Space Biomedical Engineering & Life Support

Humans in Space

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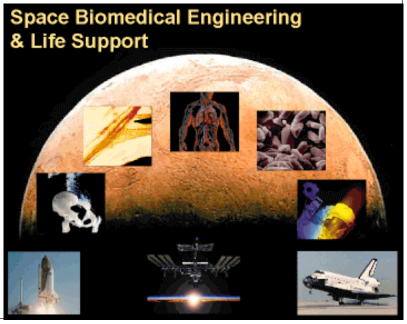
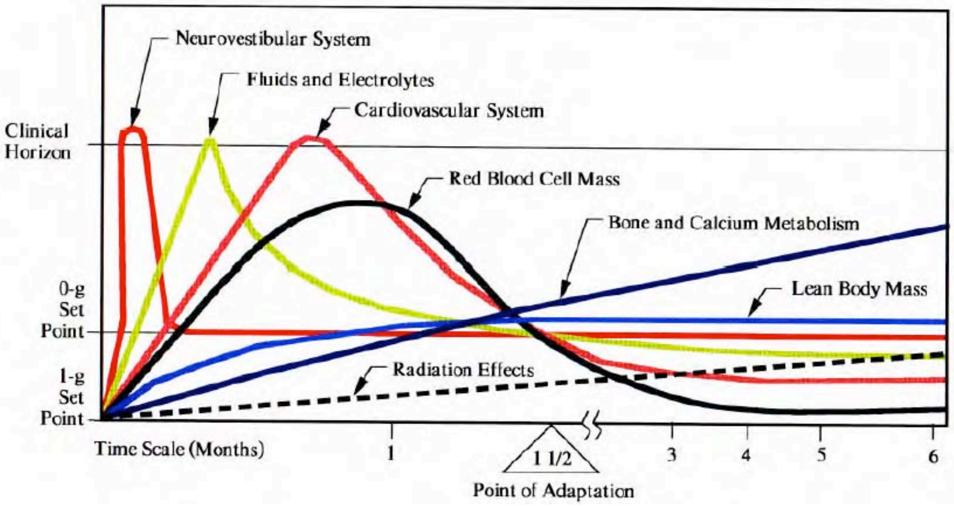
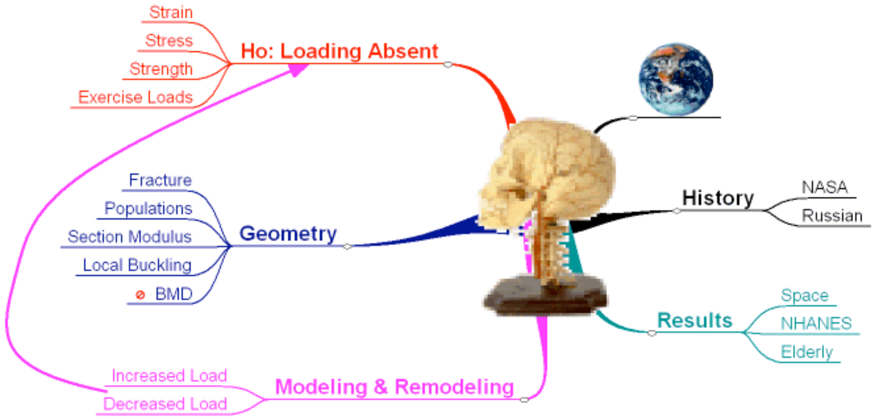


Physiological System



Bone - Summary



- Ho: Loading Absent
  - Strain
  - Stress
  - Strength
  - Exercise Loads
- Geometry
  - Fracture
  - Populations
  - Section Modulus
  - Local Buckling
  - ⊘ BMD
- Modeling & Remodeling
  - Increased Load
  - Decreased Load
- History
  - NASA
  - Russian
- Results
  - Space
  - NHANES
  - Elderly

Skeletal Consequences of Spaceflight

(Thanks to Dr. Grant Schaffner)

- Background
  - Early flights: very little idea of physiological changes to expect
    - big concerns: respiration, cardiovascular
    - bone probably wasn't a serious consideration
  - What has been learned in the past 4 decades of human spaceflight?

