Summary of Recommendations from Early Onset Osteoporosis Summit [Bone Summit] of June 2010: Occupational Risk Surveillance for Long-Duration Astronauts

Office of Chief Health and Medical Officer [OCHMO] NASA HQ

March 23, 2011

Modified Sept 26, 2011 for FE-Task Group

SK/Sibonga/3-4556
Risk for Earlier Age-Related Fractures due to Prolonged Spaceflight?

Cooper and Melton, 1992

Slide courtesy of Amin; adapted
Microgravity Effects on the Human Body
Following slides courtesy of Dr. S M Smith

NUTRITIONAL BIOCHEMISTRY LABORATORY - JSC
Calcium-regulating Hormones

Nutrition SMO, unpublished data; Courtesy Dr. SM Smith
Bone Turnover

Slide Courtesy of Dr. SM Smith; Adapted by Sibonga
Sodium/Bone

SOLO

Heer, et al.
Nutrition and Bone

Zwart, et al., JBMR, 2010
Issues for Panel to Consider


- Astronauts are exposed to *unique* set of risk factors (established and possible) during space travel (*e.g.*, *weightlessness, endocrine perturbations, suboptimal nutrition, sarcopenia, radiation, hypobaric/hyperoxic EVAs, CO2*).

- Are we doing enough *now* to address an occupational health risk that may manifest *later*?

- *Can a “new line in the sand” to be drawn based upon QCT and FEM conducted in population studies?*

- Can this Task Group come up with a set of bone parameters for new Bone medical standards?
Issues for panel to Consider. 2

- Issues:
  - QCT is currently a research tool - no clinical guidelines developed at present time
  - Limited population data of QCT and fracture outcome
  - Not enough time to collect fracture-outcome data (astronaut and/or terrestrial) and meet schedules - a role for probabilistic risk assessments.
  - Exposure to ionizing radiation (1 hip QCT ~ 5 days ISS)

- Collection of surveillance data from QCT and FEM to better inform current and future (longer missions?) decision-making
Proposed Use of QCT Technology for Clinical and Operational Decisions

Recommendations from an Expert Panel for Consideration by NASA
The Long-duration Astronaut

- Typical space mission duration - $163 \pm 32$ d (range 90-215d)
- Average Age - $46.5 \pm 4.5$ y (range 36.8 - 55.3)
- Male to Female Ratio - 3.8 : 1
- Current total # per astronauts in corps - 34 of 331
- # repeat fliers - 4
- BMI - Male BMI $25.9 \pm 2.2$ (20.6 to 30.6); Female BMI $22.6 \pm 2.2$ (20.4 to 25.4)
- Wt and Ht- Males: Males: $81 \pm 9$ kg (62 to 101 kg), $177 \pm 6$ cm (163 to 185 cm);
- Females: $65 \pm 7$ kg (57 to 80 kg), $170 \pm 4$ cm (165 to 178 cm)
June 2010

BONE SUMMIT

RECOMMENDATIONS
Use of Algorithm for Operational Decisions

- **Proposed:** For flight certification (based upon Permissible Outcome Limit), if BMD data are ambiguous (BMD continuum), then individualized FE estimates of strength will better inform decision-makers regarding flight certification (using individualized estimates vs. relative risks).

- **FE before Flight 1** gives better estimation of low fracture risk (i.e., stronger bones) than DXA BMD and thus QCT/FE used for “GO” decision only not for “NO GO” decision

- **From Standards:** “DXA scan values in the osteopenic range with a negative endocrine evaluation should not be considered disqualifying. These individuals should be closely monitored with appropriate imaging studies. Any associated underlying conditions or correctable causes of osteopenia should be treated. Long duration missions may result in significant bone loss. This should be considered when certifying astronauts with significant osteopenia for such missions.”

- **Proposed:** Apply FE bone strength threshold derived from population studies (TBD) to medical standards (consider as supplement to DXA)
Use of Research Data for Clinical Practice

- **Recommended Analysis**: Bone strength estimated by Finite Element (FE) may provide the *single best composite number* because it integrates bone mineral density, elastic modulus, loading and structure (may not be 100% but better than status quo).

