In 2011, NASA adopted the Visual Impairment-Intracranial Pressure (VIIP) risk in response to observed neuro-ocular changes due to spaceflight\(^1\). The Human Health & Performance Directorate (known at the time as Space Life Sciences Directorate) initiated a significant effort that included expanded occupational monitoring, retrospective data mining investigations, as well as prospective flight and ground research. Results from clinical data mining and ground analog studies suggest changes seen in spaceflight fall below the threshold of visual impairment\(^2,3\). While intracranial pressure (ICP) is clinically elevated post flight in some crewmembers based on the Dandy criteria (>25cm H\(_2\)O)\(^4\), elevations in ICP appear to be milder in nature than first postulated\(^5\). In 2017, NASA changed the risk title of VIIP to Spaceflight Associated Neuro-ocular Syndrome (SANS) to reflect this new evidence.

Space Medicine/LSAH continually monitors SANS related outcomes in the astronaut corps. As of 2017, 28 crewmembers have developed one or more of the ocular changes illustrated in Figure 1. A total of 15% of the ISS crewmembers have developed disc edema specifically following long duration spaceflight. While LSAH provides cohort results to the clinical, operational and research communities, LSAH has also worked with clinical risk custodians to develop a vision summary report which is provided to NASA flight surgeons after every pre-, in-, and post-flight testing session (Figure 2).

Initial data mining studies have also expanded the understanding of SANS and influenced the clinical care of crewmembers. An evaluation of pre- and post-flight optical coherence tomography (OCT) images identified novel key clinical parameters associated with spaceflight, such as retinal thickness and the angle of the blood-retina barrier near the optic nerve, which are now included in the standard clinical report\(^6\). Dr. Roberts has characterized a vertical shift of the brain due to spaceflight, and is currently evaluating the clinical significance of this shift\(^7\). 1-Carbon metabolism has also been implicated as a potential biomolecular pathway for the development of SANS. Initially, Dr. Smith evaluated polymorphisms showing an association with SANS outcomes\(^8\). They have recently expanded their study to include cardiovascular risk factors and 351 additional single nucleotide polymorphisms (SNPs) in the 1-Carbon Metabolism pathway.

While these studies have provided new tools and insight into the SANS phenomenon, they have raised even more questions. In 2013, the Heidelberg Spectralis OCT device was deployed in the JSC Clinic and on the ISS. This tool has proven invaluable in monitoring/characterizing ocular anatomical changes during spaceflight. The JSC Clinic is also using the OCT to evaluate the active and retired crewmembers to determine if there are any long-term changes associated with spaceflight. This expanded

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**From VIIP to SANS: The Evolution**

Sara Mason

In 2011, NASA adopted the Visual Impairment-Intracranial Pressure (VIIP) risk in response to observed neuro-ocular changes due to spaceflight\(^1\). The Human Health & Performance Directorate (known at the time as Space Life Sciences Directorate) initiated a significant effort that included expanded occupational monitoring, retrospective data mining investigations, as well as prospective flight and ground research. Results from clinical data mining and ground analog studies suggest changes seen in spaceflight fall below the threshold of visual impairment\(^2,3\). While intracranial pressure (ICP) is clinically elevated post flight in some crewmembers based on the Dandy criteria (>25cm H\(_2\)O)\(^4\), elevations in ICP appear to be milder in nature than first postulated\(^5\). In 2017, NASA changed the risk title of VIIP to Spaceflight Associated Neuro-ocular Syndrome (SANS) to reflect this new evidence.

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**Figure 1.** Prevalence of SANS Related Outcomes. A description for each outcome is provided at the end of the article.
screening has already identified changes to the choroid, a vascular layer in the back of the eye, in an early long duration flyer. This finding did not impact visual acuity but appears to be related to spaceflight. In 2018 NASA procured Heidelberg’s second-generation state-of-the-art OCT device, and deployed it in the JSC clinic and onboard the ISS. This latest OCT device gives new expanded capability, speed, and resolution, especially with respect to the choroid. In a recent multilateral effort, de-identified fundus images from all ISS partners were graded by blinded Neuro-Ophthalmologists from each agency for disc edema. The initial analysis shows good consensus for images with no visible signs of edema, however, grading was more variable between readers when evaluating case images with edema. This study identified a need to develop new clinical criteria for diagnosing and defining SANS, with more emphasis on changes seen on OCT.

