Epidemiologic Analyses of Risk Factors for Bone Loss and Recovery Related to Long-duration Space Flight

[Awarded in 2008]

NASA Human Research Program Investigators’ Workshop
February 3-5th, 2010

Shreyasee Amin, MD CM, FRCP(C), MPH
Associate Professor of Medicine
College of Medicine, Mayo Clinic

(Presented by Jean Sibonga, PhD)
Overview

- Study Overview
- Progress on Aims
- Unexpected Challenges
Response to NRA

- To address:
  - the risk of long-term effects on crew health regarding bone loss and fracture
  - the need to define the likelihood and/or consequence of bone health recovery post-flight
Study Overview

- Collaboration between NASA-JSC and Mayo Clinic, Rochester MN.
- Analyses of BMD and risk factor data already collected on US crew, with comparisons to a population-based cohort (Rochester Bone Health Study).
Specific Aims

AIM 1: To investigate the risk of microgravity exposure on long-term changes in bone health and fracture risk.

• compare data from crew members (“observed”) with what would be “expected” from Rochester Bone Health Study.

AIM 2: To provide a summary of current evidence available on potential risk factors for bone loss, recovery & fracture following long-duration space flight.

• integrative review of all data pre, in-, and post-flight across disciplines (cardiovascular, nutrition, muscle, etc.) and their relation to bone loss and recovery
Specific Aims

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Methods

- “Expected” BMD changes were determined based on data from the Rochester Bone Health Study cohort of 699 men and women, representing an age-stratified random sample of the adult community (age 20-95 years).

- “Observed” BMD changes following long-duration flight from 28 crew members were measured:
  - Immediately post-flight
  - ~1 year post-flight
Rochester Bone Health Study

- 348 men, age range at baseline: 22-90 years
- 351 women, age range at baseline: 21-93 years

- BMD measurements on Hologic QDR 2000 at spine, hip, radius, total body.

- BMD at baseline, 2 and 4 years for men.
- BMD at baseline, 1, 2 and 4 years for women.
Rochester Bone Health Study

- Prediction models derived using baseline and follow-up BMD data from cohort
- Prediction of “expected” BMD over follow-up using:
  - Linear mixed effects models
  - Baseline BMD, age at baseline BMD, gender, and time-to-follow-up, as predictors in model
  - Models including body mass index and total lean mass as predictors were also considered
Long-Duration Crew

- 28 men and women
  - 24 men, age range at preflight scan: 36-53 yrs
  - 4 women, age range at preflight scan: 41-53 yrs

- BMD measurements on Hologic QDR 2000, QDR 4500 and Discovery at spine, hip, radius, total body.

- BMD pre-flight, immediately post flight and ~1 year post-flight
Long-Duration Crew

- Median flight duration: 167 days (range: 95-215 days)
- Immediate post-flight BMD performed a median of 6 days (range: 3-33 days) following return on 24 men and 4 women.
- ~1 year post-flight BMD performed a median of 376 days (range: 184-534 days) following return on 22 men and 4 women.
Long-Duration Crew

- 25/28 had pre-flight BMD performed within 6 months before launch (all 28 had immediate post-flight BMD)
  - 24/25 had pre- and immediate post-flight BMD on same machine (7 QDR 2000, 11 QDR 4500 and 6 on Discovery)
- 24/28 have a pre-flight BMD within 6 months of flight and a post-flight BMD within 6-18 months of return. (26/28 had a 6-18 month BMD)
  - 22/24 have scans on same machine (7 QDR 2000, 10 QDR 4500 and 5 Discovery)
<table>
<thead>
<tr>
<th>BMD Site*</th>
<th>Mean Pre-Flight BMD (g/cm²) (Used first and last pre-flight scans available)</th>
<th>Expected</th>
<th>Observed</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>BMD</td>
<td>BMD</td>
<td></td>
</tr>
<tr>
<td>Total Hip</td>
<td>1.106</td>
<td>1.097</td>
<td>0.11</td>
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<tr>
<td>Lumbar Spine</td>
<td>1.091</td>
<td>1.080</td>
<td>0.04</td>
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<tr>
<td>Mid Shaft Radius</td>
<td>0.713</td>
<td>0.702</td>
<td>0.06</td>
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<tr>
<td>Ultradistal Radius</td>
<td>0.525</td>
<td>0.529</td>
<td>0.37</td>
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<tr>
<td>Total Body</td>
<td>1.284</td>
<td>1.281</td>
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</table>

