National Aeronautics and Space Administration

Physiological Health Challenges for Human Missions to Mars

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Disclosure Information:

I have no financial relationships to disclose.

I will not discuss off-label use and/or investigational use in this presentation.

- Weightlessness
- Radiation
- Isolation
- Stress
- Distance
- PO_2-PCO_2-changes
- Circadian rhythms
- Other

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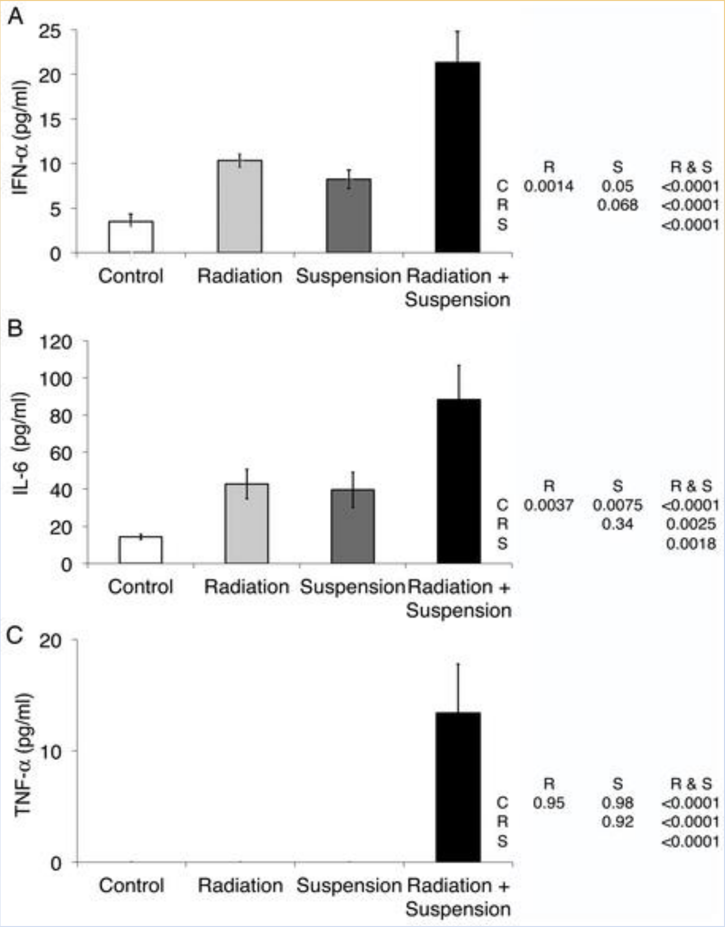
Synergistic effects?

Examples

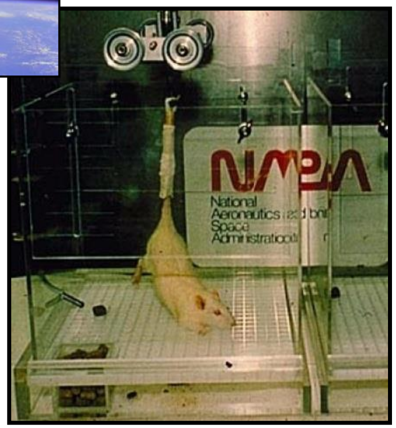


An example of synergistic effects of 0 G-simulation and radiation (2 Gy)

Zhou Y, Ni H, Li M, Sanzari JK, et al. (2012) PLoS ONE 7(9): e44329. doi:10.1371/journal.pone.0044329
http://www.plosone.org/article/info:doi/10.1371/journal.pone.0044329

PLOS | ONE

Simulated weightlessness and ionizing radiation: bone and muscle effects
(Globus et al. 2014)



Rodent Hindlimb Unloading (HU)

Ionizing Radiation

BONE

HU AND RADIATION (DOSE-DEPENDENT) EACH CAN CAUSE:

-decrements in density and architecture
-weaker mechanical properties; greater propensity to fracture
-increased bone resorption by osteoclasts
-impaired bone formation by osteoblasts
-depletion of progenitors
HU: reversible
RAD: ? irreversible

MUSCLE

-**HU CAUSES**:
-muscle fiber atrophy
-switch from slow to fast-type fibers

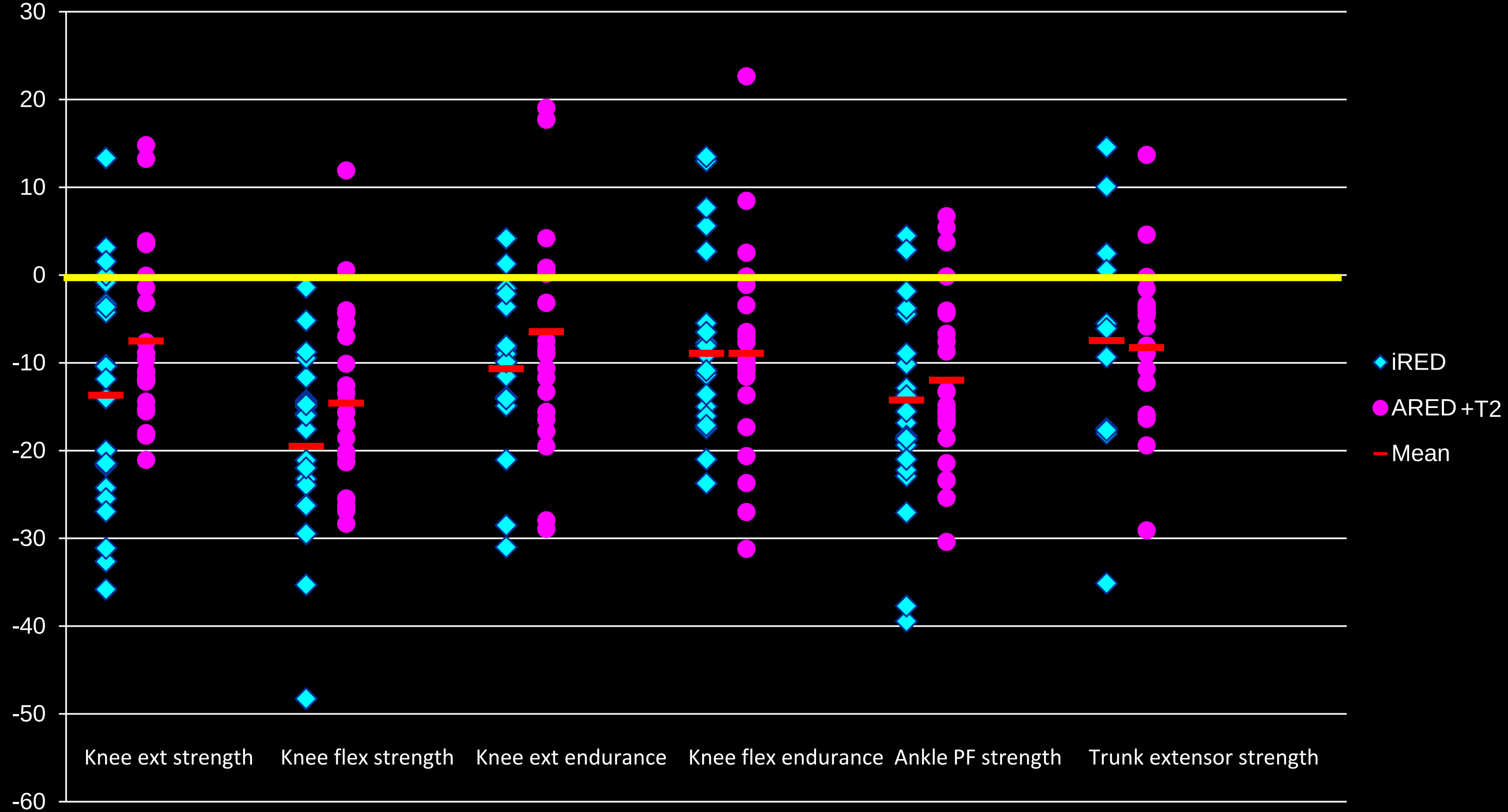
-**RADIATION (DOSE-DEPENDENT) CAN CAUSE** :
- Increase in smaller diameter fibers
- more fibers containing central nuclei
- satellite cell apoptosis

