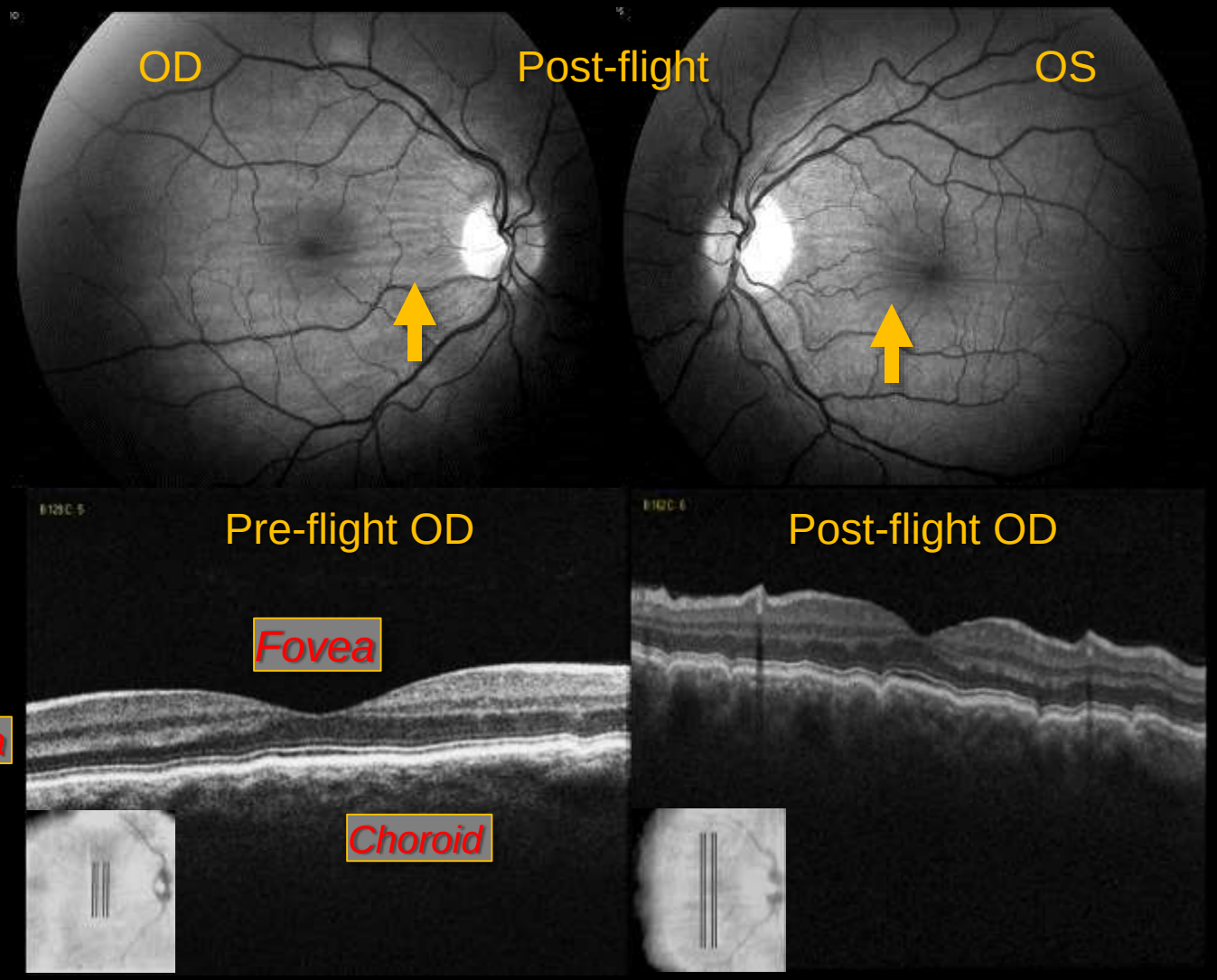
