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The human body in space: the metaphoric journal

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<u>THE HUMAN BODY IN SPACE</u>

The metamorphic journey

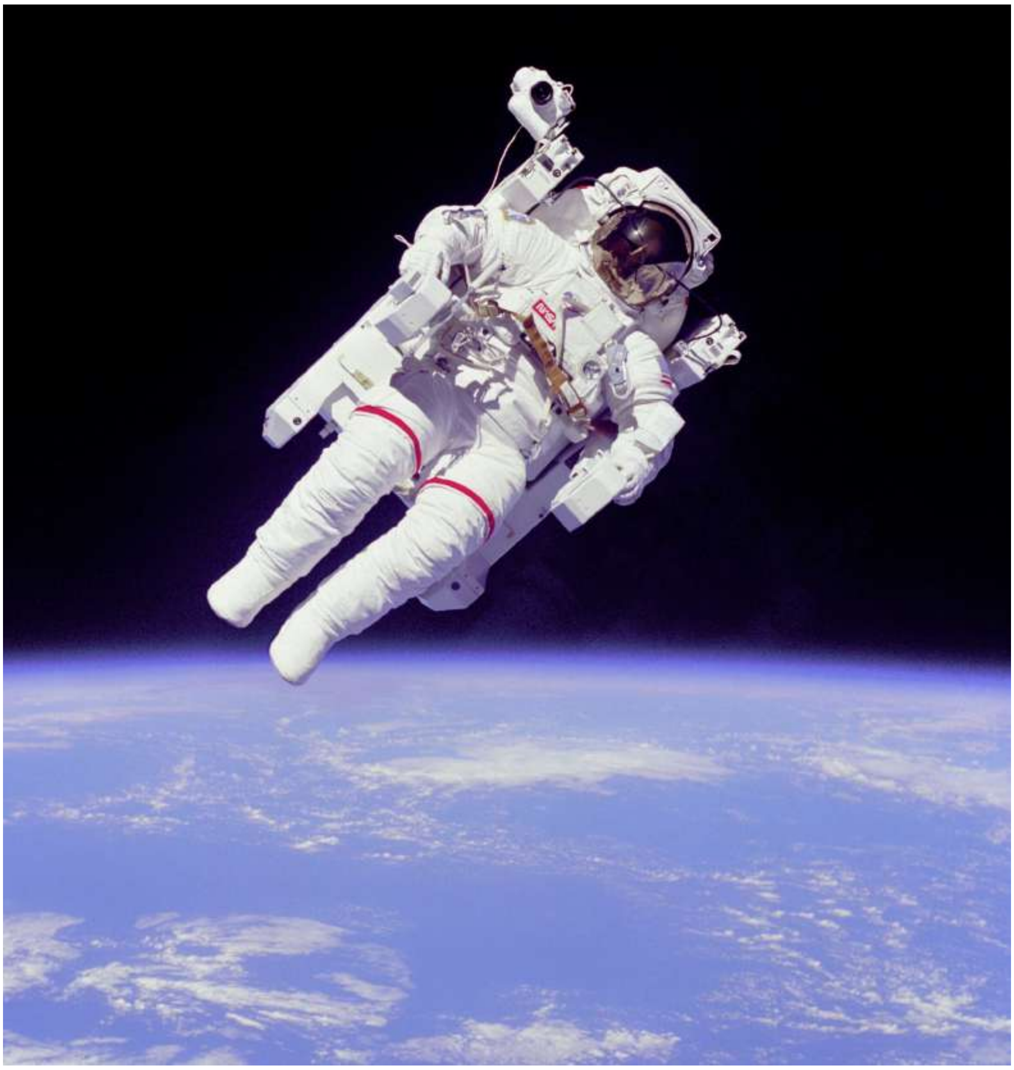

Image 1. Astronaut Bruce McCandless II, an STS-41-B mission specialist, used his hands to control his movements above the Earth during the first-ever spacewalk which didn't use restrictive tethers and umbilicals [1].

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ABSTRACT

The potential risks and harm that different systems and organs have gone through and could go through when travelling through space are assessed in this thesis. Microgravity and radiation are the main factors that make space travelling very dangerous to the human body. Gravity guides the vestibular system, keeps bone formation and bone destruction in homeostasis and makes sure the same amount of protein is being synthesised and broken down, amongst other roles that are discussed in more detail throughout the paper. The almost absence of it can therefore produce severe damage. On the other hand, the amount of radiation astronauts get exposed to increases from when they are on Earth, in the ISS, and outside the magnetic field. The latter is especially dangerous because it can cause the cell's DNA to get damaged and can lead to diseases like cancer.

The systems and organs discussed in the thesis are the vestibular system, the bones and muscles, the immune system, the cardiovascular system and the sleep/wake cycle and circadian rhythm.

The objective ultimately is to determine the viability of surviving a long spaceflight, specifically a six-year journey, to study the impact that space research has had on terrestrial medicine and to test whether some devices could be used to treat and prevent diseases on astronauts.

The research on the effects that space has on the human body shows that a long spaceflight (six years) would be life-threatening due to mainly the high radiation exposure. This paper also shows that there has been an impact on terrestrial medicine made by space research. Finally, the practical framework of the thesis has confirmed that some devices can help prevent some disease symptoms on astronauts.

Keywords:

Microgravity: A condition, such as a free fall or orbital motion, in which acceleration of an object causes it to appear weightless even in the presence of a strong gravitational force. [2]

Radiation: Energy in the form of electromagnetic waves or streams of particles, such as photons or electrons. Radiation is given off by nuclear reactions (as in fission) and by radioactive decay. [3]

Vestibular system: The sensory mechanism in the inner ear that detects movement of the head and helps to control balance. [4]

Bones: The dense, semirigid, porous, calcified connective tissue forming the major portion of the skeleton of most vertebrates. It consists of a dense organic matrix and an inorganic, mineral component. [5]

Muscles: A tissue composed of fibres capable of contracting to affect bodily movement. [6]

Immune system: The integrated body system of organs, tissues, cells, and cell products such as antibodies that differentiates self from nonself and neutralises potentially pathogenic organisms, agents, or substances, consisting in vertebrates of the adaptive and the innate immune systems. [7]

Cardiovascular system: The anatomical system consisting of the heart and blood vessels. [8]

Sleep/wake cycle - circadian rhythm: A daily rhythmic activity cycle, based on 24-hour intervals, that is exhibited by many organisms. [9]

ABSTRACT EN CATALÀ

En aquesta tesi s'avaluen els possibles riscos i danys que han patit i poden patir diferents sistemes i òrgans. La microgravetat i la radiació són els principals factors que fan que els viatges espacials siguin molt perillosos per al cos humà. La gravetat guia el sistema vestibular, manté la formació i destrucció òssia en l'homeòstasi i s'assegura que se sintetitza i descompon la mateixa quantitat de proteïna, entre altres funcions que es discuteixen amb més detall al llarg del document. Per tant, la seva gairebé absència pot produir danys greus. D'altra banda, la quantitat de radiació que els astronautes s'exposen augmenta d'ençà que es troben a la Terra, a l'ISS i fora del camp magnètic. Aquest últim és especialment perillós perquè pot danyar l'ADN de la cèl·lula i provocar malalties com el càncer.

Els sistemes i òrgans tractats a la tesi són el sistema vestibular, els ossos i els músculs, el sistema immunitari, el sistema cardiovascular i el cicle son / vigília i el ritme circadiari.

L'objectiu és, en definitiva, determinar la viabilitat de sobreviure a un llarg vol espacial, concretament a un viatge de sis anys, per estudiar l'impacte que la investigació espacial ha tingut sobre la medicina terrestre i descobrir si alguns dispositius es poden utilitzar per tractar i prevenir malalties en els astronautes.

La investigació sobre els efectes que té l'espai en el cos humà mostra que un vol espacial llarg (sis anys) posaria en perill la nostra vida a causa principalment de l'alta exposició a la radiació. Aquest treball de recerca també demostra que hi ha hagut un impacte en la medicina terrestre produït per la investigació espacial. Finalment, el marc pràctic de la tesi ha confirmat que alguns dispositius poden ajudar a prevenir alguns símptomes de malalties en els astronautes.

Paraules clau:

Microgravetat: una condició, com una caiguda lliure o un moviment orbital, en què l'acceleració d'un objecte fa que aparegui ingràvida fins i tot en presència d'una forta força gravitatòria.

Radiació: energia en forma d'ones electromagnètiques o corrents de partícules, com ara fotons o electrons. La radiació es desprèn de reaccions nuclears (com en la fissió) i de la desintegració radioactiva.

Sistema vestibular: el mecanisme sensorial de l'oïda interna que detecta el moviment del cap i ajuda a controlar l'equilibri.

Ossos: El teixit connectiu dens, semirígid, porós i calcificat que forma la porció principal de l'esquelet de la majoria dels vertebrats. Consisteix en una matriu orgànica densa i un component mineral inorgànic.

Músculs: teixit compost de fibres capaces de contraure's per a efectuar el moviment corporal.

Sistema immunitari: el sistema corporal integrat d'òrgans, teixits, cèl·lules i productes cel·lulars, com ara anticossos que es diferencia d'un mateix i neutralitza organismes, agents o substàncies potencialment patògens, que consisteixen en vertebrats del sistema immunitari adaptatiu i innat.

Sistema cardiovascular: sistema anatòmic format pel cor i els vasos sanguinis.

Cicle de son / vigília-- ritme circadiari: cicle d'activitat rítmica diària, basat en intervals de 24 hores, que exhibeixen molts organismes.

INDEX

I. INTRODUCTION

A. Motivation

Since the author was very young she has been fascinated by everything related to space, from black holes to gas nebulae, and also everything that happens inside humans; how is it that blood is capable of transporting nutrients to all the cells of the body, how is it possible that we are capable of secreting hormones and enzymes that break down and synthesise complex compounds,..... Considering that the author is interested in both topics but knows so little about them, she has decided to merge them and create this thesis: the human body in space. In it, the author talks about the effects that microgravity and space radiation have on the body, whether doing scientific research in space is beneficial to medicine used on Earth and if there is any device that can make living in space much easier.

B. Objectives

The author's objectives to write this thesis are the following:

- To discover and consolidate the author's knowledge of human anatomy and the requirements to be able to live in space, an unknown environment that includes microgravity and radiation, amongst others, and is very dangerous to the human being.
- To predict how the human body will react to a long journey through space.
- To determine whether experiments performed in space can somehow be of use to cure or treat illnesses on Earth.
- To investigate the devices that have been created to help with the astronauts' recovery once they return from space or even help them from needing such.
- To conduct an experiment that will prove one of the author's hypotheses.

C. Hypotheses

The hypotheses that the author has written in the following paragraph are the summed up objectives that have been specified to make her research less ambiguous. These are the following:

- Maybe the effects of spaceflight on the body are too harmful to allow survival on a long term basis.
- Maybe the research that scientists are doing in space has had an impact on terrestrial medicine.
- Maybe some devices can help treat or prevent possible illnesses in astronauts.

D. Methodology

The author wanted to carry out the thesis from a truly scientific point of view, that is to say, she did not want to do it just because it had to be done, but because she wanted to find out what, how and why these things happen to our bodies when we come into contact with another kind of reality.

To start with, the author did a general search about the topic to figure out how to divide and structure the thesis. Later on, she started a more detailed research of each of the points that she had chosen to write about. In addition, she gathered information from different sources, such as online journals, public theses and space-related books. Moreover, the author contacted professionals to ask advice about how to conduct an experiment that helped her prove one of her hypotheses. As a result, she ended up collaborating with Dr David Green, who is an Academic Co-ordinator at the European Space Agency and a professor at King's College London. Once the author had finished the experimental framework, she analysed the results, discussed them and elaborated a conclusion. Finally, she wrote three conclusions that demonstrated her hypotheses.

II. THEORETICAL FRAMEWORK

A. Introduction

Space is so unbelievably big that we, humans, can't even begin to understand the dangers and risks that it comprises. A journey through space will make you taller, weaker and look older. Join the author on this journey through space and discover whether it’s possible to survive in the great unknown that surrounds us.

1. Life’s must-haves

Life as we know it can only thrive under specific conditions; these are what make Earth such a unique place.

Our planet’s atmosphere is made up of vital particles and gases such as nitrogen, oxygen and carbon dioxide which allow crucial biochemical reactions to take place. For instance, oxygen is used by most organisms to carry out respiration; nitrogen (N_2) is converted into ammonia (NH_3) by bacteria and lightning and then used to create nucleotides and amino acids; and carbon dioxide is used by plants, algae and cyanobacteria for photosynthesis.

The atmosphere also presents a small but crucial amount of gases, such as ozone which absorbs harmful radiation. If organisms were exposed to high doses of radiation it would be toxic and even fatal.

Due to the friction that the atmospheric gases generate when in contact with a meteor, they burn up before reaching the Earth’s surface.

In conclusion, the atmosphere is in charge of providing essential gases; protecting us from cancerous rays, and destroying massive meteors before they reach us. Therefore, it is safe to say that the living being's survival mostly depends on our planet’s atmosphere.

Gravity is likewise related to the survival and proper development of living organisms. Our bones and muscles grow and develop following gravity's queues; the heart is designed to pump blood that can fight the force of gravity, and our senses depend on it to detect stimuli. Many other systems are regulated and operated according to the Earth-characteristic gravitational force (1G) and if it were to change, either reduce or increase, everything stated would suffer one way or another. Microgravity won't be fatal on a short-term basis but it can severely damage our body over a longer period.

Overall, Earth's atmosphere and gravitational force are one of the main, if not the most, influential factors in our lives; without them, we wouldn't be standing here.

But, humans, as curious but wreckless animals, decided to jump into the surrounding pitch blackness, the universe that they knew so little about, to find out what would happen to them if the variables were removed. Fortunately, the astronauts who had put their lives at risk for the greater scientific good were unharmed. Thanks to all the research they had done, planets, stars, and other celestial bodies were and are still being discovered. But how can scientists take further steps in the world of space research if the limitations of doing so are so extensive? The answer is within its question. Research. The only way of finding out new things about space is by first figuring out how to put scientists into space safely. What are the effects of spaceflight on the human body and how can they be prevented? This is the question that the author will try to answer through the thesis. One thing's for sure; space is not a danger-free zone.

