Introduction to Spaceflight Associated Neuro-ocular Syndrome (SANS) and its Risk to NASA Astronauts

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Why We Do What We Do…

Recent SANS 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

Health & Science

Astronauts Returning to Earth With Vision Problems

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

Video Channels

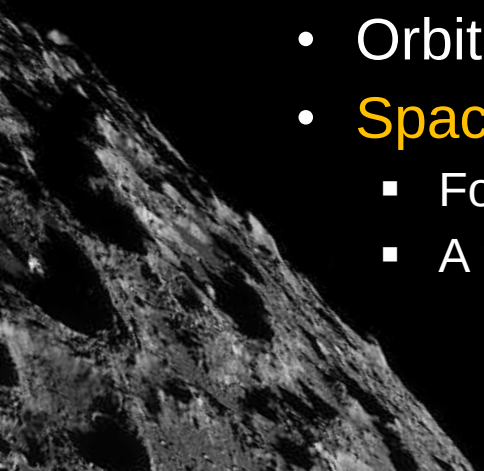
The Washington Post

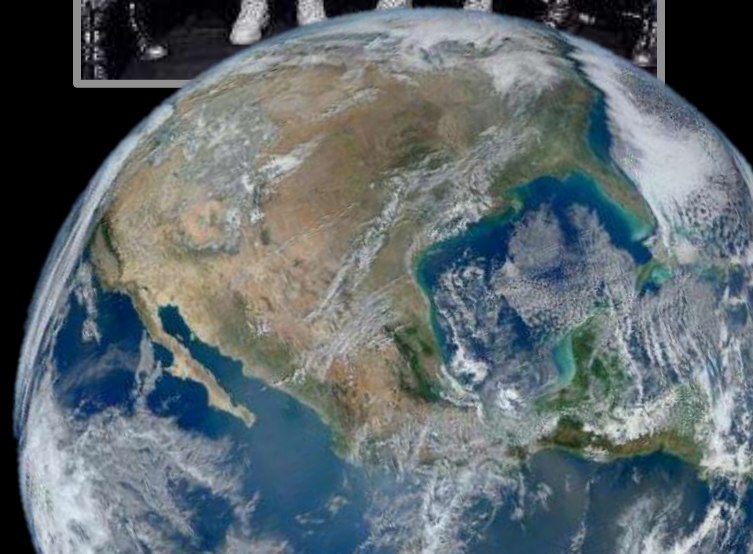
POST ORIGINALS

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

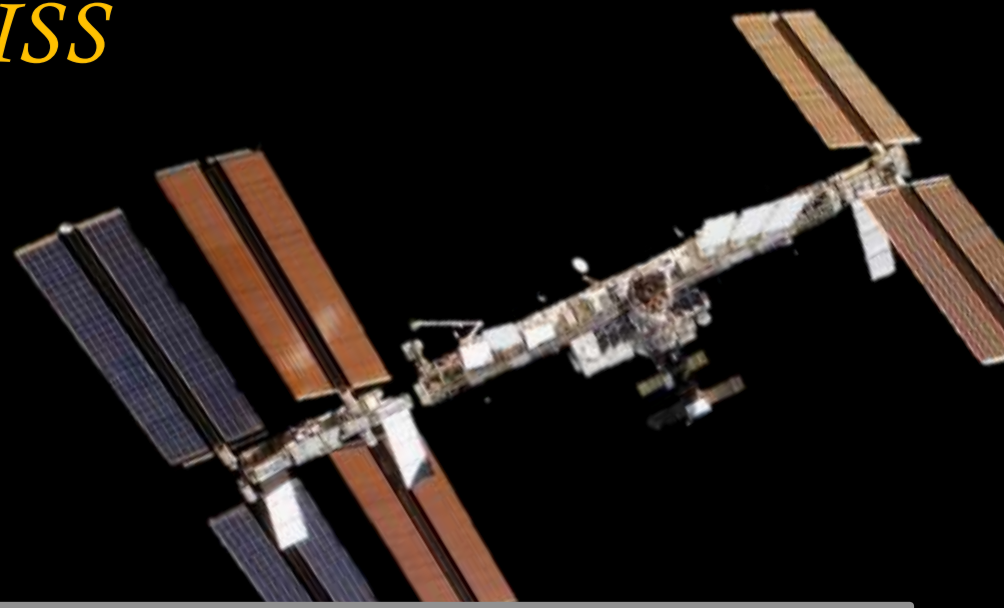
Background: *The Space Environment*

- Bottom-line: Not human friendly. For example…
  - Vacuum: No atmosphere; no air
  - Gravity
    - Gravity reduces w/ distance. ISS (@ ~200-250 mi) feels 90% of Earth's gravity…But…
    - ISS moves at ~17,500 mph, in constant freefall = "Microgravity"
  - Temperature extremes
  - Ionizing (high energy) radiation: Galactic cosmic rays, solar proton events
  - Orbiting space junk/debris: >550K larger than 1cm
  - Spaceflight Associated Neuro-ocular Syndrome (SANS)
    - Formerly called Visual Impairment Intracranial Pressure (VIIP)
    - A top risk to Deep Space Journey (e.g., mission to Mars)





Background: *ISS*

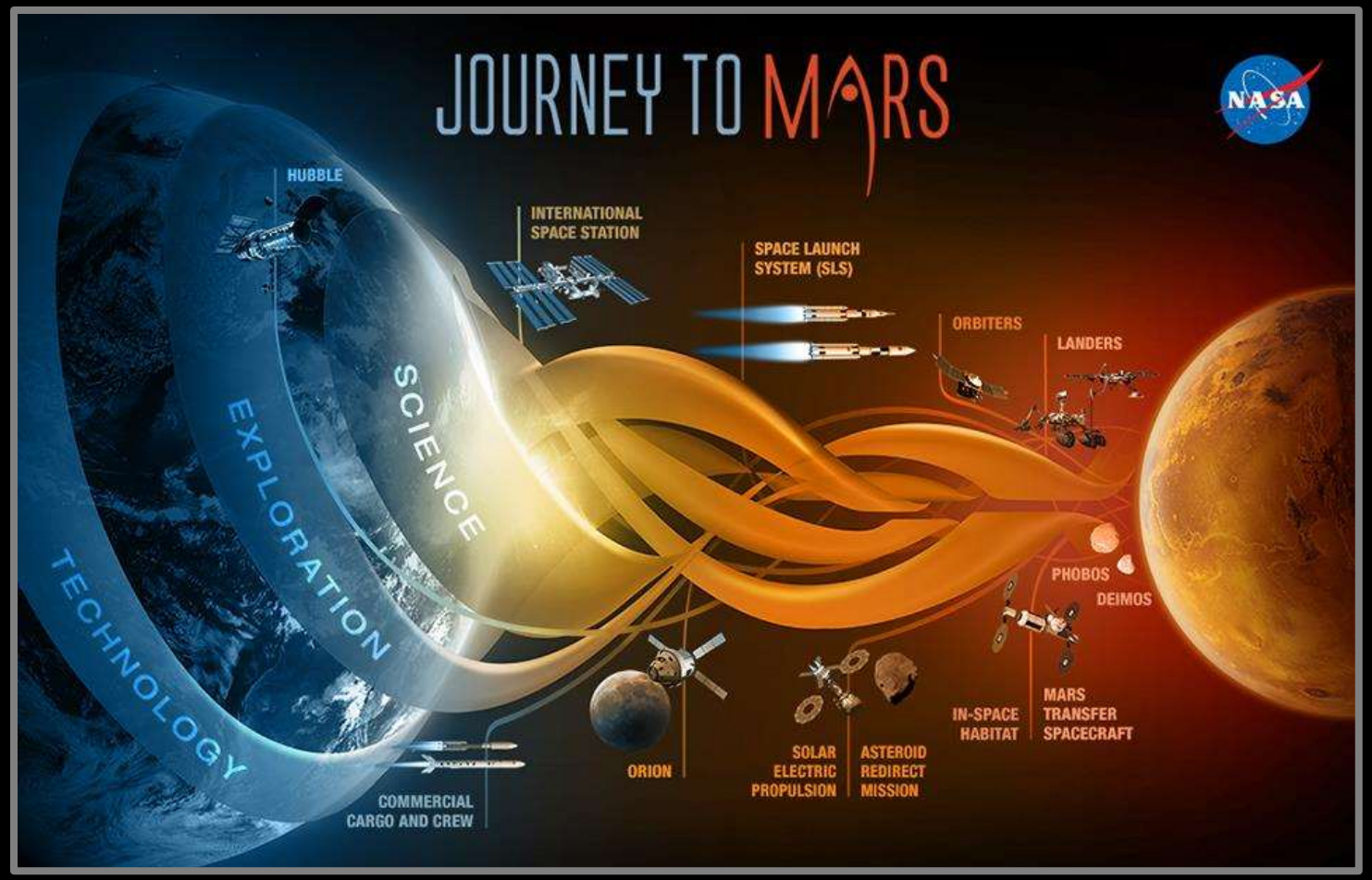


- International Space Station (ISS)
  - In use since 2000
    - 51 expeditions completed
  - *n = 58 (as of 31Jan17)
  - Duration: ~0.5 to 1y
  - International partners
    - United States
    - Russia
    - European Union
    - Canada
    - Japan
  - Crew: Typically 5-6
  - “Low Earth orbit”

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

Background: *The Future…*

- NASA to send humans to: An asteroid by 2025; Mars in the 2030s



Background: *SANS*

- Ocular testing has been performed pre- & post-flight
- Initial eye/vision testing capability on ISS was…
  - Ophthalmoscope (astro-physicians only)
  - Paper VA chart
  - Amsler grid
- Sentinel SANS case discovered in 2005, post-flight
  - Optic disc edema & cotton wool spot
- Surveillance/medical data collection has evolved
  - *Some* SANS-related testing began in 2008 (w/ Exp 18), but inconsistent
  - Feb 2010 (Exp 23): Standardized medical monitoring (i.e., “Eye MED B”) established

Ocular Surveillance

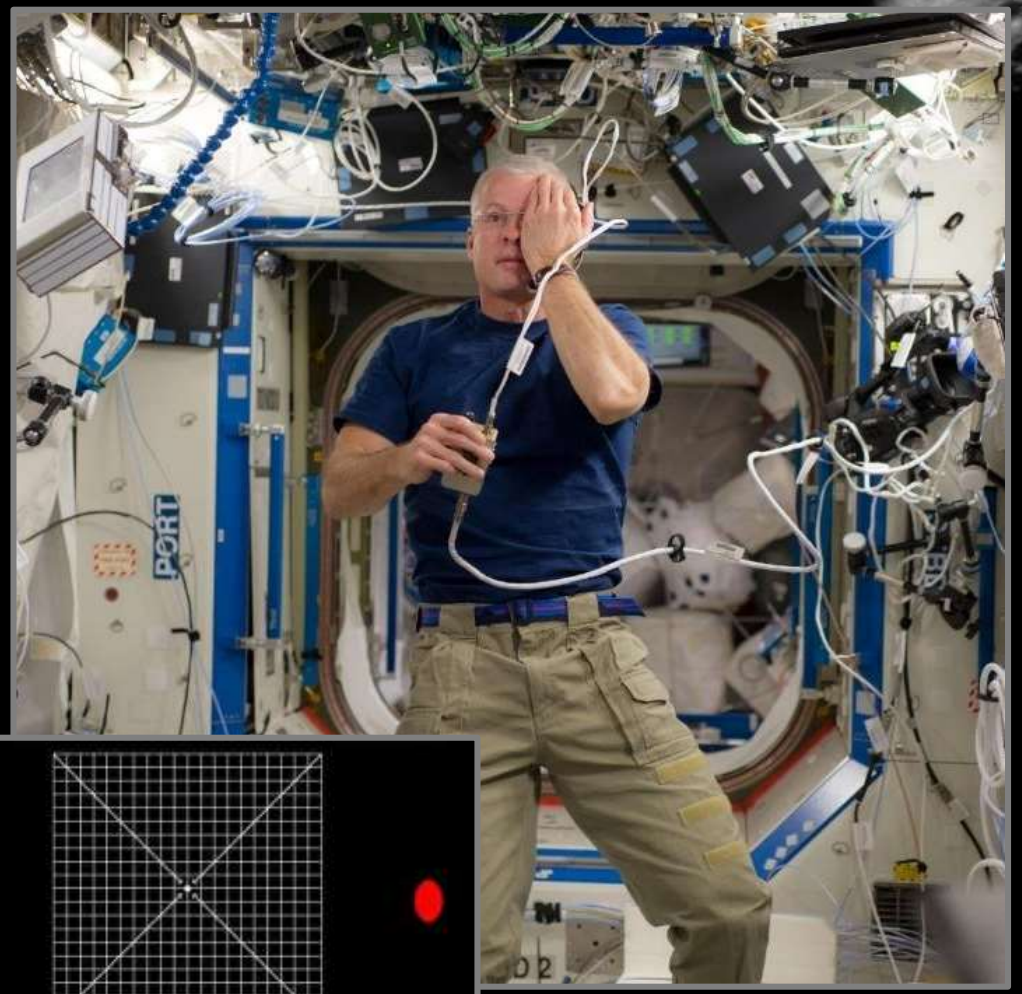
Ocular Surveillance

Terrestrially

- 3T MRI – Special “NASA Astronaut” protocol
- Visual Field (Threshold) Perimetry
- Cycloplegic Refraction

