



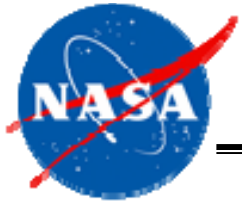
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# The Visual Impairment Intracranial Pressure Syndrome in Long Duration NASA Astronauts: An Integrated Approach

**P. Norsk<sup>1</sup>, C. Otto<sup>1</sup>, Y. Barr<sup>2</sup>, M. Shelhamer<sup>3</sup>, and J. Davis<sup>3</sup>**

*<sup>1</sup>Universities Space Research Association, Houston, TX, USA; <sup>2</sup>University of Texas Medical Branch, Galveston, Texas; & <sup>3</sup>NASA Johnson Space Center, Houston, TX, USA*

***Human in Space Symposium, IAA, Prague***



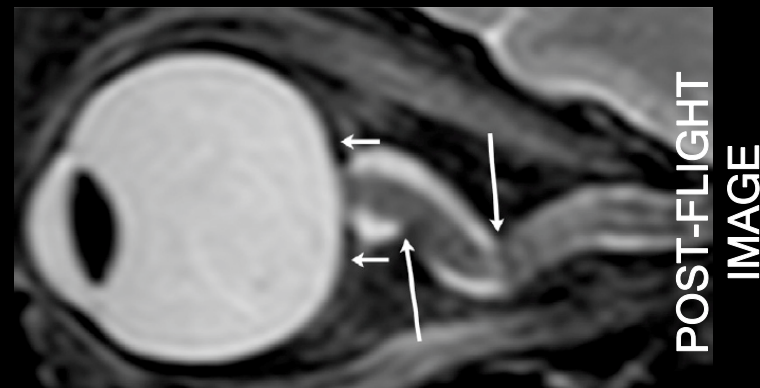
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# Background



# VIIP Clinical Findings

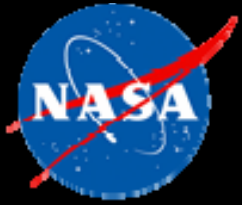
- To date 22/31 U.S. astronauts have developed some or all of the following findings either during or following a six-month spaceflight:



*Eye Findings*

- Hyperopic shift
- Choroidal folds
- Optic Nerve Sheath Distention
- Optic nerve kinking
- Globe flattening
- Optic disc edema (papilledema) N=7
- Cotton wool spots N=3
- ↑ CSF pressure postflight 5/6 subjects: 21.0-28.5 cmH<sub>2</sub>O

- Kramer et al.  
(2012)



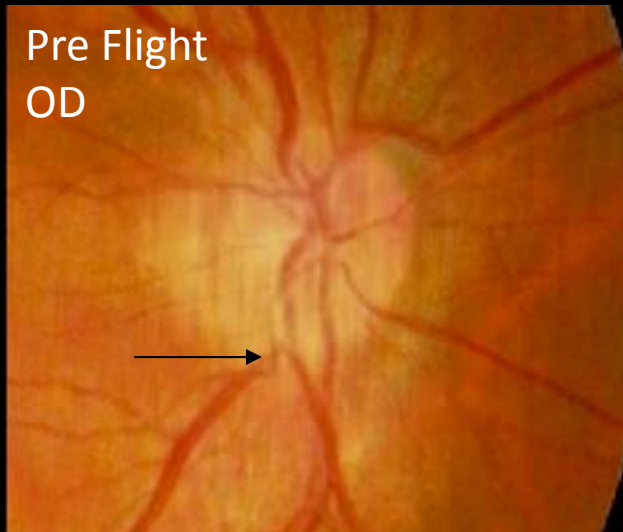
# Pre to Postflight Disc Edema (First case 2005)



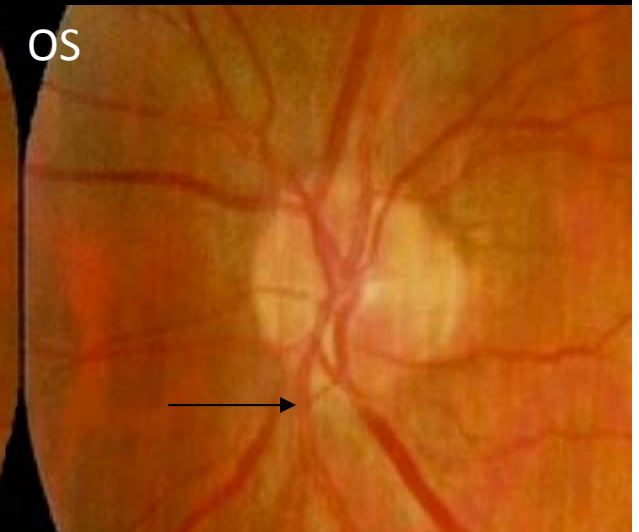
## Pre Flight

Fundoscopic images of the right and left optic discs.

Pre Flight  
OD



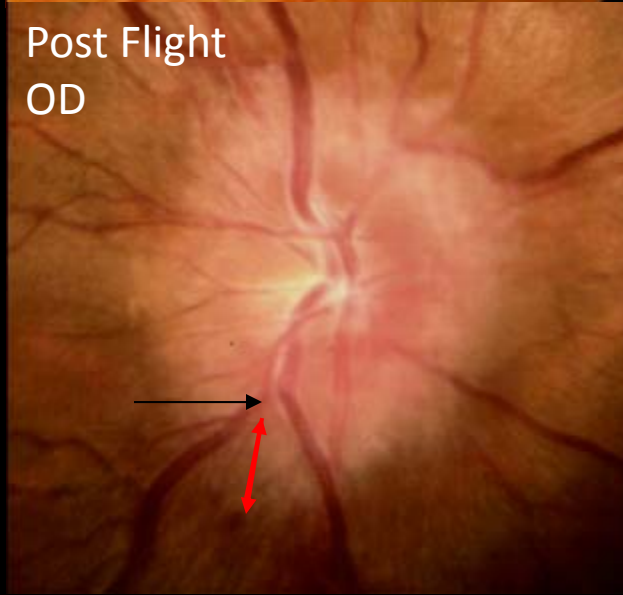
OS



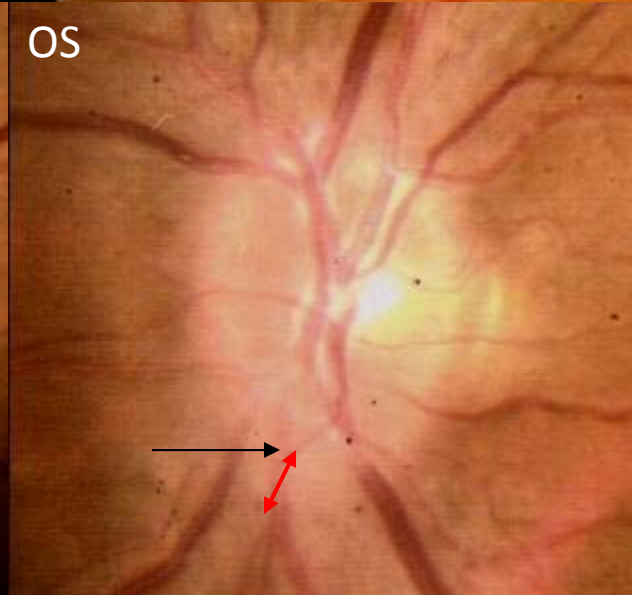
## Post Flight

Fundoscopic images of the right and left optic discs showing Grade 3 edema (right) and Grade 1 edema (left).

