Spaceflight Associated Neuro-ocular Syndrome (SANS): Clinical Update

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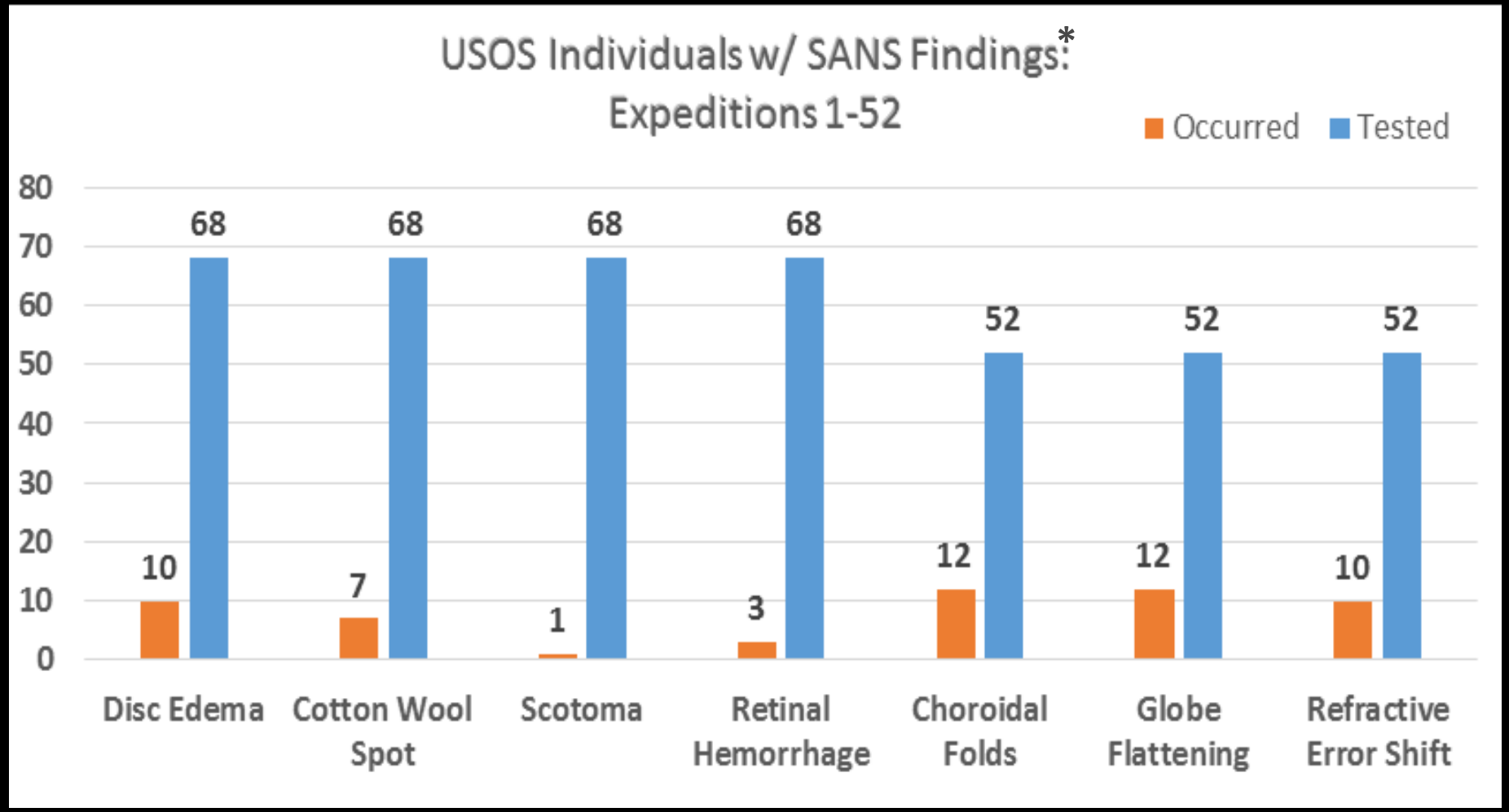
NASA Human Research Program Investigators' Workshop
24 January 2018

SANS Clinical Update

- “SANS Incidence” Update
- Space naïve crewmember SANS data (vs. veteran crewmembers)
- Clinical Highlights – 2017
  - VIIP name change
  - “Optic disc changes” w/ long-duration spaceflight
  - Association between optic nerve head (ONH) cup volume and SANS diagnosis
  - International Fundoscopy Evaluation of Crewmembers (IFEC) Review
- Clinical Tasks – 2018
  - Deployment of next-gen Optical Coherence Tomography (OCT) device
  - Evaluating visual field (VF) testing for ISS
  - Update SANS case definition

