Skeletal Adaptation to Space

Transitioning Research to the Clinical Realm

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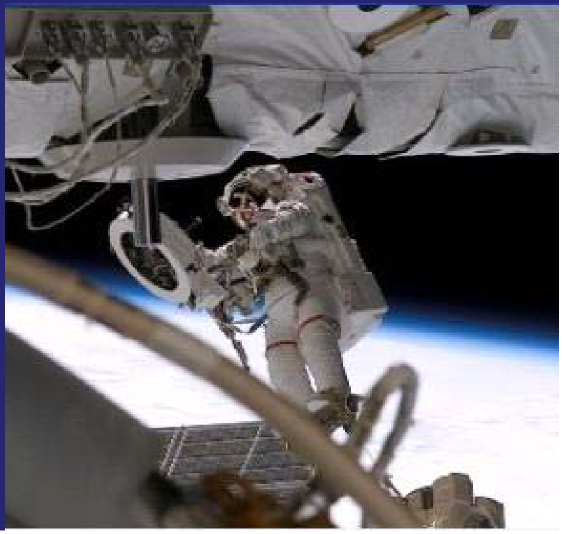
The Astronaut as the Human System

Systems Engineering &Integration

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

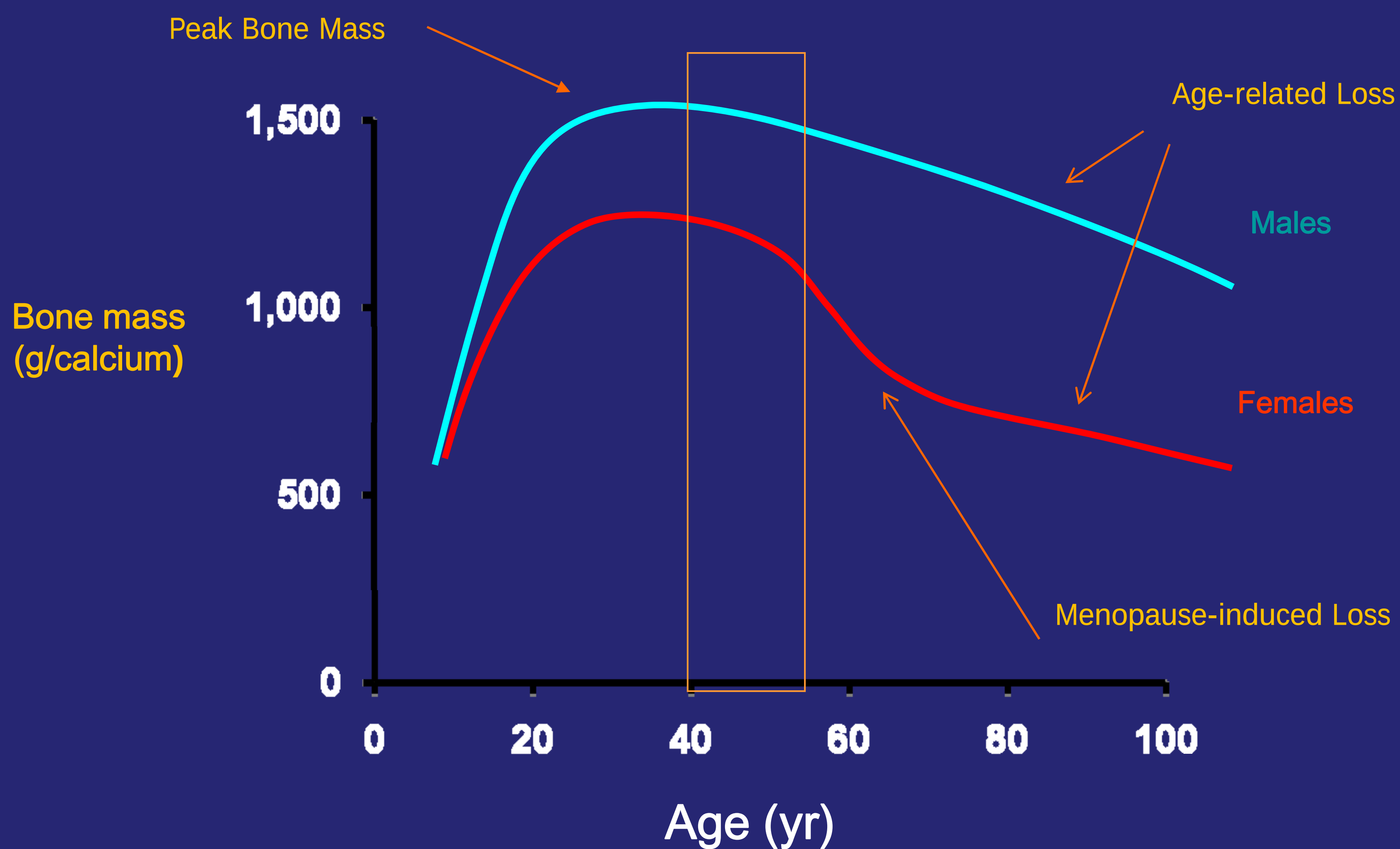


Overview

- Uniqueness of NASA
  - Three C's
- Unique Flight Data
- *Unique Recommendations*

