Skeletal Adaptation to Space

Transitioning Research to the Clinical Realm

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The Astronaut as the Human System

Systems Engineering & Integration

- Structure
- Electrical Power System
- Environ. Control Life Support
- Thermal
- I/T
- Human
Overview

• Uniqueness of NASA – Three C’s

• Unique Flight Data

• *Unique Recommendations*
How do you pitch the need for biomedical research to stakeholders who question the existence of the risk?
Does spaceflight result in irreversible changes to bone that combine with age-related losses?

Graph showing changes in bone mass over age for males and females, with indications for peak bone mass, age-related loss, and menopause-induced loss.
Consequence: Premature fractures in astronauts?

SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

Cooper and Melton, 1992
Constraints to Understanding Skeletal Adaptation
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
The Long-duration Astronaut

• Typical space mission duration – 163 ± 32d (range 90-215d)
• Average Age – 46.5 ± 4.5 y (range 36.8 – 55.3)
• Male to Female Ratio – 3.8 : 1
• Current total # per astronauts in corps – 34 of 331
• # repeat fliers – 4
• BMI – Male BMI 25.9 ± 2.2 (range 20.6 to 30.6); Female BMI 22.6 ± 2.2 (range 20.4 to 25.4)
• Wt and Ht- Males: Males: 81 ± 9 kg (range 62 to 101 kg), 177 ± 6 cm (range 163 to 185 cm);
• Females: 65 ± 7 kg (57 to 80 kg), 170 ± 4 cm (range 165 to 178 cm)
• MEDICAL PRIVACY OF THE ASTRONAUT.
Microgravity Effects on the Human Body

From Scientific American
Overview

- Uniqueness of NASA – Three C’s
- Unique Flight Data
- *Unique* Recommendations
**DXA: BMD losses are regional and rapid**

<table>
<thead>
<tr>
<th>Areal BMD g/cm²</th>
<th>%/Month Change ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole Body</td>
<td>0.3% / month</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td>-1.06±0.63*</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-1.15±0.84*</td>
</tr>
<tr>
<td>Trochanter</td>
<td>-1.56±0.99*</td>
</tr>
<tr>
<td>Total Body</td>
<td>-0.35±0.25*</td>
</tr>
<tr>
<td>Pelvis</td>
<td>-1.35±0.54*</td>
</tr>
<tr>
<td>Arm</td>
<td>-0.04±0.88</td>
</tr>
<tr>
<td>Leg</td>
<td>-0.34±0.33*</td>
</tr>
</tbody>
</table>

*p<0.01, n=16-18

LeBlanc et al, J Musculoskeletal 2000
DXA BMD increases in Postflight – is that recovery?

Sibonga et al. BONE 41:973-978, 2007
Medical Requirement, but Relative Risk based upon T-scores not very informative.

BMD T-Score Values* Expeditions 1-25 (n=33)
*Comparison to Population Normals
Change in DXA BMD after Long-Duration Mir and ISS Space Missions:
%Change Normalized to 6-Month Mission Length

n = 40 (7 Mir, 33 ISS)
Insert SMS’ slides
Research Technologies: QCT measures hip vBMD loss in trabecular bone compartment (n=16 ISS volunteers)

<table>
<thead>
<tr>
<th>Index</th>
<th>%/Month Change ± SD</th>
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<th>%/Month Change ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>aBMD Lumbar Spine</td>
<td>1.06±0.63*</td>
<td>Integral vBMD Lumbar Spine</td>
<td>0.9±0.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trabecular vBMD Lumbar Spine</td>
<td>0.7±0.6</td>
</tr>
<tr>
<td>aBMD Femoral Neck</td>
<td>1.15±0.84*</td>
<td>Integral vBMD Femoral Neck</td>
<td>1.2±0.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trabecular vBMD Femoral Neck</td>
<td>2.7±1.9</td>
</tr>
<tr>
<td>aBMD Trochanter</td>
<td>1.56±0.99*</td>
<td>Integral vBMD Trochanter</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trabecular vBMD Trochanter</td>
<td>2.2±0.9</td>
</tr>
</tbody>
</table>

