Bisphosphonates as a Countermeasure to Space Flight Induced Bone Loss Increment 31/32 Science Symposium

Principal Investigators:

• Adrian LeBlanc, Ph.D. (USRA)
• Toshio Matsumoto, M.D., Ph.D. (Univ. of Tokushima Grad. School of Medicine)

Co-Investigators:

NASA Team
Jeff Jones, M.D. (BCM)
Jay Shapiro, M.D. (Johns Hopkins)
Tom Lang, Ph.D. (UCSF)
Scott M. Smith, Ph.D. (NASA)
Linda C. Shackelford, M.D. (NASA)
Jean Sibonga, Ph.D. (NASA)
Harlan Evans, Ph.D. (Wyle)
Elisabeth Spector (Wyle)
Robert Ploutz-Snyder, Ph.D. (USRA)

JAXA Team
Toshitaka Nakamura, M.D., Ph.D (UOEH)
Kenjiro Kohri, M.D., Ph.D. (Nagoya City U.)
Hiroshi Ohshima, M.D., Ph.D. (JAXA)
Outline

• Background-MIR, ISS
  – DXA
  – QCT
• Bisphosphonate experiment
  – Hypothesis
  – Preliminary results
• Objective of current addendum
• Measurements
• Testing constraints
Change in DXA BMD after Long Duration Flight

- % Change / 6 Months
- Mir (n=36)
- ISS (n=27)
- Means

Locations:
- Lumbar Spine
- Femoral Neck (Hip)
- Trochanter (Hip)
- Pelvis
CT Methodology

Regions of Interest

Femoral Neck

Trochanteric

Total Femur

Troch intgl

Troch trab

Troch cort.
Change in QCT Trabecular BMD after ISS Flights
(n=14)

Data published by T. Lang 2004
Experiment Hypothesis

The combined effect of anti-resorptive drugs plus in-flight exercise regimen will have a measurable effect in preventing space flight induced bone mass and strength loss and reducing renal stone risk.
Experiment Status

• To date 7 subjects are enrolled -- 70-mg tablet of alendronate once a week before and during flight, starting 17 days before launch.

• 5 crewmembers have completed ISS long duration missions and will be reported here.

• 2 additional crewmembers are scheduled to complete the flight portion of the protocol this year.
Preliminary Results

%Change in DXA BMD (g/cm²)
ISS Controls (n = 14) vs. Bisphosphonate Subjects (n = 5)

<table>
<thead>
<tr>
<th>Location</th>
<th>%Change from Pre Flight BMD</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Neck</td>
<td>-20</td>
<td>p = 0.001*</td>
</tr>
<tr>
<td>Trochanter</td>
<td>-15</td>
<td>p = 0.019*</td>
</tr>
<tr>
<td>Total Hip</td>
<td>-10</td>
<td>p = 0.001*</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td>-15</td>
<td>p &lt; 0.001*</td>
</tr>
</tbody>
</table>

*p value statistically significant when Holm correction for multiple comparisons is applied
Preliminary Results

%Change in QCT Trabecular BMD (g/cm³)

%Change from Pre Flight BMD

Femoral Neck
-35
-30
-25
-20
-15
-10
-5
0
5
10
15

Trochanter
-35
-30
-25
-20
-15
-10
-5
0
5
10
15

Total Hip
-35
-30
-25
-20
-15
-10
-5
0
5
10
15

* p value statistically significant when Holm correction for multiple comparisons is applied
Preliminary Results

Urinary Calcium During and After Space Flight (Mean ± SE)
Mir n = 6; Bisphosphonate n = 4

* p < 0.05
Preliminary Results

NTX During and After Space Flight (Mean ± SD)
Mir n = 6, ISS SMO n = 3

NTX (nmol/nmol creatinine)

- Pre Flight
- Early Flight
- Mid Flight
- Late Flight
- R+0
- R+10 to 25 d
- R+1 to 4 mo

Mir
SMO
Objectives of the Current Study Extension

- Current controls are ISS astronauts who exercised using IRED.
- All subjects in the current study have used ARED, capable of higher loading and more efficient usage.
- New control group will help clarify the impact of ARED alone.
protocol

