Skeletal Health Risks Due to Spaceflight: Recommended Research Directions by a Clinical Advisory Panel

Northeast Ohio Medical University, Dept. of Anatomy and Neurobiology 2012 Spring Seminar Series

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Center for Space Medicine, Cleveland Clinic

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Overview

- Defining the risks in atypical conditions (The 3 C’s)
- Novel skeletal adaptation
- Directions for Bone Research
Overview

- Defining the risks in atypical conditions
- Novel skeletal adaptation
- Directions for Bone Research
Not a health care institution.

NASA CULTURE
NASA Human Research Program:
Mitigating Risk for the Human System

Evidence Base – Flight and Ground
- Science
- Clinical
- Operational experience

Inst of Medicine

Risks

Gaps

Standing Review Panels

Prioritization & Implementation Approach
- Need dates
- Budgets
- Research platform availability

Integrated Research Plan

Exploration Missions & Architectures

NASA Spaceflight Human System Standards

Results and Deliverables

Customer Review

Solicitations & Directed Research

Peer Review

Closure Metrics
Identified HRP “Bone” health risks due to space exploration.

1. Early Onset Osteoporosis  
   Long-term health issue
2. Bone Fracture
3. Formation of Renal Stones
4. Intervertebral Disc Injury (or Damage)  
   #2-4 Greater risk to mission operations.
Two Risks Associated with Fracture*

• Risk of Early Onset Osteoporosis Due to Spaceflight

  Osteoporosis: Condition of low bone mass and severe structural disruption leading to fractures under normal physical activities -- “fragility or atraumatic” fractures (fracture with fall from standing height)

  Osteoporosis is the INTERMEDIATE condition.

• Risk of Bone Fracture

  Factor of Risk = Ratio of Applied Load/Bone Failure Load ("Bone Strength")

  Includes TRAUMATIC FRACTURE - Biomechanics
Premature Osteoporosis fractures in astronauts?

Cooper and Melton, 1992

SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic
Does spaceflight result in irreversible changes to bone that combine with age-related losses?

Riggs BL, Melton LJ: Adapted from Involutional osteoporosis
Oxford Textbook of Geriatric Medicine
ADAPTED SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic
Given that osteoporosis is not a geriatric condition...

**WHAT SHOULD NASA MEASURE NOW TO ADDRESS AN OCCUPATIONAL HEALTH RISK THAT MAY MANIFEST *LATER*?**
Requirement for Evaluating Bone Strength

- “Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality.” JAMA 2001
- What is an index of Bone Quality? – any bone parameter that can influence bone strength independent of DXA BMD. *Supplement BMD as a predictor of fracture.*
Dual-energy X-ray Absorptiometry [DXA] BMD @ Johnson Space Center

- Monitor astronaut skeletal health
- Characterize skeletal effects of long-duration spaceflight
- Evaluate efficacy of bone loss countermeasures
- Verify restored health status
DXA measurement of areal BMD [BMD$_a$] – a 3d measure in 2d units

- Improved precision
- Low radiation
- Shorter scan times
- BMD measures over multiple skeletal sites
- Used in large prospective studies for fracture prediction
- Long established, widely-applied surrogate for bone strength
Limitation of DXA: cannot distinguish different geometries of bone and thus cannot reflect different levels of bone strength.

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<thead>
<tr>
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<tbody>
<tr>
<td>aBMD</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Compressive Strength</td>
<td>1</td>
<td>1.7</td>
<td>2.3</td>
</tr>
<tr>
<td>Bending Strength</td>
<td>1</td>
<td>4</td>
<td>8</td>
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</tbody>
</table>
DXA-based T-scores not appropriate, informative or predictive for fracture in astronaut population.

