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Studies of the conditions on board the ISS influencing the structures of oral cavity.

Nicolas Pitois

Dissertação conducente ao Grau de Mestre em Medicina Dentária (Ciclo Integrado)

Gandra, 8 de Junho de 2022

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Trabalho realizado sob a Orientação do Professor Doutor Rui Manuel Simões Pinto

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RESUMO

Introdução: O ambiente espacial é hostil para os seres humanos. Apesar disto, a curiosidade insaciável da humanidade leva-nos a explorar cada vez mais longe. Precisamos de nos armar com as ferramentas certas, de modo a podermos lidar com os problemas que iremos encontrar.

Objetivos: Os objetivos serão apresentar as condições de vida no ISS, compreender como eles influenciam a saúde oral e finalmente se existe possíveis soluções futuras? Um objetivo secundário será simular as consequências de uma viagem a Marte.

Material e métodos: Foi realizada uma pesquisa bibliográfica na base de dados PubMed. Os resultados incluem os estudos publicados que atenderem aos critérios no período de 2006 a 2022. Acrescentei dois artigos de 2005 e 2004 devido à sua elevada relevância.

Resultados: Os resultados variam muito em função da estrutura da esfera oral em questão. Uma coisa é certa: a falta de gravidade e a radiação têm efeitos deletérios sobre a saúde oral em geral. Os instrumentos de prevenção e tratamento já existem, mas são insuficientes, a ciência deve desenvolver novos meios para cumprir objetivos futuros.

Conclusões: As condições de vida na ISS são prejudiciais para a saúde oral de muitas maneiras. Perda óssea, disfunção da ATM ou mesmo o sentido do paladar. As soluções atuais existem, mas são largamente insuficientes. Os instrumentos de prevenção, diagnóstico e tratamento futuros são necessários. Finalmente, uma viagem a Marte é muito difícil de prever, dados os atuais meios científicos, com o risco de encontrar uma equipa em grande sofrimento ao regressar à Terra.

Palavras chave: "Space flight" "Spacecraft" "Bone density" "Alveolar bone loss" "Saliva" "Masticatory muscles"

ABSTRACT

Introduction: The space environment is hostile for humans. Despite this, humanity's insatiable curiosity drives us to explore further and further. We need to arm ourselves with the right tools in order to deal with the problems we will encounter.

Objectives: The objectives will be to present the living conditions on the ISS, understand how they influence oral health, and finally whether there are possible future solutions? A secondary objective will be to simulate the consequences of a trip to Mars.

Material and methods: A literature search was conducted in the PubMed database. The results include published studies that met the criteria in the period from 2006 to 2022. I added two articles from 2005 and 2004 due to their high relevance.

Results: The results vary greatly depending on the structure of the oral sphere in question. One thing is certain: lack of gravity and radiation have deleterious effects on oral health in general. Prevention and treatment tools already exist, but they are insufficient; science must develop new means to meet future goals.

Conclusions: Living conditions in the ISS are detrimental to oral health in many ways. Bone loss, TMJ dysfunction or even the sense of taste. Current solutions exist but are largely insufficient. Future tools for prevention, diagnosis and treatment are needed. Finally, a trip to Mars is very difficult to predict, given current scientific means, with the risk of finding a team in great distress upon returning to Earth.

Keywords: "Space flight" "Spacecraft" "Bone density" "Alveolar bone loss" "Saliva" "Masticatory muscles"

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LIST OF ABBREVIATIONS:

B.Ar : Bone area

CEJ-ABC : Cementoenamel junction to alveolar bone crest length

DI : Dry immersion

[E+D]Ar : Enamel+dentin area

[E+D]Ar/T.Ar : Relationship between enamel+dentina area and tissue area

FSM : Fluid shift mechanism

HDT : 6° Head down tilt

IL-6 : Interleukin 6

ISS : International Space Station

MA : Masseters muscles

M.Ar : Marrow area

MIR : Мир

NASA : National Aeronautics and Space Administration

PGE2 : Prostaglandine E2

Pu.Ar : Pulp area

RE : Resistive exercise alone

RVE : Whole-body vibration coupled with high-load resistive exercise

SCM : Sternocleidomastoid muscles

SM : Simple muscle pain

TA : Tibial anterior muscles

T.Ar : Tissue area

TMD : Temporomandibular disorder

TMJ : Temporomandibular joint

1. INTRODUCTION

The space environment is still little known and little mastered despite the great progress made in this field in the last 60 years. We are just beginning to understand the consequences of the space environment on human physiology. Dentistry is one of them. It is imperative to identify and understand the mechanisms involved in such conditions.

Humanity's project is to push back the limits of human beings in space, I am thinking, for example, of the possible trip to Mars in the next decades. It is therefore essential to know as much as possible about human physiology in the space environment in order to prepare ourselves as well as possible for the adventures of tomorrow.

Aeronautical dentistry is a term coined by Dr. Balwant Rai in 2007. It is a relatively young discipline that has its origins in the 1960s when NASA commissioned Colonel William Frome in 1966 to monitor the oral health of astronauts [(1)]. The second significant step was taken in 1988 when NASA asked Colonel Johan Young to develop instruments and protocols for preventive purposes and emergency procedures [(1)].

Aeronautical dentistry is therefore a very specialized branch, recently recognized, whose aim is to analyze the conditions of life in space, their consequences on oral health and finally to develop tools and means of prevention and treatment adapted to the astronaut's lifestyle.

Current knowledge already supports a consequent influence of the lack of gravity on several aspects of the oral sphere: change in the composition of saliva, blood distribution throughout the body, perception of flavors, muscle tone, bone density or the behavior of bacterial colonies.

Microgravity being of course the most notable and significant change, others are not to be neglected. We can note a significant increase in the dose of radiation received. Moreover, the ISS is a restricted and hermetic environment composed of people of multiple origins, so the bacterial mixing must be closely monitored. The natural circadian cycle is broken in the ISS with a sun that rises and sets 16 times a day, it is relevant to measure the likely consequences of such a change in the day/night cycle.

I will go into more depth on each of these particular life parameters and their impact on the space lifestyle and more specifically on oral health.

The main goal of this systematic review will be to exhaustively list the causes and consequences of the living conditions in the ISS leading to important changes of the oral sphere. Are these changes avoidable or mitigable with current knowledge and technology? Can they endanger a mission?

An additional part of this study will focus on the possibility of a trip to Mars and what essential role aeronautical dentistry will play.

2. AIM

The purpose of this essay will be multiple:

Main objectives:

- To present the very particular conditions of life present in the ISS (lack of gravity, ionizing radiations, restricted and hermetic environments...)

- To list past accidents and events in the MIR / ISS station in order to identify the factors involved and avoid them in the future.

- Understand the natural and artificial conditions that astronauts go through and what are their consequences on oral health (masticatory muscle, bone arch, teeth, TMJ, saliva, oral microbiota, cancer). Are these consequences avoidable or mitigable?

- What are the solutions and measures of prevention and treatment that already exist? What are the possible future solutions thanks to the evolution of medicine and technology?

Secondary objective:

- Is a trip to Mars possible, given current knowledge and means?

3. MATERIAL AND METHODS

3.1. PICo :

Population	The population of interest are the astronauts living on the ISS. They therefore have a very high level of education and understanding of the importance of dental hygiene. In addition, these people come from very different countries.
Interest	The events of interest that will be measured are osteoporosis and muscle weakness induced by microgravity, TMJ modifications, the development of teeth, modification of saliva and saliva flow and change in oral microbiota.
Context	The ISS is a very particular context subject to microgravity that leads to bone degradation due to lack of mechanical stimulation, as well as muscle weakness. In addition, the danger of space radiation must be taken into account. Astronauts living in low orbit at an altitude of 408 km on the ISS are shielded from this radiation by the atmosphere and the magnetosphere. However, scientists and doctors measure their exposure levels in real time, 24 hours a day. Furthermore, ISS is a restricted and hermetic space that does not allow exchange between the inner space and outer space of the ISS.

3.2. Eligibility criteria of the articles:

- Inclusion criteria: Published articles until the year 2006 (between 2006 and 2022). With available resume, and high relevance. I took the liberty of adding two articles from 2005 and 2004 due to their high relevance.

- Exclusion criteria: A first rejection of articles after the year 2005. A second rejection of articles that are integrative systemic reviews. A final rejection by manual reading based on titles, abstract and relevance.

3.3. Search strategy and articles selection process:

The search strategy with the keyword combination detailed above identified 2123 articles in the different database. After application of the inclusion criteria 562 articles were obtained. Following titles screening we have selected 140 hypothetically suitable for our study. After removing the duplicates, a total of 64 articles were selected for a review of the abstract. A thorough reading of the articles allowed us to select 33 of them.

