NASA-STD-3001 Technical Brief

Bone Loss

OCHMO-TB-030
Rev C

Relevant Technical Requirements

NASA-STD-3001 Volume 1, Rev C

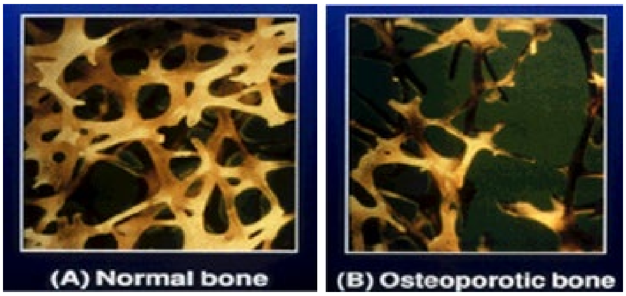
[V1 3002] Pre-Mission Preventive Health Care
[V1 3003] In-Mission Preventive Health Care
[V1 3016] Post-Mission Health Care
[V1 3017] Post-Mission Reconditioning
[V1 3018] Post-Mission Long-Term Monitoring
[V1 4020] In-Mission Nutrient Intake
[V1 4026] Pre-Mission Bone Mineral Density
[V1 4027] Pre-mission Bone Countermeasures
[V1 4028] Post-Mission Bone Reconditioning

NASA-STD-3001 Volume 2, Rev D

[V2 7038] Physiological Countermeasures Capability
[V2 7043] Medical Capability
[V2 7100] Food Nutrient Composition

Executive Summary

Bone density loss in microgravity (skeletal unloading) is a well-documented crew health concern since the Skylab mission, when it was observed that the flight crew had about 1-1.5% mineral loss per month. This was noted as being “significantly faster than normal osteoporotic individuals.” As a result, several technical requirements throughout Volumes 1 and 2 of NASA-STD-3001 provide countermeasures that can aid in the prevention of significant deterioration of overall crew heath. This will contribute to overall mission success and benefit other areas including crew mental well-being. Countermeasures such as exercise, adequate nutrition, and medications have been recommended or required in order to prevent demineralization, especially during long-duration missions such as planetary and deep-space exploration. Presently, NASA-STD-3001 Volume 1 Rev C, **[V1 4027] Pre-Mission Bone Countermeasures** provides the range of acceptable loss. In addition, there is a need for appropriate nutrition to prevent loss from various areas of concern, including that of the skeletal, muscular, and immunological systems.



(A) Normal bone (B) Osteoporotic bone

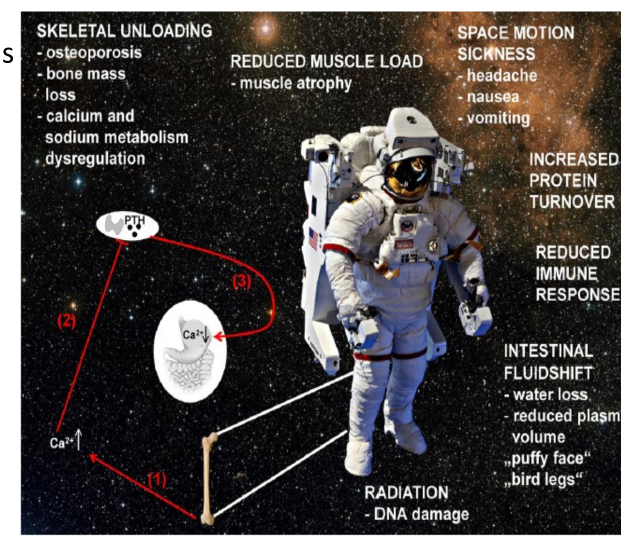
Background

Post-flight recovery of bone loss and demineralization can occur over a period of time, but the long-term effects (increased risk of osteoporosis) of these changes on the crew are not completely understood, especially in crewmembers' later years following long-duration flights. As missions increase in duration, the prevention of bone loss is necessary to avoid injuries or fractures to the crew, especially as more strenuous activities are performed, and risks are increased with the exploration of other planetary bodies and longer durations of microgravity.

