Bone Health in Spaceflight: Spinal Cord Injury Analog

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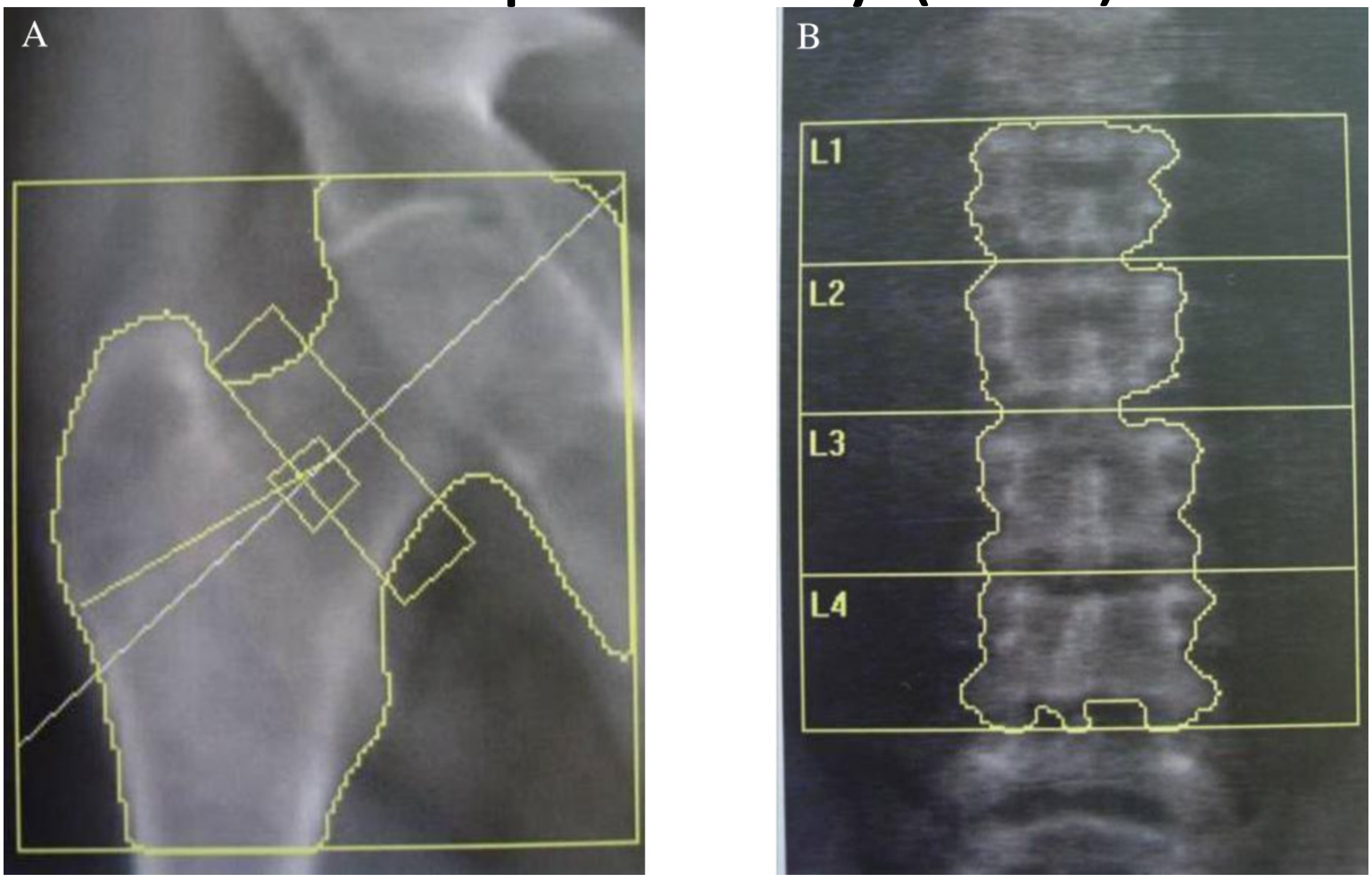
About Me