Present platform in LEO

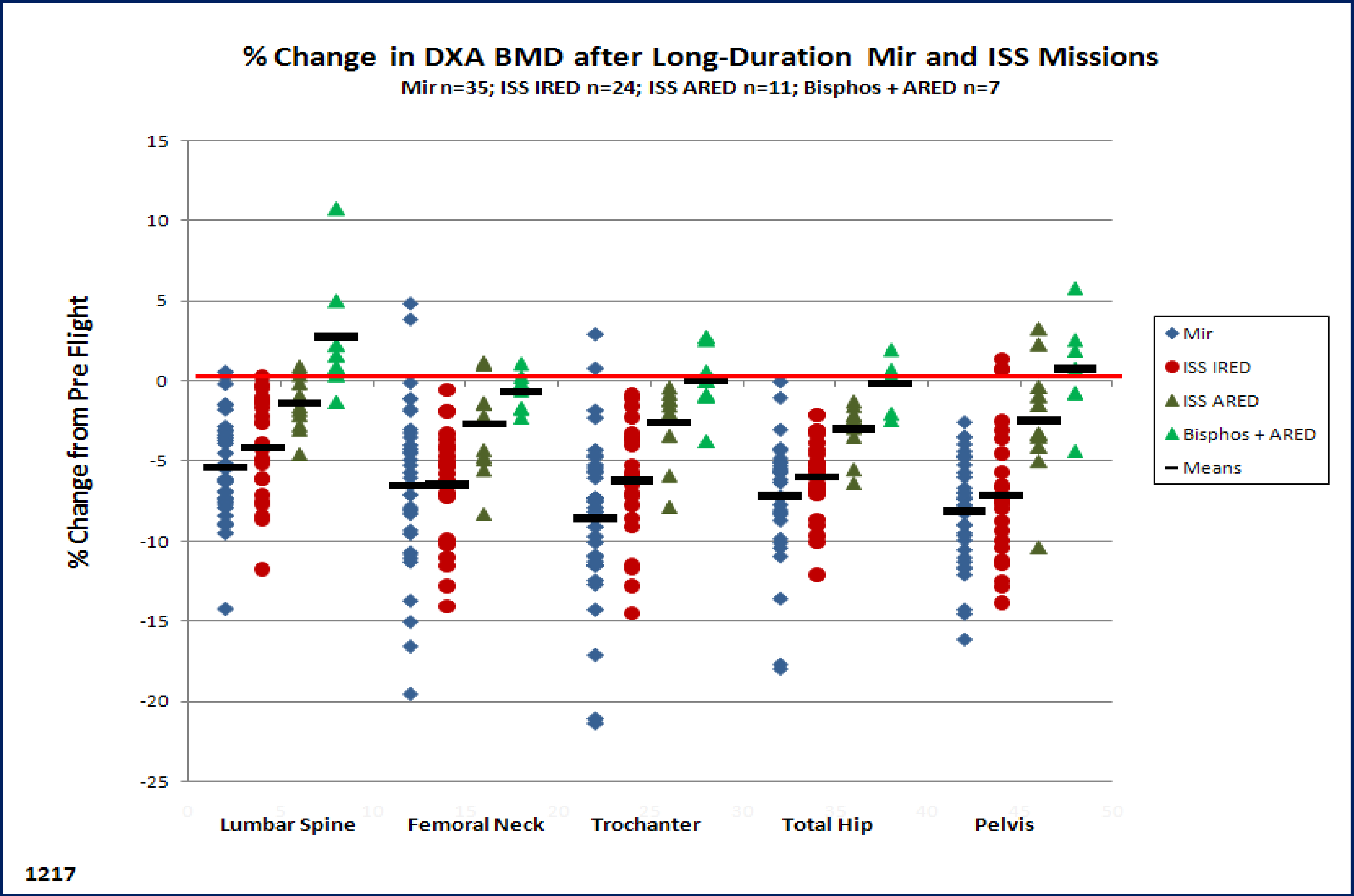


Muscle Function

Exp 1-32 (IRED n=22 ARED+T2 n=25)