Post Flight  
OD



OS

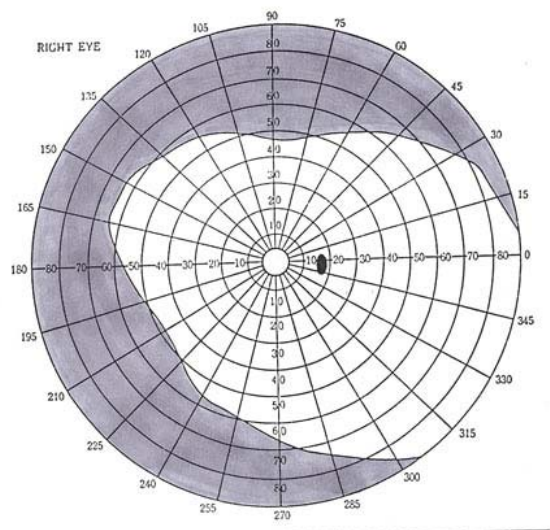




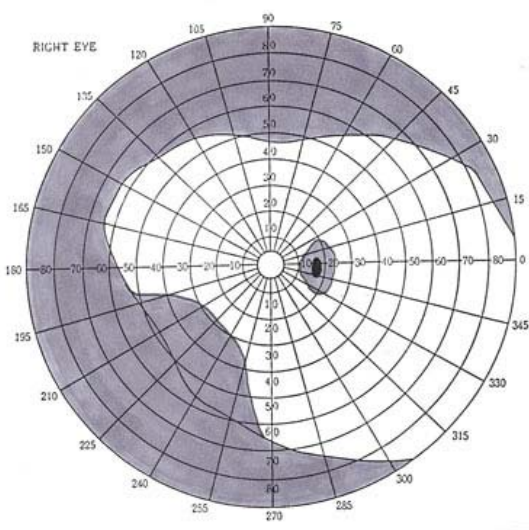
# Prolonged Disc Edema May Lead to Peripheral Visual Field Loss



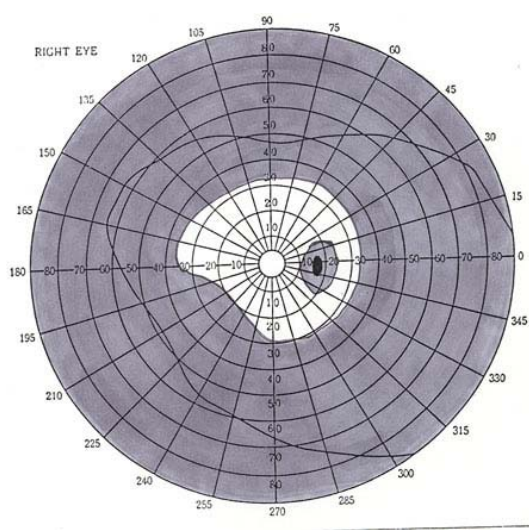
1. Normal Visual Field with normal blind spot (in black)



2. Early Defect, Enlarged Blind Spot and Inferior Nasal Loss



3. Severe Visual Constriction





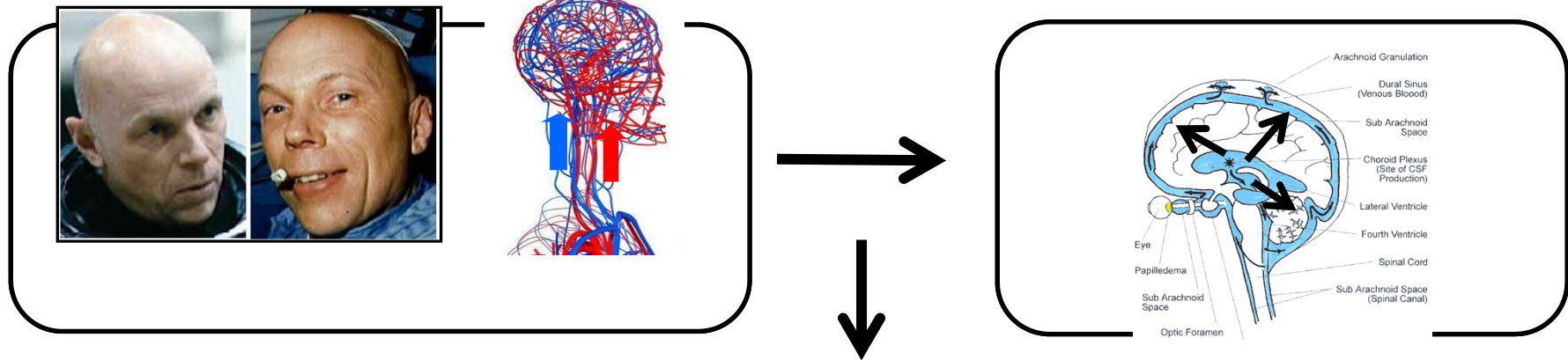
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# Main Hypothesis

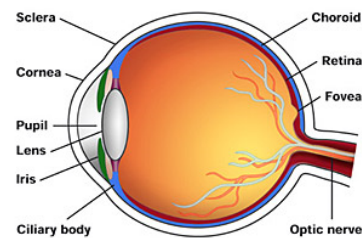


## Head-ward fluid shift due to microgravity

## Increased intracranial pressure (ICP)



## Elevated ICP transmitted to the eye and optic nerve





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# Evidence



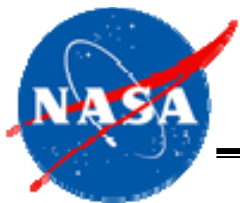


# NASA Crewmember LPs to Date



- LPs are done in crewmembers only if clinically indicated
- 6 LPs conducted postflight in crewmembers with optic disc edema, no preflight LP as baseline
- Postflight measurements of ICP via LP have demonstrated elevated ICP in 5/6, ranging 15.4-21mmHg. Clinical intervention recommended when ICP>20.0mmHg
  - → Does not reflect in-flight ICP (fluid shift + CO<sub>2</sub>), suspected to be higher

Case	Opening pressure (cm H <sub>2</sub> O) Normal range 10-20 cm H <sub>2</sub> O	Opening pressure (mmHg) Normal range 5-15 mm H <sub>2</sub> O	Time after flight (days)
D	28.5	21.0	57
C	28	20.6	12
A	22	16.2	66
F	21.5	15.9	6
B	21	15.4	19
E	18	13.2	8

