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Reflections on 20 Years of Research on the International Space Station

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Abstract

November 2, 2000 began an era of continuous human presence on the International Space Station (ISS). That first crewed expedition to the ISS had few scientific instruments and facilities to work with, yet managed to conduct 52 research investigations. Today, crew oversee upwards of 300 investigations during their time aboard. Indeed, over the past 20 years the ISS has evolved into a robust laboratory with dozens of research facilities, capabilities for the autonomous monitoring and conduct of research, and a growing array of scientific tools available and observational instruments active. As a result, the station has hosted more than 3,000 research investigations generating more than 2,400 scientific publications across every major discipline of science.

The ISS Program Science Forum is composed of senior science representatives across the station's international partnership. It provides multilateral science leadership to the ISS Program. Indeed, ISS research has evolved to become a truly international activity encompassing the participation of more than 4,000 investigators from over 100 countries whose research has been completed or is ongoing. This paper provides an overview of the research and technology development conducted to date and reflects upon the accomplishments, impacts and future direction of ISS research from the perspective of the member organizations of the Program Science Forum. Research areas which have been a focus of ISS research to date and key implications both for future space exploration and scientific advancement are presented. Major Earth benefits derived from ISS research are discussed. Finally, the paper provides insight into areas of emphasis for future research including the maturation of technological capabilities needed for deep space exploration, including lunar exploration programs such as Artemis and future missions to Mars.

Keywords: International Space Station, microgravity research, NASA, PSF, ISS, technology demonstration, benefits, humanity, human spaceflight

1. Outpost on the Edge of Space

On November 2, 2000, the crew of Expedition 1, cosmonauts Yuri Gidzenko and Sergei Krikalev and astronaut Bill Shepherd, commenced continuous operations of the world's first truly international space laboratory. At that time, the International Space Station (ISS) was more an outpost on the edge of space than a microgravity laboratory. Consisting of the U.S. "Unity" node and Russian "Zarya" and "Zvezda" modules, the station offered less than 200m³ of pressurized volume and about 3 kW of power [1-2].



Fig 1. ISS and docked Soyuz vehicle as seen from space shuttle (STS-105) in August, 2001. Credit: NASA

Over their four-month mission, the Expedition 1 crew initiated or completed 52 science experiments and technology demonstrations, many of which focused on check-out of station systems, documentation of the acceleration, vibration and the acoustic environments, and crew physiological adaptations to extended time in the microgravity environment [3].

The ability to do long-duration research in microgravity is beneficial to many areas of scientific study. Humans are uniquely tuned to Earth's gravity, which affects our entire body, from how hard our heart pumps to the density of our bones. The force of gravity also affects all experiments performed on Earth. But take gravity away and many things change, opening up opportunities to view systems in a whole new way not possible on Earth. Likewise, having a platform for in-situ testing of technologies needed for future space exploration, such as a return to the Moon, is crucial to their development.

While the first priority of Expedition 1 was appropriately placed on station assembly and systems performance, impactful science was conducted. The Plasma Kristall-3 (PK-3) investigation was one of the first physical science experiments performed [4]. The Max Planck Institute for Extraterrestrial Physics in Garching near Munich, Germany, and the Institute for High Energy Densities in Moscow, part of the Russian Academy of Sciences, collaborated on the experiment to study the formation and behavior of plasma and dust crystals in microgravity. These collaborators have continued performing experiments on the ISS over the life of the station, including the currently ongoing Plasma Kristall- 4 (PK-4) study.

Because plasma is a charged gas, it can permeate many materials, and spreads evenly and quickly. It can disinfect surfaces, and has been proven to neutralize drug-resistant bacteria such as methicillin-resistant *Staphylococcus aureus* within seconds. Thus, there are many potential Earth-bound benefits from research in plasma crystals. Indeed, this ISS research has contributed to the licensing of seven families of patents and the creation of three companies active in hygiene, medicine, water purification, odor control, car exhaust technology and medical treatments for wound care and skin disease treatment. Products in development include a miniaturized wound treatment device that can create plasma from ambient air without using a gas tank. [5].

Expedition 1 also initiated crew photography-based Earth observations research on the ISS. Utilizing the station's unique vantage-point, orbiting 400 kilometers up and circling our planet every 90 minutes, the crew used hand-held cameras to capture images of hurricanes, cities and geographical features of interest. These photos added to long-running image-capture programs reaching back to the 1960's for both the Russian and U.S. space programs.



Fig. 2. Canadian Space Agency astronaut David Saint-Jacques takes a photograph through the windows of the space station's cupola. Credits: Canadian Space Agency/NASA

As of September 2021, more than 3.5 million Earth photos are publicly available to researchers interested in environmental changes over many years and decades. These images have supported programs such as the Avian Migration Aerial Surface Space (AMASS) research project, a collaboration between the Roberta Bondar Foundation, NASA and the Canadian Space Agency (CSA), which takes advantage of thousands of images captured by astronauts to give people an appreciation of the migrations many birds undertake across the planet.