- 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

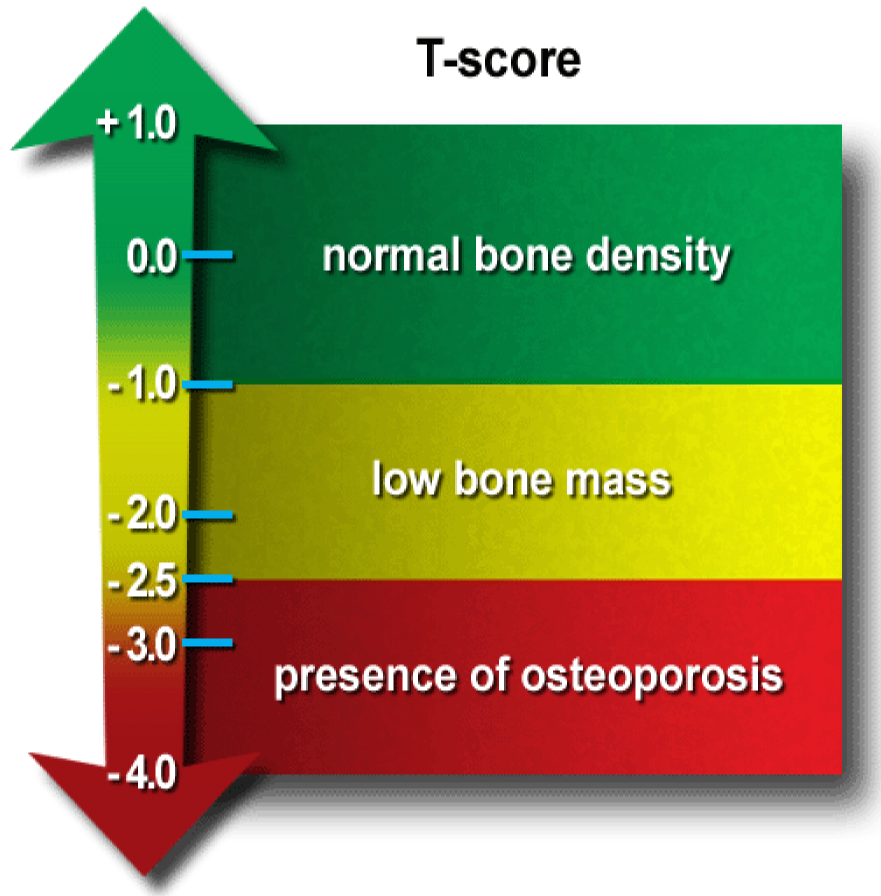
Clinical - Dual-Energy X-ray Absorptiometry (DXA)



D. P. Germain: *Fabry disease.* In: *Orphanet journal of rare diseases* Vol. 5, 2010, 30
Canadian Space Agency. <http://www.asc-csa.gc.ca/eng/missions/expedition34-35/health.asp>

