Spaceflight-Induced Changes to Bone

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Human Research Program [HRP]
Johnson Space Center, Houston, TX
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By the end of this lecture...

1. Bone is a complicated tissue.
2. NASA has constraints: low subject #’s; slow data acquisition.
3. Astronauts are understudied group.
4. Spaceflight effects on bone are unique.
5. Clinically-accepted guidelines not applicable.
6. Widely-applied imaging technology (for Bone Mineral Density – BMD) is insufficient fully understanding bone changes due to spaceflight exposure.

Given NASA’s constraints for decision-making, Bone Discipline is investigating/advocating the transition of innovative research technologies to support decision-making (mission planning and risk management) and time-efficiency.
Whether the bone problem is “solved” depends upon the stakeholder’s perspective.

1. Program Managers – Have we mitigated risks to astronaut health and performance to ensure mission objectives can be accomplished while minimizing impact on power/mass/volume/time/expense?

2. Human Risk Board – Does spaceflight increase the probability of fracture both during mission operations and long-term health [LTH]? Can we ensure that astronauts are working within the operating standards of bone health? Is current risk management considered CONTROLLED?

3. Space & Clinical Operations – Do/will the results of proven clinical tests substantiate that the bone health of astronauts is impaired and requires a clinical response? Do we know what should be the therapeutic response?
Whether the bone problem is “solved” depends upon uncertainties willing to accept.

5. Bone Biomedical Research: Are we collecting the right data to sufficiently assess the probability of fracture during missions (and after return)? To assess the causality of IVD/back injury to spaceflight? Do we know which risk factors for bone loss/for overloading bones we should target first for mitigation? Can we identify which astronauts are at greatest need for mitigation?

6. Human Systems Engineering: Can we sufficiently engineer-out hazards (e.g., mechanical loads) to the skeleton to prevent injury?

7. Challenge: Not all stakeholders are on the same page regarding what is an acceptable and controlled risk. (Not understanding Bone physiology).
Skeletal Sites: Different composition of Bone Types with different contributions (a GAP) to Bone Integrity

PROXIMAL FEMUR

Trochanter
50% BMD

Femoral Neck
25% BMD

Cortical Bone/ "Compact Bone"

Cancellous “Spongy” Bone/Trabecular Bone

VERTEBRAL BODY – 66% BMD

Sources: L. Mosekilde; SL Bonnick; P Crompton
Different Distribution and Turnover Rates for Bone Types to Support Skeletal Functions

Entire skeleton turns-over 10%/year: 3% cortical bone but 25% of cancellous bone

Cortical Bone 80% of total skeleton (long bones)

Cancellous Bone 20% of total skeleton (vertebrae, ribs, ends of long bones) Contains 80% of bone surfaces
Remodeling of Bone Tissue in Adults is Highly Regulated* - Perturbations to Relative Rates can Influence Skeletal Integrity

*Resorption occurs at faster rate, occurs first, relative to formation. Requires communication between cells.
Some insight gained by comparison to Earth-based disorders of increased bone resorption.
Research Specialties in Bone & Mineral Field

- Endocrinology (704)
- Cell Biology (637)
- Biomechanics (250)
- Orthopaedics (336)
- Molecular Biology (460)

Figure Courtesy of the ASBMR 2014; adapted
Human Bone Risk: It’s all about fracture.

“Osteoporotic/Fragility Fractures” – low to atraumatic Fractures due to Osteoporosis (Causality - SKELETAL CONDITION)

You don’t have to be OLD.

Applied Load > Bone Strength = FRACTURE
(Key Causality – BIOMECHANICS)

You don’t have to have OSTEOPOROSIS.
Gain and Loss of Bone Mass in the Aging Human

Peak Bone Mass

Bone mass (g/calcium)

0 20 40 60 80 100

Age (yr)

Riggs BL, Melton LJ: Adapted from Involutional osteoporosis
Oxford Textbook of Geriatric Medicine
ADAPTED SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic
FRAGILITY FRACTURES in long-duration [LD] astronauts: Are they at risk for premature low trauma fractures due to prolonged exposure to space?

Cooper and Melton, 1992

SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic
Bone is a complicated tissue. Clinicians evaluate the multifactorial nature of bone loss and fracture risk for at-risk patients here on Earth.

Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
Bone loss in space is novel. While astronauts are not “patients” unique operationally-induced* factors in astronauts are possible contributors to fracture risk.

Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
Characterizing Bone Changes* in Space

- **Mercury** 1961-63
- **Gemini** 1965-66
- **Apollo** 1968-72
- **Skylab** 1973-74
- **Shuttle** 1981-2010
- **Intl Space Station** 2000-present

**Soyuz/Salyut** 1974-85
- SPA
- Urine, fecal Ca

**Mir** 1986-2000
- DXA

- SPA
- Urine, fecal Ca
- Heel,Wrist
- DXA
- QCT
- pQCT
- BTO
- Heel,Wrist

SPA=Single Photon Absorptiometry
DXA=Dual-energy X-ray Absorptiometry
QCT=Quantitative Computed Tomography
pQCT = peripheral QCT
BTO=biochemical markers of bone turnover

*Two functions of skeleton
FRAGILITY FRACTURES during LTH: Quantifying # premature low trauma fractures in astronauts not practical.

Cooper and Melton, 1992

SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic
Thus, NASA adapted the clinical surrogate for fracture (BMD) and WHO guidelines for 1° Osteoporosis for bone health standards in long-duration astronauts (Circa 2000)

*T-scores* (Not BMD change).

*T-score is # Standard Deviations from mean BMD of young normal “peak bone mass”*
Bone Densitometry more than a fracture surrogate in ISS Astronauts (MedB 1.11)

• Describe skeletal effects of spaceflight
• Track individual bone loss and recovery after long-duration flights.
• Informs rehabilitation efforts
• Facilitates recertification for long-duration missions
• For evaluation of in-flight exercise countermeasures and postflight rehabilitation processes.
Meanwhile, Terrestrial Observation of Reduced Sensitivity of DXA Test: “T-score Osteoporosis” Misses Over 50% of Fragility Fractures

Only 44% of women (21% of men) who sustain non-vertebral fractures have “osteoporosis” by BMD*

![Graph showing number of non-vertebral fractures by BMD status]

5794 participants in the Rotterdam study; Mean follow-up 6.8 yrs FN BMD at baseline

(Female data presented here)

Adapted from Schuit, Bone. 2004;34:195-202. Slide from J Shaker, MD; ISCD 2015 Annual Meeting

*Also disconnects evident with clinical trials—reduced ability to monitor therapeutic response to pharm agents.
Addtl shortcoming with BMD Guidelines: Cannot identify high risk persons in patients with other patterns of sub-regional bone loss (i.e., distinct from bone loss with aging – relevance to spaceflight-induced changes).

Seeman, JCI 1992
DPA measure of BMD
DXA BMD test/guidelines have limited clinical utility for younger-aged astronauts.

Kanis et al JBMR 9(8):1137, 1994

* it is the probability of fracture that drives the requirement for interventions, not declines in BMD.
Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: **bone density and bone quality.**” JAMA 2001

“Bone Quality: What is it and Can we measure it?”

May 2005
SD Clinical Test: Not clinically applicable to younger-aged astronaut population (Bone Summit, 2010).

BMD T-Score Values* Expeditions 1-25 (n=33)
*Comparison to Population Normals
What about BMD as a metric for bone strength?
The good, the bad, and the ugly.
### Seminal DXA study of Mir Crew Members

*Declines in bone mass are rapid and site-specific.*

*vs. 0.5 – 1.0 % BMD loss/yr in the aged*

<table>
<thead>
<tr>
<th>Areal BMD g/cm²</th>
<th>%/Month Change ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar Spine</td>
<td>-1.06±0.63*</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>-1.15±0.84*</td>
</tr>
<tr>
<td>Trochanter</td>
<td>-1.56±0.99*</td>
</tr>
<tr>
<td>Total Body</td>
<td>-0.35±0.25*</td>
</tr>
<tr>
<td>Pelvis</td>
<td>-1.35±0.54*</td>
</tr>
<tr>
<td>Arm</td>
<td>-0.04±0.88</td>
</tr>
<tr>
<td>Leg</td>
<td>-0.34±0.33*</td>
</tr>
</tbody>
</table>

* *p<0.01, n=16-18


Whole Body

0.3% / month

Lumbar Spine

1% / month

Hip

1.5% / month
**In vitro** studies: DXA BMD underestimates bone strength relative to QCT and QCT-FEM.

QCT estimates fracture loads better than DXA  \( R^2 = .66 \) QCT

QCT + FEM has superior capabilities for estimating fracture loads  \( R^2 = .84 \) FEM

DD Cody: Femoral strength is better predicted by finite element models than QCT and DXA. J Biomechanics 32:1013 1999.
DXA 2-D Limitation for BMD as a surrogate for bone strength: BMD g/cm$^2$ cannot delineate different sizes (which influences bone strength).