The first of many investigations of viral shedding on station was also initiated by the crew of Expedition 1. First documented on shuttle missions, studies into this phenomena led to the identification of reactivation of latent herpes viruses in crew as a health risk on long-duration space missions. Additionally, the space-flight derived technologies for saliva and urine-testing used for this research were patented and led to rapid virus-detection tests employed today for diagnosing common ailments on Earth such as mono, herpes, and chicken pox. [6]

2. From Outpost to Orbiting Laboratory



Fig 3. ISS and the docked space shuttle Endeavour in May 2011, as photographed by Expedition 27 crew member Paolo Nespoli from the Soyuz TMA-20. Credits: ESA/Roscosmos

Over more than 20 years of continuous habitation, the ISS has grown to include over a dozen major components, expanding the interior pressurized volume by a factor of 5 (over 900m³) and power generation by more than an order of magnitude (75 - 90 kW) [7]. Expedition 1 saw the addition of the first dedicated science lab, the U.S. “Destiny” module. Three additional science-dedicated modules have been added since – the ESA (European Space Agency) “Columbus” and JAXA (Japan Aerospace Exploration Agency) “Kibo” modules,

both launched in 2008, and the Russian “Nauka” module (2021).

Other additions supporting research include the station’s iconic Cupola and several external platforms. The Cupola greatly increases capability to provide crew photographs of Earth and celestial objects for use by researchers. It also provides an observation and work area for the ISS crew giving visibility to support the control of the space station’s remote manipulator system anchored by the CSA’s Canadarm2.

In addition to supporting spacewalks, maintenance, and arriving vehicles, impactful spinoff technologies have been created thanks to the Canadarm2. Related technology transformed the way surgery is performed, with tools such as neuroArm, an image-guided, computer-assisted neurosurgery device, and the Image-Guided Autonomous Robot (IGAR), which is a digital surgical tool that provides increased access, precision and dexterity for performing highly accurate, minimally invasive procedures.

External experiments on station can take advantage of exposure to the harsh environment of space surrounding the orbiting lab. The space station’s first external science experiment, the Materials on ISS Experiment (MISSE), was initiated in 2001. MISSE consisted of two suitcase-sized pallets containing a variety of materials exposed to the external environment around the station. Tests like these continue today aboard the ISS, providing insights that support development of better materials for future spacecraft, spacesuits, structures, and other components needed for space exploration. Testing materials in space has the potential to significantly speed up their development. Materials capable of standing up to space have possible applications in both space and in harsh environments on Earth, via advances such as improved radiation protection, better solar cell performance, and more durable concrete.

The external platforms also provide valuable opportunities for conducting Earth observation and astrophysical research. They essentially serve as a satellite bus, providing power, command, thermal control, and data-throughput for instruments looking down to capture data on Earth’s atmosphere, oceans and ecosystems or looking up to collect data on cosmic rays or observing at wavelengths largely masked from ground instruments by the atmosphere. Payloads from around the world such as the Global Ecosystem Dynamics Investigation (GEDI), Orbiting Carbon Observatory-3 (OCO-3), DLR Earth Sensing Imaging Spectrometer (DESI), Total and Spectral Solar Irradiance Sensor-1 (TSIS-1), Atmosphere-Space Interactions Monitor (ASIM), STP-H5-Lightning Imaging Sensor (ISS-LIS), and Hyper-Spectral Imager Suite (HISUI) individually collect data helping us study the effects of climate change and other ecological phenomena by observing weather,

oceans, vegetation, and more. In combination, they provide a unique set of measurements that could push the leading edge of environmental research.

The external platforms on ISS also provide researchers an opportunity to test and refine their instruments before committing them to long-duration satellite or robotic exploration missions. Due to its unique orbit, ISS provides a vantage point that compliments data gathered from other satellites. [8]

In 2011, the ISS program officially transitioned from a focus on space station assembly to prioritizing utilization, which includes research, technology development and demonstration, educational engagement, and commercial development. Crew time available for scientific and technology demonstrations increased from lows of 10-20 hours/week to highs in excess of 125 hours/week. Bandwidth for data downlinks increased, first to 300Mb/s in 2016 and again in 2019 to 600Mb/s. This allows faster transmission of 10's of terabytes of research data daily, while simultaneously generating a greater capacity for real-time monitoring of experiments and real-time support of crew conducting hands-on science by the principle investigators on the ground. [9]

Figure 3 shows the cumulative number of ISS investigations over time. It illustrates that the steady build-up of station size and capabilities, coupled with the transition of crew focus from construction to utilization, has resulted in a steady increase in the cadence of scientific research on board.

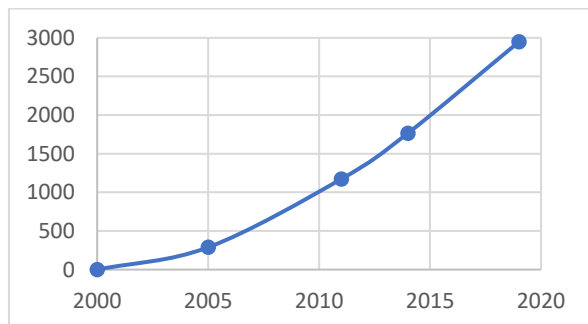


Fig 4. Cumulative Total ISS Investigations through October, 2019.