Spaceflight Bone Loss in Humans

Flight / Study	Finding	References
Gemini 4, 5, and 7	4-14 days; Calcaneus and metacarpal bone density losses of 2-4% for 5 astronauts, and 9% for sixth	Vose, 1974
Soyuz 9	18 days; 8-10% decrease in calcaneus density for both cosmonauts	Birykov and Krasnykh, 1970
Apollo 17	12.6 days; mean Ca loss of 0.2% of total body and mean Phosphorus loss of 0.7% of total body through increased urinary and fecal excretion	Rambaut, et al., 1975
Skylab 2 Mission	No significant bone mineral content changes in arm; calcaneus loss returned to normal by 87th day postfl.	Vogel & Whittle, 1976
Long Term Follow-Up of Skylab Bone Demin.	Statistically significant loss of os calcis mineral in nine Skylab crewmembers, 5 years after flight	Tilton, et al., 1980
Combined U.S. / U.S.S.R. Study of Long Term Flight	QCT of spine; Up to 8 months; No loss in vertebral bodies, but 8% loss in posterior elements (4% loss in volume of attached muscles); exercise countermeasures only partially successful	Oganov, et al., 1990
Mir 366-Day Mission	One cosmonaut averaged 10% loss of trabecular bone from L1, L2, L3; measured by QCT	Grigoriev, et al., 1991
Mir 4.5-6 Month Flights	QDR assessment of BMD; total body mineral losses averaged 0.4%; most marked local loss was in ***femoral neck and greater trochanter -- up to 14%***	Oganov, et al., 1992
Mir 1 and 6 Month Flights	pQCT; noticeable loss of trabecular and cortical bone in tibia after 6 months	Collet, et al., 1997
NASDA Study of 2 NASA Astronauts	42 y.o. female and 32 y.o. male; short flight; negative calcium balance; 3.0% loss of BMD in L2-4	Miyamoto, et al., 1998

Spaceflight Bone Loss in Animals

Flight / Study	Finding	References
Cosmos 605	Rats; Bone formation reduced in metaphyses of long bones	Yagodovsky, et al., 1976
Cosmos 782	Rats; 40% reduction in length of primary spongiosa due to reduced formation and increased resorption	Asling, 1978
Cosmos 782?	Rats; Osteoblast differentiation in *non-weight-bearing site* suppressed during weightlessness	Roberts, 1981
Cosmos 936	Rats; 30% decrease in femoral breaking strength of femora with recovery of normal properties after 25d	Spector, et al., 1983
Cosmos 782 & 936	Rats; Arrest line separating bone formed during and post-spaceflight; defective and hypomineralized bone	Turner, et al., 1985
Rat Tail Suspension, 1984	Up to 15 days; Calcium content: tibia = 86.2 +/- 2.5%, vertebra = 75.5 +/- 3.5% of control	Globus, et al., 1984
Cosmos 1514	Primates; 5 days; resorption increased during flight	Cann, et al., 1986
Cosmos 1667, 1887, 2044	Primates; 13 days; lower mineralization rate and less bone mineralized; longitudinal growth slowed	Cann, et al., 1990
Cosmos 1667	Rats; 7d spaceflight vs 7d tail-suspension; loss of trabecular bone in prox tibial metaph more extensive in flight rats	Vico, et al., 1991
Cosmos 2044	Rats; Fracture repair process impaired during flight	Kaplansky, et al., 1991
Cosmos 2229	Primates; 11.5 days; tendency toward decreased BMC during flight; only partial recovey 1 month after	Zerath, et al., 1996
Rat Tail Suspension, 1998	Unloaded bones display reduced osteoblast number, growth, and mineralization rate in trabecular bone	Morey-Holton and Globus, 1998

