Space: The Final Frontier of Bone Density

Jean D. Sibonga, Ph.D., Lead Bone Discipline, NASA Human Research Program at Johnson Space Center, Houston, TX

It is a medical requirement at NASA to evaluate the skeletal integrity of “long-duration” astronauts by measuring bone mineral density [BMD] with DXA technology. A long-duration mission is a spaceflight that is greater than 30 days but is typically the continuous 120-180 day missions aboard the International Space Station [ISS]. Not only does NASA use the BMD index to monitor fracture risk in this astronaut population, but these measures are also used to describe the effects of spaceflight, to certify skeletal health readiness for flight, to monitor the recovery of lost bone mass after return to earth, and to evaluate the efficacy of countermeasures to bone loss. However, despite the fact that DXA-based BMD is a widely-applied surrogate for bone strength that is grounded in an abundance of population-based fracture data, its applicability to the long-duration astronaut is limited. The cohort of long-duration astronauts is not the typical group for evaluating osteoporosis or determining age-related fracture risk. The cohort is young (< 55 years), predominantly male and exposed to novel risk factors for bone loss besides the weightlessness of space. NASA is concerned about early onset osteoporosis in the astronaut exposed to long-duration spaceflight, especially since any detectable symptoms are likely to manifest after return to earth and perhaps years after space travel. This risk raises the question: is NASA doing enough now to mitigate a fracture event that may manifest later? This presentation will discuss the limitations and constraints to understanding skeletal changes due to prolonged spaceflight and the recommendations, by clinical experts in osteoporosis and BMD, to transition research technologies for clinical decision-making by NASA.
Space: The Final Frontier of Bone Density

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Insert video

• editing of video
The Astronaut as the Human System

Systems Engineering & Integration

- Structure
- Electrical Power System
- Environ. Control Life Support
- Thermal
- I/T
- ... Human
Gain & Loss of Bone Mass with Aging

- Peak Bone Mass
- Age-related Loss
- Menopause-induced Loss

Legend:
- Males
- Females

Bone mass (g/calcium)

Age (yr)

0 20 40 60 80 100

Riggs BL, Melton LJ: Adapted from Involutional osteoporosis Oxford Textbook of Geriatric Medicine ADAPTED SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic
Age-Related Fractures

Cooper and Melton, 1992

SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

Cooper and Melton, 1992
History of Bone Imaging in Space

- **Mercury** (1961-63)
  - X-ray densitometry

- **Apollo** (1965-66)
  - SPA heel and wrist

- **Gemini** (1968-72)
  - SPA heel and wrist

- **Skylab** (1973-74)
  - SPA heel and wrist

- **Soyuz/Salyut** (1974-85)
  - SPA
  - DPA

- **Mir** (1974-85)
  - DXA whole body
  - CT of lumbar spine BMD

- **ISS** (2000-present)
  - DXA
  - QCT
  - **HR3DpQCT (ESA)**

Slide adapted from Dr. Jean Sibonga, NASA JSC
Overview

- Uniqueness of NASA

- Spaceflight Effects: *Out-of-this-World Data*

- *Bold* Approaches to Managing Bone Risk
The Long-duration Astronaut

- Typical mission duration – 163 ± 32d (range 90-215d)
- Average Age – 46.5 ± 4.5 y (range 36.8 – 55.3)
- T-score at first* DXA BMD –
- Male to Female Ratio – 3.8 : 1
- Current total number out of total # astronauts in Corps – TBD
- # repeat fliers – 4
- BMI etc– Males 25.9 ± 2.2; Females 22.6 ± 2.2 kg/m²
- Wt and Ht- Males: 179 ± 20 lbs, 5.8 ± 0.2 ft; Females: 143 ± 15 lbs, 5.6 ± 0.1 ft
Constraints to Understanding Skeletal Adaptation
Adapted from: Cooper C, Melton LJ
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