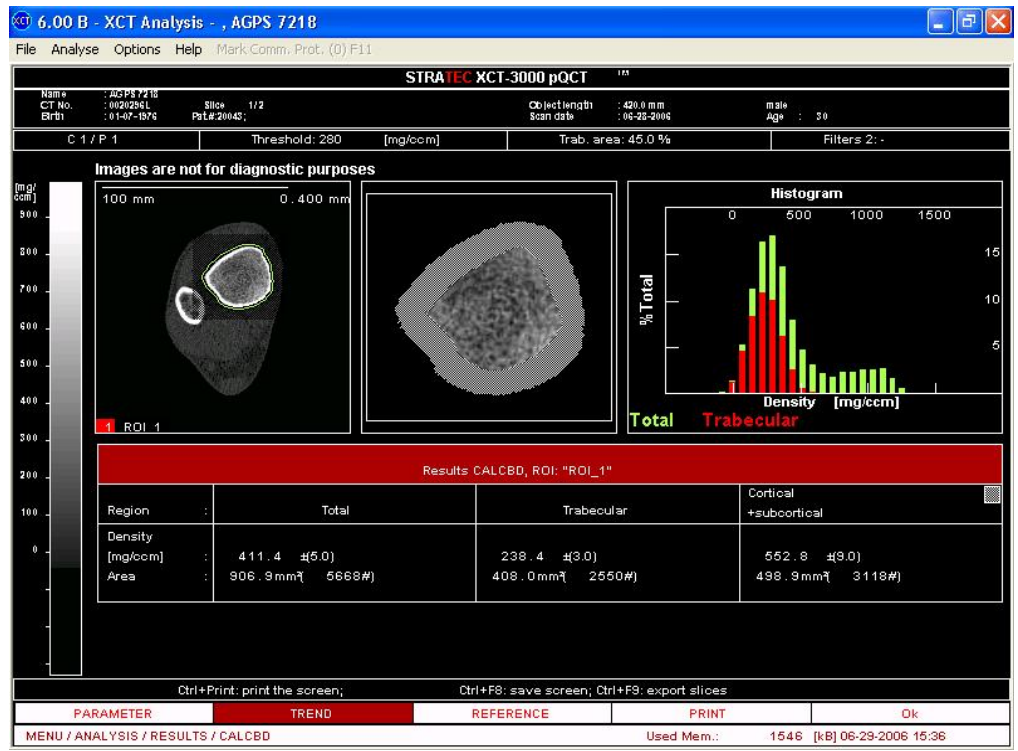
Clinical - DXA Standard

- 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



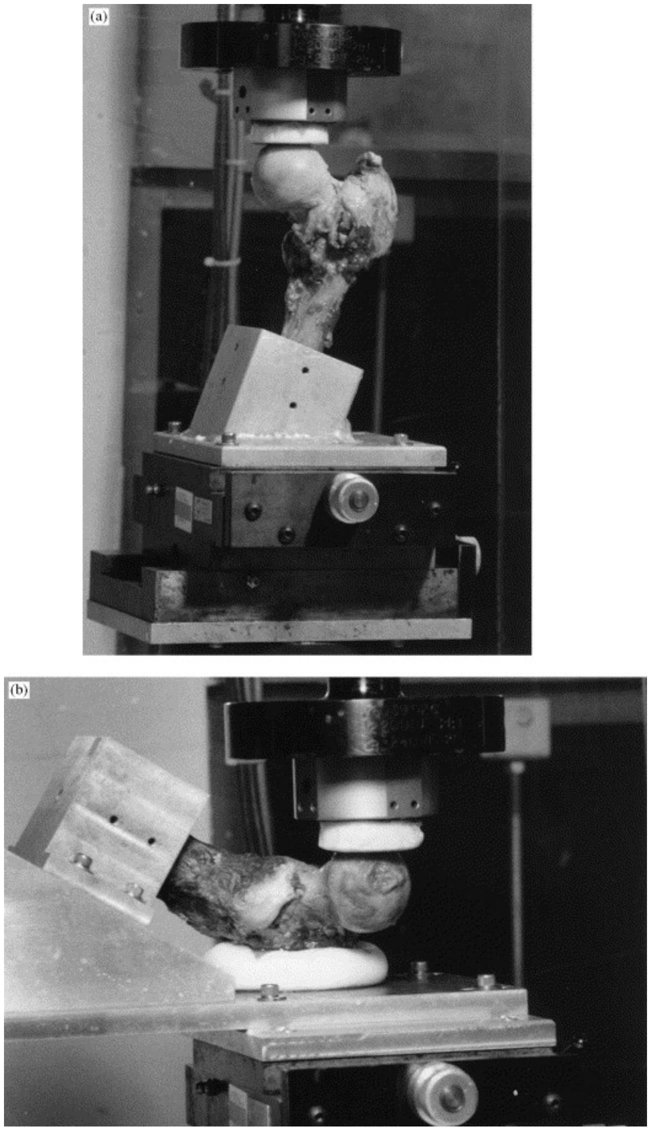
Orwoll et al. (2013). “Skeletal Health in Long-Duration Astronauts: Nature, Assessment, and Management Recommendations from the NASA Bone Summit”

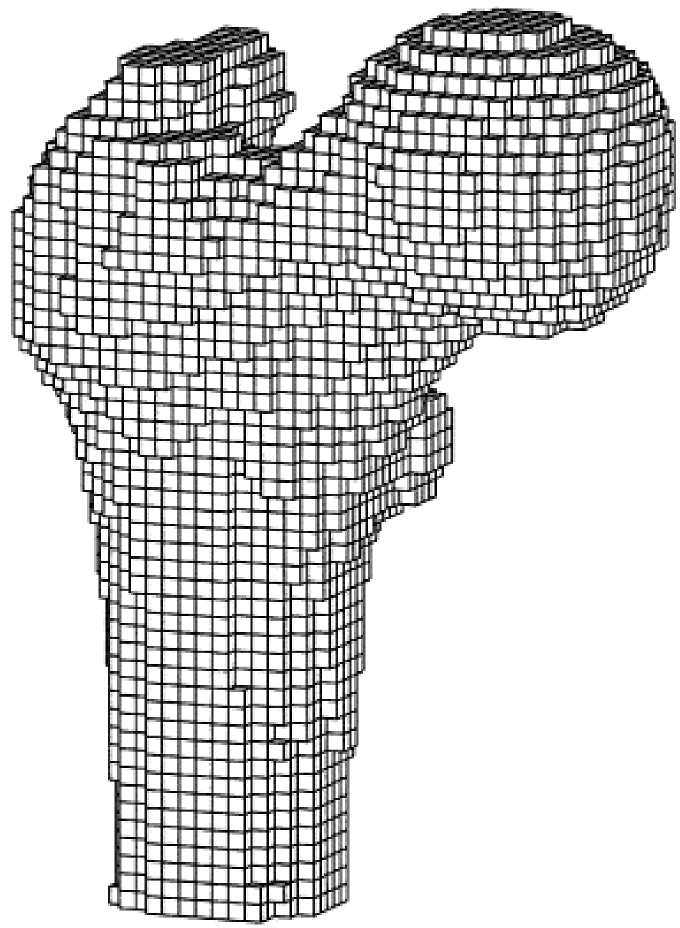
Research - Peripheral Quantitative Computed Tomography (pQCT)



Canadian Space Agency. <http://www.asc-csa.gc.ca/eng/missions/expedition34-35/health.asp>

Research - Finite Element Analysis





Keyak et al. (1997). “Prediction of femoral fracture load using automated finite element modeling.“

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

*fine*SA a New MR-Based Technique can Accurately Distinguish Normal From Osteopenic or Osteoporotic Trabecular Bone Structure

Amanda Cox[1], Michael Stone[2], Jane Turton[2], Irene Debiram[3], Kristin James[1], Richard Hugtenburg[4], Juliet E. Compston[3]

[1]Acuitas Medical, Swansea, United Kingdom, [2]University Hospital Llandough, United Kingdom, [3]University of Cambridge School of Clinical Medicine, Cambridge, United Kingdom, [4]Swansea University, Swansea, United Kingdom