2-d projected *areal* bone mineral density (BMD = g/cm$^2$)

Areal BMD is not a good measurement to monitor *restoration to* or *maintenance of preflight status*.

Adapted figure from M. Bouxsein, PhD Presentation, Bone Quality May 2-3, 2005; Bethesda, MD
Literature: Exercise changes **geometry/size** of whole bone (adult skeleton)-
Suggests DXA not good for monitoring exercise as countermeasure.  (2011)


Bottom Line: Difficult to interpret % change in a DXA BMD over mission because cannot delineate bone gains or losses in different bone types.
Additionally, assays for biochemical markers in serum and urine suggest trends in cellular activities.

**Serum:**
- Total and bone-specific alkaline phosphatase (formation)
- Osteocalcin (formation)
- Total serum Calcium (40% protein bound; calcium complexes)

**Urine:**
- Pyridinium cross-links (resorption)
- Deoxypyridinoline cross-links (resorption)
- n-telopeptide (resorption)

**Hormones:**
- Parathyroid hormone – glands - main calcium sensing organ
- 1,25Dihydroxyvitamin D – stimulates Ca conservation
- 25Hydroxyvitamin D – assayed vitamin D metabolite (substrate)
Urinary calcium excretion (trend same as bone resorption markers) help elucidate how countermeasures affect bone cell activities Suggests that Exercise does not suppress breakdown

*Significantly different from pre-flight, p < 0.05
Bone Turnover Markers: suggest uncoupling of remodeling -- may result in net loss in bone mass *from skeleton.*
Subsequent Pilot Study:
Hip QCT to monitor response to countermeasure.

1. Utility: QCT will distinguish the effects of biochemical from mechanical countermeasures.

2. Important to use QCT to evaluate Countermeasures that affect different bone types (anti-resorptives vs. anabolic drugs).

3. Utility: QCT data to estimate hip strength to answer “so what?” question.

From J.W.Jaworski
Images Courtesy of D Carter, PhD
Fractures
Bone Research Plan
Densitometry for Bone Macroarchitecture

DXA reports areal BMD (aBMD)

QCT quantifies volumetric BMD

$g/cm^2$ averaged for cortical + trabecular bone

$g/cm^3$ for separate cortical & trabecular bones
Flight Research: QCT detects different rate of vBMD loss in separate bone compartments of hip. (n=16 ISS volunteers)

<table>
<thead>
<tr>
<th>Index DXA</th>
<th>%/Month Change ± SD</th>
<th>Index QCT</th>
<th>%/Month Change ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>aBMD Lumbar Spine</td>
<td>1.06±0.63*</td>
<td>Integral vBMD Lumbar Spine</td>
<td>0.9±0.5</td>
</tr>
<tr>
<td>aBMD Femoral Neck</td>
<td>1.15±0.84*</td>
<td>Integral vBMD Femoral Neck</td>
<td>1.2±0.7</td>
</tr>
<tr>
<td>aBMD Trochanter</td>
<td>1.56±0.99*</td>
<td>Integral vBMD Trochanter</td>
<td>1.5±0.9</td>
</tr>
</tbody>
</table>

*p<0.01, n=16-18

LeBlanc, J Musculoskelet Neuronal Interact. 2000; Lang, J Bone Miner Res, 2004;
Bone Turnover Markers: suggest uncoupling of remodeling -- may result in net loss in bone mass \textit{from skeleton}. 
Bone Strength (a contributor to fracture risk) is affected by factors not detected by DXA BMD.

*Osteoporosis is a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality.” JAMA 285(6):785-95, 2001

“Bone Quality: What is it and Can we measure it?” Bethesda, MD, May 2005

“The other 30-50%”
QCT in aging populations increases knowledge of macroarchitectural changes: Bone loss occurs at earlier age than expected. (Rec. from Bone Lead)

Macroarchitecture of Spine in 8 ISS astronauts of Extension Study: Discordant Recovery Patterns After Spaceflight

Adapted by Sibonga
DXA vs. QCT Proximal Femur of Extension Study: Clinical Advisory Panel identifies a clinical trigger for long-duration astronauts. “Failure to recover in trabecular BMD by R + 2 years” *

*SD response – seek osteoporosis specialist for evaluation and possible intervention.