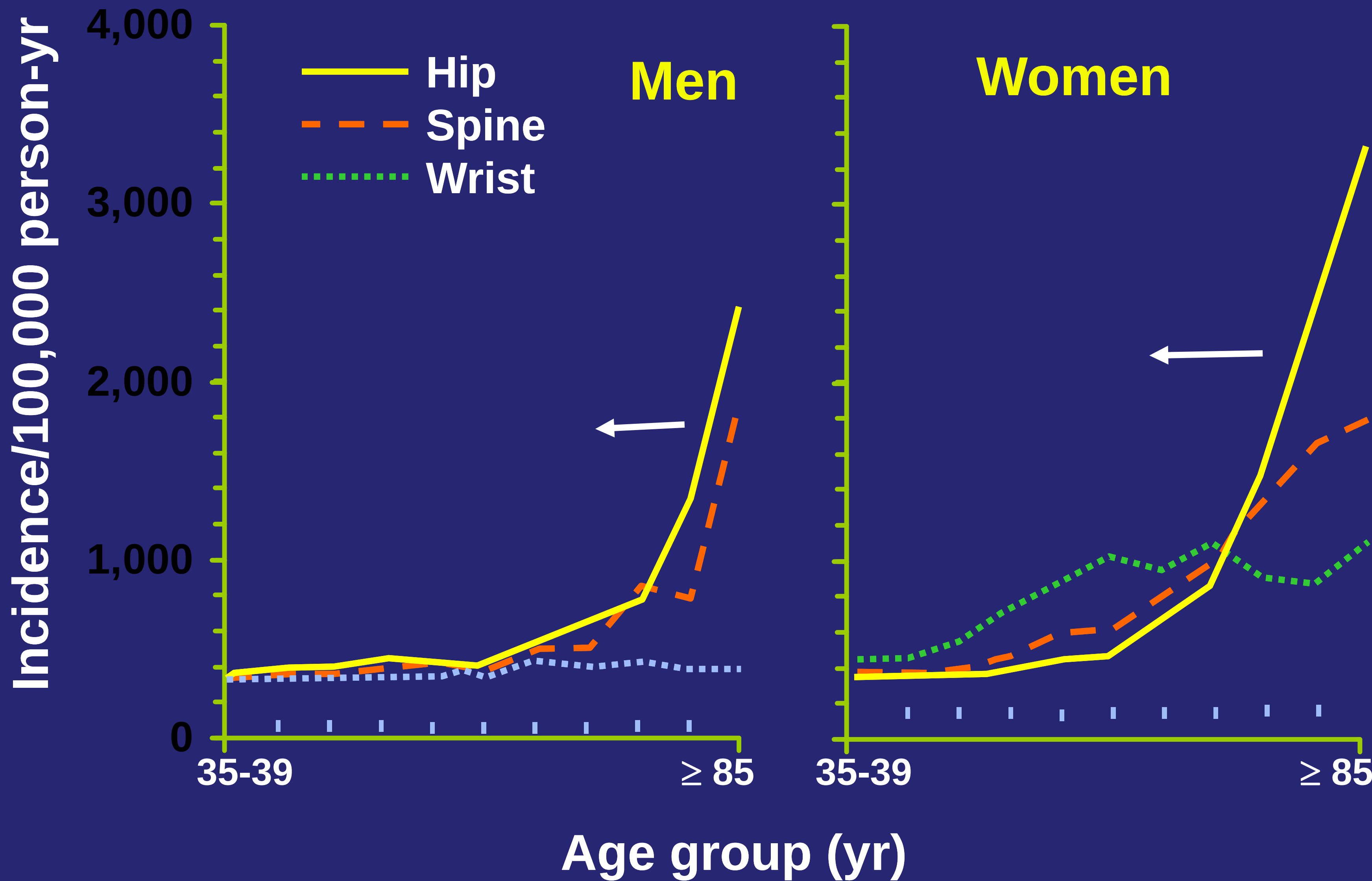
How do you pitch the need for biomedical research to stakeholders who question the existence of the risk?

Does spaceflight result in irreversible changes to bone that combine with age-related losses?



Riggs BL, Melton LJ: Adapted from Involutional osteoporosis
Oxford Textbook of Geriatric Medicine
ADAPTED SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

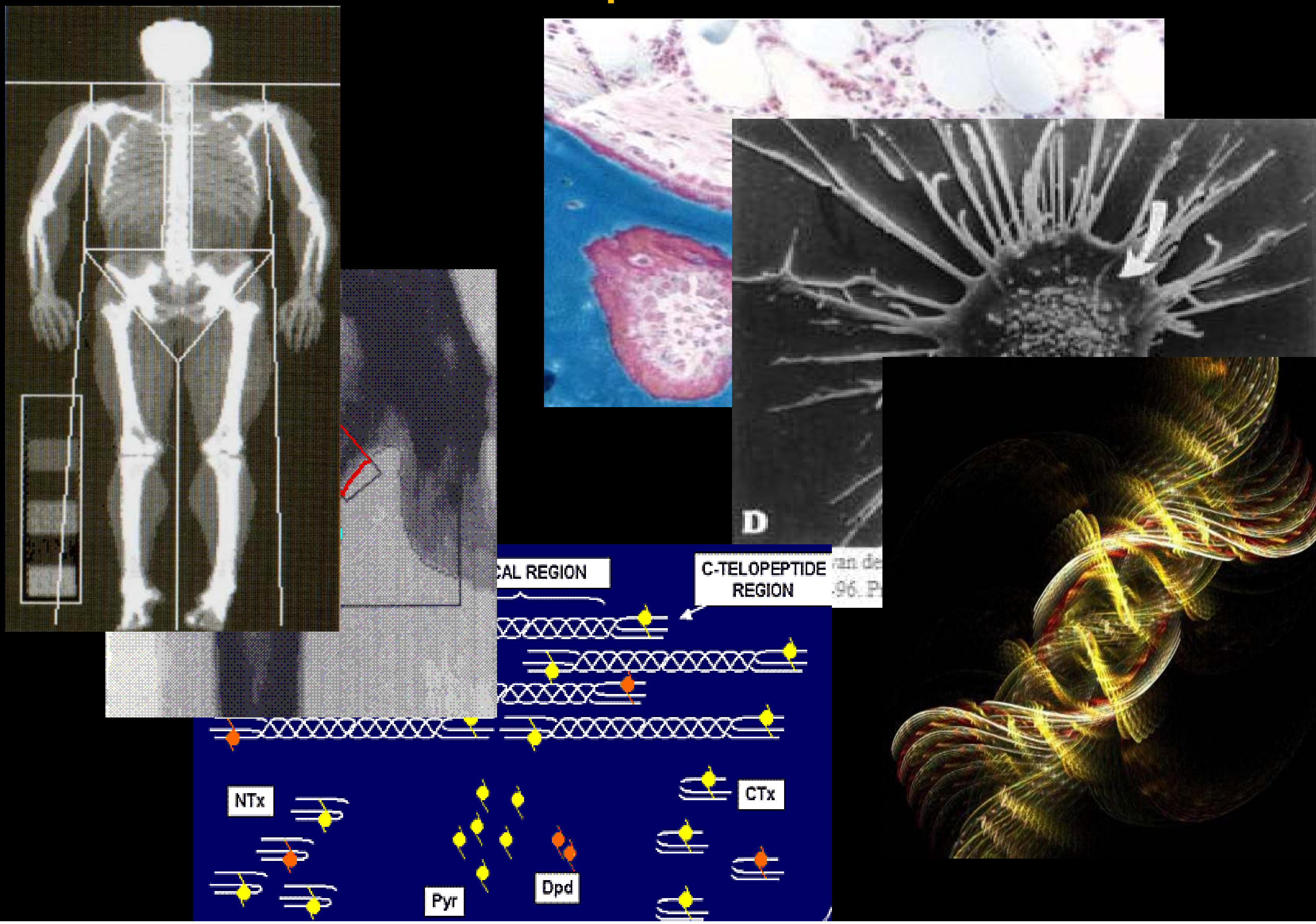
Consequence: Premature fractures in astronauts?



SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

Cooper and Melton, 1992

Constraints to Understanding Skeletal Adaptation



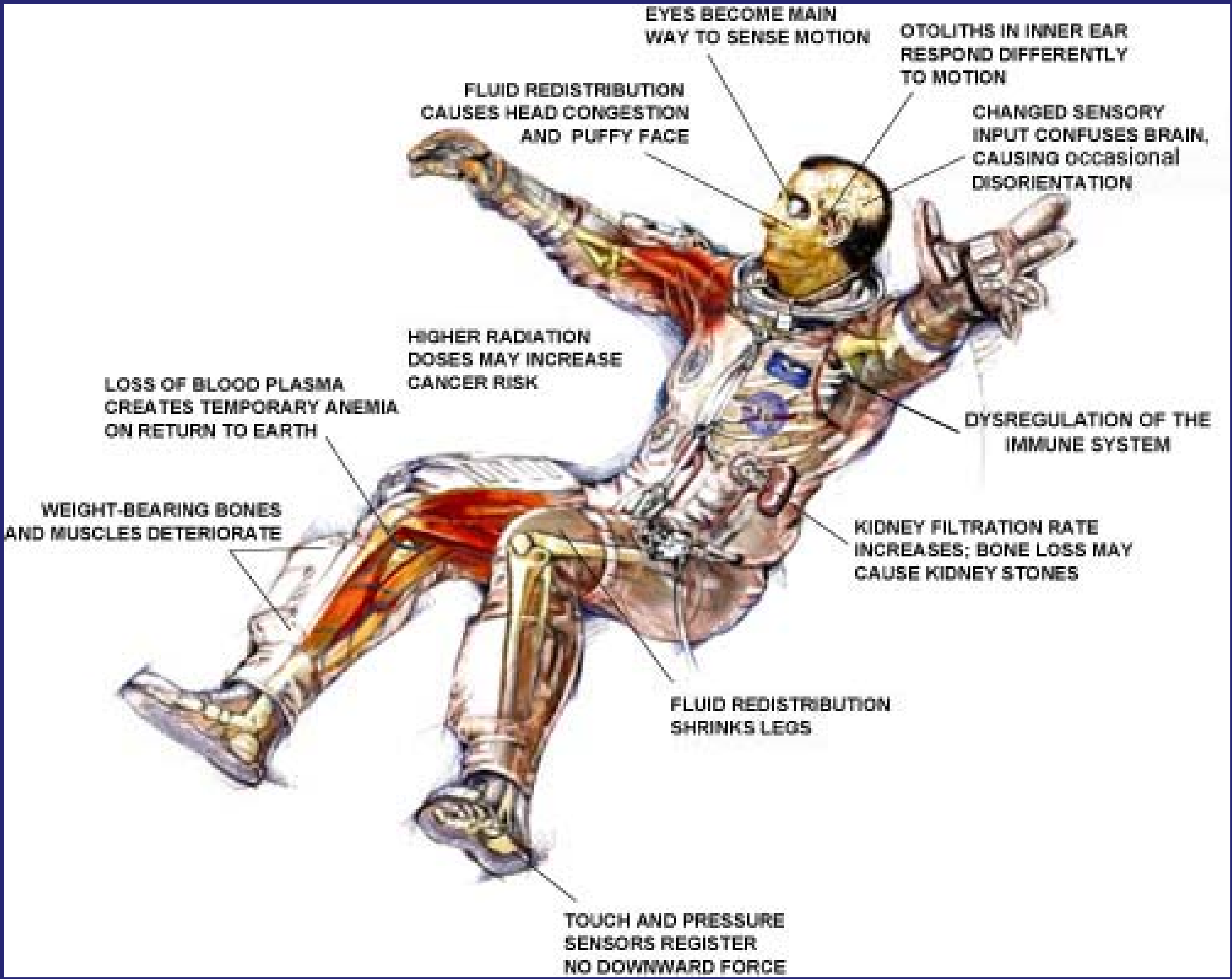
Dual-energy X-ray Absorptiometry [DXA] BMD @ Johnson Space Center

- Monitor astronaut skeletal health
- Characterize skeletal effects of long-duration spaceflight
- Evaluate efficacy of bone loss countermeasures
- Verify restored health status

The Long-duration Astronaut

- Typical space mission duration – 163 ± 32d (range 90-215d)
- Average Age – 46.5 ± 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 ± 2.2 *(range 20.6 to 30.6);* Female BMI 22.6 ± 2.2 *(range 20.4 to 25.4)*
- Wt and Ht- Males: Males: 81 ± 9 kg *(range 62 to 101 kg),* 177 ± 6 cm *(range 163 to 185 cm)*;
- Females: 65 ± 7 kg *(57 to 80 kg),* 170 ± 4 cm *(range 165 to 178 cm)*
- *MEDICAL PRIVACY OF THE ASTRONAUT.*

Microgravity Effects on the Human Body



From Scientific American

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  - Three C’s
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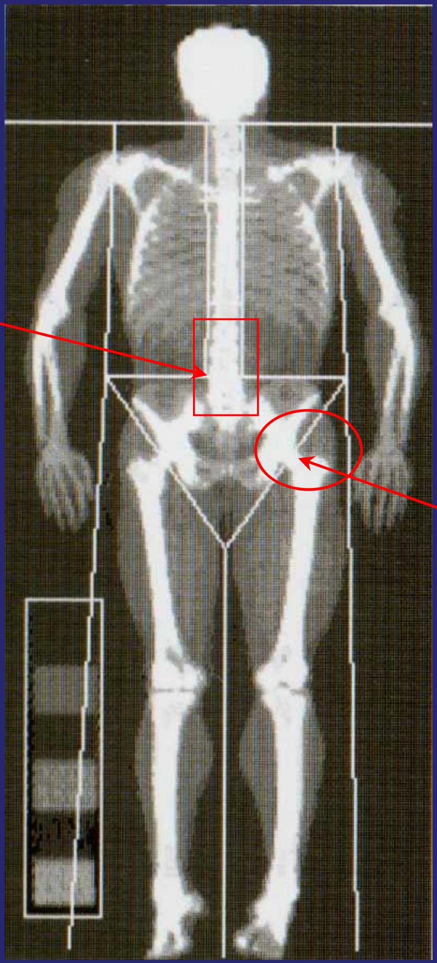
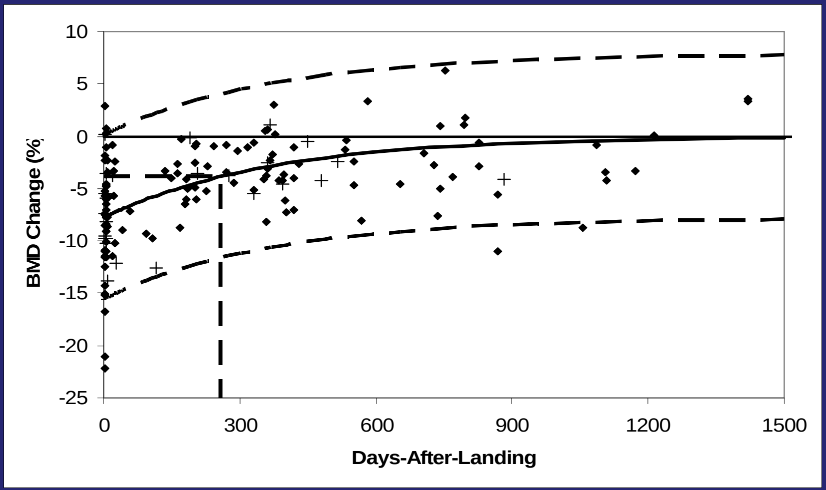
DXA: BMD losses are regional and rapid

Areal BMD g/cm2	%/Month Change ± SD
Lumbar Spine	-1.06±0.63*
Femoral Neck	-1.15±0.84*
Trochanter	-1.56±0.99*
Total Body	-0.35±0.25*
Pelvis	-1.35±0.54*
Arm	-0.04±0.88
Leg	-0.34±0.33*
*p<0.01, n=16-18	