ACUiTAS medical

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

Literature Search

	A	B	C	D	E	F	G	H	I	J	K
1	Site Measured	Author	Type of Study	Duration of Injury	Extent of Injury, cor	Para or Tetrapelgic	Males	Females	Age	Type of Imaging	BMD (Z-score, SD, or % lo
2	**Upper Extremity**	Clasey_2004	X-Sectional	0.6-35.3 yrs	29C	Not specified	21	8	23-56 yrs	DXA	11.10%
3		Dauty_2000	X-Sectional	>1 yr	22C, 9I		31		18-60 yrs	DPX	6%
4		Demirel_1998	X-Sectional	2-30 months	21C, 9I		32	9	19-49 yrs	DEXA	0.09 +/- 0.15 SD
5											
6	**Forearm**										
7	forearm distal diaphysis	Finsen_1992	X-Sectional	7 months-33 yrs	Not specified		19		15-64 yrs		-5%
8	forearm distal metaphysis	Finsen_1992	X-Sectional	7 months-33 yrs	Not specified		19		15-64 yrs		-13%
9	distal forearm	Sabo_2001	X-Sectional	1-26 yrs	33C, 13I		46		<50 yrs	DXA	-6.10%
10											
11	**Radius**										
12	distal radius trabecular	DeBruin_2005	Prospective	3.5 yrs	4C, 6I		9	1	19-81 yrs	pQCT	-10 to +14%
13	radius trabecular	FreyRindova_2000	Prospective	12 months	10C, 19I	18 para, 6 tetra	27	2	19-59 yrs	pQCT	-28% tetra, 0% para
14	radius cortical	FreyRindova_2000	Prospective	12 months	10C, 19I	18 para, 6 tetra	27	2	19-59 yrs	pQCT	-3% tetra, +1% para
15	radius shaft 1/3	Zehnder_2004	X-Sectional	<1 yr	94C, 6I		16		18-60 yrs	DXA	0 +/- 0.41 SD
16	radius shaft 1/3	Zehnder_2004	X-Sectional	1-9 yrs	94C, 6I		38		18-60 yrs	DXA	0.4 +/- 0.17 SD
17	radius shaft 1/3	Zehnder_2004	X-Sectional	10-19 yrs	94C, 6I		31		18-60 yrs	DXA	0.97 +/- 0.2 SD
18	radius shaft 1/3	Zehnder_2004	X-Sectional	20-29 yrs	94C, 6I		13		18-60 yrs	DXA	0.27 +/- 0.31 SD
19	ultradistal radius	Zehnder_2004	X-Sectional	<1 yr	94C, 6I		16		18-60 yrs	DXA	0.02 +/- 0.24 SD
20	ultradistal radius	Zehnder_2004	X-Sectional	1-9 yrs	94C, 6I		38		18-60 yrs	DXA	0.01 +/- 0.15 SD
21	ultradistal radius	Zehnder_2004	X-Sectional	10-19 yrs	94C, 6I		31		18-60 yrs	DXA	0.52 +/- 0.20 SD
22	ultradistal radius	Zehnder_2004	X-Sectional	20-29 yrs	94C, 6I		13		18-60 yrs	DXA	0.44 +/- 0.32 SD
23											
24	**Ulna**										
25	ulna trabecular	FreyRindova_2000	Prospective	12 months	10C, 19I	18 para, 6 tetra	27	2	19-59 yrs	pQCT	-15% tetra, 0% para
26	ulna cortical	FreyRindova_2000	Prospective	12 months	10C, 19I	18para, 6 tetra	27	2	19-59 yrs	pQCT	-4% tetra, 0% para