2. Problems faced during spaceflight

Before the author jumps into the specific known effects that space has on the body, the author should find out what are the causes, or in other words, what is the root of the problem. One of the main concerns about travelling in space is, as the author has already stated, gravity.

a) Gravity

Gravity is an attractive force, not as in handsomeness, but as a force that pulls objects with mass closer together. Gravity has existed since the beginnings of time, maybe even before. Without gravity, the big, bang would have never happened, and consequently, none of us would exist. Gravity is responsible for amazing phenomena: from collapsing molecular clouds to giant supernovas.

During spaceflight, astronauts experience a multitude of gravitational forces. The Earth has one gravitational force (1 G); but during the launch, the forces may vary from 1 to 3 g. But, what does this mean? It means that during spaceflight, the human body undergoes a huge amount of stimuli and stress that affect the body in different ways. The repercussions can vary from changes in vision, balance, and orientation, to loss of bone density to even an increase in intracranial pressure.

b) Radiation

The other protagonist of the movie is space radiation. It's not as popular as gravity but still has an important role in making our journey to space even more difficult than it is. Radiation can be defined as energy in transit in the form of high-speed particles and electromagnetic waves. Electromagnetic radiation is very common in our daily lives in the form of visible light, radio and television waves, and microwaves. Radiation is divided into two categories: ionising radiation and non-ionising radiation.

Ionising radiation is radiation with sufficient energy to remove electrons from the orbits of atoms, giving rise to charged particles, and it is this type of radiation that is evaluated for radiation protection purposes. Examples of ionising radiation include gamma rays, alpha and beta particles.

Non-ionising radiation, on the other hand, is radiation without sufficient energy to remove electrons from their orbits. Some examples are microwaves, radio waves, and visible light.

Space radiation consists mainly of ionising radiation that exists in the form of high-energy charged particles. There are three natural sources of space radiation: trapped radiation, galactic cosmic radiation and protects

On Earth, the magnetic field protects against most space radiation, but once out of our planet's orbit, radiation is free to penetrate our skin. Even though space stations are equipped with protective measures, they aren't enough to ensure total safety from radiation, putting the astronauts at risk for degenerative diseases, cancer, and changes in the central nervous system.

c) Mental health issues

Space travel also affects the mind in many different ways. In the late-1950's, scientists working in the National Aeronautics and Space Administration weren't sure how space would affect the human mind. They believed that once outside Earth's gravity, they would become impulsive, suicidal, and sexually aberrant thrill-seekers; that's why they decided to call it space madness (Hersch, 2012) [10]. Fortunately, these scientists were proven wrong. They overestimated the effects of weightlessness amongst others, on the human body, but they didn't get it completely wrong. Some astronauts have had to deal with mental health issues when orbiting the space station.

Isolation, another problem of spaceflight may not seem very important when compared to microgravity and radiation, but that isn't entirely true. Confinement can have a big impact on our mental health and subsequently on our physical health. Just as we get homesick when we travel to a foreign country, astronauts can get *planetsick* when staying in space for long periods.

Astronauts go through psychiatric tests to make sure they are mentally suited for a mission like this. For instance, they are tested to see if they can handle the pressure of knowing that a mistake could put their crewmates' lives and theirs at risk. Consequently, isolation can cause a lot of stress and strain on their body.

They train and train to make sure they know what to do in every single situation. Chris Haldfiled, a former NASA astronaut explained in a TED talk how astronauts are trained to keep calm in very stressful situations. He described what his thoughts were when he suddenly went blind during a spacewalk. He managed to overcome the situation by following an old saying astronauts used to say: "there is no problem so bad that you can't make it worse"[11] (TED, 2014).

d) Food supply

Supplies are a major aspect to consider when travelling to space. The amount of effort, money and time needed to launch a rocket to space is so enormous that all supplies need to be thought of much before the launch.

Food starts to get prepared a month before astronauts leave for space. It goes through a meticulous process of selection, packaging and evaluation and is stored in refrigerators. There are very specific guidelines as to what foods can go and how they are prepared to go to space. They need to be compact, easy to prepare and nutritious.

How can they make sure that food doesn't go off while in space? Well, space scientists had the same question. Eventually, they managed to develop several methods that helped preserve food. They learned how to avoid bacteria and other organisms from growing on food by heat processing it and exposing it to radiation. They also discovered that water could be removed from specific foods, like pasta, and then once up in space, be rehydrated.

Image 2. Astronauts eating onboard the International Space Station. Seated at the table, clockwise from bottom left, are Frank De Winne, Christopher Cassidy, Mike Barratt, Tim Kopra, Robert Thirsk and Mark Polansky. From left to right at top are Koichi Wakata, Roman Romanenko and Gennady Padalka [12].

Space food isn't delicatessen food, but anyone on Earth would happily trade spots with an astronaut to have dinner among the stars.

B. Effects of spaceflight on different systems and organs of the body

Astronauts may seem like fictional characters who fly and snap their fingers so it's easy to forget that they are actual human beings who sometimes get ill. You might wonder what astronauts have to do when they get sick.

Before going into space, astronauts are the healthiest people on the planet. The Space Associations can't risk sending someone to space who then needs to come back because of health issues. That's why, a few weeks before the launch, astronauts go into quarantine to make sure they don't carry any virus into the space station.

So far, there haven't been any medical emergencies onboard the space station, but what if there were? That's a very important topic that scientists need to think of before sending their astronauts into space. As long as only a few go to space, the possibilities of getting sick are not great, but if our long-term plan is to send more and more people, scientists are going to need to find alternative solutions.

1. Vestibular system

As stated earlier in the paper, gravity produces a vast range of effects on the human body. The first thing astronauts experience when abandoning Earth's soil and arriving at the ISS is the confusion their senses have because of all the gravitational forces or the absence of them that they have and are experiencing. During the launch, they undergo the effects of several gravitational forces, from 1G (Earth's gravity) up to 3G, and then once in the ISS, they experience the effect of weightlessness. Weightlessness is not caused by the lack of gravity but because they are orbiting Earth in a state of constant free fall. Due to this, up to 70 % of astronauts have suffered from stomach discomfort, nausea, vomiting, fatigue, and other symptoms which they refer to as space motion sickness. There are multiple hypotheses as to why this occurs but the two main ones are explained by sensorial conflict and fluid shift theories. It is widely accepted that space motion sickness (SMS) has a connection with how the brain interprets the stimuli received from the senses. The ‘’why’ and the ‘’how’’ this happens is the part where scientists start to disagree.

The ear is divided into three parts which are the outer ear, middle ear, and inner ear. The way our body perceives balance and orientation is through our vestibular system which is located in the inner ear. Our vestibular system is in charge of providing information to our brain about motion, head position and spatial orientation. It also is involved with motor functions that allow us to keep our balance, stabilise our head and body during movement, and maintain posture [13].

The vestibular system is divided into two main parts: the central system (brain and brainstem) and the peripheral system (the inner ear and the pathways to the brainstem). The peripheral system organs are in charge of detecting head motion and position in space related to gravity [14]. The inner ear is made up of the cochlea, the semicircular canals and the vestibule. The cochlea is in charge of converting the sound waves into nerve signals and the semicircular canals and vestibule are responsible for the sense of balance and posture. The semicircular canals are filled with a liquid called endolymph and lined with hair cells that detect stimuli in the form of movement [15]. These sensors carry the sensory impulses to the main primary processing centres in the brainstem and cerebellum. These areas in return, send inputs to coordinate other reflexes such as the vestibuloocular reflexes, an ocular movement responsible for stabilising the gaze during head movements, and vestibulospinal reflexes, head and neck movement responsible for maintaining the head in an upright position. [16]

The stimuli are interpreted and put together along with the other sensory impulses received. Thanks to the combination of all impulses the brain understands and predicts what you are and will be doing immediately.

a) Sensory conflict

The brain is used to interpreting the signals from the eyes and ears in a certain way (e. g. the brain knows when we’re upside down thanks to these messages). In a weightless environment, the body no longer knows what's up and what's down so the signals it sends do not match with what the astronaut is seeing [17]. This is commonly referred to as sensorial conflict and it can lead to nausea, dizziness, tiredness and fatigue. Fortunately, astronauts recover quite quickly and are able to continue with their onboard duties.

To conclude, the sensory conflict theory supports that the inputs provided by different sensors (eyes, skin, joints, muscles and the vestibular receptors) do not coincide, therefore the brain's assessment and interpretation of reality gets altered and disrupted [18].

b) Headward fluid shift

Gravity also plays a big role in how our fluids are distributed around the body. Fluids and blood tend to accumulate in the lower half of our body because of it. When exposed to microgravity the blood and fluids no longer have a force pushing down on them so they get displaced into the upper part of the body. Likewise, it produces movements of the liquid in the vestibular system, subsequently altering receptors' responses in the inner ear. The swelling of the endolymphatic duct may restrict the flow of the endolymph sac, resulting in hydrops, a syndrome that affects the inner ear resulting from the abnormal quantity, composition or pressure of the endolymph in the endolymphatic sac [19].

Based on the author's research, she can conclude that both theories don't cancel each other out but instead complement each other. It may be that the combination of both, sensory conflict and headward fluid shift, causes space motion sickness.

Space motion sickness is not a long term severe medical condition, but rather a short term one that can make astronauts unable to perform necessary procedures. Therefore, astronauts must train their senses before going into space.

2. Musculoskeletal System

Constantly pushing our muscles and bones, gravity acts like our own personal trainer. We may not realise this, but every time we take a step we are making our muscles and bones work.

a) Muscles

Our so-called antigravity muscles are those which support our body and fight against gravity. In a microgravity environment, these muscles no longer have to support the body's weight, in other words, the muscles get lazy. Consequently, the lack of use provokes a loss of muscle mass. But why does this exactly happen and how severe can it actually be?

Replacement of skeletal muscle proteins is regulated by a complex process involving biochemical and mechanical signals. Skeletal muscle size and composition is maintained through balanced protein synthesis and breakdown. Any disruptions to this process may result in a gain or loss of size and muscle strength. Space induced muscle loss occurs because of biochemical alterations in metabolism and the myofibrillar protein (contractile protein) content. According to NASA, astronauts can lose up to 20 % of their muscle mass in spaceflight lasting from 5 to 11 days if they don't do any kind of exercise. [20] (What happens to muscles in space? 2006)

Studies have shown that long term bed-rest has similar effects to prolonged exposure to weightlessness. Therefore, potential muscle loss studies have been conducted in patients on bed rest. The following study, *''Proteomic investigation of human skeletal muscle before and after 70 days of head-down bed rest with or without exercise and testosterone countermeasures''* [21], used exercise and testosterone as means to prevent muscle loss in patients on bed-rest. The studies showed that exercise stimulated structural protein synthesis while testosterone reduced the breakdown of complex molecules and induced overall muscle growth.

Although exercise and testosterone have been proven to be effective countermeasures, they don't fully prevent muscle loss. Due to this, muscle loss is one of the main concerns about performing long-duration spaceflights. Astronauts must be able to perform laborious procedures, but because of the effects of microgravity in the skeletal muscles, their overall performance is severely compromised.

So far the author has talked about how muscle loss affects the astronauts' capability of performing strenuous activities, such as emergency landings or extravehicular activities, but what about when astronauts have to return to Earth: Do their muscles readapt to Earth's gravity? According to NASA, the muscle will eventually go back to its pre-flight stage within a month of re-entering Earth, even though complete recovery of muscle mass may take longer [22].

b) Bones

Bones go through processes of bone formation and destruction, just like muscles do. Consequently, bones are not fixed calcium structures, instead, they are constantly reshaping [23]. The amount of bone created or broken-down is regulated by metabolic changes alongside other factors such as hormones, daily activities and diet [24]. Bone loss happens when the formation of new bone cells is not enough to compensate for the destruction of such. This condition is called osteoporosis and affects not only astronauts but millions of people across the globe. Due to multiple countermeasures such as exercise, astronauts don't suffer from osteoporosis but instead suffer from osteoporosis-like symptoms [25].

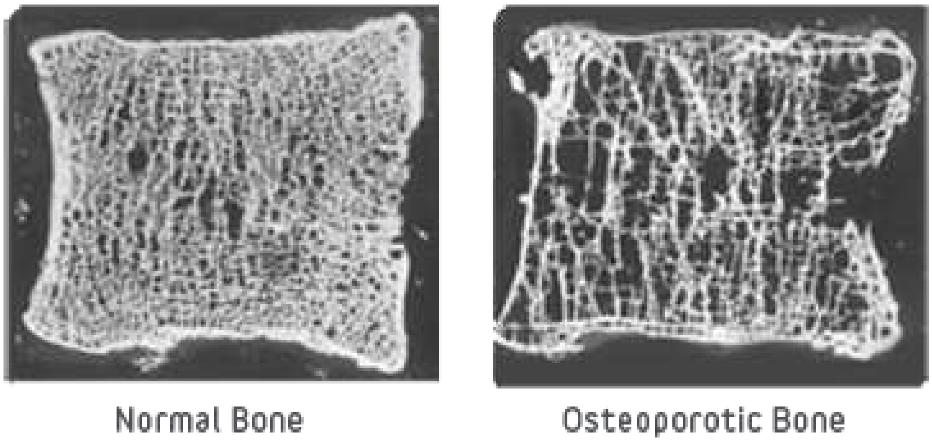

Image 3. Two slides comparing the vertebrae of a healthy 37 year old male with a 75 year old female suffering from osteoporosis. The osteoporotic bone presents bigger pores which makes it weaker and more susceptible to fractures [26].

The process of replacing mature bone tissue with new tissue is called bone remodelling and it is divided into bone resorption, the destruction of bone cells, and ossification, the formation of bone cells.

Bone resorption is carried out by osteoclasts, a type of bone cell, which other than breaking down bone tissue they release bone minerals, subsequently transferring calcium into the blood. Apart from destroying bone tissue so that it can be replaced, bone resorption is also stimulated or regulated by the demand for calcium around the body. If the demand is very high, too much calcium is transferred into the blood and it can produce damage and conditions such as kidney stones.

Bone formation, on the other hand, is carried out by osteoblasts, bone-forming cells. Bone formation is directly proportional to the stress it has been under, in other words, how much the bones have been used. Areas of the body in which bones are subjected to higher stress present a denser bone mass. When exposed to weightlessness, the loading stimuli received is almost none, therefore, osteoblasts' formations are slowed down, resulting in bone loss [27].