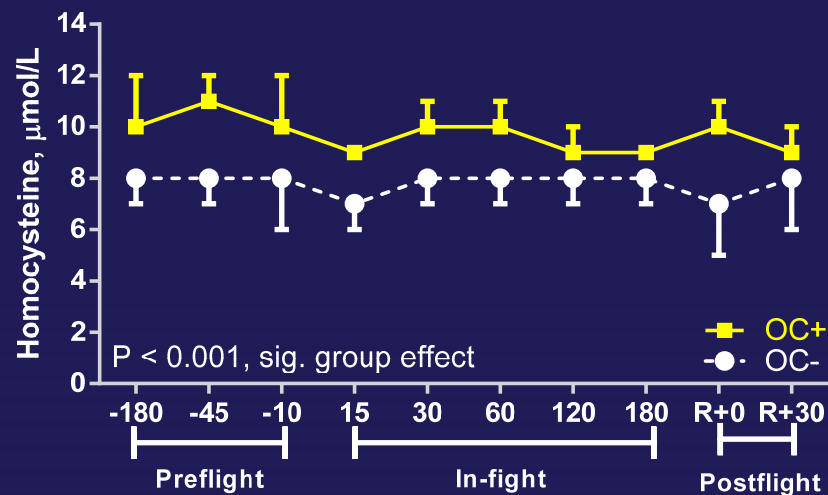
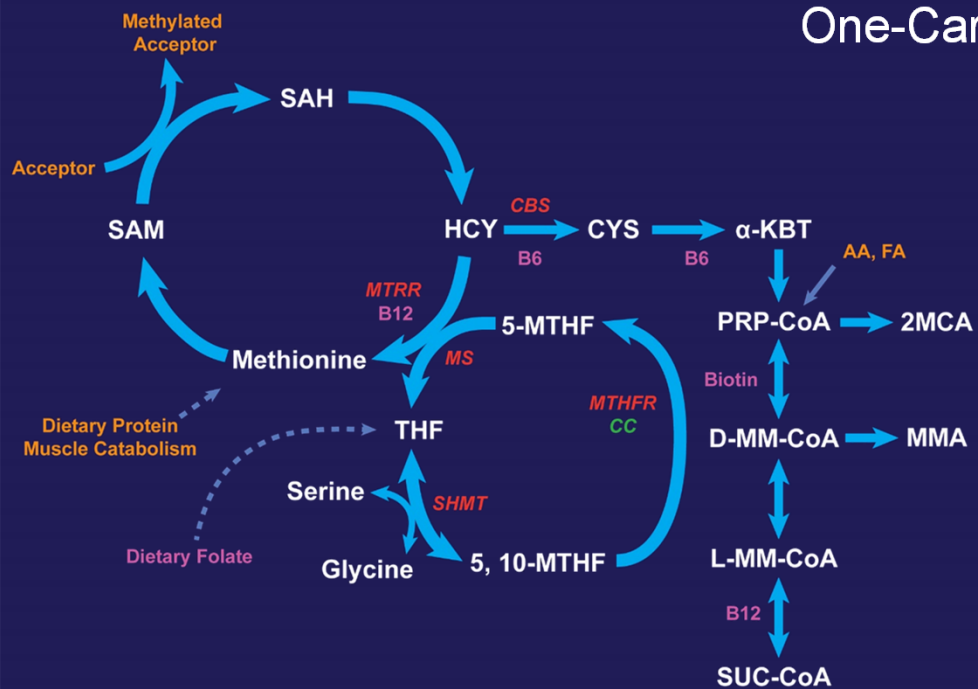


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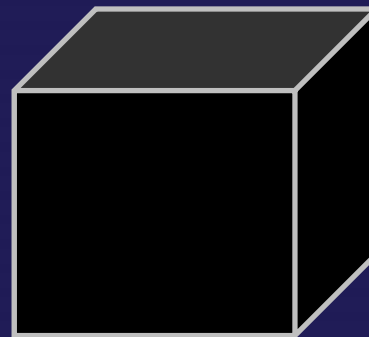
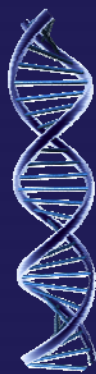
## Alternative Hypotheses:

1. Genetic VIIP predisposition to the spaceflight environment

# One-Carbon Metabolism



Smith & Zwart et al. 2015





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## Alternative Hypotheses:

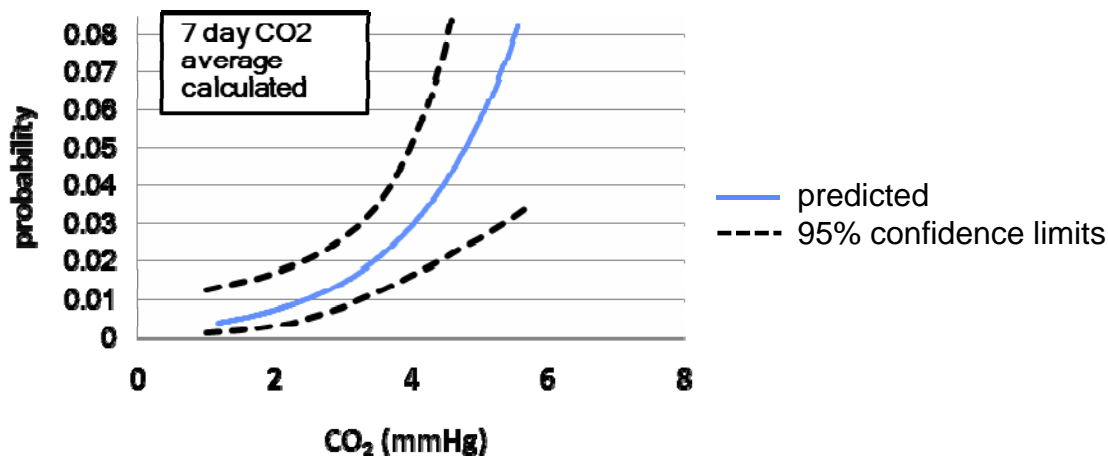
1. Genetic VIIP predisposition to the spaceflight environment
2. CO<sub>2</sub> induced VIIP



# A Possible Role for CO<sub>2</sub> in VIIP?

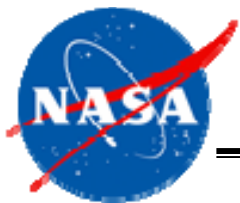


- CO<sub>2</sub> is an extremely potent vasodilator, and its levels on ISS are x10 of Earth levels
- A study by a joint NASA team (medical operations, LSAH, toxicology) evaluated in-flight data from expeditions 2-31, looking for a relationship between levels of CO<sub>2</sub> and symptoms



- A statistically significant association was found between the probability of headaches and average CO<sub>2</sub>, for both 24-hour and 7-day averages

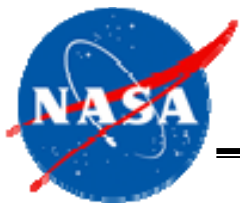
Law J, Van Baalen M, Foy M, Mason SS, Mendez C, Wear ML, Meyers VE, Alexander D. Relationship Between Carbon Dioxide Levels and Reported Headaches on the International Space Station. *Journal of Occupational and Environmental Medicine* 2014; 56 (5):477-483



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## Alternative Hypotheses:

1. Genetic VIIP predisposition to the spaceflight environment
2. CO<sub>2</sub> induced VIIP
3. Ocular structural changes



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4. Brain structural changes



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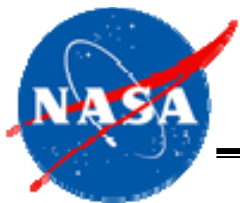
Probably a combination or other causes as well!