- **Recommended Use**: FE bone strength estimates in conjunction with physical medicine and rehabilitation approaches in returning astronaut (Dr. Sinaki consult)

- **Required Use of QCT** for Countermeasure Evaluation: clinical trigger based upon trabecular bone compartment - not detectable by DXA but by QCT

- **Recommended Threshold**: Apply FE bone strength as flight certification threshold but most pertinent for 2nd long duration flight (threshold based upon FE cut-points derived from population - and upon FE declines from first long duration flight - Space Med also provides input for acceptable declines)
Rationale

- “Although we are used to DXA measurements as clinical assessment of risk, the situation in the astronaut corps may be different. Rather than think in population terms, it might be better to think in individual terms.” (Panel member)

- Spaceflight-induced changes to bones are not detectable by DXA (poor correlation) (see slide 28)

- FE provides better assessment of bone strength following spaceflight.

- Panel recognizes that fracture risk is LOW during an ISS mission although risk for stress fractures during flight exercise regimens may exist (opportunity for occupational surveillance data to inform Bone Fracture Module of IMM).

- If an astronaut has deficits in hip bone strength equivalent to the elderly (at L2- 1 year) (See slides 30-31), then re-exposing to long-duration space likely to increase the risk for early onset age-related fractures after return.
Summary Panel Recommendations

- Recommend: QCT Technology for Occupational Risk Surveillance & Countermeasure validation

- **Four scans per one LD mission (per scan radiation < 5 day ISS)**
  - Preflight 30-45 days before Launch
  - Postflight by Return+22 days (or whenever return to US)
  - R+ 1 y
  - R+2 y

- To monitor changes in **hip structure and strength** (not lumbar spine because of variability)
  - Describe spaceflight effect (Risk for Fracture)
  - Monitor effect of peri-menopause prior to flight
  - Monitor recovery after return (Risk for Early Onset Osteoporosis)
Summary Panel Recommendations (cont)

- To provide a clinical trigger* for medical response
- To facilitate *individualized* estimations of bone strength,
  - To supplement DXA BMD measures when making clinical decisions,
  - To certify astronaut for long-duration flights by algorithm vs. Permissible Outcome Standard based upon projected BMD (1-2% loss/month)

*Failure to recovery BMD in hip trabecular bone compartment by R+ 2 years. See endocrine evaluation by bone specialist for astronaut.
BACKGROUND DATA SLIDES
T-scores not appropriate for monitoring spaceflight-induced changes or for predicting fractures in astronauts.

BMD T-Score Values* Expeditions 1-25 (n=33)
*Comparison to Population Normals
%Change in DXA BMD after Long-Duration Mir and ISS Space Missions

Mir n = 33; ISS n = 26; SMO n = 5; ARED = 8; Partial SMO = 1
DXA BMD increases in Postflight – is that recovery?

Sibonga et al. BONE 41:973-978, 2007
Recovery of Lumbar Spine BMD after ISS Flights
n= 17 Crewmembers with Measurements at R+5, R+1yr and R+2yr
Recovery of Femur Neck BMD after ISS Flights

n = 17 Crewmembers with Measurements at R+5, R+1yr and R+2yr
Recovery of Trochanter BMD after ISS Flights
n= 17 Crewmembers with Measurements at R+5, R+1yr and R+2yr
Recovery of Total Hip BMD after ISS Flights
n= 17 Crewmembers with Measurements at R+5, R+1yr and R+2yr
Research Study: QCT measures loss hip vBMD due to spaceflight in trabecular bone compartment (n=16 ISS)

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<th>%/Month Change ± SD</th>
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*p<0.01, n=16-18

QCT Postflight – Changes in bone mass and structure at Femoral Neck 12 months after return

**Bone Mineral Content (g)**

![Femoral Neck](#)  

**Volumetric Bone Mineral Density (g/cm³)**

![Femoral Neck](#)  

**Minimum Cross-sectional Area (cm²)**

![Minimum CSA](#)

$P < 0.05$ with respect to preflight*, postflight*

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Slide adapted from T. Lang., JBMR 2006.
Astronaut Data: Surrogates of bone strength do not correlate. Suggest that FE can pick up space-induced changes in strength that DXA cannot.
Results

Stance Loading

Mean post-menopausal white women (SD=2 kN)

Mean pre-menopausal white women

Max loss 30%
Results

Fall Loading

Time (months)

Hip Strength (kN)

Max loss
Mean post-menopausal white women
24%
Mean pre-menopausal white women

(SD=0.6 kN)
QCT: Trabecular BMD at Femoral neck does not appear to show a recovery 2 to 4 years postflight