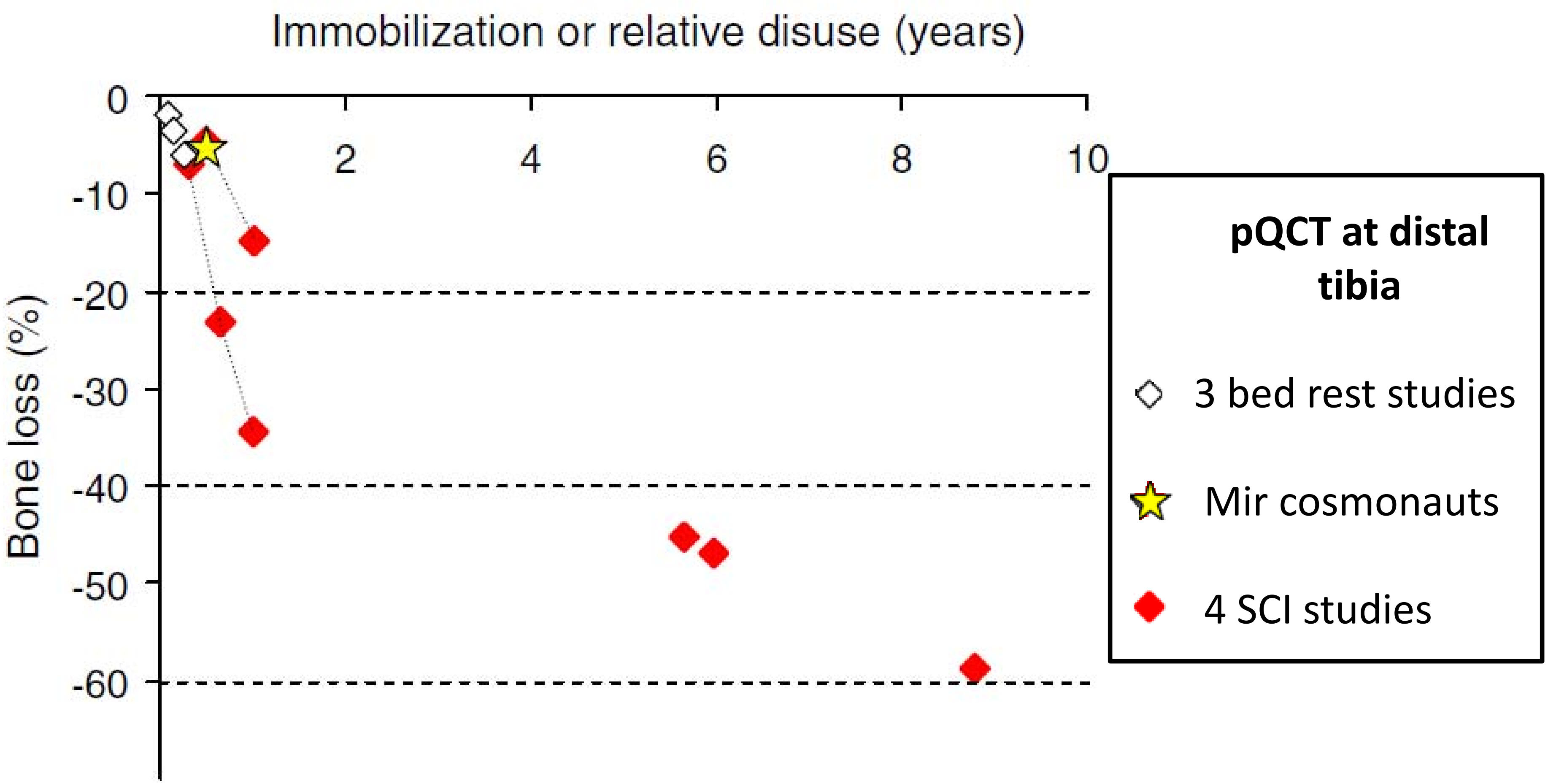
Comparison of BMD Loss

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

*Orwoll et al. (2013). "Skeletal Health in Long-Duration Astronauts: Nature, Assessment, and Management Recommendations from the NASA Bone Summit"

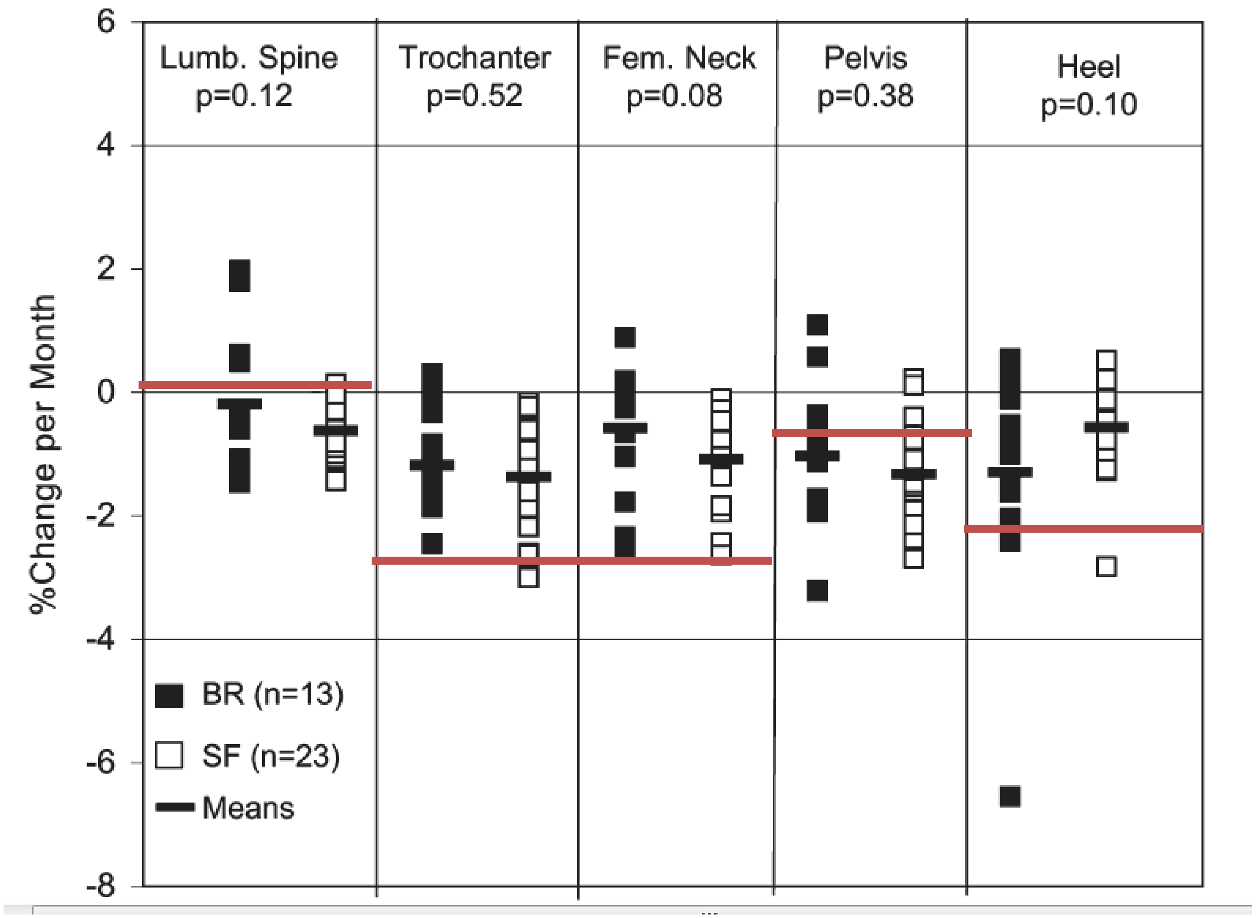
**Modlesky et al. (2004). "Trabecular Bone Microarchitecture Is Deteriorated in Men With Spinal Cord Injury"