Terrestrially & On-Orbit

- Vision Exam
  - Distance visual acuity (ISS: Acuity Pro on laptop)
  - Near visual acuity (ISS: Handheld card)
  - Amsler grid (ISS: Laptop)
- Ocular Ultrasound
- Tonometry (when clinically indicated)
- Fundoscopy
- Optical Coherence Tomography (OCT)



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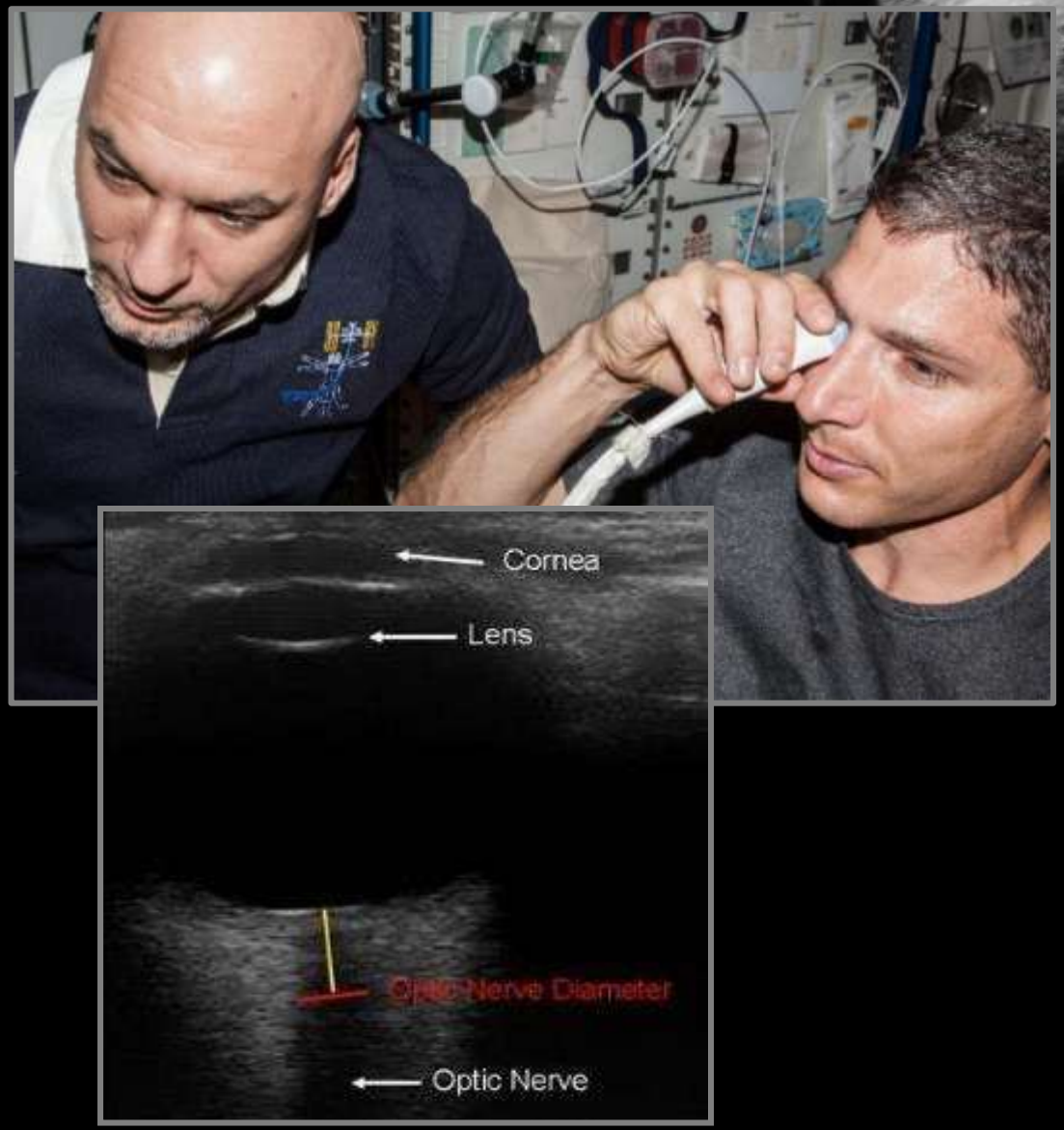

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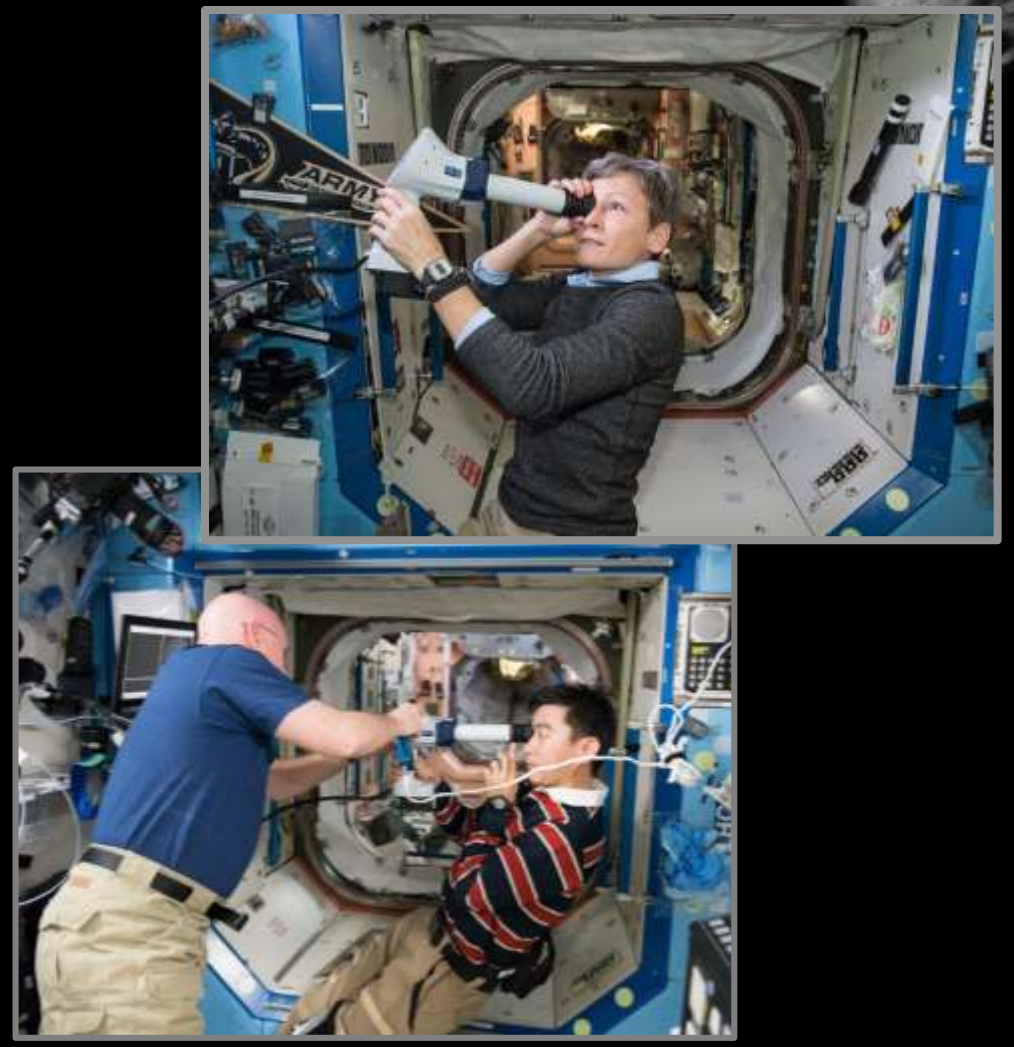