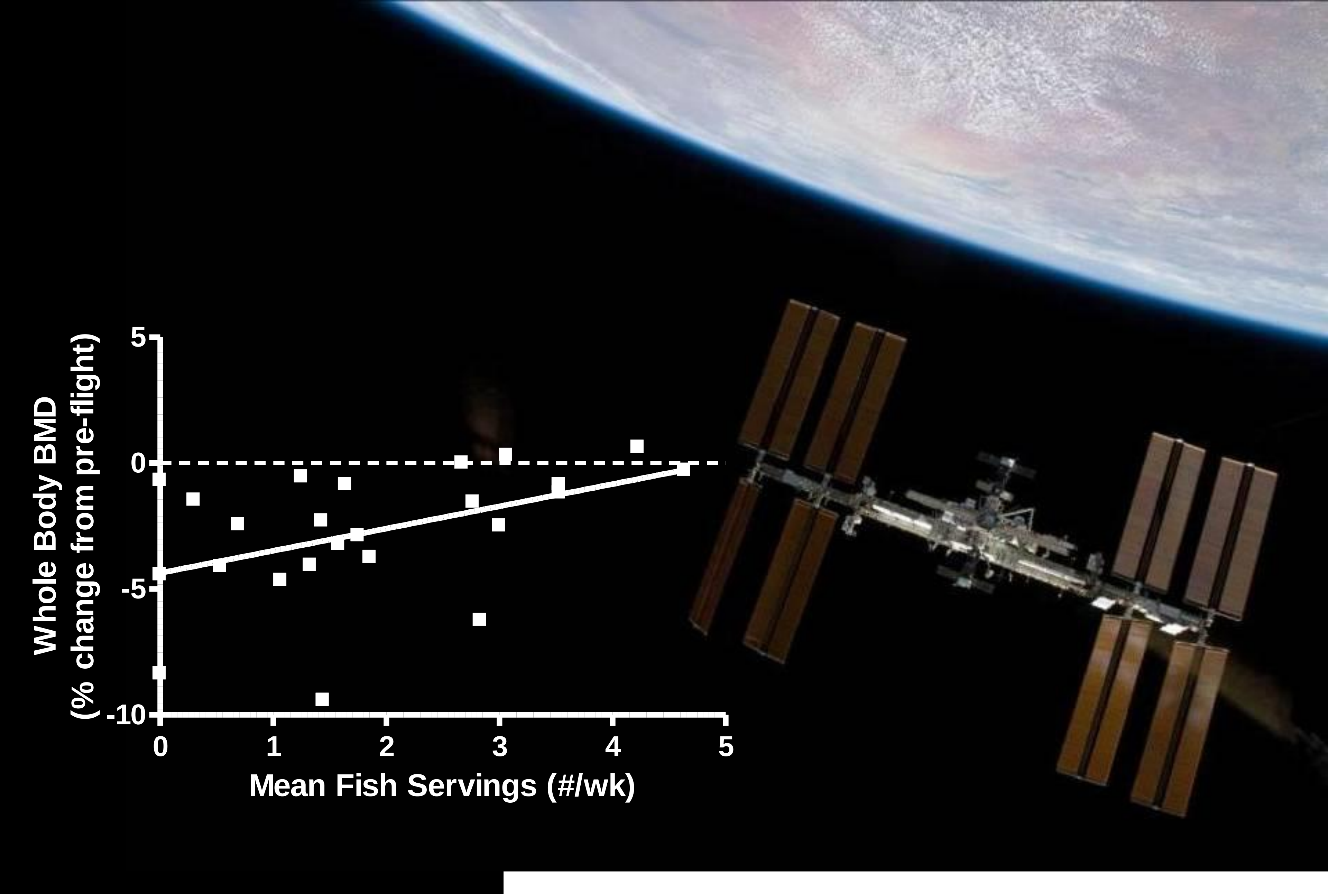


Ploutz-Snyder et al. 2014



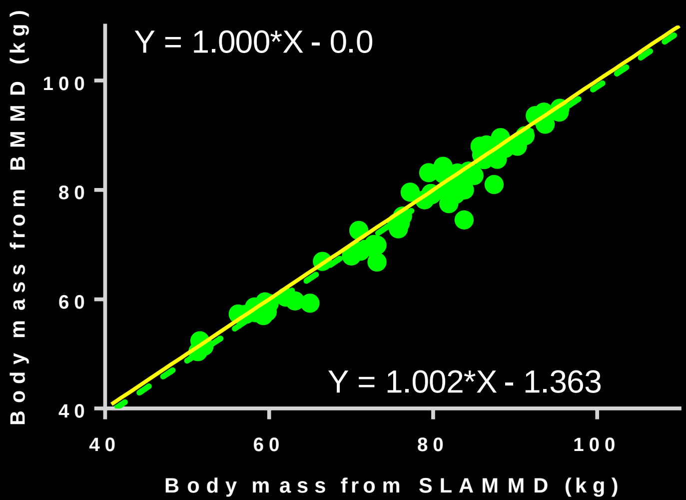
* Updated data since 2010 Bone Summit

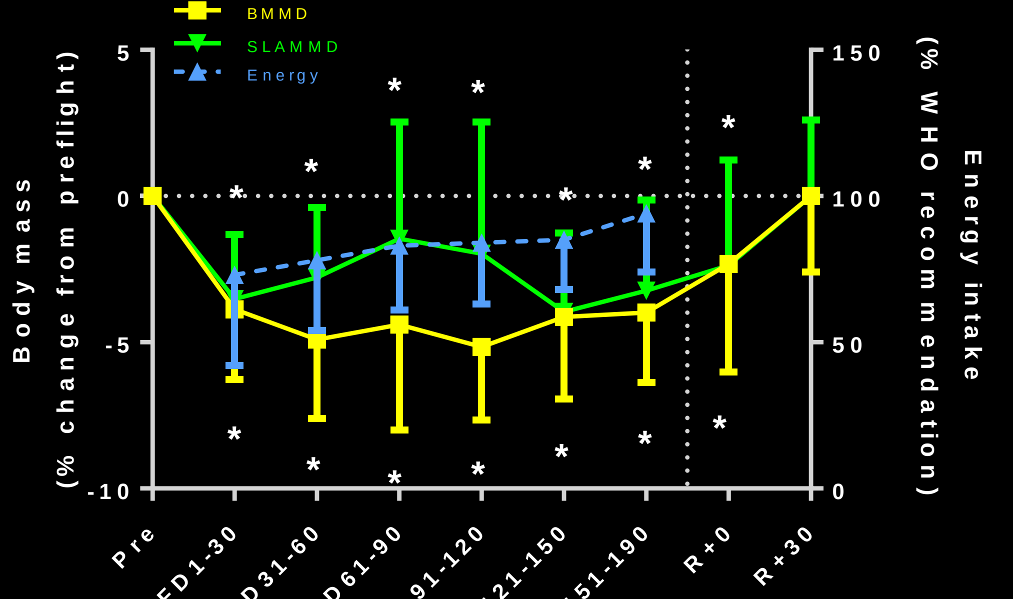
Sibonga et al. 2014



Smith et al. 2010

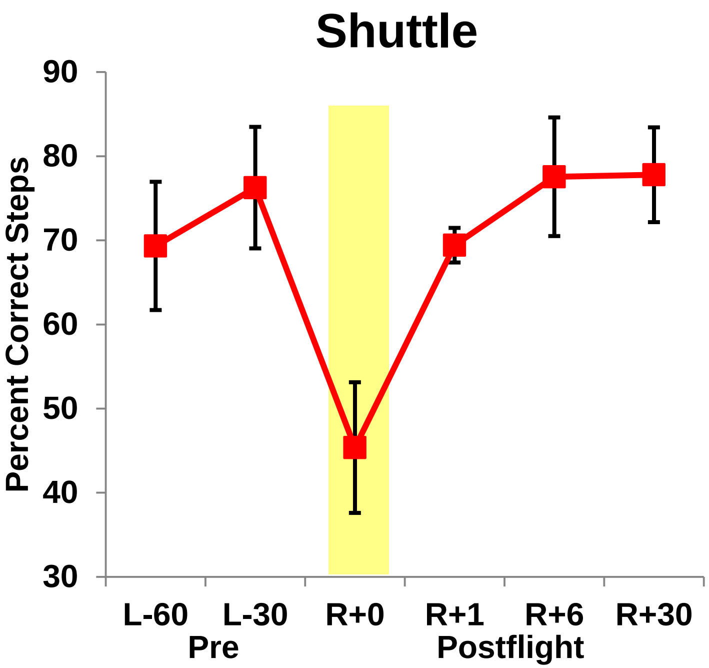
Body Mass

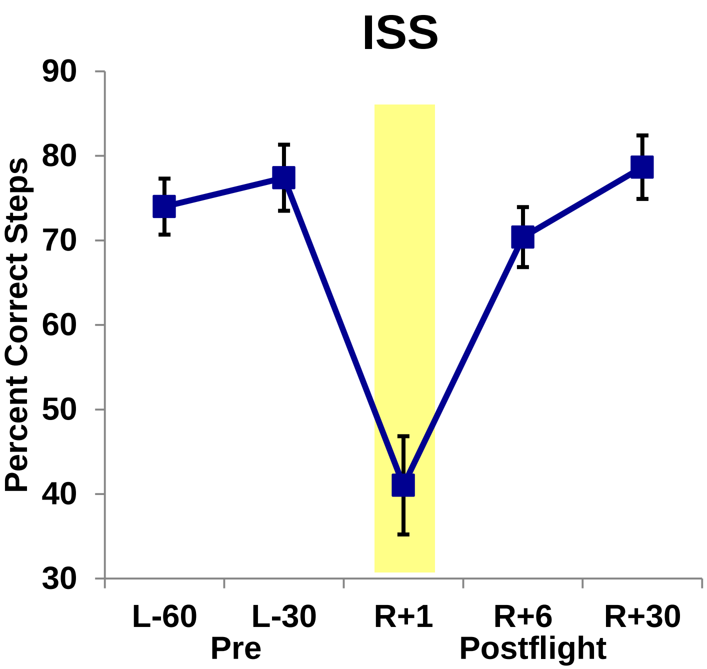




Zwart et al., *Aviation, Space, Environ Med,* 2014

Tandem Walk Test

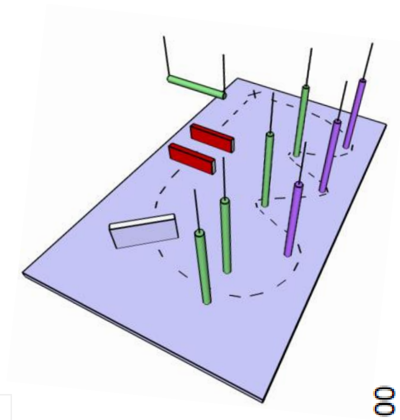




<u>Incorrect Steps</u>:
sidestepped, opened eyes,
or paused for more than
three seconds between steps

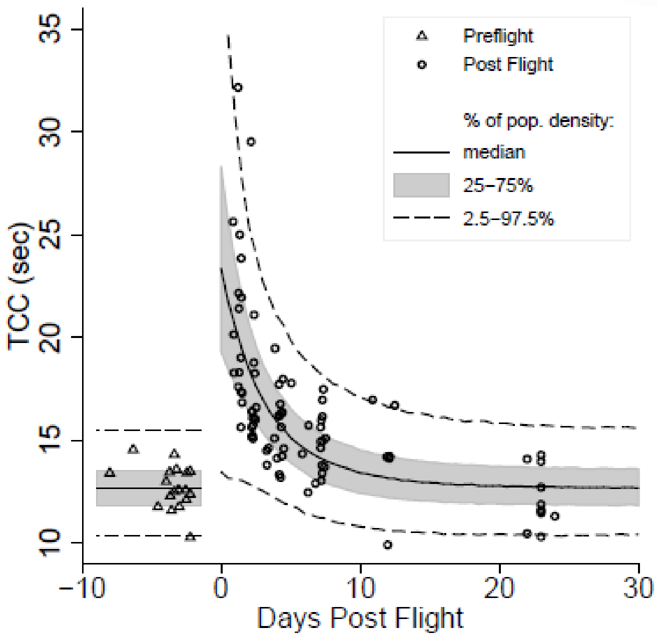
Bloomberg et al. 2014

Functional Mobility after Long-Duration Spaceflight (ISS)