Bedrest / Hypokinesia Studies Models for Weightlessness of Spaceflight

Study	Finding	References
5-36 Weeks Bedrest	90 healthy young men; 5% loss of calcaneal minerla each month; mechanical and biochemical countermeasures not successful	Schneider and McDonald, 1984
120-day Bedrest	Mineralization rate slowed; contradictory results demonstrate difficulties of bedrest as space analog	Vico, et al., 1987
17-week Bedrest	6 healthy young males; 6 months of reambulation; ***BMD % change (p < .05): femoral neck (FN) -3.6, trochanter (T) -4.6; % / week (p < .05): FN -.21 +/- .05, T -.27 +/- .05; Reambulation % recovery: FN 0.00 +/- .06, T 0.05 +/- .05 (prox. femur did not recover well)***	LeBlanc, et al., 1990
370-day Antiorthostatic Hypokinesia Test	Highest losses in foot bones; remedial measures delay osteoporosis but do not completely exclude it; results obtained by different methods often conflicting	Zaichick and Morukov, 1998

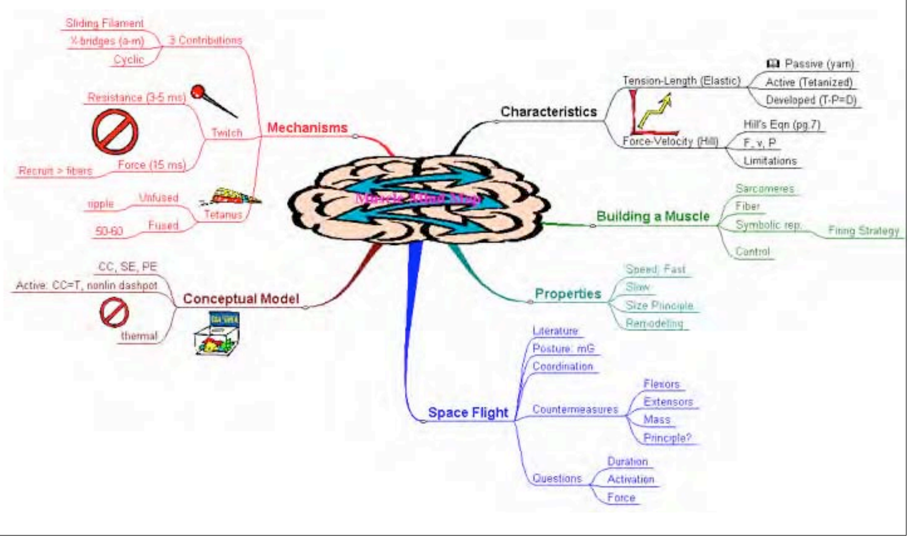
Bone Summary Findings

- Significant bone loss in weightlessness
- Calcium excretion increases– negative balance
- Bone mineral density decreases
  - weight bearing areas: 1-2% per month
- Osteoblast (builders) proliferation and activity reduced, while osteoclasts (consumers) appear to be unaffected
- Fracture repair may be impaired
- **Bone strength is reduced**

Bone Research Questions

- What is the rate of bone loss in critical areas?
- How does this affect bone strength?
- What is the risk of fracture?
  - duration of spaceflight
  - activity, gravity level
  - bone habitus: body weight, etc.
- What countermeasures are possible and how effective are they?

Muscle - Summary



Muscle Strength Loss in Microgravity

Strength loss over time

- Reported 40% lower at 6 months, 60% at 12 months
  - 21% lower peak activate force 17-day flight [Widrick, 1999]
  - 120 days HDT bed rest [Koryak 1999]
    - 44% / 33% (M/F) decline in isometric max. voluntary contraction (MVC)
    - 36% / 11% (M/F) decline in isometric twitch contraction
    - 34% / 24% (M/F) decline in tetanic contraction force
  - Maximal explosive power (MEP) reduced to 67% after 31 days, 45% after 180 days of space flight [Antonutto et al., 1999]

Effectors of the Motor System

- The major output of the elaborate information processing that takes place in our brain is the generation of a contractile force in our skeletal muscles.