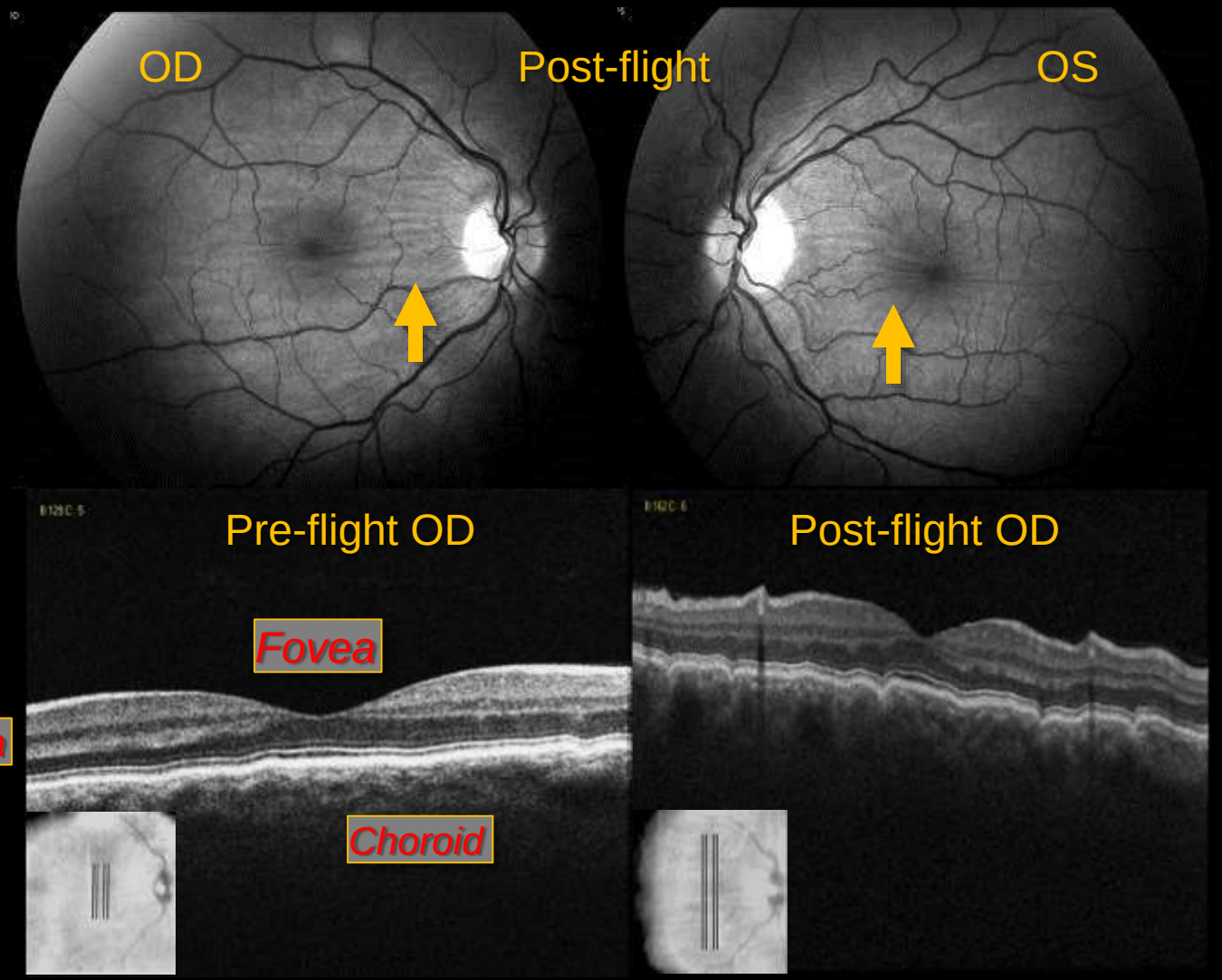
Clinical Findings: *Choroidal Folds*