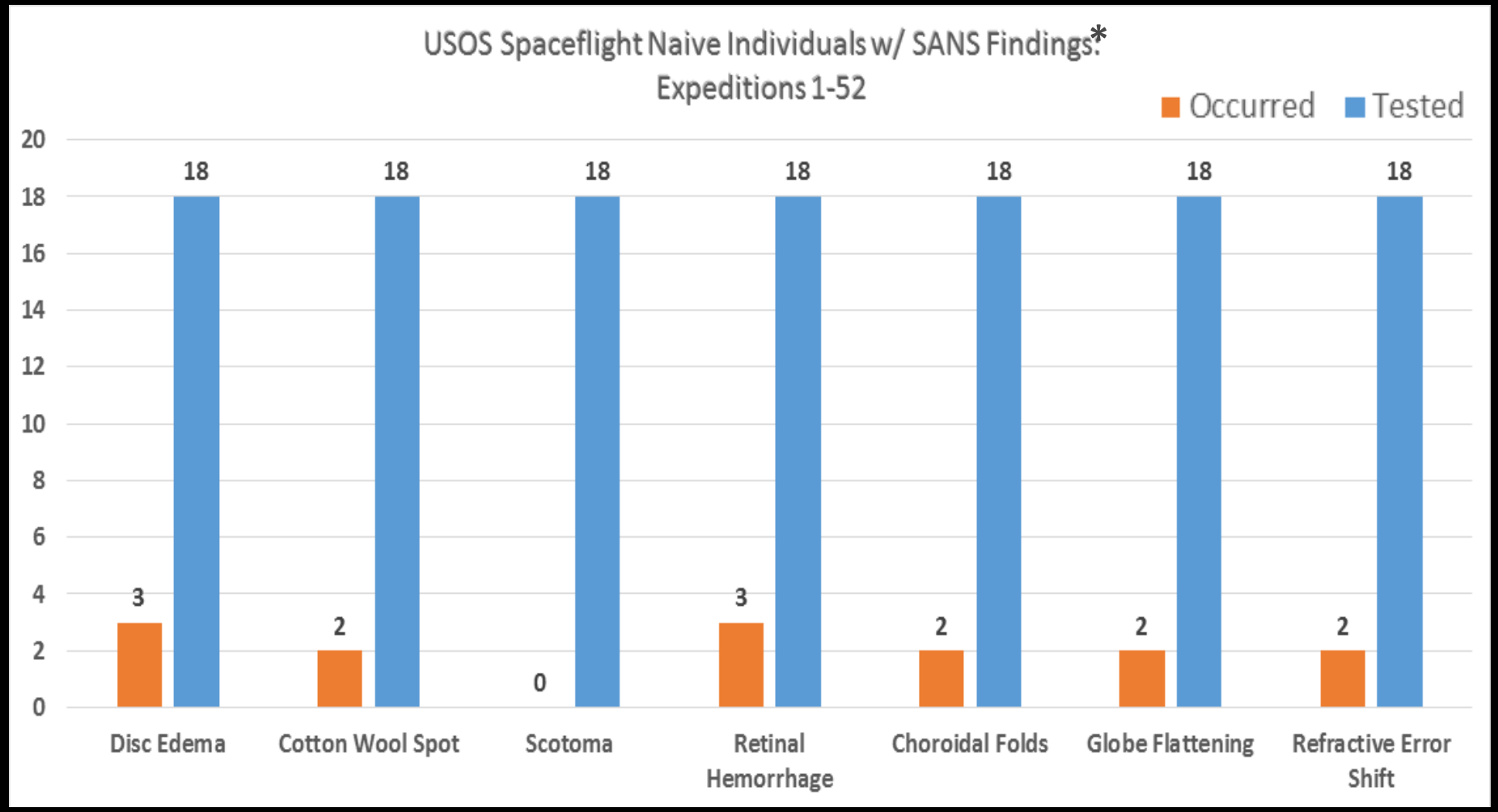


Post-flight - OD



* 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*

	All Crew	Space Naïve
D Edema	15%	17%
CWS	10%	11%
Scotoma	1.5%	0%
R Heme	4%	17%
Chor Folds	23%	11%
G Flattening	23%	11%
Ref Error Δ	19%	11%



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Clinical Highlights - 2017



- VIIP name change: Why?