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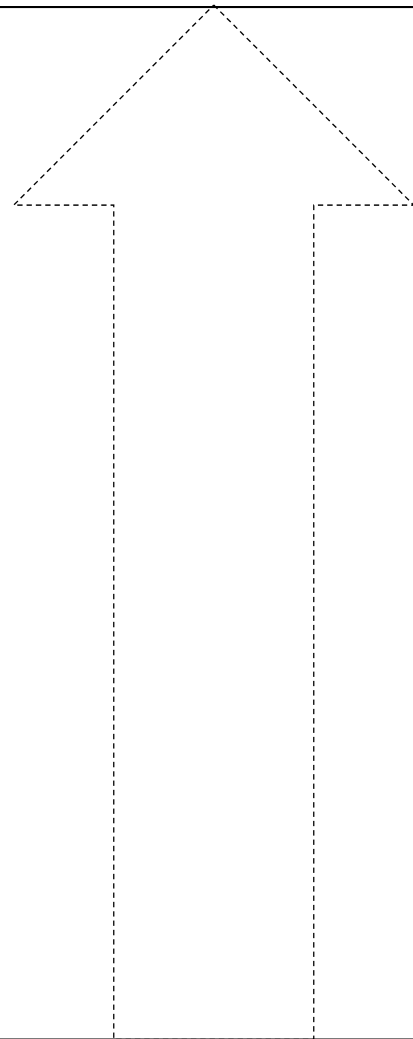
# Research Approach



# The VIIP Research Plan

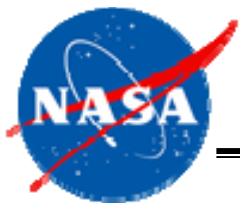


*Zero VIIP Incidence*



Human Research Program  
NSBRI  
Medical Operations  
LSAH

*Current Incidence of VIIP Findings = 66.7%*



# The VIIP Research Plan



*Zero VIIP Incidence*

Human Research Program  
NSBRI  
Medical Operations  
LSAH

**VIIP 1 - Knowledge Acquisition**

*Current Incidence of VIIP Findings = 66.7%*



# The VIIP Research Plan



*Zero VIIP Incidence*

Human Research Program  
NSBRI  
Medical Operations  
LSAH



*Current Incidence of VIIP Findings = 66.7%*

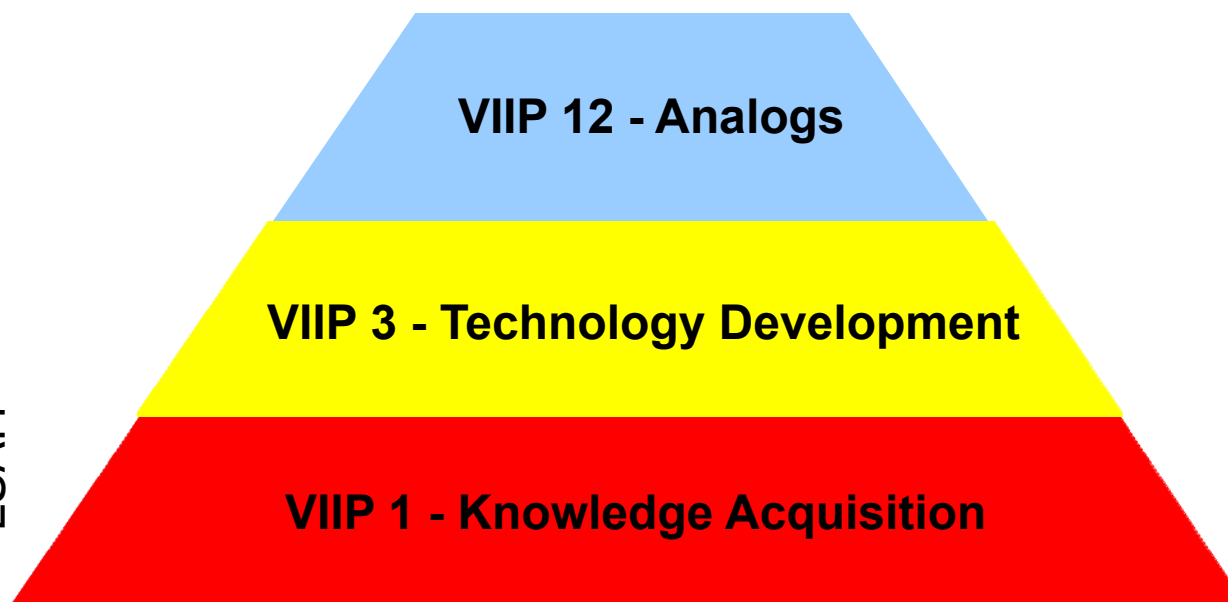


# The VIIP Research Plan

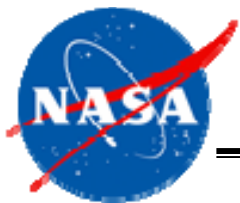


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*Current Incidence of VIIP Findings = 66.7%*