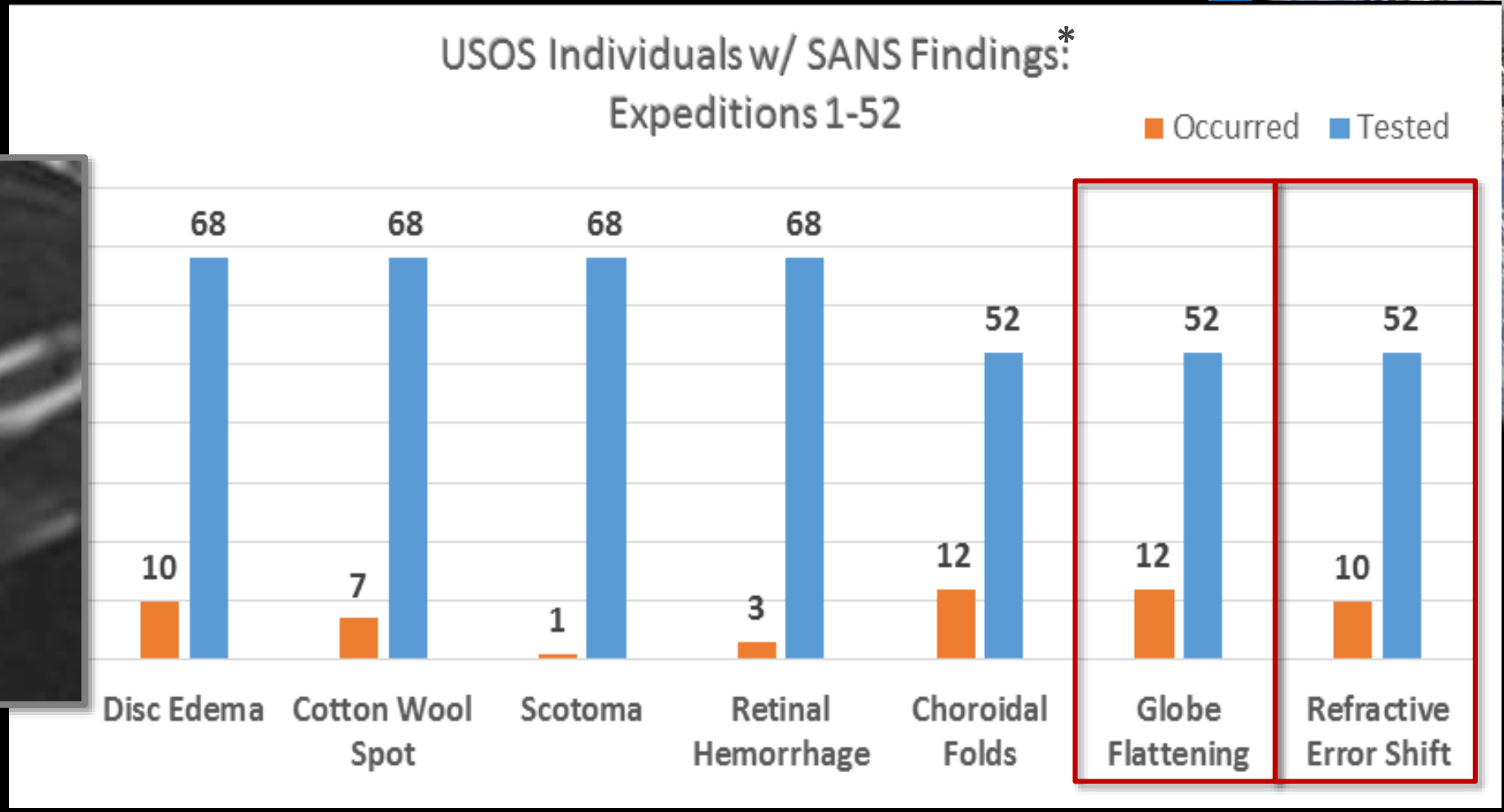


- SANS cases:
  - Choroidal thickening due to vessel engorgement → induces choroidal (and sometimes retinal) folds

Clinical Findings: *Choroidal Folds*



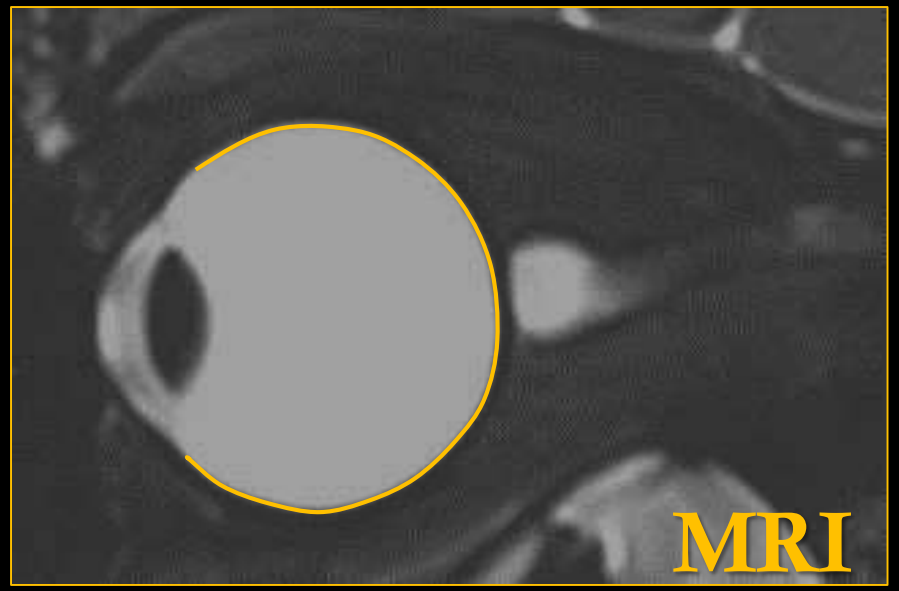
- SANS cases:
  - Choroidal thickening due to vessel engorgement → induces choroidal (and sometimes retinal) folds
  - Usually run horizontally
  - Can resolve post-flight or persist (for 12+ yrs)
  - So far, no significant impact on best-corrected visual acuity (BCVA)…*but is a significant risk*
- *Terrestrially:* Assoc. w/ choroidal or orbital tumors, scleritis, IIH