Despite a strict exercise regime, astronauts lose up to 1 % of their bone mass per month. On Earth, an elderly person loses the same amount of bone in a single year [28]. Just so you can get an idea about how much bone is lost, imagine the following: a middle-aged healthy astronaut who weighs 70 kilos. Out of the 70 kilos, 10 kilos are bone mass (14 % of a man's body is bone). If each month an astronaut loses around 1 % of his bone mass, after 10 months of prolonged spaceflight, the astronaut would have lost almost a kilo of bone.

Bone loss can be worrying because of the great range of repercussions it has. The most obvious effect is the weakening of them which results in a higher risk of fracturing and breaking bones. If this were to happen, astronauts would not be able to go through demanding activities (e.g. spacewalks), and missions and studies would be compromised.

Besides this known effect, there is also hypercalcemia. As stated earlier on, calcium is released into the blood when bones are broken down by osteoclasts. If too much bone is being destroyed, the amount of calcium being released into the bloodstream may surpass the limit. This can lead to hypercalcemia, which can cause kidney stones, kidney failure and abnormal heart rhythms.

Even though many measures are applied to prevent bone mass loss, such as antiresorptive[1] drugs and exercise, the loss is still significant and worrying. This proves that bone loss is one of the most, if not the most, challenging aspects of travelling to space.

[1]Antiresorptive: An agent that prevents or slows the progress of osteoporosis by blocking or opposing the destruction of bone by osteoclasts [95].

3. <u>Immune system</u>

The immune system is responsible for protecting the body against harmful proteins, viruses, bacteria, fungi, parasites and other pathogens. Depending on the pathogen, the immune system's reaction varies. The two primary parts of the immune system are the bone marrow and the thymus, which are responsible for the formation of immune cells.

Humans are born with innate immunity, which is in charge of preventing the spread of pathogens around the body. It provides physical barriers, such as the skin, chemical barriers (e.g. secretions), and cellular defences, such as inflammation. The innate immune system offers immediate general protection against pathogens and is activated through detecting antigens and their chemical proteins. Phagocytes are the main innate immune system cells and are constantly circulating in the bloodstream searching for pathogens to destroy. It is important not to confuse antigens with pathogens. Antigens are components of the pathogen's membrane which antibodies use to identify pathogens.

Adaptive immunity, on the other hand, is a type of specific immune response. This type of immunity is characterised by the ability to detect certain antigens and respond accordingly to them. Adaptive immunity cells are also capable of remembering specific antigens and consequently, generating a measured immunological response through T cells and B cells [29]. Adaptive immunity has two different types of immunity within itself: humoral immunity and cellular mediated immunity.

Humoral immunity is mediated by B cells which produce antibodies to fight off toxins and free pathogens (pathogens that have not been absorbed by a phagocyte) in body fluids. Antibodies neutralise pathogens outside the cell. On the other side, cellular mediated immunity does not produce antibodies, instead, it generates T cells which neutralise infected cells.

Although the immune system may seem like a powerful army which is undefeatable, that is not the way it is. Aspects of the immune system can be weakened, leading to infections or others might be overactive, resulting in autoimmune diseases. In a weightless environment, both of these disruptions occur.

The thymus gland, where most of the T cells are formed, can be easily altered by physiological and psychological stressors, hence the atrophy it undergoes when in microgravity. Some of the gland's functions might be disrupted because of it. Results of a study (Benjamin, C.L. et al. 2016) [30] suggested that T cell counts had decreased post-flight, implying the deterioration of the thymus gland.

On spaceflights, pathogenic microorganisms replace large parts of the gut flora due to the effects of space motion sickness on their body. According to a study on the gut's microbiome, food intake is a key factor to the well being of the gut microbiome. Because of space motion sickness, astronauts may not reach their required nutritional needs, resulting in a profound impact on the gastrointestinal tract [31]. Someone might wonder what does the gut microbiome have to do with the immune system, well, they work together in fighting diseases and keeping the different systems balanced (homeostasis). The microbiome plays an important role in the formation of innate and adaptive immune cells, and in return, the immune system regulates the symbiotic relationship between the gut flora and our intestines [32]. Dysbiosis[2] (microbial imbalance) of the gut flora can lead to chronic diseases such as inflammatory bowel disease, obesity and cancer. [33].

Stress on the human body can lead to the reactivation of latent herpes viruses. Herpes viruses, for those who might not know, are a family of double Deoxyribonucleic Acid (DNA) strand viruses that are characterised for being latent and recurring. Astronauts' saliva and urine samples indicated the recurrence of some herpes viruses when onboard the Space Station. These viruses are generally not life-threatening, but in a hostile environment, like space, any sort of virus can weaken the already fragile immune system and set off a chain reaction that could compromise the health of the astronauts [34].

[2] Dysbiosis: An unhealthy change in the normal bacterial ecology of a part of the body, e.g., of the intestines or the oral cavity [96].

4. <u>Cardiovascular system</u>

The cardiovascular system is highly dependent on the pressure gravity produces. Our cardiovascular system has evolved to develop specific reflexes and mechanisms to compensate for the tendency that blood has to accumulate in the lower extremities.

a) Blood pressure and blood cells

Our body has got several mechanisms that regulate blood pressure in required situations. These mechanisms are activated thanks to sensors that detect mechanical pressure or distortion. These sensory cells are called baroreceptors and are located in the carotid sinus.

As mentioned at the beginning of the paper, headward fluid shifts cause fluids, including blood, to distribute evenly throughout the body. This shift in blood distribution causes face oedema(swelling) and volume loss on the lower extremities. Even though these modifications are pronounced, they don't pose a major risk to astronaut's health.

Plasma, the liquid part of blood, faces a 20 % [35] loss of its volume. Subsequently, the brain detects an excess of red blood cells per volume of blood. Thus, the brain sends signals to get rid of some of it. In these situations, kidneys stop the secretion of erythropoietin, a type of protein that stimulates the production of erythroid cells (red blood cells). When the release of these proteins stops, the bone marrow ceases the production of pre red blood cells and stimulates neocytolysis, a process in charge of destroying the excess of erythrocytes.

The reduction of red blood cells causes a decrease in the oxygen that other cells of the body receive. This condition is denominated anaemia and affects not only astronauts but also millions of people around the world. Anaemia's symptoms include fatigue, shortness of breath, chest pain and lightheadedness [36]. It is important to note that astronauts suffer from anaemia temporarily. This is because their plasma volume and red blood cell concentration restore to preflight levels when astronauts return to Earth [37]. Also, a recent study (Kunz, H., *et al*, 2017) [38] seems to indicate that anaemia may not be a concern on long-term spaceflight, because the results showed an increase in red blood cells on long-duration spaceflights. According to NASA [39], the early reductions of red blood cells that have been reported in other studies are just temporary adaptations to microgravity and that spending more time in space might partially compensate for the reductions in red blood cells.

b) Heart

The heart, likewise, gets affected by the decrease in blood pressure. Just as any other muscle, the heart atrophies when it isn't being used. So it is correct to assume that unless astronauts' hearts stopped beating, there wouldn't be any damage done to the heart. The thing is, the amount of blood the heart has to pump is inferior to what it normally does, leading up to significant damage due to its lack of use. In essence, the heart loses part of its tissue and, consequently, shrinks.

As a result of the heart's atrophy, astronauts can develop a series of symptoms which are commonly referred to as orthostatic intolerance. The symptoms include, amongst others, nausea, fatigue and presyncope[3]. These appear when standing up from a lying or sitting down position. Standing upright demands compensatory responses to maintain blood pressure, cerebral blood flow and consciousness. If the cardiovascular and neurological systems fail to generate a compensatory response, astronauts can develop this syndrome.

Around 25 % of astronauts who have been on short-term spaceflights have reported symptoms and 80 % of the astronauts of those who have returned after long journeys have also experienced orthostatic intolerance. Orthostatic intolerance is a challenging condition, not just because of the impairments it causes on the astronaut's day to day lives but when having to perform emergency procedures. Astronauts become unable to pilot the vehicles or stand upright when they have landed on Earth. Astronauts who go on long-duration spaceflight have a higher risk of developing this condition.

[3] Presyncope: An episode of near-fainting which may include lightheadedness, dizziness, severe weakness, blurred vision, which may precede a syncopal episode [97].

5. <u>Sleep/wake cycle and circadian rhythm</u>

Not long ago, sleep was thought to just be the brain's way of shutting down and resting. Nowadays, scientists have realised that there's much more to it and that it has a crucial impact on the body's wellbeing. In the past few decades, sleep has been researched thoroughly to understand more about how it works.

Sleep is regulated by internal factors and is influenced by external factors like light, noise… Living beings count on two processes to regulate their sleep cycles. These are called sleep/wake homeostasis and circadian biological clock. Homeostasis is defined as the compensating mechanisms which try to keep the substances in our body balanced. In this case, keep the sleep and wake hormones balanced out. On the other hand, the circadian biological clock is in charge of determining what substances are needed the most throughout the day and subsequently, changing the levels.

The sleep cycle begins with the optic nerves sensing the morning light. Then, it sends these signals to a specific area of the brain called the suprachiasmatic nucleus (SCN). The SCN, which is located in the hypothalamus [4], then sets off the release of cortisol and other hormones to wake you up and inhibits the pineal gland's[5] melatonin (sleep hormone) secretion. Once you're awake, the nerve cells in your brainstem release neurotransmitters, which their role is to keep the brain alert and functioning properly. Night comes and the optic nerves send signals to the pineal gland, which triggers the release of melatonin. Along with melatonin, other hormones contribute to the sleep-inducing process. Amongst them, there's adenosine, a hormone in charge of blocking the neurotransmitters that tell you to stay awake [40][41].

On the international space station, astronauts see about 16 sunsets a day, meaning their day is 90 minutes long. Consequently, their internal clock gets disrupted. This can lead to several sleep disorders which can cause increased sensitivity to stress, emotional distress and memory and performance deficits. In the long-term, sleep deprivation can lead to

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[4] Hypothalamus: A structure within the brain responsible for a large number of normal functions throughout the body, including regulating sleep, temperature, eating, and sexual development. [98].

[5] Pineal gland: A small, cone-shaped organ in the brain of most vertebrates that secretes the hormone melatonin [99].

hypertension, cardiovascular diseases, dyslipidemia [6], metabolic syndromes, diabetes and colorectal cancer.

6. Radiation effects

In the paper's introduction, the author briefly pointed out what radiation was and why it is dangerous for us. Now she will go into further detail to find out what happens to our body on a molecular level when exposed to radiation.

According to the United States Nuclear Regulatory Commission [42] radiation is energy given off by matter in the form of rays or high-speed particles. All matter is made up of atoms that have got a positively charged nucleus, containing protons and neutrons and a negatively charged shell that contains electrons. Both these forces work together towards balance by getting rid of excess atomic energy. In this process, unstable nuclei can emit spontaneous energy emissions which are called radiation.

Depending on the effects and properties, radiation can be divided into ionising and non-ionising radiation. Ionising is highly energetic and consists of electromagnetic waves that are powerful enough to remove electrons from their atoms. Meanwhile, non-ionising radiation does not have enough energy to break down particles when passing through matter.

Space radiation is made up of particles trapped in the Earth's magnetic field [7], solar energetic particles and galactic cosmic rays.

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[6] Dyslipidemia: Abnormality in, or abnormal amounts of, lipids and lipoproteins in the blood [100].

[7] Earth's magnetic field: Earth's magnetic field is a magnetic field that emanates from Earth's core and encircles the Earth. It can be looked at as sort of a force field that encompasses the Earth and protects our planet from solar radiation [101].

Trapped radiation occurs when charged particles coming from the sun are trapped by the Earth's magnetic field. If astronauts were to leave the magnetic field, this type of radiation wouldn't be a problem to them [43].

Solar energetic particles are charged particles that have been accelerated during a solar particle event (solar flare or coronal mass ejection) [44].

Finally, galactic cosmic rays are high-energy charged particles that come from outside the solar system. Even though their rate of flow is very low, they travel at almost the speed of light which causes intense ionisation of matter when it passes through it [45]. This type of space radiation is the hardest to shield against.

Solar energetic particles galactic cosmic rays are the type of space radiation that scientists are trying to shield us from.

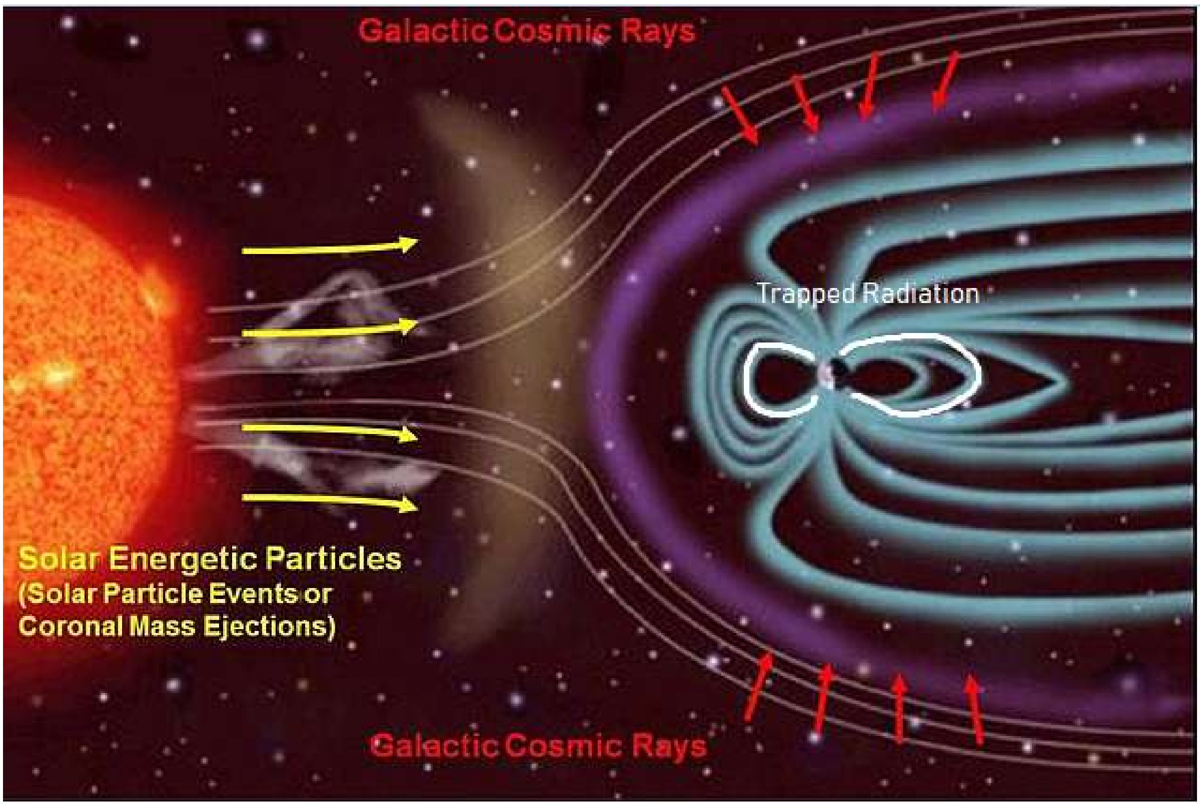


Image 4. Representation of the three types of space radiation. Solar energetic particles come from the sun. Galactic cosmic rays originate outside the solar system. Trapped radiation is particles that are trapped in the Van Allen belts [46].