QCT measures are independent predictors of hip fracture in addition to aBMD. Persistent deficits may combine with age-related changes. Clinical advisory panel recommends clinical trigger for possible intervention (monitor for recovery by two years after return).
How can we assess fracture risk in astronauts from QCT data?

Clinical advisory panel: Explore the emerging data from population studies to propose how Finite Element Models of QCT data could be used to reflect fracture risk due to spaceflight. (Report back to the clinical advisory panel).


- More from the ISCD 2015 position development (22 total for QCT and FEM).
Individual Astronaut Results
Stance Loading (4 to 30% loss in strength)

Max loss 30%

Hip Strength (kN)

Time (months)

Individual Astronaut Results
Fall Loading (3 gain to 24% loss in strength)

The FEM knowledge, gained from population studies – how can it be used to support the monitoring of astronaut bone health?

E. Orwoll MD, S Khosla MD, S Amin MD, T Lang PhD, J Keyak PhD, T Keaveny PhD, D Cody PhD, JD Sibonga, Ph.D.
RESEARCH MTL807: Recommendation of FE Operating Bands of “Bone Health” - by FE Task Group II - to be used together with DXA BMD Standards to inform clinical/operational decision-making.

E. Orwoll MD, S Khosla MD, A Cheung, MD, S Amin MD, T Lang PhD, J Keyak PhD, D Nicolella PhD, T Keaveny PhD, D Cody PhD, and J Sibonga, PhD

*Red, Yellow and Green Operating Bands for Astronauts – Example Only

Minimum FE strength for Bone Health*

Minimum Permissible Outcome

E. Orwoll MD, S Khosla MD, A Cheung, MD, S Amin MD, T Lang PhD, J Keyak PhD, D Nicolella PhD, T Keaveny PhD, D Cody PhD, and J Sibonga, PhD

*Red, Yellow and Green Operating Bands for Astronauts – Example Only

REPRESENTATIVE POPULATION DATA

Data slide courtesy of Keyak. NOT FOR DISTRIBUTION
Additional Goal is to integrate QCT and FEM hip strength to assess probability of Bone Fracture -- NASA Glenn Research Center’s Probabilistic Risk Assessment [PRA] Model for Fracture Likelihood

*Current PRA using DXA BMD for bone strength is insensitive to BMD changes due to ARED or Bisphosphonates. FE strength reduces uncertainty; can be used to individualize risk management.

Probability of Fracture

Probability of event

Probability bone will fail to support load

Bone Changes in Space

Estimate of Fracture Probability

Clinical and Engineering Characteristics of Bone Strength

Figure 2. Summary of literature survey on fracture load as a function of femoral neck BMD
Bone *Micro*architecture

Knowledge and Technology Gap
High Resorption → Disrupts Microarchitecture → Fractures* 
GAPS persist.

Male Astronauts? 
Spaceflight Effect? 
The Hip?
Indices of bone microarchitecture reflect changes in trabeculae size and spatial orientation – need to identify non-permissible outcome

Images courtesy of Ralph Müller, PhD, Switzerland

Adapted by Sibonga
Monitoring microarchitectural changes: Establish when perforation may occur. Mechanism of disruption informs countermeasure (anti-resorptive or anabolic)

Electron Microscopic Images to demonstrate mechanism of disruption ONLY
Recap

It’s challenging.
Sole use of BMD data as a surrogate for fracture risk and skeletal integrity in astronauts may incur the following risks:

1. Restricting our understanding spaceflight effects on hip and spine integrity
2. Inadequately evaluating efficacy of countermeasures
3. Failing to identify astronauts at greater risk (both during and after spaceflight)
4. Subsequently failing to provide greater protection against risk

Hence, Bone Research is taking the following Path to Risk Reduction:
Fracture Risk during Mission Operations [OPS]: Collecting new bone data to estimate bone strength and inform NASA’s PRA module for Applied Loads > Bone Strength

- Peak Bone Mass
- Overloading during OPS
- Age-related Loss
- Males
- Females
- Menopause-induced Loss

Bone mass (g/calcium)

Age (yr)

Riggs BL, Melton LJ: Adapted from Involutional osteoporosis
Oxford Textbook of Geriatric Medicine
ADAPTED SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic
Fracture Risk during Long-term Health (LTH): a) Monitor for persistent space-induced changes (*clinical trigger at R + 2 years*) and b) Develop new FE strength-based bands of bone health based upon predicted fractures for advanced ages.