"Vision Impairment Intracranial Pressure"

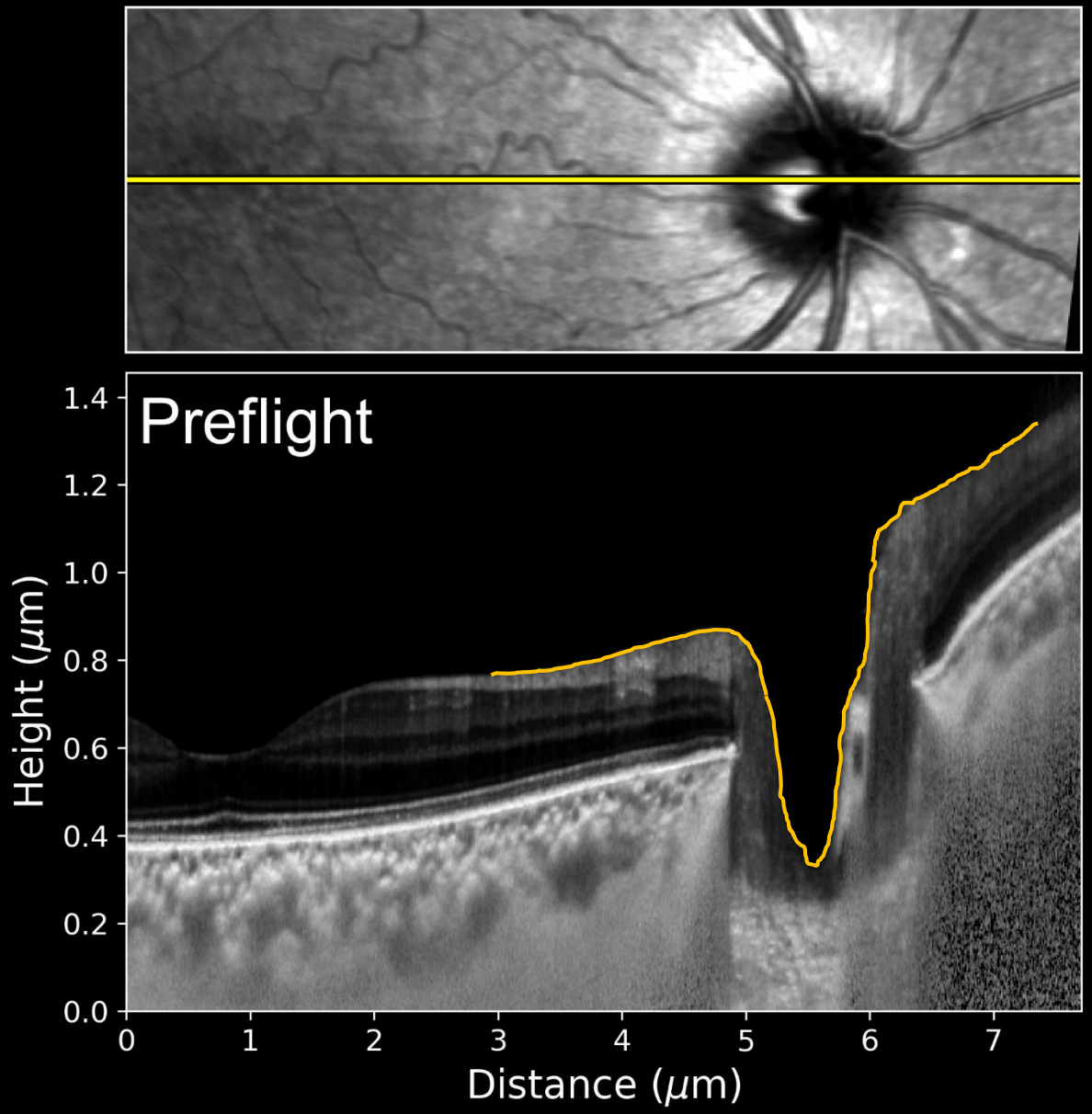
- Vision Impairment: Defined as the best-corrected visual acuity worse than 20/40 in the better-seeing eye (National Institutes of Health)
  - *Not applicable* to long-duration astronauts; all correctable to 20/20 or better
- Intracranial Pressure: Not conclusively tied to astronaut vision issues

"Spaceflight Associated Neuro-ocular Syndrome"