The magnetosphere is the area surrounding the globe which is in charge of protecting the planet from galactic cosmic rays, solar energetic particles and shielding the atmosphere from the solar wind, a stream of charged particles released by the sun's atmosphere. The atmosphere's job then is to shield us from the remaining space radiation that has managed to go through the magnetic field.

The ISS orbits in the thermosphere, an atmosphere's layer, which indicates that astronauts are still relatively protected from space radiation, but it can not be forgotten that the further away they are from the Earth's surface the more exposed to radiation they are. Consequently, we can not assume that the doses which the astronauts are receiving daily are the same as the ones they would receive on a journey through space [47].

Non-ionising radiation may not seem dangerous because it can not break down atoms when passing through them. Although this is true, some types of non-ionising radiation such as UV radiation can indeed be harmful to the body. UV radiation does not penetrate deep into the body but it can cause damage to the skin and eyes if exposed to it for a long time. The damage done could eventually lead to cancer and the formation of cataracts. Spacecrafts' windows are made up of UV-blocking materials which makes the absence of atmosphere in space, not a problem for preventing damage to the body.

On the other hand, ionising radiation can penetrate the body's tissues. Living cells, which are made of atoms, can therefore suffer from alterations in their chemical composition due to the loss of electrons caused by radiation.

a) Types of radiation effects

There are direct and indirect effects of radiation depending on the molecules they interact with.

(1) Direct effects

Direct effects involve radiation interacting with DNA molecules. They can affect the cells ability to reproduce, and hence survive. DNA is the guide that each cell in our body follows. Think of it as a book full of recipes; each one of them represents a dish to cook, or in other words, a role to play. Every recipe in the book explains how to cook certain food, the same happens with the DNA: it is divided into genes, sections of the genetic information that code for specific proteins. Proteins have lots of different jobs; transporting substances through the bloodstream, protecting the body from harmful pathogens and producing enzymes, amongst others. Going back to the kitchen metaphor, proteins would be like the chefs, the ones in charge of actually cooking the dishes.

In a process called transcription, a segment of the DNA is copied in the form of a single molecule strand: messenger RNA. Once messenger RNA has been successfully transcripted, it leaves the nucleus to go and find a ribosome. Ribosomes are made up of proteins and another type of RNA, and act as a binding amino acid machine. Once the RNA has arrived, the ribosome starts translation. Through this process, transfer RNA brings amino acids which, following the RNA's messenger information, the ribosome puts together in the correct sequence. To sum everything up, the genetic information that the DNA contains is the key factor in protein synthesis.

When DNA molecules are exposed to ionising radiation, their double helix strands can be ruptured or can suffer losses or modifications in their nitrogenate bases. In several cases, the damage can be fixed by repairing mechanisms. However, there are times when it can not be reversed. If the cell has already started to replicate before the repairing mechanisms have found the damage, there is a possibility that a nucleotide is mistaken for another one. In consequence, gene expression can differ, therefore synthesising a different polypeptide chain. It can be the case that the mutation does not affect the proteins' function, nevertheless, if it does happen, the damages can include cellular and tissue anomalies. Radiation can activate and deactivate genes, which in some cases can lead to the activation of cancer genes.

There are four different outcomes of direct effects of radiation on cells. The first one is that the cell repairs the damage, the second one is that the cell dies, the third is that the descendant from the damaged cell dies and last is that there is no repair or non-identical repair before reproduction of the damaged cell. Out of these, only one manages to survive and replicate successfully. This is a clear indication of how dangerous radiation is.

So far the author has gone over the consequences of radiation in DNA molecules, but what about the effects on other biomolecules? Considering the fact that most of our body is made up of water, it is worthwhile researching what effects space radiation could have on these molecules.

(2) Indirect effects

Indirect effects are caused by the dissociation of water molecules caused by ionising radiation, commonly referred to as radiolysis of intracellular water, and are very high when exposed to ionising radiation because of the great portion of such in cells. Radiolysis causes water molecules to break down into H^+ and OH^- radicals. These chemicals recombine in highly reactive molecules such as superoxide (HO_2) and peroxide (H_2O_2) that can be toxic and damaging to the cell's molecules [48].

The effects radiation has on the human body is determined by the dose and duration of the exposure and can be classified into acute and chronic effects. Acute effects occur when the human body is exposed to a high quantity of radiation in a short amount of time and the symptoms include nausea, vomiting and fatigue. On the other side, chronic effects happen as a consequence of the accumulation of radiation over an extended period.

Since every cell in our body has DNA and is made up of water, radiation exposure affects a vast range of systems in the body. Numerous cases from people exposed to ionising radiation, due to radiation therapy or survivors of bombings, have led to lung, colorectal, breast, stomach, liver, brain, ovarian, oesophagal and bladder cancers, and several types of leukaemia [49].

b) Effects on the cardiovascular system

The cardiovascular system is affected by the extreme nature of radiation. Heart diseases were and are still being reported in patients undergoing radiation therapy and people who have been exposed to high doses of radiation (i.e bombing in Hiroshima). The effects of exposure include myocardial fibrosis, which is characterised by an increase in collagenous scar tissue in the heart muscle and cardiac conduction and valve abnormalities, which are alterations in the heart's rhythm (arrhythmias) and the closing of the heart valves, respectively. In some cases, symptoms didn't start to show until several decades after the exposure. Effects on blood vessels were also reported such as; accelerated atherosclerosis which is the narrowing and hardening of the arteries that can lead to a blocked blood flow; and also the loss of blood vessels after a high skin dose exposure to radiation. A study performed on a pig's dermis (Kennedy, 2014) [50], suggested that radiation exposure led to the disappearance of the blood vessels beneath the epidermis. Due to this, the skin would not receive enough blood and would have to be removed surgically.

c) Effects in neuronal cells and the central nervous system

(1) Neurogenesis

Neurons are likewise severely affected by space radiation. The process in which nerve cells are generated is called neurogenesis and is highly compromised when exposed to radiation. Not only are neurons affected by irradiating them but also their progenitors, or in other words, the neural precursor cells. Their proliferation and differentiation are compromised because of their high sensitivity to radiation. Investigators from the study "*Hippocampal neurogenesis and PSA-NCAM expression following exposure to 56Fe particles mimics that seen during aging in rats*" [51] stated that the changes were similar to ones seen in ageing studies, therefore suggesting that irradiating neuron cells could model the ageing process [52].

(2) Oxidative damage

A study (Limoli, *et al* 2004) [53] that investigated the effects of ionising radiation on the neural precursor cells indicated that these presented an apoptotic response to radiation exposure. The study was focused on the brain's oxidative damage because the brain has a high oxygen consumption and therefore is more susceptible to it than other organs. The response was followed by an increase in reactive oxygen species which is directly related to oxidative stress.

According to the following study, "*Oxidative Stress: Harms and Benefits for Human Health study"* [54], " oxidative stress is a phenomenon caused by an imbalance between production and accumulation of oxygen reactive species (ROS) in cells and tissues" Reactive-oxygen species are a type of highly reactive unstable molecules that contain oxygen and are the product of aerobic oxygen metabolism and play an important role in cell signalling and maintaining homeostasis [55].

Considering the fact that cells are primarily composed of water, the radiolysis of water is the main contributor to the increase of reactive oxygen species formation [56]. Reactive-oxygen species can lead to cell dysfunction and even cell death due to their interaction with macromolecules (proteins, nucleic acids and proteins). Oxidative stress has been proved to cause neurodegenerative diseases such as Alzheimer disease, Huntington disease, and Parkinson disease, also in neuropsychiatric disorders, including anxiety disorders and depression [57].

(3) Behavioural effects

As stated in the previous paragraphs, the central nervous system is severely impaired when exposed to radiation and because of it, cognitive functions and behavioural patterns are altered. A study (Raber *et al*, 2004)[58] on rats and mice provided insight into the behavioural effects of ionising radiation on the brain. The results indicated that the effects on behaviour depended on the strain, the subject's species and the method used to assess them. For example, two groups of X-irradiated mice who were tested differently showed contradicting results; one group presented spatial learning and memory deficits and the other one did not. Despite these results, the study was still able to reach the conclusion that the mice had suffered from cognitive deficits and behavioural changes. Another study (Joseph *et al*. 1992) [59] (Joseph *et al* 1993) [60] indicated that rats exposed to low-doses of Fe (a type of radiation) experienced neurochemical changes and their sensorimotor system was affected.

From an overall point of view, behavioural changes and cognitive deficits were observed in animal studies. Therefore we can conclude that the effects of ionising radiation on our behaviour will also change.

d) Effects on the skin

Most people would immediately think of skin damage when they are asked about the consequences of radiation exposure. This may be because we can see the repercussions without any medical equipment. When exposed to high doses of radiation the skin can develop lymphedematous, a condition in which the skin is very sensitive to touch, blisters, burns and epithelial dysfunction. The most serious condition from exposure to high doses of irradiation is skin cancer. Skin cancer is caused by the alteration of the skin cell's DNA, that leads to uncontrolled skin cell growth. [61].

e) Effects on the eyes

Another of the many consequences that radiation has on human cells, is the formation of cataracts. Cataracts are defined as cloudy areas of the eye's crystalline lens that make eyesight blurry. The eye's lenses are covered by a layer of epithelial cells. They maintain the lens's function by constantly dividing peripheral or equator cells and then slowly growing towards the centre of the lenses. Because radiation has a bigger impact on those cells which are constantly reproducing, the equator epithelial cells are very prone to radiation damage. Once exposed to radiation, damaged cells travel to the backside of the lens and then concentrate at the centre, causing patches of opacity and cloudiness which block light from travelling forward [62].

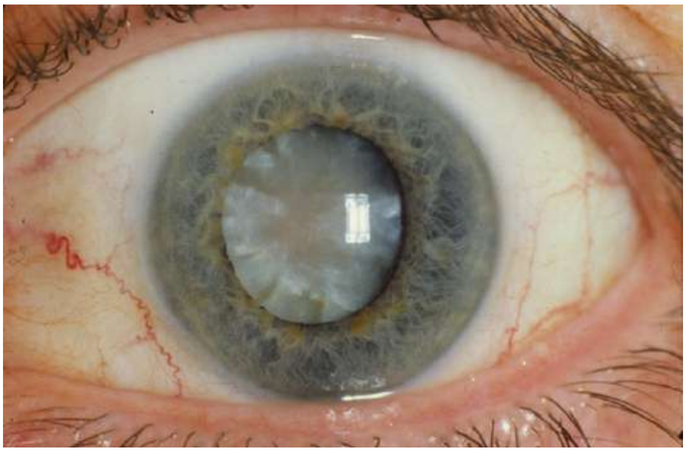


Image 5. Cataract in a human eye [63].

C. Impact of space research on terrestrial medicine

1. Cancer cell cultures

Space has provided an alternative way of researching diseases on a biomolecular level that is not possible in Earth's gravitational force. Researchers have been trying to find a cure for cancer for years. They've come together to conduct studies in different parts of the world, with different subjects and methods. Despite their many efforts, it hasn't been possible to recreate the exact conditions in which cancerous cells grow. Scientists can learn more about tumours if they find out how they reproduce and why, but certain parameters limit these types of research. For instance, Earth's gravitational force does not allow cell cultures created in labs to form three-dimensional structures. The cell's structure is directly related to the way the cell functions, to how it activates genes and to how they interact with other cells. Therefore if their structure is modified or isn't formed as it should, they won't act the same way as they would inside a living organism.

When it comes to studying the behaviour of cancerous cells, the conditions to which they are exposed inside the body must be the same as in *in vitro* cells. Nowadays, researchers commonly use culture techniques called 2D monolayers which consist in transferring cells to a flask to analyse their performance. Once the first step is done, gravity then pulls them down to the bottom of the container. Cancerous cells start dividing in a flattened shape. The change in position causes alterations in their structure and subsequently in the way they act. Because of it, cancerous cell cultures may provide information about their patterns of behaviour which aren't entirely accurate.

The variable that makes these results unreliable is gravity. Once removed from the equation, cells can grow properly in a 3D shape. This is where space comes in.

Investigations were conducted in the early 1970s on the US Skylab Program concerning the changes of cells when exposed to microgravity. Weightlessness allowed the cells to form 3D structures that were accurate biological representations of *in vivo* growth. These studies revealed alterations in cells which then became the base to further experiments.

3D cultures were considered to be a breakthrough discovery in medicine because of the similarity it could provide to *in vivo* cells. It made a profound impact on tumour progression and chemoresistance research. Cell cultures were designed to recreate different types of tumours, from their drug resistance to their access to nutrients and oxygen. For instance, small, rapidly dividing multicellular constructs simulated those parts of the tumour which had unlimited access to nutrients, oxygen and were responsive to chemotherapeutic drugs. On the contrary, this approach was also used to investigate voluminous tumours which showed high drug resistance. This 3D cell culture technique was used to investigate colorectal and pancreatic cancer which's responsiveness to antitumour agents was low.

2. Human ageing and insulin resistance

According to NASA, spaceflight acts like a stimulant for rapid ageing acceleration. It produces symptoms that mimic the ageing process. The symptoms include loss of muscle mass, increased insulin resistance, and neuron deterioration, all of which allows scientists to understand how human ageing works. Martina Heer, a professor in nutrition physiology at the University of Bonn, talked about the benefits of studying the changes that astronauts experienced to study human ageing- "They can shed light on aspects of ageing that are hard to disentangle in a heterogeneous elderly population and also aid in the quest for countermeasures that would help people age in a healthier way."