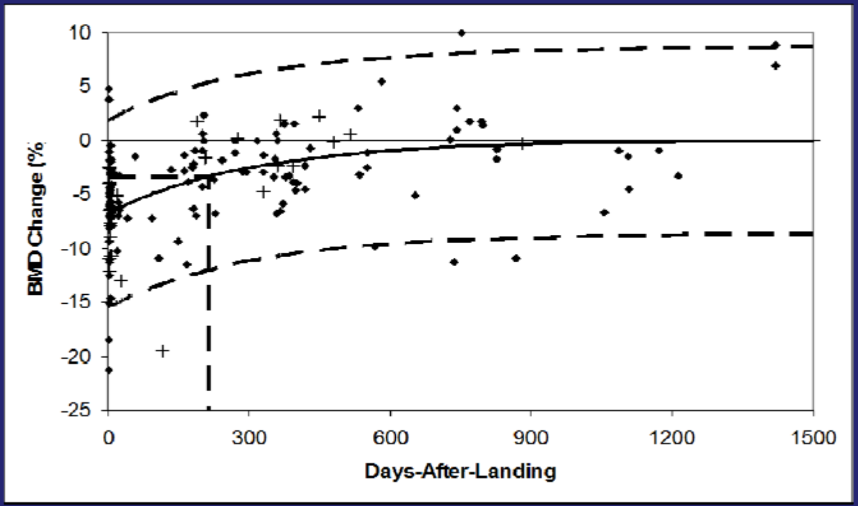


LeBlanc et al, J Musculoskeletal 2000

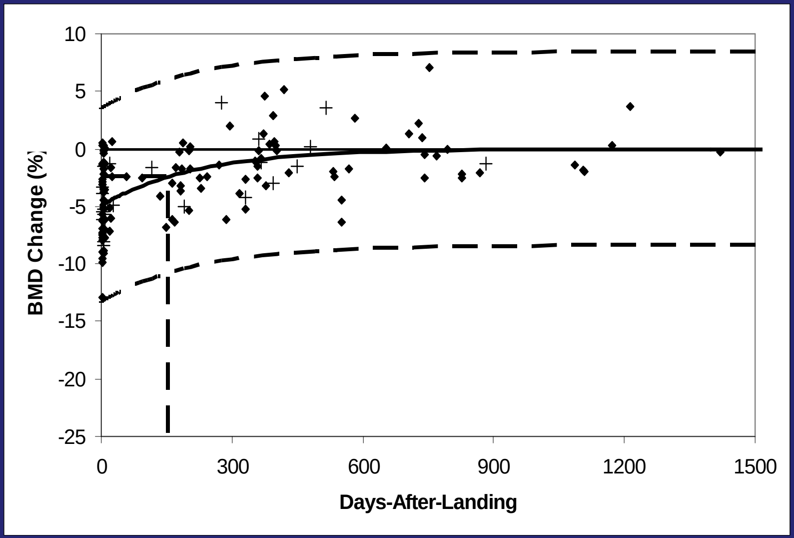
DXA BMD increases in Postflight – is that recovery?



