PREVENTION OF BONE FRACTURES AND OSTEOPOROSIS IN SPACE USING HIGH FREQUENCY MECHANICAL LOADING. P. A. Johnson[1,2], J. C. Johnson[1,2], and A. A. Mardon[1,2]. [1]University of Alberta, Edmonton AB, Canada, (jcj2@ualberta.ca) [2]Antarctic Institute of Canada (116 St 85 Ave NW, Edmonton AB, Canada, paj1@ualberta.ca).

Problem: After 50 years of age, the risk factors for osteoporotic fractures increases significantly from ~10% to ~50% of the general population, re-emphasizing the need for tools, technologies, and techniques to mitigate bone resorption. Perhaps unsurprisingly, disuse osteoporosis, the loss of bone secondary to a lack of mechanical stimulus, increases with age and is further exacerbated by fractures especially in the geriatric population. Osteoporosis is a disease of the bone, characterized by a loss in bone mineral density. Although this disease is commonly diagnosed in adults, it is not directly associated with increasing age. There are many links and potential risk factors to developing osteoporosis, including hormonal imbalances, nutrient deficiency, cardiovascular health and exercise. Risk factors for osteoporosis also include genetic inheritance patterns, body mass index, age, and a multitude of lifestyle factors (including alcohol consumption, smoking, and physical exercise).

Strikingly similar effects are well-recognized as a common complication of space travel and prolonged exposure to microgravity conditions - namely, the acceleration of bone loss and development of osteopenia. This is thought to be a result of the lack of gravitational stresses that permit optimal bone osteoblast/osteoclast resorption, formation, and turnover. Excessive bone turnover and loss leads to elevated serum calcium ion levels, which can thereby precipitate headaches, confusion or disorientation, weakness, muscle pain, and a multitude of gastrointestinal symptoms including a loss of appetite, upset stomach, nausea, vomiting, and constipation, making it difficult to perform tasks on missions, let alone routine tasks of daily living. In more serious cases, high serum calcium ion levels and increased bone turnover can lead to loss of consciousness, seizures, kidney stones, heart arrhythmias or heart attacks, coma, and/or irreversible skeletal damage.

This can be observed in patients living with osteoporosis as these individuals commonly suffer from a decreased quality of life due to loss of mobility and autonomy. Severe osteoporotic fractures occurring in the hip and spine require hospitalization time and carry a 20% increase in mortality rate. Patients commonly feel socially isolated, and show signs of feeling anxious about their health and changing lifestyles after their diagnosis. Most patients also have fears regarding another fracture. After a fracture, patients have decreased mobility in their body, which makes it difficult for these individuals to complete their activities of daily living (e.g., personal hygiene, getting dressed, continence management, cleaning, cooking, etc.)

Not only is this problem an ongoing and significant challenge faced by a substantial proportion of the aging population, it also has an impact on nearly all astronauts exposed to microgravity conditions for prolonged periods of time. As we embark on more missions in orbit and beyond, the future of space exploration and ultimately, the long-term survival of humanity, would critically depend on astronauts having an effective means of preventing these adverse health effects. A solution would also open the door for novel therapeutic strategies in bone health and orthopedic medicine enhancing health and quality of life for ~1-4 billion people in the general population who are at-risk for bone fractures.

Solution: Currently, the prophylactic use of bisphosphonates, vitamin D supplements, or newly available monoclonal antibodies utilized for osteoporosis, such as Romosozumab, are the only strategy for enhancing bone health to combat the challenges posed by prolonged exposure to microgravity. Unfortunately, while these pharmacological strategies may be effective, it is not sustainable during prolonged space missions especially if there are delays and limited access to these medications. Many of these medications also have side effects including bone and joint pain, fatigue, muscle weakness, cardiovascular issues, a plethora of gastrointestinal adverse effects, and occasionally even paradoxically increase the risk of fractures.