When humans grow old, numerous systems of their body start to slowly malfunction, which can lead to disorders such as diabetes. A study performed on astronauts who spent months aboard the space station led by Richard Hughson, director of the University of Waterloo lab**,** indicated that their levels of insulin and other blood components were higher than usual. This was due to insulin resistance, a condition in which muscle, fat and liver cells don't respond to the hormone and therefore can't use the glucose as a source of energy [64]. Insulin resistance can lead up to Type 2 Diabetes, a disease that can be very harmful especially for astronauts when living in space [65].

All the studies being performed aboard the space station have both Space and Earth applications because not only astronauts can experience diabetes, but millions underneath their feet too.

3. Neurodegenerative diseases: Parkinson's and Multiple Sclerosis

Parkinson's and Multiple Sclerosis are both neurodegenerative diseases that induce damage to the brain and central nervous system. The reason to write about these diseases is because of the similarity they present with other spaceflight-induced immune system changes. The study of astronaut's alterations in their immune system has had its use when researching Parkinson's disease and Multiple Sclerosis.

Parkinson's disease is caused by the breaking down of neurons which are responsible for segregating a chemical messenger called dopamine. Due to the decrease in this neurotransmitter, some areas of the brain present abnormal activity leading to difficulties in movement [66].

Multiple Sclerosis is an autoimmune disease in which its body's immune system attacks myelin, the fatty tissues that protect nerve fibres and the spinal cord [67].

A study led by stem cell expert Andres Bratt-Leal of Aspen Neuroscience in La Jolla, California, and Valentina Fossati, a Multiple Sclerosis researcher with the New York Stem Foundation Research Institute in New York, is researching the effects of weightlessness in the nervous system, repercussions that both illnesses suffer from, and how it affects resembling cells. The experiment has been carried to the space station aboard the SpaceX CRS-18 cargo flight.

The experiment revolves around the two main types of cells which trigger the illnesses. These include neurons, the cells that produce them and microglia, immune cells which are responsible for protecting the brain from harmful substances and maintaining homeostasis. Valentina Fossati, the stem cell expert, said that one of the hypotheses they had was that microglial cells were the cause of such neurodegenerative diseases; they were attacking their own neurons.

This experiment will allow Bratt-Leal and Fossati the chance to find out if gene expression is altered in microgravity and subsequently help them understand how Parkinson's disease and Multiple Sclerosis work. On top of that it will give an insight as to what the astronaut's nervous system exactly undergoes and what can be done to countermeasure the effects of spaceflight [68].

D. <u>Survival on a long spaceflight</u>

So far the author has talked about the effects that spaceflight has on the human body on a relatively short-term basis. One of the purposes of this thesis is to determine whether we can or can't live in space for prolonged periods with the goal of ending in a planet that has a gravitational force similar to Earth's. In this section of the thesis, the author will go over which medical hazards can be overcome with the help of technology and which can not.

All of the thesis has come down to this simple question. Could we survive a long journey through space?. But what is considered a "long" spaceflight? Well, in the author's case, she will be referring to a long spaceflight as the duration of a trip to Jupiter, meaning a 6-year journey.

You might be wondering how it can be possible to survive all of the impairments and dangers that the author has mentioned throughout the paper. Well, you are not wrong to ask yourself that question, because she has also done the same. Out of all the effects spaceflight has on the body, some are only harmful when arriving into space or landing on Earth. Others might be harmful only on a short-term basis. Different variables should be taken into consideration when planning a spaceflight.

1. <u>Vestibular system</u>

The vestibular system is altered due to the confusion the brain suffers concerning its spatial orientation and balance: the senses detect stimuli that don't match the inputs detected by the other ones. Therefore, the brain gets confused trying to interpret all the different signals. Eventually, the brain manages to figure out where it is and the confusion ceases. Scientists have developed drugs that mitigate almost all the effects of SMS, such as intramuscular (medication injected into the muscle) promethazine. According to RxList [69], promethazine is an antihistamine [8] and works by blocking a certain natural substance (histamine [9]) that your body makes during an allergic reaction. Its other effects (such as anti-nausea, calming, pain relief) may work by affecting other natural substances and by acting directly on certain parts of the brain.

Besides this, astronauts have to go through specific training to make sure space motion sickness doesn't prevent them from performing day to day required activities or even precise manoeuvres (e.g. extravehicular activities, landing procedures). Virtual reality, flight simulators and rotatory chairs (Barany's chair) are the sorts of training that they must undergo to reduce the symptoms of space motion sickness.

Thanks to the brain's ability to adapt, humans don't need to worry about suffering from space motion sickness for 6 years, unless they plan to stop over at Mars to greet the aliens.

2. Musculoskeletal system

a) Muscles

Muscle loss is a major concern when it comes to spaceflight. For humans to be able to live on a 6-year space journey, different aspects are needed to minimise muscle atrophy.

Each astronaut's diet is carefully taken into consideration and designed. The diets have in common that they are high in protein, especially in Leucine, an amino acid in charge of maintaining muscle mass [70]. Exercise is also very important to prevent muscle loss. In order to preserve our muscle mass on a spaceflight to Jupiter, at a very minimum we would need to exercise for at least two hours a day for 6 years. This may be an issue because some people would not be able to exercise due to their age, health or physical condition. On the

[8] Antihistamine:A drug used to counteract the physiological effects of histamine production in allergic reactions and colds [102].

[9] Histamine: A physiologically active amine, $C_5H_9N_3$, found in plant and animal tissue and released from mast cells as part of an allergic reaction in humans. It stimulates gastric secretion and causes dilation of capillaries, constriction of bronchial smooth muscle, and decreased blood pressure [103].

other hand, a study (Dillon *et al.,* 2019) [71] has suggested that testosterone reduces the breakdown of skeletal muscle and helps it develop.

So a combination of exercise, a proper diet and a drug that helps maintain muscle mass such as testosterone, could be the main pillars of preventing muscle loss during spaceflight. Unfortunately, these countermeasures are not long-term solutions because these just mitigate the effects, they don't fully eliminate them.

In conclusion, from the point of view of preserving muscle mass, a spaceflight to Jupiter can be plausible but only for those who are in good physical shape to perform such strict exercise programmes.

B) Bones

Bone loss is another aspect to bear in mind on long journeys. Bone loss can be treated but not cured. The treatment is a combination of a proper diet, exercise and medicine. The diet is rich in calcium and Vitamin D, which helps absorb calcium into the body. As noted in the paragraph above, the inability of certain age groups (e.g. very young, very old) to exercise regularly can be a hindrance when trying to prevent bone loss. On the other hand, drugs can help by slowing down bone decay and stimulating bone growth. If just the exercise routine was followed, bone density would still decrease at a rate of 1 % a month (approximately), therefore, after a 6-year journey to Jupiter, a healthy middle-aged man or woman would have lost 72 % of their bone mass. Fortunately, a study (Leblanc *et al,* 2013) [72] from NASA in collaboration with the JAXA space agencies, indicated that an antiresorptive drug, alendronate[10] (bisphosphonate)[11] decreased the amount of bone loss and levels of urinary calcium during a 5.5 months mission on the ISS. The amount of bone that was still lost was not specified.

[10]Alendronate: A calcium-regulating agent used in the form of the sodium salt to inhibit resorption of bone in the treatment of osteitis deformans, osteoporosis, and hypercalcemia related to malignancy; administered orally [104].

[11]Bisphosphonate: Member of a class of drugs used for treatment of osteoporosis; works by inhibiting osteoclast-mediated resorption of bone [105].

Another study (Tavella *et al*, 2012) [73] tried to prove that pleiotrophin, a growth-factor protein, could stop the decrease in bone density. The subjects of the study were 6 mice; of which 3 were genetically engineered to produce more pleiotrophin. The results were very positive because they showed that the mice that produced more pleiotrophin presented only a 3 % bone loss in contrast with the control group that lost 41.5 % of their bone density over the course of 91 days. Scientists are confident that even though the experiment was performed on mice, humans will also react in a similar way to pleiotrophin [74].

The author can conclude that even though exercise alone is not enough to stop bone decay, astronauts can survive a 6-year spaceflight as long as they remain in microgravity. If they were to somehow return to a 1g or hypergravity environment their bones would most likely not be able to manage the stress.

3. <u>Immune system</u>

The immune system is compromised due to the decrease in T cells and the replacement of large portions of the gut microbiome by pathogenic microorganisms. The weakening of the immune system can result in it not being able to fight possible infections or diseases. Due to this, countermeasures would have to be taken into consideration when planning for a six years spaceflight.

Even though further countermeasures will have to be thought of, plenty of evidence about astronauts going on short journeys to the ISS has proven that the immune system is not severely damaged to the point where it is a danger to our survival, therefore it is not far-fetched to assume that a long spaceflight will not be very damaging to our immune system.

4. Cardiovascular system

The main concern about spaceflight on the cardiovascular system is heart atrophy. The heart is affected in space because of its decrease in use. A study published in the Circulation journal [75] reported that Scott Kelly, an astronaut who had spent 340 days on the ISS, had undergone severe heart atrophy despite exercising two and a half hours a day. The largest chamber of his heart had shrunk in mass by more than one-quarter after returning to Earth. The mass reduction in his heart didn't make it dysfunctional but it proved that in longer missions it could be a serious concern.

The study compared Scott Kelly's heart atrophy with the one that the long-distance endurance swimmer, Benoît Lecomte, had also undergone when he attempted to cross the Pacific in 2018. The swimmer spent most of the time in a horizontal position, thus, the heart didn't have to fight against gravity to pump blood into the brain [76].

The study concluded that despite the rigorous exercise regime that both, Scott Kelly and Benoît Lecomte, had followed, heart atrophy was almost inevitable if gravity wasn't there to pose resistance against the heart. Even though the results indicate that heart atrophy is not avoidable, astronauts can indeed survive a 6-years spaceflight as long as they stay in a microgravity environment.

5. Sleep/wake cycle and circadian rhythm

Sleeping in space is easier said than done. Due to the alteration in their circadian rhythm and sleep/ wake cycle, a long journey can make astronauts suffer from cardiovascular diseases, metabolic syndromes, diabetes and colorectal cancer, amongst others. Scientists have developed countermeasures that can help prevent these diseases. These go from changes in the environment and equipment, such as exposure to light and dark goggles, to drugs. Almost half of the medications used in the space station are sleep-related. Zolpidem, a sedative-hypnotic drug, is used to treat insomnia in astronauts even though scientists are not completely sure if these types of drugs react in the same way as they do on Earth. Even though the disruption of the sleep cycle is not very damaging, it would be ideal to have new drugs designed specifically for astronauts [77].

The author's conclusion is that the alteration of the sleep/wake cycle and the circadian rhythm during a 6-year spaceflight is not a life threatening condition.

6. Radiation effects

Radiation comes in different frequencies and wavelengths, depending on them, radiation can be more or less harmful to the human body. The more harmful it is, the more protection we need from it.

Non-ionising is a type of radiation that isn't as dangerous as ionising but some types can still be harmful to the body. UV radiation, for example, can not penetrate tissues of the body but can harm the skin and eyes, leading to cancer, cataracts and others. Fortunately, non-ionising radiation can be easy to block or protect from. UV-protection windows are enough to prevent harmful effects from happening.

The effects that ionising radiation produces can be prevented by proper shielding. As explained in the radiation effects section, galactic cosmic rays and solar energetic particles are the two types of cosmic radiation which scientists are currently working on to shield us from. The issue is that meanwhile solar energetic particles can be almost shielded against the spacecraft itself, galactic cosmic rays can not. Therefore, shielding will only be effective against both types of radiation if the material of the shield is effective against galactic cosmic rays.

Shielding can either be done by putting a lot of mass between the source of radiation and the human being or by using more efficient protective shielding materials. The second way of shielding is more effective because less material is required, therefore it's economically better. However, using more efficient protective shielding materials is not as easy as it sounds. Scientists started their search for the perfect protective material following the premise that “the best way of stopping particle radiation is by running that energetic particle into something that’s a similar size.” (Quote by Jonathan Pellish, a space radiation engineer at Goddard, NASA).

Aluminium is currently used in the ISS and blocks 95 % of the radiation that manages to get through the Earth’s magnetosphere. However, if astronauts were to leave the Earth’s magnetic field and go to Jupiter, aluminium wouldn't be the material used. Why is that? Because when ionising radiation passes through heavy matter such as aluminium, a nuclear reaction happens that produces secondary particles, also called secondary radiation. This type of radiation can even be more harmful to humans than space radiation. Therefore, other shielding materials need to be thought of.

Hydrogen-rich materials are perfect for shielding because of hydrogen’s composition. It is made up of one proton and one electron which makes it the lightest element. Because of this, it produces far less secondary radiation than heavier elements like aluminium. Hydrogen makes compounds such as water and polyethylene (plastic) which can be used in a spacecraft as a form of protection. Nevertheless, there are disadvantages to using water and polyethylene. Water would have to be replaced by recycled water from advanced life support systems and polyethylene wouldn’t be strong enough to be part of the spacecraft.

One of the most promising ingredients that scientists have developed is hydrogenated boron nitride nanotubes (hydrogenated BNNTs). The material in which it is made is both a shielding and a structural material, which makes it perfect for implementing it on a spacecraft. Scientists are planning on using the hydrogenated BNNTs in space suits too in order to protect them on spacewalks.

There are other ways of protecting us from radiation than just shielding. Researchers are contemplating the idea of force fields, just like the Earth’s magnetic field but at a much smaller scale. With the technology that we currently have, it would take a massive amount of energy and material to fabricate the force field, therefore more research is needed.

Drugs could be used to treat the effects of radiation. The problem then would be that we would be treating the symptoms instead of the cause.

To conclude the section about radiation being a major hazard when going to Jupiter, the author uses another quote from Jonathan Pellish: “Ultimately, the solution to radiation will have to be a combination of things. Some of the solutions are technology we have already, like hydrogen-rich materials, but some of it will necessarily be cutting edge concepts that we haven’t even thought of yet.”

III. EXPERIMENTAL FRAMEWORK

A. <u>Effect of posture upon blood volume in the nasal mucosa</u>

1. <u>How did the author come across this experiment?</u>

The author is part of an educational program for young people involved in clinical trials (KIDS Barcelona) at the Hospital of Sant Joan de Déu. The head of the KIDS advisory group, Begonya Nafria, put her in contact with the European Space Agency, who then directed her to Dr. David Green and Roger Huerta. David Green works as a Human Space Physiologist at the European Astronaut Center, ESA and is also a professor at King's College London. Roger Huerta works as a Medical Projects Engineer at the European Astronaut Center, ESA. Doctor Green informed the author about an experiment that he had already started and asked her if she wanted to be involved in it, to which she agreed.