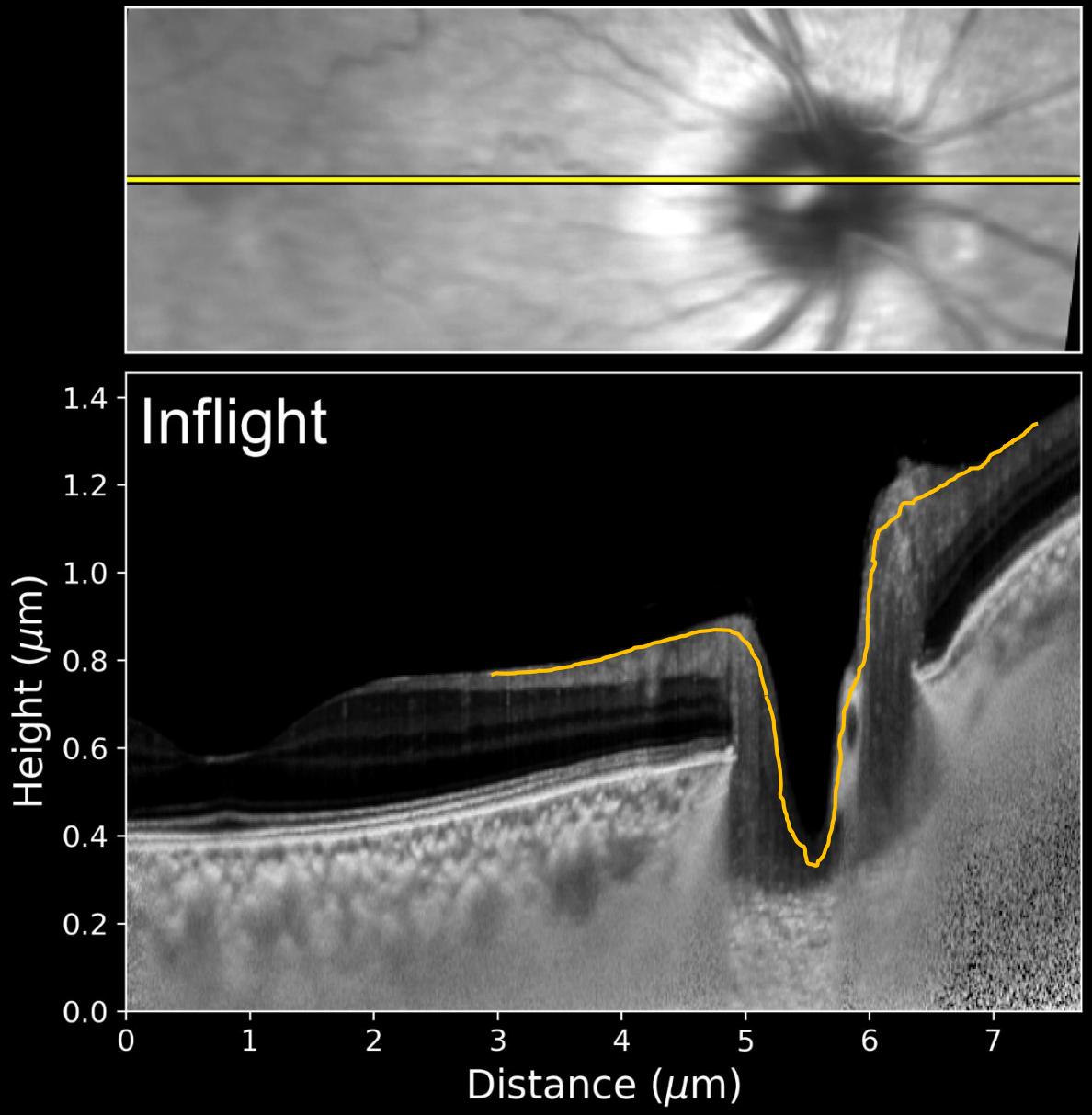
- More accurate, given current evidence
- More general; includes wider range of pathogenesis possibilities

Clinical Highlights - 2017

- "Optic disc changes" w/ long-duration spaceflight
  - David Brown, MD – SANS Research & Clinical Advisory Panel (RCAP); Retinal specialist, Retinal Consultants of Houston
  - Analyzed 14 crewmembers having complete pre-flight & on-orbit OCT data, *ALL* showed signs of:
    - Choroidal thickening
    - Venous engorgement
    - *Optic disc edema*, extending into the retinal nerve fiber layer
    - Optic discs tend to expand forward *and backward*. This posterior displacement is opposite to that seen in terrestrial-based papilledema/idiopathic intracranial hypertension (IIH) cases
  - Edema findings also reported by others (e.g., Nimesh Patel, OD, PhD; Brandon Macias, PhD; Steven Laurie, PhD)