3. An Expanding Portfolio of Research

As the ISS has grown, it's research capabilities have expanded. ISS research databases identify more than 180 instruments and facilities that have been employed to conduct ISS research as of 2021. [3] The Expedition 1 crew had only a handful of these to conduct research, including equipment to support protein crystal growth, the frozen storage of biological samples for return to Earth, and measurements characterizing the acceleration and vibrational environment on board. Some of these

early tools and facilities had previously been used on the Russian Mir space station or on U.S. Space Shuttle missions.

For example, the Autonomous Biological System (ABS), used in Expeditions 1-4, was a self-contained, isolated aquatic habitat that could house aquatic plants and animals for up to 18 months with the goal of understanding the effects of microgravity on species multigenerational propagation.

Over time, ISS capabilities for supporting biological and human health research expanded to include facilities for studying the impact and adaptation to microgravity of plants, microbes, and animals. Species as diverse as tardigrades, nematodes, fruitflies, squid and rodents have all been studied on the station and investigations focused at the genetic, cellular, and systems levels have been supported. [10-12]

Being able to identify microbes in space in real time – without having to send them back to Earth for identification – is revolutionary for the world of microbiology and space exploration. The Genes in Space-3 team successfully demonstrated this capability when they completed the first-ever sample-to-sequence process entirely aboard the space station in 2017.

Building on this research, the Genes in Space-6 team successfully demonstrated a complete molecular biology process to allow the study of DNA repair entirely. [13] These scientists demonstrated they could break, repair, and sequence DNA in space, expanding the orbiting laboratory's capabilities to include research on the repair of damaged DNA caused by radiation.

Although not originally designed to be used for this purpose, the ISS has also become a prolific deployer of small satellites and, more specifically, CubeSats (small satellites traditionally measuring 10 x 10 x 10 centimeters [~4 x 4 x 4 inches]). In 2005, cosmonauts kicked things off by manually launching Nanospudnik during a spacewalk. This satellite flew for four months, successfully performing a full program of flight experiments.



Fig. 5. AzTech Sat-1 floats away from the ISS. It is the first satellite designed and built by students in Mexico

that is deployed from the International Space Station. Credits: NASA/Nanoracks

Facilities were later installed on the ISS by JAXA and U.S.-based company Nanoracks to automate the deployment process. Northrop Grumman even installed a satellite launcher on its space station resupply vehicle Cygnus that could propel these satellites into higher orbits as the spacecraft departed the ISS. As of November 2020, more than 250 CubeSats have deployed from the ISS into low-Earth orbit (LEO).

Since 2012, nano-satellites and CubeSats from many countries around the world have been deployed from the Japanese “Kibo” module. On many occasions these CubeSats represent the first satellites designed and built by students or engineers from these countries. The KiboCUBE program, initiated in 2015, is a collaboration between the United Nations Office for Outer Space Affairs and JAXA. KiboCUBE aims to provide educational or research institutions from developing countries of United Nations membership with opportunities to deploy CubeSats.

Many of the CubeSats deployed from ISS have served to demonstrate and mature the technological capabilities of these small satellites. In late 2017, the Integrated Solar Array and Reflectarray Antenna (ISARA) demonstrated a new hybrid antenna and power system for use in CubeSats. In 2018, “Raincube” was deployed demonstrating a small radar and providing a profile of the Earth’s vertically falling precipitation such as rain and snow. Raincube’s planned three-month mission turned into more than 2 years. Its accomplishments included providing researchers with a 3D look inside several hurricanes when its data was combined with another CubeSat, TEMPEST-D, to collect complementary data that could be combined with Raincube’s. TEMPEST-D, launched from the Cygnus resupply vehicle to ISS in 2018, demonstrated use of a compact radiometer.

CubeSat launches from ISS also served to demonstrate business models, opening up new markets for services from low-Earth orbit (LEO). From 2013 through 2016, Earth observation company Planet used the space station to validate its business model. Planet was able to enter the marketplace 2 years earlier than planned by demonstrating its ability to provide snapshots of the Earth at a useful resolution of 3 to 5 meters (10 to 16 feet) on a daily basis using a fleet of CubeSats deployed from the ISS. Planet no longer utilizes the ISS, having moved to commercial launch providers to expand its services and constellation of satellites. [14]

The addition of the Combustion Integrated Rack (CIR) in 2009 opened up unique opportunities to the combustion research community that have helped move that field of science forward over the past decade. Removing the effects of gravity from combustion studies

allows for exploration of the basic principles of flames. [15]