Trochanter



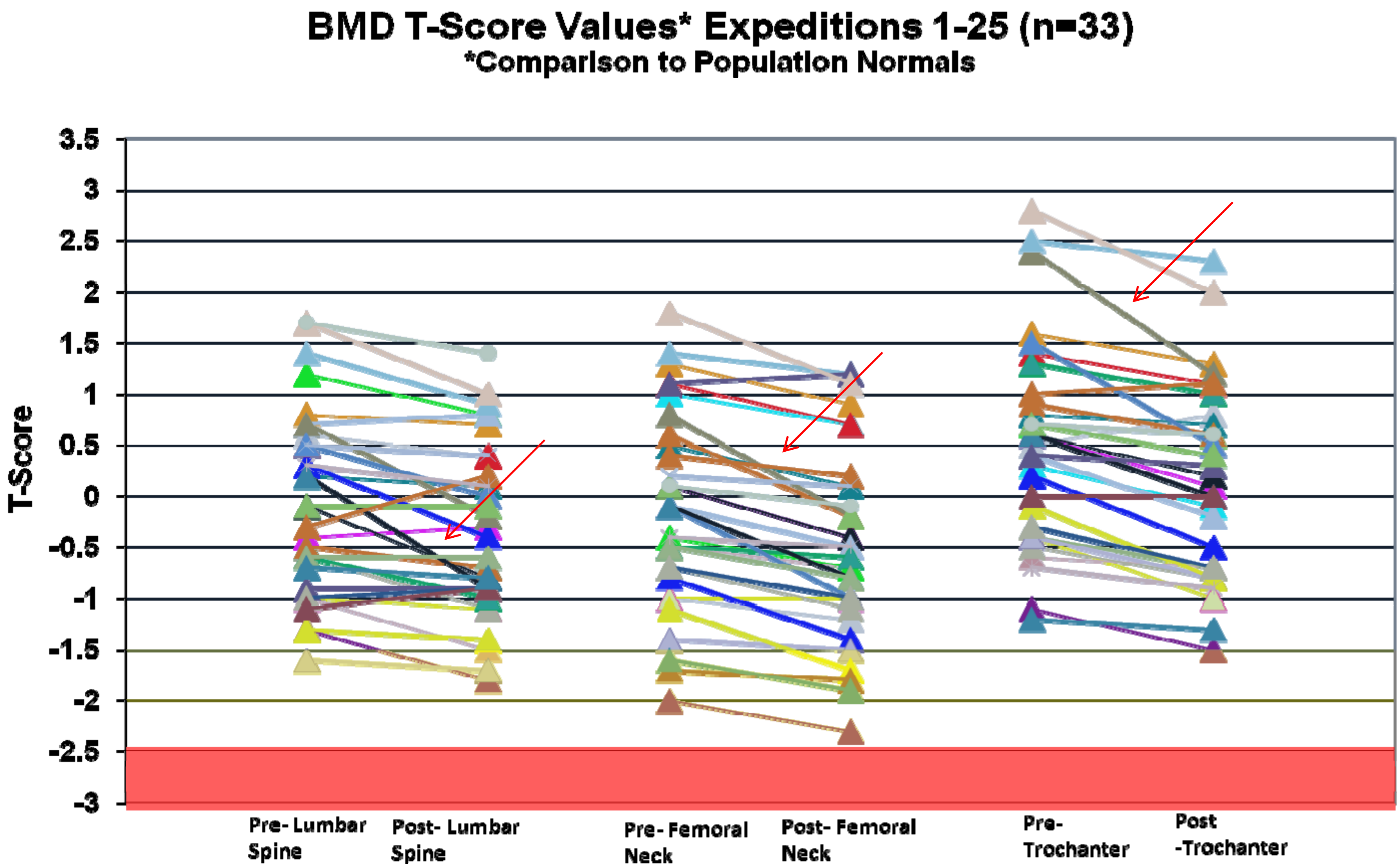
Femoral neck

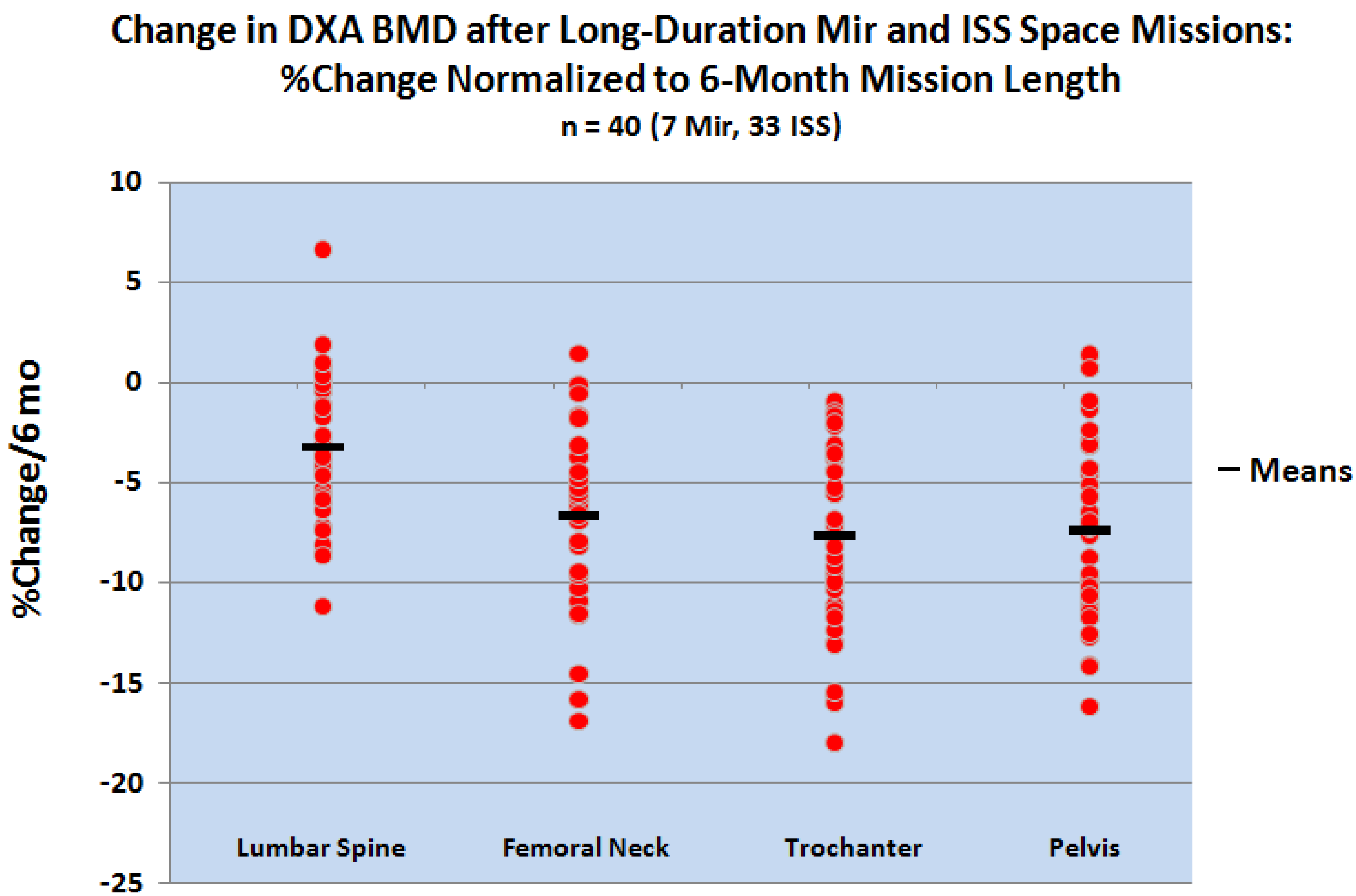


Lumbar Spine

Sibonga et al. BONE 41:973-978, 2007

Medical Requirement, but Relative Risk based upon T-scores not very informative.




Change in DXA BMD after Long-Duration Mir and ISS Space Missions:
%Change Normalized to 6-Month Mission Length
n = 40 (7 Mir, 33 ISS)
%Change/6 mo
10
5
0
-5
-10
-15
-20
-25
Lumbar Spine
Femoral Neck
Trochanter
Pelvis
— Means

Insert SMS' slides

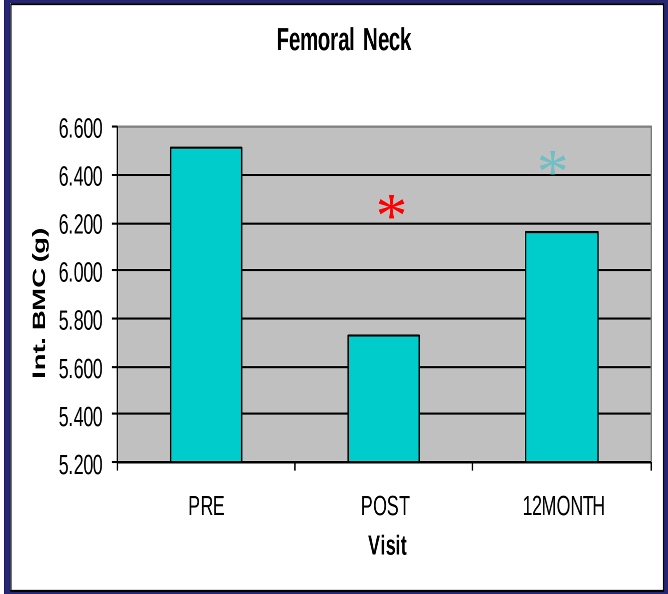
Research Technologies: QCT measures hip vBMD loss in trabecular bone compartment (n=16 ISS volunteers)

Index DXA	%/Month Change $\pm$ SD	Index QCT	%/Month Change $\pm$ SD
aBMD Lumbar Spine	1.06 ± 0.63*	Integral vBMD Lumbar Spine	0.9 ± 0.5
		Trabecular vBMD Lumbar Spine	0.7 ± 0.6
aBMD Femoral Neck	1.15 ± 0.84*	Integral vBMD Femoral Neck	1.2 ± 0.7
		Trabecular vBMD Femoral Neck	2.7 ± 1.9
aBMD Trochanter	1.56 ± 0.99*	Integral vBMD Trochanter	1.5+0.9
*p<0.01, n=16-18		Trabecular vBMD Trochanter	2.2+0.9

LeBlanc, J Musculoskelet Neuronal Interact. 2000 ;
Lang , J Bone Miner Res, 2004;

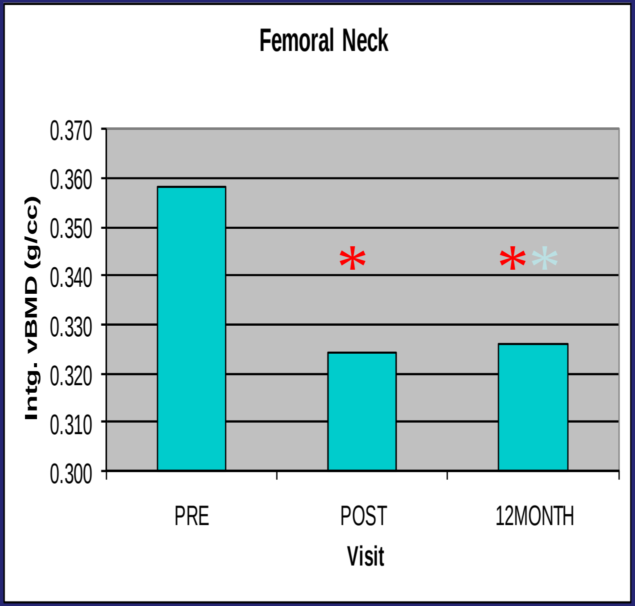
QCT Postflight – Changes in at Femoral Neck 12 months after return