Data from the recently completed Ocular Health Study are currently being reviewed and analyzed. This study expanded on the current medical monitoring protocol (pre-, in-, and post-flight). This will provide valuable insight into the progression and recovery of the changes seen in the neuro-ocular system due to spaceflight. Fluid Shifts is another study that is looking at the vascular changes of the neuro-ocular system, with a focus on potential countermeasures such as Chibis (negative pressure body suit), which can partially reverse the headward fluid shift observed during spaceflight. This study is truly an international effort, including United States Operating Segment and Russian Space Agency crewmembers and investigators. The Fluid Shifts study is anticipated to conclude in 2020, but preliminary data analyses are already underway.

The next SANS study planned for the ISS is Direct ICP, where direct measurements of ICP pre- and post-flight by lumbar punctures will be performed in conjunction with non-invasive measurements of ICP by Cerebral Cochlear Fluid Pressure (CCFP) Analyzer, Transient Evoked Otoacoustic Emissions, and Transcranial Doppler (model based). In-flight, these same non-invasive indirect measures of ICP will be collected to ascertain the magnitude of change in intracranial pressure, and to compare the data with the direct and indirect measures on the ground. This study will be invaluable in understanding the underlying mechanism of SANS.

Two different teams are using computational models and ground physiological data to predict the potential pathways and mechanisms for SANS. NASA Digital Astronaut Program is collaborating with Georgia Tech and the University of Alabama Birmingham, combining lumped parameter models of the cardiovascular and eye systems with finite element models of the microstructure of the eye. Dr. Buckey and his lab at Dartmouth University are collaborating with Creare, Inc to model the cranial venous circulation and its effects on the eye. With the re-use of crewmember clinical data, NASA hopes to gain valuable insight into etiology of SANS.

LSAH is involved in several exploratory analyses to look at potential risk factors and relationships with...

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**SANS Related Outcomes Definitions:**

- **Disc Edema** - swelling of optic nerve head
- **Cotton Wool Spot** - retinal infarct
- **Choroidal Folds** - abnormal undulations of the choroid layer
- **Globe Flattening** - deformation of the back of the eye globe
- **Refractive Error Shift** - change in eye's optical power ≥0.75 Diopters
- **Retinal Hemorrhage** - small bleed in the retinal layer
- **Scotoma** - blind spot
clinical data that will allow flight surgeons to better understand and manage their crewmember’s visual health during a mission. We are also collaborating with NASA’s Space Medicine Operations Division and the Cardiovascular and Vision Laboratory in a special effort to identify relationships with previously unexplored, multi-system data. A list of SANS Research Studies is provided for your information. 

**SANS Research Studies**

*Optical Coherence Tomography Analysis of the Optic Nerve Head and Surrounding Structures in Long Duration ISS Crew Members; Principle Investigator: Namesh Patel*

*Human Cerebral Vascular Autoregulation and Venous Outflow in Response to Microgravity-Induced Cerebral Fluid Redistribution; Principle Investigator: Donna Roberts*

*Risk of Visual Impairment and Intracranial Hypertension after Space Flight: Evaluation of the Role of Polymorphism of Enzymes Involved in One-Carbon Metabolism; Principle Investigator: Scott Smith*

*VIP and One-Carbon Metabolism: Expanded Polymorphism Evaluation and Polycystic Ovary Syndrome Pilot Study; Principle Investigator: Scott Smith*

*Prospective Observational Study of Ocular Health in ISS Crews; Principle Investigator: Brandon Macias*

*Distribution of Body Fluids during Long Duration Space Flight and Subsequent Effects on Intraocular Pressure and Vision Disturbance; Principle Investigator: Michael Stenger*

*Zero G and ICP: Invasive and Noninvasive ICP Monitoring of Astronauts on the ISS; Principle Investigator: Michael Williams*

*VIIP Simulations of CSF, Hemodynamics and Ocular Risk; Principle Investigator: Christopher Ethier*

*Role of the Cranial Venous Circulation in Microgravity-Associated Visual Changes; Principle Investigator: Jay Buckey*

*Effects of Long Duration Spaceflight on Venous and Arterial Compliance in Astronauts; Principle Investigator: Steven Platts*

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**Cancer among NASA Astronauts**

Jacqueline Charvat, Ph.D

Cancer, by definition, is a group of diseases characterized by the uncontrolled growth and spread of abnormal cells. In the United States (U.S.), it is estimated that 1.7 million new cancer cases will be diagnosed in 2018.¹ Cancer is one of the leading causes of death in the U.S., second only to cardiovascular disease. It is expected that 1 in 5 individuals (20%) in the general U.S. population will have a cancer-related death.