2. <u>Purpose and predictions of the experiment</u>

As the author has mentioned throughout the thesis, astronauts experience changes in their blood flow when being "weightless" in space. Blood no longer needs to be pumped against gravity to get to the upper half of the body and therefore the heart does not need to work as hard as it would in a 1G environment. This diminished use of the heart can be a problem when astronauts return to Earth due to the fact that the heart has to readapt to Earth's gravity. During the heart's process of acclimatisation, astronauts experience light-headedness or orthostatic intolerance resulting from a sudden shortfall in blood flow to the brain when standing up.

One way of tracking the blood flow that goes into the head is by measuring the amount of blood in the nasal mucosa. At the moment, there are devices capable of measuring this but have not been used to track the astronaut's blood flow when returning from space. <u>If it were</u>

to be used in this scenario, it could alert astronauts before they faint or feel light-headed to sit down or get help. Because of it, David Green decided to conduct a study to find this out.

The experiment aims to prove that the device works properly and is capable of measuring the blood flow to the brain during different posture changes. Dr David Green and the author expect blood flow in the nasal mucosa to vary depending on the person's position because gravity can facilitate or complicate the effort the heart has to do to pump the blood towards the brain. The amount of blood should increase when the subjects change from a complicating (e.g. standing) or neutral position (supine) to a facilitating position (e.g. PLA). Blood flow should decrease when subjects change from a facilitating or neutral position to a complicating position. If the results match with the predictions, the hypothesis "Maybe some devices can help treat or prevent possible illnesses on astronauts" would be true.

3. Social application

If the device proves out to function properly, it could also be used on people who suffer from orthostatic intolerance, elderly people, etc, and could be implemented in nursing homes.

4. Procedure

To test the effectiveness of the device, David Green has designed an experiment with 24 subjects, from ages 16 to 60, to adopt different postures during 1 and 3-minute intervals summing up to a total of 27 minutes. David Green has already started this experiment in the UK with 7 healthy individuals. The author will be in charge of doing the experiment on the other 17 people.

As the table shows, the first minute is preparation before actually starting the experiment. This makes starting the experiment with all the subjects in the same conditions easier.

There are also 1-minute intervals of sitting down which are just to make sure the subjects are feeling well and to check that the device is tracking correctly.

Minutes	Positions
-1	1 minute: SITTING DOWN
0	3 minutes: SUPINE
3	3 minutes: STANDING UP
6	3 minutes: SUPINE
9	3 minutes: LEGS UP AT A 90-DEGREE-ANGLE (PLA)
12	1 minute: SITTING DOWN
13	3 minutes: PRONE
16	3 minutes: SUPINE
19	1 minute: SITTING DOWN
20	3 minutes: STANDING UP
23	1 minute: SITTING DOWN
24	3 minutes: SUPINE
27	END

Table 1. Positions that the subjects will adopt.

5. <u>Elements of the experiment</u>

* Due to the ongoing pandemic, the experiment has been carried out by disinfecting the infrared device (glasses), the yoga mat and by wearing masks.

The different parts of the experiment include:

1. An infrared device that is worn like a pair of glasses.

Image 6. Infrared device. [78]

An infrared light comes out of the emitter at the frequency required to detect haemoglobin and is captured by the photodetector that's in front of it. Haemoglobin is a protein found in red blood cells. The photodetector is able to measure how much blood is going through the nasal mucosa because of the amount of infrared light that it is receiving.

2. Rhinolux

Image 7. Rhinolux device [79]

3. A computer that contains specific software that allows the data to be monitored.

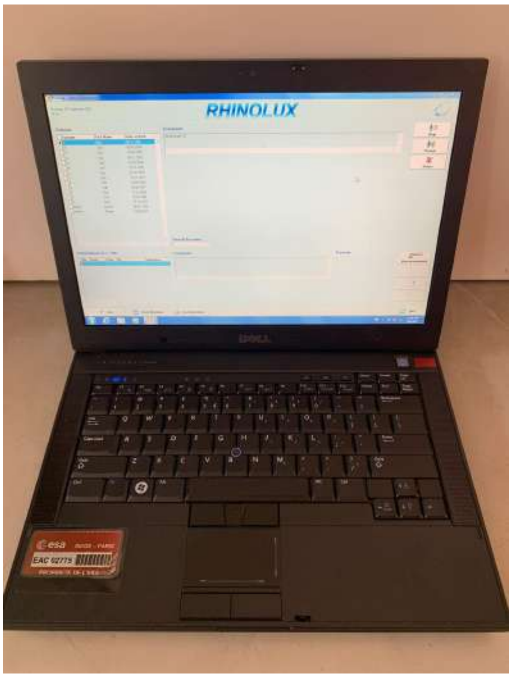


Image 8. Computer provided by ESA. It contains the program that monitors the changes in blood flow. [80]

The program is called Rhinolux, just like the device. Before the subject puts on the device, the examiner creates a new profile.

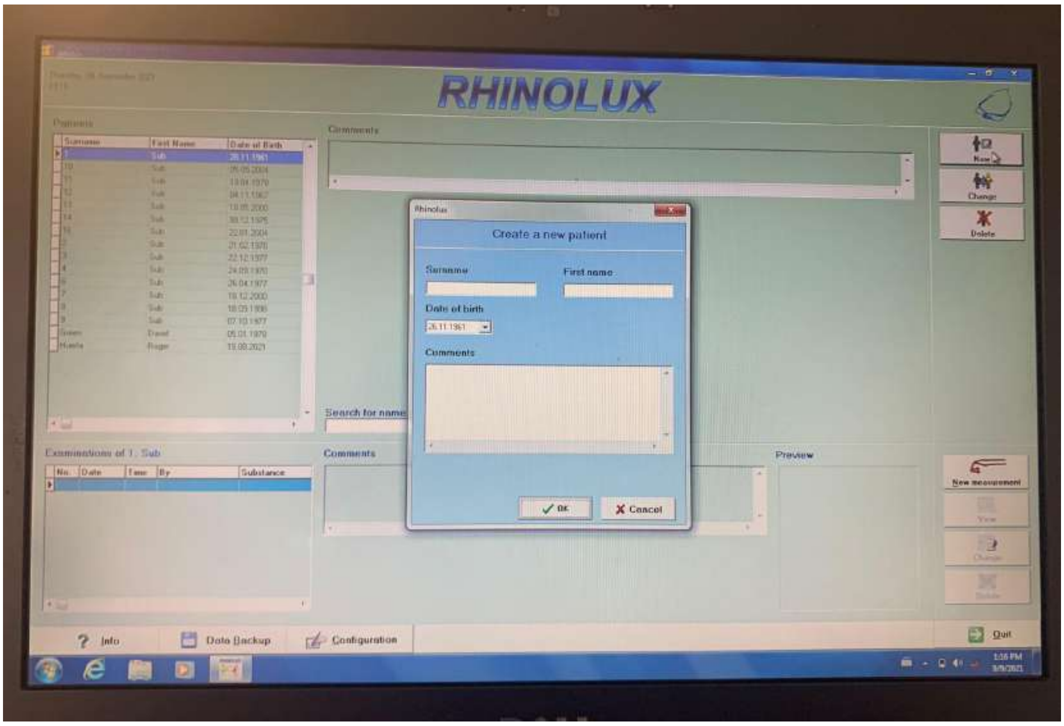


Image 9. Rhinolux program. Creating a new profile for a subject. [81]

Once the profile has been created, the examiner indicates who they are and sets the experiment to officially start in a minute.

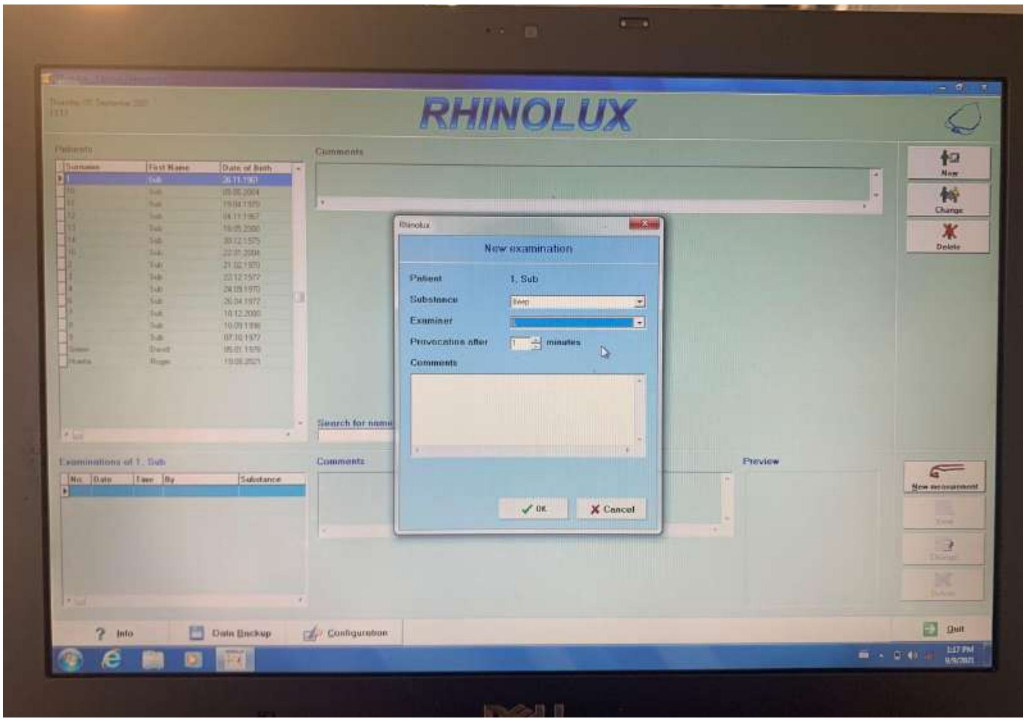


Image 10. Rhinolux program. Starting the examination. [82]

The program takes around 30 seconds to warm up and then the 1-minute preparation starts.

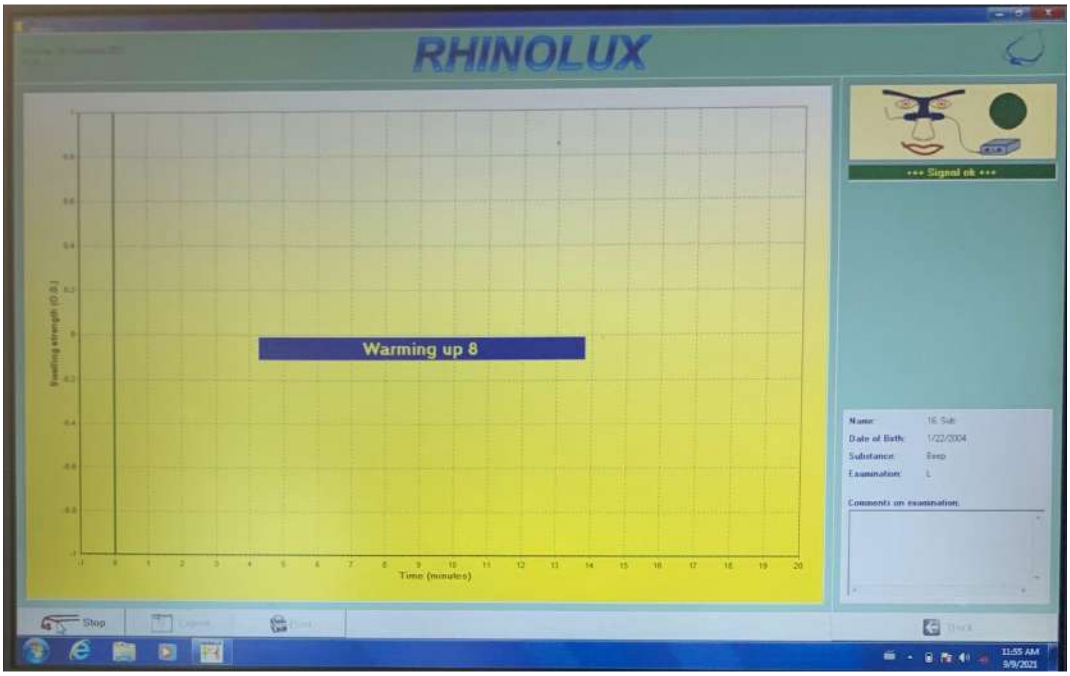


Image 11. Rhinolux program. Warming up. [83]

As you can see in the image below, the amount of blood that goes through the nasal mucosa is shown on the screen as a graph.

The quantity of blood increases when the subject is in a supine position because gravity is a vertical force which means that blood doesn't have to get to the head.

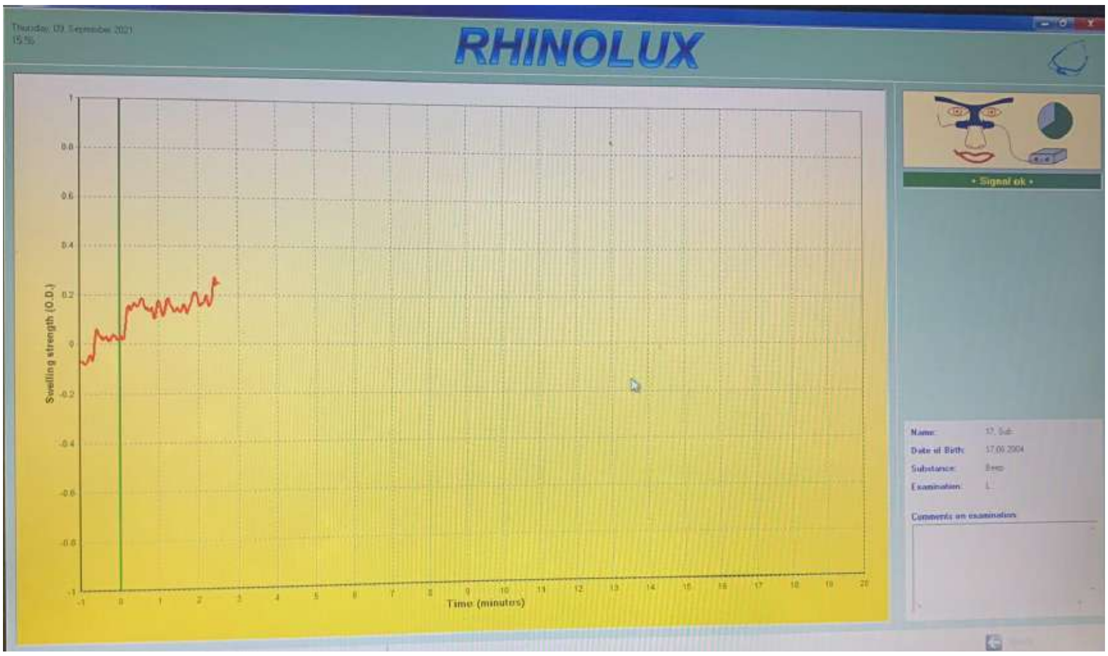


Image 12. Rhinolux program. [84]

The amount of blood going to the brain decreases when the subject is standing up.