Exercise as a Countermeasure[1]

It is noted in the Human Integration Design Handbook (HIDH) Section 5.2.4.2 that "it is critical for crewmembers to have frequent access (potentially multiple daily sessions) to exercise equipment that can provide high levels of loading, and diversity in load application, on the skeletal system. These exercise countermeasures should be targeted primarily toward protecting the lower body and hip regions." It has been observed that the areas of most concern for skeletal unloading are in the lower areas of the body (i.e., hips and trochanter).

As mentioned by Shackelford et al. "Spaceflight can be considered the ultimate model to determine the role of gravity on the human skeleton. There is a consensus among exercise scientists that both endurance (aerobic) and resistance exercises are needed as countermeasures to maintain overall crew health and performance during and after spaceflight. An exercise countermeasure has the advantage of benefiting multiple body systems (musculoskeletal, cardiovascular, immunological) and can be targeted to those body regions needing protection. Maintenance of muscle strength also reduces risk of injury during falls and impact. Increased muscle strength reduces the risk of impact injury by decreasing joint angular velocity, providing damping of impact loads. Muscles protect bone from fracture by resisting bending moments across long bones."



Grimm et al.

[Risk of Bone Fracture due to Spaceflight-induced Changes to Bone]

1. [OCHMO-TB-031Exercise Technical Brief]

Background

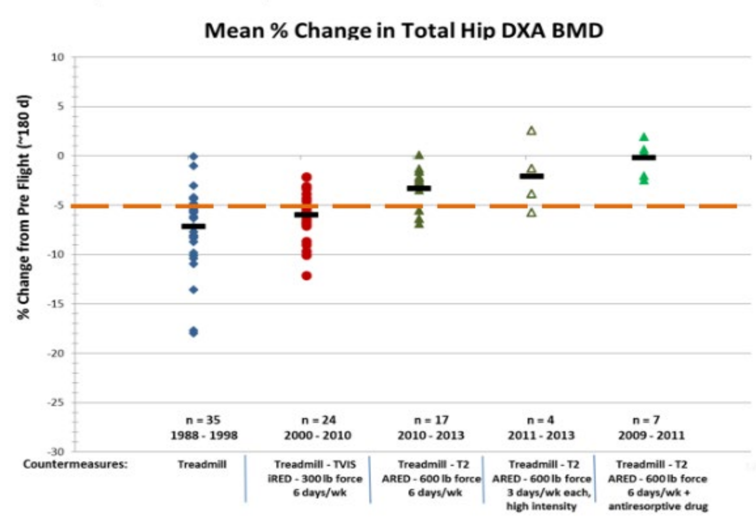
Level	Definition
Normal	Bone density is within 1 SD (+1 or −1) of the young adult mean.
Low bone mass	Bone density is between 1 and 2.5 SD below the young adult mean (−1 to −2.5 SD).
Osteoporosis	Bone density is 2.5 SD or more below the young adult mean (−2.5 SD or lower).
Severe (established) osteoporosis	Bone density is more than 2.5 SD below the young adult mean, and there have been one or more osteoporotic fractures.

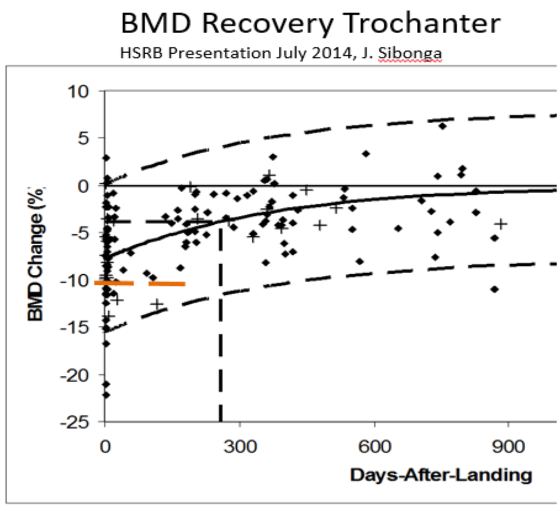
World Health Organization Definitions Based on Bone Density Levels