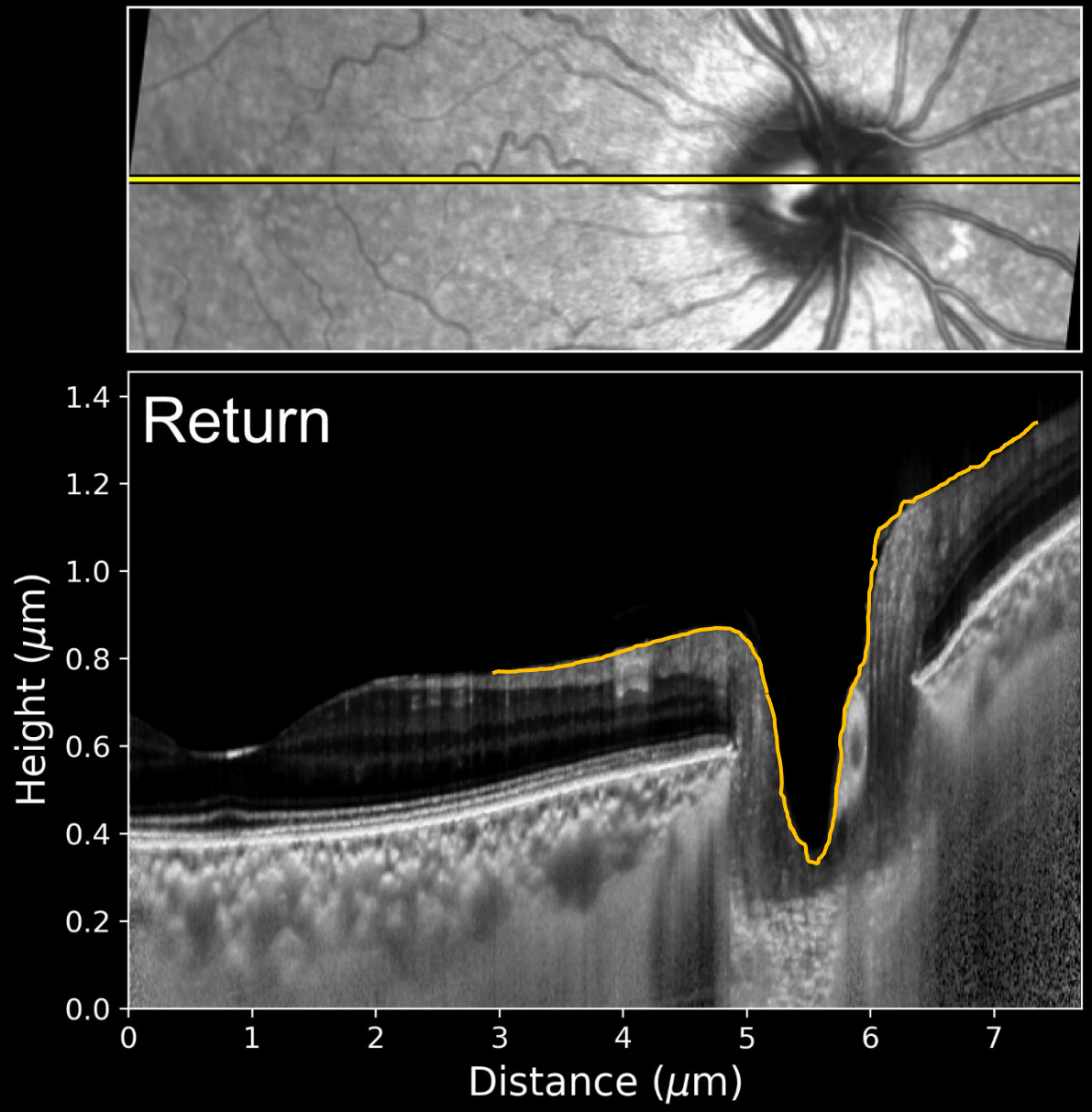


Source: Mayra Nelman & Simon Clemett, PhD



Non-Case w/ “subclinical edema”

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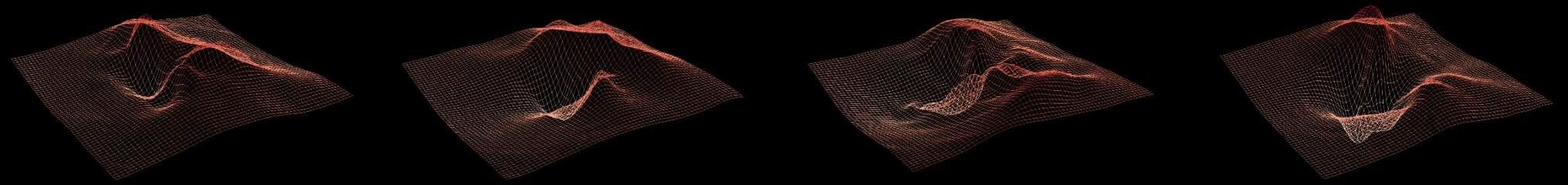
Non-Case w/ “subclinical edema”

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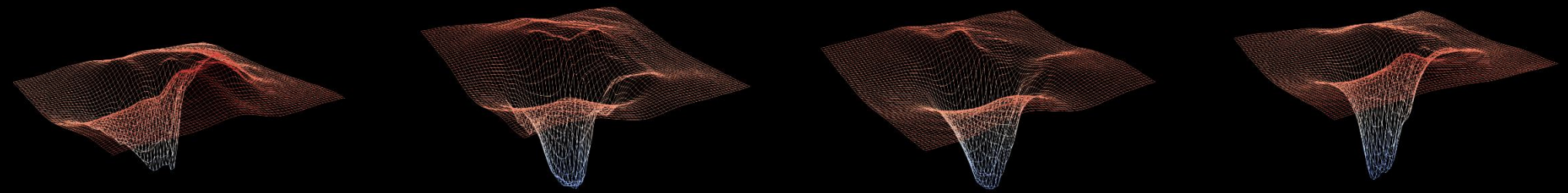
Association between ONH cup volume & SANS diagnosis?