As of December 31, 2017, 65 NASA astronauts have died, with accidental events (including occupational and non-occupational) as the leading cause of death among astronauts (27 of 65) and cancer as the second leading cause (20 of 65). Numerous risk factors for cancer have been identified in the U.S. general population. These include family history, radiation exposure, alcohol consumption, smoking, and obesity. Increasing age is also a major risk factor for cancer in the general population – nearly 90% of all cancer cases are diagnosed after age 50.² Each unique type of cancer may also have additional risk factors. For instance, a risk factor for liver cancer is chronic infection with Hepatitis B or C. Among astronauts, the risk factors for cancer are similar to those of the general population, with a few exceptions. The primary additional risk of concern being monitored is radiation exposure, not only from spaceflight, but also from medical testing and jet pilot training.

As part of the Lifetime Surveillance of Astronaut Health (LSAH), epidemiologists strive to understand the risk of cancer among astronauts. LSAH annually updates the incidence and mortality of all types of cancer and related diseases. Types of cancer, total number of cases, and attributable deaths among astronauts as of December 31, 2017 are reported in Table 1. The most commonly diagnosed cancer among male astronauts is prostate cancer (30), which

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**References**


Cancer among NASA astronauts continued

is consistent with the most frequent diagnosis among American men (preceding lung, colorectal, bladder and melanoma). Among women in the U.S., the most frequently diagnosed cancers are breast, lung, colorectal, uterine and thyroid. There have only been five reports of malignancy among female astronauts, with all five being different types of cancer.

The most common types of cancer seen in the general population have not been seen as frequently among astronauts (with the exception of prostate cancer in men). Some of this may be attributed to diligent screening protocols at selection into the astronaut corps, surrounding a mission, and even after leaving the active corps. For example, screening can help prevent colorectal and cervical cancers through early detection and removal of precancerous lesions (i.e. polyps). Screening also offers the opportunity to detect some cancers early, when treatment is more likely to be successful. Screening is known to help reduce mortality for certain cancers including breast, colorectal and cervical. The United States Preventive Services Task Force guidelines shape US medical screen protocols as well as many astronaut screening requirements. NASA goes above and beyond these screening requirements. NASA goes above and beyond these screening requirements. As part of your physical exam at the JSC Clinic, you can discuss your personal risk factors with your flight surgeon and together plan for screenings that may be beneficial to you.

References

<table>
<thead>
<tr>
<th>Body Site</th>
<th>Number of Cases (%) (n=238)</th>
<th>Number of Deaths (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain (Glioblastoma, Lymphoma)</td>
<td>3 (1.3)</td>
<td>3</td>
</tr>
<tr>
<td>Head and Neck (Nasopharyngeal, Parotid, Thyroid)</td>
<td>3 (1.3)</td>
<td>1</td>
</tr>
<tr>
<td>Breast</td>
<td>1 (0.4)</td>
<td>1</td>
</tr>
<tr>
<td>Lung - Adenocarcinoma</td>
<td>2 (0.8)</td>
<td>1</td>
</tr>
<tr>
<td>Gastrointestinal (Gallbladder, Pancreas, Colon)</td>
<td>4 (1.7)</td>
<td>4</td>
</tr>
<tr>
<td>Genitourinary (Kidney, Prostate, Cervix, Endometrium)</td>
<td>34 (14.3)</td>
<td>3</td>
</tr>
<tr>
<td>Hematologic (Leukemia, lymphoma)</td>
<td>4 (1.7)</td>
<td>2</td>
</tr>
<tr>
<td>Skin - Melanoma</td>
<td>12 (5.0)</td>
<td>3</td>
</tr>
<tr>
<td>Skin - Non-Melanoma Skin Cancer</td>
<td>171 (71.8)</td>
<td>--</td>
</tr>
<tr>
<td>Soft Tissue (Sarcoma)</td>
<td>2 (0.8)</td>
<td>--</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>1 (0.4)</td>
<td>1</td>
</tr>
<tr>
<td>Unknown Type</td>
<td>1 (0.4)</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1. Type of cancer by body site, number of cases, and number of deaths among astronauts, as of 12/31/2017

Publications Corner (2018)

Attached are publications related to LSAH data requests and other papers that may be of interest. For your convenience, each publication has a link according to the Digital Object Identifier (DOI) system, if available, to take you directly to the abstract or publication online. For papers not available via open source, the corresponding author may be able to provide you with a copy.


GBI, Wotring VE: Biomedical Findings from NASA's Project Mercury: A Case Series. NPJ Microgravity, 4;2018; https://doi.org/10.1038/s41526-018-0040-5

Five years have passed since LSAH and the Life Sciences Data Archive (LSDA) began consenting the astronaut population for the medical and research data repositories. Whether the data are used for clinical, operational, occupational surveillance, or research purposes, the data is being used to understand the effects of spaceflight on humans. Since LSAH and LSDA started this process in 2012 over 220 crewmembers have agreed to participate in the data repositories!

