Bone Health in Spaceflight: Spinal Cord Injury Analog

By Chen Zhuang
Mentor: Dr. Jean Sibonga
SK3
About Me

- B.S. in Bioengineering at University of California, Los Angeles
- M.S. in Biomedical Engineering at University of Michigan, Ann Arbor
- Fremont, California
Bone Lab

• Scans of astronauts
  – selection
  – pre-flight
  – post-flight
  – life-time

• Database and surveillance of bone health, no fracture so far

• No basic research done in lab
Clinical - Dual-Energy X-ray Absorptiometry (DXA)

Clinical - DXA Standard

• Since 1998, NASA medically required measurements of aBMD by DXA to assess skeletal integrity of astronauts.

• a T-score of greater than –1.0 at the hip or lumbar spine qualifies an applicant for the astronaut corps and long-duration missions

Research - Peripheral Quantitative Computed Tomography (pQCT)

Research - Finite Element Analysis

Project:
SPINAL CORD INJURY ANALOG
Purpose of the Analog

PROBLEM: no direct way to quantify bone health

• **Validate** new technology NMR to assess bone microarchitecture

• fineSA software by Acuitas Medical (Open Innovation)

PROJECT: Write background section of proposal
fineSA a New MR-Based Technique
can Accurately Distinguish Normal
From Osteopenic or Osteoporotic
Trabecular Bone Structure

Amanda Cox¹, Michael Stone², Jane Turton², Irene Debiram³,
Kristin James¹, Richard Hugtenburg⁴, Juliet E. Compston³

¹Acuitas Medical, Swansea, United Kingdom, ²University Hospital Llandough, United Kingdom,
³University of Cambridge School of Clinical Medicine, Cambridge, United Kingdom, ⁴Swansea
University, Swansea, United Kingdom
Advantages of Spinal Cord Injury Analog

Bed Rest
- Small sample size/Large variability
- Recruitment
- Facilities
- Relocation and Testing

Spaceflight
- Small sample size/Large variability
- Approval and consent
- Recruitment

Spinal Cord Injury (SCI)
- Large sample size/Large variability
- Contract with surgeon and 800+ patients
- Similar mechanical unloading of bone
<table>
<thead>
<tr>
<th>Site Measured</th>
<th>Author</th>
<th>Type of Study</th>
<th>Duration of Injury</th>
<th>Extent of Injury, Core</th>
<th>Para or Tetraradicular</th>
<th>Males</th>
<th>Females</th>
<th>Age</th>
<th>Type of Imaging</th>
<th>BMD Z-score, SD, or % lo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper Extremity</td>
<td>Clyney 2004</td>
<td>X-Sectional</td>
<td>0.6-3.3 yrs</td>
<td>Not specified</td>
<td>20C</td>
<td>21</td>
<td>8</td>
<td>23-56 yrs</td>
<td>DXA</td>
<td>11.10%</td>
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<tr>
<td>Daity 2000</td>
<td></td>
<td>X-Sectional</td>
<td>&gt;1 yr</td>
<td>20C</td>
<td>31</td>
<td>9</td>
<td>18-60 yrs</td>
<td>6%</td>
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<tr>
<td>Demirag 1998</td>
<td></td>
<td>X-Sectional</td>
<td>2-30 months</td>
<td>21C, 9I</td>
<td>32</td>
<td>9</td>
<td>19-49 yrs</td>
<td>0.09 +/- 0.15 SD</td>
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<tr>
<td>Forearm</td>
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<tr>
<td>Forearm distal diaphysis</td>
<td>Finsen 1992</td>
<td>X-Sectional</td>
<td>7 months-33 yrs</td>
<td>Not specified</td>
<td>19</td>
<td>15-64 yrs</td>
<td>5%</td>
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<tr>
<td>Forearm distal metaphysis</td>
<td>Finsen 1992</td>
<td>X-Sectional</td>
<td>7 months-33 yrs</td>
<td>Not specified</td>
<td>19</td>
<td>15-64 yrs</td>
<td>-13%</td>
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<tr>
<td>Distal forearm</td>
<td>Sabo 2001</td>
<td>X-Sectional</td>
<td>1-26 yrs</td>
<td>33C, 13I</td>
<td>46</td>
<td>&lt;50 yrs</td>
<td>6.10%</td>
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<tr>
<td>Radius</td>
<td></td>
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<tr>
<td>Distal radius trabeular</td>
<td>D’Saumur 2005</td>
<td>Prospective</td>
<td>3.5 yrs</td>
<td>4C, 6I</td>
<td>9</td>
<td>19-81 yrs</td>
<td>-10 to +14%</td>
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<tr>
<td>Radius trabeular</td>
<td>FreyRindova 2000</td>
<td>Prospective</td>
<td>12 months</td>
<td>10C, 19I</td>
<td>27</td>
<td>19-59 yrs</td>
<td>-28% para, 0% para</td>
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<tr>
<td>Radius cortical</td>
<td>FreyRindova 2000</td>
<td>Prospective</td>
<td>12 months</td>
<td>10C, 19I</td>
<td>27</td>
<td>19-59 yrs</td>
<td>-3% para, +1% para</td>
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<tr>
<td>Radius shaft 1/3</td>
<td>Zehnder 2004</td>
<td>X-Sectional</td>
<td>&lt;1 yr</td>
<td>94C, 6I</td>
<td>16</td>
<td>18-60 yrs</td>
<td>0 +/- 0.41 SD</td>
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<tr>
<td>Radius shaft 1/3</td>
<td>Zehnder 2004</td>
<td>X-Sectional</td>
<td>1-9 yrs</td>
<td>94C, 6I</td>
<td>16</td>
<td>18-60 yrs</td>
<td>0.4 +/- 0.17 SD</td>
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<tr>
<td>Radius shaft 1/3</td>
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<td>X-Sectional</td>
<td>10-19 yrs</td>
<td>94C, 6I</td>
<td>31</td>
<td>18-60 yrs</td>
<td>0.97 +/- 0.2 SD</td>
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<td>Radius shaft 1/3</td>
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<td>X-Sectional</td>
<td>20-29 yrs</td>
<td>94C, 6I</td>
<td>13</td>
<td>18-60 yrs</td>
<td>0.27 +/- 0.31 SD</td>
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<tr>
<td>Radius shaft 1/3</td>
<td>Zehnder 2004</td>
<td>X-Sectional</td>
<td>&lt;1 yr</td>
<td>94C, 6I</td>
<td>16</td>
<td>18-60 yrs</td>
<td>0.02 +/- 0.24 SD</td>
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<tr>
<td>Radius shaft 1/3</td>
<td>Zehnder 2004</td>
<td>X-Sectional</td>
<td>1-9 yrs</td>
<td>94C, 6I</td>
<td>38</td>
<td>18-60 yrs</td>
<td>0.01 +/- 0.15 SD</td>
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<tr>
<td>Radius shaft 1/3</td>
<td>FreyRindova 2000</td>
<td>X-Sectional</td>
<td>10-19 yrs</td>
<td>94C, 6I</td>
<td>31</td>
<td>18-60 yrs</td>
<td>0.52 +/- 0.20 SD</td>
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<tr>
<td>Radius shaft 1/3</td>
<td>FreyRindova 2000</td>
<td>X-Sectional</td>
<td>20-29 yrs</td>
<td>94C, 6I</td>
<td>13</td>
<td>18-60 yrs</td>
<td>0.44 +/- 0.32 SD</td>
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<tr>
<td>Ulna</td>
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</tr>
<tr>
<td>Ulna trabeular</td>
<td>FreyRindova 2000</td>
<td>Prospective</td>
<td>12 months</td>
<td>10C, 19I</td>
<td>27</td>
<td>19-59 yrs</td>
<td>-15% para, 0% para</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ulna cortical</td>
<td>FreyRindova 2000</td>
<td>Prospective</td>
<td>12 months</td>
<td>10C, 19I</td>
<td>27</td>
<td>19-59 yrs</td>
<td>-4% para, 0% para</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
# Comparison of BMD Loss

