The goal of the Human Research Program is to provide human health and performance knowledge, countermeasures, technologies, and tools to enable safe, reliable, and productive human space exploration.
Ocular Health in ISS Crews

Jennifer Villarreal, M.S.E.

NASA Human Research Program
What is VIIP?

The Visual Impairment Intracranial Pressure (VIIP) syndrome
- NASA’s number one human spaceflight risk
- Related to microgravity exposure
- Characterized by changes in eye structure, visual acuity, and ↑ intracranial pressure (ICP)

Leading hypotheses
- Microgravity ➔ Headward fluid shift and loss of gravity-assisted drainage of venous blood from brain
- Leads to increased ICP

Potential consequences of prolonged ↑ ICP
- Long-term ocular structural changes
- Reduced visual acuity
- Mild short-term memory impairment (reported in an analog terrestrial population)
Ocular Health in ISS Crews

1. Contributing factors

- CO₂

2. Intracranial pressure (ICP) ↑

3. Elevated ICP & fluid shift affect the eye

- Hyperopic Shifts
  - Up to +1.75 diopters

- “Cotton wool” Spots
  - Altered blood flow

- Choroidal Folds
  - Ridges in back

- Optic Disc Edema
  - (Swelling)

- Scotoma
  - Abnormal visual field

- Increased Optic Nerve Sheath

- Globe Flattening
  - Normal Globe
  - Flat Globe
Current U.S. ISS VIIP Incidence

45 U.S. crewmembers completed ISS missions (as of Feb. 2014):
- First 16 crewmembers not evaluated (no MRI, OCT or ocular ultrasound)
- Latest 29 crewmembers evaluated:
  - Non-cases N=8
  - Confirmed cases N=21

Clinical Practice Guidelines (CPG) classification for the 21 cases:
- CPG Class One N=2
- CPG Class Two N=13
- CPG Class Three N=2
- CPG Class Four N=4

71.2 % Class 1&2
28.6 % Class 3&4

Current VIIP Incidence as a % of U.S. ISS crew tested = 72.4%
Systems Affected in VIIP:

1. The Vascular System

2. The Brain

3. The Eye
**Ocular Health in ISS Crews**

**Data mining in ISS crew reveals correlations between cardiovascular variables & VIIP severity**

<table>
<thead>
<tr>
<th>Cardiovascular Variable</th>
<th>Significant Correlation Across CPG Classification</th>
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<tbody>
<tr>
<td><strong>Biochemistry:</strong></td>
<td></td>
</tr>
<tr>
<td>LDL</td>
<td>√</td>
</tr>
<tr>
<td>HDL</td>
<td>-</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>-</td>
</tr>
<tr>
<td>Hemoglobin A1c</td>
<td>√</td>
</tr>
<tr>
<td>Fasting serum glucose</td>
<td>√</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>√</td>
</tr>
<tr>
<td><strong>Body Composition:</strong></td>
<td></td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>√</td>
</tr>
<tr>
<td>Percentage Body Fat</td>
<td>√</td>
</tr>
<tr>
<td><strong>Cardiac:</strong></td>
<td></td>
</tr>
<tr>
<td>Resting blood pressure (pre-in-post flight)</td>
<td>√</td>
</tr>
<tr>
<td>Pulse Pressure (pre-in-post flight)</td>
<td>√</td>
</tr>
<tr>
<td>CT Coronary Calcium Score</td>
<td>-</td>
</tr>
<tr>
<td><strong>Aerobic Capacity:</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased Maximal Oxygen Uptake</td>
<td>√</td>
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</tbody>
</table>
Initial Identification of VIIP: Changes in Vision

- 50% of long-duration (ISS) mission astronauts report a subjective degradation in vision, primarily increasing farsightedness
- Hyperopic shift

Decreased near visual acuity, distant vision intact

(1mm decrease in axial length is equivalent to a 3 diopter hyperoptic shift)
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Refractive Change in Diopters:
ISS Preflight to Postflight vs CPG Class