*Osteoporosis due to changes due to aging.*
Fracture Risk soon after return to Earth: Explore a Factor of Risk (Applied load/bone strength) to inform astronauts about potential hazardous conditions?*

Overloading due to preflight activities performed on reduced bone strength.

Peak Bone Mass

Bone mass (g/calcium)

Age-related Loss

Males

Females

Menopause-induced Loss

*Counseling the “athlete vs. the office worker”?*
Questions

Thanks for your attention.
Backup Slides
Path to Risk Reduction – what is **Essential vs. Good-to-Know?**

*Optimize risk definition by end of ISS platform. (2020-2024)*

*Focus on risk factors that are modifiable.*

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**Fracture 1.** We don’t understand how the space flight environment affects bone fracture healing in-flight.  
**KNOWLEDGE GAP – RISK CHARACTERIZATION**

**Fracture 2.** We need to characterize the loads applied to bone for standard in-mission activities.  
**KNOWLEDGE GAP – RISK CHARACTERIZATION**

**Fracture 3.** We need a validated method to estimate the Risk of Fracture by evaluating the ratio of applied loads to bone fracture loads for expected mechanically-loaded activities during a mission.  
**MITIGATION GAP - TOOL**

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**Osteo 1.** A new acceptable bone health standard using an improved surrogate for bone strength needs to be defined for the flight environment.  
**POLICY ON STANDARDS**

**Osteo 2.** We need a validated, clinically-relevant method for assessing the effect of spaceflight on osteoporosis or fracture risk in LD astronauts.  
**KNOWLEDGE GAP – ENABLING TECHNOLOGY**

**Osteo 3.** We don’t know the contribution of each risk factor on bone loss and recovery of bone strength and which factors are the best targets for countermeasure application.  
**KNOWLEDGE GAP – DATA**

**Osteo 4.** We need an in-flight capability to monitor bone turnover and bone mass changes during spaceflight.  
**MITIGATION GAP - DETECT**

**Osteo 5.** We need to identify options for mitigating early onset osteoporosis before, during and after spaceflight.  
**MITIGATION GAP – PREVENTION & TREATMENT**

**Osteo 6.** How do skeletal changes due to spaceflight modify the terrestrial risk of osteoporotic fractures?  
**MITIGATION GAP – SURVEILLANCE**

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(*) Risk Custodian: J. Sibonga

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**Research for CPGs**

**PRA for LTH**

**Hip QCT, Back, Microarchitecture**

**CPGs – clinical practice guidelines**

**PRA=probabilistic Risk Assessment**

**LTH = Long term Health**

**FEM = Finite Element Models/Modeling**

**BMD=bone mineral density; QCT = quantitative computed tomography**
Human System Risks – Proposed Likelihood vs Consequence

### Mission Health and Performance (OPS)
- **Consequence**
  - **Low**
  - Minor injury/illness that is self-limiting
  - Minor impact to performance and operations - requires additional resources (time, consumables)
  - Temporary discomfort
  - Insignificant impact to performance and operations - no additional resources required

  - **Medium**
  - Significant injury, illness, or incapacitation - may affect personal safety
  - Significant reduction in performance results in the loss of some mission objectives

  - **High**
  - Death or permanently disabling injury to one or more crew (LOC)
  - Severe reduction of performance that results in loss of most mission objectives (LOM)

### Long Term Health (post mission) (LTH)
- **Consequence**
  - **Very Low**
  - Return to baseline values within 3 months with limited intervention (time, exercise, nutrition, lenses)
  - No effect on the quality of life

  - **Low**
  - Return to baseline values within 1 year with nominal intervention (time, exercise, nutrition, lenses)
  - Negligible effect on quality of life

  - **Medium**
  - Unknown and improbable return to baseline (requires drastic intervention surgery & therapy)
  - Major impact on quality of life (permanent reduced function, premature death)

  - **High**
  - Return to near baseline requires extended medical intervention w/ known clinical methods/technologies (pharmaceuticals, etc.)
  - Moderate impact on quality of life

- **Quality of Life** is defined as impact on day to day physical and mental functional capability and/or lifetime loss of years

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CM = Countermeasure
LOC = Loss of Crew
LOM = Loss of Mission

Do not delete this slide - may be needed for discussion at the HSRB
“Mega-analysis” for Fracture Prediction

Constraint: “Fracture Prediction” requires large # subjects.