<table>
<thead>
<tr>
<th>Method of Loss</th>
<th>Short Term Average aBMD% Decline in Lower Limbs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed Rest (up to 4 months)</td>
<td>-1.0% to -1.5% per month*</td>
</tr>
<tr>
<td>Spaceflight (up to 6 months)</td>
<td>Pre-ARED: -1.0% to -1.5% per month*</td>
</tr>
<tr>
<td></td>
<td>Post-ARED: -0.3% to -0.5% per month*</td>
</tr>
<tr>
<td>Spinal Cord Injury (3-12 months)</td>
<td>-1.5% to -5% per month**</td>
</tr>
<tr>
<td>Typical Aging</td>
<td>-0.5% to -1.0% per year*</td>
</tr>
</tbody>
</table>


**Modlesky et al. (2004). “Trabecular Bone Microarchitecture Is Deteriorated in Men With Spinal Cord Injury”
Comparison of BMD Loss

Comparison of BMD Loss

“New steady-state levels for BMC were reached at 2 years post-injury for the proximal tibia and the femoral neck at 40-50% and 60-70%, respectively of normal values. (Biering-Sorensen, 1990)”

“These patterns indicate that there is no steady state of bone mineral density following 3 years of spinal cord injury. (de Bruin, 2005)”
## Comparison of Bone Turnover

<table>
<thead>
<tr>
<th>Bed Rest</th>
<th>Space Flight</th>
<th>Spinal Cord Injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary Ca ↑</td>
<td>Urinary Ca ↑</td>
<td>Urinary Ca ↑↑</td>
</tr>
<tr>
<td>Ca Balance ↓</td>
<td>Ca Balance ↓↓</td>
<td>Ca Balance ↓↓</td>
</tr>
<tr>
<td>BMD ↓</td>
<td>BMD ↓↓</td>
<td>BMD ↓↓↓</td>
</tr>
<tr>
<td>Resorption ↑</td>
<td>Resorption ↑↑</td>
<td>Resorption ↑↑↑</td>
</tr>
<tr>
<td>Formation ↔</td>
<td>Formation ↔</td>
<td>Formation ↔</td>
</tr>
<tr>
<td>PTH ↓</td>
<td>PTH ↓</td>
<td>PTH ↓</td>
</tr>
<tr>
<td>Ca Absorption ↓</td>
<td>Ca Absorption ↓</td>
<td>Ca Absorption ↓</td>
</tr>
<tr>
<td>Ca+, Serum Ca++ ↔</td>
<td>Ca+, Serum Ca++ ↔</td>
<td>Ca+, Serum Ca++ ↔</td>
</tr>
</tbody>
</table>

LeBlanc et al. (2007). “Skeletal responses to space flight and the bed rest analog: A review”
Comparison Summary

**Similarity**
- Loss of BMD in lower extremity
- Trabecular loss greater than cortical
- Similar bone turnover

**Difference**
- Acute Stage -> Chronic Stage
- Different intensity and location of injury
- Loss of BMD in upper for tetraplegics
- Neurological
- Trauma
- Loss of muscle use
- No recovery, steady state?
Summary

• NASA responsible for astronaut health
• Bone is complicated
• Spinal Cord Injury Analog: Validation of new imaging technology
• Sievänen et al. (2010). “Immobilization and bone structure in humans.” Archives of Biochemistry and Biophysics. 503: 146-152.
Thank you

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• Lauren Merkle
• Diego Rodriguez
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Extra Slides