- Muscle fasciculus
  - Muscle fiber
    - Myofibril
      - Sarcomere

- Each muscle fiber is innervated by only one motor neuron, although each motor neuron innervates a number of muscle fibers

- The motor neuron and all the fibers it innervates is called a motor unit (the smallest functional unit controlled by the motor system)

Innervation and Force

- The number of muscle fibers innervated by one motor neuron is called the innervation ratio. The innervation ratio can vary between 10 and 2000
- A low innervation ratio indicates a greater capacity for finely tuning the muscle total force

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Action Potential (AP)

From AP generation to muscular contraction

- Motor neuron fires an action potential
- It propagates down the motor axon until it reaches the neuro-muscular junction
- It triggers an AP in the muscle fiber
- This AP is propagated rapidly over the surface of the fiber and conducted into the myofibril by mean of the T-tubule system
- This in turn releases Ca^{++} from the Sarcoplasmic Reticulum (SR)-the SR serves as a store of Ca^{++}
- This in turn triggers the cyclic motion of Myosin heads, attaching and detaching on the Actin filaments, thus forming cross-bridges and generating the pulling force
- Ca^{++} are pumped back to the SR

Muscle Contraction

- The force of contraction depends on the length of the muscle (length-tension relationship)
- The force of contraction also depends on the relative rates of movement of the Actin and Myosin filaments (tension-velocity relationship, Hill's curve)
- Motor units are recruited in a fixed order from the weakest to the strongest (Henneman size principle): The weakest inputs recruit the slow units which generate the smallest force and are most resistant to fatigue. The fast fatigue-resistant are recruited next, followed by the fast fatigable units which generate the strongest force.

Cardiovascular System

- Cardiovascular problems following spaceflight have been encountered since the Mercury missions
- Drastically increased heart rates have been noted in upright tilt-table testing during the Gemini missions
- Post-spaceflight orthostatic intolerance was noted in Apollo astronauts for up to 3 days after landing
- Skylab (1970s) mission explored human physiology during long-term space missions
- Spacelab (1980s) provided a framework for studying human physiology with emphasis on various organs systems
- Neurolab (1998) explored several hypotheses regarding the the mechanisms underlying post-spaceflight OI.
- Orthostatic Intolerance (OI) still persists!

Orthostatic Intolerance

Presenting symptoms:

- Lightheadedness
- Palpitations
- Fatigue
- Blurred Vision
- Dizziness
- Syncope

Clinical Findings:

- Drop in Mean Arterial Pressure
- DRAMATIC Increase in Heart Rate

… upon assumption of the upright posture.

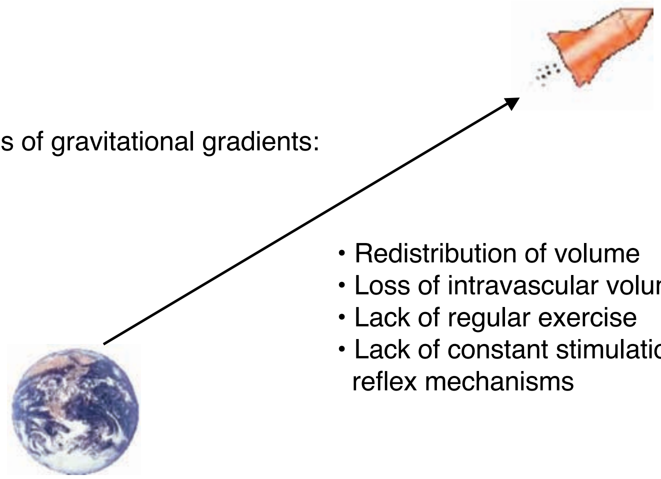
Research/Data Problems

- High variability in individual responses
- Small number of subjects studied
- Environmental effects unclear
- Conflicting experimental observations

Cardiovascular Problems Associated with Spaceflight

- Orthostatic Intolerance upon Re-entry
- Arrhythmias
- Loss of Cardiac Mass
- Reduced Exercise Capacity
- Manifestation of Pre-Existing Cardiovascular Diseases

Transition from 1g to Microgravity



Loss of gravitational gradients:

- Redistribution of volume
- Loss of intravascular volume
- Lack of regular exercise
- Lack of constant stimulation of reflex mechanisms

Hypotheses

- Cardiac Atrophy
- Hypovolemia
- Downregulation of Effector mechanisms
- Muscle Atrophy / Changes in Properties of Leg Circulation
- ...

Cardiovascular Summary

- Even after 30+ years of research, OI is still poorly understood.

- Current efforts rely on ground-based analogs such as bedrest.

- Computational models can:
  - help interpret experimental observations
  - test hypotheses
  - simulate the effects of countermeasures.

→ Computational Models will save the world!