Bone Mineral Content
(g)



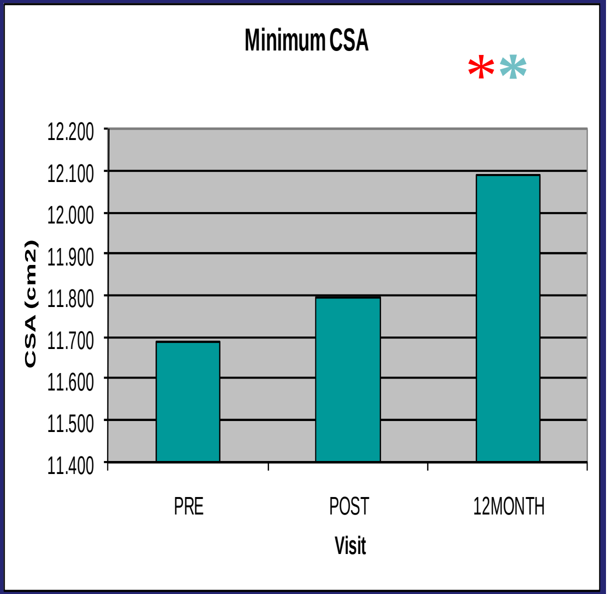
Pre Post 12

Volumetric Bone Mineral Density
g/cm^3



Pre Post 12

Minimum Cross-sectional Area
cm^2

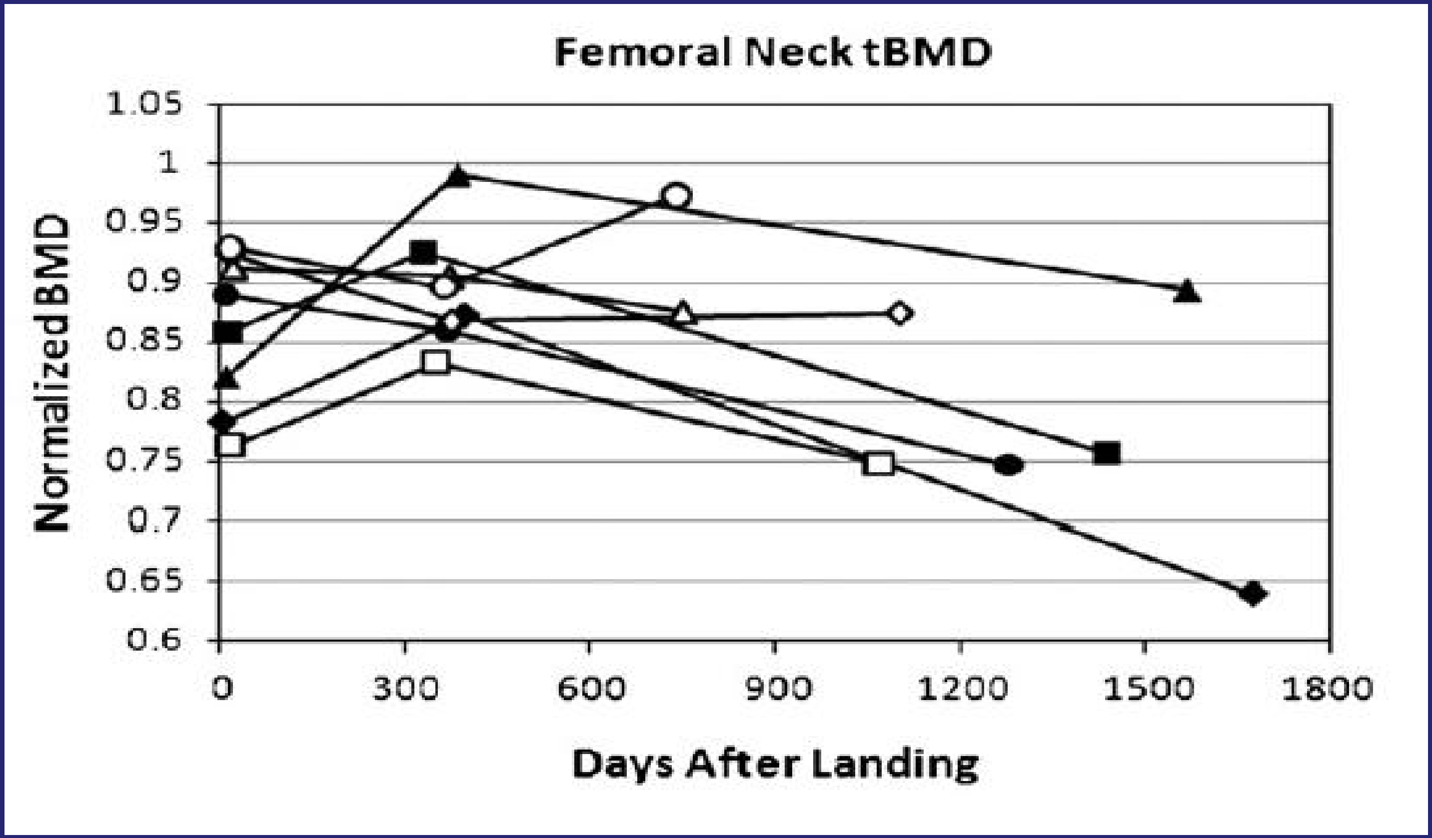


Pre Post 12

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

Slide adapted from T. Lang., JBMR 2006.

QCT: Trabecular BMD at Femoral neck does not appear to show a recovery 2 to 4 years postflight



QCT Extension Study (n=8) Postflight Trabecular BMD in hip. Carpenter, D et al. Acta Astronautica, 2010.

GAP: What is the impact of Trabecular Bone Loss on whole hip bone strength?

JOURNAL OF BONE AND MINERAL RESEARCH
Volume 23, Number 8, 2008
Published online on March 17, 2008; doi: 10.1359/JBMR.080316

Proximal Femoral Structure and the Prediction of Hip Fracture in Men: A Large Prospective Study Using QCT*

Dennis M Black,[1] Mary L Bouxsein,[2] Lynn M Marshall,[3] Steven R Cummings,[4] Thomas F Lang,[5] Jane A Cauley,[6] Kristine E Ensrud,[7] Carrie M Nielson[3] and Eric S Orwoll[3] for the Osteoporotic Fractures in Men (MrOS) Research Group

Lower trabecular BMD was an independent predictor of hip fracture in elderly men.
Overall, QCT measures provide useful information regarding causation of hip fracture, evaluation of hip fracture risk and possible targets for intervention.