Comparison of BMD Loss



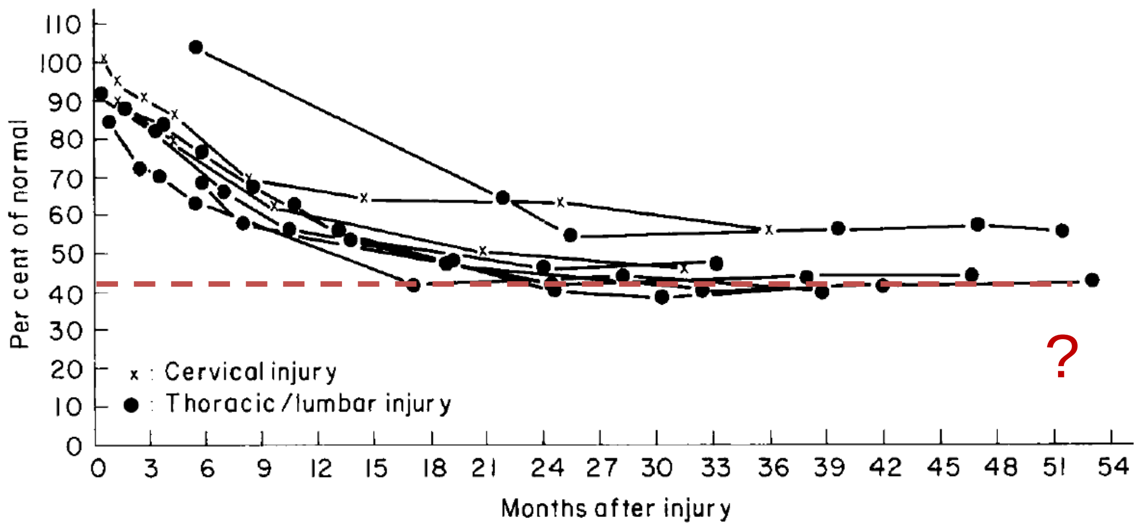
Harri Sievänen. (2010). “Immobilization and bone structure in humans.”

Comparison of BMD Loss



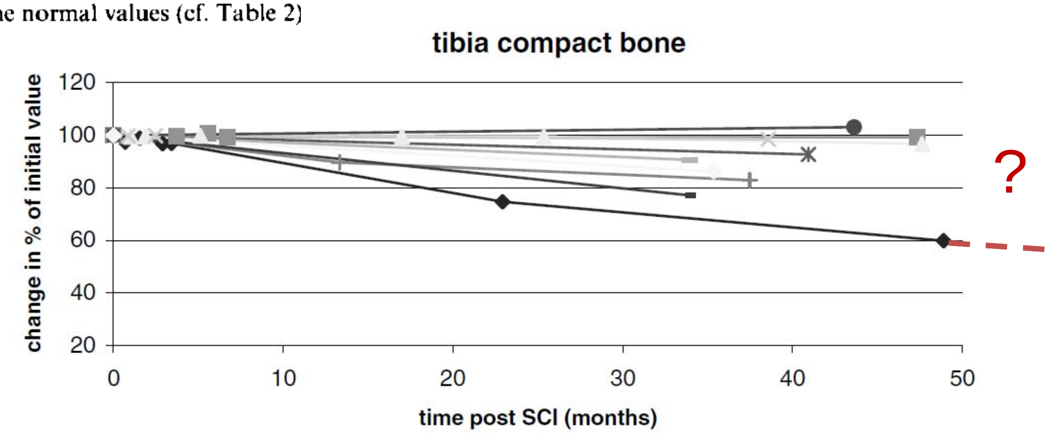
Distal Femur and Proximal Tibia

Sibonga et al. (2008). “Adaptation of the Skeletal System During Long-Duration Spaceflight.”