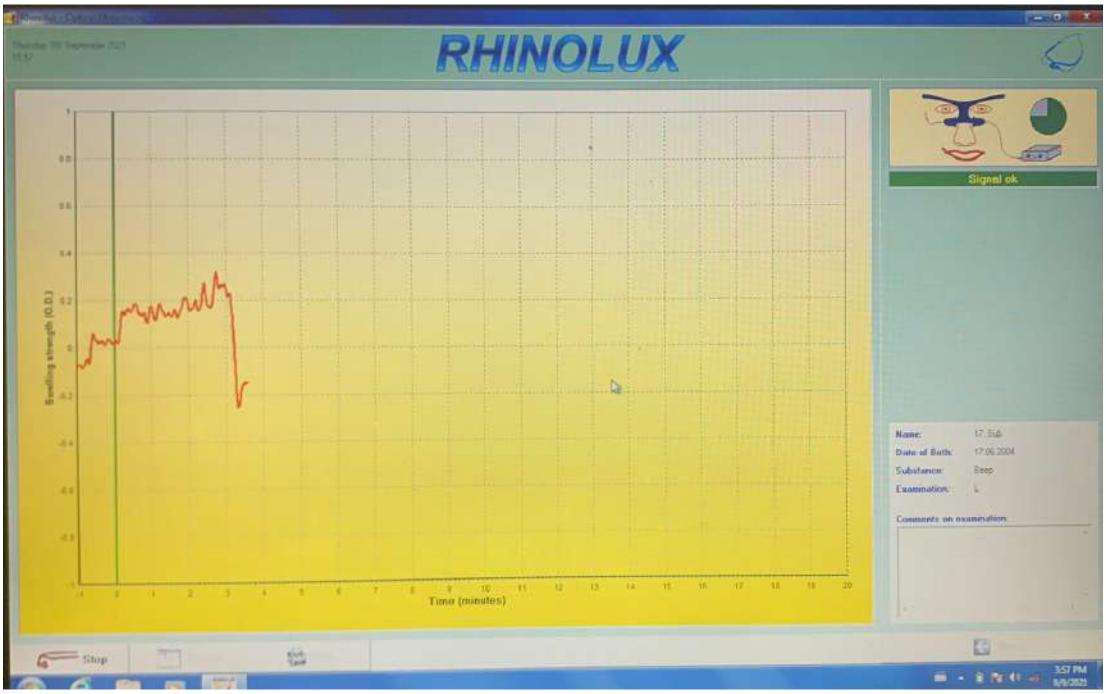


Image 13. Rhinolux program. [85]

During the rest of the experiment, the postures that the subjects adopt are reflected in the graph: if gravity is working against the blood flow (standing up) the amount will decrease and if gravity is giving an advantage to blood to get to the brain (PLA position) the amount of blood flow will increase.

When 27 minutes have passed the examiner stops the measuring and exports the files to the computer. The data is then sent to David Green to analyse.

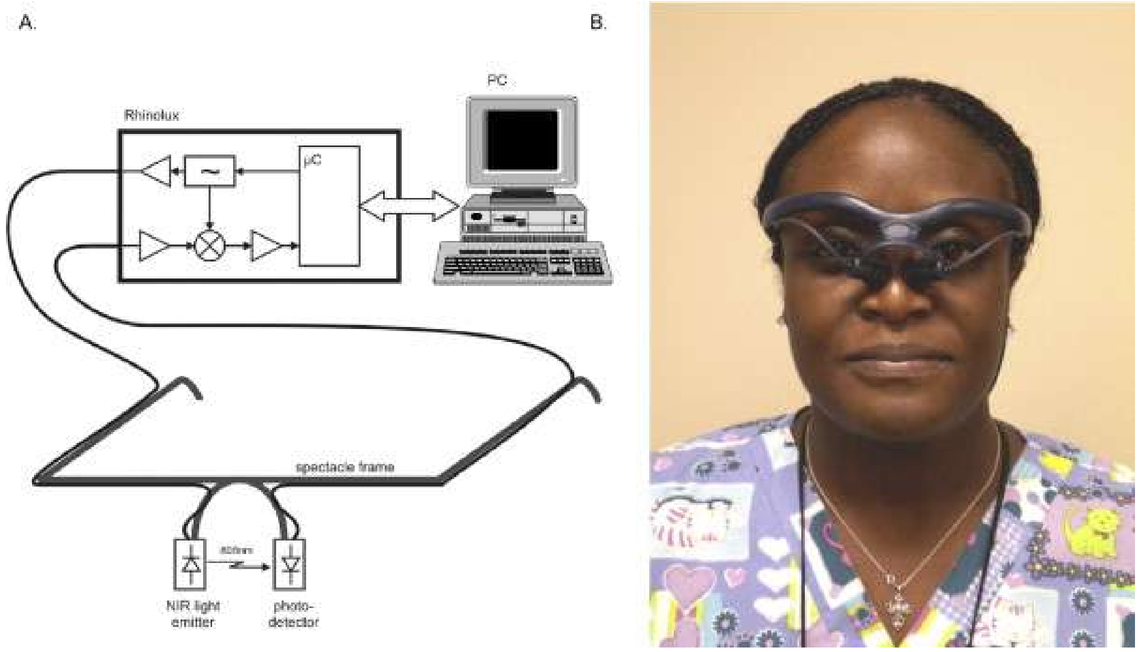


Image 14. A. Representation of the computer, the rhinolux and the infrared device all connected. B. Infrared device that is worn like a pair of glasses. [86]

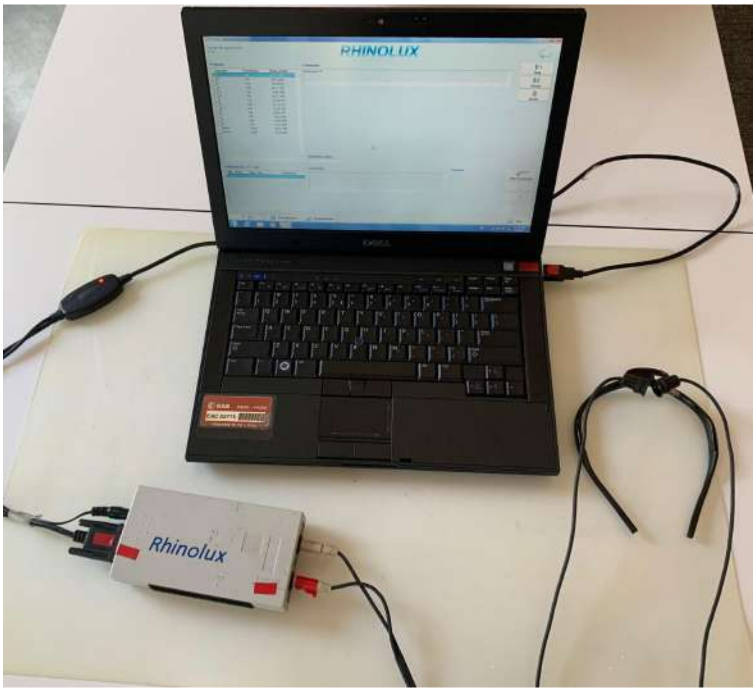


Image 15. Image of the computer, the Rhinolux and the infrared device. [87]

SUBJECTS	GENDER	YEAR OF BIRTH
Sub 1	Male	1961
Sub 2	Female	1970
Sub 3	Female	1977
Sub 4	Female	1970
Sub 5	Female	1967
Sub 6	Male	1977
Sub 7	Male	2000
Sub 8	Male	1998
Sub 9	Female	1977
Sub 10	Female	2004
Sub 11	Male	1970
Sub 12	Male	1967
Sub 13	Male	2000
Sub 14	Female	1975
Sub 15	Male	1998
Sub 16	Female	2004
Sub 17	Male	2004

Table 2. Gender date of birth of the 17 subjects.

6. Photographic report

Image 16 . Subject sitting [88].

Image 17 . Subject standing [89].

Image 18 . Subject in a prone position [90].

Image 19. Subject in a supine position [91].

Image 20. Subject in a PLA position [92].

Image 21. The author and a subject during the experiment [93].

7. Results

The following image shows the variation of blood flow in the nasal mucosa of one of the subjects. This graph shows the increase and decrease in blood flow when changing positions. For example, in the sixth minute, there's a rapid increase in the blood flow which is caused by changing from a standing position to a supine position. And, if we look at minute 12 we see there's a sudden drop caused by going from a PLA position to sitting down. These changes in blood flow are caused because some positions are advantageous when getting blood to the head.

Image 22. Graph representing the amount of blood going through the nasal mucosa while changing positions during 27 minutes. [94]

The following box indicates the difference in the blood flow between standing, sitting and PLA when coming from a supine position.