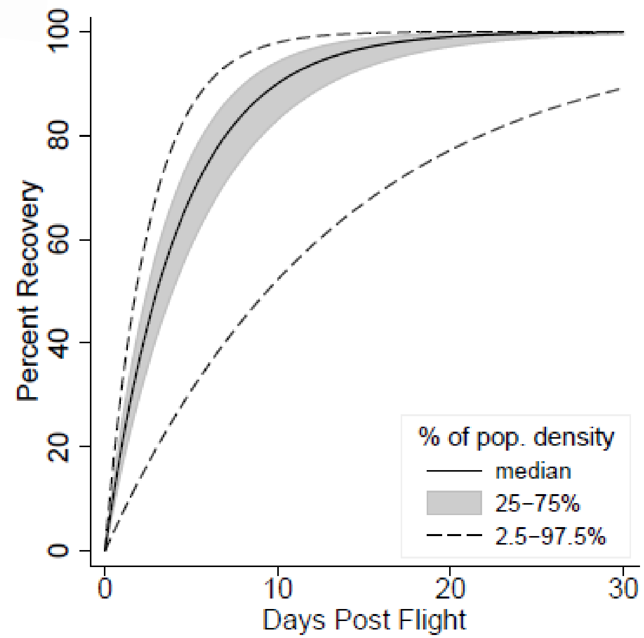
Functional Mobility Test

Time to Complete Course



N = 18

Percent Recovery

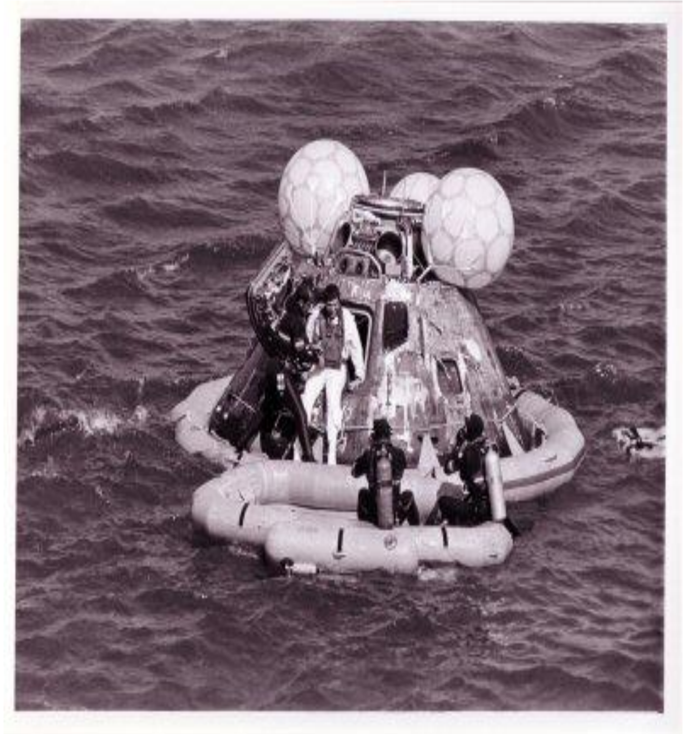


- Subjects showed a 48% increase in time to complete the course on R+1
- Recovery of functional mobility to 95% of preflight level took 15 days

Mulavara AP, Feiveson A, Feidler J, Cohen HS, Peters BT, Miller CA, Brady R, Bloomberg JJ. Experimental Brain Research. 202(3): 649-59. 2010.

Considerations from Apollo

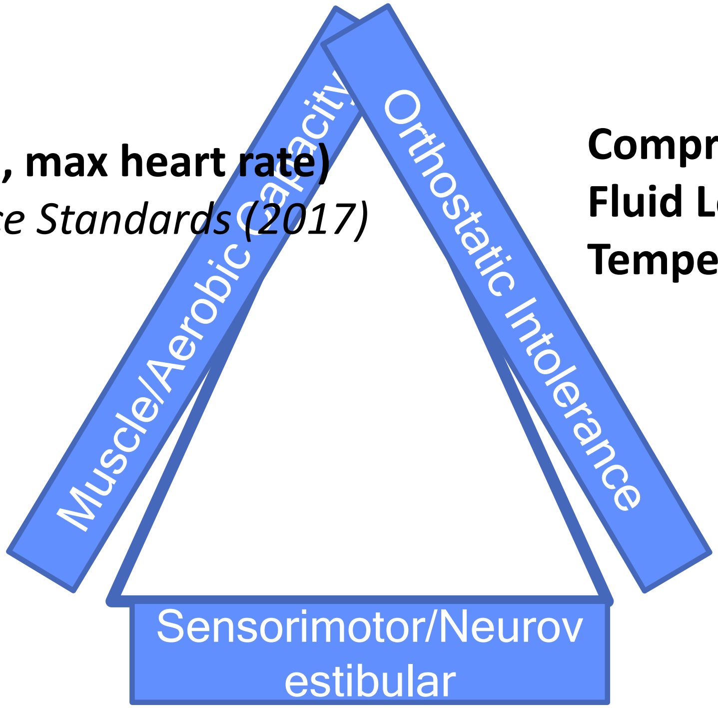
- Apollo 17 splashdown
  - 12.5 day mission, 3 day lunar stay
  - https://www.youtube.com/watch?v=_c2mDEdCJIc
  - Jack Schmitt, Ron Evans, Gene Cernan
- Biomedical Results of Apollo (http://history.nasa.gov/SP-368/s3ch8.htm):
  - With one important exception on the Apollo 15 mission, no crewmen experienced pronounced vestibular disturbances after returning from space flight. This finding suggests that adaptive processes that occur during weightless space flight missions of up to two weeks in duration do not render the vestibular system significantly hyposensitive or hypersensitive following sudden return to a one-g environment.
    - ✓ 33 subjects, 12 landed on moon, 6 to 12 day missions
  - Whether or not an individual is likely to develop inflight vestibular problems cannot be predicted reliably from his previous history of motion sickness.
  - Data relied heavily on crew self-reporting
- Principles of Clinical Medicine for Space Flight (Barratt,



Jack Schmitt egressing Apollo 17 Command Module

Recommended MPCV Countermeasures (Date Available)

Inflight Exercise
(max contractions, max heart rate)
Preflight Performance Standards (2017)



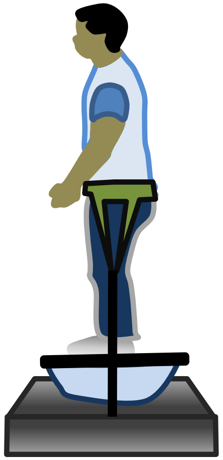
Compression Garments
Fluid Loading
Temperature Control

Preflight Adaptation Training (today)
Inflight Load + balance challenge (2018 MPCV AEC)
Vehicle/Suit/Operations design (in work)

Status of Integrated Sensorimotor Countermeasures

Sensorimotor Countermeasures	CRL	Reference
Preflight Sensorimotor Adaptability Training (w/ Stochastic Resonance)	CRL 5	Sensorimotor Adaptability Training Review Paper
Visual Flow/Virtual Reality with Treadmill walking (high % body loading)	CRL 4	Sensorimotor Adaptability Training Review Paper/ FTT final report
Inflight balance challenge with load	CRL 4	FTT final report
Space Motion Sickness Training	CRL 4	Preflight Adaptation Training and AFTE manuscripts and reports

Balance/Sensorimotor Adaptability Training



Preflight

Sensorimotor Adaptability Training

•Support surface motion (motion base treadmill system)