* Additional SANS signs not included: Optic nerve (ON) sheath distension, ON kinking/tortuosity, Retinal nerve fiber layer thickening, Retinal folds, Choroidal thickening. *Data analysis ongoing*

Clinical Findings: *Globe Flattening*

- Can resolve post-flight or can persist (for 7+ yrs)
- Case Example:
  - Male, mid 40s at time of flight
  - No significant PMH/PSH/PFH
  - No meds
  - Normal BP (118/64)
  - Normal lipids
  - ECG Stress test normal w/ VO_2 max of 51ml/kg



Pre-flight

Clinical Findings: *Globe Flattening*

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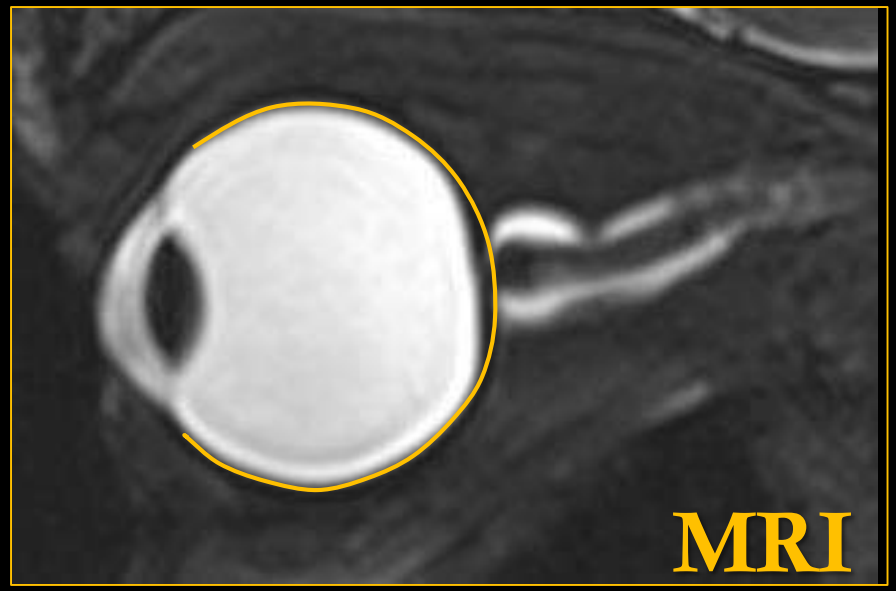