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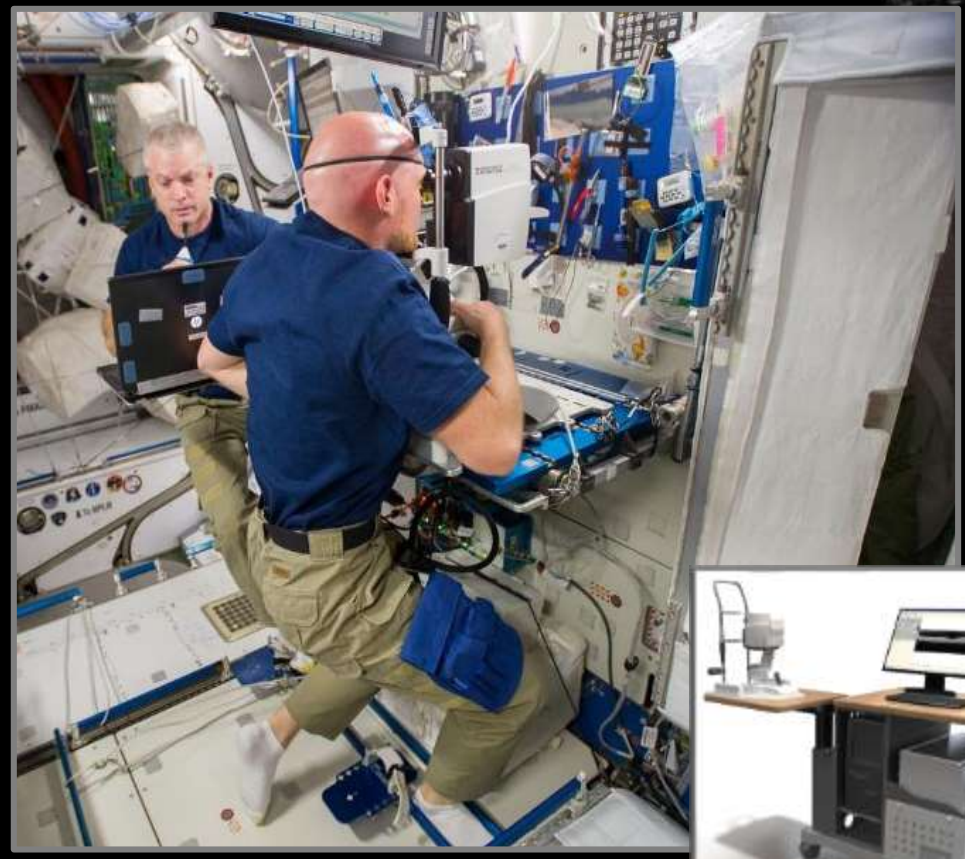
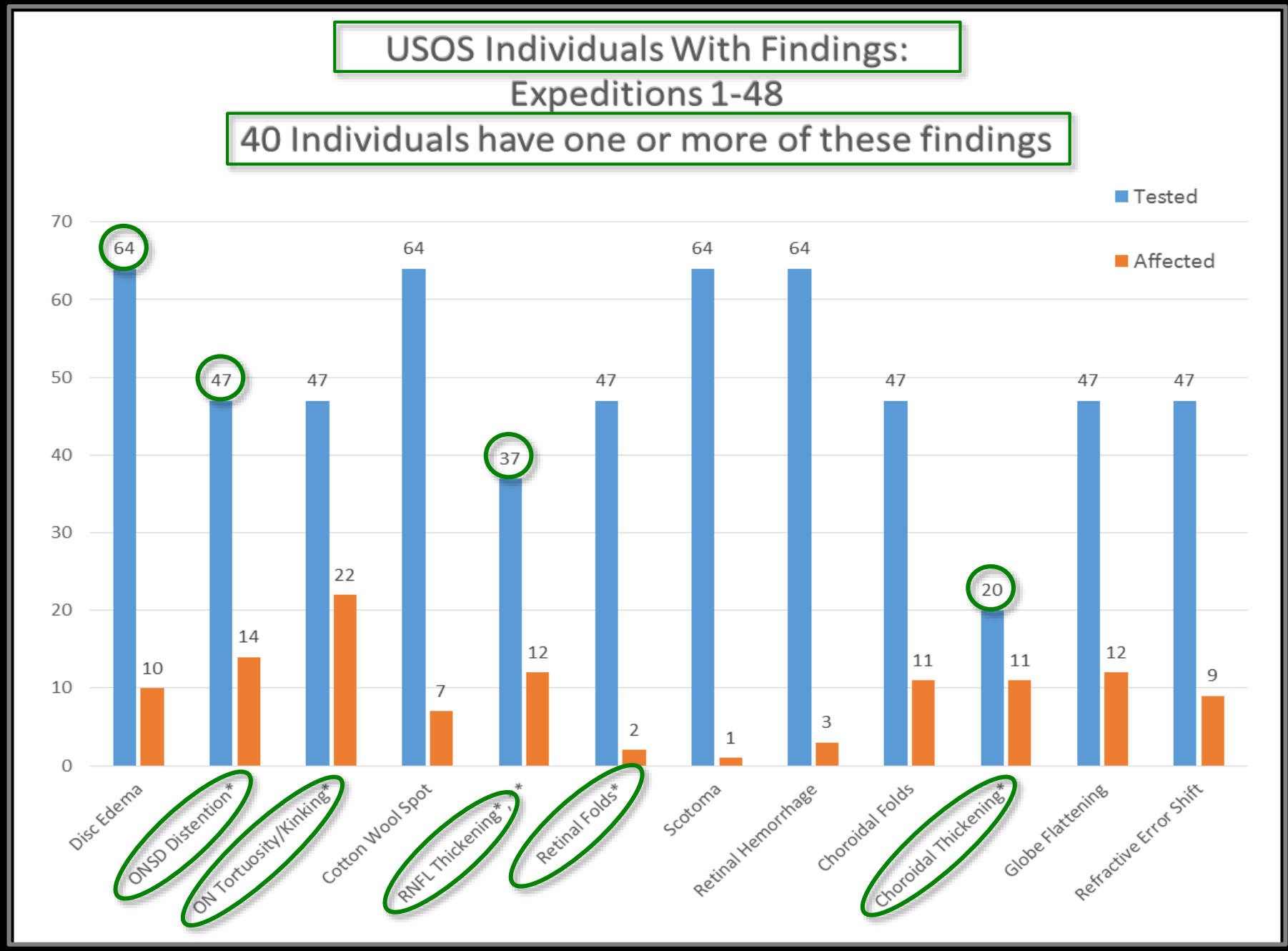
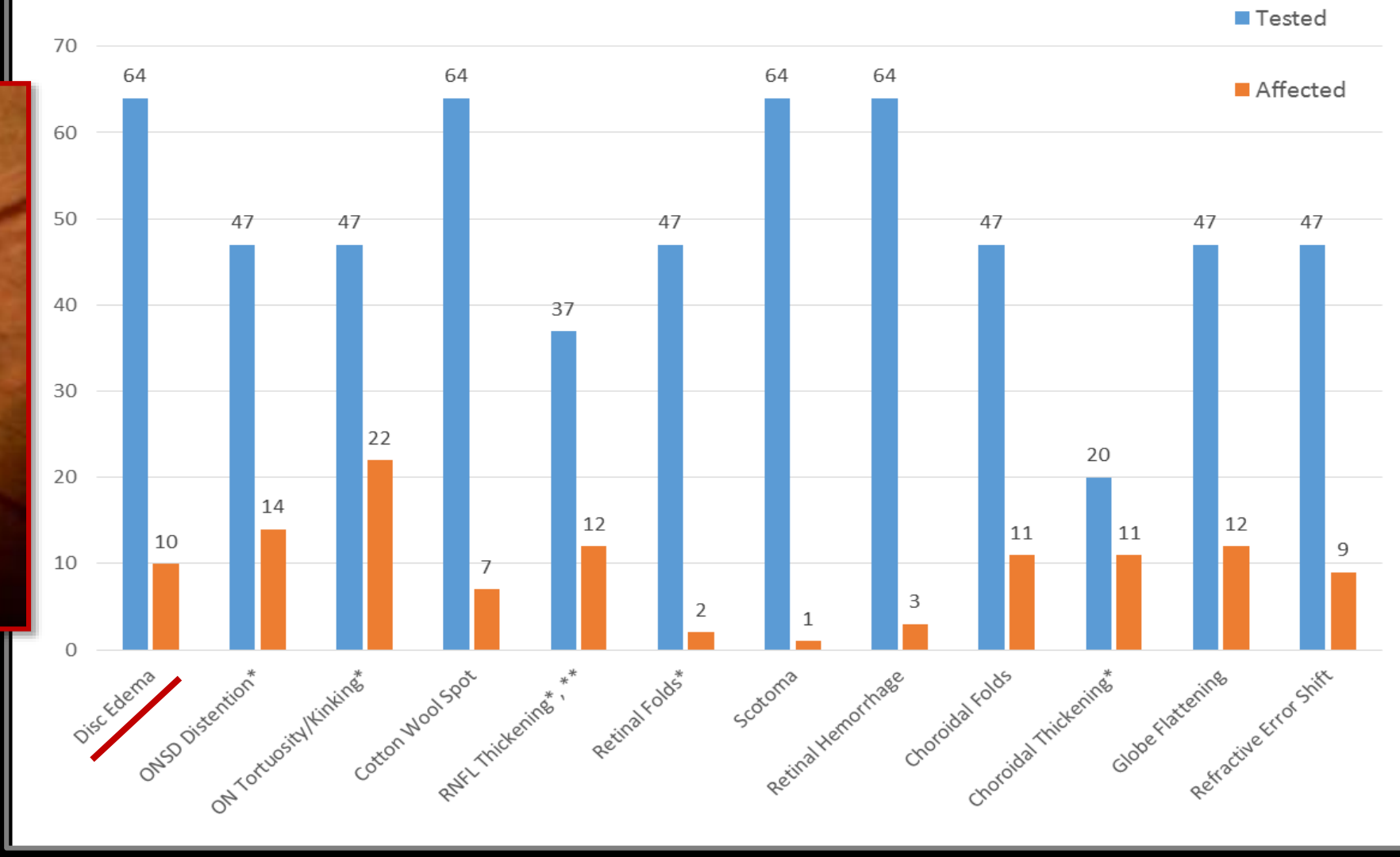


Clinical Findings


USOS Individuals With Findings:
Expeditions 1-48
40 Individuals have one or more of these findings
Tested
Affected
70
60
50
40
30
20
10
0
64
10
47
14
47
22
64
7
37
12
47
2
64
1
64
3
47
11
20
11
47
12
47
9
Disc Edema
ONSD Distention*
ON Tortuosity/Kinking*
Cotton Wool Spot
RNFL Thickening*, *
Retinal Folds*
Scotoma
Retinal Hemorrhage
Choroidal Folds
Choroidal Thickening*
Globe Flattening
Refractive Error Shift

USOS Individuals With Findings: Expeditions 1-48

40 Individuals have one or more of these findings



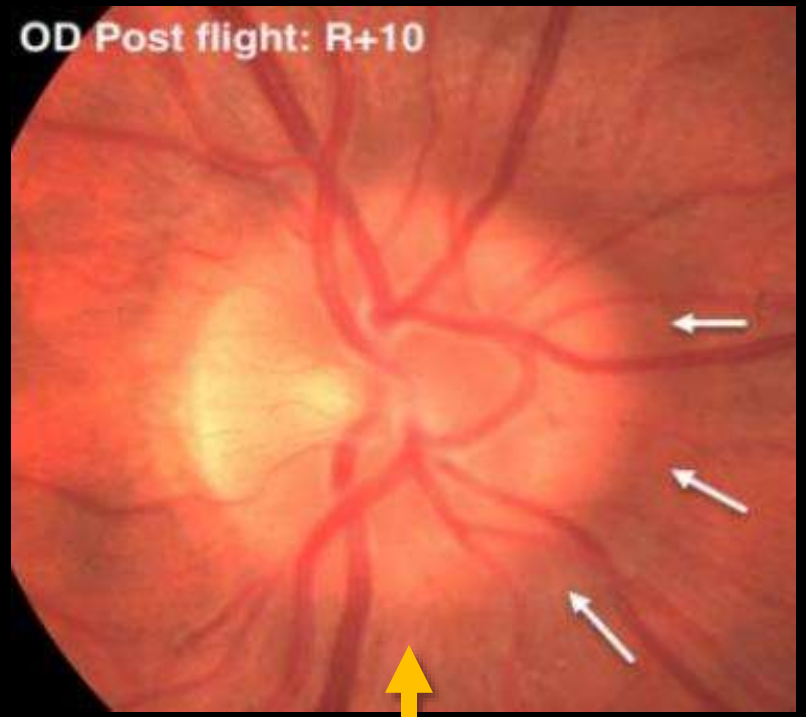
Clinical Findings: *Optic Disc Edema*

Pre-flight fundoscopic images of the optic discs

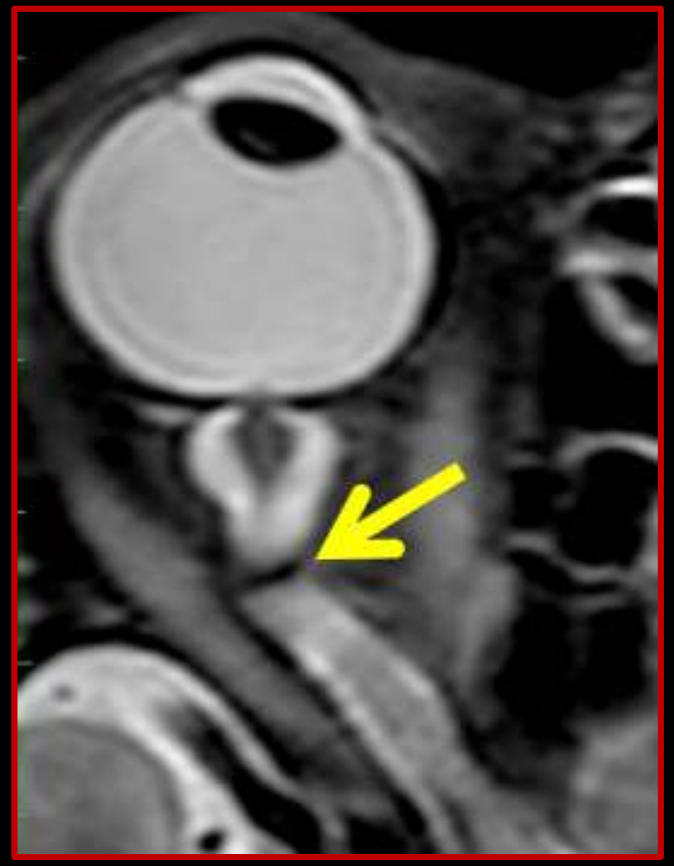
Post-flight images of optic discs, showing *Grade 3 edema OD & Grade 1 edema OS*

Clinical Findings: *Optic Disc Edema*

- *Terrestrially:* Optic disc edema is associated with:
  - Unilateral: Optic neuritis, optic neuropathy, retinal artery/vein occlusion
  - Bilateral: Increase in ICP…
    - IIH (→ "papilledema")
    - Intracranial mass
    - Obstructive hydrocephalus
    - Cerebral edema
    - Increased CSF production
    - Decreased CSF absorption
    - Venous outflow obstruction
  - Typically reduces VA, enlarges blind spot, causes relative afferent pupillary defect & color impairment



Fundoscopic image of optic disc OD, 10 days after return to Earth
- Arrows: "C" shaped halo of edema