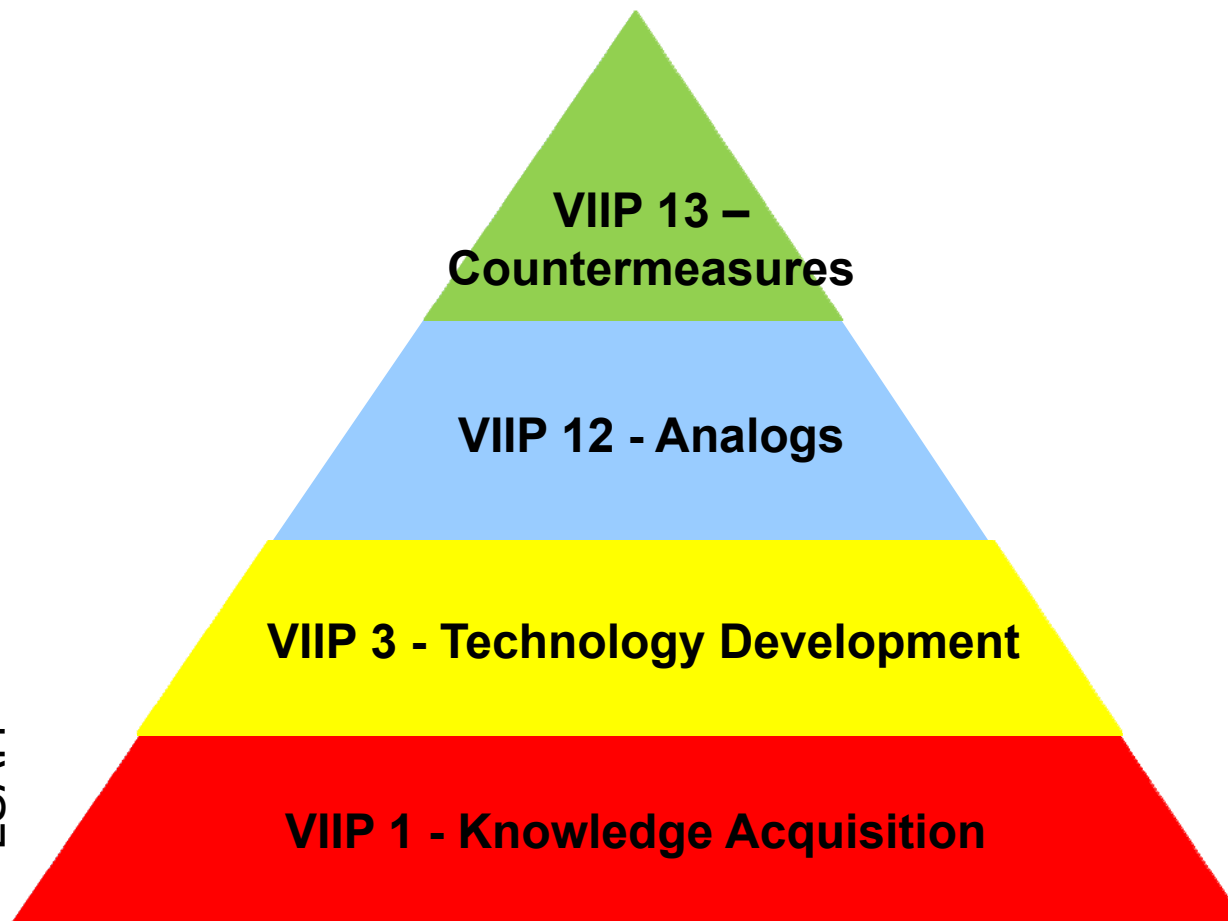


# The VIIP Research Plan

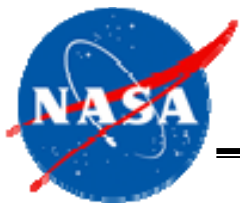


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Human Research Program  
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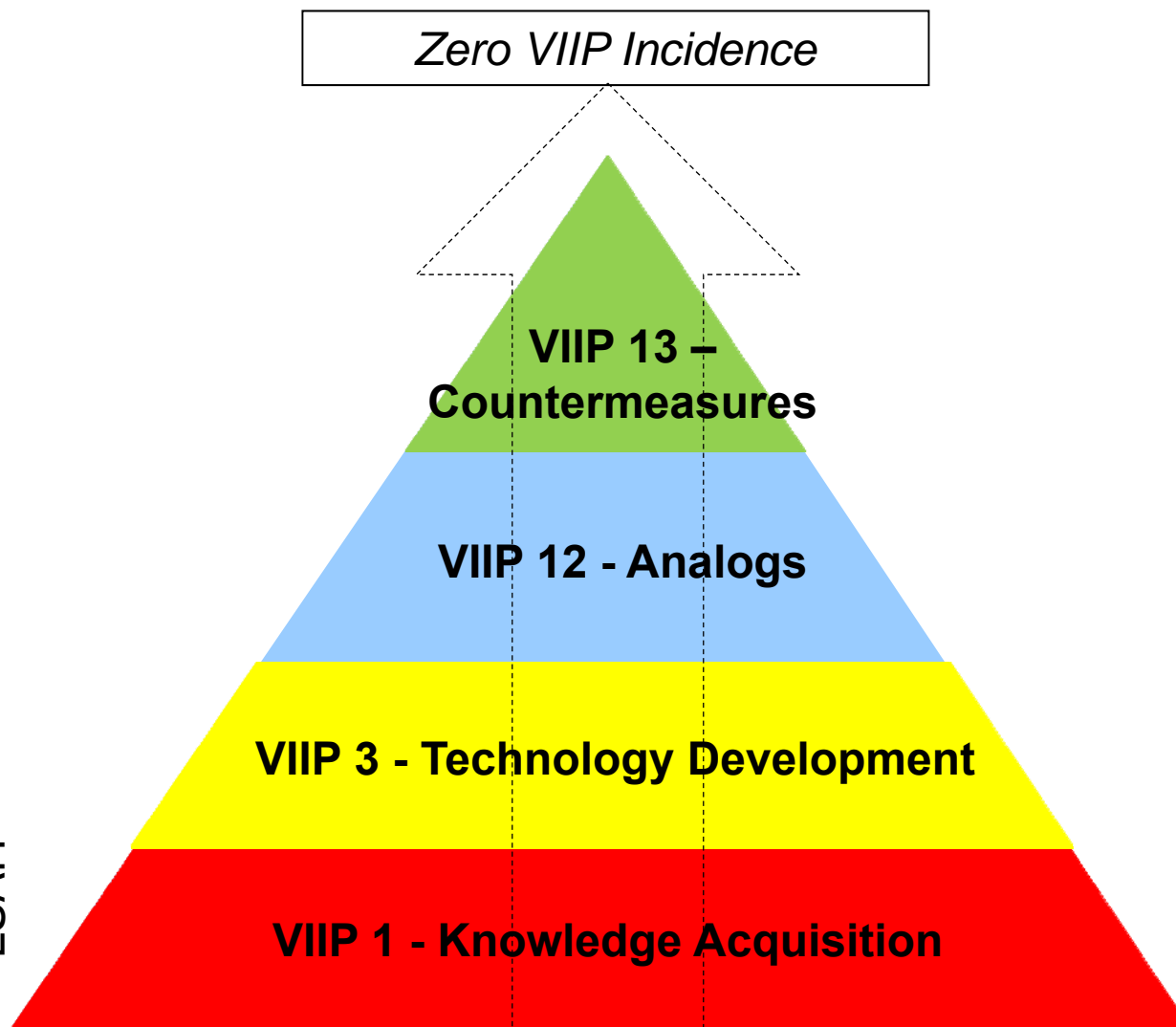
*Current Incidence of VIIP Findings = 66.7%*



# The VIIP Research Plan



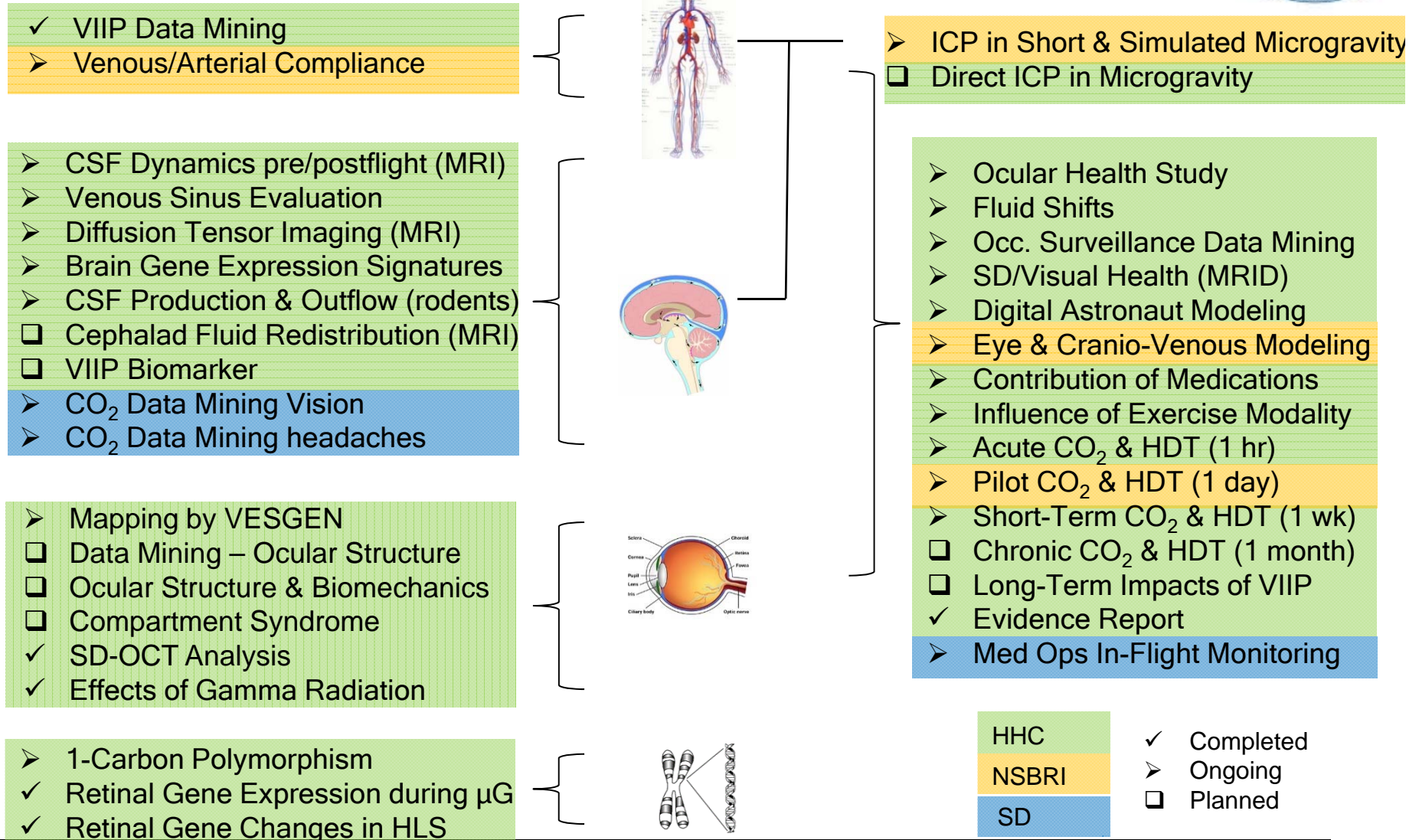
Human Research Program  
NSBRI  
Medical Operations  
LSAH