6 days post-flight

Clinical Findings: *Globe Flattening*

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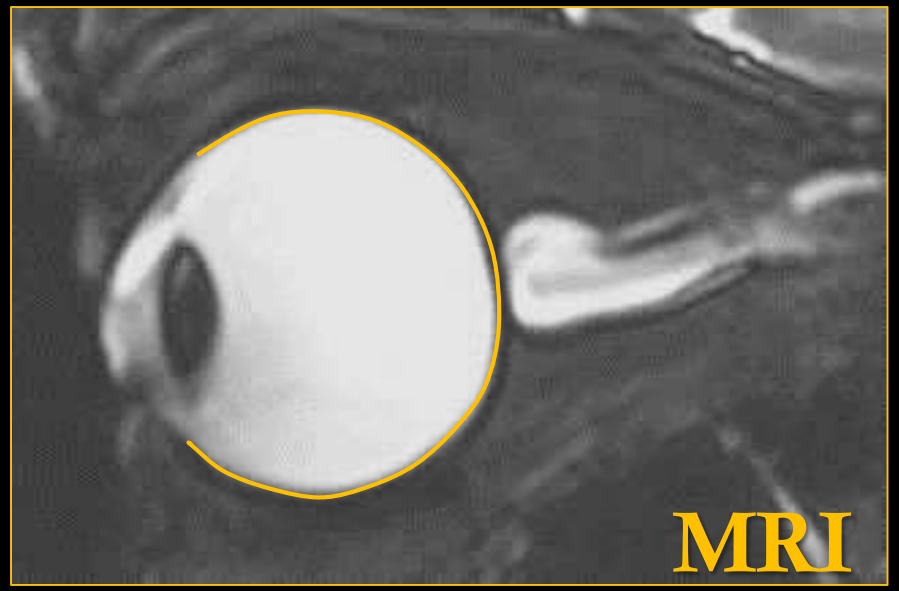
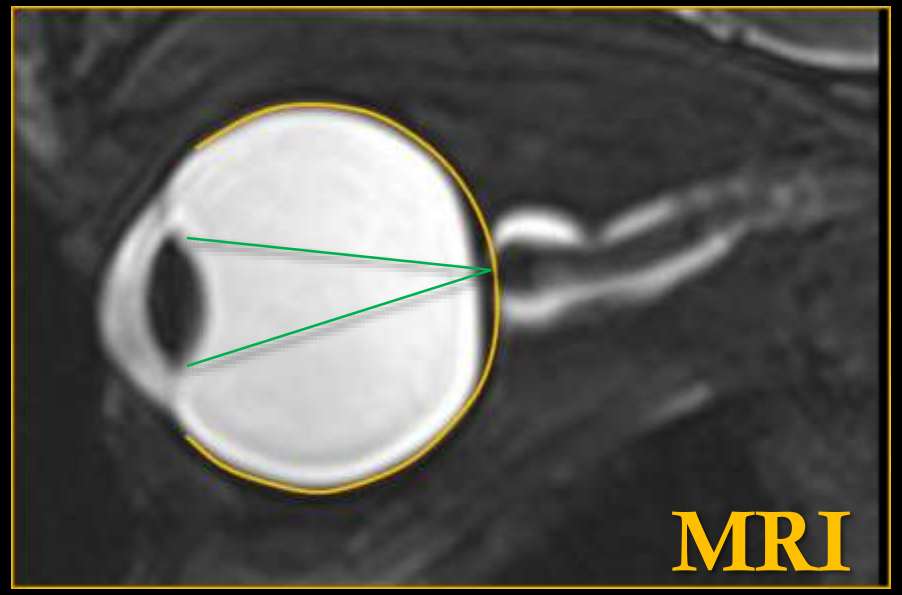
  - No meds
  - Normal BP (118/64)
  - Normal lipids
  - ECG Stress test normal w/ VO_2 max of 51ml/kg
- *Terrestrially*: Typically associated w/ increased intracranial pressure (e.g., IIH); typically bilateral



1 year post-flight

Clinical Findings: *Hyperopic Shift*

- Post-flight questionnaires (1989 - 2011): *23% of short- & 49% of long-duration mission astronauts report a degradation in vision* (especially at *near distances*)
  - Provided “Space Anticipation Glasses”
- *Mostly* attributable to globe flattening
- Pre-to-post-flight change
  - Up to +1.75D
  - Like globe flattening, can rebound or persist (7+ years)
- *No loss in BCVA* (i.e., 20/20 or better)



6 days post-flight

Common Characteristics of the Cases

Common Characteristics of the Cases

- Almost all were long duration *ISS mission crewmembers*
  - *Is severity related to flight duration??* [If so, what about a *3-yr Mars mission*??]
- *Healthy individuals w/ normal* medical history *& normal* pre-flight eye exams
  - *Negative* for uncontrolled systemic disease
- ISS cabin
  - Elevated CO_2: 8-10x terrestrial levels (~0.33-0.5% avg)
    - CO_2 is a potent vasodilator – *A potential SANS contributor??*
- *None* experienced loss in visual performance (e.g., BCVA, color vision, or depth perception)
- *None* complained of classic symptoms of idiopathic intracranial hypertension (IIH)
  (e.g., Severe headaches, transient vision loss/obscurations, double vision, pulsatile tinnitus, etc.)
- Tendency for SANS signs to be *right-hand biased*

Why is this Happening?

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Microgravity → Cephalad fluid shift → Cerebral venous congestion (i.e., overfilling & distension)

Confounding variables: Resistive exercise / Sodium intake / CO_2 levels / Pharmaceuticals??