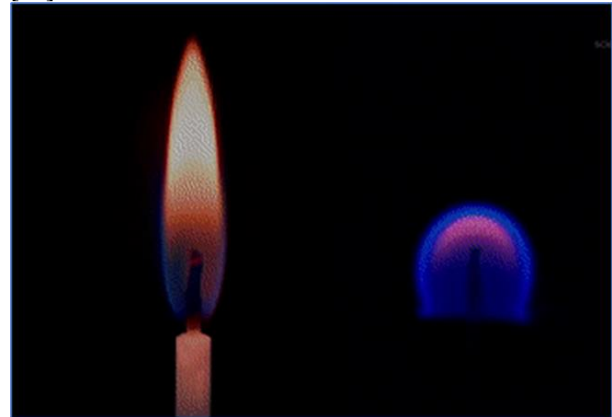


Fig. 6. On Earth, hot air rises, making flames long and thin, but in microgravity flames are spherical in shape. Credits: NASA

When scientists burned fuel droplets in CIR during the Flame Extinguishing Experiment (FLEX) study in 2012, they received surprising results. A fuel droplet appeared to extinguish but actually continued to burn without a visible flame. The fire went out twice—once with and once without a visible flame. This is the first time scientists observed large droplets of heptane fuel that had dual modes of combustion and extinction. The second stage was sustained by what is known as cool flame chemical heat release. Cool flames have been produced on Earth, but they quickly flicker out. On station, cool flames can burn for minutes, giving scientists a better opportunity to study them.

Numerous combustion experiments have followed, further diving into this exploration of cool flames and advancing our understanding of fire safety. While the flames created aboard station in 2012 burned liquid fuel, new cool flames created during a 2021 experiment burned gaseous fuels. This was the first time spherical non-premixed cool flames have been observed burning gaseous fuels. [16]

Typical flames produce soot, carbon dioxide, and water. Cool flames produce carbon monoxide and formaldehyde. Learning more about the behavior of these chemically different flames could lead to the development of more efficient, less-polluting vehicles.

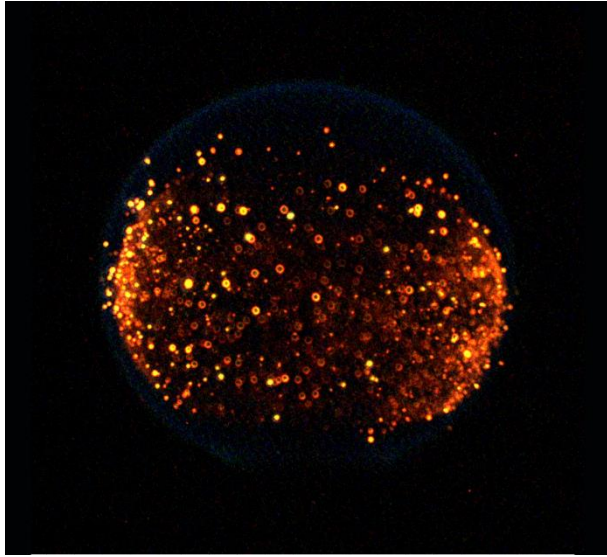


Fig. 7. This flame was one of many ignited as part of the Flame Design investigation inside of CIR to investigate the amount of soot that is produced in different conditions. The yellow spots are soot clusters that glow yellow when hot. These clusters grow larger in microgravity than on Earth because the soot remains within the flame longer. Credits: NASA

As the ISS research portfolio has expanded, a significant amount of investigations have focused on disease. Microgravity research has provided new insights to scientists studying ailments ranging from heart disease to Parkinson's Disease to cancer.

For example, more than 500 protein crystal growth experiments have been conducted to date, with many more planned. Researchers discovered that they could produce higher-quality protein crystals in microgravity than on Earth in experiments conducted on Mir and on space shuttle missions. So, from the very beginning the ISS has been used as a platform for growing crystals to help identify the structures of proteins that are instrumental in our understanding and/or treatment of disease.

Humans contain more than 100,000 types of proteins. Each protein provides information related to our health. Studying these proteins by crystallizing them helps us learn more about our bodies and potential disease treatments.

The JAXA PCG investigation has studied protein crystal growth in microgravity for more than 10 years, providing precise structures of many protein types and leading to discovery of potential drugs for breast cancer, periodontal or gum disease, and Duchenne's Muscular Dystrophy. While details cannot yet be disclosed, the investigators behind these studies say development of those drugs is going well, with some in preclinical trials. Muscular dystrophy drugs have advanced to the third phase of clinical trials, the most advanced result.

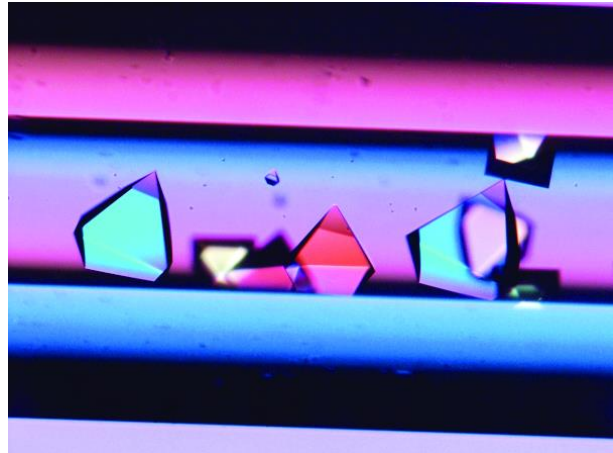


Fig. 8. Protein crystals formed in microgravity in the space station's Kibo Module. Credits: JAXA