* SANS Case

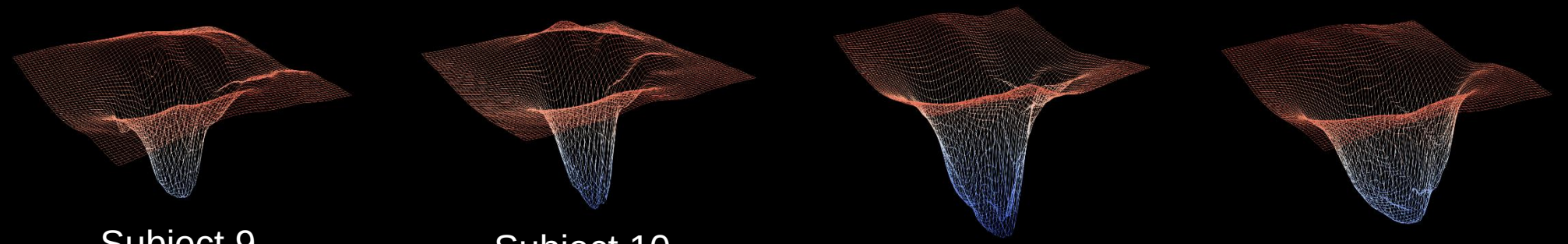
* Non-Case w/ "subclinical edema"