*Current Incidence of VIIP Findings = 66.7%*



# VIIP 1: Etiology and Risk Factors





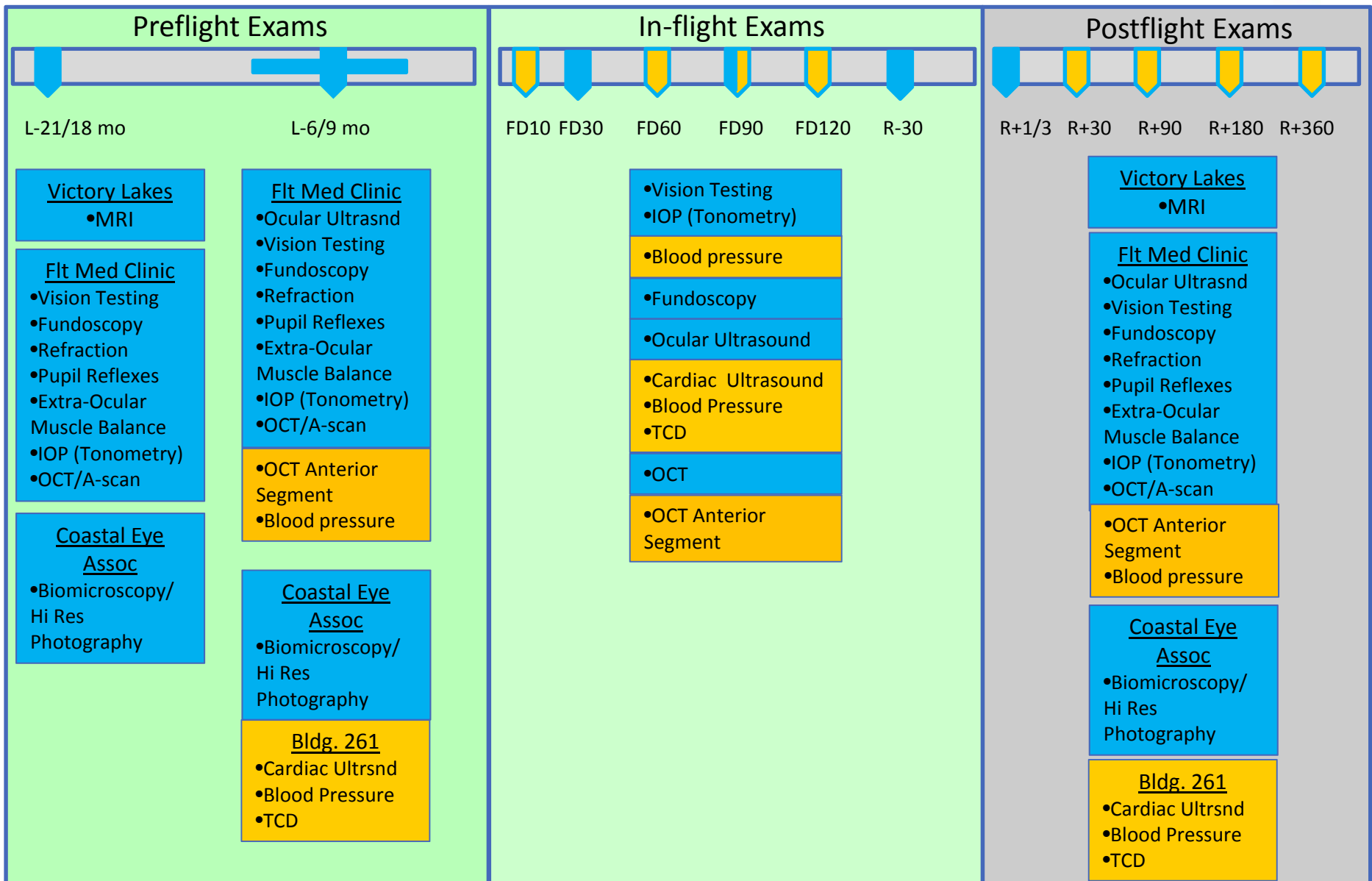


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Example:

**The Ocular Health Study on ISS**

**(PI: Christian Otto)**

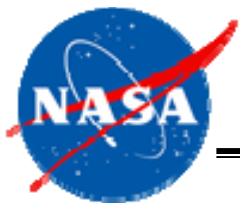


Medical Activity

Research Additional Activity

Medical Session

Research Additional Session



# Comprehensive Examinations in Ocular Health



B-scan Ocular Ultrasound



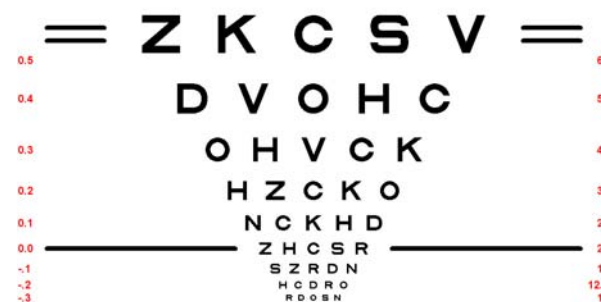
Intraocular Pressure



Optical Coherence Tomography (OCT)



Fundoscopy



Computer-based vision testing



Cardiac and transcranial Doppler for vascular compliance

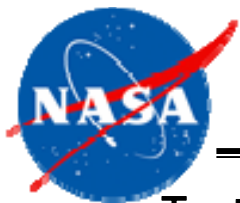


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## Example:

### The Fluid Shifts Study on ISS

(PI's: Michael Stenger, Alan Hargens &  
Scott Dulchavsky)



# In-Flight Sessions (FD 45, R-45)



## Test Day 1

### Fluid compartmentalization measures:

- Total Body Water ( $D_2O$ )
- Extracellular (NaBr)
- Intracellular (Calculated)

## Test Day 2

### Ultrasound measures of fluid shifts:

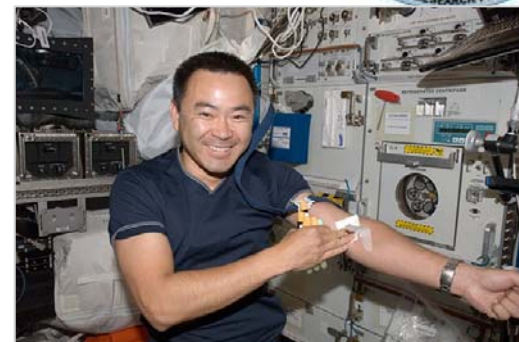
- Vascular measures of head/neck (i.e., carotid, jugular, vertebral, cerebral)
- Cardiovascular, ophthalmic, and portal vein measures
- Tissue thickness forehead and eyelid

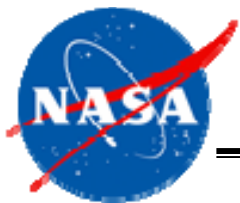
### Other physiological measures:

- Intracranial Pressure (CCFP/DPOAE)
- Intraocular Pressure (Tonopen/iCare and Ultrasound)
- Ocular Structure (OCT)
- Blood Pressure / Heart Rate / Vascular Resistance