Reference Information

"Observations of astronauts and cosmonauts indicate that skeletal unloading causes loss of calcium from the skeleton, which increases the risk of kidney stones and bone fracture (both during the mission and potentially as a lifelong consequence). By using single photon absorptiometry, the bone density of the calcaneus in astronauts aboard Skylabs 2, 3, and 4 had a decrease of as much as 8% with an average of 4% on the longest flights of 59 and 84 days. Similar observations have been made in cosmonauts, where losses in bone density of the calcaneus have been reported to be as much as 19% after 140 days in microgravity" (Holick). Additionally, Shackelford et al. reported "to date, we have collected pre-and post-flight bone densitometry measurements on 47 individuals from such flights. Although losses show significant heterogeneity among individuals and between bones of a given subject, bone loss is a consistent finding after spaceflight. Among astronauts and cosmonauts who participated in long duration (average of 170 days) flights aboard Mir and the ISS, >50% of the crew members had a 10% loss in at least one skeletal site, and 22% of the Mir cosmonauts had a 15–20% loss in at least one site. This bone loss has been shown to be a regional phenomenon in which the areas with the greatest decrease in weight bearing lose the most bone; losses average 1–2%/mo in such regions as the lumbar spine and hip compared with no change in the arms or radius (Mir and ISS astronauts, arms: 0.1%/mo; ISS astronauts, radius and ulna: -0.1%/mo)."

1371B - January 2014 Bone Lab Data Analysis





Reference Data

In a review of the information from the Apollo Medical Summit, NASA/TM-2007-214755, it was noted that "the astronauts demanded exercise capability for the Command Module for rest and relaxation purposes," which supports Volume 1 of NASA-STD-3001 stating that countermeasures should be used to "mitigate undesirable physical, physiological, and psychological effects of space flight upon crewmembers."

Due to the rarity of persons in microgravity for the purposes of studying bone loss, numerous studies have been performed using bed-rest as an analogue to better understand the physiology during skeletal unloading, as well as efficacy of various prevention techniques (exercise, medications, diet, etc.). The following tables show the results of these studies and the impact of unloading, regardless of the presence of microgravity (Tables 1 and 2 from Grimm et al.).

Table 1
Recent bed-rest studies investigating the influence of simulated microgravity on bone.

Type of bed-rest	Duration	Observations	Reference
HDT with or without exercise	5 d	Bone resorption increased during BR, locomotion replacement training or 25 min of upright standing had no effect	[176]
HDT with or without resistive vibration exercise or resistive exercise	60 d	Increases of sclerostin and dickkopf-1 in all groups, no evidence for an influence of exercise on the rise in serum sclerostin and dickkopf-1 levels	[177]
HDT with or without resistive vibration exercise	60 d	Serum osteocalcin was significantly associated with serum insulin and leptin (increased during BR in both groups)	[178]
HDT	35 d	Increased bone demineralization, increased urinary calcium and decreased aquaporin-2 excretion	[179]
HDT with or without 30 min centrifugation (1g at center of mass)	5 d	Serum sCD200 levels fall and sCD200R1 levels rise (the author proposes them as useful surrogate markers for bone loss). Centrifugation abolished or attenuated these changes.	[180]
HDT	14 and 21 d	The Wnt-pathway is involved in bone loss under microgravity. Sclerostin levels rose during BR and declined at the ends of the studies. Bone formation marker PINP decreased and bone resorption marker NTx increased during BR	[124]
HDT	30 d	Urinary markers of bone resorption increased, and serum parathyroid hormone decreased. Urinary oxalate excretion decreased and correlated inversely with urinary calcium	[49]
HDT	90 d	Bone mineral density declined significantly, serum sclerostin was elevated. Serum PTH levels were reduced, urinary bone resorption markers and calcium were significantly elevated	[181]
HDT with or without vibration training	14 d	Increase in bone resorption, no effect of vibration on bone resorption markers, bone formation markers, and calcium excretion.	[182]
HDT with or without exercise or high-protein nutrition	60 d	Deterioration of bone microstructure and density, no effect of exercise and nutrition.	[183]
HDT with or without exercise or high-protein nutrition	60 d	Regional differences in bone loss in women with incomplete recovery one-year after bed-rest. No effects of exercise or nutrition	[184]
HDT	21–90 d	No changes in phylloquinone, urinary γ-carboxyglutamic acid, or undercarboxylated osteocalcin, comparable to spaceflights, indicating that vitamin K supplementation in microgravity is not needed to counteract bone loss	[185]
HDT with or without resistive vibration exercise or resistive exercise	60 d	Reductions in cortical area, cortical thickness and bone density at the distal tibia, but increases in periosteal perimeter and trabecular area. Recovery within 180 d after BR. At the distal radius, persistent increases in cortical area, cortical thickness, cortical density and total density and decreases in trabecular area. Resistive vibration exercise had a significant effect only on the cortical area at the distal tibia.	[186]