The combination of keywords and their results on PubMed:

Keywords	Numbers of results
(space flight OR space craft OR extraterrestrial environment OR weightlessness Simulation OR Mars) **AND** (bone and bones OR bone density OR alveolar bone loss)	932 articles
(space flight OR space craft OR extraterrestrial environment OR weightlessness Simulation OR Mars) **AND** Saliva	50 articles
(space flight OR space craft OR extraterrestrial environment OR weightlessness Simulation OR Mars) **AND** Masticatory Muscles	3 articles
(space flight OR space craft OR extraterrestrial environment OR weightlessness Simulation OR Mars) **AND** Mandible	13 articles
Total :	998 articles

3.4. Flowchart:

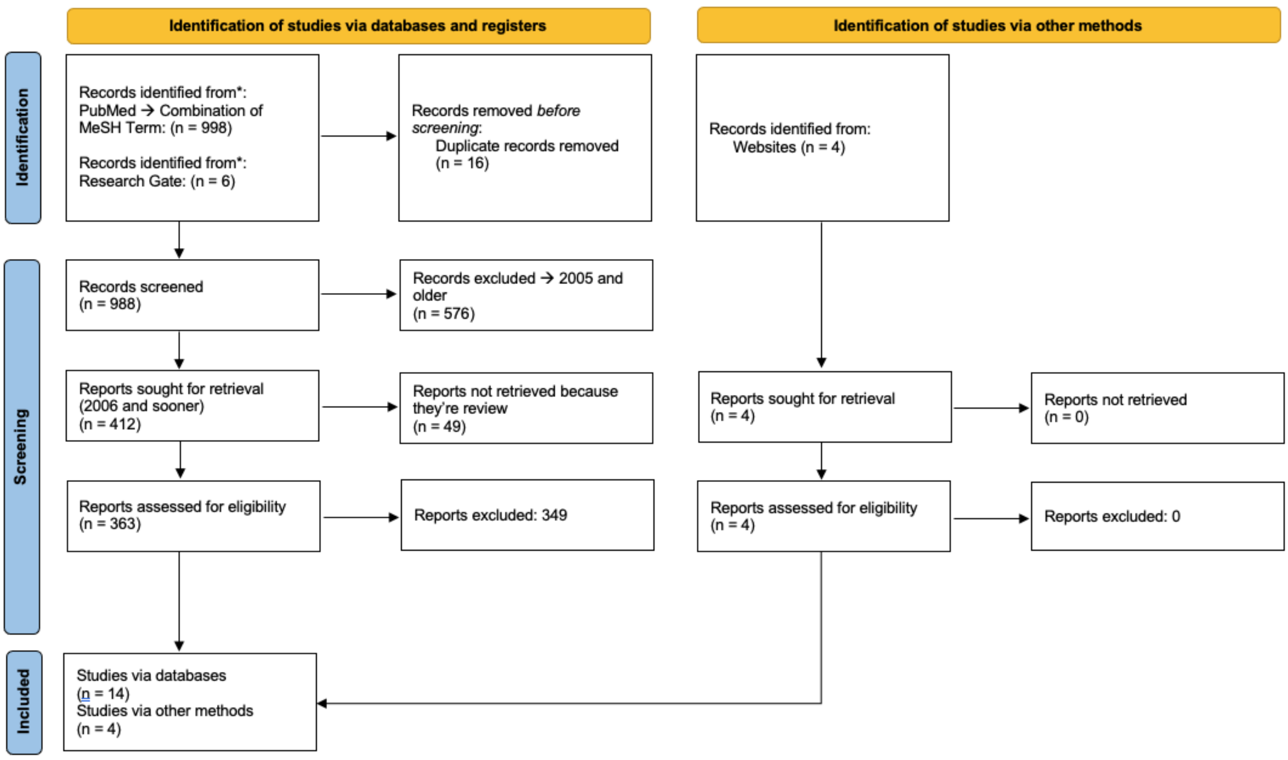

Figure 1: *Flow diagram of the research strategy*

4. RESULTS

Autor Year Reference	Material and Methods	Objectives	Mean results	Conclusion
Dadwal et al. 2019 (2)	- For the mandible (n = 9–10) the region of interest (ROI) was a single coronal slice taken through the middle of the posterior root of the first molar. The molar was then subtracted from the ROI prior to performing a 2D analysis on the mandible with the incisor. A separate 2D analysis was also completed on just the incisor. Mandible variables included Tissue Area (T.Ar), Bone Area (B.Ar), and Marrow Area (M.Ar). The latter was calculated as follows : M.Ar = T.Ar – B.Ar. Of note, the mandible values were obtained by subtracting the equivalent incisor values. - The lingual cementum–enamel to alveolar bone crest distance (CEJ–ABC) was acquired by measuring the distance from the cementum edge on the lingual tooth surface to the alveolar bone apex.		- No significant differences were detected between any of the groups. - There was a non-significant 15% increase in the cementoenamel junction to alveolar bone crest for the Flight + Surgery compared to Flight + Sham group. - We report a decrease in enamel and dentin T.Ar in Flight + Sham incisors compared to Ground + Sham incisors due to a 40% increase in dental pulp cavity or area (Pu.Ar) in the Flight + Sham incisors. - Normal dental growth of the incisor may be impaired in spaceflight mice.	- The most important findings in this study were changes observed in the tibia.
Dagdeviren et al. 2018 (3)	- Mandibles and incisors of mice flown on the US STS-135 space shuttle mission and the Russian Bion-M1 satellite were studied using micro-computed tomography and immunohistochemistry. Ground controls were mice housed in standard vivarium cages and flight habitats.	- To determine if spaceflight and microgravity affect non-weight bearing bones and development and mineralization of teeth, reasoning that combining an organ and a cellular level approach can lead to greater insights about these effects.	- Incisor length was greater in the 13-day STS-135 flight mice than in either control group. Initial incisor mineralization occurred more posteriorly, and incisor, enamel and dentin volumes and enamel and dentin thicknesses were greater in the 30-day Bion-M1 flight. - Mandibular bone volume (BV) was increased in STS-135 flight and habitat groups and decreased in Bion-M1 flight and habitat groups compared to vivarium controls.	- Microgravity has measurable effects on mandibular bone physiology and incisor development and mineralization. The results also showed that the habitat had an effect either in flight or ground control samples, as demonstrated by the changes in BV and apparent slowing of incisor eruption. Therefore, developing appropriate habitats is critical for future spaceflight missions.

Treffel et al. 2016 (4)	- Twelve healthy male volunteers participated in a 3-day dry immersion study. Before and immediately after exposure we measured maximal bite, force using piezoresistive sensors. - The mechanical properties of the jaw and cervical muscles were evaluated before, during, and after dry immersion using MyotonPRO. - Stabilometric measurements of center of pressure were performed before and after dry immersion in two mandibular positions: rest position without jaw clenching, and intercuspidal position during voluntary teeth clenching.	- The objective of the study was to determine the influence of simulated microgravity by exposure to dry immersion on the craniomandibular system.	- Results revealed no significant changes of maximal bite force after dry immersion. All postural parameters were significantly altered by dry immersion. - There were however no significant differences in stabilometric data according to mandibular position. Moreover, the masseter tonicity increased immediately after the end of dry immersion period.	- This study reveals that there is no evidence of masticatory muscles and maximal byte force dysfunctions during 3 days of dry immersion. - Our results suggest a link between postural disturbance after dry immersion and masseter tonicity. Posturographic measurements of the center of pressure were not affected by dental occlusion. - However, it should be mentioned that postural sway parameters were measured in healthy subjects without dental or temporomandibular disorders. - Dental occlusion disorder could disturb the postural balance. Jaw clenching should be taken into account as a condition, like eyes closed and eyes open, in postural studies.
Bohra et al. 2016 (5)		- List the different main parameters that have a significant impact on the maxillofacial sphere.	- Prevalence of periodontitis, dental caries, bone loss, pain and numbness of teeth and oral tissues, salivary duct calculi, and cancer in microgravity conditions, along with certain radiographic changes in weightlessness condition. - Bone loss results after each space flight leading to osteoporotic changes and teeth mobility. Normal oral mucosal flora gets altered with the changes in the salivary flow rate and alterations in the quality of saliva - Cosmic radiations have the capacity to induce malignant changes, thus resulting in precancerous changes in the oral mucosa.	- Aeronautical dentistry is an upcoming branch which needs to be flourished by proper understanding of the extra-terrestrial environmental conditions and their respective effect on oral microflora - Further knowledge of exobiological condition is required to protect us from cosmologic health hazards.