* Subject 1 * Subject 2 * Subject 3 * Subject 4



* Subject 5 * Subject 6 * Subject 7 * Subject 8

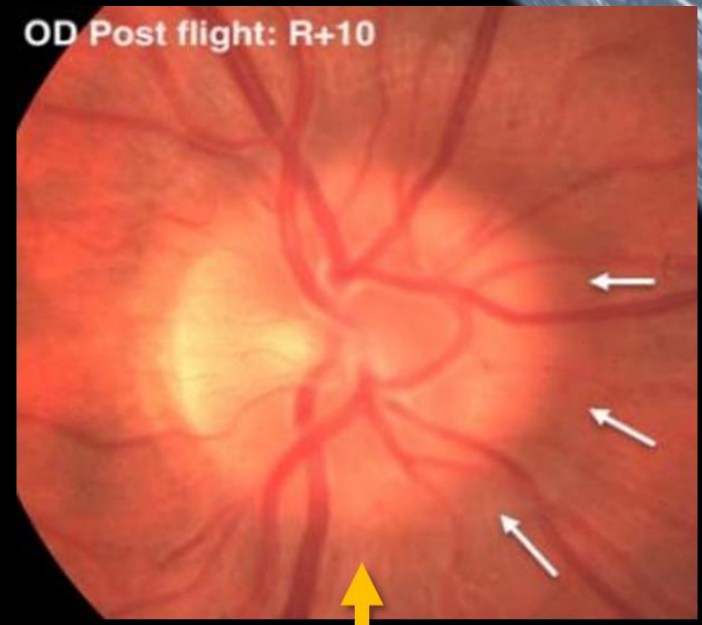


Subject 9 Subject 10 Subject 11 Subject 12

Source: Mayra Nelman & Simon Clemett, PhD

Clinical Highlights - 2017

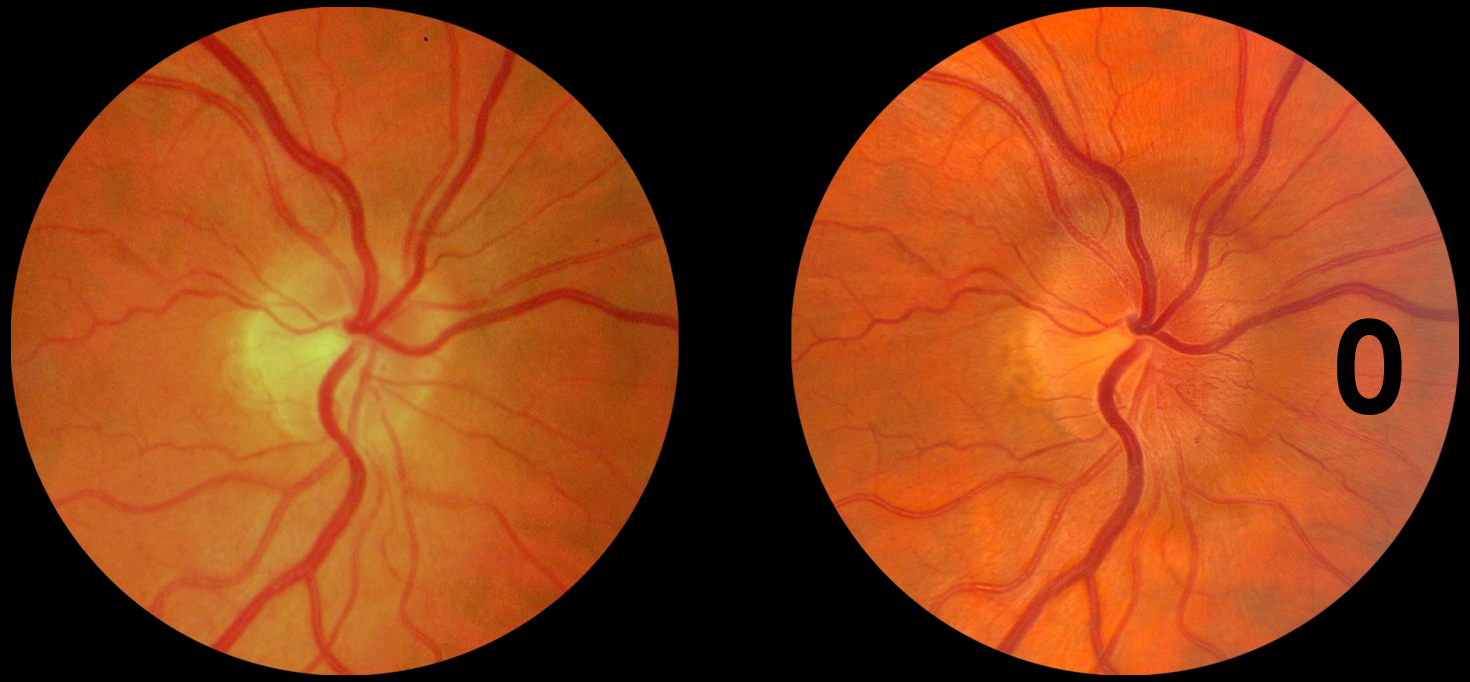
- Association between ONH cup volume and SANS diagnosis?
  - Appears that ONH edema (which occurs to some extent in most/all long-duration crewmembers):
    1. Engorges neurons just anterior to lamina cribrosa
    2. Edematous neurons fill cup (i.e., empty space)
    3. If occupies enough volume, "spills out" of ONH
    4. SANS diagnosed if edema extends ≥270-deg around disc (as visualized via fundoscopy)
  - So, *is a large ONH cup protective against SANS*? Or *are large cups just as susceptible to edema-induced vision loss*…but are being under-diagnosed w/ SANS?



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

Clinical Highlights - 2017

- Intl Fundoscopy Evaluation of Crewmembers (IFEC) – 23-25 Oct 17
  - Face-to-face mtg of SANS SubWG of MMOP's Inflight Clinical Med WG
  - Goals: (1) Conduct retrospective, blinded eval of pre- & post-flight fundoscopic images for signs of SANS across long-duration ISS crewmembers. (2) Establish standard eval process for fundoscopic images across Partner Agencies



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  - Preliminary results:
    - Results ranged from Frisen Grade 0 to 2. 10 of 52 crew rated Grade 1-2 (i.e., SANS)
    - "Several Grade 0" crew showed edema, but not ≥ 270^{o} (i.e., Grade 1)
    - Wide inter-rater variability (very subjective)
  - All Partner Agencies agree:
    - To use standardized Frisen scale to evaluate retinal images
    - Frisen scale is useful, but inadequate for our needs. OCT + fundoscopy = synergy
    - SANS case definition must be updated – Too limited; 100% based on fundo images; underestimates presence of SANS (i.e., Grade 0 ≠ No changes)

Clinical Tasks - 2018

- Deployment of next-gen Heidelberg OCT2 device
  - Same form & basic function as current on-orbit OCT
  - Head operates at 2X speed of current OCT = ~60% reduction in scan time
    - Permits denser datasets w/in same time rqmts
  - Deeper tissue penetration in standard scan mode
  - Angiography Module – 3D rep. of perfused retinal & choroidal vasculature
  - MultiColor imaging capability
    - May replace routine fundoscopy