Radiation on bone marrow cells
Fluid shifts and reduce regional blood flow

Postural instability

Kinetic Energy of Mass

EVA Suit

Exercise Loads

Skeletal fragility

Fracture

PRA Models

Excessive bone loading

Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
Overview

• Uniqueness of NASA

• Spaceflight Effects: *Out-of-this-World Data*

• *Bold* Approaches to Managing Bone Risk
DXA: BMD losses are regional and rapid

<table>
<thead>
<tr>
<th>Areal BMD</th>
<th>%/Month Change ± SD</th>
<th>%/Month</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar Spine</td>
<td>-1.06±0.63*</td>
<td>1%</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-1.15±0.84*</td>
<td></td>
</tr>
<tr>
<td>Trochanter</td>
<td>-1.56±0.99*</td>
<td></td>
</tr>
<tr>
<td>Total Body</td>
<td>-0.35±0.25*</td>
<td></td>
</tr>
<tr>
<td>Pelvis</td>
<td>-1.35±0.54*</td>
<td></td>
</tr>
<tr>
<td>Arm</td>
<td>-0.04±0.88</td>
<td></td>
</tr>
<tr>
<td>Leg</td>
<td>-0.34±0.33*</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.01, n=16-18

LeBlanc et al, 2000
What about recovery?

Trochanter: \( \text{Loss}_0 = 7.8\% \quad \text{50\% Recovery} = 255\text{d} \)

DXA BMD increases in Postflight Period after long-duration flights.
Research Study: QCT measures loss hip vBMD due to spaceflight in trabecular bone compartment (n=16 ISS)

<table>
<thead>
<tr>
<th>Index</th>
<th>%/Month Change ± SD</th>
<th>Index</th>
<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>Trabecular vBMD Lumbar Spine</td>
<td>0.7±0.6</td>
<td>Integral vBMD Femoral Neck</td>
<td>1.2±0.7</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>Trabecular vBMD Femoral Neck</td>
<td>2.7±1.9</td>
<td>Integral vBMD Trochanter</td>
<td>1.5±0.9</td>
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<tr>
<td>aBMD Trochanter</td>
<td>1.56±0.99*</td>
<td>Integral vBMD Trochanter</td>
<td>1.5±0.9</td>
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<td>2.2±0.9</td>
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*p<0.01, n=16-18

QCT Postflight – Changes in bone mass and structure at Femoral Neck 12 months after return

Bone Mineral Content (g)

Femoral Neck

Volumetric Bone Mineral Density g/cm³

Minimum Cross-sectional Area cm²

P < 0.05 with respect to preflight*, postflight*

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

PRE: n=16   POST: n=16   1 YEAR: n=16   EXT: n=8
What is the impact of Trabecular Bone Loss on whole hip bone strength?

http://depts.washington.edu/bonebio/ASBMRed/structure.html

Photo by Paul Crompton
©University of Wales College of Medicine
And what has happened to bone microarchitecture of hip?

L Mosekilde
Overview

• Uniqueness of NASA

• Spaceflight Effects: 
  *Out-of-this-World Data*

• *Bold* Approaches to Managing Bone Risk
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 that uses QCT data to estimate hip bone 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.
FEM to estimate changes to hip bone strength after spaceflight.

- Geometry
- Material Properties
- BMD
- Loading

Finite Element Strength

Individualized Fracture Risk
Individual Results

Stance Loading (4 to 30% loss in strength)

![Graph showing hip strength over time with a max loss of 30%](image-url)
Individual Results

Fall Loading (3 gain to 24% loss in strength)
Surrogates of bone strength do not correlate.
Summary

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

• QCT – added measures of bone that increase our knowledge about how spaceflight affects bone structure – changes that may combine with aging effects

• FE estimates of strength – an improved surrogate for NASA by individualizing the estimates of hip bone strength per astronaut.
Final Comments

• Clinical goal: Prevention of fractures by identifying those at highest risk – risk factors to enhance DXA predictive capabilities