BR = bed-rest, HDT = head down tilt, d = days, NTx = amino-terminal collagen crosslinks, PINP = procollagen type I N-terminal propeptide, sCD200 = soluble CD200, cCD200R1 = soluble CD200R1.

Reference Data

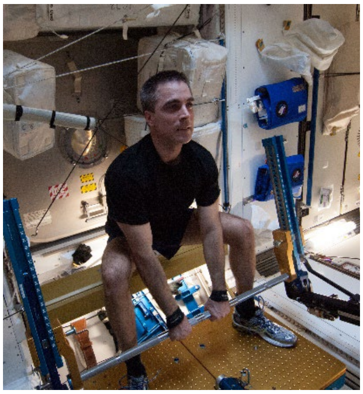
Table 2
Overview of the bone loss countermeasures used in real and simulated microgravity.

Countermeasure	Microgravity stimulus	Duration	Observations	Reference
iRED	Real (ISS)	6 months	No effects on bone loss	[42]
ARED	Real (ISS)	6 months	Helps maintaining bone mass when combined with adequate energy intake	[42]
70 mg alendronate once/week + iRED or ARED	Real (ISS)	5.5 months	High variability of data, hints towards superiority of combination vs. training alone	[107]
HEM (resistance exercise training)	Simulated (horizontal bed-rest)	17 weeks	Prevention of BMD loss in total hip, calcaneus, pelvis and total body, significantly increased bone metabolism markers and net calcium balance	[149]
Resistive exercise ± vibration	Simulated (HDT bed-rest)	60 d	The combination of vibration and resistive exercise prevents bone loss at the tibial diaphysis and proximal femur more efficiently than resistive exercise alone	[150]
Supine treadmill exercise within LBNP/flywheel resistive exercise	Simulated (HDT bed-rest)	60 d	Exercise treatment significantly attenuated loss of hip and leg bone mineral density	[51]
Artificial gravity (1g at center of mass)	Simulated (HDT bed-rest)	3 × 5 d	No protection by artificial gravity	[100]
Alendronate (10 mg/d)	Simulated (horizontal bed-rest)	17 weeks	Alendronate attenuated most of the changes in bone occurring during bed rest	[158]
EHDP (5 or 2 × 20 mg/d)	Simulated (horizontal bed-rest)	20 weeks	Only minor effects, no change in skeletal mineral loss	[161]
Flywheel resistance training + 1 × 60 mg pamidronate 14 d before start of bed-rest	Simulated (HDT bed-rest)	90 d	No effect of pamidronate on bone metabolism	[160]