Ghosh et al. 2015 (6)	- Mandible properties were assessed using high-resolution micro-CT. Bones were wrapped in parafilm and scanned at 60 kV. - A single slice from the central region of the first mandible molar was analyzed for three parameters: total bone volume (both cortical and trabecular bone, excluding the molar and incisor) and lingual cementum–enamel to alveolar bone crest distance (CEJ–AC), and tissue mineralization. - CEJ–AC, as its name indicates, is the measured distance from the cementum edge on lingual tooth surface to the alveolar bone apex.	- To determine the effects of spaceflight on mandibular bone properties	- There were no differences in tissue mineralization with spaceflight in either mission. - Mandibles from SF mice from the STS-135 mission had no difference in bone volume/tissue volume, however it was lower in in space flight mice from STS-131. - The distance from the CEJ–AC was shorter in SF mice from STS-131 with no difference in mice from STS-135.	- Spaceflight led to mandibular bone changes in mice, suggesting that non-weight bearing bones are altered in a weightless environment - Results from the present study of mandibles combined with those of the calvaria from the same animals suggest that other factors associated with spaceflight may also be important factors which modulate the remodeling process of non-weight bearing bones in the head.
Philippou et al. 2015 (7)	- Masticatory muscles in mice was subjected to a liquid diet, which eliminates the loading from normal chewing but still affords muscle movement and activity. - Muscles were blotted, weighed, and rapidly frozen in liquid nitrogen for immunoblotting and expression analysis or myofibril isolation for function, or they were placed in 4% paraformaldehyde for up to 4 hours at 4°C, incubated with 20% sucrose overnight on a shaker at 4°C - Frozen cross-sections (10 mm thick) were cut from the mid-belly of each left MA muscle and subjected to immunohistochemistry for laminin.	- Comparing the signaling, expression, and functional responses of appendicular versus masticatory muscles to the microgravity environment of space flight.	- Myofibril-specific force from both control and flight MAs were similar to flight TA muscles, yet power was compromised by 40% following flight. Continued loading in microgravity prevents atrophy, but masticatory muscles have a different set point that mimics disuse atrophy in the appendicular muscle.	- These findings indicate that continued mechanical loading of skeletal muscle in a weightlessness environment can prevent atrophy but may not be sufficient to protect against loss of power.
Zaitsu et al. 2014 (8)		- Possible dental/oral problems in the space environment and the current dental management of astronauts by NASA are described and the countermeasures will be discussed.		- Several symptoms of dental/oral problems occur on astronauts in the space environment to date and the current countermeasure is only the dental examination before mission launch and treatment manual for some dental emergency in spacecraft. - Examination of salivary conditions and programs promoting oral hygiene of astronauts in spacecraft are to be urgently prepared for the prolonged spaceflight for lunar and Mars exploration.

Rai et al. 2013 (9)	- The 24 healthy crew members were recruited. The orofacial pain questionnaire was applied to measure pain experience using descriptors from the McGill Pain Questionnaire. Salivary cortisol and melatonin were measured.	- The aim of this study was to test the association between quality of sleep and stress in individuals with TMD (temporomandibular joint dysfunction) in simulated Mars mission.	- The 15 crew members reported temporomandibular joint pain after 6 days of mission. On dental examination, 5 crew members reported simple muscle pain (SM) and other 10 crew members with TMD. Compared to the TMD group, the SM group also reported significantly poorer sleep duration. The TMD group reported non-significantly more daytime dysfunction than the control. Higher levels of salivary cortisol and salivary melatonin were reported in the TMD group as compared to other group.	- This study concludes that both quality of sleep and stress levels due to extreme condition (simulated Mars mission) were associated with TMD in simulated Mars mission.
Rai et al. 2013 (10)	- The 12 crew members were selected from Mars desert research stations. - Intraoral samples were taken from each crew member between 7:00 and 7:30 AM before brushing, rinsing with water, and breakfast. Different samples (e.g., dental plaque and stimulated saliva) were taken before the mission, at 1 week, and at mission completion. Oral clinical examinations were done to establish the extent of dental plaque, calculus formation, and alterations in tooth, bone, gingiva, and other soft tissues. - Probing depth at six sites per tooth was measured using a manual probe. Clinical loss of attachment was determined by measuring interproximal sites only. - A wax carver was used to collect dental plaque from buccal, lingual, and proximal surfaces of two anterior and posterior maxillary and mandibular teeth. - Unstimulated saliva was collected, as described in a previous study. Stimulated saliva was collected using a saliva collection device. Salivary flow rate was measured using a standardized technique. Salivary cortisol and α-amylase were also measured.	- The present study was designed to investigate the effects of a simulated Mars mission on oral health, including periodontal status, using a simulated Skylab mission at the Mars desert research station, USA.	- Values for probing depth, clinical loss of attachment, and bleeding on probing were significantly higher at 1 week and mission end, as compared with baseline (before mission). - As compared with baseline, levels of total anaerobes, *Bacteroides*, *Fusobacterium*, and *Veillonella* were higher at 1 week and mostly remained so at 2 weeks. In addition, levels of total aerobes, *Neisseria*, *Lactobacilli*, *Staphylococci*, *Candida*, and *enteric bacilli* were higher at 1 week as compared with baseline and were almost unchanged at 2 weeks. The level of *Streptococcus mutans* was significantly higher as compared with baseline - Salivary cortisol, α-amylase, and current stress scores were significantly higher at the end of the mission as compared with baseline. Salivary IgG levels were significantly lower at 1 week as compared with baseline and is positively correlated with clinical periodontal parameters. - *S. mutans* level strongly positively correlated with salivary IgG, and with salivary cortisol, and α-amylase.	- Our findings suggest that effects on periodontal parameters and oral immunity were increased in the simulated environment, which could be due to stress factors. Furthermore, reduction in salivary flow and Ig levels in saliva were probably responsible for increases in bacteria and yeast levels. - To verify the relationship between stress status and periodontal health in simulated Mars missions, future studies will need to use larger patient samples and a longer duration of follow-up.

Rachna et al. 2013 (11)		- This article highlight the effects of microgravity on human body with emphasis on oro-facial structures. - It also gives information regarding the newly emerged speciality of aeronautical dentistry.	- Bone loss of 1-2 % per month in flight. - Peri-implant bone levels remains stable after 6 month in microgravity, and the implant continued to function without complications.	- It is time to recognize the speciality of aeraunautical dentistry since oral health plays a pivotal role in the overall health and wellbeing of astronauts.
Rai et al. 2012 (12)	- Twelve crew members were selected. Taste reactions and intensity of the taste sensations to quinine sulfate, citric acid, and sucrose were tested before and after mental and physical tasks for one hour. - Psychological mood states by profile of mood state, salivary, salivary alpha amylase and cortisol, and current stress test scores were measured before and after mental and physical tasks.	- This study was planned to find the effects of physical and mental workload on taste sensitivity and salivary stress biomarkers.	- After the mental and physical tasks, the perceived duration of bitter, sour, and sweet taste sensations was significantly shortened relative to control group. There were good correlations between average time intensity of sweetness, bitterness, sourness and cortisol levels.	- Taste alterations due to stress can have an effect on the health and confidence of astronauts in long-term space missions. Thus, this issue remains one of the important issues for future human explorations.
Anil Menon 2012 (13)		- The objective is to identify which dental emergency is most likely to occur in-flight and near-flight. What's are the odd for each of them to appear, and which one is most problematic onboard the ISS.	- There is no written documentation of an in-flight dental emergency in US astronauts. - The medical conditions most likely to end in an evacuation of the ISS is a dental abscess.	- In-flight dental emergencies have been a rare event regarding current data records. - Pre-flight events requiring root canals had the potential for significant mission impact.
Belavý et al. 2010 (14)	- Twenty-four male subjects as part of the 2nd Berlin Bed Rest Study performed RVE (n=7), RE (n=8) or no exercise (control, n = 9) during 60-day head-down tilt bed rest. - Whole-body, spine and total hip dual X-ray absorptiometry (DXA) measurements as well as peripheral quantitative computed tomography measurements of the tibia were conducted during bed rest and up to 90 days afterwards.	- The addition of whole-body vibration to high-load resistive exercise (RVE) may be more effective in preventing bone loss in spaceflight and its simulation (bed rest) than resistive exercise alone (RE), though this hypothesis has not been tested in humans.	- A better retention of bone mass in RVE than RE was seen at the tibial diaphysis and proximal femur. - Compared to control, RVE retained bone mass at the distal tibia and DXA leg sub-region but with no significant difference to RE - RE impacted significantly on DXA leg sub-region bone mass only. Calf muscle size was impacted similarly by both RVE and RE.	- Combining whole-body vibration and high-load resistance exercise may be more efficient than high-load resistive exercise alone in preventing bone loss at some skeletal sites during and after prolonged bed rest. - The effects of exercise during bed rest impact upon bone recovery up to 3 months afterwards.