BMD T-Score Values* Expeditions 1-25 (n=33)
*Comparison to Population Normals
Understudied population for osteoporosis/novel risk factors

ASTRONAUT COHORT
The Long-duration Astronaut

- Typical space mission duration – $164 \pm 33d$ (range 58-215d)
- Average Age – $46.9 \pm 4.2 \text{ y}$ (range 36.8 – 55.3)
- Male to Female Ratio – 3.9 : 1
- Current total # per astronauts in corps – 44 of 331
- # repeat fliers – 4
- BMI – Male BMI $26.4 \pm 2.0$ (range 22.3 to 30.7); Female BMI $21.7 \pm 1.9$ (range 20.1 to 25.8)
- Wt and Ht- Males: Males: $82 \pm 9 \text{ kg}$ (range 63 to 101 kg), $177 \pm 6 \text{ cm}$ (range 163 to 188 cm);
- Wt and Ht Females: $61 \pm 6 \text{ kg}$ (52 to 72 kg), $168 \pm 3 \text{ cm}$ (range 163 to 173 cm)
Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
ASTRONAUTS EXPOSED TO UNIQUE SET OF RISK FACTORS DURING SPACEFLIGHT

- Aging
- Muscle Atrophy
- Ca/Nutrition/Vit D
- Increased and unbalanced bone resorption
- Inadequate peak bone mass
- Increased bone loss
- Low bone density
- Impaired bone quality/Stress risers

Skeletal fragility

Fracture

CO2; Radiation on bone marrow cells
Fluid shifts and regional blood flow

Postural instability
EVA Suit
Exercise Loads
Excessive bone loading

Kinetic Energy of Mass
Subject Numbers/Scheduling/Budget/Platform Availability/Therapeutic Windows

NASA CONSTRAINTS
The long-duration astronaut – Constraints to clinical practice guidelines

- Current total # per astronauts in corps – 44 of 331
- # repeat fliers – 4
- Male to Female Ratio – ~4:1
- Restricted presentation of sex-specific data – *Medical privacy*
- Limited Medical Assessment Tests – DXA, Biochemical bone turnover markers
- Limited expeditions/yr – 3 to 4
- Limited platform availability – 2020
Overview

• Defining the risks in atypical conditions

• Novel Skeletal Adaptation

• New Directions for Research
DXA BMD reveals changes that are unique & complex. Drives requirement for research.

Rapid (1-1.5%/mo) and site-specific BMD loss (means local regulation occurring).

<table>
<thead>
<tr>
<th>BMD Site</th>
<th>Mean Immediate Post Flight BMD (% change/month)</th>
<th>Mean Three Year Post Flight BMD (% change/month)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Predicted</td>
<td>Observed</td>
</tr>
<tr>
<td>Total Hip</td>
<td>1.063</td>
<td>0.994</td>
</tr>
<tr>
<td></td>
<td>(0.05)</td>
<td>(-0.76)</td>
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<tr>
<td>Lumbar Spine</td>
<td>1.081</td>
<td>1.016</td>
</tr>
<tr>
<td></td>
<td>(0.11)</td>
<td>(-0.58)</td>
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<tr>
<td>Ultra-Distal Radius</td>
<td>0.558</td>
<td>0.550</td>
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<tr>
<td></td>
<td>(-0.05)</td>
<td>(-0.20)</td>
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<tr>
<td>Mid-Shaft Radius</td>
<td>0.755</td>
<td>0.741</td>
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<tr>
<td></td>
<td>(0.19)</td>
<td>(-0.00)</td>
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<tr>
<td>Total Body</td>
<td>1.288</td>
<td>1.262</td>
</tr>
<tr>
<td></td>
<td>(-0.04)</td>
<td>(-0.26)</td>
</tr>
</tbody>
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Total BMD loss greater and persist compared to BMD changes predicted from algorithms derived from earth-based population.

Loss is variable.
Recovery is variable.
Recovery is prolonged.
Indicates: Multiple Risk Factors at play.
More informative. – but how do we translate to fracture risk in astronauts?
Bone Turnover Markers suggest a net loss in bone mass in the skeleton.