USOS Individuals With Findings: Expeditions 1-48

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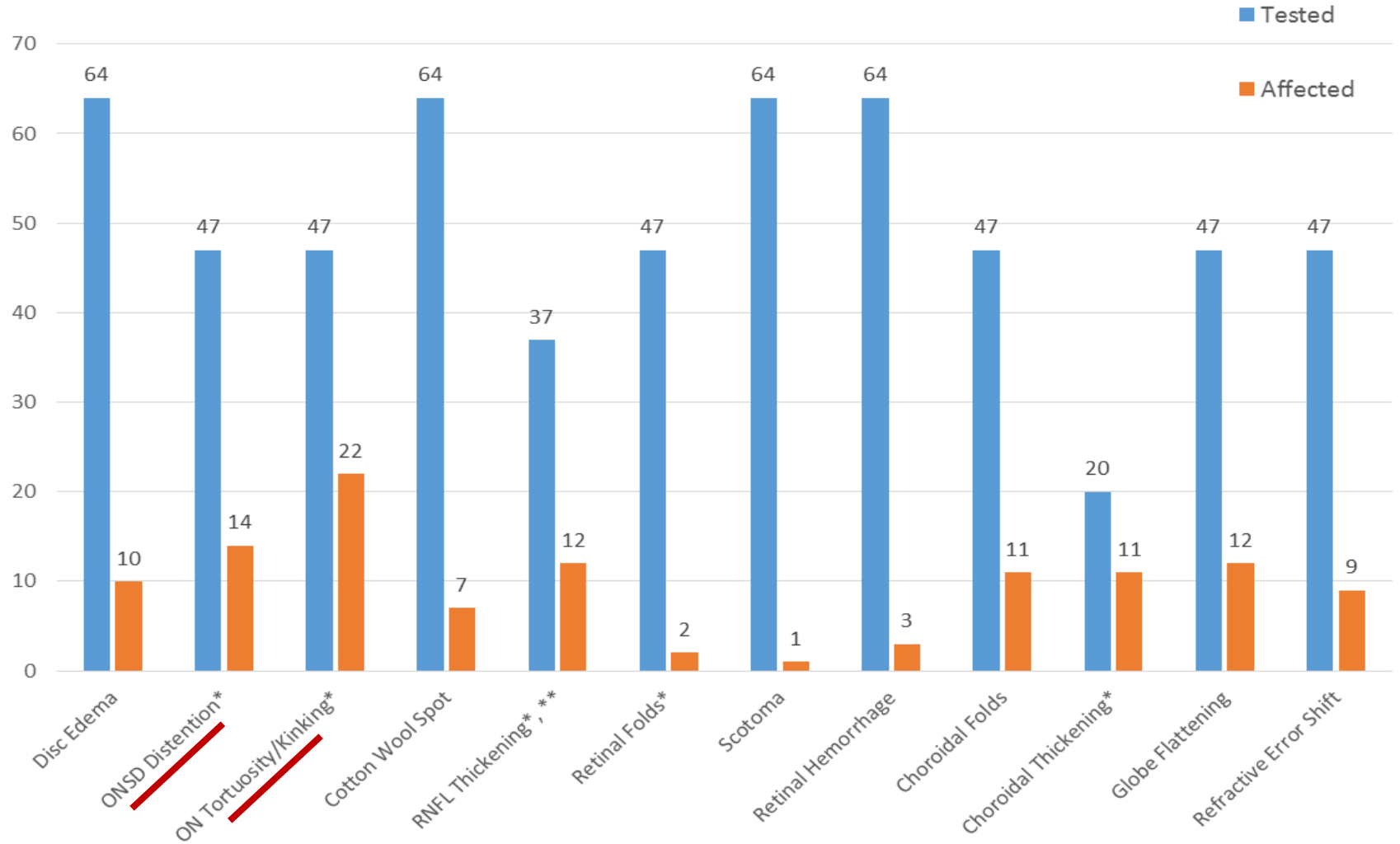
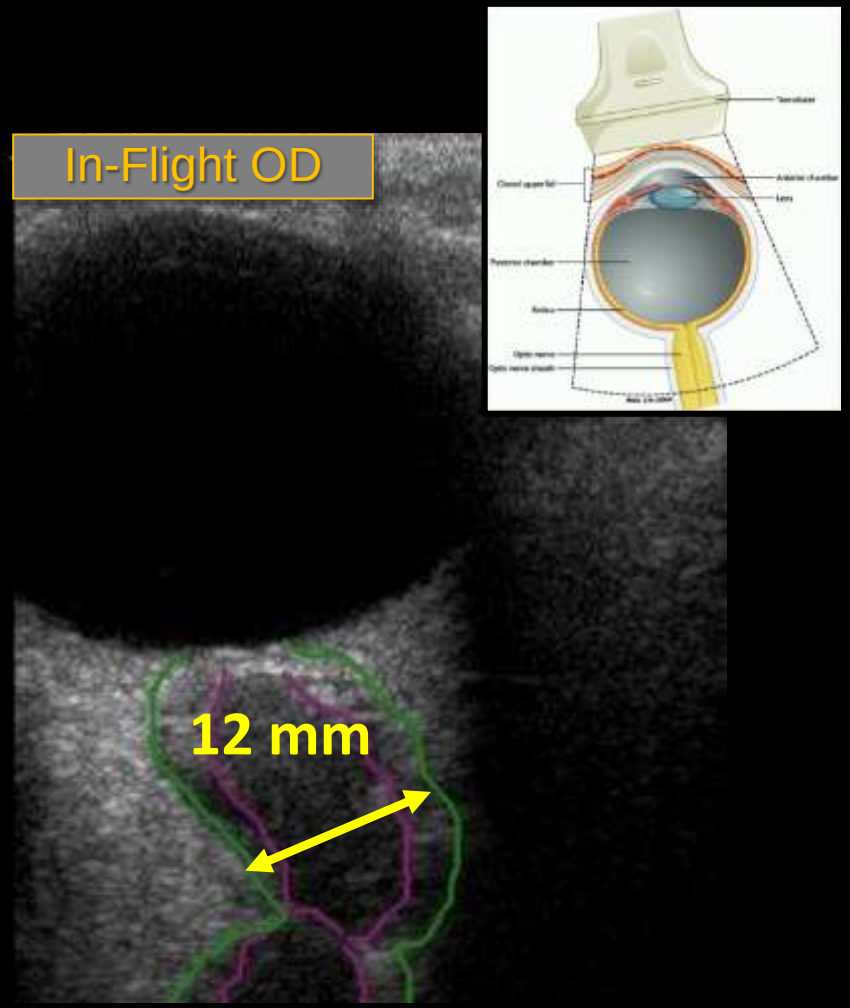


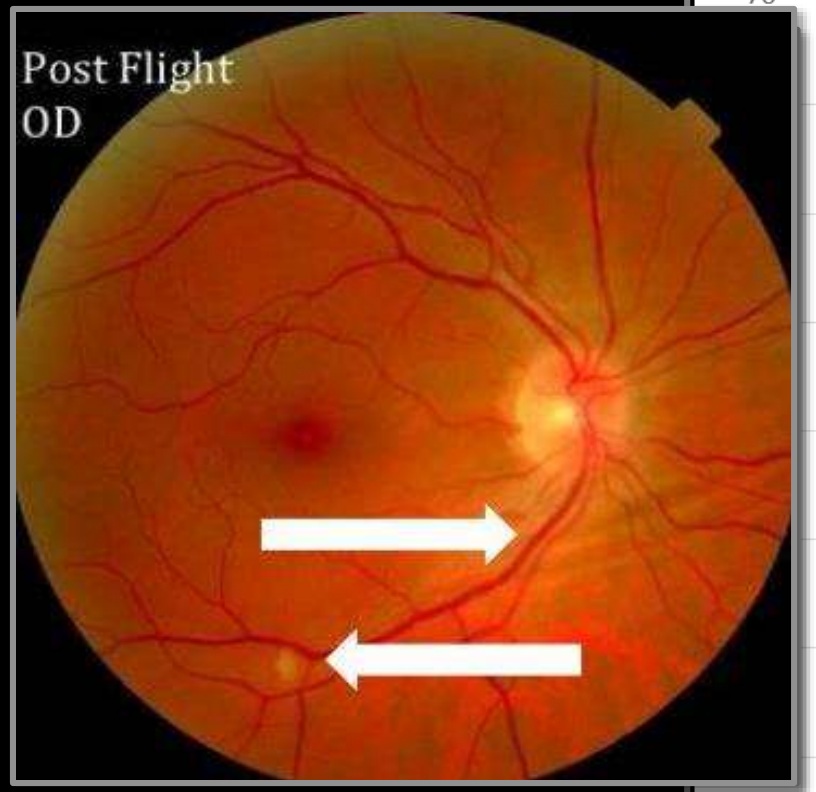
Clinical Findings: *Optic Nerve Sheath Distention*

Post-flight ultrasound image of globe, optic nerve (ON; purple), and optic nerve sheath (green). Showing:

- ON Sheath distention
- ON tortuosity



- ON Sheath *terrestrially:*
  - Normal diameter (ONSD) < 5.9 mm
  - Enlargement typically associated w/ increased ICP



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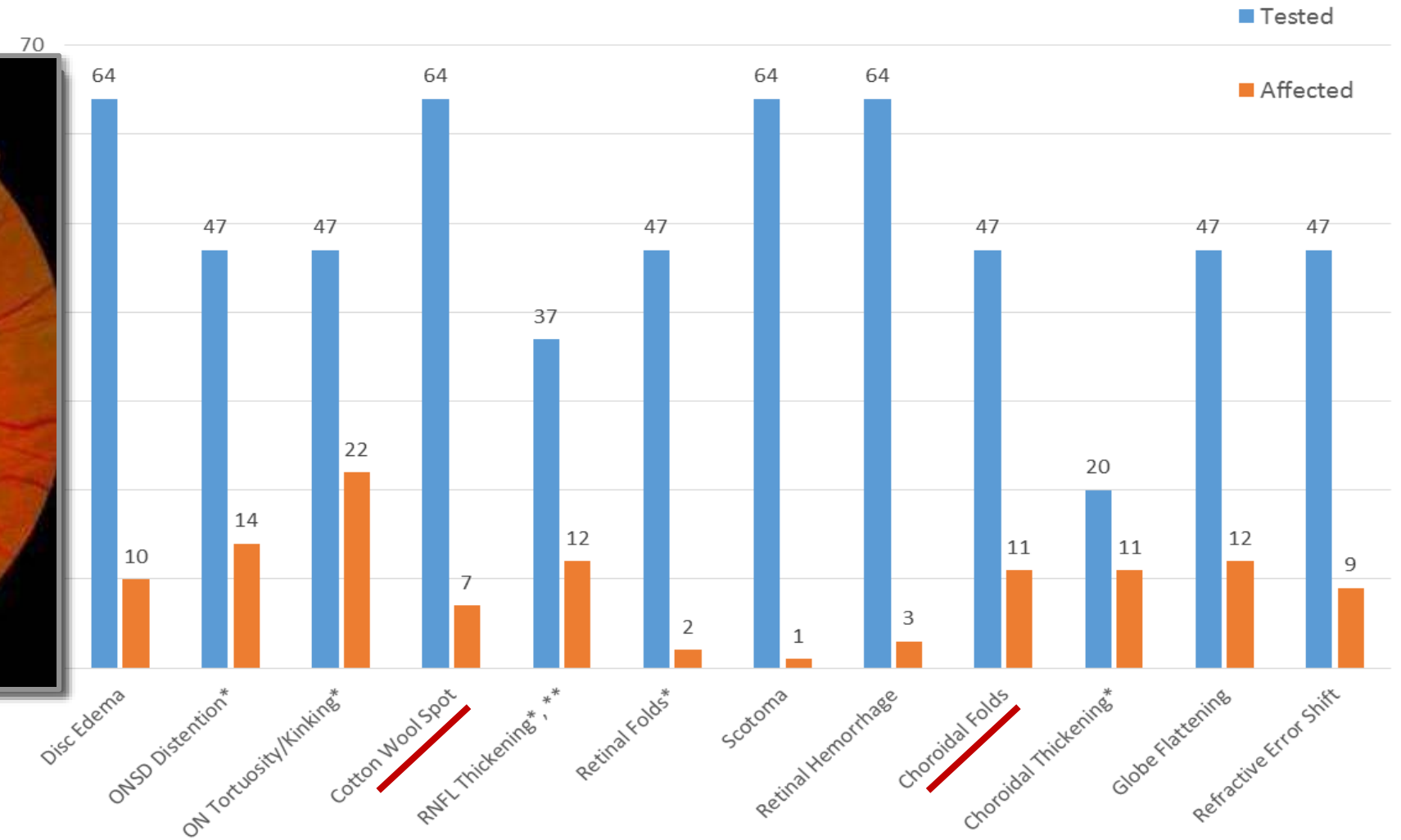