Rai et al. 2010 (15)	- The subjects of this investigation were 10 male and 10 female volunteers who were exposed to 3 weeks of -6°HDT bed rest. - Dual-energy X-ray absorptiometry was used to measure bone density and bone mineral content in alveolar bone from the mandibular canine to the third molar, as well as in the mandibular ramus, before, during, and after exposure to conditions of simulated microgravity. - GCF (ie, MMP-8, MMP-9, cathepsin K, and osteocalcin) and salivary and serum osteocalcin levels were measured by enzyme-linked immunosorbent assays.	- This study was designed to assess bone mineral density, bone mineral content, GCF (ie, cathepsin K, MMP-8, MMP-9, and osteocalcin), and salivary and serum osteocalcin in normal healthy men and women under conditions of simulated microgravity, namely, -6°head-down tilt (HDT) bed rest.	- Bone mineral density and bone mineral content were significantly lower under conditions of simulated microgravity in both sexes. The decreases were greater in women than in men, but the differences between sexes were not significant. - Cathepsin, osteocalcin, MMP-8, and MMP-9 levels were significantly higher under conditions of simulated microgravity than under normal conditions; the increases were greater in women than in men, but the differences were not significant.	- The findings suggest that bone loss is greater in women than in men. Additional comprehensive studies with larger sample sizes are required for the investigation of simulated microgravity and microgravity. - Although there were a number of limitations in this study, including the fact that dietary factors, demographic data, and other important factors were not included in the analysis,
Rai et al. 2009 (16)	- 20 healthy male volunteers were studied before, during, just after and after 12 hr of the simulated microgravity condition of 6° head-down-tilt (HDT) bed rest - Facial function tests, mouth opening, jaw movements, tongue movements, facial sensation (Touch, pressure, temperature), taste, odour, perception of food, Salivary vitamins E and C, lactate dehygrogenase isoenzyme, MIP 1 á, Glucosyltransfer â, Malonaldehyde, 8-hydroxydeoxyguanosine, Thiocynate, salivary contents and salivary flow rate were measured.	- To determine the influence of a simulated microgravity on oral cavity.	- Flow rate, sodium, potassium, calcium, phosphate, protein, lactate dehygrogenase, MIP 1 alpha, Malonaldehyde, 8-hydroxydeoxyguanosine, thiocynate were found to increase significantly - Amylase activity, vitamin E & C and mouth opening were decreased in simulation environments in contradiction to normal and recovery stage. - Mild pain of teeth, facial oedema, mild pain mandibular angle regions, pain in sublingual and submandibular opening duct regions, abnormal facial expression, loss of sensation of pain and temperature, decreased the tongue and mandibular movement in simulation microgravity environments.	- The reversible effect of microgravity is oedema of face, change in taste, abnormal expression of face, teeth pain and xerostomia. - The non reversible effect of microgravity such as prevalence of periodontal disease, dental caries but different pattern than normal, stone formation in salivary duct, pre cancer or cancer, fracture of maxillary and mandibular bone and xerostomia more in astronaut as compared to normal persons. - Further study will be required on large scale and long term effect of microgavity on oral cavity to prevent the adverse effect on oral cavity.

William Stenberg 2005 (17)	- Since we do not yet have a lot of long-term data on the fate of the oral structures in space, we can look at the condition of the oral structures in analogous environments. (submarine experience, space travel environment, space shuttle experience, MIR experience, related studies and Mars expedition planning)	- To determine the consequences of space travel on the oral structure, more specifically on the oral bone.	- Recent research in periodontology has shown that osteoporotic periodontal bone is more susceptible to breakdown than healthy bone, and that tooth loss is more frequent in subjects with osteoporosis. The strategies which may prove useful in the long bones, exercise, etc., are not adaptable to the oral bone. The bone surrounding the teeth is very susceptible to damage from the type of overloading that this would cause. - Strategies to preserve the oral bone may include dietary and pharmacologic measures, as well as artificial gravity.	- Tooth loss will occur with unabated osteoporosis, so something has to be done when travelling through zero G environments. Space osteoporosis need not be a showstopper if we manage it with care, and continue to develop research as we proceed. - If we can provide artificial gravity, it appears that problems will be limited.
Sforza et al. 2004 (18)	- Eleven male astronauts currently training at the Russian Cosmonauts Center of Star City aged 31 to 54 years, were analyzed. All subjects were in general good health and free from pathologies of the neck and stomatognathic apparatus. - An alginate impression of their dental arches was taken and cast in dental stone, had only posterior contacts (from second premolar to second/first permanent molar), and modified the occlusal contacts to obtain a more symmetric standardized contraction of the jaw elevator and neck muscles during teeth clenching. - Surface electromyography (EMG) of the masseter, temporalis anterior, and sternocleidomastoid (SCM) muscles was measured in all subjects with and without the occlusal splint. Body postural oscillations, as assessed by the modification of the position of the center of foot pressure (COP), were measured with eyes open and closed, with and without the occlusal splint.	- The current pilot study used normal gravity conditions to investigate the hypothesis of a functional coupling between occlusion and neck muscles and body postural oscillations.	- In almost all subjects, one or more pairs of muscles showed asymmetric standardized activity while clenching in intercuspal position (without splint) - When clenching on the occlusal splint, the standardized activity of all three muscular pairs became more equilibrated and symmetric in all subjects. - On average, the area of oscillation of COP was larger without the splint than with the EMG adjusted splint	- A functionally more symmetric maxillo-mandibular position resulted in a more symmetric sternocleido-mastoid muscle contraction pattern and less body sway. - The current data underline how modifications in the contraction of the muscles may affect the body as a whole and could be considered a first approach to this field of investigation. If a reversible modification of the occlusal surface could reduce body sway in basal conditions, its effect during or after a journey in microgravity is worth investigating.

Table 1: *Table of results*

5. DISCUSSION

5.1. SETTING THE CONTEXT FOR AERONAUTICAL DENTISTRY:

5.1.1. Living conditions on the ISS:

The International Space Station (ISS) is a set of modules from different countries/organizations (Russian, American, Japanese, European ...). Long of 108 meters and wide of 73 meters, it allows a habitable volume of 388 m3.

In order to realize in which conditions the ISS evolves, we must explain how the atmosphere is cut. The atmosphere extends from the ground to 800 Kms of altitude and stretches up to 10000 Kms of altitude. It is composed of several layers organized as such:

- The troposphere from 0 to 16km of altitude
- The stratosphere from 16 to 50 km of altitude
- The mesosphere from 50 to 80 km altitude
- The thermosphere from 80 to 640 km altitude
- The exosphere from 640 to 10000 km of altitude

The ISS evolves in an orbit located at 408 Kms of altitude, it is thus located in the thermosphere. This orbit measures 42543 kms, it makes the revolution in 1h30. It has a speed of approximately 28000 km/h.

The content of the ISS is located in a state of microgravity. This means that the sum of the force of gravity and the inertial force is zero. It is therefore possible to "float" freely in the ISS.

The ISS is also subject to strong radiation due to the solar wind. An astronaut is exposed to an average of 5 mSv/week. On Earth, it is estimated that a person subjected to daily radiation due to his professional activity must remain below 20 mSv/year! An astronaut undergoes in 6 months of life in the ISS 120 mSv! Some examples of possible exposure on Earth to put into perspective the very high doses suffered by astronauts:

- Mammography: 0.4 mSv
- Computed Tomography of the head: 2 mSv
- Computed Tomography of the whole body: 20 mSv
- A pilot of transatlantic flights: 2 mSv / year

Finally, the ISS is a system that operates in isolation since the year 2000. It is a restricted and hermetic environment where water and air are recycled to the maximum for more than 20 years!

5.1.2. History of accidents of the oral sphere in spatial history:

Accidents involving the oral sphere have appeared several times in space history. Beyond being problematic and disabling for the astronaut's missions, they have the interest to highlight the causes of their appearances. We can thus anticipate the complications, the situations most likely to occur.

Some notable examples:

Regarding crowns, during a flight to Мир station (MIR) there was a crown displacement [8]. Some tooth fractures, as well as dislodged teeth due to vibrations [8][13], a crown displacement that was put back in place in the station [13].

Several problems due to pulpitis, abscesses, poorly performed endodontics and the resulting pain have also occurred. A cosmonaut in 1978 indeed reported to have suffered from very disabling tooth pain, during the last two weeks of his 96-day mission on the Salut 6 [8]. An astronaut suffered from a pulpitis 3 months before the takeoff, another astronaut at his return on Earth [8]. These characteristic pains would have been particularly heavy to support in the middle of a mission and could have seriously affected the capacity of the astronauts to carry out their tasks [13]. A last case was reported 2 weeks before a flight, 2 periapical abscesses were detected and were caused by the bad condition of an amalgam [13]. Finally, an endodontia was dislodged due to the vibrations of the rocket launch [13].