- 10 long duration ISS crew-male or female
- Exercise with ARED protocol
- Exclude subjects participating in Sprint protocol-Sprint controls can be enrolled
- Exclude subjects taking drugs targeting bone loss
Experiment Measurements

**QCT:**  L-45 to L-30, R+5, R+360
Imaging scan of the hip for measurement of volumetric bone density, strength modeling
Performed at local hospital
Scan takes < 15 minutes; 1 hour allotted for travel time + scanning
Can data share with Sprint study if subject is a Sprint control

**DXA:**  L-60 to L-30, R+5, R+360
Imaging scan of the whole body, hip, spine, heel and wrist for measurement of areal bone mineral density
Performed at JSC
Scans take ~ 1 hour
Will data share with existing DXA Medical Requirement

**pQCT:**  L-60 to L-30, R+5, R+360
Imaging scan of the lower leg (tibia) for measurement of volumetric bone density
Performed at JSC
Scans take ~50 minutes
Experiment Measurements

Urine Collections:
L-45, Early In-Flight, Mid In-Flight, Late In-Flight, R+0, R+30, R+360
Levels of various markers of bone metabolism will be measured
24-hour void-by-void
Can data share with Medical Requirements or other studies (e.g., Nutrition SMO)

Blood Draws:
L-45, R+0, R+30, R+360
Levels of various markers of bone metabolism will be measured
Standard blood draw
Can data share with Medical Requirements or other studies (e.g., Nutrition SMO)
Blood draw takes < 10 minutes

Abdominal Ultrasound:
L-30 to 180, R+30
Imaging of bladder, ureters and kidneys for presence of renal stones
Performed at local imaging facility
Ultrasound takes ~ 1.5 hour, including travel time

Calcium and Vitamin D supplements:
Vitamin D: 800 IU daily from L-45 to launch; Ca: 1000 mg daily from L-17 to launch
# Test Constraints

<table>
<thead>
<tr>
<th>Test</th>
<th>Constraints</th>
</tr>
</thead>
<tbody>
<tr>
<td>QCT</td>
<td>Remove all metal (i.e., jewelry) or clothes containing metal No radioisotopes or radio opaque contrast agents for one week prior to test.</td>
</tr>
<tr>
<td>DXA</td>
<td>Remove all metal (i.e., jewelry) or clothes containing metal No radioisotopes or radio opaque contrast agents for one week prior to test.</td>
</tr>
<tr>
<td>pQCT</td>
<td>Remove all metal (i.e., jewelry) or clothes containing metal No radioisotopes or radio opaque contrast agents for one week prior to test.</td>
</tr>
<tr>
<td>Urine collections</td>
<td>24-hr. urine collection starts with first void of the day and concludes with first void of the following day</td>
</tr>
<tr>
<td>Blood draws</td>
<td>Overnight fast</td>
</tr>
<tr>
<td>Ultrasound</td>
<td>Overnight fast Arrive at imaging center with full bladder (drink 32 oz. of water before arrival)</td>
</tr>
</tbody>
</table>
## Summary

<table>
<thead>
<tr>
<th>Preflight</th>
<th>Inflight</th>
<th>Postflight</th>
</tr>
</thead>
<tbody>
<tr>
<td>QCT: 60 min *</td>
<td></td>
<td>QCT: 120 min *</td>
</tr>
<tr>
<td>DXA: 60 min *</td>
<td></td>
<td>DXA: 120 min *</td>
</tr>
<tr>
<td>pQCT: 50 min</td>
<td></td>
<td>pQCT: 100 min</td>
</tr>
<tr>
<td>Blood draw: 10 min *</td>
<td></td>
<td>Blood draw: 30 min *</td>
</tr>
<tr>
<td>Urine collection: 30 min *</td>
<td>Urine collections: 510 min *</td>
<td>Urine collection: 90 min *</td>
</tr>
<tr>
<td>Abdominal ultrasound: 90 min</td>
<td></td>
<td>Abdominal ultrasound: 90 min</td>
</tr>
<tr>
<td>Ca and Vitamin D: 30 sec/day, 22.5 min total</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total Time:</strong> 322.5 min</td>
<td><strong>Total Time:</strong> 510 min</td>
<td><strong>Total Time:</strong> 550 min</td>
</tr>
</tbody>
</table>

* Potential for data sharing with Med Requirements or other studies