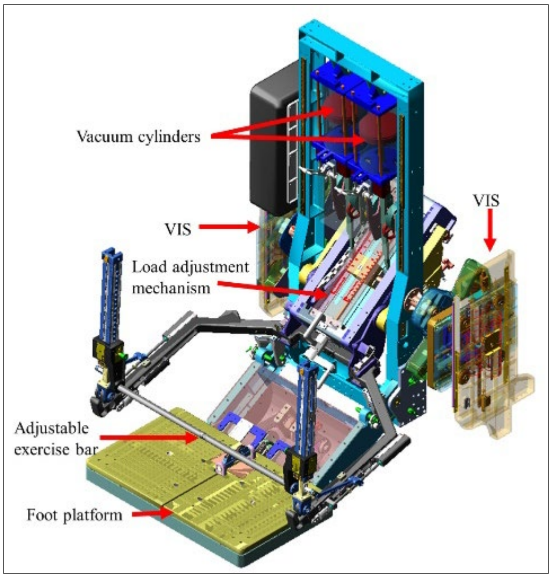
HEM = horizontal exercise machine, BMD = bone mineral density, iRED = interim resistive device, ARED = advanced resistive exercise device, HDT = head down tilt, d = days, LBNP = lower body negative pressure, EHDP = disodium ethane-1-hydroxy-1,1-diphosphonate or ethane-1-hydroxy-1,1-diphosphonate.

Application

Information noted in the NASA-STD-3001 Volumes 1 and 2, along with details from the HIDH, provide reference details and guidance to aid in the understanding of crew needs. Some examples that have helped in the implementation of the exercise equipment include items from ISS, such as the **Advanced Resistive Exercise Device (aRED)** – This device, while similar to the Interim Resistive Exercise Device (iRED), is capable of higher concentric resistance and eccentric-to-concentric ratio close to that recommended by expert panels and confirmed effective by exercise scientists. The aRED also collects data regarding the parameters associated with crew exercise and transmits it to the ground.



NASA astronaut Chris Cassidy using the aRED device

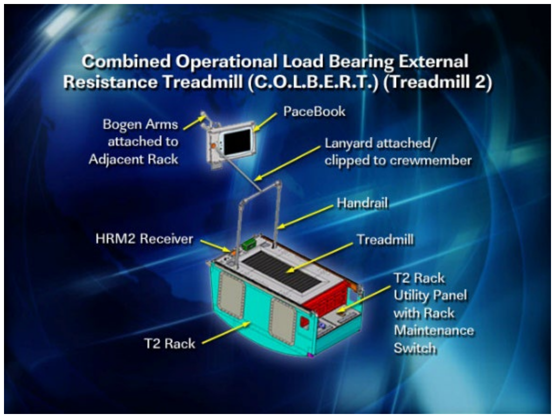


aRED Diagram; NASA, 2012

1. [OCHMO-TB-013 Food and Nutrition Technical Brief]

Application

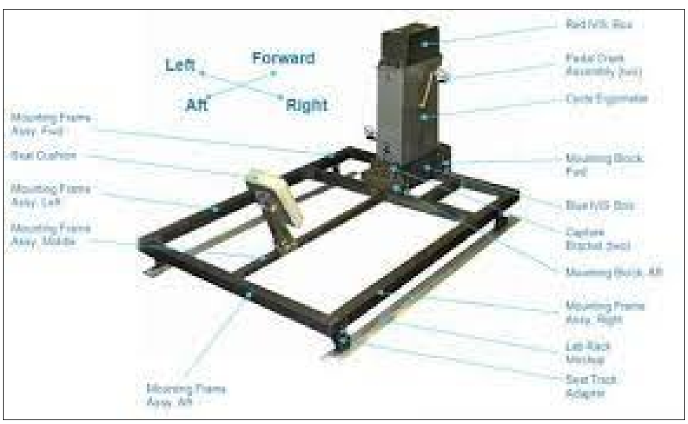
- **Treadmill 2 (COLBERT)** – An exercise treadmill that can also be used to collect data such as body loading, duration of session, and speed for each crewmember.