A few caries presences are also to be noted, fortunately they were temporarily treated thanks to a dental kit present in the station [13].

5.1.3. Current NASA/ESA knowledge of risks to astronauts:

There are few publications that relate the effects of missions in microgravity conditions on the oral sphere. However, some trends have been observed in the probability of periodontitis, caries, bone loss, pain, salivary duct calculus and finally cancers [11].

Thanks to twenty years of experience, NASA succeeded identifying and quantifying the probability of occurrence of 6 major dental problems [8]. They are considered the most important to be treated on long term missions:

- Abcess ≈ 0.02 pers/year
- Avulsion / Tooth loss ≈ 0.003 pers/year
- Caries ≈ 0.39 pers/year
- Crown Replacement ≈ 0.005 pers/year
- Exposed pulp / Pulptis ≈ 0.02 pers/year
- Filling replacement ≈ 0.005 pers/year

Several observations have been made and confirmed over the years and situations. Caries, acute periodontitis as well as pulpitis can greatly affect the astronaut's ability to concentrate and perform daily tasks on the ISS [8]. Abscesses and root events are the most likely pathological conditions to lead to evacuation from the ISS [13].

Increase of dental plaque and aggravation of gingivitis [8]. Deterioration of the periodontal structure, and a decrease in salivary flow. Moreover, it has been observed in simulated microgravity conditions (bed rest study) a decrease of oral defense capacity, as well as an increase of molecules present in saliva traducing an increase of stress [8]. Different studies conducted in terrestrial conditions similar to space travel (Antarctica, submarines, wild and hostile environments) reflect this high incidence of dental problems [13].

A trend has been observed on the probability of occurrence of dental complications. Longer missions increase the risk of in-flight dental problems in a similar way to those measured pre-flight [13].

Fortunately, in-flight events are quite rare according to the observations made [13].

5.1.4. The importance of creating new methods of diagnosis, prevention and treatment in the space environment:

The creation of aeronautical dentistry is highly desirable, in order to adequately prepare astronauts to face dental emergencies [11]. In the coming decades, humans are destined to be in contact with microgravity more and more often and for longer periods of time.

Thus, more advanced knowledge on exobiology is an essential prerequisite in order to protect us from the various threats that the universe presents [5]. Aeronautical dentistry is therefore an essential branch to be developed in order to provide us with the tools and adequate treatments regarding oral health complications in microgravity [5].

Simple tools such as saliva testing or programs to promote oral hygiene do not yet formally exist and must be quickly and urgently prepared [8].

5.2. PROBLEMS / IMPACTS OF LIVING CONDITIONS IN THE ISS ON ORAL HEALTH:

Few studies have been carried out on the impact of microgravity on oral health [5]. Nevertheless, some studies have been conducted on animal models, others in situations similar to microgravity such as the bed rest studies, 6° Head Down Tilt (HDT) or Dry Immersion. They allow us to see the consequences of the space environment on oral health.

5.2.1. The masticatory muscles:

There is little data available on the effects of microgravity regarding the mastication's muscles [11].

A study was conducted on an animal model (mice), in order to compare the differences in response and adaptation to microgravity of the appendicular muscle (tibialis anterior = TA) and the masticatory muscle (masseter = MA) [7]. After 13 days in space, it was noted that the MA was not affected by microgravity. There was no major change in the size of the fibers or their distribution within the muscle compared to the control group on the ground [7]. It seems that a continuous load in microgravity is able to prevent atrophy phenomena. A liquid diet effectively results in the atrophy of the superficial fibers of the MAs [4], this reinforces the idea that the mechanical stimulation by chewing or repeated effort support a protective effect against muscle atrophy [4][7].

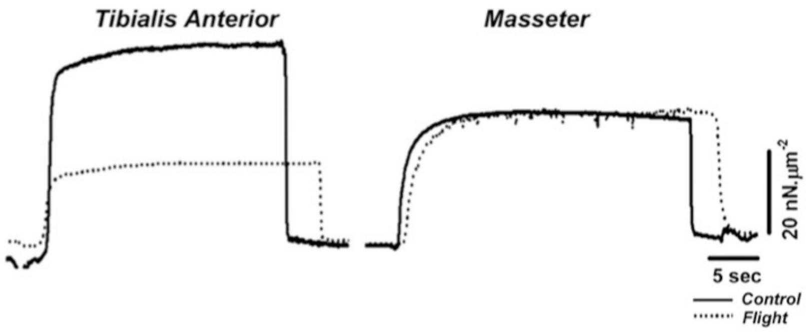

Figure 2: *Superimposition of isometric contractions produced by myofibrils isolated from TA (left) and MA (right) muscles in control and flight groups* [7].

An evaluation of the gene expression of TAs and MAs reveals an altered and predictable genetic response of TAs to microgravity, whereas MAs do not seem to express genetic sensitivity to microgravity [7]. The MAs keep intact their molecular signaling pathway related to load sensitivity, they do not follow this change in gene expression related to load decrease, as observed in appendicular muscles [7].

The specific strength of the MAs remained unchanged between the control group (on the ground) and the group in flight. Contrary to the TAs where a significant difference between the ground and the flight group is observed (*) :

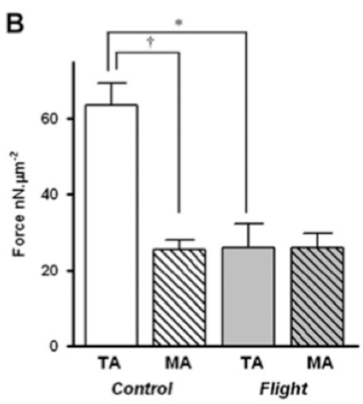

Figure 3: *Mean values of specific forces (B) calculated after experiments with myofibrils isolated from TA (open bars) and MA (hatched bars) muscles from control (white bars) and flight (gray bars) groups* [7].

The strength, power and muscle velocity of the TAs is greatly decreased between the control group and the flight group, this decrease is much less pronounced for the MAs :

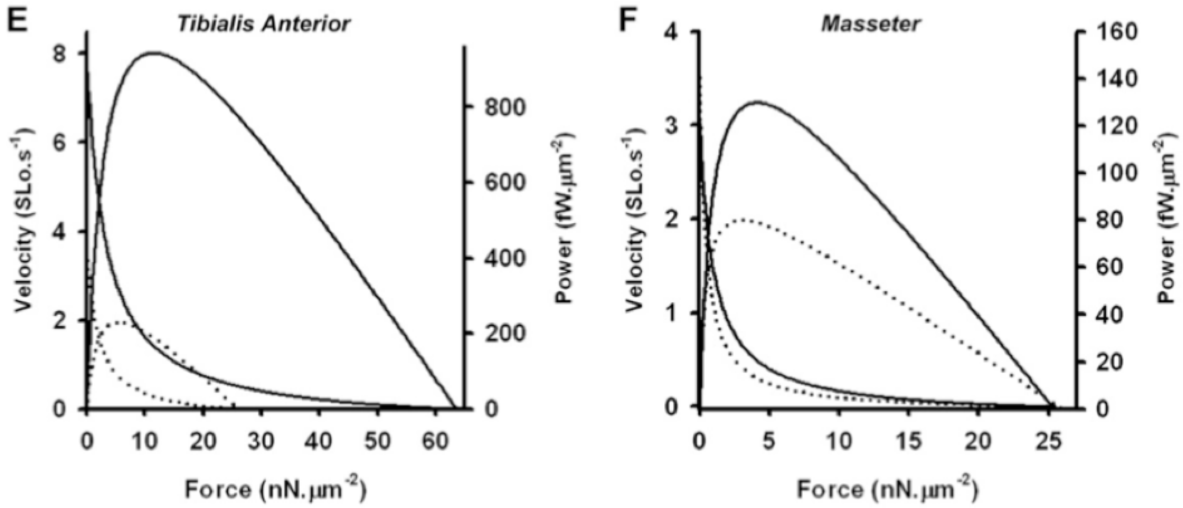

Figure 4: *Velocity and power plotted against absolute forces compiled from all measurements for TA (E) and MA (F). Solid lines are control, and dotted lines are flight*[7].

