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

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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

- Mir (n=36)
- ISS (n=27)
- Means

- % Change / 6 Months
  - Lumbar Spine
  - Femoral Neck (Hip)
  - Trochanter (Hip)
  - Pelvis
CT Methodology

Regions of Interest

Fem. Neck

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

-35 -30 -25 -20 -15 -10 -5 0 5 10 15 20
% Change / 6 Months

Lumbar Spine  Femoral Neck (Hip)  Trochanter (Hip)  Total Hip

Means

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>Region</th>
<th>Controls</th>
<th>Bisphosphonate</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral Neck</td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>Trochanter</td>
<td></td>
<td></td>
<td>0.019*</td>
</tr>
<tr>
<td>Total Hip</td>
<td></td>
<td></td>
<td>0.001*</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td></td>
<td></td>
<td>&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)

<table>
<thead>
<tr>
<th>Femoral Neck</th>
<th>Trochanter</th>
<th>Total Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>p &lt; 0.000 *</td>
<td>p = 0.055</td>
<td>p = 0.034</td>
</tr>
</tbody>
</table>

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

**Total Time:** 322.5 min  
**Total Time:** 510 min  
**Total Time:** 550 min

* Potential for data sharing with Med Requirements or other studies