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
CT Methodology

Regions of Interest

Fem. Neck

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></th>
<th>Femoral Neck</th>
<th>Trochanter</th>
<th>Total Hip</th>
<th>Lumbar Spine</th>
</tr>
</thead>
<tbody>
<tr>
<td>p value</td>
<td>p = 0.001*</td>
<td>p = 0.019*</td>
<td>p = 0.001*</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)

<table>
<thead>
<tr>
<th></th>
<th>Femoral Neck</th>
<th>Trochanter</th>
<th>Total Hip</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bisphosphonate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Femoral Neck: p < 0.000 *
- Trochanter: p = 0.055
- Total Hip: p = 0.034

* 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
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>
</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