A second study was conducted in a simulated state of microgravity, Dry Immersion (DI). The contraction capacities (stiffness, frequency, relaxation time) of the MAs and the sternocleidomastoid muscles (SCM) were measured [4]:

Parameter	BDC-1 (n = 9)	DI 1 (n = 9)	DI 3 (n = 9)	R0 (n = 9)	*p* value
Masseters					
Stiffness (N. m^{-1})	334.1 ± 8.0	329.8 ± 10.3	323.2 ± 15.5	367.9 ± 21.3 *	0.028
Frequency (Hz)	16.5 ± 0.3	16.2 ± 0.3	16.2 ± 0.4	17.8 ± 0.7 *	0.003
Relaxation time (ms)	16.7 ± 0.4	16.7 ± 0.4	17.3± 0.8	15.2 ± 0.7 **	0.011
Sternocleidomastoid					
Stiffness (N. m^{-1})	211.0 ± 17.7	190.3 ± 8.9	199.8 ± 12.0	197.8 ± 10.5	0.485
Frequency (Hz)	13.7 ± 0.5	13.1 ± 0.3	13.4 ± 0.3	13.4 ± 0.3	0.478
Relaxation time (ms)	23.2 ± 0.8	24.3 ± 0.7	23.5 ± 0.8	23.4 ± 0.9	0.663

Days are indicated as follows: the last day of control period (BDC-1), the first day (DI 1) and third day (DI 3) of dry immersion, and the first day of recovery period (R0). Values are means ± standard error.

Table 2: *Combined (left and right) changes in jaw and cervical muscles stiffness, frequency and relaxation time before, during and after dry immersion*[4].

There is a significant difference between the 3 contraction parameters concerning the MAs. The stifness and frequency is significantly higher on the first day of rest compared to the last control day (before the beginning of the experiment). The relaxation time is significantly shorter on the first rest day compared to the last control day. Other measures concerning maximal byte force and contraction symmetry did not measure a significant difference [4].

The authors put the results into perspective, stating that this type of test and measurement requires longer experimental times and a diet with a consistency similar to that of astronauts, in order to get as close as possible to physical reality.

5.2.2. Bony arcades:

The mandibular and maxillary bony arcades are essential structures in the maintenance of the teeth and are the support of the periodontium. A significant alteration of the structure of the bony arcades would have serious consequences on oral health in general. They are therefore privileged targets in the various studies concerning space travel.

It has been estimated that the loss of bone mass due to demineralization under microgravity is about 1-2%. Thus, it was reported an osteoporosis of the maxilla and the mandible in space environment, as well as in simulated HDT environment. In the HDT environment, the bone mineral density and bone mineral content was significantly reduced in both men and women. Measurements revealed a pronounced loss in women, however the difference was not significant compared to men [15].

Unfortunately, due to the limited number of studies it is difficult to extrapolate the loss of bone mass density under simulated HDT conditions to the actual flight conditions experienced by astronauts [15].

Some molecular factors and cellular actors have been identified as being responsible for bone loss. Prostaglandin E2 (PGE2) and Interleukin-6 (IL-6) are both known to be responsible for the formation of osteoclasts, the cells that resorb bone. PGE2 concentrations were measured 4.5 to 136 higher in samples present in flight compared to ground cultures. Regarding IL-6 mRNA, concentrations of 6.4 to 9.3 were measured to be higher in flight compared to ground cultures. Osteoclasts produce MMP-8, MMP-9, Osteocalcin and Cathepsin K. These 4 molecules were also measured at higher levels in microgravity conditions. Osteocalcin has a role in bone resorption, while MMP-8 has a protective and anti-inflammatory role that prevents bone loss [15]. This increase in MMP-8 suggests that it also exerts a negative feedback role on the effect of osteocalcin, to prevent excessive bone loss.

A study was conducted on mice to estimate the Bone Area (B.Ar), Tissue Area (T.Ar), the relationship between the two (B.Ar/T.Ar), the Marrow Area (M.Ar) and finally the cementoenamel junction to alveolar bone crest length (CEJ-ABC) [2]:

Parameters	Ground		Flight	
	Sham	Surgery	Sham	Surgery
Mandible				
B.Ar/T.Ar (%)	69 (2)	68 (2)	68 (2)	69 (1)
M.Ar (mm^2)	0.61 (0.05)	0.63 (0.04)	0.63 (0.05)	0.61 (0.03)
T.Ar (mm^2)	1.96 (0.08)	1.94 (0.02)	1.96 (0.06)	1.95 (0.05)
B.Ar (mm^2)	1.34 (0.04)	1.31 (0.02)	1.32 (0.05)	1.33 (0.04)
CEJ-ABC (mm)	0.204 (0.036)	0.192 (0.008)	0.193 (0.025)	0.221 (0.027)

Table 3: *Bone parameters for the mandible [2].*

The mandible was analyzed after extraction of the molars and incisors. On the 5 parameters evaluated there were no significant differences between the ground control group and the flight group. A non-significant increase of 15% was measured between the CEJ-ABC of the Flight + Surgery group compared to the Flight + Sham group [2].

To conclude, the bony arcades are undoubtedly subject to structural and physiological changes in a microgravity environment. We could therefore think of preserving the structure of the bony arcades by subjecting them to repeated mechanical stimuli, which have been proven to be useful for preserving appendicular bones. Unfortunately, this strategy is not suitable in this situation, as the bone surrounding the tooth is very susceptible to damage due to mechanical overload. By clenching the teeth with excessive force, the lower jaw acts as a lever concentrating the force on the contact area between the mandible and the temporal bone. The cartilage separating them would be subjected to inappropriate stresses resulting in deformation, perforation or destruction of the cartilage. Thus, closing the jaw with force would not result in a strengthening of the bone, but in its deterioration. An adequate strategy to preserve the bone would have to turn to pharmacological means, an adapted diet or artificial gravity [17].

5.2.3. Teeth:

We have just seen that osteoporosis of the bony arcades is inevitable in a microgravity situation. Despite a possible recovery of the bone after the return to Earth, this so-called space osteoporosis is worrying in several aspects. One of these aspects is the loss of teeth that would result. It's a major problem cause it's, by nature, irreversible [17].

Several studies have been conducted on mice incisors [2][3]. The previous study [2] which measured different parameters on the mandible also measured that parameters on the incisors. Three additional parameters inherent to the incisors were measured, the enamel+dentin area ([E+D]Ar), the relationship between the enamel+dentin area and the tissue area ([E+D]Ar/T.Ar) and the pulp area (Pu.Ar) :

Parameters	Ground		Flight	
	Sham	Surgery	Sham	Surgery
Incisor				
[E+D]Ar/T.Ar (%)	82 (6)	80 (9)	75 (6)†	82 (5)
T.Ar (mm^2)	0.468 (0.015)	0.466 (0.005)	0.474 (0.012)	0.481 (0.015)
[E+D]Ar (mm^2)	0.38 (0.03)	0.38 (0.03)	0.36 (0.03)	0.39 (0.04)
Pu.Ar (mm^2)	0.083 (0.027)	0.089 (0.030)	0.116 (0.027)†	0.087 ± (0.023)

Table 4: *Bone parameters for the incisor [2].*

The Flight+Sham group observed a significant decrease of 9% on [E+D]Ar/T.Ar parameter compared to the Ground+Sham group. This decrease in [E+D]Ar/T.Ar appears to be a consequence of the 40% increase in Pu.Ar observed in the Flight+Sham group. These data suggest that incisor growth is spatially altered, with a spatially increased pulp/(dentin+enamel) surface area relationship [2].

A second study was conducted on mice populations on board the US STS-135 space shuttle mission for 13 days and the Russian Bion-M1 satellite for 30 days. The incisor teeth's development and mineralization were compromised. The 30-day mission saw an increase in incisor and enamel volume, as well as enamel and dentin thickness, while the 13-day mission saw an increase in incisor length [3].

Regulatory proteins present in enamel and dentin were studied in order to observe a response / adaptation to microgravity conditions. The major enamel matrix protein, Amelogenin, is involved in the regulation of hydroxyapatite crystal formation as well as the development of normal enamel thickness. Amelogenin reactivity was reduced in the maturation ameloblasts of the 13-day STS-135 flight mice, despite enamel thickness being unaltered. This could indicate that the enamel matrix's deterioration and resorption have been changed. As a result, the impacts on Amelogenin expression could be a physiologic response to microgravity. Dentin sialoprotein, an important non-collagenous protein thought to be responsible for the regulation of dentin mineralization, was also studied. However, no changes in this protein were observed [(3)].

These modifications may have an impact on human dentition during long-duration spaceflight. Reduced mandibular bone volume, for example, could impact tooth support. Changes in the activity and metabolism of odontoblasts, or tooth pulp cells, can affect dental nerves and cause pain [(3)].

5.2.4. *Temporo-mandibular joint:*

The temporomandibular joint (TMJ) is a joint structure that is quite sensitive to many stimuli such as stress, circadian rhythm, sleep quality or physiological balance [(5)(9)].