COLBERT Diagram; NASA, 2009

ESA astronaut Luca Parmitano exercising on the COLBERT

- **Cycle-Ergometer with Vibration Isolation System (CEVIS**) – A structurally isolated aerobic exercise cycle that serves as a countermeasure to cardiovascular deconditioning on orbit.



CEVIS Diagram; Ambrose et al, 2014

ESA astronaut Samantha Cristoforetti exercising on the CEVIS

The crew is required to exercise a minimum of time dependent on the program mission as dictated by the medical team, however previous requirements have been as little as 2.5 hours per workday with a strict exercise program. Additionally, the medical team may instruct the crew to take medication, such as bisphosphonates, to prevent bone loss, but this is not currently required for all crew.

Furthermore, the food lab and nutritionists have developed appropriate nutritional foods to ensure that the crew have enough micro- and macronutrients to promote crew mental and physical health. The interactions of the various technical requirements from both NASA-STD-3001 Volumes 1 and 2, along with the supported information from the appendices, will allow for successful missions.[1]

While it is important to review and update the individual technical requirements that address crew health or related areas, considerations should be taken to ensure that all the technical requirements are reviewed holistically so they can be applied appropriately for planning and future requirements.

Back-Up

Major Changes Between Revisions

Rev B → Rev C

- Updated information to reflect the revisions to language throughout both volumes of NASA-STD-3001.
- Updated/added website links due to new NASA website launch

Rev A → Rev B

- Updated information to be consistent with NASA-STD-3001 Volume 1 Rev B and Volume 2 Rev C.

Original → Rev A

- Overview
    - Added executive summary
    - Updated standards to Volume 2 Rev B
- Background
    - Added subcategory "Exercise as a countermeasure" after description in order to have more separation in the information
    - Added picture to support subcategory for more visual interest
- Application
    - Added diagrams of exercise equipment for more visual interest
- Other
    - Added revision page
    - Added referenced standards page

View the current versions of NASA-STD-3001 Volume 1 & Volume 2 on the OCHMO Standards website

Referenced Technical Requirements

NASA-STD-3001 Volume 1 Revision C

[V1 3002] Pre-Mission Preventive Health Care Pre-mission preventive strategies shall be used to reduce in-mission and long-term health medical risks, including, but not limited to: (see NASA-STD-3001, Volume 1 Rev C for full technical requirement).

[V1 3003] In-Mission Preventive Health Care All programs shall provide training, in-mission capabilities, and resources to monitor physiological and psychosocial well-being and enable delivery of in-mission preventive health care, based on epidemiological evidence-based probabilistic risk assessment (PRA), individual crewmember needs, clinical practice guidelines, flight surgeon expertise, historical review, mission parameters, and vehicle-derived limitations. These analyses consider the needs and limitations of each specific vehicle and design reference mission (DRM) with particular attention to parameters such as mission duration, expected return time to Earth, mission route and destination, expected radiation profile, concept of operations, and more. In-mission preventive care includes, but is not limited to: (see NASA-STD-3001, Volume 1 Rev C for full technical requirement).

[V1 3016] Post-Mission Health Care Post-mission health care shall be provided to minimize occurrence of deconditioning-related illness or injury, including but not limited to: (see NASA-STD-3001, Volume 1 Rev C for full technical requirement).

[V1 3017] Post-Mission Reconditioning All programs shall provide the planning, coordination, and resources for an individualized post-mission reconditioning program, specific to each crewmember, mission type, and mission duration. The post-mission reconditioning starts with crew egress at landing and includes a guided, phased reconditioning protocol. The goals of the reconditioning program include the following:

a. To ensure the health and safety of returning crew.
b. To actively assist the crew's return to full functional abilities and return-to-flight status.
c. To actively assist in the crew’s return to pre-mission fitness

[V1 3018] Post-Mission Long-Term Monitoring Crewmembers returning from spaceflight shall be monitored longitudinally for health, behavioral health, and well-being parameters in a standardized manner.