Recent studies have pushed the potential of protein crystal growth further with the addition of real time monitoring and adjustments to experiments. Launched in February 2021, the Real-Time Protein Crystal Growth 2 experiment afforded scientists the opportunity to grow, monitor, and optimize protein crystal growth in microgravity through real-time communication with space station crew members. Astronauts were able to check the crystals, report on their growth, and then make changes based on initial observations. [17]

Researchers investigating the mechanisms of certain diseases on Earth must contend with the forces of gravity and the interaction between liquids and solid containers. These forces differ from interfaces in the body they are attempting to model, such as those in arteries and brain tissue, and can affect results.

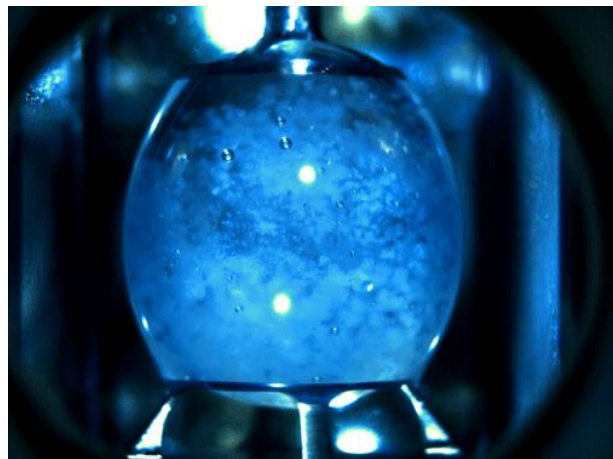


Fig. 9. Image of a drop of insulin solution contained by surface tension in the Ring Sheared Drop device. The RSD investigation studies protein aggregates called amyloid fibrils that play a role in diseases such as

Alzheimer's, Parkinson's, prions, and type 2 diabetes. Credits: Joe A. Adam and Patrick M. McMackin.

The Ring Sheared Drop (RSD) experiment team developed a specialized device [Fig. 7.] that uses surface tension rather than a solid container to hold liquids, allowing for this type of research to be performed in microgravity. Researchers used the device to study protein aggregates called amyloid fibrils. These abnormal fibrous, extracellular, proteinaceous deposits found in organs and tissues are associated with neurodegenerative diseases such as Alzheimer's. [3] The device pins a drop of liquid between two rings and rotates one while keeping the other stationary to create shear flow, or a difference in velocity between adjacent liquid layers.

Previous research shows that this shear flow plays a significant role in formation of amyloid fibrils. The study confirmed that the surface tension concept of RSD works for containing protein solutions in space. Researchers are studying the fluid extracted after each run to determine the extent of protein fibril formation, study their structure, and compare both to what happens in ground-based controls. Results could improve the fundamental understanding of how amyloid fibrils form and are transported, as well as the effects of shear at fluid interfaces relevant to conditions in the body.

Station experiments also extend to areas that directly benefit products consumers use on a daily basis. Toothpaste, 3D printing, pharmaceuticals, and shampoo all stand to benefit from improvements made thanks to years of research on colloids aboard the space station. Mixtures of tiny particles suspended in a liquid, colloids occur in many forms. These forms include natural mixtures such as milk and muddy water as well as a range of manufactured products from shampoo to medicine to salad dressing. Space station research has explored subjects such as stabilizing these mixtures and colloid behaviors that can be applied to products on Earth. [18]



Fig 10. NASA astronaut Jessica Meir configures the Light Microscopy Module (LMM) for the Advanced Colloids Experiment-Temperature-4 (ACE-T-4) study. Introducing disorder to a crystalline system in a

controlled way can form glass. ACE-T-4 examines the transition of an ordered crystal to a disordered glass to determine how increasing disorder affects structural and dynamic properties. Credits: NASA

Studying colloids on Earth is complicated by gravity, which causes some particles to rise and others to sink. Microgravity removes that complication and makes possible research that can help companies design better products. Companies such as Procter & Gamble have used station research to study how to keep a product liquid enough to dispense easily and yet prevent ingredients, or particles, from clumping together and settling. Space station research has contributed to three new patents for the company.

Facilities supporting many other areas of research have also expanded. Plastic, ceramic and biological 3D printers have been installed aboard the ISS to test manufacturing capabilities in microgravity for exploration.

As humanity continues to look further into the solar system, research aboard the ISS has continued to evolve into a testing ground for technology and science that could benefit those missions. Plastic 3D printing is one of those tools being tested. ASI and NASA collaborated on the Portable On Board Printer 3D experiment which paved the way for printing on station. Now hundreds of samples have been created in multiple printing facilities. Astronauts on long voyages need to be able to make their own spare parts, tools and materials essentially on demand – both for routine needs and to adapt quickly to unforeseen ones. In-space manufacturing using 3D printing technology could be an answer.