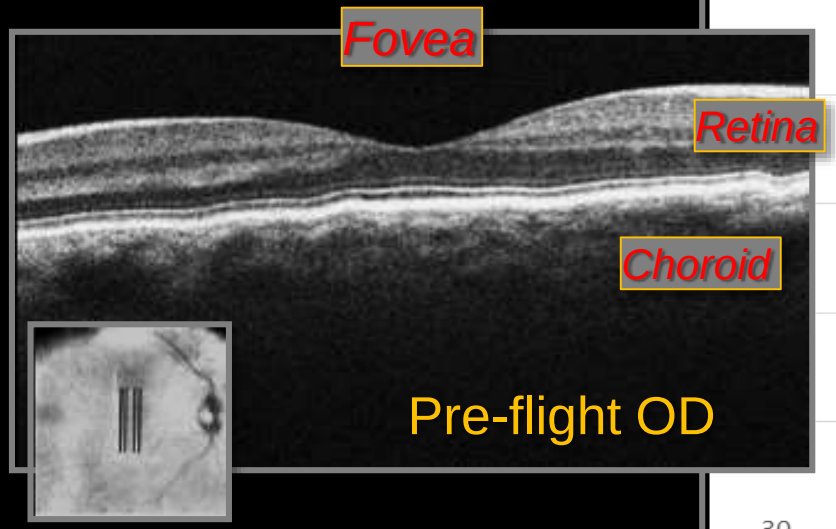

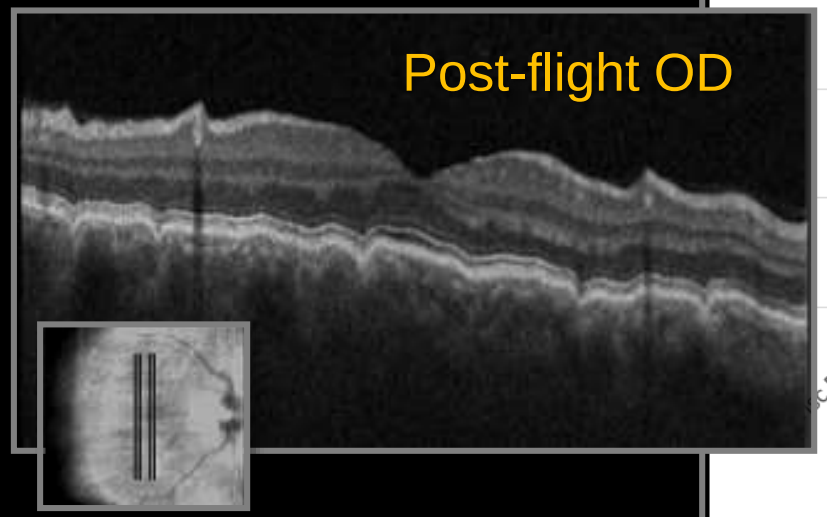

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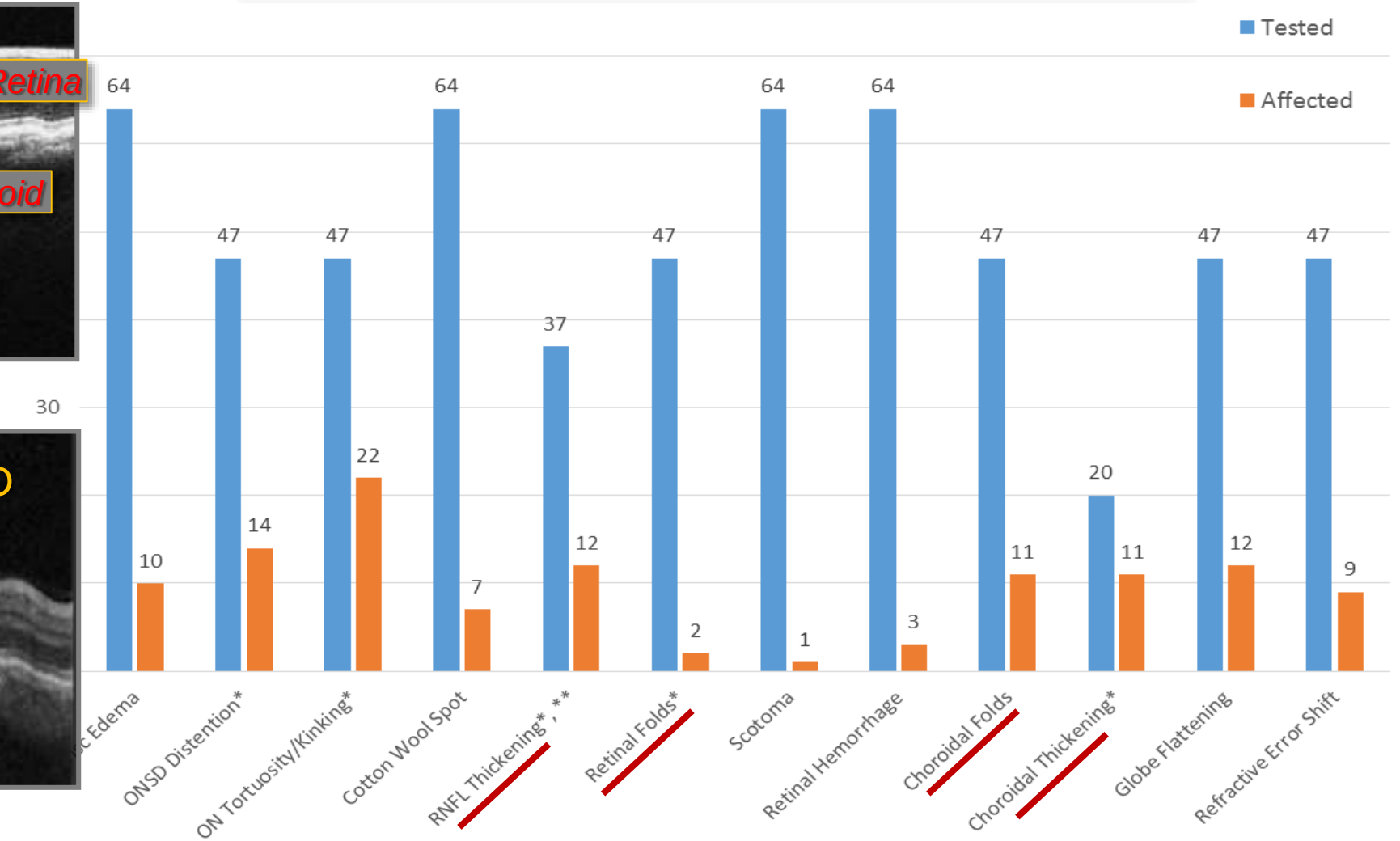
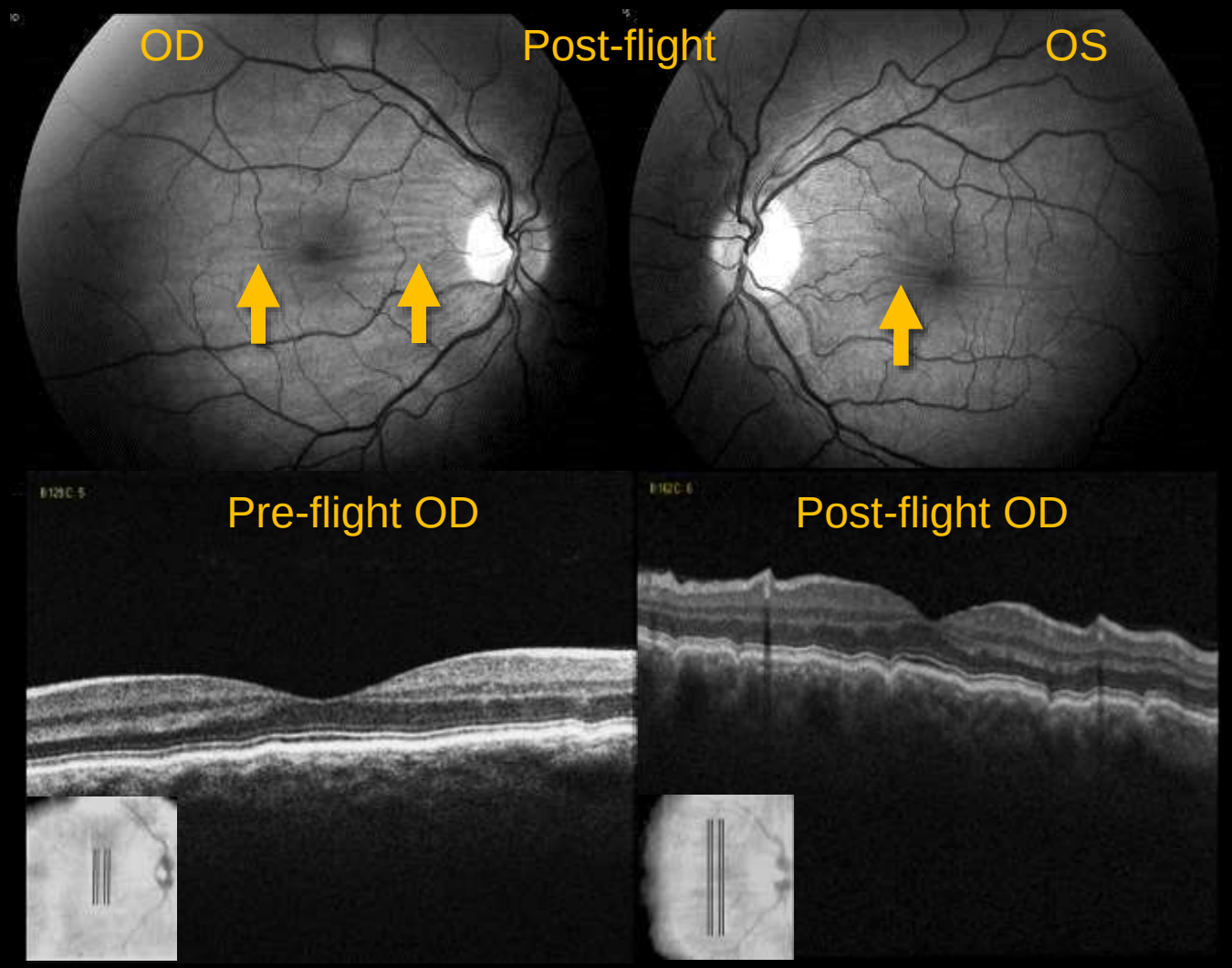


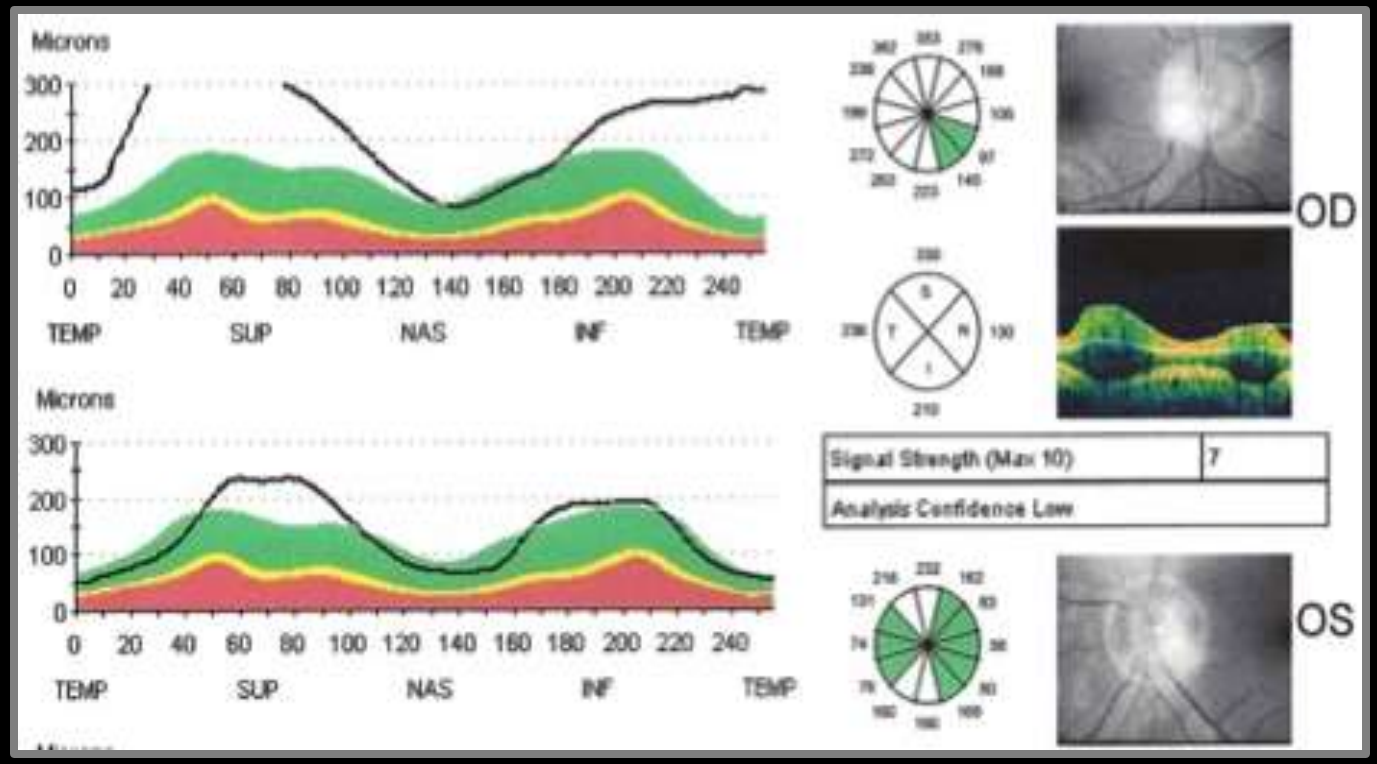
Clinical Findings: *Choroidal Folds*



- Choroidal thickening due to vessel engorgement → induces choroidal (and sometimes retinal) folds
- Usually run horizontally (not concentrically around ONH)
- Can resolve post-flight or can persist (for 5+ yrs)
- So far, no clinically-significant impact on BCVA