Mean Dioptr Change per CPG

<table>
<thead>
<tr>
<th>CPG</th>
<th>OD</th>
<th>OS</th>
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</thead>
<tbody>
<tr>
<td>CPG 3, 4</td>
<td>0.95</td>
<td>0.75</td>
</tr>
<tr>
<td>CPG 1, 2</td>
<td>0.175</td>
<td>0</td>
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</tbody>
</table>

Manifest Refraction Delta

CPG Classification

OD Delta

OS Delta
ISS Inflight Crew Ultrasound Imaging: Signs of Raised Intracranial Pressure

1. Increased Optic Nerve Sheath Diameter

2. Posterior Globe Flattening

3. Raised Optic Disc
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Fluid Shift, Venous Congestion & the Formation of Choroidal Folds
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Pre to Postflight Disk Edema: A Clinical Sign of Raised Intracranial Pressure

Post Flight

Endoscopic images of the right and left optic disc showing Grade 3 edema right and Grade 4 edema left.
Redistribution of Venous Pressures
From 1G to 0G

Standing 1G

0G

-20
0
20
40
60
80
100

venous pressure (mmHg)

9.8m/s²

15-20
7-9

venous pressure (mmHg)

Cranium is rigid
Venous congestion
Obligate arterial flow
Transcapillary leak
++ICP～30-40
Ocular Health in ISS Crews

The Lamina Cribosa & the Translaminar Pressure Gradient: A Mechanism for Papilledema

Area of Interest:

Translaminar Pressure Gradients:

1G 0G

Area of Magnification

CSFp

IOP

Translaminar Pressure Gradient

vitreal cavity

retinal pigmented epithelium (RPE)

optic disc (or optic papilla)

lamina cribrosa

sclera

sensory retina

choroid

optic nerve

dural sheath of optic nerve

retina vessels

15

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### Potential Long Term Consequences of VIIP

1. Hyperopic shift in vision resulting in decreased near visual acuity requiring correction  
2. Development of scotoma (blind spot) due to cotton wool spot (retinal infarction) resulting in direct operational impact  
3. Peripheral vision loss, initially undetected until threshold of 50% loss occurs  
4. Persistent elevation in ICP postflight  
5. Neurocognitive changes:  
   - Association between chronically elevated ICP and white matter changes i.e. degenerative changes. Due to inability to adequately clear toxic metabolites secondary to CNS metabolism such as amyloid and beta proteins  
6. Dose response effect appears to be present, and may be higher in susceptible individuals  
   - E.g. cohort of Shuttle-only flyers found to have grade 1-2 VIIP signs postflight  
7. Higher risk, greater consequences likely on longer exploration missions (*dose-response*)
Ocular Health Study Rationale & Aims

1. The current frequency of crew medical testing is insufficient to:
   a) Define the temporal sequence for the appearance of signs and symptoms in-flight and resolution of signs and symptoms postflight
   b) Identify whether VIIP signs and symptoms recover postflight and determine the impact of prolonged changes on crew health
   c) Delineate the interaction between duration of weightlessness and severity of symptoms, i.e. the dose-response
   d) Outline the mechanism for the VIIP syndrome to aid in the development of protective countermeasures and treatments

2. Data from this study will:
   a) Improve the understanding of VIIP incidence, signs, symptoms, susceptibilities, and timeline for development and recovery
   b) Guide development of countermeasures and targeted treatments to prevent VIIP and its complications
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Ocular Health in ISS Crews

Postflight Exams

Victory Lakes
- MRI

Flt Med Clinic
- Vision Testing
- Fundoscopy
- Refraction
- Pupil Reflexes
- Extra-Ocular Muscle Balance
- IOP (Tonometry)
- OCT
- Optical Biometry

Coastal Eye Assoc
- Biomicroscopy/Hi Res Photography

Preflight Exams

L-21/18 mo
L-6/9 mo

Flt Med Clinic
- Ocular Ultrasound
- Vision Testing
- Fundoscopy
- Refraction
- Pupil Reflexes
- Extra-Ocular Muscle Balance
- IOP (Tonometry)
- OCT
- Optical Biometry