Delta from preceding SUPINE

1st 10s - No effect

2nd 10s – p = 0.001*

Standing vs. PLA – p = 0.009

Standing vs. Sitting – No effect

Sitting vs. PLA – p = 0.007

3rd 10s – p = 0.001*

Standing vs. PLA – p = 0.032

Standing vs. Sitting – No effect

Sitting vs. PLA – p = 0.070 trend

Last 30s – p = 0.005*

Standing vs. PLA – p = 0.010

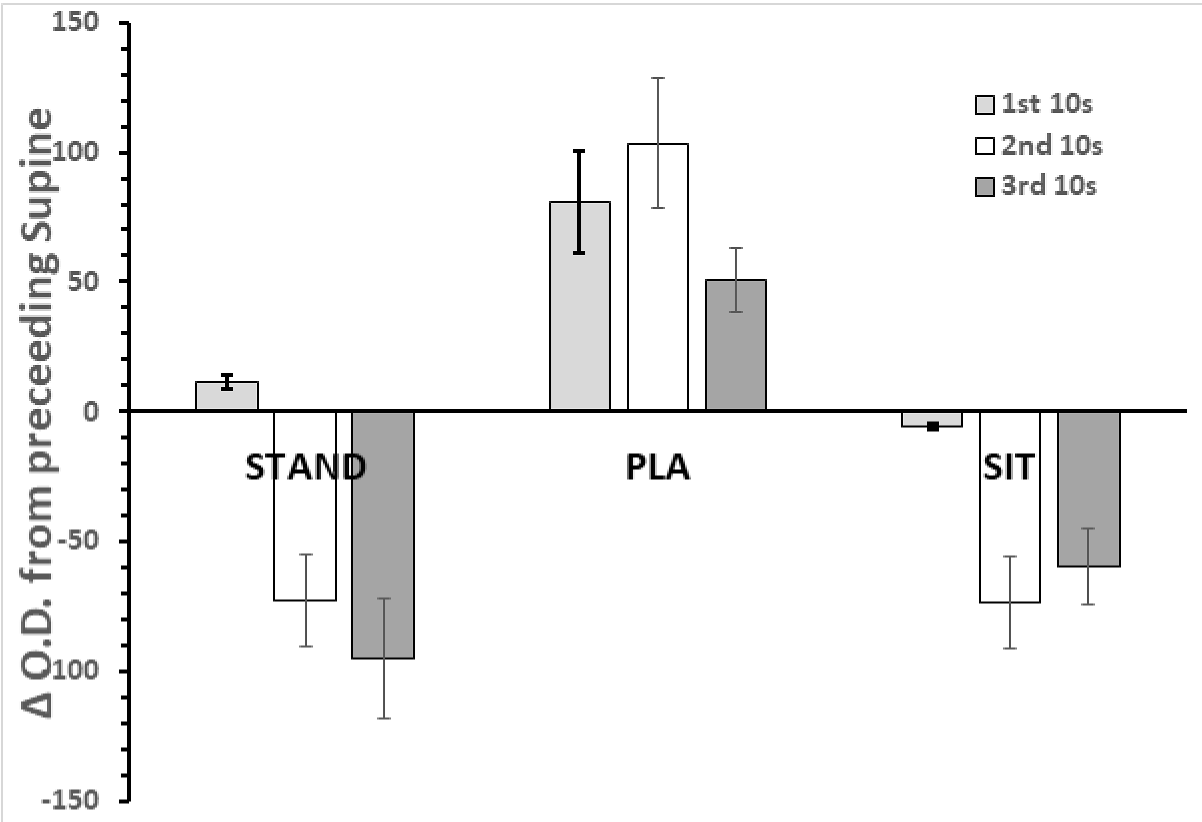
Standing vs. Sitting - p = 0.001

Sitting vs. PLA – No effect

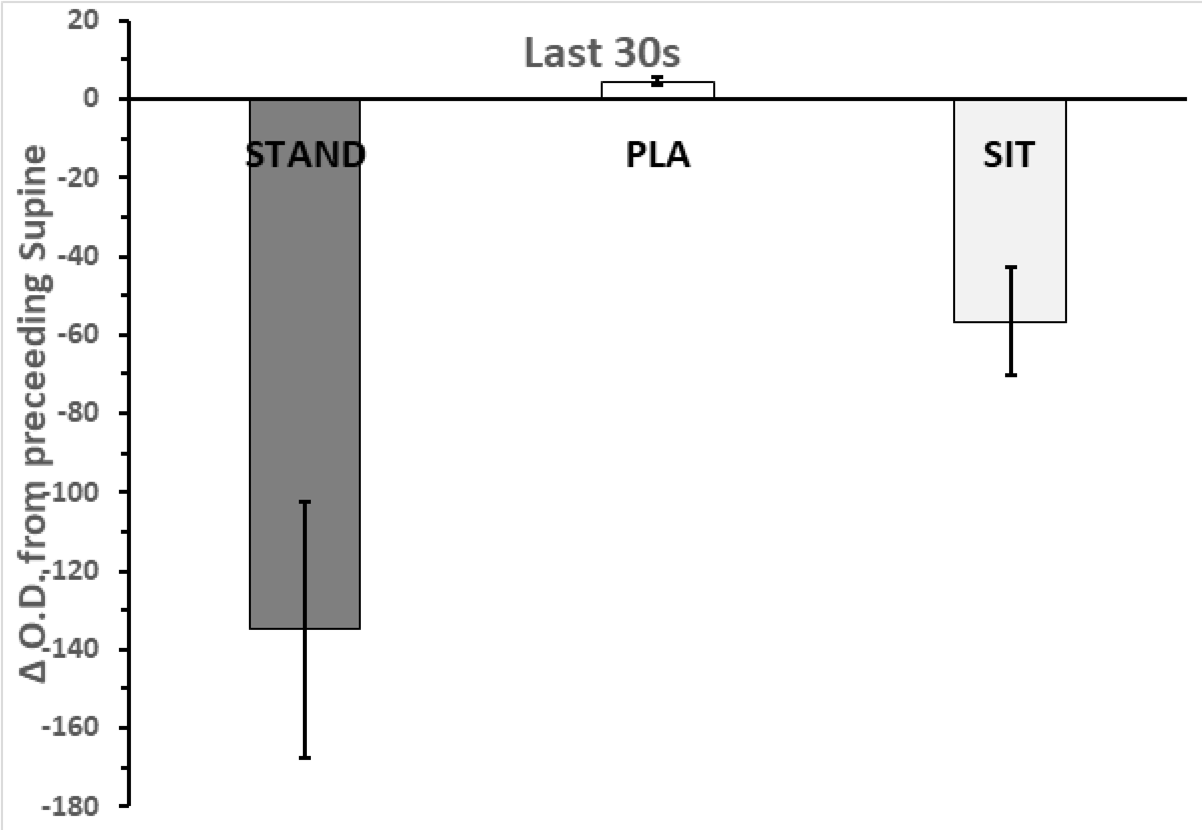
* When you perform a statistical test, a *p*-value helps you determine the significance of your results in relation to your hypothesis. The lower the p-value is the less likely it is that what you found is to do with chance. The general rule is that a significant value is when the *p*-value is less than 0.05, which means that there is a 5 % chance that the difference you see is just a coincidence. As you can see in the summary above, the *p*-values, which have been calculated

by David Green, are below 0.05 which is an indication that the data collected by the infrared device is accurate.

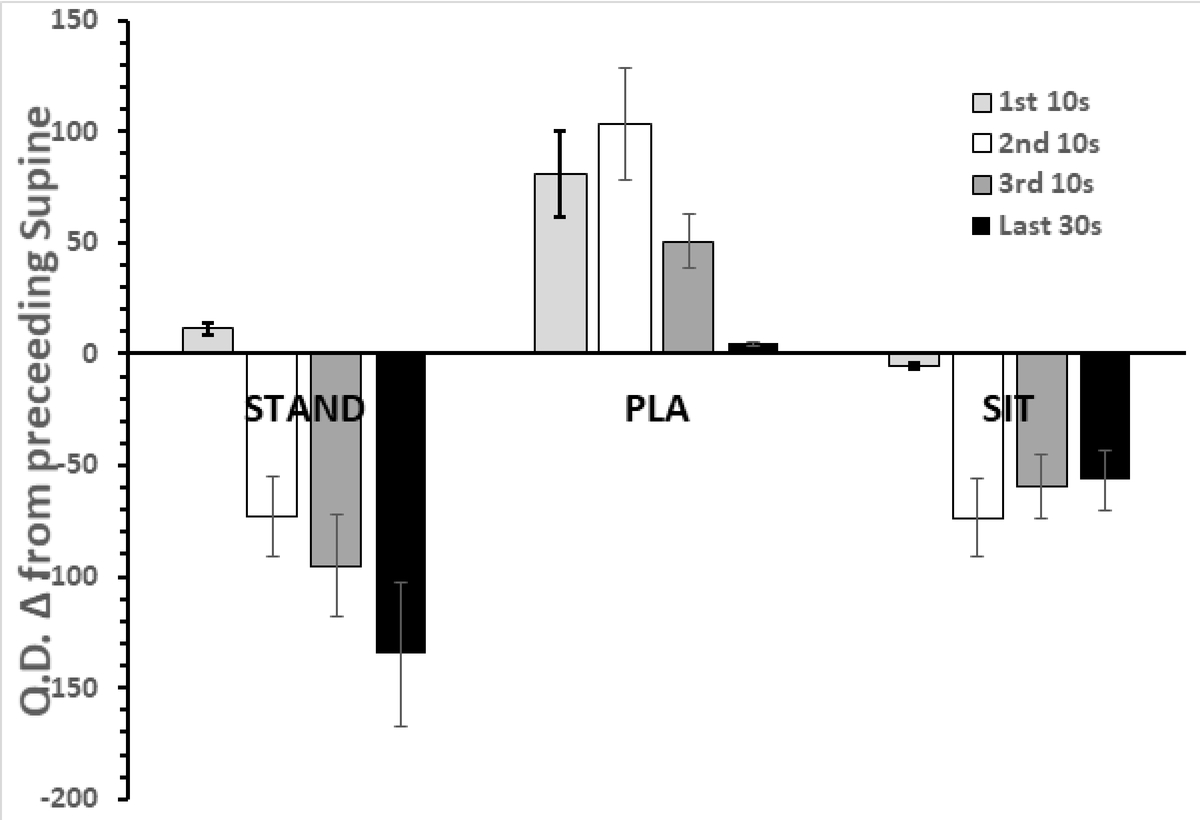
The following graphs show the effects in the first and last 30 seconds of every 3-minute position interval. We only looked at these values because we are evaluating the changes in blood flow between every position.



Graph 1. Graphic representation of the variation in blood flow from a supine position to a standing, sitting and PLA position during the first 30 seconds of each interval.



Graph 2. Graphic representation of the variation in blood flow from a supine position to a standing, sitting and PLA position during the last 30 seconds of each interval.



Graph 3. Graphic representation of the variation in blood flow from a supine position to a standing, sitting and PLA position during the first and last 30 seconds of each interval.

These columns represent the changes in blood flow from going from a supine position to a standing, sitting and PLA position. The high and the lows of the columns are the averages of the 17 subjects during that interval of time.

The mean value could be contaminated by one person having a massive or very small response and the average could change just for that one subject. The way of representing this uncertainty in this reported measurement is with error bars, which show the variability of the data in the graph. In the graph, the error bars are much smaller than the effects that we see which proves two things: that the experiment was done well and that the people's responses were very similar.

8. Discussion

The first 10 seconds of every interval are statistically insignificant, which means that the infra-red device doesn’t develop a strong enough signal to be considered relevant. This suggests that the device takes around 10 seconds to properly detect changes in blood flow.

In the second 10 seconds of every interval, there is an increase in the amount of blood flow in the nasal mucosa in changes in position going from a supine to a PLA position, and a decrease going from a supine to a standing or sitting position. The amount of blood that decreases when changing to both of these positions is almost the same because standing and sitting are in the same direction of change that's why the difference is so small and is considered insignificant.

In the third 10 seconds of every interval going from a supine position to a PLA position, the amount of blood decreases slightly because we have numerous mechanisms in the body to deal with the extra fluid in our head. Basically, the increase in blood peaks in the second 10 seconds and then slowly starts decreasing. The blood flow continues to decrease in the changes in position from supine to standing or sitting.

In the last 30 seconds of every interval, the blood flow continues to increase from a supine position to standing. The amount of blood in the nasal mucosa when going from a supine position to sitting stays almost the same as the third 10 seconds. The amount of blood from a supine position to a PLA position in the last 30 seconds continues to decrease.

9. <u>Experiment's conclusion</u>

The low *p*-value is a great indication that the experiment was performed adequately and that the results are not a product of chance, this is why we are confident that the following conclusions are accurate.

The experiment has shown that the amount of blood increases when the subjects change from a complicating position to a facilitating position and decreases when subjects change from a facilitating position to a complicating position.

Consequently, we can ensure that the predictions made about the device being able to detect the amount of blood that goes through the nasal mucosa and the results obtained by the experiment coincide. We can conclude that the device is capable of correctly detecting the amount of blood that goes through the nasal mucosa.

IV. THESIS’ CONCLUSIONS

First hypothesis: Maybe the effects of spaceflight on the body are too harmful to allow survival on a long term basis.

In the final analysis, the research on the topic has led the author to the conclusion that the damage that a 6-year spaceflight would do to the vestibular system, the muscles, the bones, the cardiovascular system, the immune system, the sleep/wake cycle and circadian rhythm, wouldn’t be serious enough to put the astronauts in a life-threatening situation. On the other hand, the effects that ionising radiation has on the human body would be very harmful and could lead to death.

Therefore, the answer to the hypothesis is that with the current technology and resources that we have, humans would not survive a long spaceflight (6 years journey). Despite this, the author firmly believes that with enough money and time, humans will eventually find a way to survive a long spatial journey.

Second hypothesis: Maybe the research that scientists are doing in space has had an impact on terrestrial medicine.

Space research has given the opportunity to study diseases from another perspective. Thanks to the research that the author has done, she has been able to find out how studying cancer from space, human ageing, insulin resistance and neurodegenerative diseases has had a positive influence on the way medicine on Earth is practised and studied.

Third hypothesis: Maybe there are devices that can help treat or prevent possible illnesses on astronauts.

By means of the experiment performed by David Green, Roger Huerta, and the author, she has been able to confirm that there are devices, such as the infrared that we used, that can help astronauts prevent, cure or treat illnesses and medical conditions. Thanks to it, the author has been able to confirm that there is an infrared device that can correctly detect the amount of blood that goes through the nasal mucosa and therefore can alert astronauts from feeling light-headed or even fainting.

V. RESEARCH CONTINUATION

If anyone were to continue the research, the author would advise them to dig deeper into the effects of travelling through space during long periods, due to the fact that this field of study is constantly evolving and is only a matter of time before a breakthrough comes that will change the course of history.

In case somebody wants to perform other experiments, such as recreating what the astronauts experience when abandoning the Earth's surface, or wanting to imitate how cells grow in a microgravity environment, the author is free to offer the research that she has collected that was not included in the thesis' final version.

VI. WEBGRAPHY / BIBLIOGRAPHY

A. Images

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[78] **Image 6.** Scales, L. (2021). *Infrared device.* [Photograph].

[79] **Image 7.** Scales, L. (2021). *Infrared device.* [Photograph].

[80] **Image 8.**Scales, L. (2021). *Rhinolux device.* [Photograph].

[81] **Image 9.**Scales, L. (2021). *Computer provided by ESA* [Photograph].

[82] **Image 35.** Scales, L. (2021). *Rhinolux program.* [Photograph].

[83] **Image 36.** Scales, L. (2021). *Rhinolux program.* [Photograph].

[84] **Image 37.** Scales, L. (2021). *Rhinolux program.* [Photograph].

[85] **Image 38.** Scales, L. (2021). *Rhinolux program.* [Photograph].

[86] **Image 39.** Luong, A., Cheung, E. J., Citardi, M. J., & Batra, P. S. (2009, October 3). *Rhinolux, PC, spectacle frame* [Illustration and Photograph]. https://ars.els-cdn.com/content/image/1-s2.0-S0194599810003517-gr1.jpg

[87] **Image 40.** Scales, L. (2021). *Image of the computer, the Rhinolux and the infrared device.*[Photograph].

[88] **Image 41.** Scales, L. (2021). *Subject sitting* [Photograph].

[89] **Image 42.** Scales, L. (2021). *Subject standing* [Photograph].

[90] **Image 43.** Scales, L. (2021). *Subject in a prone position* [Photograph].

[91] **Image 44.** Scales, L. (2021). *Subject in a supine position* [Photograph].

[92] **Image 45.** Scales, L. (2021). *Subject in a 90-degree-angle leg raise position* [Photograph].

[93] **Image 46.** Scales, L. (2021). *The author and a subject during the experiment* [Photograph].

[94] **Image 47.** Scales, L. (2021). *Graph representing the amount of blood going through the nasal mucosa while changing positions during 27 minutes.* [Photograph].

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C. Quotes

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VII. ANNEX

A. Interviews

1. Sergi Vaquer Araujo

Dr Vaquer Araujo is a certified ISS Flight Surgeon currently working for the European Space Agency at the European Astronaut Centre in Cologne, Germany. He studied medicine at the Autonomous University of Barcelona, Spain and specialised in Emergency Medicine and Critical Care. His main professional interests are human physiology, pre-hospital medicine and advanced trauma medical management. He has also participated in several research activities related to human spaceflight, including microgravity research on parabolic flights.

The interview was very informative and useful for completing the thesis. He provided the author with very valuable insight into how the astronauts prepare to go to space and what the training looks like. The information that he gave her was implemented throughout the paper and was also used to confirm previous data that she had collected. He also gave the author several ideas about what to do for the practical framework. Even though she didn't end up doing them, they helped her develop other ideas and gave her backup experiments to do.

2. Ben Hayward

Ben Hayward is a Mission Design & Flight Dynamics Engineer at Aerospacelab. He has a background in mathematics and physics, with an interest in research and entrepreneurship - currently exploring both Space and Health-related technology. He has worked in the European Space Agency, specifically in the Space Applications sector.

The purpose of the interview was to gather information about several experiments that the author could perform. One of the ideas was to use a clinostat because by changing the angle of it, an analogue for gravity on Mars or the Moon could be achieved. Another idea was to use magnetic fields to simulate microgravity. The author didn't end up doing any of these experiments because another and more plausible experiment was brought to the author's attention by another expert.

Even though the author didn't end up doing them, the interview was really helpful because it gave her the opportunity to have a lot of experiments to choose from.

B. Ethical consent and information sheets

Previous to the experiment, all 17 subjects had to read and understand the information sheet that is attached below. Along with that, they had to sign an ethical consent sheet that stated their voluntary participation in the experiment.

Information sheet: Information sheet for participants

Ethical consent sheet: Consent sheet

Signed ethical consent sheets:

- SUB 1
- SUB 2
- SUB 3
- SUB 4
- SUB 5
- SUB 6
- SUB 7
- SUB 8
- SUB 9
- SUB 10
- SUB 11
- SUB 12
- SUB 13
- SUB 14
- SUB 15
- SUB 16
- SUB 17

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