## Test Days 3 & 4

- Similar to Day 2 w/ addition of Chibis LBNP



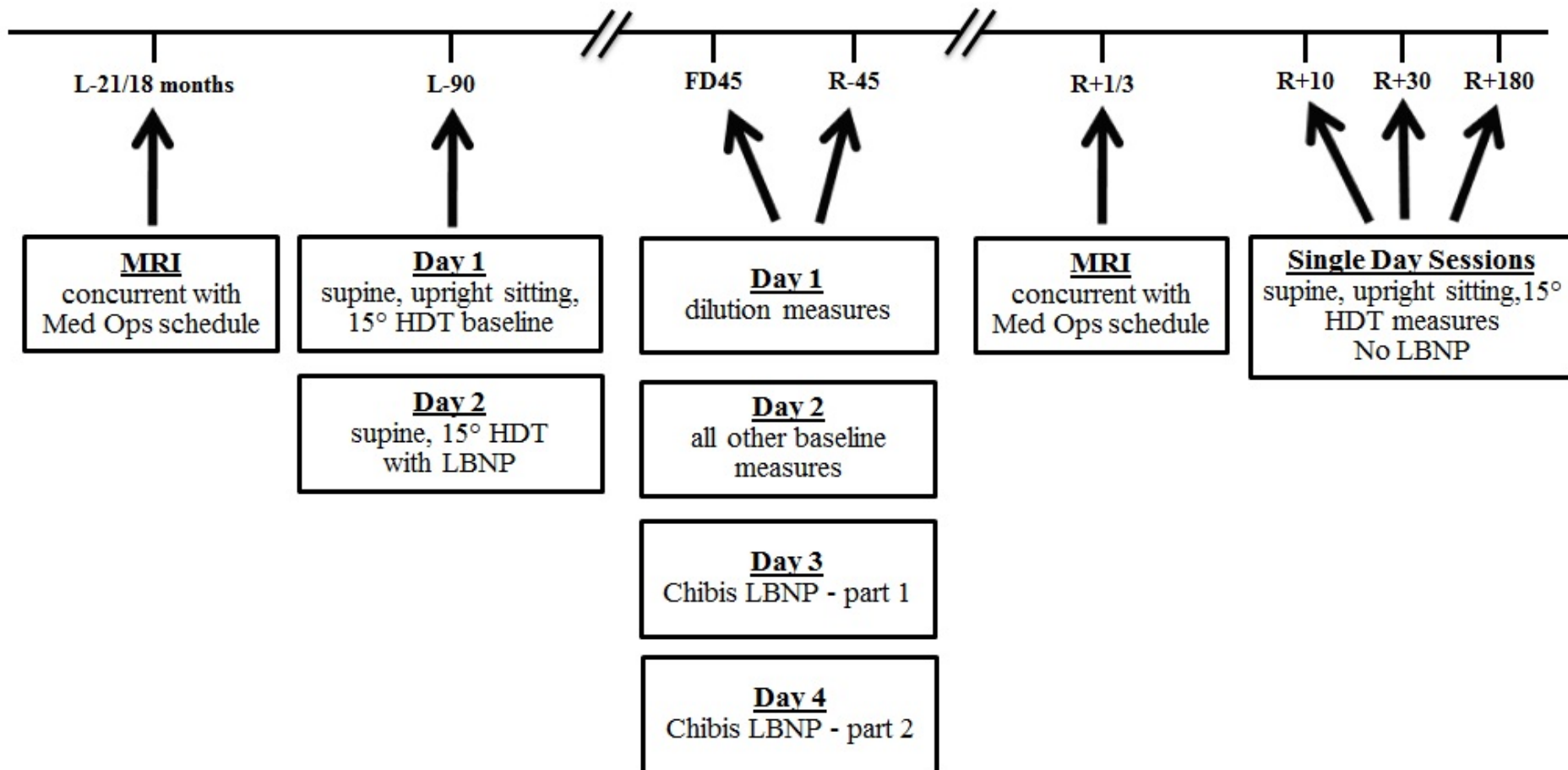


## Reversal of Fluid Shift by LBNP (Chibis)





# Fluid Shifts Timeline





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## Preliminary Results:

Intracranial pressure during parabolic  
flight induced zero G





# Ommaya, 0 G Flight Protocol



**Ommaya Reservoir** - Commonly used intraventricular chemotherapeutic delivery device. Allows access to brain's ventricular system through overlying skin allowing pressure measurement.

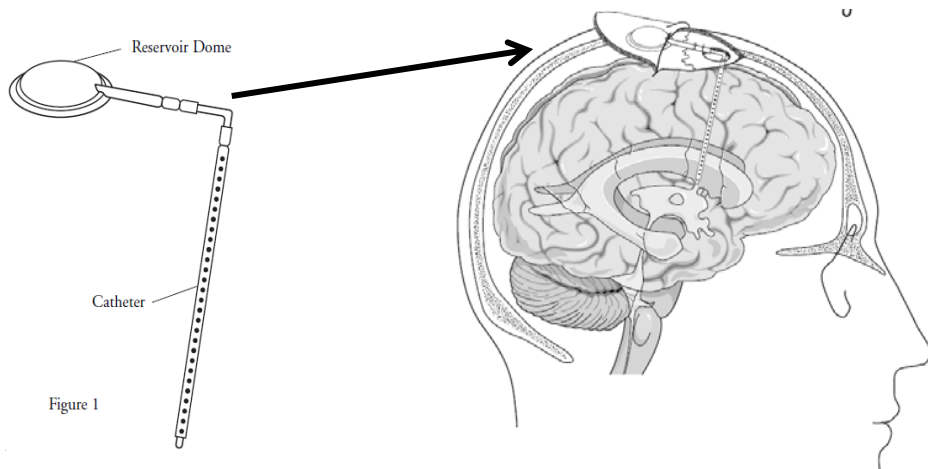
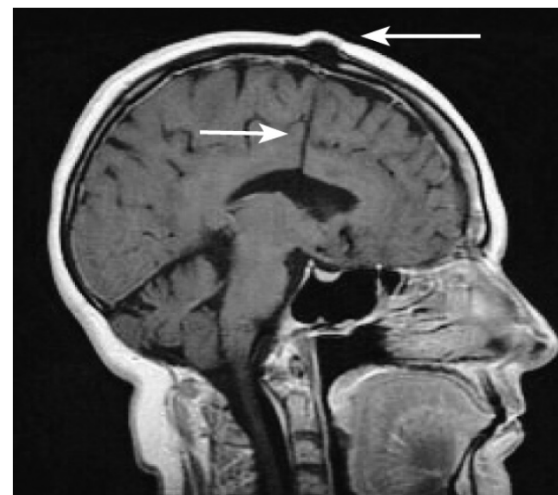