Coastal Eye Assoc
- Biomicroscopy/Hi Res Photography

In-flight Exams

FD10 FD30 FD60 FD90 FD120 R-30

Victory Lakes
- MRI

Flt Med Clinic
- Ocular Ultrasound
- Vision Testing
- Fundoscopy
- Refraction
- Pupil Reflexes
- Extra-Ocular Muscle Balance
- IOP (Tonometry)
- OCT
- Optical Biometry

Coastal Eye Assoc
- Biomicroscopy/Hi Res Photography

Postflight Exams

R+1/3 R+30 R+90 R+180 R+360

Bldg. 261
- Cardiac Ultrasound
- Blood Pressure
- TCD

Bldg. 261
- Cardiac Ultrasound
- Blood Pressure
- TCD

Medical Activity
- Research Additional Activity

Medical Session

Research Additional Session
Inflight Tests – Flight Day 10, 30, 60, 90, 120, R-30

Fundoscopy – 85 minutes per session
- Fundoscopy will take images and video clips of the eye.
- Crew will set up fundoscope and video camera, dilate the subject’s eyes, and perform the fundoscopy exam.

Tonometry with Blood Pressure – 80 minutes per session
- Tonometry will measure the subject’s intraocular pressure.
- Crew will setup the Tonometer and video camera, and numb the subject’s eyes.
- Operator will take the subject’s blood pressure after five minutes of quiet rest, and then perform the tonometry exam.

Visual Testing – 50 minutes per session
- Subject will perform standard computer-based visual tests including Visual Acuity, Amsler Grid, Contrast Sensitivity, and a vision questionnaire.
Inflight Tests – Flight Day 10, 30, 60, 90, 120, R-30

Ocular Ultrasound, Vascular Compliance, & Transcranial Doppler – 250 min/session
- Subject will perform ocular ultrasound, vascular compliance (cardiac ultrasound, ECG, blood pressure), and Transcranial Doppler exams.
- Blood pressure measurement taken prior to the cardiac ultrasound.

Optical Coherence Tomography (OCT) – 185 minutes/session
- OCT exam will capture images of the retina and optic nerve. Operator and remote guidance are required.
- Crew will setup OCT Camera and Spectrometer on the MWA, configure the OCT Laptop software, and perform exam.
**Experiment Summary**

The Ocular Health study will systematically collect physiological data from ISS crewmembers to:

- Provide a greater understanding of the causes and effects of changes to the eye and brain resulting from the space environment
- Define individual susceptibilities
- Develop preventive and treatment strategies for use before, during and after spaceflight.

Terrestrial Benefits:

- The VIIP syndrome has similarities to terrestrial medical conditions such as glaucoma, Normal Pressure Hydrocephalus, Idiopathic Intracranial Hypertension, and high-altitude related illnesses
- Advances in the tools, techniques, and countermeasures that NASA develops in its VIIP research will benefit these terrestrial clinical populations
- Identifying the cause(s) and risk factors for the VIIP syndrome will also inform the cause(s) and risk factors for these terrestrial conditions.
Ocular Health in ISS Crews

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Improved Diagnostic Tools on Space Station
Ocular Health in ISS Crews

NASA Human Research Program
Jennifer Villarreal, M.S.E.

How Heidelberg Engineering Helps
Extraordinary Effort Exceeds Expectations

• Early delivery
• Solved microgravity incompatibility with alternate XYZ Stage configuration
• Performed vibration testing of camera & power box to optimize schedule
• Solved laptop interface challenge with softward mods (Danke Tilman Otto!)
• Excellent training and proactive problem resolution planning (Danke Roland Dosch!)
• Extra training, problem resolution, operational support (Danke Steve Thomas!)
• Responsive technical and logistical support (Danke Tom Tomasso!)
• Knowledgable and flexible sales support including loaner units (Danke Andy Lackey and Ali Trafreshi!)
• And special thanks to Gerhard Zinser, the driving spirit behind it all!
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What’s next?
The National Aeronautics and Space Administration recognizes and thanks Heidelberg Engineering for their outstanding contribution to the international space program, exemplary customer service and technical support.