•Altered visual information

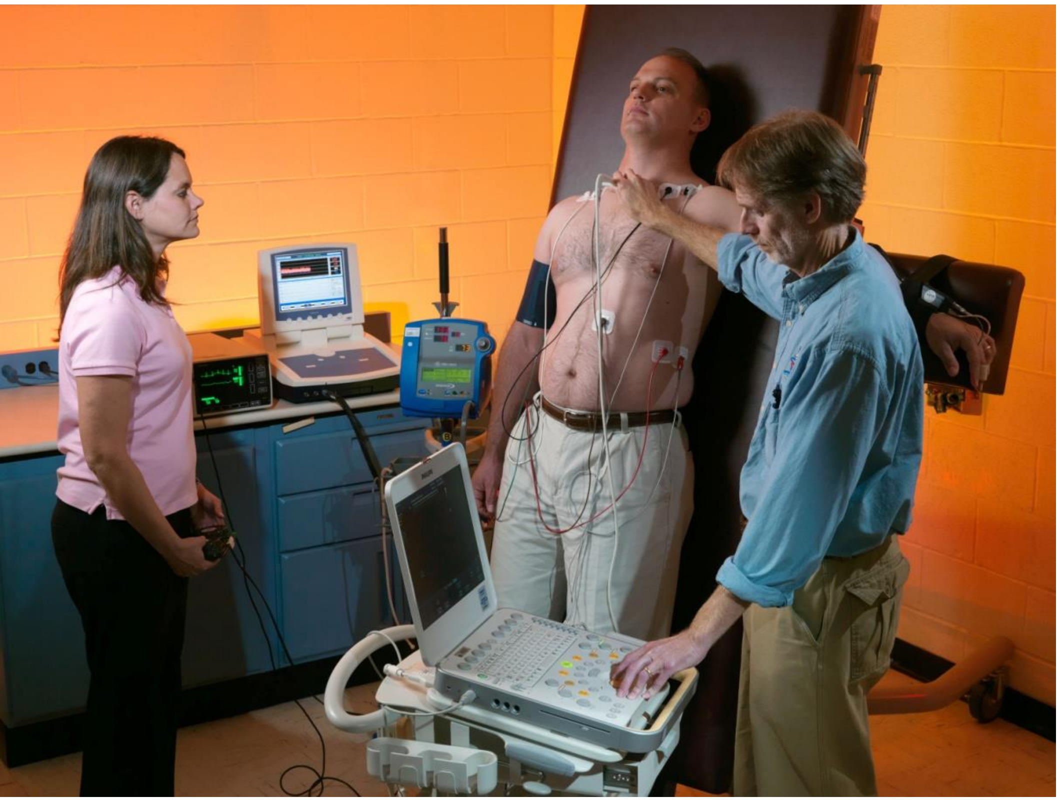
Inflight

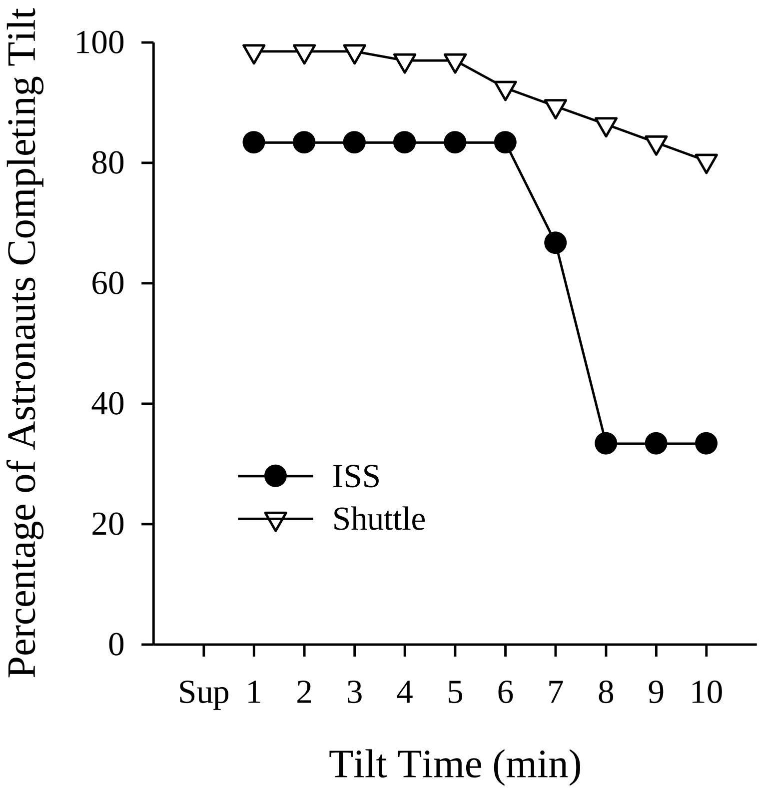
Balance and Sensorimotor Adaptability Training

•***Treadmill Walking***: 1-g body load, variation in head movements and visual flow

•***Balance Training***: Self-directed perturbations on unstable surface, 1-g body load, visual flow

Stenger et al., Pers. Com. 2015).



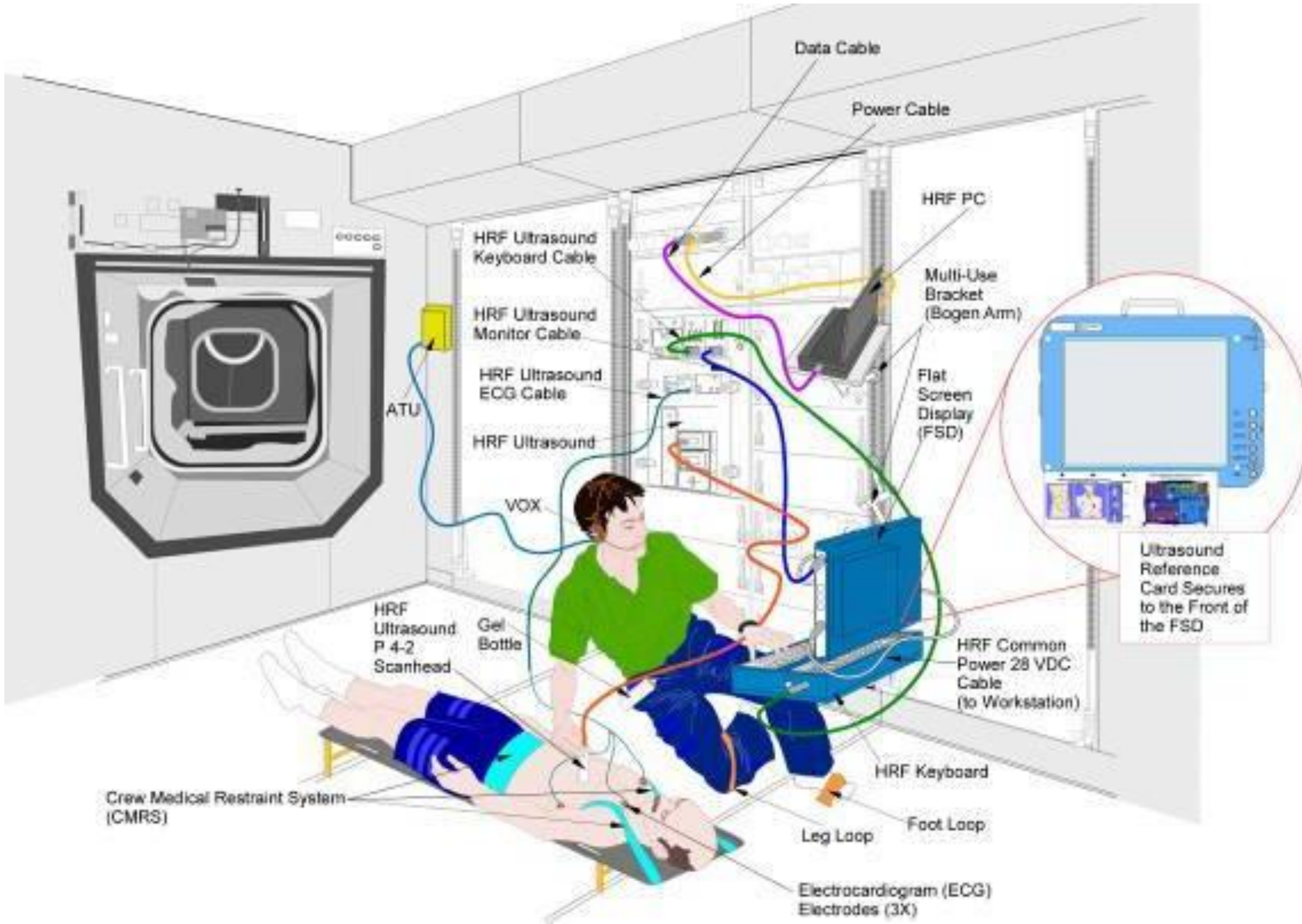


Orthostatic Intolerance

- Mitigated by:
  - Oral salt and fluid loading
  - Antigravity garment
  - Additional clinical i.v fluid treatment

Platts et al. 2012

'Integrated Cardiovascular'



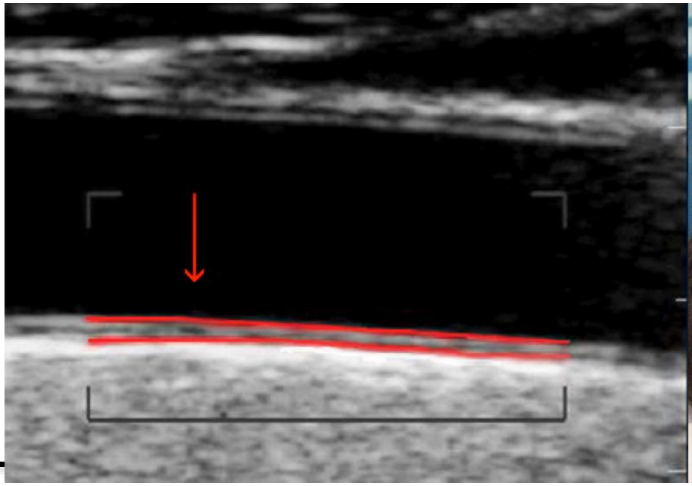
Levine & Bungo et al. 2014

Vascular Effects - II

Arbeille – 2014 – Assessment of the Carotid and Femoral Arteries wall thickness during 6 month ISS Flights (Vessel Imaging Experiment) 35th Annual International Gravitational Physiology Meeting

Carotid Artery Intimal Media Thickness (IMT), a subclinical precursor to atherosclerosis, increased by 15% between FD 110 – FD 135 as compared to FD 15 (n=10)
Remained elevated at R+4 testing.

