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Hip QCT for Assessment of Trabecular Bone Loss and Recovery after Space Flight: A Pilot Study

E.R. Spector³, T. Lang², H. Evans³, J.D. Sibonga¹

¹NASA Johnson Space Center, Houston, TX
²University of California, San Francisco, CA
³KBrWyle, Houston, TX
Introduction

Monitoring the effects of space flight on skeletal health and fracture risk in astronauts at NASA Johnson Space Center [JSC] -

• 1990: Research Study - DXA used to measure effects of spaceflight in cosmonauts (n=18 total) flown on Mir spacecraft (LeBlanc, 2000) – reported % BMD change/month.

• 1994: World Health Organization - published guidelines for using DXA BMD T-scores to diagnose osteoporosis (Kanis, 1994).

• 1997-to date : DXA testing of active astronauts on triennial basis.

• 2000-to date : Preflight and postflight DXA testing required for astronauts flown on expeditions aboard the International Space Station [ISS] (~180 d spaceflights).

• 2006-to date : DXA testing of retired astronauts on triennial basis.
Preflight and Postflight BMD T-scores in ISS astronauts: Is this a clinically-useful metric to assess effects of spaceflight on the skeletal health of long-duration* astronauts?

*DXA performed with spaceflights > 60 days but typically ~180 day spaceflight durations.
DXA BMD: Changes due to space flight that are unique & complex. Drives requirement for research to increase understanding of spaceflight effects.

**Rapid** (1-1.5%/mo) and **site-specific** BMD loss attributed to local regulation of bone cells (LeBlanc, 2000).

<table>
<thead>
<tr>
<th>BMD Site</th>
<th>Mean Immediate Post Flight BMD (% change/month)</th>
<th>Mean Three Year Post Flight BMD (% change/month)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Predicted</td>
<td>Observed</td>
</tr>
<tr>
<td>Total Hip</td>
<td>1.063</td>
<td>0.994</td>
</tr>
<tr>
<td></td>
<td>(0.05)</td>
<td>(-0.76)</td>
</tr>
<tr>
<td>Lumbar Spine</td>
<td>1.081</td>
<td>1.016</td>
</tr>
<tr>
<td></td>
<td>(0.11)</td>
<td>(-0.58)</td>
</tr>
<tr>
<td>Ultra-Distal</td>
<td>0.558</td>
<td>0.550</td>
</tr>
<tr>
<td>Radius</td>
<td>(-0.05)</td>
<td>(-0.20)</td>
</tr>
<tr>
<td>Mid-Shaft</td>
<td>0.755</td>
<td>0.741</td>
</tr>
<tr>
<td>Radius</td>
<td>(0.19)</td>
<td>(-0.00)</td>
</tr>
<tr>
<td>Total Body</td>
<td>1.288</td>
<td>1.262</td>
</tr>
</tbody>
</table>

Total BMD loss greater and **persist** compared to BMD changes predicted from algorithms derived from earth-based population (Amin, 2011).

Loss is variable. Recovery is variable. Recovery is prolonged. **Indicates: Multiple risk factors at play.** (Sibonga, 2009)
Discordant assessment of recovery by DXA vs. QCT for the hip: DXA fails to capture i) spaceflight effects specific to hip trabecular volumetric BMD (Trb vBMD) and ii) the delayed recovery/additional losses after return to Earth. Supports the value of QCT monitoring.

Adapted by Sibonga – side by side comparison
Do the profound skeletal changes observed with spaceflight (medical and research measurements) have any clinical relevance? How should NASA use the research data to enhance its clinical management of crew skeletal health?

In response to these issues, experts in osteoporosis & bone densitometry have been assembled near Johnson Space Center [JSC] (Houston, TX) to provide periodic reviews (“Bone Summits” 2010, 2013, 2016) of bone densitometry and other bone-relevant data of astronauts serving on long-duration spaceflights (~ 180 days aboard the International Space Station [ISS]).
2010 Bone Summit Panel identified a clinical “trigger” to monitor in astronauts – a trigger to evaluate for possible intervention.

(excerpts from JBMR Vol. 28, No. 6, June 2013, pp 1243–1255)

An osteoporosis specialist should evaluate astronauts for treatable risk factors if his/her DXA postflight aBMD T-score is less than −2.0 or if hip QCT results do not recover to preflight values (within LSC of preflight measure) by 2 years after return.

... it could be clinically meaningful to implement QCT hip scans to assess the efficacy of new in-flight countermeasures and for surveillance postflight, in which an absence of recovery could be a trigger to review bone health risk factors and/or to consider intervention to prevent expected age-related bone loss...
Hip QCT: A Pilot Study

Study Purpose:

• To demonstrate the use and value of QCT as a surveillance tool to augment standard DXA measurements in astronauts flying on missions $\geq 180$ days: i) to monitor space flight bone loss and recovery and ii) to assess for a trigger to evaluate astronaut for possible intervention.

Evidence in Terrestrial Medicine:

• Hip QCT measurements can predict fractures in the elderly (Black, JBMR 2008; Bousson, JBMR 2011).