A study measured the association between these different stimuli and temporomandibular disorder (TMD). TMD is a frequent stress-related illness, which have a multifactorial etiology. TMD is linked to cortical and melatonin secretion abnormalities. This study recruited 24 crew members on a simulated Mars Mission. After 6 days on the mission, 15 crew members complained of temporomandibular joint pain. 5 crew members expressed simple muscle pain (SM) after a dental checkup, while the other 10 crew members had TMD. More emotive descriptors of their pain experience were endorsed by the TMD group. The SM group also reported considerably shorter sleep duration than the TMD group. In comparison to the other groups, the TMD group had higher levels of salivary cortisol and salivary melatonin. The TMD and SM groups had higher levels of psychological distress than the control group. In Earth, space, and harsh environments, melatonin therapy and improved sleep may aid in the reduction of stress, and TMD problems[(9)].

The TMJ turns out to be an important parameter in maintaining the balance and the body sway in weightlessness. Thus, a study wanted to test the hypothesis of a causal link between the occlusion, the muscles of the neck and the body sway. Body sway was measured with and without an occlusal splint, with and without the eyes open. Bivariate analysis was used to examine the fluctuations in the center of foot pressure. With both eyes open and closed, the region of oscillation of the center of foot pressure was bigger without the splint than with the splint. The changes in sternocleidomastoid muscle symmetry, caused by the occlusal splint, and the center of foot pressure differential area with closed eyes were found to be significantly related: the greater the increase in muscular symmetry, the smaller the area of oscillation with the splint compared to without the splint. As a result, changes in the contraction of the masticatory muscles may have an impact on the entire body. In conclusion a more functionally symmetric maxillo-mandibular posture was associated with a more symmetric sternocleido-mastoid muscle contraction pattern and reduced body sway [18].

5.2.5.Saliva:

Saliva is one of the easiest components of the oral sphere to collect and analyze. It will certainly become an essential tool for measuring the astronaut's physiological state. The quantity and properties of saliva during the pre-flight phase have a high predictive value [8].

A study therefore tried to establish a relationship between the level of cortisol and salivary melatonin and the level of stress. Stress-related adaptation has been determined using early morning responses in salivary cortisol excretion profiles. An increased degree of stress is linked to a higher cortisol awakening reaction. Melatonin and cortisol in saliva could be used as a biomarker for circadian disruption and stress [9].

A second study highlighted the increase in salivary 8-hydroxyguanosine concentration due to the increase in oxidative stress, as well as an increase in glucosyltransferase B which means an increased prevalence of caries in microgravity. Other adverse effects have been observed such as obstruction of the opening ducts in the sublingual and submandibular areas [5].

Finally, a last study was conducted in HDT, several measurements of the salivary composition were made before, during, just after and 12 hours after the HDT, and show this result [11]:

Increase	Decrease
Flow rate*	Vitamine E
Calcium*	Vitamine C
Potassium*	Sodium Chloride
Phosphate*	
Protein levels*	
Sodium	
Free radical	
—> So 8-hydroxy-deoxyguanosine	
Malonaldehyde	
Capsaicin	
Lactate deshydrogenase	

Table 5: *Increased and decreased of different saliva components over the HDT simulation* [11]*. (*) Return to normal level after the HDT simulation.*

5.2.6. Oral microbiota:

The oral microbiota is also not spared by the change in the extreme living conditions of the space environment. It is obviously altered [5]. Bacteria become less susceptible to anti-microbial agents, bacteria's growth is rapid, including the oral bacteria's [11]. Caries is more likely to occur due to the decrease in salivary flow, as well as an increased level of glucosyltransferase B as we have seen in the previous point [5]. Finally, the immune system is diminished during prolonged space flights, so all these factors together lead us to believe that dental problems will become a major medical emergency in long-term space missions [11].

A study carried out in a simulated Martian environment tried to measure the variations in the count of the different bacterial colonies forming the oral microbiota. Thus, 12 healthy volunteers were studied at several stages of the experiment: before, after one week of the experiment, after two weeks of the experiment and finally after the completion of the experiment. The analysis of the different bacterial populations was done in samples of dental plaque and saliva. Here are the results concerning the different populations [10]:

- Anaerobic bacteria: Total anaerobes, *Bacteroides*, *Fusobacterium*, and *Veillonella* levels were greater at 1 week than at baseline, and remained essentially the same at 2 weeks.
- Aerobic bacteria: Total aerobes, *Neisseria*, *Lactobacilli*, *Staphylococci*, *Candida*, and enteric bacilli levels were increased at 1 week and nearly constant at 2 weeks when compared to baseline.

- *Streptococcus mutans*: When compared to the baseline, the level of Streptococcus mutans was considerably greater. Salivary IgG levels were considerably lower at 1 week than at baseline, and the amount of *S. mutans* was highly linked with salivary IgG. Salivary cortisol, α-amylase, and current stress levels were significantly higher by the end of the mission, and *S. mutans* is known to be strongly and positively correlated with salivary cortisol and α-amylase.

5.2.7. Cancer:

As we have seen previously, the ISS is subjected to high doses of radiation, despite the fact that it is protected by the Earth's magnetosphere. Cosmic ionizing radiation have the ability to cause malignant changes in the oral mucosa, leading in precancerous changes. The ripping of DNA in cells by high-speed atomic particles causes cellular damage, then mutations occur in damaged DNA, resulting in carcinogenic alterations. A 1 Sv dose is enough to greatly enhance the risk of malignant potential in tissues (5).

5.2.8. Implant:

Very few observations have been made in real conditions, in other words, implants worn by astronauts on a mission in space. After 6 months in microgravity, the peri-implant bone levels stayed unchanged, and the implant functioned normally (11).

5.2.9. Fluid Shift Mechanism:

It is considered that a Fluid Shift Mechanism (FSM) happens in humans when there is no major head-to-foot gravitational vector in space, resulting in a redistribution of fluid pressures throughout the body (6).

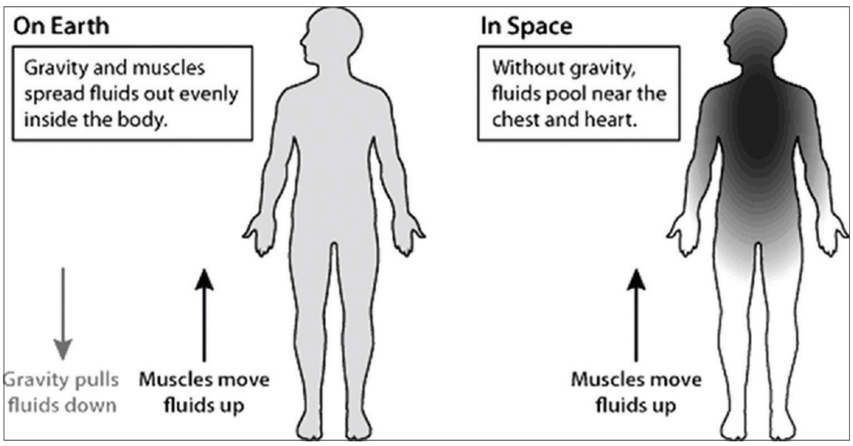

Figure 5: *Fluid Shift Mechanism* (5).

This change in blood flow throughout the body concentrates part of the blood flow in the skull. It therefore has notable effects on the oral sphere [11][5] such as:

- Abnormal facial expression
- Decrease of pain and temperature sensations
- Decreased tongue
- Xerostomie
- Modification of taste, due to the olfactory component attenuation
- Edema of face
- Mandibular mobility is restricted
- Moderate pain of teeth

FSM also has a limiting, a protecting effect on spatial osteoporosis. Increased bone blood flow raises bone interstitial fluid flow, which may increase osteoblastic nitric oxide and PGE2 release, favoring osteoblastic bone formation and limiting osteoclastic bone resorption. Gains in skull and mandibular bone mineral density would correlate to such a change in bone cell activity [6].

5.2.10. *Diet:*

Food plays a fundamental role in society. It allows to create links between individuals, to share moments of conviviality. It is an important facet of every culture in the world. All these truths are amplified in space. Due to the extremely difficult living conditions up there and the very busy days of the astronauts who must carry out several complex missions per day, these moments of rest and sharing are precious.

In addition, the form of the meals is designed for the ISS environment. Restrictions are imposed to prevent any interference between the form of the meals and the proper functioning of the ISS. For example, any form of bread or food that could produce crumbs is strictly prohibited so that it does not enter the air filtration and recycling system.

In general, food consumption is reduced by about 20% during space missions. A major problem is maintaining an adequate balance between food intake and the high volume of physical effort required. According to the research, a regular, well-balanced diet with lots of fluids will be just as healthy in space as it is on Earth [11].

We also face unique environmental conditions in space travel that cause nutritional depletion in the body, although it appears that the main issue in space flight is calcium homeostasis rather than vitamin depletion [17]. However, the spacecraft's low quantities of lightning may not be enough to induce vitamin D production [11].