- *Terrestrially:* Assoc. w/ choroidal tumors, scleritis, retrobulbar mass, papilledema/IIH

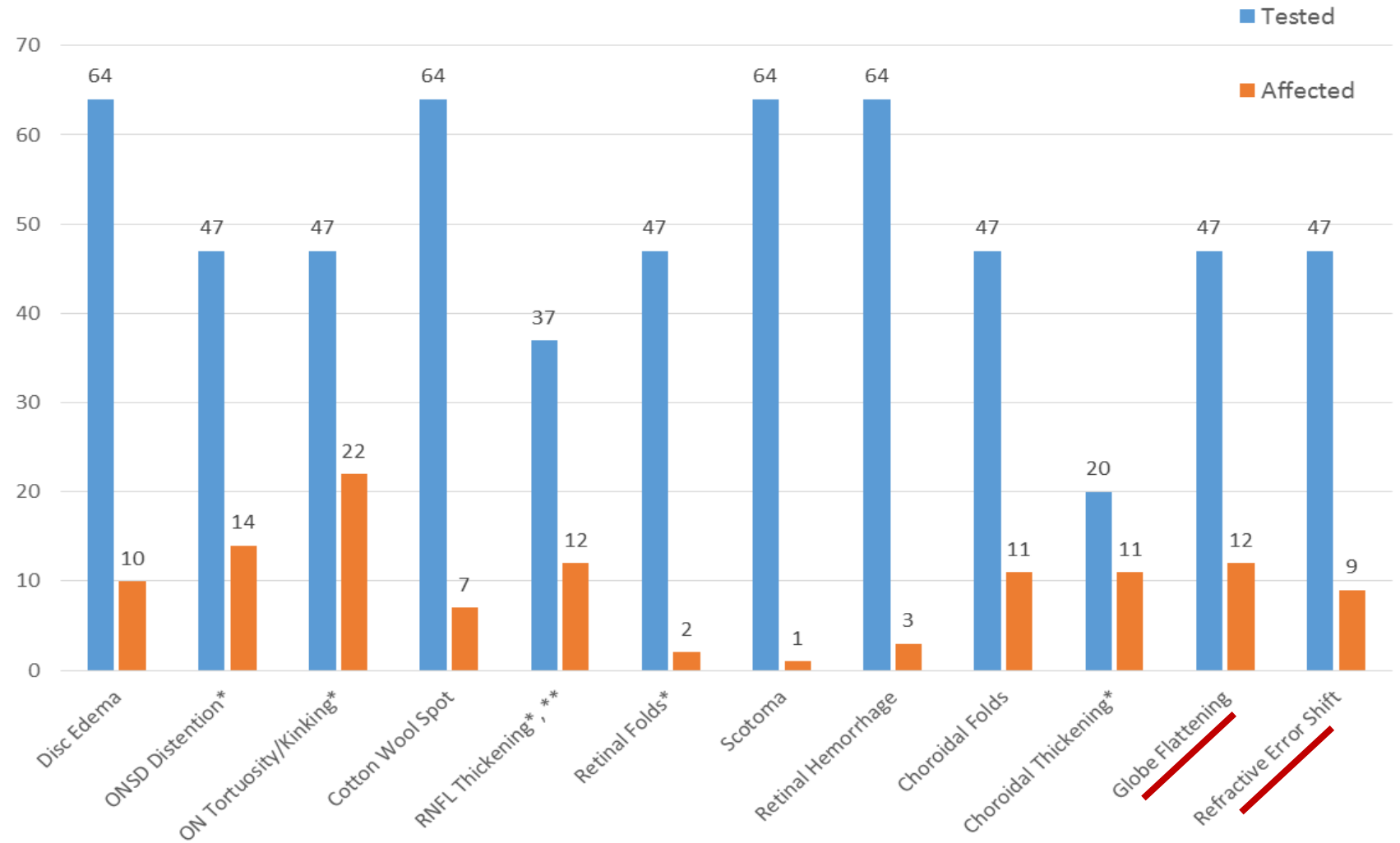
Clinical Findings: *Retinal Nerve Fiber Layer Thickening*



Post-flight OCT “circle scans” showing RNFL thickening consistent w/ observed optic disc edema OU

USOS Individuals With Findings: Expeditions 1-48

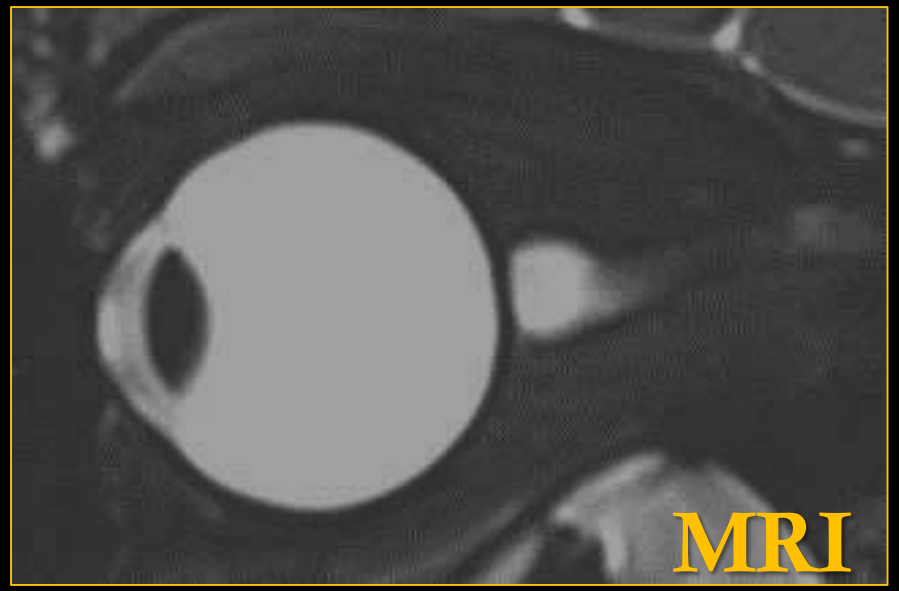
40 Individuals have one or more of these findings



Clinical Findings: *Globe Flattening*

- 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

- *Terrestrially*: Globe flattening associated w/ papilledema (i.e., disc edema 2º to increased intracranial pressure); typically bilateral



Pre-flight

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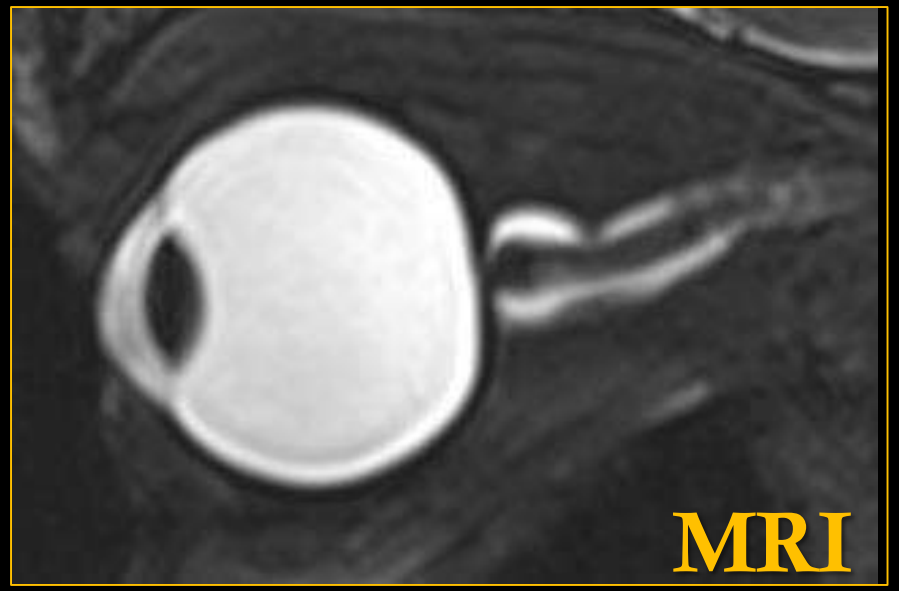

6 days post-flight

Clinical Findings: *Globe Flattening*

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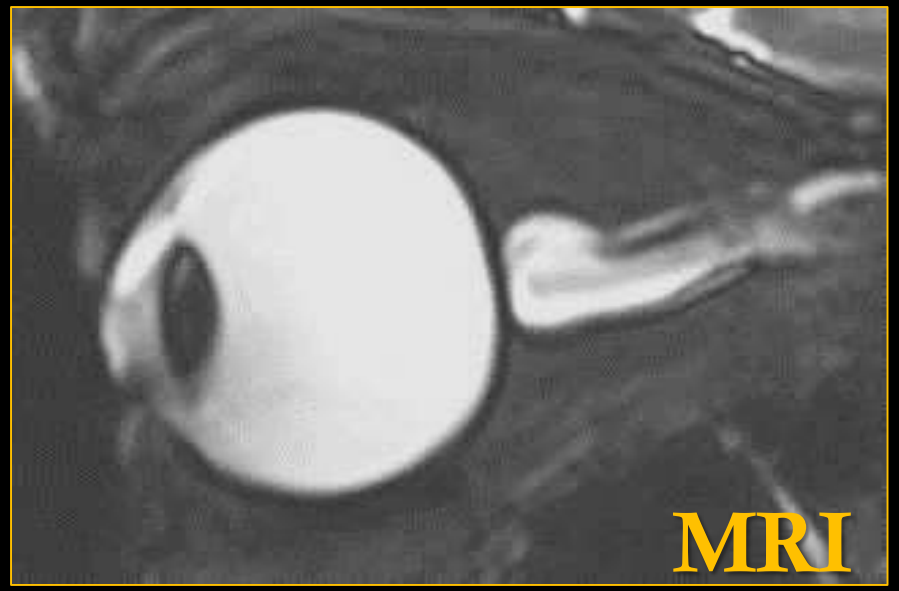

1 year post-flight

Clinical Findings: *Globe Flattening*

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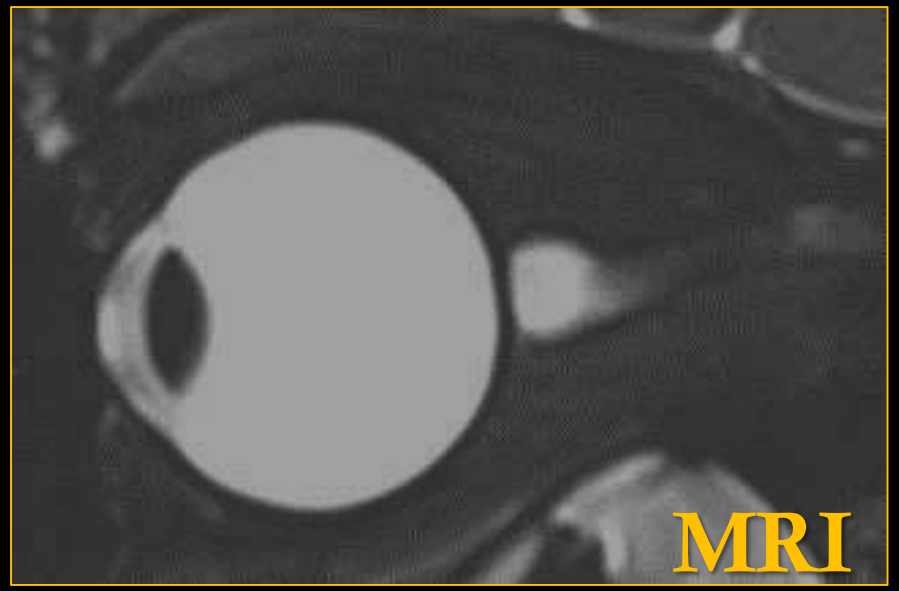


Pre-flight

Clinical Findings: *Hyperopic Shift*

- Of the active astronaut population…
  - 80% wear vision correction (32% contact lenses)
  - Mean age = 47 yrs
  - Majority are presbyopic (i.e., a normal, age-related, progressively worsening inability to focus clearly on near objects)
- Post-flight questionnaires (1989 - 2011): *29% of short- & 60% of long-duration mission astronauts report a subjective degradation in vision*, especially at near
  - Provided “Space Anticipation Glasses”

Why is this Happening?

Why is this Happening?