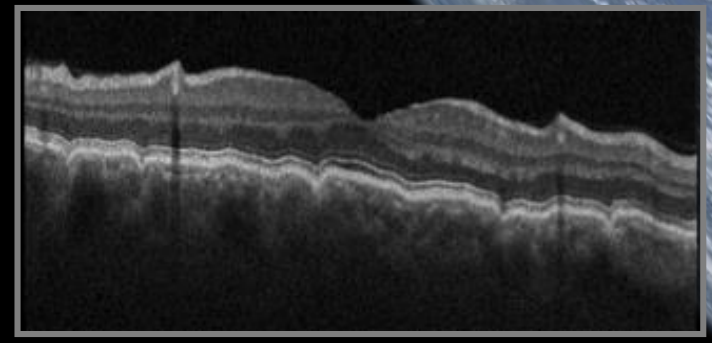
ISS ETA: Summer 2018

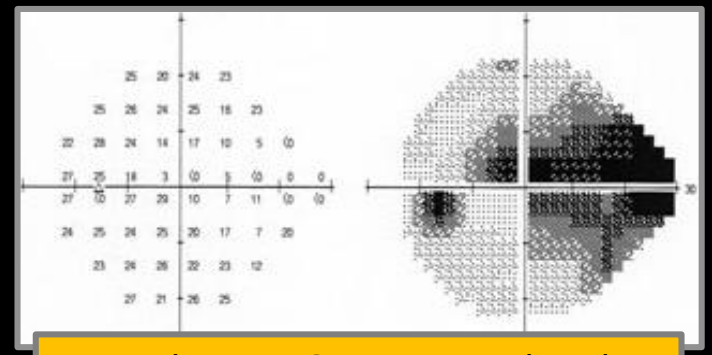




Clinical Tasks - 2018

- Evaluating visual field (VF) testing for ISS
  - OCT: Gold standard for evaluating ocular *STRUCTURE*
  - VF testing
    - Measurement of retinal sensitivity over a visual area
    - A gold standard for evaluating visual *FUNCTION*
    - Performed *terrestrially* by NASA for >10 years; <u>not yet on-orbit</u>
    - Ocular structural changes occur during long-duration spaceflight; however, functional losses are required before treatment can occur. VF testing may:
      - Detect neuro defects (occurring btwn retina & occipital cortex)
      - Track progression of the pathology
      - Monitor effectiveness of med interventions

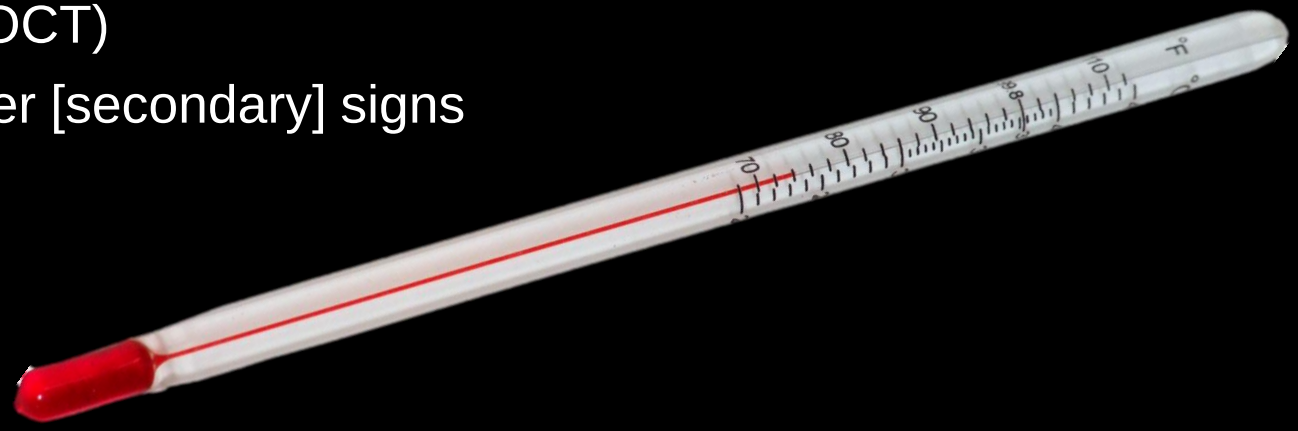




Example VF. NOT crewmember data

Clinical Tasks - 2018

- Update SANS case definition
  - Diagnosis currently based solely on:
    - Optic disc edema of *Frisen grade of ≥ 1* (i.e., edema extending ≥ 270^{o} around ONH) as evaluated via *fundoscopy*
      - Subjective / Binary / Ignores other SANS signs & diagnostic tech
    - Most/all long-duration crewmembers have some “optic disc changes.” Suggests that SANS should be…
      - Described on a continuous scale, w/ a threshold btwn physiological/pathological
      - Measured more objectively (e.g., OCT)
      - Evaluated for edema, but also other [secondary] signs



Questions?

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