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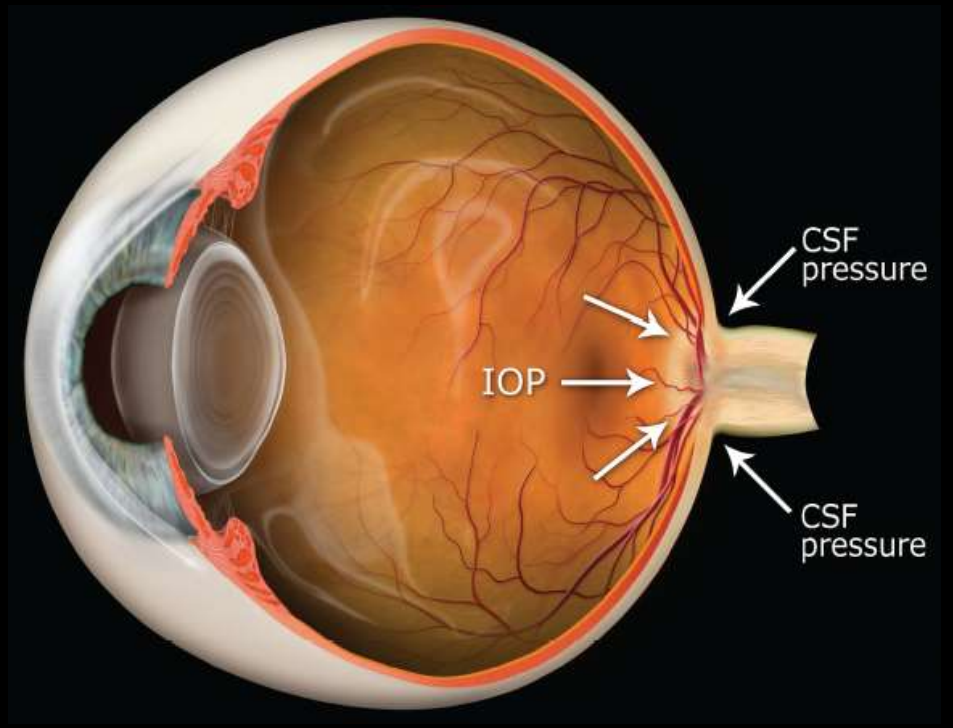
Microgravity → Cephalad fluid shift → Cerebral venous congestion (i.e., overfilling & distension)

Confounding variables: Resistive exercise / Sodium intake / CO_2 levels / Pharmaceuticals??

- Hypothesis #1: *Increased intracranial pressure* (ICP)
  - e.g., Enough to cause an imbalance between ICP & intraocular pressure (i.e., translaminar pressure gradient)
- Hypothesis #2: *A local eye problem*
  - e.g., Compartmentalization of perioptic subarchnoid spaces → local increase in ICP
- Hypothesis #3: *Venous congestion* alters local physiology and/or places direct pressure on retinal axons
- Hypothesis #4: *Individual anatomical/genetic factors*
  - e.g., Altered folate-dependent 1-carbon metabolism



Take-Home Messages

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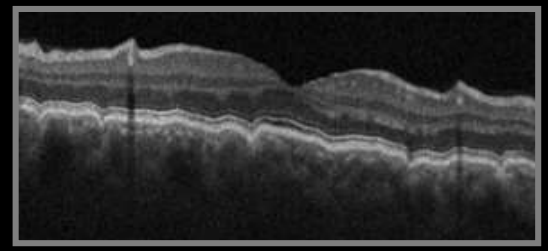

- Top SANS-related risk: *Optic disc edema*
  - Part of CNS – Susceptible to permanent loss, depending on *severity & duration*
  - Currently, no evidence of true vision impairment in long-duration astronauts
  - Most/all ISS astronauts have ocular “changes” in-flight, including disc edema
  - Cannot yet predict impact of SANS during expeditionary spaceflight
- *Choroidal folds*, if under fovea, also pose a mission risk
  - Could potentially decrease best-corrected VA to 20/40 – 20/60
- Small sample sizes & confounding variables hamper definitive conclusions

- There are potential opportunities for *win-win DoD/NASA collaborations*
  - Details / Fellowships / Clerkships / Research ??
  - Dozens of NASA projects that could benefit from aerospace physiologist expertise & experience, especially those w/ a research-based PhD

Questions?

CAPT Tyson Brunstetter, MSC (AsO), USN
COM: 281-792-7705
Email: Tyson.J.Brunstetter@nasa.gov

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