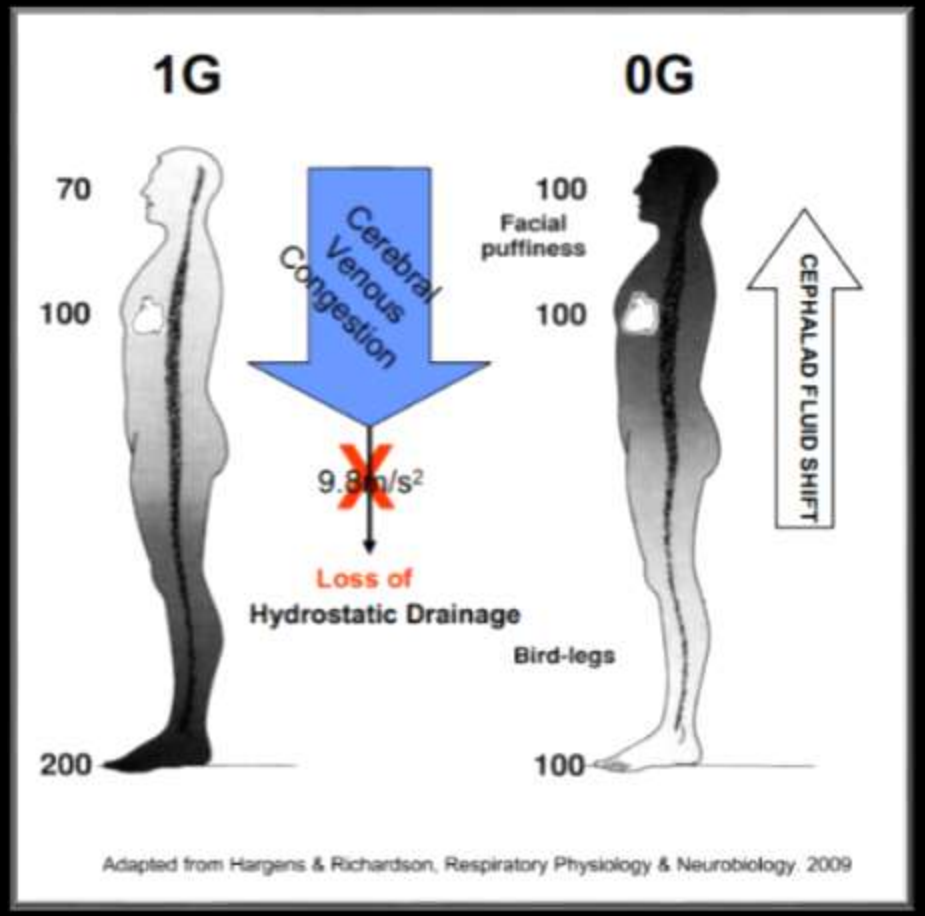
- Terrestrially → Fluid is pulled downward by gravity (i.e., hydrostatic pressure)
- Microgravity → Fluid is free to uniformly distribute (i.e., hydrostatic pressure is eliminated)

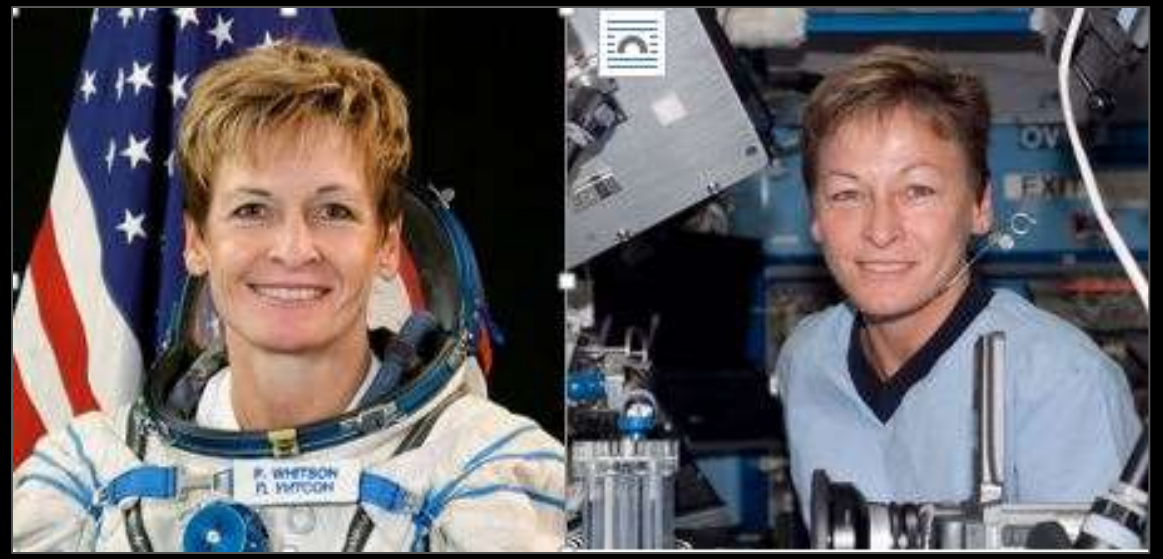
Consider how hydrostatic pressure affects fluid/blood distribution in humans…

And what happens in its absence…

Why is this Happening?

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

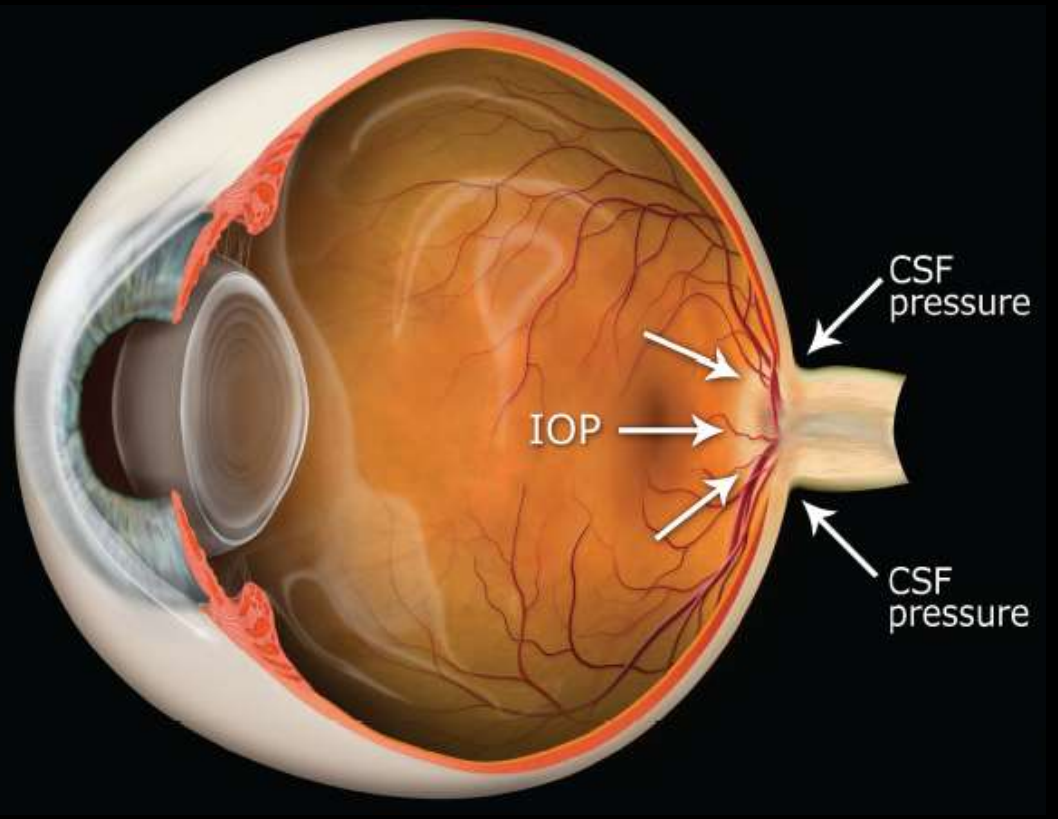




Why is this Happening?

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

- 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
- Hypothesis #3: *Individual anatomical/genetic factors*
  - e.g., Altered folate-dependent 1-carbon metabolism
- Hypothesis #4: *Venous congestion* alters local physiology and/or places direct pressure on retinal axons



In-flight Exacerbating Factors??

Resistive Exercise

High Oral Sodium Intake
Prepackaged Foods…
Up to 5000+ mg/day

High CO_2
~10x terrestrial levels

In-flight Pharmaceuticals

Common Characteristics of the Cases

Common Characteristics of the Cases

- Almost all were "long duration" (i.e., >30 day) *ISS mission crewmembers*
  - One short-duration case w/ subtle disc edema (discovered retrospectively)
  - *Severity related to flight duration?*? [So…what about a *3-yr Mars mission*??]

- *Normal* past medical history:
  - *Negative* for uncontrolled systemic disease
  - None used medications before/during mission that would increase ICP (e.g., vitamin A, tetracycline, corticosteroids, or nalidixic acid)
- ISS cabin
  - Normal pressure & oxygen
  - Elevated CO_2
    - ~0.33-0.5% avg, w/ avg peak ~0.7%; 10x terrestrially: ~0.03-0.04%

Common Characteristics of the Cases

- All had *normal* pre-flight eye exams
- *None* experienced loss in BCVA, color vision, or stereopsis
- *None* complained of severe headaches, transient vision obscurations, double vision, pulsatile tinnitus, or vision changes during eye movements (i.e., classic symptoms of idiopathic intracranial hypertension)
- OD affected more than OS *in all cases*. *If monocular, always OD*
- For 14 crewmembers having complete pre-flight & on-orbit OCT data, regardless of SANS diagnosis, *ALL* show signs of:
  - *Choroidal engorgement*, *Optic disc edema* (*subclinical or clinical*), extending into the retinal nerve fiber layer; *Retinal venous engorgement*

