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

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

Photo: International Space Station
Gain & Loss of Bone Mass with Aging

Peak Bone Mass

Age-related Loss

Menopause-induced Loss

Bone mass (g/calcium)

Age (yr)

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
<table>
<thead>
<tr>
<th>Mercury</th>
<th>1961-63</th>
<th>X-ray densitometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gemini</td>
<td>1965-66</td>
<td>SPA heel and wrist</td>
</tr>
<tr>
<td>Apollo</td>
<td>1968-72</td>
<td>SPA heel and wrist</td>
</tr>
<tr>
<td>Skylab</td>
<td>1973-74</td>
<td>SPA heel and wrist</td>
</tr>
<tr>
<td>Soyuz/Salyut</td>
<td>1974-85</td>
<td>SPA, DPA</td>
</tr>
<tr>
<td>Space Shuttle</td>
<td>1974-85</td>
<td>DXA whole body, CT of lumbar spine BMD</td>
</tr>
<tr>
<td>ISS</td>
<td>2000-present</td>
<td>DXA, QCT, HR3DpQCT (ESA)</td>
</tr>
</tbody>
</table>

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
BMD T-Score Values* Expeditions 1-25 (n=33)
*Comparison to Population Normals
Adapted from: Cooper C, Melton LJ

- Aging
- Hypogonadism & Menopause
- Clinical risk factors
- High bone turnover
  - Inadequate peak bone mass
  - Increased bone loss
  - Low bone density
  - Impaired bone quality
  - Fall mechanics
  - Propensity to fall
  - Falls
  - Certain activities
  - Excessive bone loading
  - Skeletal fragility
  - Fracture

Clinical risk factors:
- High bone turnover
- Inadequate peak bone mass
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- Propensity to fall
- Falls
- Certain activities
- Excessive bone loading
- Skeletal fragility
- Fracture
Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
Microgravity Effects on the Human Body

- Eyes become main way to sense motion.
- Otoliths in inner ear respond differently to motion.
- Fluid redistribution causes head congestion and puffy face.
- Changed sensory input confuses brain, causing occasional disorientation.
- Higher radiation doses may increase cancer risk.
- Loss of blood plasma creates temporary anemia on return to Earth.
- Kidney filtration rate increases; bone loss may cause kidney stones.
- Dysregulation of the immune system.
- Fluid redistribution shrinks legs.
- Weight-bearing bones and muscles deteriorate.
- Touch and pressure sensors register no downward force.

From Scientific American
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>
</tr>
</thead>
<tbody>
<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, 2000
What about recovery?

Trochanter: \( \text{Loss}_0 = 7.8\% \) \hspace{1cm} 50\% \text{ Recovery} = 255\text{d}

DXA BMD increases in Postflight Period after long-duration flights.

Trochanter

Femoral neck

Lumbar Spine
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>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>aBMD Trochanter</td>
<td>1.56±0.99*</td>
<td>Integral vBMD Trochanter</td>
<td>1.5±0.9</td>
</tr>
<tr>
<td>*p&lt;0.01, n=16-18</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

**Bone Mineral Content (g)**

- **Femoral Neck**
  - Pre: 6.400
  - Post: 6.000
  - 12MONTH: 6.600

**Volumetric Bone Mineral Density (g/cm³)**

- **Femoral Neck**
  - Pre: 0.350
  - Post: 0.340
  - 12MONTH: 0.350

**Minimum Cross-sectional Area (cm²)**

- **Minimum CSA**
  - Pre: 11.900
  - Post: 11.900
  - 12MONTH: 12.000

* * 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?
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.

Individualized Fracture Risk

BMD -> Finite Element Strength

Geometry

Material Properties

Loading
Individual Results

Stance Loading (4 to 30% loss in strength)

Max loss 30%

Graph showing individual hip strength loss over time (0 to 6 months) with a decline pattern and a max loss of 30%.
Individual Results

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

Change in areal BMD from QCT

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

Slide courtesy of J Keyak
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.
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• Jackie Reeves (NASA JSC)
• Robert Ploutz-Snyder, Ph.D (NASA JSC)
• Clarence Sams, Ph.D (NASA JSC)
• Linda C. Shackelford, M.D. (NASA JSC)
• Scott M. Smith, Ph.D. (NASA JSC)
• Elisabeth R. Spector (NASA JSC)
• Piotr Truszkowski (NSBRI, Harvard Medical School)
• Robert Wermers, M.D. (Mayo Clinic)
QCT does not outperform DXA-BMD for fracture prediction but provides extra information that DXA does not
Bone Fracture Risk Module (BFxRM)

Biomechanics and Mission Operations

courses.washington.edu/me598rc

Bone Loss in Space

Estimate of Fracture Probability

Clinical and Engineering Characteristics of Bone Strength

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

Beck et al., 1990
Hayes, Myers, 1996 (2mm/s)
Hayes, Myers, 1996 (100mm/s)
Kukla et al., 2002

Probability of event
Probability of Fracture
Probability bone will fail to support load
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.
What is the impact of Trabecular Bone Loss on bone microarchitecture?

- 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></td>
<td><strong>2.2% loss/month</strong></td>
<td></td>
<td></td>
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<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
QCT Postflight: Structural changes do not reflect a restoration of bone strength

Bone Strength Indices

![Bar chart showing bone strength indices preflight and postflight](chart.png)

- 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.
Aging
Triennials

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

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

Stance

Fall

Number of Astronauts

<table>
<thead>
<tr>
<th>% Reduction</th>
<th>0</th>
<th>10</th>
<th>20</th>
<th>30</th>
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<tbody>
<tr>
<td>% Reduction</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
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</table>

<table>
<thead>
<tr>
<th>% Reduction</th>
<th>-10</th>
<th>0</th>
<th>10</th>
<th>20</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Reduction</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>1</td>
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