*N=25 for all sites except radius sites where N=17*
<table>
<thead>
<tr>
<th>BMD Site*</th>
<th>Expected</th>
<th>Observed</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMD</td>
<td>% chg/mos (95% CI)</td>
<td>BMD</td>
</tr>
<tr>
<td>Total Hip</td>
<td>1.082</td>
<td>-0.00 (-0.05, 0.04)</td>
<td>1.012</td>
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<tr>
<td>Lumbar Spine</td>
<td>1.078</td>
<td>0.12 (0.10, 0.13)</td>
<td>1.028</td>
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<tr>
<td>Mid Shaft Radius</td>
<td>0.710</td>
<td>0.17 (0.11, 0.23)</td>
<td>0.695</td>
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<tr>
<td>Ultradistal Radius</td>
<td>0.519</td>
<td>-0.02 (-0.05, -0.00)</td>
<td>0.511</td>
</tr>
<tr>
<td>Total Body</td>
<td>1.264</td>
<td>-0.05 (-0.05, -0.04)</td>
<td>1.240</td>
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</table>

*N=25 for all sites except radius sites where N=17*
<table>
<thead>
<tr>
<th>BMD Site*</th>
<th>Mean ~1 Year Post-Flight BMD (g/cm²)</th>
<th>% Change per Month (% chg/mos)</th>
<th>Expected</th>
<th>Observed</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BMD</td>
<td>% chg/mos (95% CI)</td>
<td>BMD</td>
<td>% chg/mos (95% CI)</td>
<td></td>
</tr>
<tr>
<td>Total Hip</td>
<td>1.086</td>
<td>0.01 (-0.01, 0.02)</td>
<td>1.062</td>
<td>-0.10 (-0.15, -0.06)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td>1.086</td>
<td>0.05 (0.05, 0.06)</td>
<td>1.068</td>
<td>-0.03 (-0.01, 0.03)</td>
<td>0.004</td>
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<tr>
<td>Mid Shaft Radius</td>
<td>0.705</td>
<td>0.06 (0.03, 0.09)</td>
<td>0.694</td>
<td>-0.01 (-0.06, 0.04)</td>
<td>0.02</td>
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<td>Ultradistal Radius</td>
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<td>-0.07 (-0.07,-0.06)</td>
<td>0.517</td>
<td>-0.02 (-0.07, 0.02)</td>
<td>0.03</td>
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<tr>
<td>Total Body</td>
<td>1.264</td>
<td>-0.02 (-0.03,-0.02)</td>
<td>1.248</td>
<td>-0.08 (-0.15, -0.01)</td>
<td>0.08</td>
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</tbody>
</table>

*N=24 for all sites except radius sites where N=16
Findings to Date

• Our simple BMD prediction models appear to work well…

• Models including body mass index or lean mass yielded similar findings, but work is ongoing to improve models.

• Overall, BMD ~1 year post-flight still show lower than expected BMD values at most sites, particularly weightbearing sites.

• Still exploring differences between men and women
Unexpected Challenges…

- Signed consent required to access and view collected data from long-duration crew as age, gender, race/ethnicity are attributable data.
- Inability to export data with scan dates or flight dates, despite informed consent.
- Recently informed that will also need signed consent to access short-duration crew BMD.

Lack of 100% consent limits access and analyses of available data which may have potential limitations on interpretation of results.
Other Unexpected Challenges...

- Took >1 year to achieve secure remote access from Mayo Clinic to JSC-NASA in order to view and export data.

- Lack of standardized procedures for data access
  - Establishment of standards with concurrent input from CPHS (Committee for the Protection of Human Subjects), LSAH (Longitudinal Study of Astronaut Health) and Crew Office would be ideal
On-going work

- Better calibration of BMD between 2 cohorts at each region of interest using pre-maiden flight BMD from all US crew members available.

- Assembly of risk factor data available from long-duration crew

- Further refinement of fracture prediction models based on Rochester cohort using BMD, risk factor data collected and observed fractures over ~20 years of follow-up.