ESA's BioRock experiment has even explored the potential to use microbes to extract materials on other planetary bodies which could be used to support deep space explorers. The team showed that microbes can not only help mine elements in space, but some microbes may also perform even better under such altered gravitational conditions than they do on Earth. [19]

Having a crewed space station in orbit for more than 20 years means we have uncovered crucial information about how the human body responds to living in space for extended periods. For example, Space-Associated Neuro-Ocular Syndrome (SANS) was identified in many station astronauts. Symptoms include swelling in the optic disc, which is where the optic nerve enters the retina, and flattening of the eye shape. The ISS serves as a platform for testing ways to prevent or reverse these changes and preserve astronaut vision throughout future missions and when they return. [20]

Many other studies are working to identify and mitigate other potential surprises like SANS. The CSA's Vascular series of studies analyzes the effects of weightlessness on astronauts' blood vessels and hearts, including how arteries react to changes in blood pressure,

and if and when insulin resistance occurs during spaceflight. ESA and ASI experiment NutriISS has even given a closer look at ideal body composition in order to avoid an increase in the fat mass/lean mass ratio due to inactivity from microgravity. ESA's Airway Monitoring research studied the occurrence and indicators of airway inflammation in crewmembers due to dust in spacecraft. This study is also opening new avenues to understanding what goes wrong in patients with airway inflammation. The results have contributed to the development of rapid, non-invasive lung tests for an improved quality of life—both on Earth and in space.

4. Building on Past Success

Thanks to the more than 3,000 experiments conducted to date, ISS now has established a base of research, knowledge and understanding. While new areas of science are still being explored researchers are now building on the knowledge we have learned. Scientists are flying new experiments based on insights gained from their first flights or other ISS investigations. New facilities are being installed to handle growing interest. Researchers are combining their knowledge for novel results.

A good example of this involves tissue chips. Tissue chips are small models of human organs containing multiple cell types that behave much the same as they do in the body. After a number of successful experiments, these tissue chips are getting their chance at a second flight.

Many changes occurring in the human body during spaceflight resemble the onset and progression of aging and diseases on Earth, but occur much more quickly in microgravity. Scientists use specialized tissue chips in space to model diseases that affect specific organs in the human body but that might take months or years to develop on Earth.

Tissue chips were first sent to space in 2018. [21]. The initial flights served as a validation of the system. The second flight is now testing a therapy or therapeutics. These chips may make it possible to identify safe and effective therapeutics – drugs or vaccines – much more quickly than the standard process.

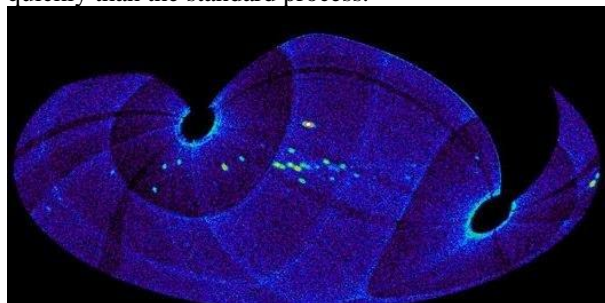


Fig. 11. The "First Light" all-sky X-ray image obtained with the Gas Slit Camera (GSC) of Monitor of All-sky

X-ray Image (MAXI) over one International Space Station orbit. Credit: JAXA

The ISS provides a platform to study not only the innermost workings of the human body but also the vast workings of the cosmos itself. An international collaboration between NASA's Neutron Star Interior Composition Explorer (NICER) instrument and fellow space station astrophysics experiment, JAXA's Monitor of All-sky X-ray Image (MAXI), has jump-started discovery of new parts of the sky that may teach us about our universe. From new insights about neutron stars, to the discovery of new black holes, these two experiments are moving the field of astrophysics forward. Now the research teams are taking their collaboration to the next level.

The differing time zones between the United States and Japan has been an ongoing complication to the collaboration. The On-orbit Hookup of MAXI and NICER (OHMAN) project is taking on this challenge by automating the relationship between the two tools. MAXI will perform an automated analysis to determine whether something is worth NICER's attention. Then NICER can follow up on the X-ray source automatically, cutting the response time from hours or days to minutes.

Earth-science research aboard the ISS will also be getting an upgrade with the planned launch of CLARREO Pathfinder and the Atmospheric Waves Experiment (AWE). The researchers behind this project previously designed and launched TSIS-1, an external space station instrument tracking solar irradiance, the total energy flowing into Earth from the Sun. Solar irradiance represents one of the longest climate data records derived from space-based observations and researchers have been able to maintain continuity of that record with TSIS-1.