(Arbeille et al. 2014, ISGP Waterloo).




- Weightlessness
- Radiation
- Isolation
- Stress
- Distance
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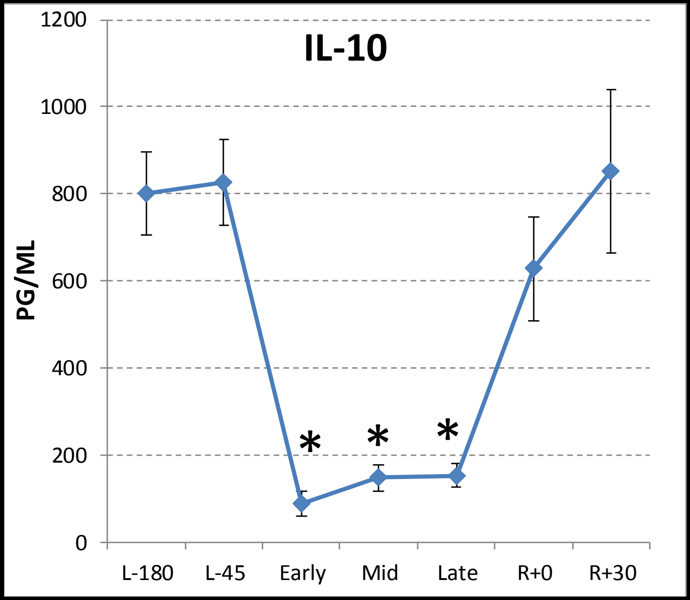
Synergistic effects?

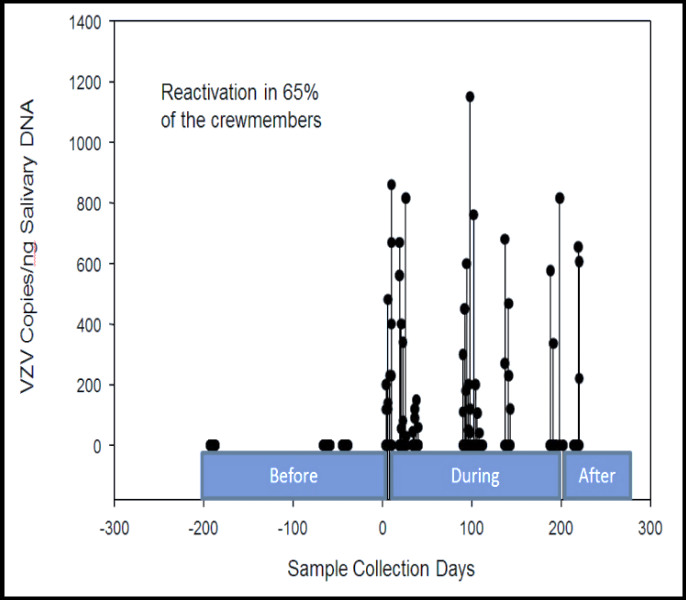
Immunity is Altered During Long-duration Spaceflight onboard ISS

Cytokine Production Profiles



N = 22

Latent Herpesvirus Reactivation



Crucian et al. 2014

VIIP Syndrome

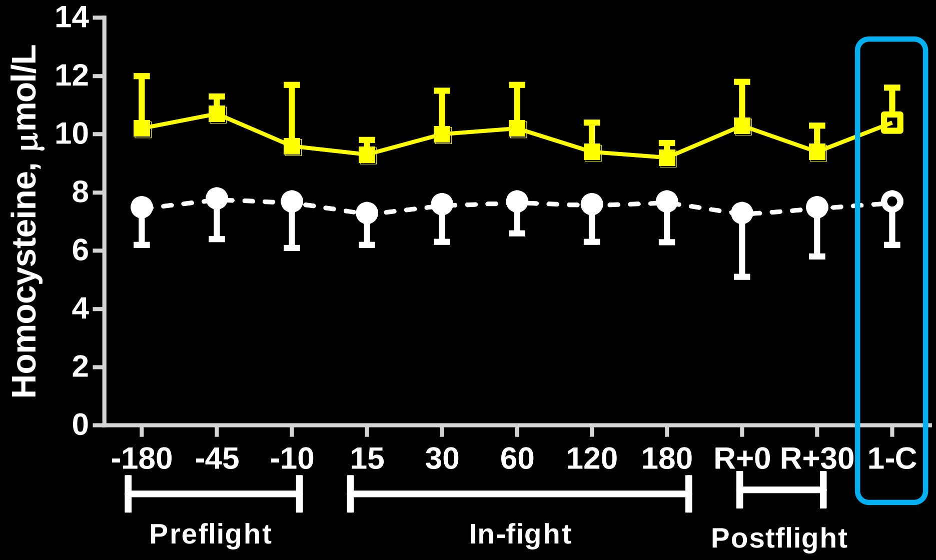
Fluid shift induced vision and intracranial pressure changes!

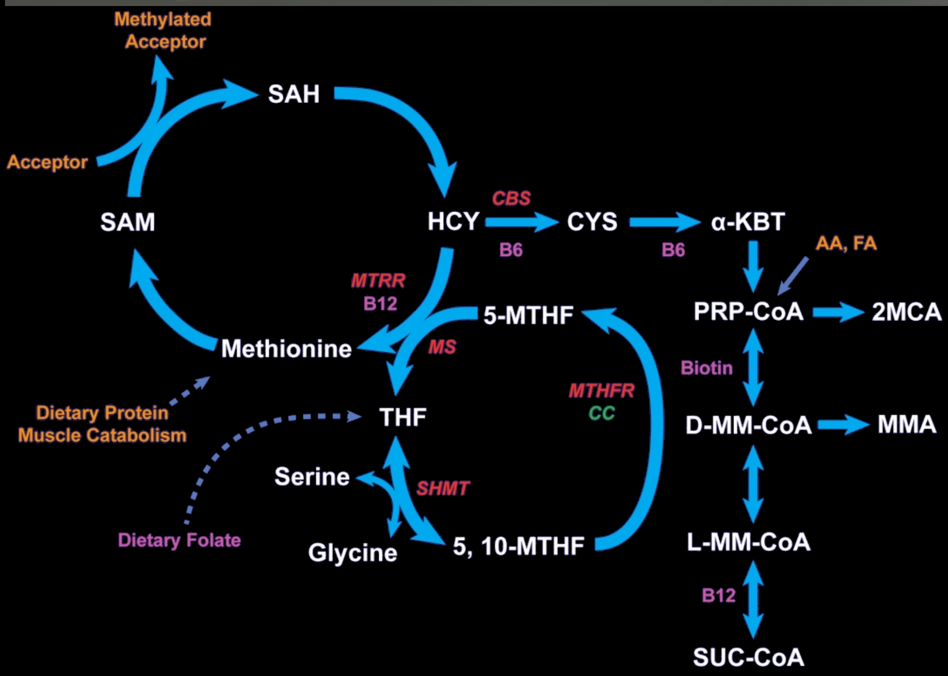
Example of cephalad fluid shift

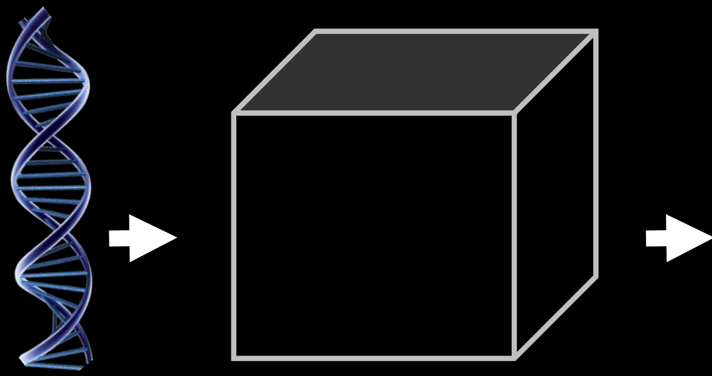
Preflight press briefing

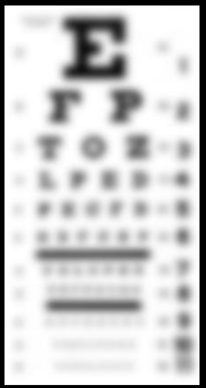
FD-2

One Carbon Metabolism/VIIP









Zwart et al., *J Nutr,* 2012

Future approach

IPCS:

IPCS:

IPCS:

Integrated
Physiological
Countermeasure
Suite

Based on ISS Research

Integrated Physiological Countermeasure Suite

Pre-flight

- Establish healthy life style: Exercise, food intake
- Develop individualized CM-protection programs: Computer modeling, G-transition training

Integrated Physiological Countermeasure Suite

In-flight

Monitoring

- Immune/OSaD-biomarkers (Lab analysis of urine, blood, saliva)
- Cardiovascular, VIIP, muscle/bone (ultrasound, ECG, BP, OCT, CCFP/TCD, vision, cognition)

Training & Prevention

- Sensory-motor adaptability training: Computer programs , vestibular (galvanic) stimulation
- Exercise prescriptions: Aerobic and resistive
- EVA pre-breathing
- Functional food items: Omega-3, anti-oxidants, low salt and iron
- Anti-osteoporotic medications: Bisphosphonates, anabolics, ACE-inhibitors

Treatment and prevention

- Anti-VIIP bracelets (+/- dynamic exercise) and/or medication
- Anti-motion sickness & anti-inflammatory medications (medication stability monitoring)
- Anti-orthostatic pre-landing fluid and salt ingestion

Integrated Physiological Countermeasure Suite

Planetary landing

- Anti-orthostatic garment and fluid/salt treatment
- G-transition medication, vestibular (galvanic) stimulation

Integrated Physiological Countermeasure Suite

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Planetary landing:

- Anti-orthostatic garment and fluid/salt treatment
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But -

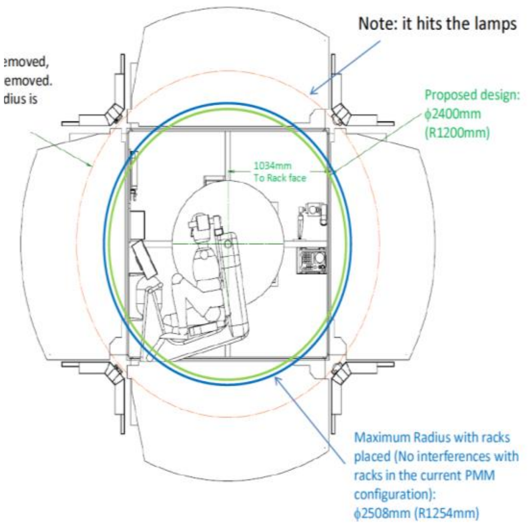
But – why not bring gravity?