Overview

- Uniqueness of NASA
  – Three C's
- Unique Flight Data
- *Unique* Recommendations

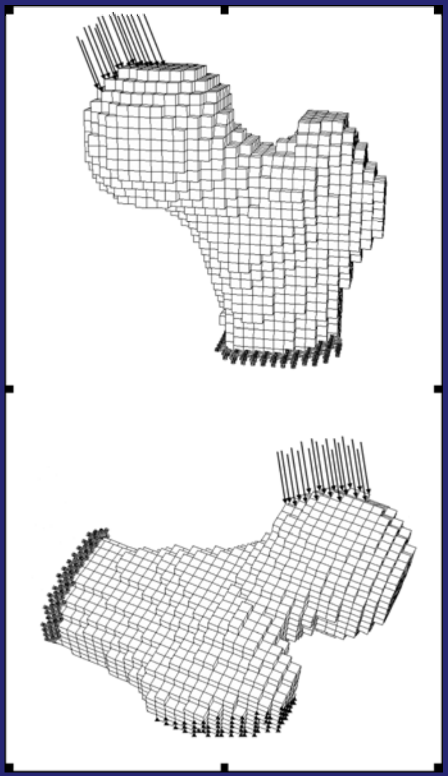
Bone Summit Panel Members

- Eric Orwoll, MD
  - Endocrinology and Male Osteoporosis
- E. Michael Lewiecki, MD, FACP, FACE
  - Endocrinology, ISCD
- Neil Binkley, MD, CCD
  - ISCD, Geriatrics and Vitamin D
- Shreyasee Amin, MD
  - Rheumatology, Male Osteoporosis and Epidemiology
- Sue Shapses, PhD
  - Nutritional Sciences and Weight-loss
- Robert A. Adler, MD
  - Male Osteoporosis and Epidemiology
- Steven Petak, MD, JD, FACE
  - Endocrinology, ISCD (
- Mehrsheed Sinaki, MD
  - Physical Medicine & Rehabilitation
- Nelson B. Watts, MD
  - Endocrinology, ISCD

Left to Right, Top Row down

Finite Element Modeling [FEM]:
What is it and what can it tell NASA about hip fracture risk in the long-duration astronaut?

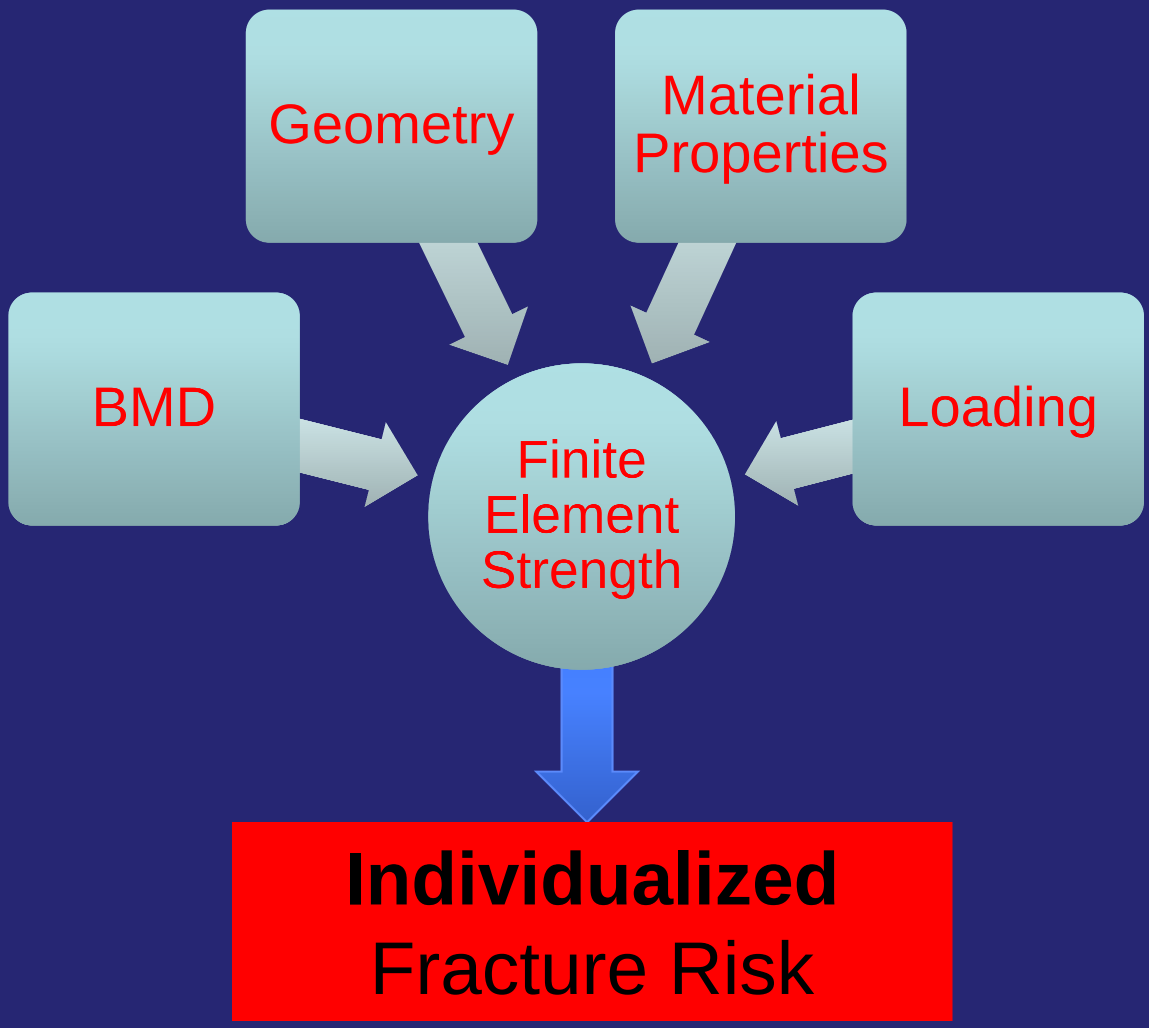
FEM – a computational tool to estimate failure loads to complex structures.



J. Keyak et al, 1998, 2001, 2005

Images courtesy of Dr. J Keyak

FEM of QCT data integrates multiple factors associated with fracture to provide a single composite number to estimate bone strength.