• NASA goal: To reduce the uncertainty of fracture risks (fragility and traumatic fractures) during a mission, after a mission and as the astronaut ages by employing the best technologies and analyses available.
Thank you!
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• Robert Wermers, M.D. (Mayo Clinic)
Backup Slides
QCT does not outperform DXA-BMD for fracture prediction but provides extra information that DXA does not

| Table 4. HRs of Multivariate Models of Skeletal Parameters at the Femoral Neck for Hip Fracture Adjusted for Clinic Site, Age, and Body Mass Index |
|------------------------------------------|------------------------------------------|------------------------------------------|
| Model A (HR per SD decrease)            | Model B (HR per SD decrease)             | Model C (HR per SD decrease)             |
|                                        | HR    | 95% CI        | p   | HR    | 95% CI        | p   | HR    | 95% CI        | p   |
| Trabecular bone, volumetric BMD (g/cm³) |        | —             |     | 1.65  | 1.15, 2.37    | 0.007 | 1.29  | 0.84, 1.98    | 0.250 |
| Percent cortical volume                 |        | —             |     | 3.19  | 2.23, 4.57    | <0.001| 2.42  | 1.56, 3.76    | <0.001|
| Minimum cross-sectional area (cm²)      |        | —             |     | 1.59  | 1.24, 2.05    | <0.001| 1.48  | 1.14, 1.94    | 0.004 |
| Areal BMD from DXA (g/cm²)              | 4.13   | 2.67, 6.38    | <0.001| —     |              |     | 1.91  | 1.06, 3.46    | 0.033 |

Area under the ROC curve for Models A, B, and C were 0.853, 0.855, and 0.860, respectively.
Bone Fracture Risk Module (BFxRM)

Biomechanics and Mission Operations

courses.washington.edu/me598rc

Bone Loss in Space

Figure 2. Summary of literature survey on fracture load as a function of femoral neck BMD

Estimate of Fracture Probability

Probability of Fracture

Probability of event

Probability bone will fail to support load

Clinical and Engineering Characteristics of Bone Strength
ES Nelson et al. Development and validation of a predictive bone fracture risk model for astronauts NASA Glenn Research Center, Cleveland, OH

*Ann Biomed Eng, 37(11), 2009, pg. 2337 - 2359.*
• Impact on HIPmicroarchitecture UNKNOWN*
• Knowledge base: Vertebral trabecular bone loss with menopause.
• Loss of horizontal trabecular struts and directionality, perforation of trabeculae*, reduction in mechanical strength, and increase in fracture risk (Mosekilde, 2000; Seeman, 2002, Silva 1997; Kleerekoper 1985)
## Results in Astronauts – 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>Fall</td>
<td>2,580 N (560 N)</td>
<td>2,280 N (590 N)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

2.2% loss/month

1.9% loss/month

1.0-1.5% BMD loss /month
QCT Postflight: Structural changes do not reflect a restoration of bone strength

Bone Strength Indices

- **Bending (cm³)**
- **Compressive (g²/cm⁴)**

* : p<0.05 with respect to preflight

DXA: Losses at total hip and spine after ~6 months in space exceed 2-year losses on Earth in similar-aged population.
Fracture
Aging
Hypogonadism & Menopause
Sex Hormones
Clinical risk factors
High bone turnover
BTO markers

Inadequate peak bone mass
Selection Std

Increased bone loss
NTX/DPd

Low bone density
BMD Algorithm

Impaired bone quality

Skeletal fragility

Falls
Certain activities
RE Loads
Biomech Models

Excessive bone loading

Propensity to fall
Postural Sway

Fall mechanics

Reduced Activity
Endocrine Levels
Ca/Nutrition/Vit D
Muscle Atrophy

Triennials

Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
Percentage Reduction in Hip Strength

Stance

Fall

<table>
<thead>
<tr>
<th>% Reduction</th>
<th>Number of Astronauts</th>
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<tr>
<td>0</td>
<td>2</td>
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<tr>
<td>10</td>
<td>4</td>
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<td>30</td>
<td>2</td>
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<table>
<thead>
<tr>
<th>% Reduction</th>
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</thead>
<tbody>
<tr>
<td>-10</td>
<td>2</td>
</tr>
<tr>
<td>0</td>
<td>2</td>
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<tr>
<td>10</td>
<td>3</td>
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<td>3</td>
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