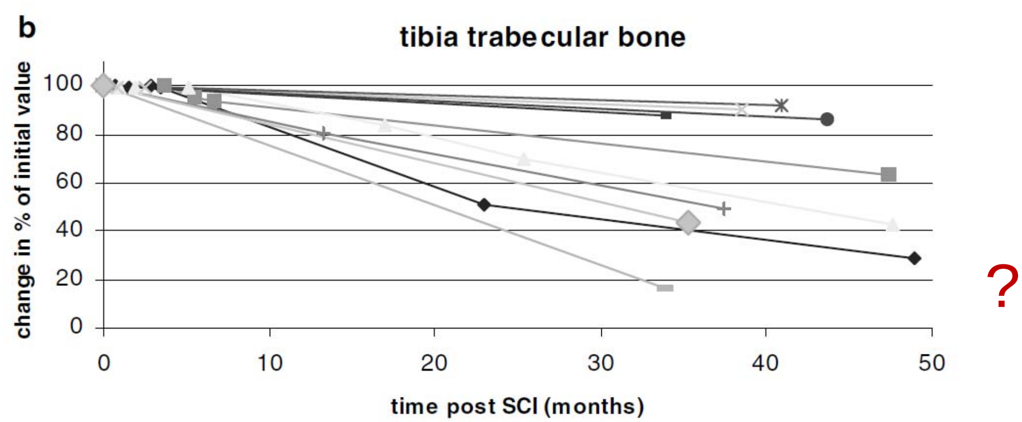


. Bone mineral content (BMC) in the proximal tibia in per cent of the mean of the normal values (cf. Table 2) ord injured patients (cf. Table 1) measured several times after injury.

"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)"