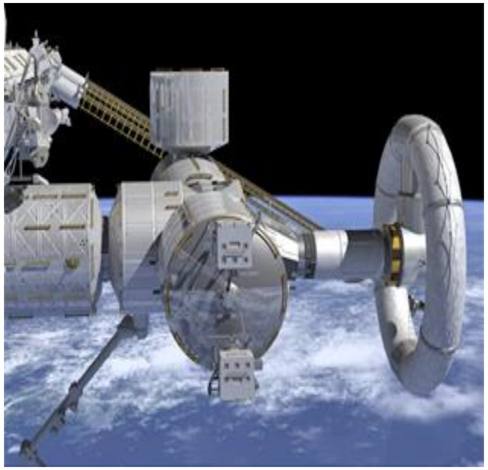
Example of cephalad fluid shift

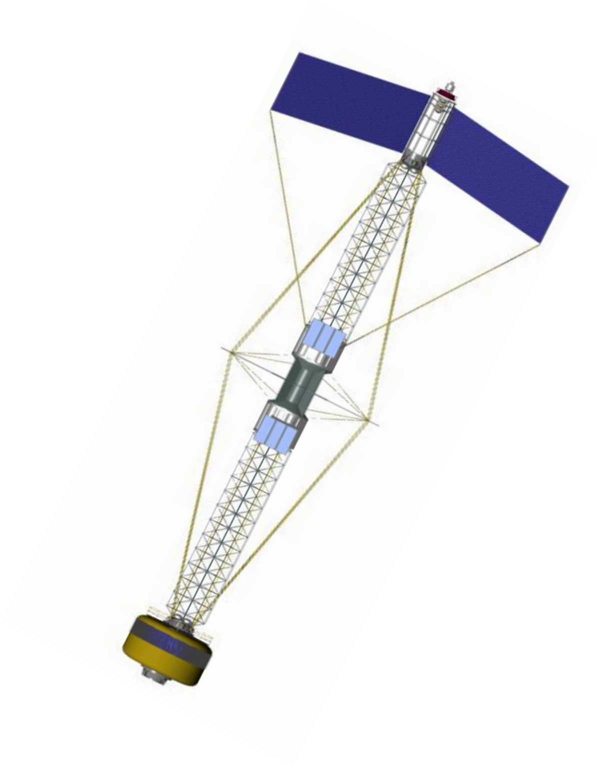
Preflight press briefing

FD-2

Artificial Gravity

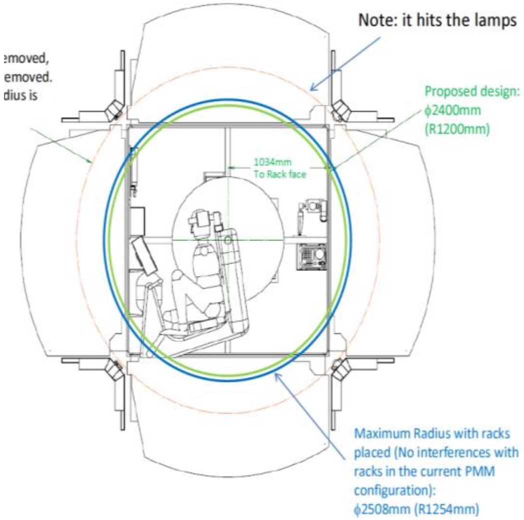


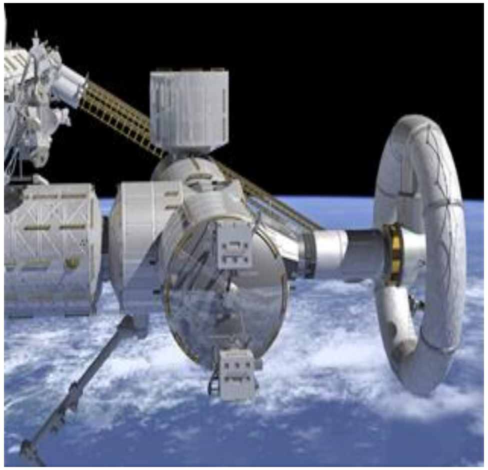


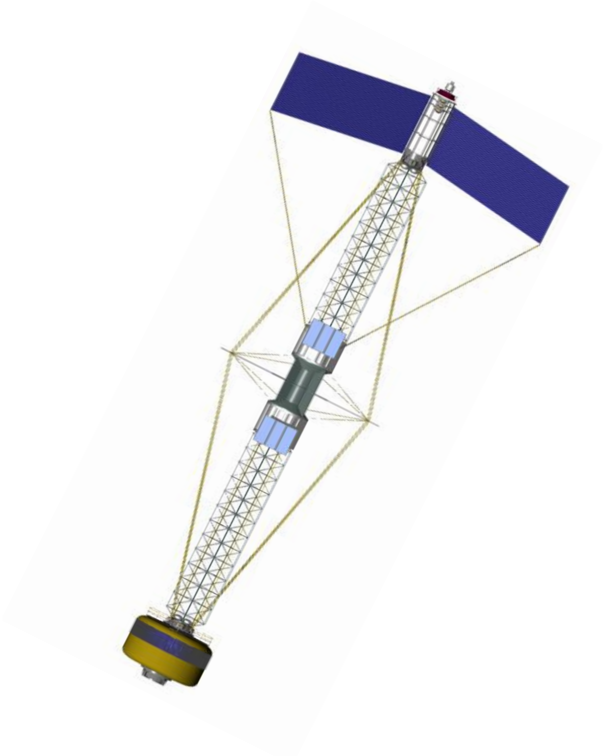


<u>Spinning:</u>

Artificial Gravity



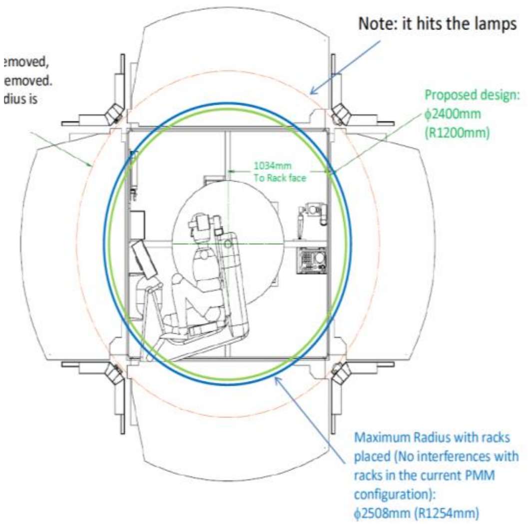


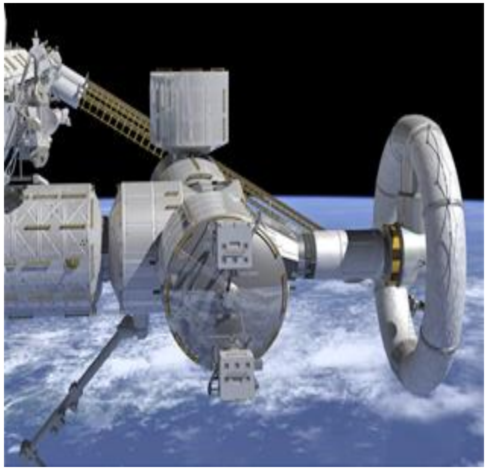


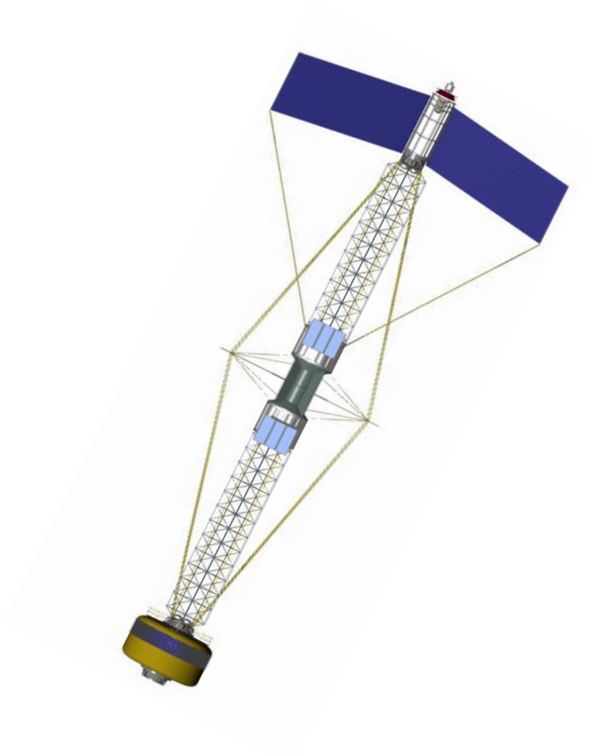
Spinning:

Inside

Artificial Gravity





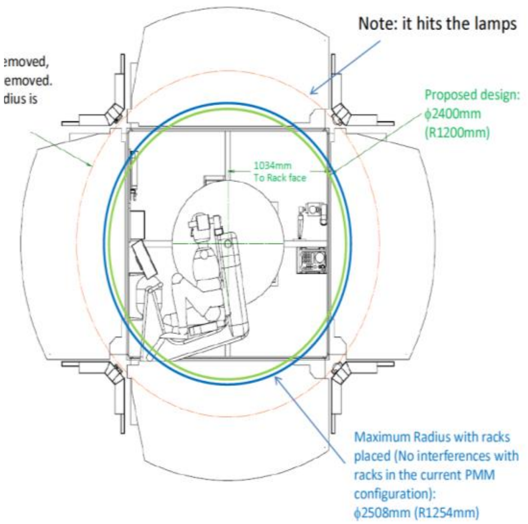


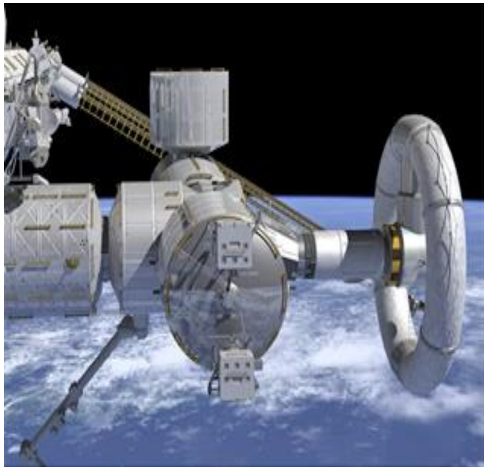
<u>Spinning:</u>

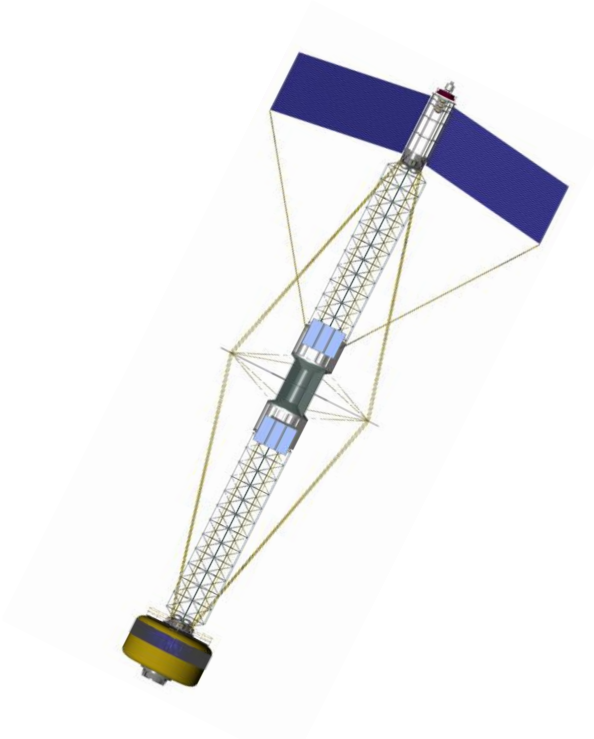
Part of

Inside

Artificial Gravity







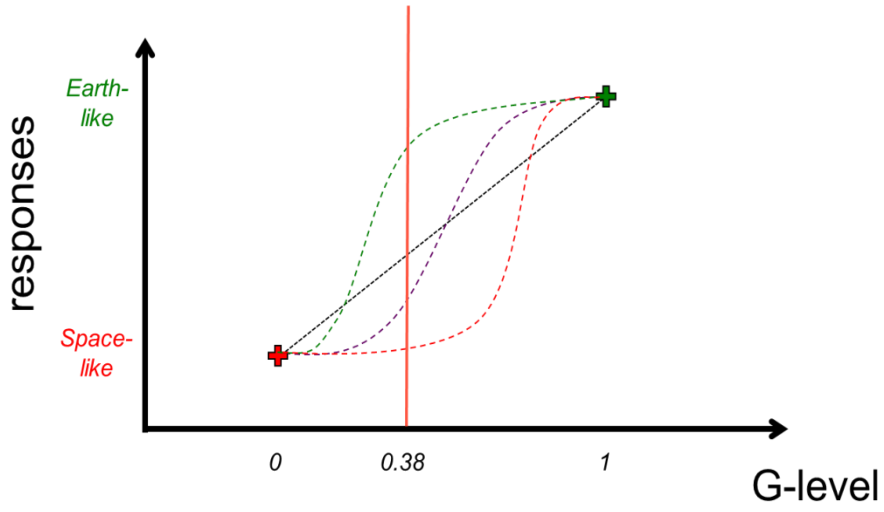
Spinning:

Inside

Part of

Whole vehicle

Physiological Responses to Hypogravity?



<u>We don't know:</u>

- The minimum artificial gravity level?
- The protection of Martian gravity?

Paloski 2014

Thank you!