QCT + FEM has superior capabilities for estimating mechanical strength

QCT estimates fracture loads better than DXA

QCT + FEM has superior capabilities for estimating fracture loads

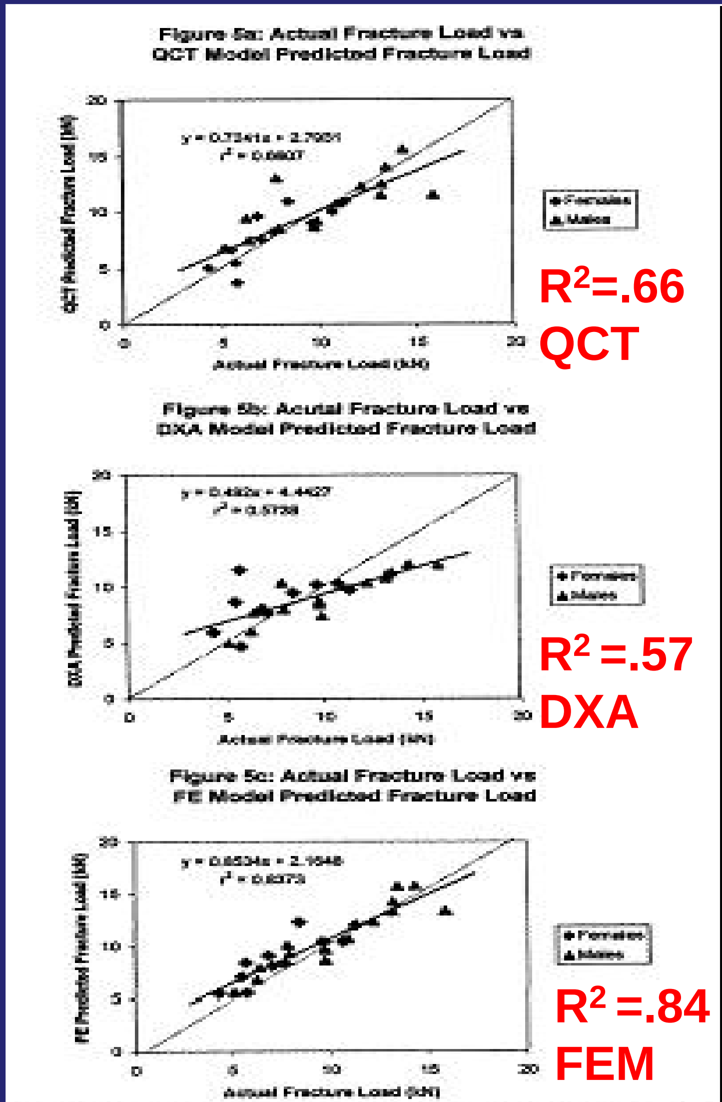


Fig. 5. The predicted strength of the specimens in the test set (developed from the models generated using the training set) plotted against their actual measured values for each of the three methods (a: QCT; b: DXA; c: FEM).

DD Cody: Femoral strength is better predicted by finite element models than QCT and DXA. J Biomechanics 32:1013 1999.

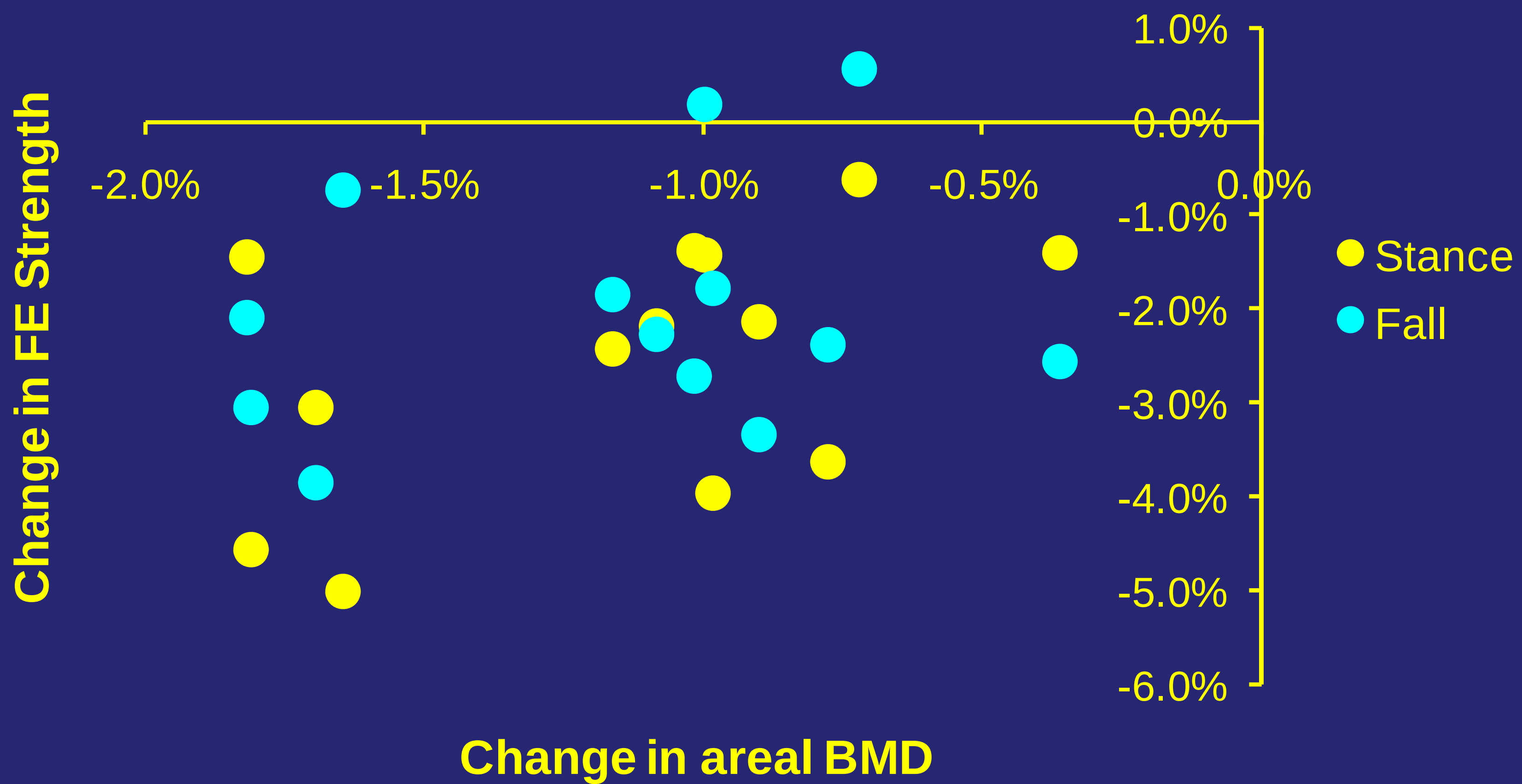
Astronaut Data– Hip Strength

N=11 crewmembers

Loading Condition	Mean (SD) Pre-flight	Mean (SD) Post-flight	*p*
Stance	13,200 N (2300 N)	11,200 N (2400 N)	<0.001
	2.2% loss/month		
Fall	2,580 N (560 N)	2,280 N (590 N)	0.003
	1.9% loss/month		

1.0-1.5% BMD loss /month

Astronaut Data: Surrogates of bone strength do not correlate.



Stance: R^2=0.23

Fall: R^2=0.05

Slides courtesy of J Keyak; Bone. 2009 Mar;44(3):449-53.

Summary

- Unique cohort, unique environment, unique changes in bone structure during long-duration missions in microgravity
- DXA – A widely-applied medical test to predict fracture risk in population at risk (menopausal, elderly)
- QCT – A Research Imaging Technology that increases our knowledge but applied on limited volunteer basis.
- FE modeling of strength – An improved estimate of hip bone strength for NASA to consider for clinical decisions.

Closing Remark

NASA Goal: To reduce the uncertainty of *spaceflight-induced* fracture risks in astronauts by increasing our understanding of spaceflight effects on bone -- by employing the best technologies and analyses available.

Thank you.

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NASA