By applying the knowledge gained from the design and implementation of TSIS-1, the creation of CLARREO was much more streamlined. With its Power Converter Unit now completed [22], the experiment is scheduled to launch in late 2023. CLARREO will study Earth's climate by taking measurements of sunlight reflected by Earth and the Moon with five to ten times lower uncertainty than measurements from existing sensors. [23]

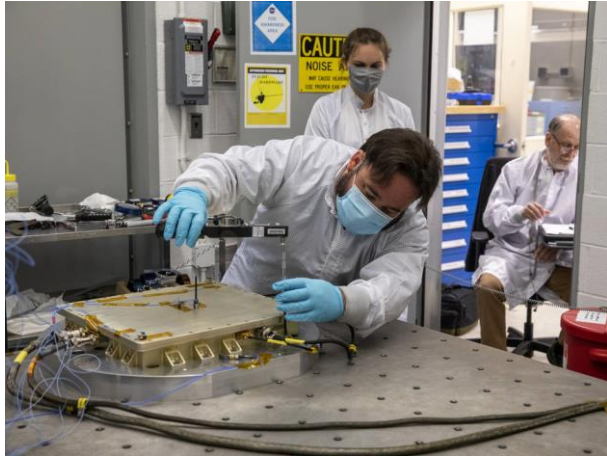


Fig. 12. NASA Langley vibe technician Dave McIn helped build crucial hardware for the CLARREO Pathfinder mission. Credits: NASA/David C. Bowman.

The AWE, planned to launch in late 2022, will also attach to the exterior of the ISS, and look back at Earth. From its space station perch, AWE will focus on colorful bands of light in Earth's atmosphere, called airglow, to determine what combination of forces drive space weather in the upper atmosphere. AWE is the first dedicated NASA mission designed specifically to characterize the properties of global mesospheric gravity waves. [24]

Fluid physics research has benefited greatly from the availability of a microgravity research laboratory, building significantly on the scientific community's knowledge of the topic since April 2004 when the first Capillary Flow Experiment (CFE) was conducted onboard the ISS. This initial study investigated capillary flows and flows of fluids in containers with complex geometries. The work began as a series of fundamental fluid physics investigations led by Dr. Mark Weislogel of Portland State University. These investigations led to patents that involve multiphase fluidics in technology applications associated with space exploration such as thermal control systems and liquid fuel tanks.

The fundamental equations for capillary flow have broad applications in the area of microfluidics. Since the completion of those initial fluids studies, the ISS has provided a unique venue for exploring the nature and applications of fluidics, leading to dozens of scientific publications and multiple patents.

For example, Dr. Alessandro Grattoni of the Houston Methodist Research Institute (HMRI) spearheaded one set of ISS investigations focusing on using nanofluidics to create a new and novel drug delivery mechanism. Based on research done on the ISS and additional research conducted in his labs, Dr. Grattoni and his team received a grant from the National Institute of Allergy and Infectious Diseases in 2016 to study a transcutaneously refillable implant that

administers pre-exposure prophylaxis drugs to those at risk of HIV. The experiment was successfully completed and the implant, which was developed in partnership with Gilead, is in clinical trials and could be approved for usage soon.

In 2014 and 2015, Novartis successfully conducted the Rodent Research (RR)-1 and the follow-up RR-2 investigations, which focused on muscle atrophy and bone mineral loss in the microgravity environment. Novartis partnered with HMRI and Dr. Grattoni's group to conduct a drug delivery fluidics investigation (RR-6) aboard the ISS in fall of 2017. RR-6 tested the performance of an implantable nanochannel system for delivery of therapeutics that are specifically for muscle atrophy.

Fundamental research such as Weislogel's CFE generate new knowledge with a broad range of potential uses. Follow-up activities, such as the nanochannel drug delivery work performed by Dr. Grattoni validate specific applications and demonstrate potential new products.

Overall, research conducted by Dr. Grattoni's group at HMRI has led to nine patents and 21 scientific publications, as well as two highly cited literature reviews on nanochannel drug delivery systems. The many emerging applications of Dr. Grattoni's work, for which the ISS has served as a catalyst, illustrate how basic research can lead to multiple emerging applications. [14]

5. Looking Forward

ESA has also performed microgravity fluids research, contributing greatly to our understanding of boiling, heat transfer, and fluid flows. For example, their Multiscale Boiling experiment analyzed bubbles that form during boiling. Without gravity, boiling takes place in slow motion and produces larger bubbles. Multiscale Boiling allows scientists to observe and measure effects that are too fast and too small on Earth, getting a more complete understanding of heat transfer during the boiling process. This information could be applied to help cool electronics like laptops more efficiently.

Looking forward, ESA plans to launch a new facility to station that will build on the results of Multiscale Boiling. The new Heat Transfer Host facility intended for launch to station in a few years will contain a series of experiments designed around the Multiscale Boiling data.



Fig. 13. ESA astronaut Luca Parmitano installing the MultiScale Boiling Experiment Container (EC) in the Fluid Science Laboratory (FSL) in the Columbus Module aboard the ISS. Credits: NASA/ESA

ROSCOSMOS launched the first bioprinter, Organ.Aut, to the ISS kicking off a new area of research that could one day lead to the creation of organs for use in transplants. The printer was used to culture cartilage cells in space using a magnetic field. U.S.-based company Techshot's BioFabrication Facility (BFF) launched in 2019 further explored the possibility of printing human tissue in orbit. BFF conducted multiple test prints to determine what is necessary to manufacture 3D constructs with cardiac cells, and condition them into tissue. The company also successfully conducted preliminary test prints of components of a human meniscus. [25] In 2022, it expects to continue testing the on-orbit manufacture of cardiac and orthopedic tissue and start a new program aimed at testing the manufacturing of vasculature in space.