[V1 4020] In-Mission Nutrient Intake Programs shall provide each crewmember with 100% of their calculated nutrient and energy requirements, based on an individual’s age, sex, body mass (kg), height (m), and appropriate activity factor.

[V1 4026] Pre-Mission Bone Mineral Density Crewmembers’ pre-mission bone mineral density (BMD) T-scores for total hip and lumbar spine (L1-L4), as measured by mass dual energy X-ray absorptiometry (DXA) shall be consistent with an age, sex, gender, and ethnic-matched population.

[V1 4027] Pre-mission Bone Countermeasures Countermeasures shall maintain bone mineral density of the hip and spine at or above 95% of pre-mission values and at or above 90% for the femoral neck.

[V1 4028] Post-Mission Bone Reconditioning Post-mission reconditioning shall be aimed at returning bone mineral density to pre-mission baseline values.

Referenced Technical Requirements

View the current versions of NASA-STD-3001 Volume 1 & Volume 2 on the [OCHMO Standards website]

NASA-STD-3001 Volume 2 Revision D

[V2 7038] Physiological Countermeasures Capability The system shall provide countermeasures to meet crew bone, muscle, sensorimotor, thermoregulation, and aerobic/cardiovascular requirements defined in NASA-STD-3001, Volume 1.

[V2 7043] Medical Capability A medical system shall be provided to the crew to meet the medical requirements of NASA-STD-3001, Volume 1.

[V2 7100] Food Nutrient Composition The system shall provide a food system with a diet including the nutrient composition that is indicated in the Dietary Reference Intake (DRI) values as recommended by the National Institutes of Health, with the exception of those adjusted for spaceflight as noted in Table 7.1-2—Nutrient Guidelines for Spaceflight.

All referenced tables and figures are available in NASA-STD-3001 Volume 2 Revision D.

Reference List

1. National Institutes of Health. *Bone Mass Measurement: What the Numbers Mean.* https://www.bones.nih.gov/health-info/bone/bone-health/bone-mass-measurement-what-numbers-mean
2. Apollo Medical Summit, NASA/TM-2007-214755
3. Shackelford et al. Resistance exercise as a countermeasure to disuse-induced bone loss. *J Appl Physiol* 97: 119–129, 2004.
4. D Grimm, J Grosse, M Wehland, V Mann, JE Reseland, A Sundaresan and TJ Corydon. The impact of microgravity on bone in humans. *Bone* 87 (2016) 44–56
5. Holick, M.F. 2000. Microgravity-induced bone loss - will it limit human space exploration? *Lancet*, 355:1569-70.
6. Reference Guide to the International Space Station. Utilization Edition September 2015. NP-2015-05-022-JSC
7. Internation Space Station Facilites: Research in Space 2017 and Beyond. NP-2017-04-014-B-JSC
8. Schneider SM, Amonette WE, Blazine K, Bentley J, Lee SM, Loehr JA, Moore AD Jr, Rapley M, Mulder ER, Smith SM (2003) Training with the International Space Station interim resistive exercise device. Med Sci Sports Exerc 35(11):1935–1945
9. Hilliard-Robertson PC, Schneider SM, Bishop SL, Guilliams ME (2003) Strength gains following different combined concentric and eccentric exercise regimens. Aviat Space EnvironMed 74(4):342–347
10. Smith SM, Heer MA, Shackelford L, Sibonga JD, Ploutz-Snyder L, Zwart SR (2012) Benefits for bone from resistance exercise and nutrition in long-duration spaceflight: evidence from biochemistry and densitometry. J Bone Miner Res 27(9):1896–1906
11. R. Ambrose, P. Bevill, M. Murray, S. Reddy, D. Blank, and H. Goetz, "Sustaining Engineering Description for the Treadmill with Vibration Isolation and Stabilization (TVIS) System," NASA JSC63712, Rev. B, 2011
12. Human Integration Design Handbook (HIDH), Revision 1. (2014). https://www.nasa.gov/sites/default/files/atoms/files/human_integration_design_handbook_revision_1.pdf