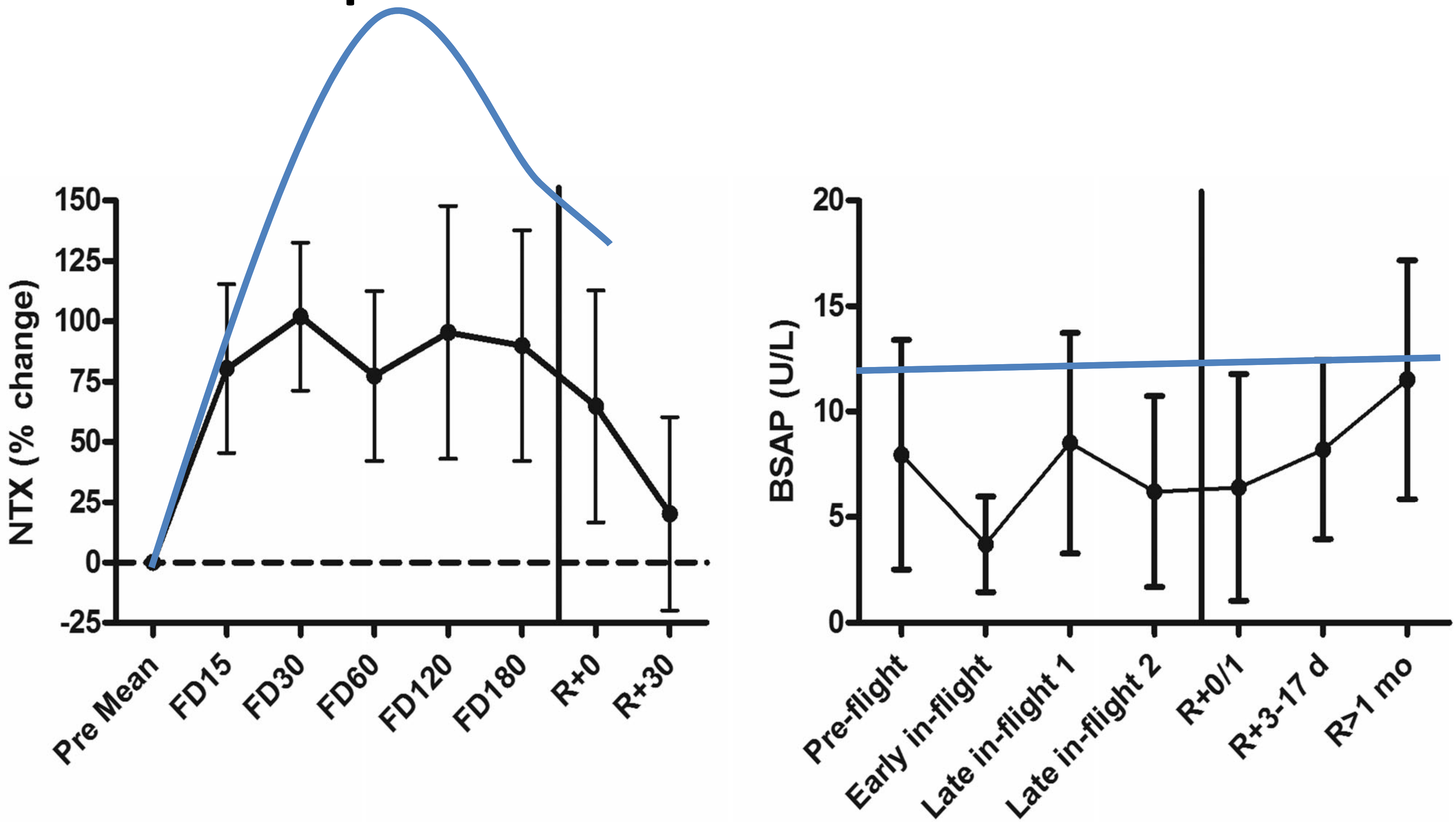


Comparison of Bone Turnover

Bed Rest	**Space Flight**	**Spinal Cord Injury**
Urinary Ca ↑	Urinary Ca ↑	Urinary Ca ↑↑
Ca Balance ↓	Ca Balance ↓↓	Ca Balance ↓↓
BMD ↓	BMD ↓↓	BMD ↓↓↓
Resorption ↑	Resorption ↑↑	Resorption ↑↑↑
Formation ↔	Formation ↔	Formation ↔
PTH ↓	PTH ↓	PTH ↓
Ca Absorption ↓	Ca Absorption ↓	Ca Absorption ↓
Ca+, Serum Ca++ ↔	Ca+, Serum Ca++ ↔	Ca+, Serum Ca++ ↔

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

Comparison of Bone Turnover



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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 tetrapelgics
- 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

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Thank you

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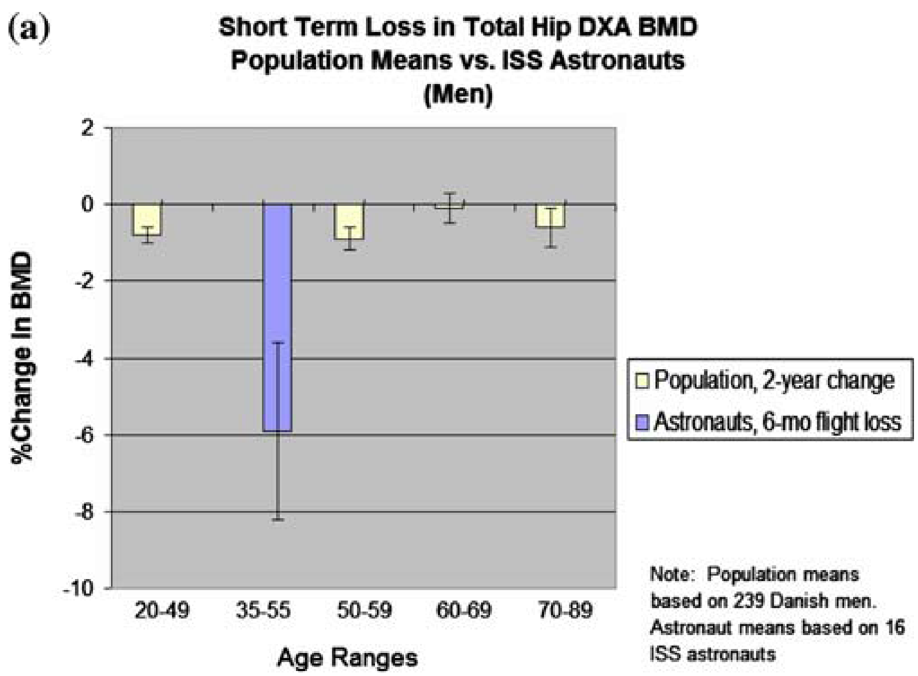
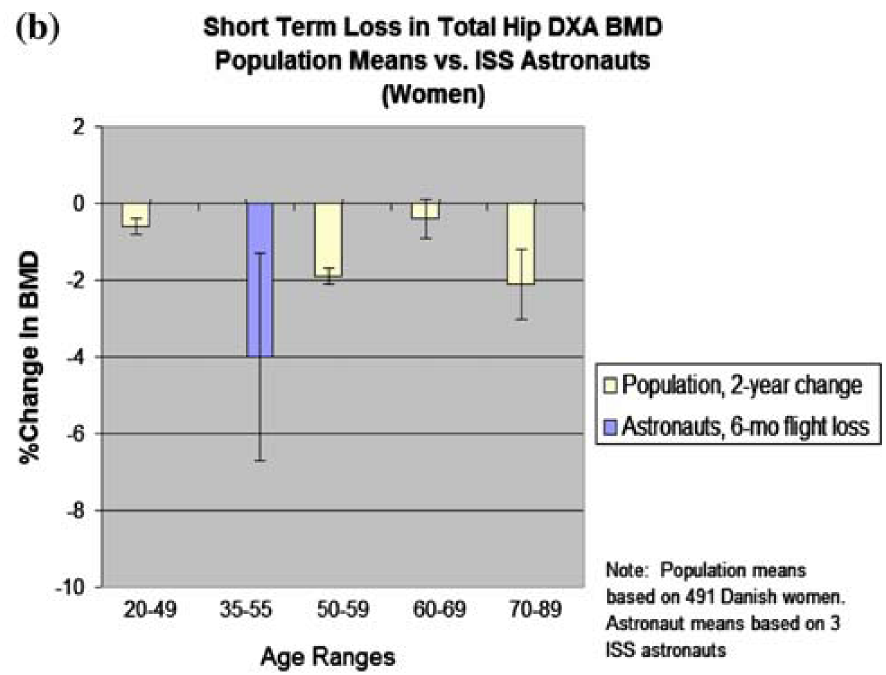
Extra Slides





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