What are the data repositories again?
Given that it has been five years since introducing the repository and consent options to the astronaut corps, here are brief descriptions of each repository:

**LSAH - Medical Data Repository.** This repository contains all medical data (past and future) in Space Medicine records from selection through retirement including LSAH exams for former astronauts. This may include medically related information such as hazard exposures, training, and other records pertinent to occupational health.

**LSDA - Research Data Repository.** This is an active archive of information containing experiment data from 1961 (Mercury Project) through current flight and flight analog studies (International Space Station, Shuttle, bed rest studies, etc.) consisting of data from completed research studies.

Each repository has its own separate consent form so each astronaut can make decisions about use of specific medical and research data.

**What is the reason for re-consent?**
During each initial informed consent briefing, astronauts were informed that their consent options can be changed at any time. Simultaneously, LSAH outlined that it would take steps to confirm the initial option is still consistent with each astronaut’s choice.

**What can be expected during this process?**
During the initial informed consent briefing, a tiered set of options was presented. As a refresher, here are the options presented during the initial consent briefing:

**Option 1:** Authorizes the release of any data stored in either the LSAH-Repository or the LSDA-Repository to approved researchers for research,
LSAH and LSDA repository 5-year re-consent process continued

Presentation, or publication without the need for further contact.

Option 2: A request for informed consent will be issued to the astronaut for each individual study requesting possibly attributable data. Otherwise, the astronaut’s data will not be used.

Option 3: Authorizes that only the data categories selected on the Medical Data Authorization Checklist or the Research Data Authorization Checklist may be released for research, presentation, or publication without the need for further contact.

During the re-consent process, LSAH and/or LSDA will contact each astronaut via email. Please expect this email during the fifth anniversary of the original signature. Each person will have two choices: retain the current option or choose a different option. To keep the current option, all that is needed is a response (via email or mail) stating no change is required. In order to change the initial option, a new consent form should be completed. This new form should be sent to LSAH via mail with a postage paid return envelope. Once received, the updated consent option will be valid from the new signature date.

Please note that with the new changes to the Common Rule*, re-consenting will only be needed once. However, it is each astronaut’s data and each individual can thereby choose how it is used. Each astronaut can still change their current option at any time by contacting Kim Montague at 281-244-1545 or kimberly.montague-1@nasa.gov.

*The “Common Rule” is the popular term for the Federal (U.S.) Policy for the Protection of Human Subjects, 45 CFR part 46, which outlines processes for IRB review of human subjects research.

News and Notes

Travel Tidbits!

For those traveling from out of town to JSC for your annual LSAH physical examination, here are some facts and tidbits to keep in mind when making your arrangements.

Are you driving your RV to Houston for your annual examination? Planning to fly your personal plane? Any other mode of transportation? Plan ahead; call Denise Patterson at 281-244-5195 to get a comparison flight quote; you will be reimbursed at the lower of the two costs; mileage (land/nautical) or economy airfare from your home city. Include a copy of your flight plan if you travel by private plane.

2019 Houston area Federal Per Diem hotel rates are: Oct. 2018 – May 2019, $131 per night; and June through September 2019, $120 per night; plus tax. Hotel “GOV” rates may be different from the Federal per diem rate; reimbursement is based upon Federal per diem rate. You will receive $61 a day for meals and miscellaneous expenses (which includes, tips for cabs, porters, etc.) calculated at 75% on both the first and last days of travel. Follow this link for more Travel information:

https://www.defensetravel.dod.mil/site/faqraterrev.cfm

You may book your choice of airfare, or rental car, but as a NASA contractor, KBR can only reimburse your expenses according to Federal regulations. Reminder: Original receipts are required for travel reimbursement. You will be given a Professional Services Invoice and return envelope during your annual LSAH exam in the Flight Medicine Clinic. More travel tips are included in your annual invitational letter.

Coffee with CB

The Astronaut Office would like to keep you informed about office happenings, and hear what you’re up to. If you are interested in meeting with some fellow astronauts over coffee or lunch while in Houston for your annual exam, please contact Karen Nyberg (Karen.Nyberg@nasa.gov). Her backup is Stephanie Wilson (Stephanie.Wilson@nasa.gov).

FYI

Did you move? New Email address? Remember to update us so we can continue to send you the LSAH Newsletter, LSAH Invitational physical exam letters and any other news we may need to share with you. Contact Denise Patterson at 281-244-5195 or denise.a.patterson@nasa.gov.

You may also write us at:
Lifetime Surveillance of Astronaut Health (LSAH)
Flight Medicine Clinic/SD3
NASA Johnson Space Center
2101 NASA Parkway
Houston, TX 77058-3696

Or email us at: Jsc-lsah@mail.nasa.gov

For past newsletters, please visit the LSAH website.