• The postflight surveillance of all space-induced skeletal changes in astronauts is required to assess the restoration of skeletal changes to preflight status.

Clinical Concern:

• An intervention for astronauts may be required to prevent the combination of deficits due to spaceflight with deficits due to aging.
Methods

- Astronauts (n=10) to be flown on typical 180-day missions aboard the ISS were consented to participate in a QCT surveillance program. Two astronauts took alendronate as participants in the bisphosphonate flight experiment (data not shown to avoid identifiable status).

- In Houston, QCT (GE LightSpeed VCT) and DXA (Hologic Discovery) scans of the left and right hip were obtained on 8 astronauts before flight (duration 154 ± 23 days), approximately 1 week after flight and again at 1 year of recovery (R+1yr).

- All subjects exercised 6 days/wk during spaceflight using some combination of resistive exercise on the “ARED” and aerobic exercise (i.e., cycle ergometer and treadmill).

- If a subject’s R+1yr QCT Trb vBMD did not return to baseline (i.e., within established measurement error of 2.3%) in one or both hips, an additional QCT session was obtained at R+2yr.

- For Risk Surveillance, the lack of recovery in hip Trb vBMD by R+2yr would serve as a trigger* to crew surgeon for astronaut to be evaluated further by an osteoporosis expert.

- Notably, a non-Hip QCT study participant may have hips scanned by QCT as a research outcome but not for surveillance of skeletal recovery at R+2yr.

ARED = Advanced Resistive Exercise Device with capability of providing resistance of 600 lb force.

Risk: Radiation Exposure for 1 hip scan by Quantitative Computed Tomography [QCT]

1.50 mSv men, 1.22 mSv women
0.5 x annual United States background (excl. medical exposures)

~ 1 week onboard ISS
RESULTS

Change in Bone Mineral Density after Space Flight: DXA areal BMD vs. QCT Trabecular vBMD

Mean %Change ± SD

* P < 0.05, Student’s paired t-test for post-flight vs. pre-flight means

n=8 ARED users
n=5 of 8, with non-detected recovery of Trb vBMD at R+1yr
Individualized Assessments: DXA fails i) to assess for clinical trigger and ii) misses non-participants in Study who may need evaluation for possible intervention (i.e., n=2 not in Hip QCT study for surveillance).

Next DXA scan on triennial schedule.

DXA aBMD %ch in ARED Astronauts with QCT + DXA Scans through R+1Y (Hip with Greatest Loss) n=10

QCT Trab vBMD %ch in ARED Astronauts with Scans Through at Least R+1Yr (Hip with Greatest Loss) n=10

Denotes Least Significant Change

* not a Hip QCT subject
Influence of in-flight alendronate on hip Trb vBMD loss and recovery at R + 1 yr.

QCT Trb vBMD %ch in ARED Astronauts with Scans Through at Least R+1Yr
Hip with Greatest Loss n=17
Includes 7 Bisphosphonate Subjects (Dashed Lines)

%Change from Pre Flight

Pre R+5 R+1yr R+2yr

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

ARED, Not in Hip QCT Study
ARED, In Hip QCT Study
ARED + Bisphosphonates, not in Hip QCT Study
ARED + Bisphosphonates, In Hip QCT Study

Denotes Least Significant Change
Individualized Assessments of Space Flight Effects
An estimate of hip strength (by Finite Element Models) - a more useful “biomarker” for fracture risk management?

FE NLS = Finite Element Non-linear Stance (left hip strength estimate)      Trb = Trabecular      Cort = Cortical      aBMD and vBMD = areal BMD and volumetric BMD
Summary and Discussion

Is the use of QCT justified in the absence of fractures in astronauts?

1. DXA hip scans as sole surveillance will not detect full restoration from spaceflight-induced losses in bone mass.

2. Intervention trigger to mitigate long-term fracture risk may be missed in astronauts who do not participate in Hip QCT surveillance program.

3. Using QCT scans to estimate the hip Fracture Load (i.e., kN load to failure by Finite Element Modeling) may enhance the assessment and management of hip fracture risk in astronauts – especially due to younger age and the higher level of physical activity.

4. Hip QCT measurements are predictors of fractures in the elderly and intervention may be required to mitigate any combination of deficits following spaceflight with expected deficits with aging.
Conclusions

Collectively,

• the conflicting surveillance of bone densitometry by DXA and QCT,
• the inability to predict which astronauts will lose or fail to recover bone mass,
• the unknown - possibly detrimental - effects of rapid bone loss especially on Trb bone microarchitecture,
• the efficacy of the bisphosphonate alendronate during spaceflight and in bed rest analogs of space to suppress the stimulation of biomarkers for bone resorption and
• the opinions of osteoporosis experts (Bone Summit 2016)

support the recommendations for i) preflight infusion of the bisphosphonate Zoledronic Acid in astronauts to prevent osteoclast-driven bone loss during spaceflight missions >180 days and ii) QCT, as an adjunct to DXA, to monitor postflight bone loss and recovery in different bone compartments of hip.


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