Clinical & Research Update

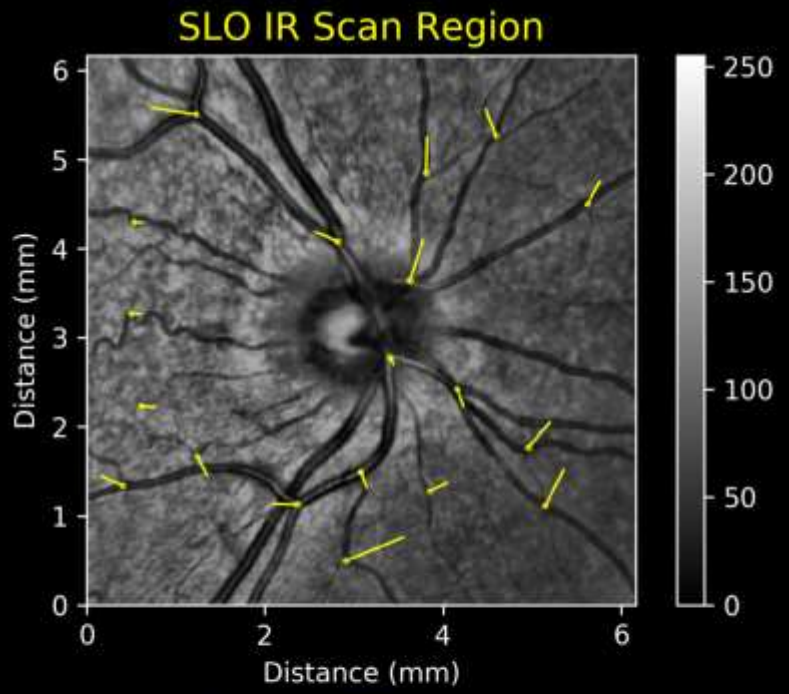
Ongoing SANS Efforts: Clinical/Research

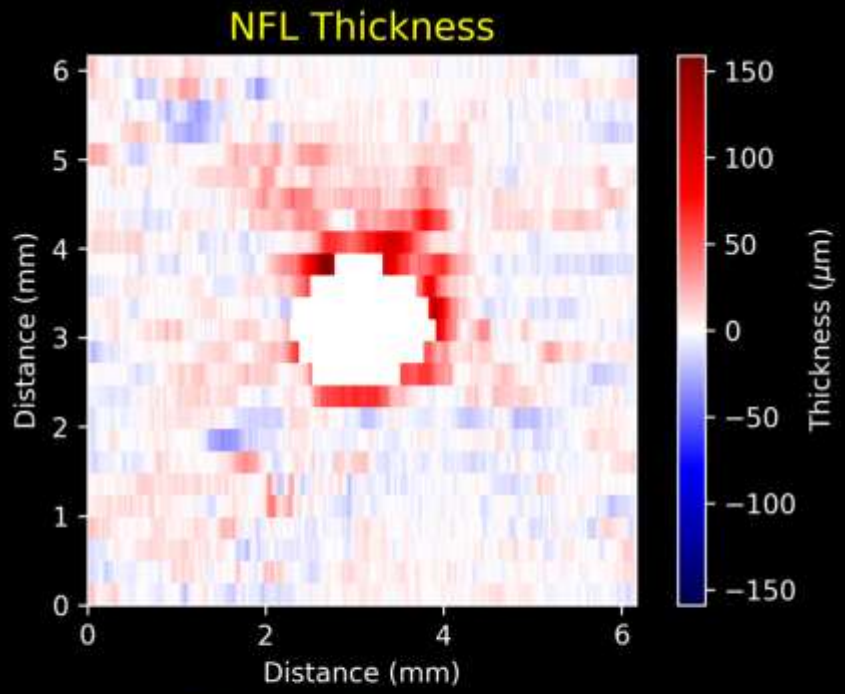
Clinical

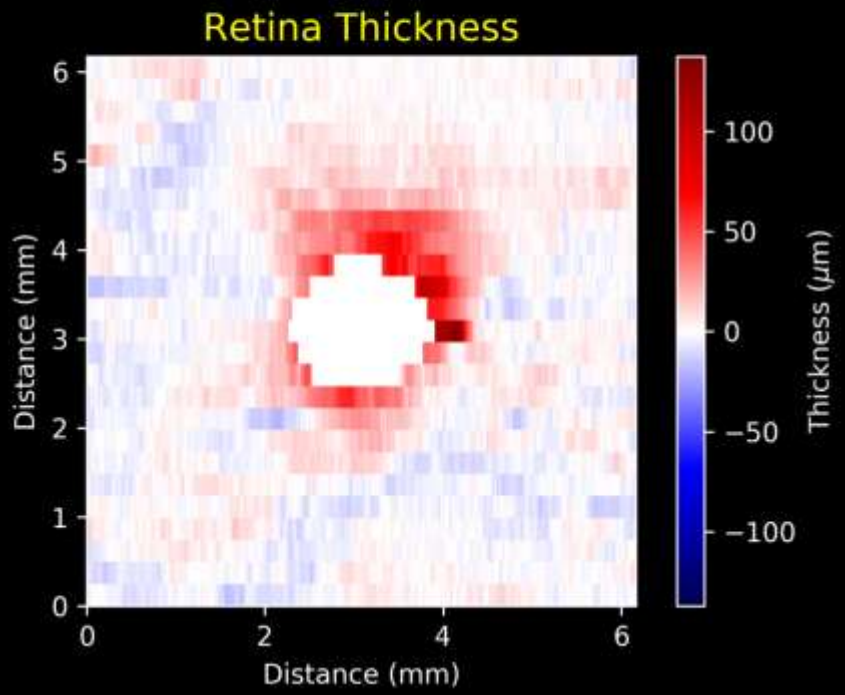
- "*Form & Function*": Are there any RNFL thickness losses (*via OCT*)? If so, are there correlations w/ any reduction in visual sensitivity (*via visual field*)?
  - KEY Concern/Risk: Potential impact of *disc/retinal edema* during longer duration missions (>>12 months)
- Deploy *next-generation OCT*:
  - Faster (~60%); better signal-to-noise; MultiColor imaging
- Consider deploying an ISS *visual field device*
- Consider possibility of *venous congestion* as a SANS contributing factor

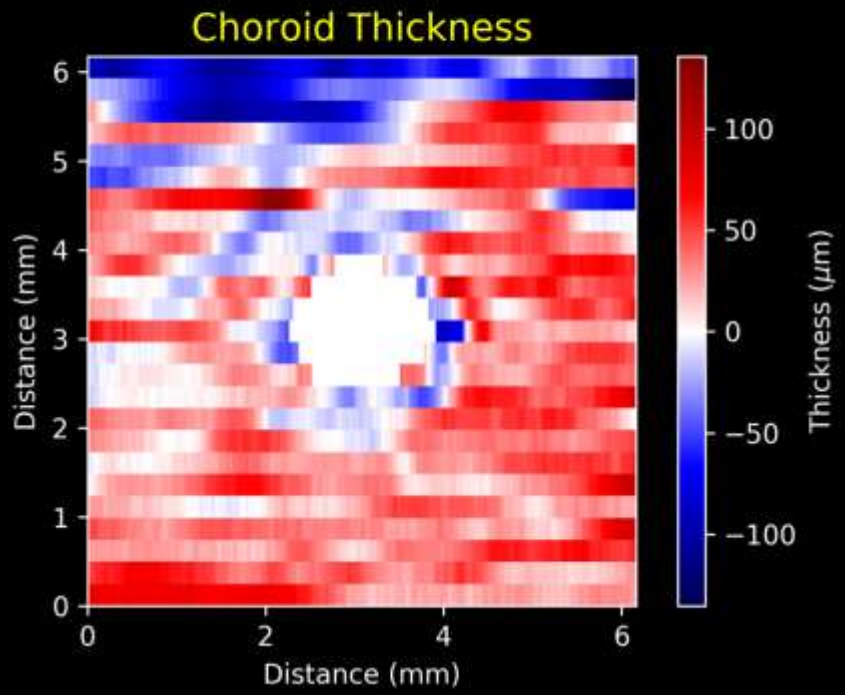
Research

- Ocular Health Study & Fluid Shifts Study
- Clinical relevance of MRI-based findings
- Implementation of direct ICP measures (Lumbar puncture pre- & post-mission)
- Correlation btwn SANS & CO_2 using HDT (EnviHab)



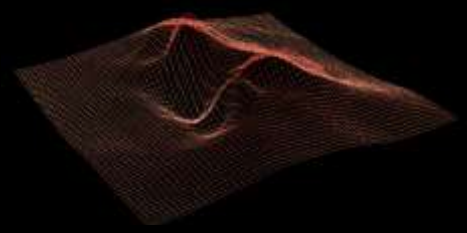




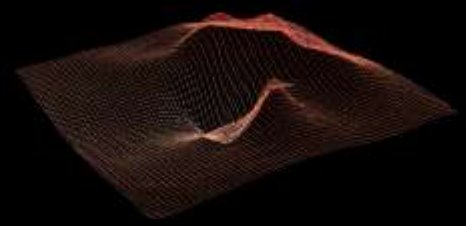


Source: Mayra Nelman & Simon Clemett, PhD

ONH Surface Topography



* Subject 1



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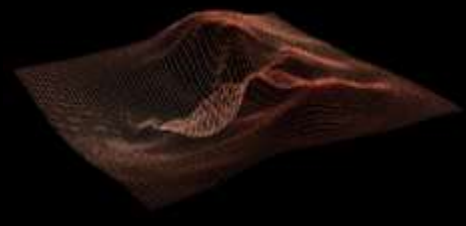
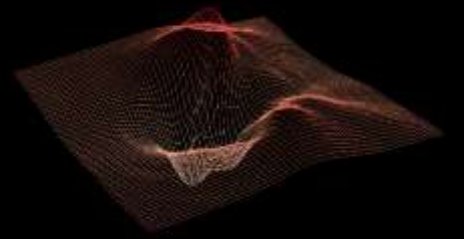
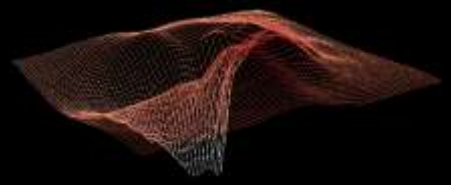


* Subject 3



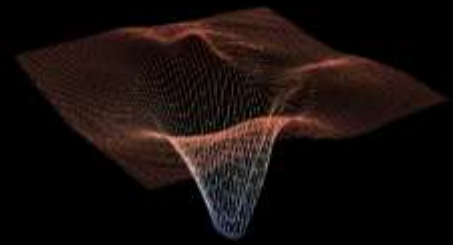
* Subject 4

* Indicates Case

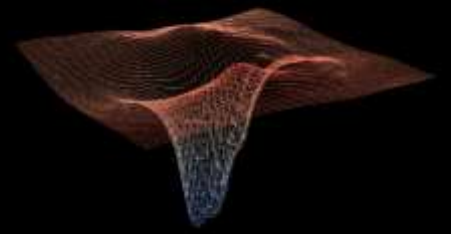


* Subject 5

* Subject 6



* Subject 7



Subject 8

Subject 9

Subject 10

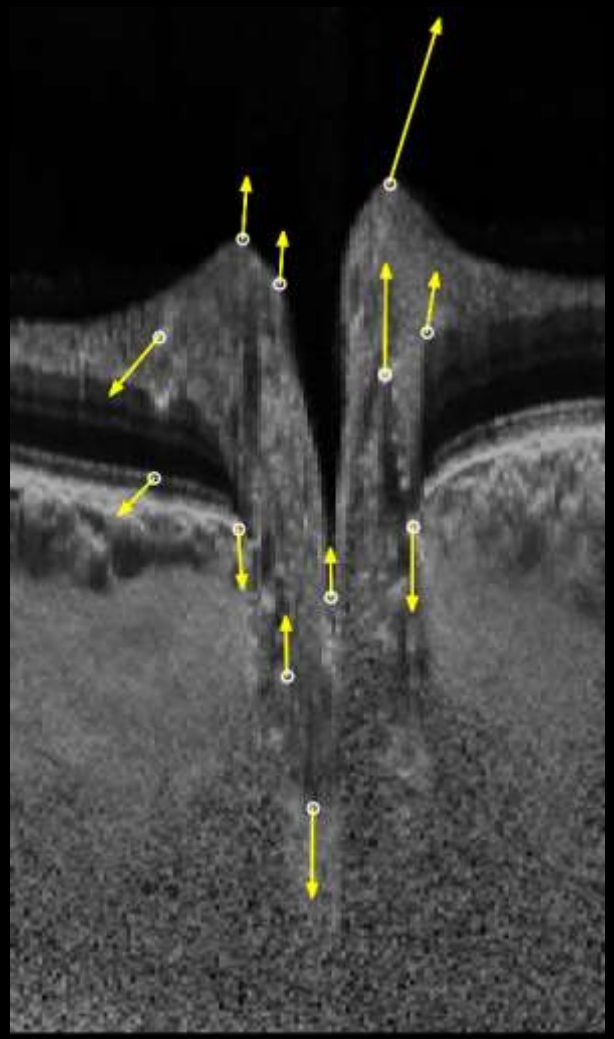
Subject 11

Subject 12

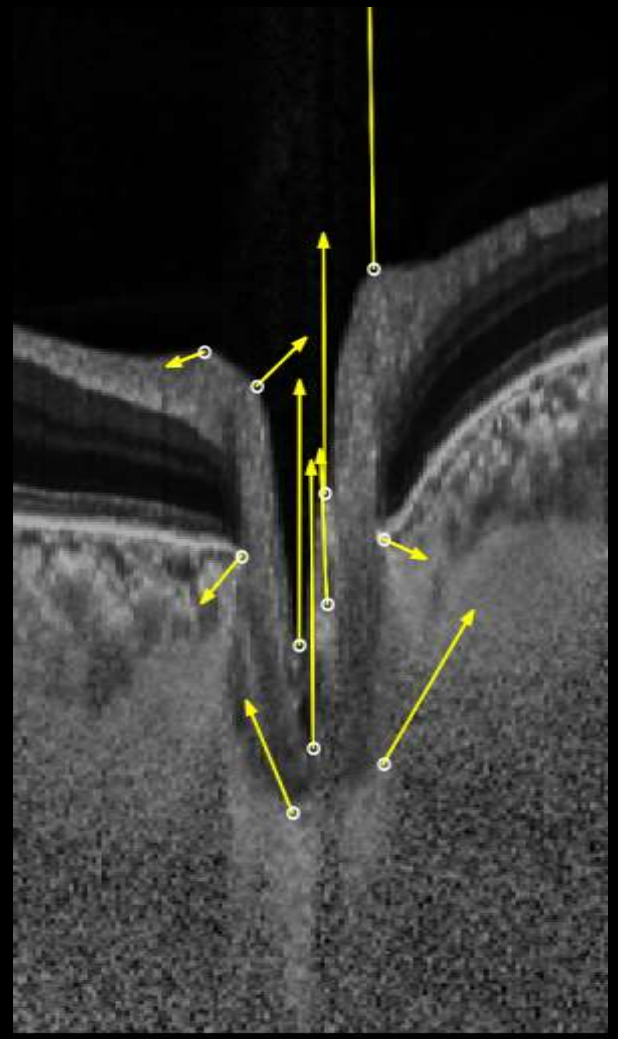
Source: Mayra Nelman & Simon Clemett, PhD

Lamina Cribrosa Movement

* Indicates Case



* Subject 5



Subject 8

Source: Mayra Nelman & Simon Clemett, PhD

Questions?

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