In the past decade, literature has suggested low magnitude, high frequency mechanical loading as a potentially effective countermeasure to bone loss. In one study, it was shown that brief bouts of 0.2-g stimulus at 30 Hz by a vibration platform (Optimass model 1000 Mechanical Strain Device) at 2 x 10 min/day for a total of 12 months in postmenopausal Caucasian women with low bone mass showed a 2% increase in total bone mineral density. As such, we propose the development of a vibrational platform using a mechanical strain device (MSD) capable of replicating the delivery of an optimized stimulus in near 0-g microgravity conditions. This device would not only be able to improve bone adaptability to load bearing, it would also offer a sustainable technology for astronauts to combat microgravity-induced osteopenia in prolonged flights as the device can be re-charged.

We propose for the development of the MSD to be designed as a six degrees of freedom platform with soft robotic appendages that offer the adjustment of required levels of frequency and strain, while accounting for on-board ergonomics. For physical exertion tasks, such as running, peak strain magnitudes of 2000–3500 micro-strains may be generated. Additionally, standing imposes strains in the optimal spectral range of 10–50Hz. Optimal prescription may be calculated using the Fourier method, an equation that describes bone adaptation as a function of strain magnitude. This calculation can enable us to determine the optimal frequency of vibration and degree of force for the MSD. Thus, these parameters can be reflected by this instrument to permit astronauts to take part in exercise activities. As a result, more robust extraterrestrial exercise programming can be engineered by developers around this manufactured MSD. Noting that bone loss tends to be critical around long bones, optimal landmarks should use joints such as the shoulder, hip, and ankle, which would allow for the effective application of compressional and tensional forces along and around the plane of the bone shaft (diaphysis). Our proposed MSD model (OsTrek) offers a practical approach to mechanically load the skeleton to enhance bone strength and prevent fractures in a safe, passive, non-invasive, and low strain with no adverse side effects, compared to pharmacological management. It is based on evidence validated in a population of patients with high risk of fractures and could be optimized even further in microgravity conditions not only for astronauts, but also the general population at-risk for osteopenia and osteoporosis.

Space station relevance: Access to a space station is vital element to the success of our product as critical testing and validation can only be performed in microgravity conditions. While simulated conditions of spaceflight on ground offer some value prior to venturing out, it is limited in its rigour and external validity to the environment experienced in true spaceflight. In addition to the real-world testing in the same microgravity conditions that astronauts are exposed to over an extended period of time, these conditions also offer excellent controlled settings to conduct experiments and research this device. Manipulating the g-force utilized for stimulus and the g-force in the environment may also be critical for testing this device as it would offer insights into its viability for use in different environments (i.e., on Earth, in orbit, and on other celestial bodies such as the Moon or Mars).

Moreover advancing research in bone atrophy and osteoporosis in space has many implications for medical advances on Earth. Compared to Earth, both immobilization and illnesses can be observed at a higher rate than normal aging. However, both conditions precipitate as a result of bone resorption occurring faster than the formation of new bone. That means that developing a trainer device to treat osteopenia and bone loss, which are of benefit to astronauts in space missions will also prove beneficial for people on Earth. For example, a number of exercise training regimens and devices such as the Advanced Resistive Exercise Device (ARED) on the space station, which is utilized for high-intensity resistive training, were developed based on trainers used for cable, bar, and weight exercises on Earth. These findings also translate back from space to Earth if we consider developments like the cool suits manufactured by CoolSystems Inc. culminating from application of NASA technology for down-to-earth problems such as multiple sclerosis, neurological conditions, injured athletes, and post-operative care for symptom control in lowering body temperature.

When we consider the future of space exploration, research at the space station is essential in helping us understand strategies to combat bone loss in missions beyond orbit. In many cases, astronauts may need to perform activities in microgravity conditions for extended periods of time or even embark on voyage for a number of days or months. Devices like ARED are not always readily available depending on the mission and available technologies. Under these conditions, access to a portable MSD trainer that could be transported outside of the space station could be critical for both exercise and as a countermeasure for astronauts to prevent bone loss and its associated adverse effects. Nevertheless, there is an expanding necessity for this essential research aboard the space station in order for us to prepare effective countermeasures for the current and future generation of space travellers while simultaneously advancing treatments through the implementation of these acquired knowledge, technology, and application for people on Earth.

References: [1] Johnson J. C. et al. (2020) *Pac J Sci Tech.,* 21(1):274-275. [2] Johnson P. A. et al. (2021) *Lect. Notes Eng. Comput. Sci.* doi: 10.1007/978-981-33-6926-9_30. pp. 355-366