Figure 1



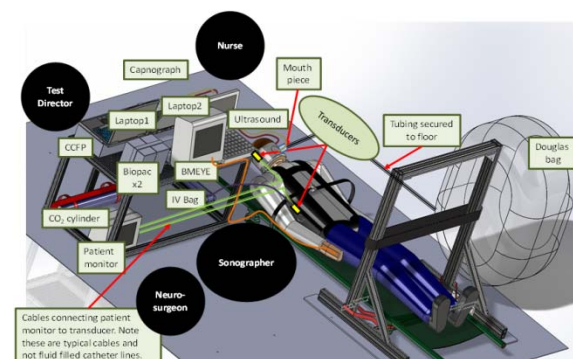
Ommaya Reservoir catheterized

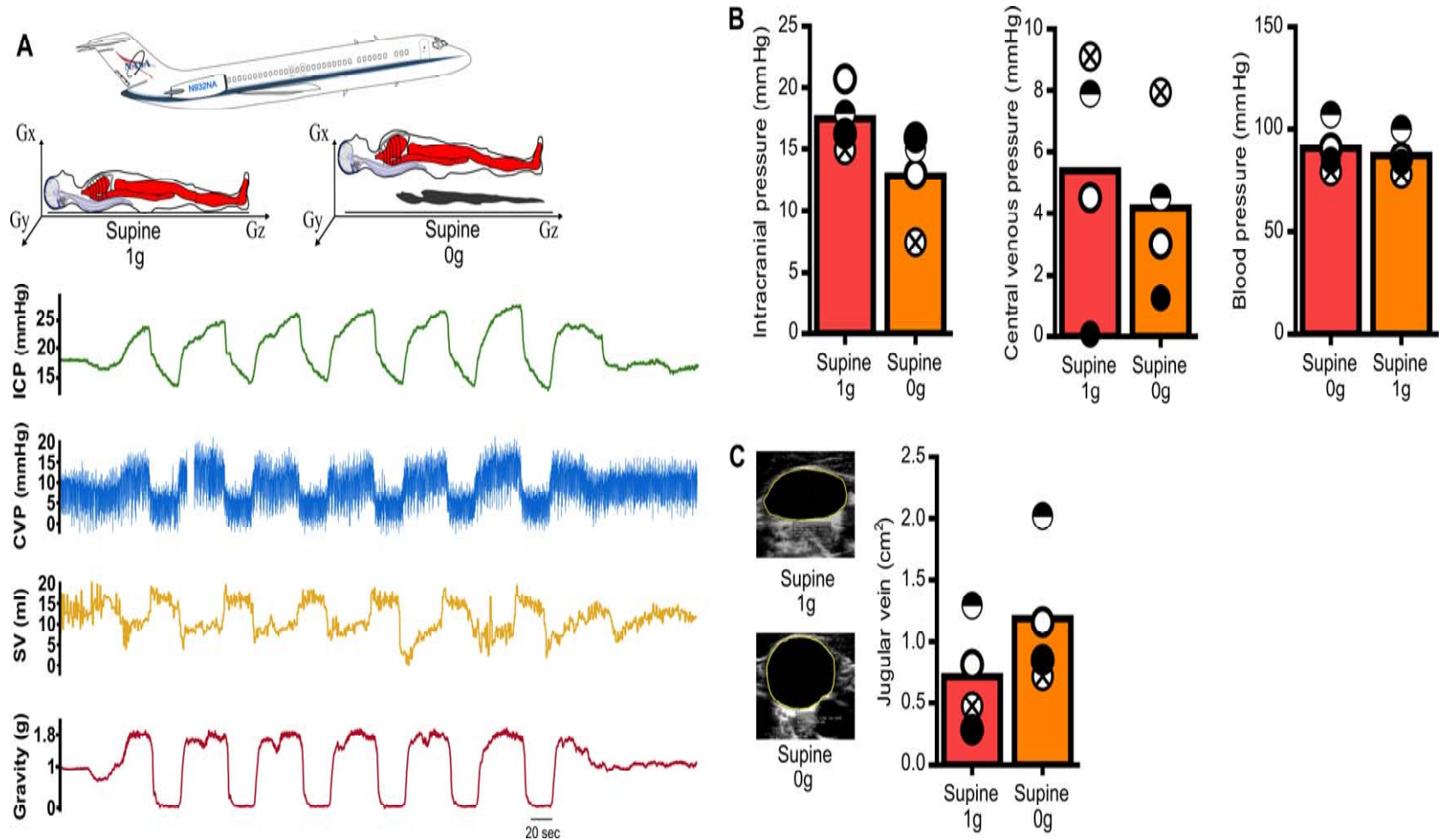


Catheter attached to pressure transducer

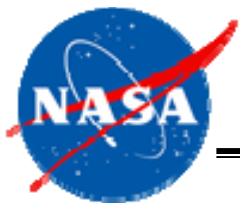


Patient Supine in Aircraft





Levine & Lawley, personal communication (2015)



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# Preliminary Results: Cardiovascular predisposition



# Correlation of Preflight Cardiovascular Score and Postflight Eye Outcomes



Best correlation = 0.91, Max = .96, Min .86,  $P < 0.001$

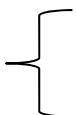




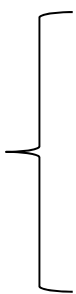
# VIIP 3: Diagnostic Tools



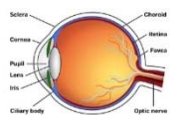
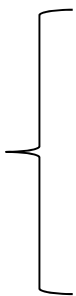
✓ Pilot Study: Non-Invasive CVP Device



- Vittedmed ICP Device Evaluation
- Non-Invasive ICP Ground Comparison
- ✓ ICP Tech Search
- ✓ CCFP Data Mining
- ✓ Cerebrotech
- ☐ Non-Invasive ICP Flight Hardware Development
- ☐ Validation of Non-Invasive ICP



- Retinal Vascular Remodeling
- ✓ SD/Visual Acuity Software & In-Flight Tonometer Upgrade
- ✓ SD/Flight Fundoscopy Trade Study
- ✓ SD/Flight Fundoscopy Upgrade
- ✓ SD/Diagnostic OCT Trade Study
- ✓ SD/Development In-Flight diagnostic OCT



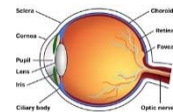
- Volumetric Ophthalmic Ultrasound & ICP
- VIIP Hardware TechWatch

HHC
NSBRI
SD

- ✓ Completed
- Ongoing
- ☐ Planned



# VIIP 12: Ground-based Analogs & Models

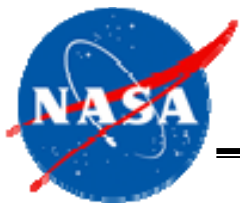


➤ Ophthalmic and Optic nerve Sheath Modeling

- HLS Rodent Model for VIIP
- Digital Astronaut: VIIP Modeling
- Cranial Venous Circulation Modeling
- Acute CO<sub>2</sub> & HDT (1 hr)
- Pilot CO<sub>2</sub> & HDT (1 day)
- ❑ Short-Term CO<sub>2</sub> & HDT (1 week)
- ❑ Chronic CO<sub>2</sub> & HDT (1 month)
- ✓ Rodent Retinal Changes with HLS
- ✓ Rodent Retinal Changes with Spaceflight
- ✓ Rodent Retinal Changes with Radiation

HHC
NSBRI
SD

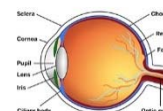
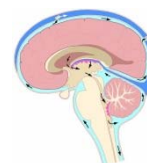
- ✓ Completed
- Ongoing
- ❑ Planned



# VIIP 13: Countermeasures

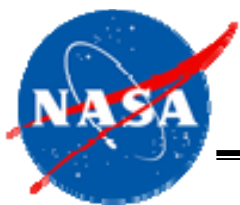


- In-Flight CO<sub>2</sub> Reduction
- Fluid Shifts Flight Study (LBNP)
- Influence of Exercise Modality
- Evaluation of an Impedance Threshold Device
- Mechanical Countermeasures - Evaluation of Marketed Devices
- Thigh Cuffs Ground Evaluation
- ☐ Pharmacological Countermeasures
- ☐ Countermeasure Optimization Ground Study
- ☐ Countermeasure Optimization In-Flight



HHC
NSBRI
SD

- ✓ Completed
- Ongoing
- ☐ Planned



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Thank you!