Fig. 14. The Nanoracks Bishop Airlock can be opened to space to release satellites and run experiments. It can also be detached and moved to different locations. Taking advantage of the opportunity to expose experiments to different elements such as sunlight or atomic oxygen, this flexibility enables a wide range of research possibilities. Credits: Nanoracks

The space station is gearing up for many more years of technological, scientific, and commercial breakthroughs to come. New commercial facilities are further expanding ISS research capabilities to support future efforts in low-Earth orbit.

The Bishop Airlock, constructed by Nanoracks, was launched in 2020 and is the first commercially owned and operated ISS structure. This airlock allows movement of larger payloads inside and outside the station. This will alleviate one bottleneck slowing down the deployment of small satellites and CubeSats from the space station. [26]

One of the first technology demonstrations to be installed on the Bishop airlock, the Nanoracks-GITAI Robotic Arm, demonstrates the versatility and dexterity in microgravity of a robot designed by GITAI Japan Inc. Results could support development of robotic labor to support crew activities and tasks, as well as servicing, assembly, and manufacturing tasks while in orbit.

Coming soon, U.S.-based company Axiom plans to launch the first habitable commercial module to be attached to the ISS. The element will attach to the space station's Node 2 forward port to demonstrate its ability to provide products and services and begin the transition to a sustainable low-Earth orbit economy in which NASA is one of many customers. Axiom is also launching a private crew of astronauts to the ISS next year who will spend eight days aboard the orbiting laboratory conducting their own research investigations.

Developing commercial destinations in low-Earth orbit is one of five elements of NASA's plan to open the ISS to new commercial and marketing opportunities. The other elements include efforts to make station and crew resources available for commercial use through a new commercial use and pricing policy; enable private astronaut missions to the station; seek out and pursue opportunities to stimulate long-term, sustainable demand for these services; and quantify NASA's long-term demand for activities in low-Earth orbit. [27]

The ISS is preparing for these many continued years of operations through the installation of a series of new ISS Roll-out Solar Arrays (iROSA). iROSA is made up of compact arrays, based on technology previously demonstrated on station, that open like unrolling a long rug. The first pair of arrays were installed in 2021, with the next set launching in 2022. The combination of the eight original, larger ISS arrays, and the smaller, more efficient new arrays will provide a 20% to 30% increase in power for space station research and operations. The roll out arrays are also a technology demonstration for Moon missions. The same solar array design will be used to power elements of the Gateway lunar-orbiting outpost. [28]

As we return to the Moon as a part of the Artemis program, the space station will become an even more crucial resource for testing new exploration technologies.

The station's regenerative life support hardware, called the Environmental Control and Life Support System, provides clean air and water for station crews, and is getting a number of upgrades. These upgrades demonstrate technology that could get spacecraft to the level of reusability needed for deep space missions.



Fig. 15. A full Moon seen from the International Space Station as it orbits 251 miles above the Andaman and Nicobar Islands, territories of India in the Bay of Bengal. Credits: NASA

The Universal Waste Management System (UWMS) is being tested aboard the ISS for future use aboard Orion for the Artemis II flight test that will send astronauts on a 10-day mission beyond the Moon and back. The toilet was designed to address astronaut feedback about comfort and ease of use. It also features a 65% smaller and 40% lighter build than the current space station toilet. Improved integration with other components of the space station water system will aid in recycling more urine.

A newly upgraded distillation system for the space station's Urine Processor Assembly was also tested in 2020 after engineers found the station's previous system suffered an issue common to many machines – deteriorating belts. NASA engineering teams determined they could 3D print a plastic-toothed drive pulley. Previously, the distillation assembly could see parts failures after approximately 1,400 hours of service. With the upgrades included in the latest iteration, engineers anticipate a service life of more than 4,300 hours without parts replacement. The Brine Processor Assembly (BPA) which allows more water to be recovered from crew urine was also implemented as a system upgrade.

There are many more ISS tests preparing us for future exploration. The Four Bed CO₂ Scrubber is testing a technology to remove carbon dioxide from a spacecraft as well. Astronauts tested a sextant in the Cupola of the space station for use aboard Orion as an emergency navigation tool. Built as the primary radiation detection system for the Orion spacecraft, the Hybrid Electronic Radiation Assessor (HERA) was modified for testing on the ISS as a part of the A-HOSS experiment.

In total, these ISS technology demonstrations are setting the stage for humanity's future in space. [29]

6. In Conclusion

The results of more than two decades of research in orbit are being delivered to humanity in the form of numerous breakthroughs. From advances in consumer products to medical treatments to pushing the frontiers of scientific knowledge, ISS research is moving humankind forward into the future from 400 kilometers above our planet.

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