A study conducted on a simulated Mars field aimed to measure changes in food perception and the consequences of this sensory change on food intake [12]. An important aspect of the physiological changes generated by the space environment is the modification of the chemical receptors responsible for the perception of flavors. This facet has been underestimated in scientific research, surely due to the lack of benefit that this research would bring to the Earth environment. However, food is one of humanity's most basic necessities, and any disruption in the pleasure of eating different meals related to taste changes might have an impact on astronaut's health and confidence during long-term space missions. As we seen previously microgravity causes physiological changes such as an upward transfer of body fluids toward the skull, which may result in a loss of olfactory component in food flavor. In fact, the Mars Desert Research team 78 and other microgravity simulation subjects have reported a change in their taste perception [12].

With this context in place, the aim of this research [12] is to measure the average time intensity for different flavors (bitterness, sourness, sweetness) once the participants are subjected to stress. Thus, compared to the pre-stress baseline values:

- Bitterness: a reduction in maximum intensity, a decrease in after-taste duration, and a diminution in total bitterness
- Sourness: a decrease in time as well as a drop in total sourness, and also a modification in maximum intensity.
- Sweetness: the pattern for sweetness was comparable to that for sourness, and the duration of after-taste was shorter.

Additional measurements were made, and allowed this study to conclude that sleep deprivation and leisure time do not cause a change in taste. Low calcium levels and an acidic environment have also been linked to the inhibition of taste reactions. Taste and smell loss, as well as related symptoms, are not linked to reduced energy consumption [12].

Finally, to prove the impact of simulated and real microgravity or extreme conditions on taste sense, more research with a large sample size is needed, taking into consideration all physiological and physiological aspects. As a result, this is a vital challenge for future human adventures [12].

5.3. *POSSIBLE SOLUTIONS TO AVOID OR MITIGATE THESE PROBLEMS/IMPACTS:*

5.3.1. *Solutions that already exist:*

NASA, ESA and other actors involved in the conquest of space have not yet sufficiently developed the tools necessary to prevent and cure dental problems.

Dental emergencies such as caries, pulpitis, abscesses, fractures, and crown displacement must be taught to crew members. Any dental emergency will have to be handled in-flight with limited equipment and personnel who may not have extensive dental training [13].

The current state of dental/oral health management for astronauts is insufficient, and a method that allows appropriate prevention, diagnosis and treatment in astronauts is urgently required. There is still no clear and systematic protocol for risk assessment. There is no manual on how to maintain proper oral hygiene in spacecraft. The only practical prophylaxis for dental/oral diseases among astronauts on the ISS is tooth brushing [8]. Finally, crew members have a dental examination six months before launch, and if any dental treatment is considered necessary, it is completed three months before launch to reduce the risk of problems during flight [11]. To conclude, dental treatment innovation in the space environment must be developed as soon as possible [8].

5.3.2. *Possible solutions for the future:*

The different situations that will occur will require protocols adapted to the space environment: a limited use of water and sharp instruments, the protocols will have to be operated without difficulties and an obligation to fix the astronaut patient and the astronaut dentist. An important challenge will be to offer the astronaut dentist the possibility to exercise single precision movements during the entire treatment phase [8].

Several approaches are possible to find future solutions. Prevention tools for example: tailored dentistry for each astronaut should be prepared and incorporated into the mission's health management, introducing interdental brush, dental floss, or fluoride application. Also chewing dental gum is a good way to improve oral self-defense [8].

We can also imagine more reliable and efficient diagnostic tools. The development of a remote diagnostic system might be beneficial for periodic oral health examinations. An oral camera would be used to photograph the oral cavity, which would then be sent to the control room in the ground. The amount of jawbone, oral malodor, occlusion, and taste sensation will all be investigated further as part of the dental/oral symptoms [8].

Artificial gravity generated by the centrifugal force of a rotating cylinder could also solve some problems. The majority of studies have compared zero gravity to 1 G forces, while fractional levels of gravity have received less attention. Lower levels of gravity could help to preserve bone and would be simpler to design [17].

One study attempted to compare the difference in effectiveness between resistive exercise alone (RE) and whole-body vibration coupled with high-load resistive exercise (RVE). The hypothesis was that the addition of vibration stimulates the bones in a more efficient way and limits bone loss. It was observed that when large-magnitude bone strain is combined with a low-amplitude vibration stimulus, more bone is formed than when large-magnitude bone strain is used alone. Although the loading duration (5 to 6 minutes per activity day) and repetition (3 days per week) were short, the RVE group's findings support the idea that when a loading stimulus is substantial enough, it is not necessary to do a significant number of loading cycles each day to affect bone metabolism. While further research is needed to enhance the countermeasures, the findings show that RVE may be more effective than RE in preventing bone loss. To conclude more research is needed in this area to refine the parameters of vibration loading, such as vibration frequencies, the duration of the stimulation or the number of sessions to be performed over a given time (day, week) [14].

5.4. MARS:

A manned trip to Mars is the next big step in human space exploration. Humans have proved their ability to explore hostile space environments during missions to and around the moon. An expedition to Mars, on the other hand, will oblige humans to react to systemic and complex conditions that are beyond the capacity of the human body. During the flight to Mars and the return to Earth, astronauts will be exposed to physiological and psychological challenges [(12)].

Human physiological status is known to fluctuate in response to extreme conditions encounter in space environment such as microgravity, high workload, cosmopolite environment (different cultures, languages or habits), limited internet access, radiations, isolation, limited resources... During a mission, these factors will have an impact on human performance and well-being, they are already known to have been a source of stress in a simulated Mars environment [(9)].

NASA's current flight plan for a trip to Mars calls for 5 to 6 months of transit to and from the planet. It should also be taken into account that the crew will stay a little less than 2 years on the surface of Mars, the time for the orbits of Earth and Mars to coincide again for a return flight. Due to its size, Mars exerts a gravitational force of about 0.38 G. Some plans call for a crewmember to stay in orbit while the landing team is on the ground. The orbiting astronaut would be subjected to zero gravity for an extended length of time, resulting in significant bone degeneration. To summarize, the astronauts will have to live in a 0 G environment during the 10 to 12 months of the round-trip flight, as well as 0.38 G for 2 years. The estimated amount of bone loss during a three-year mission due to zero gravity would equal about thirty years of earthly bone loss due to aging. Thus, even if the environment of Mars will allow to slow down the bone loss, the final result is more than worrying [(16)(17)].

It seems obvious that the astronauts who will be chosen for such a long mission, will have to observe an optimal bone density (due to their age, sexes, health), or naturally constituted of a bone structure more important than the average. This can be accomplished by consuming a calcium-rich diet, intense exercise program and by avoiding bone depleting substances such as caffeine, tobacco and alcohol. Estrogen levels in female astronauts would need to be checked, and supplementation would be necessary if levels are low. Supplementing with calcium and vitamin D appears to be required, but it is not enough to prevent degeneration [(17)].

6. CONCLUSION

In conclusion, the conditions of life in the ISS are difficult to bear for the human race. The high doses of ionizing radiation received, the weightlessness, the confined spaces, the constant sharing of living space with other people from different backgrounds. Astronauts are trained to deal with all this, but it undoubtedly has an impact on their health.

Accidents involving the oral sphere have appeared several times in space history. Beyond being problematic and disabling for the astronaut's missions, they have the interest to highlight the causes of their appearances. We can thus anticipate the complications, the situations most likely to occur.

Of all the parameters characterizing the space environment, the most problematic regarding human health is undoubtedly microgravity. Concerning oral health in general, microgravity has reversible and irreversible effects. The edema of the face, alteration in taste, abnormal facial expression, teeth pain, and xerostomia are reversible effects of microgravity. Microgravity's non-reversible effects include periodontal disease, dental caries with a different pattern than usual, stone formation in the salivary duct, pre-cancer or cancer, maxillary and mandibular bone fractures.

The space environment is a hostile environment for man in many ways. To preserve ourselves from cosmologic health risks, we need to learn more about exobiological conditions. There are currently not enough tools and measures for care and prevention. Aeronautical Dentistry will contribute to the management and treatment of microgravity-related oral health issues. Astronaut's oral health is crucial to their general health and well-being, that's why this type of research should be encouraged and supported.

Space is the new *Terra Incognita* of the 21st century. It is cold, hostile and silent. Yet it is a source of history and contemplation that has accompanied the human race for millennia. It is now our turn to explore, understand and apprehend it. Henceforth, the next big step is Mars. At present, a trip to Mars is very difficult to envisage. The circumstances are such and the solutions do not exist yet, that the state of health of the astronauts on their return to Earth will be more than worrying.

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