~60,000 subjects
~5,400 total fractures
~250,000 person-years
~3,500 OP fractures
~1,000 hip fractures

• Rotterdam
• EVOS/EPOS
• CaMos
• Rochester
• Sheffield
• Dubbo

• EPIDOS
• OFELY
• Kuopio
• Hiroshima
• Gothenburg 1
• Gothenburg 2

Cohorts analyzed but not merged: MEDOS, NHANES, Asia
Possible future cohorts: OFELY extension, OPUS, SOF

Adapted, Slide courtesy of S. Petak, M.D.
Background: Bone is a complicated tissue. Clinical assessment evaluates multifactorial nature of bone loss and fracture risk.*

* Presented cohort trends and individual case reports in closed meeting.

Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
Bone loss in space is novel: Operationally-induced* factors in astronauts are possible contributors to fracture risk.

Aging
- Hypogonadism and Menopause
- Ca/Nutrition/Vit D/Endocrine Perturbations/Muscle Atrophy
- Unbalanced and increased bone resorption
- Reduced activity, weightbearing; diet
- Family History
- Medications
- Disorders

Inadequate peak bone mass
- Low bone density
- Impaired bone quality
- Increased bone loss
- Postural instability/Gait impairment
- Falling in partial gravity
- Certain Activities Extravehicular Activities Exercise loading
- Fall Mechanics in hypog G Hazardous environment/Kinetic energy

Skeletal fragility
- Excessive bone loading
- Fracture Probability

CO2; Radiation on bone marrow cells, Fluid shifts and regional blood flow

*exposure to space environment and mission operations

Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ
Constraint: Astronauts are understudied population—very limited baseline knowledge (1/2015).

- Typical **space** mission duration – **160 ± 32d** (range 49-215d)
- Average **Age** – **47 ± 5 y** (range 36 – 56)
- **Male to Female** Ratio – **4.7 : 1** (56:12)
- Current **total #** per astronauts in corps – **68 of 365**
- # repeat fliers – **7**
- **BMI** – **Male BMI 25.7 ± 2.2** (range 21.2 to 30.7) **Female BMI 22.3 ± 2.3** (range 20.1 to 25.9)
- **Wt and Ht**- Males: **Males: 82 ± 9 (63 to 103); 177 ± 6 (163 to 188)**
  Females : **65 ± 7 (54 to 81), 169 ± 4 (163 to 178)**
- **% Body Fat**: Males: **23 ± 4 (14 to 31)** Females: **29 ± 6 (22 to 44)**
Which is better?
Fracture risk assessment by 1 measurement or by > 1 measurement?
It’s not complicated.

Finite Element Strength

- aBMD
- Geometry
- Material Properties
- BMD
- Loading

Bone Strength Surrogate
- Relative Fracture Risk

Individualized Fracture Risk
Reported “ Disconnects” and Limitations of DXA BMD (Slide from 2007)


Effects of exercise regimens described using DXA BMD

Note: No population data linking % BMD loss to Fracture Outcome

* Updated data since 2010 Bone Summit
Skeletal Health in Long-Duration Astronauts: Nature, Assessment, and Management Recommendations from the NASA Bone Summit

Eric S Orwoll, Robert A Adler, Shreyasee Amin, Neil Binkley, E Michael Lewiecki, Steven M Petak, Sue A Shapses, Mehrsheed Sinaki, Nelson B Watts, and Jean D Sibonga
“Bottom Line” Bone Summit II (2013)

“Overall, NASA’s strategy of assessing relative fracture risk in astronauts by T-score BMD-based guidelines alone needs to be refined. Accurately determining the absolute fracture risk in astronauts is an ambitious goal that may never be fully realized. A concerted effort however should be made to expand NASA’s technical and scientific capabilities toward objectively assessing the factors contributing to the risk since long-duration space flight is expected to:

i) have profound and possibly irreversible bone changes that would not be adequately addressed by DXA BMD, ii) affect other physiological systems (e.g., muscle) that determine fracture likelihood and

iii) expose astronauts to novel situations that involve a greater probability of overloading bones.”
Calcium-regulating Hormones – Endocrine system is "normal" but perturbed.

Nutrition SMO, unpublished data; Courtesy Dr. SM Smith
QCT critical for detecting countermeasure effects on different compartments of bone (cortical vs. trabecular BMDs)
NASA is an engineering agency in the business of space exploration – i.e., extending human capabilities in space.


Systems Engineering & Integration

- Structure
- Electrical Power System
- Environ. Control Life Support
- Thermal
- I/T
- ... Human