*p<0.01, n=16-18

LeBlanc, J Musculoskelet Neuronal Interact. 2000; Lang, J Bone Miner Res, 2004;
QCT Postflight – Changes in at Femoral Neck 12 months after return

Bone Mineral Content (g)

Volumetric Bone Mineral Density g/cm³

Minimum Cross-sectional Area cm²

<table>
<thead>
<tr>
<th>Pre</th>
<th>Post</th>
<th>12</th>
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</thead>
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<td>Post</td>
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</tr>
<tr>
<td>Pre</td>
<td>Post</td>
<td>12</td>
</tr>
</tbody>
</table>

P < 0.05 with respect to preflight*, postflight*

Slide adapted from T. Lang., JBMR 2006.
QCT: Trabecular BMD at Femoral neck does not appear to show a recovery 2 to 4 years postflight.

GAP: What is the impact of Trabecular Bone Loss on whole hip bone strength?

Lower trabecular BMD was an independent predictor of hip fracture in elderly men. Overall, QCT measures provide useful information regarding causation of hip fracture, evaluation of hip fracture risk and possible targets for intervention.
Overview

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• Unique Flight Data

• *Unique* Recommendations
Bone Summit Panel Members

- **Eric Orwoll, MD**
  - Endocrinology and Male Osteoporosis
- **E. Michael Lewiecki, MD, FACP, FACE**
  - Endocrinology, ISCD
- **Neil Binkley, MD, CCD**
  - ISCD, Geriatrics and Vitamin D
- **Shreyasee Amin, MD**
  - Rheumatology, Male Osteoporosis and Epidemiology
- **Sue Shapses, PhD**
  - Nutritional Sciences and Weight-loss
- **Robert A. Adler, MD**
  - Male Osteoporosis and Epidemiology
- **Steven Petak, MD, JD, FACE**
  - Endocrinology, ISCD
- **Mehrsheed Sinaki, MD**
  - Physical Medicine & Rehabilitation
- **Nelson B. Watts, MD**
  - Endocrinology, ISCD

Left to Right, Top Row down
Finite Element Modeling [FEM]:
What is it and what can it tell NASA about hip fracture risk in the long-duration astronaut?
FEM – a computational tool to estimate failure loads to complex structures.

Images courtesy of Dr. J Keyak

FEM of QCT data integrates multiple factors associated with fracture to provide a single composite number to estimate bone strength.

Geometry

Material Properties

BMD

Loading

Finite Element Strength

Individualized Fracture Risk
QCT + FEM has superior capabilities for estimating mechanical strength

QCT estimates fracture loads better than DXA

QCT + FEM has superior capabilities for estimating fracture loads

DD Cody: Femoral strength is better predicted by finite element models than QCT and DXA. J Biomechanics 32:1013 1999.
# Astronaut Data—Hip Strength

$N=11$ crewmembers

<table>
<thead>
<tr>
<th>Loading Condition</th>
<th>Mean (SD) Pre-flight</th>
<th>Mean (SD) Post-flight</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stance</td>
<td>13,200 N (2300 N)</td>
<td>11,200 N (2400 N)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td><strong>2.2% loss/month</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fall</td>
<td>2,580 N (560 N)</td>
<td>2,280 N (590 N)</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td><strong>1.9% loss/month</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1.0-1.5% BMD loss / month
Astronaut Data: Surrogates of bone strength do not correlate.

Stance: $R^2=0.23$
Fall: $R^2=0.05$

Summary

• Unique cohort, unique environment, unique changes in bone structure during long-duration missions in microgravity

• DXA – A widely-applied medical test to predict fracture risk in population at risk (menopausal, elderly)

• QCT – A Research Imaging Technology that increases our knowledge but applied on limited volunteer basis.

• FE modeling of strength – An improved estimate of hip bone strength for NASA to consider for clinical decisions.
Closing Remark

NASA Goal: To reduce the uncertainty of *spaceflight-induced* fracture risks in astronauts by increasing our understanding of spaceflight effects on bone -- by employing the best technologies and analyses available.
Thank you.
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- Piotr Truszkowski (NSBRI, Harvard Medical School)
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