Space: The Final Frontier of Bone Density

Jean D. Sibonga, Ph.D., Lead Bone Discipline, NASA Human Research Program at Johnson Space Center, Houston, TX

It is a medical requirement at NASA to evaluate the skeletal integrity of “long-duration” astronauts by measuring bone mineral density [BMD] with DXA technology. A long-duration mission is a spaceflight that is greater than 30 days but is typically the continuous 120-180 day missions aboard the International Space Station [ISS]. Not only does NASA use the BMD index to monitor fracture risk in this astronaut population, but these measures are also used to describe the effects of spaceflight, to certify skeletal health readiness for flight, to monitor the recovery of lost bone mass after return to earth, and to evaluate the efficacy of countermeasures to bone loss. However, despite the fact that DXA-based BMD is a widely-applied surrogate for bone strength that is grounded in an abundance of population-based fracture data, its applicability to the long-duration astronaut is limited.   The cohort of long-duration astronauts is not the typical group for evaluating osteoporosis or determining age-related fracture risk.   The cohort is young (< 55 years), predominantly male and exposed to novel risk factors for bone loss besides the weightlessness of space. NASA is concerned about early onset osteoporosis in the astronaut exposed to long-duration spaceflight, especially since any detectable symptoms are likely to manifest after return to earth and perhaps years after space travel. This risk raises the question: is NASA doing enough *now* to mitigate a fracture event that may manifest *later*? This presentation will discuss the limitations and constraints to understanding skeletal changes due to prolonged spaceflight and the recommendations, by clinical experts in osteoporosis and BMD, to transition research technologies for clinical decision-making by NASA.

National Aeronautics and Space Administration

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Insert video

- editing of video

The Astronaut as the Human System

Systems Engineering &Integration

Structure

Electrical Power System

Environ. Control Life Support

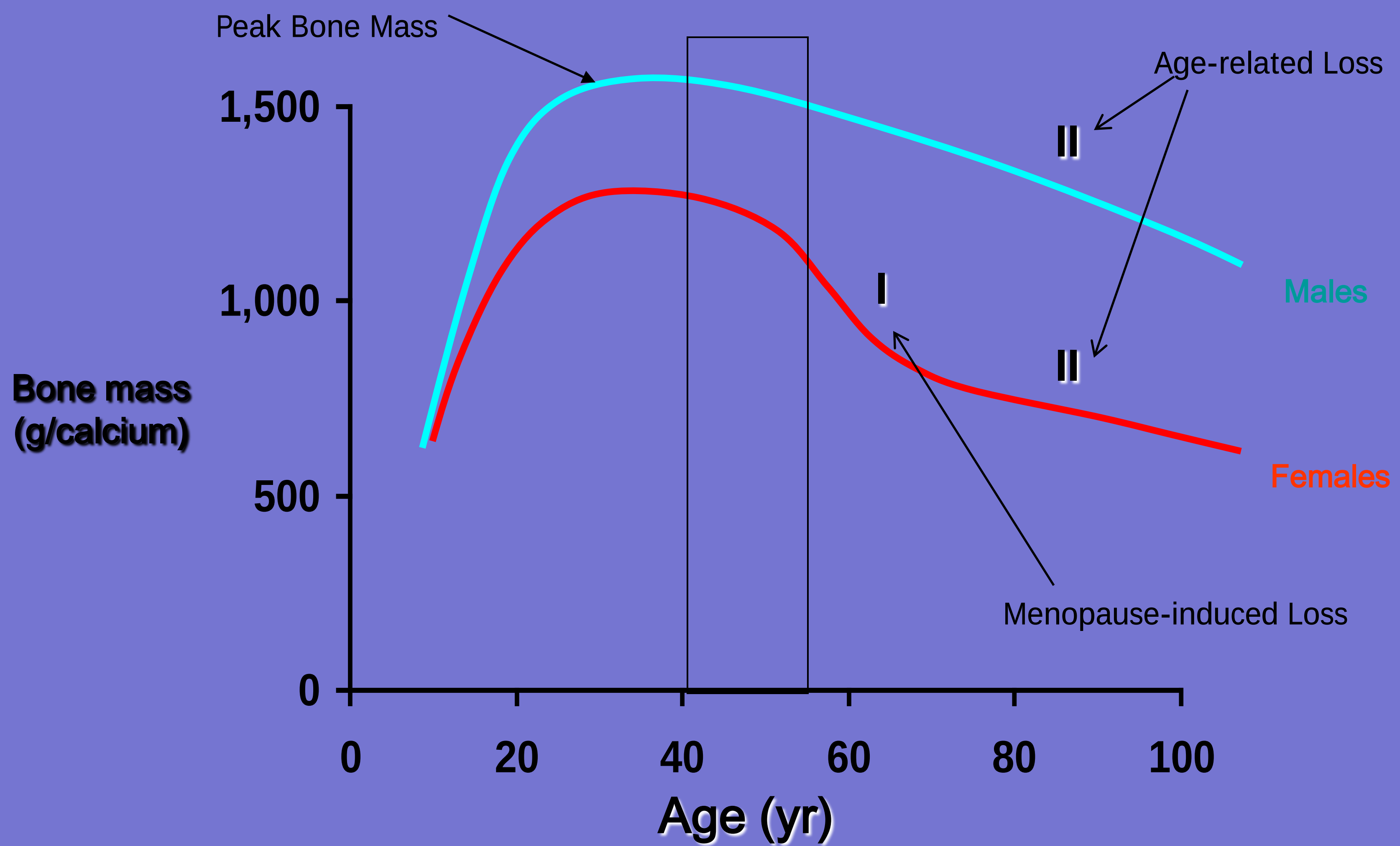
Thermal

I/T

…

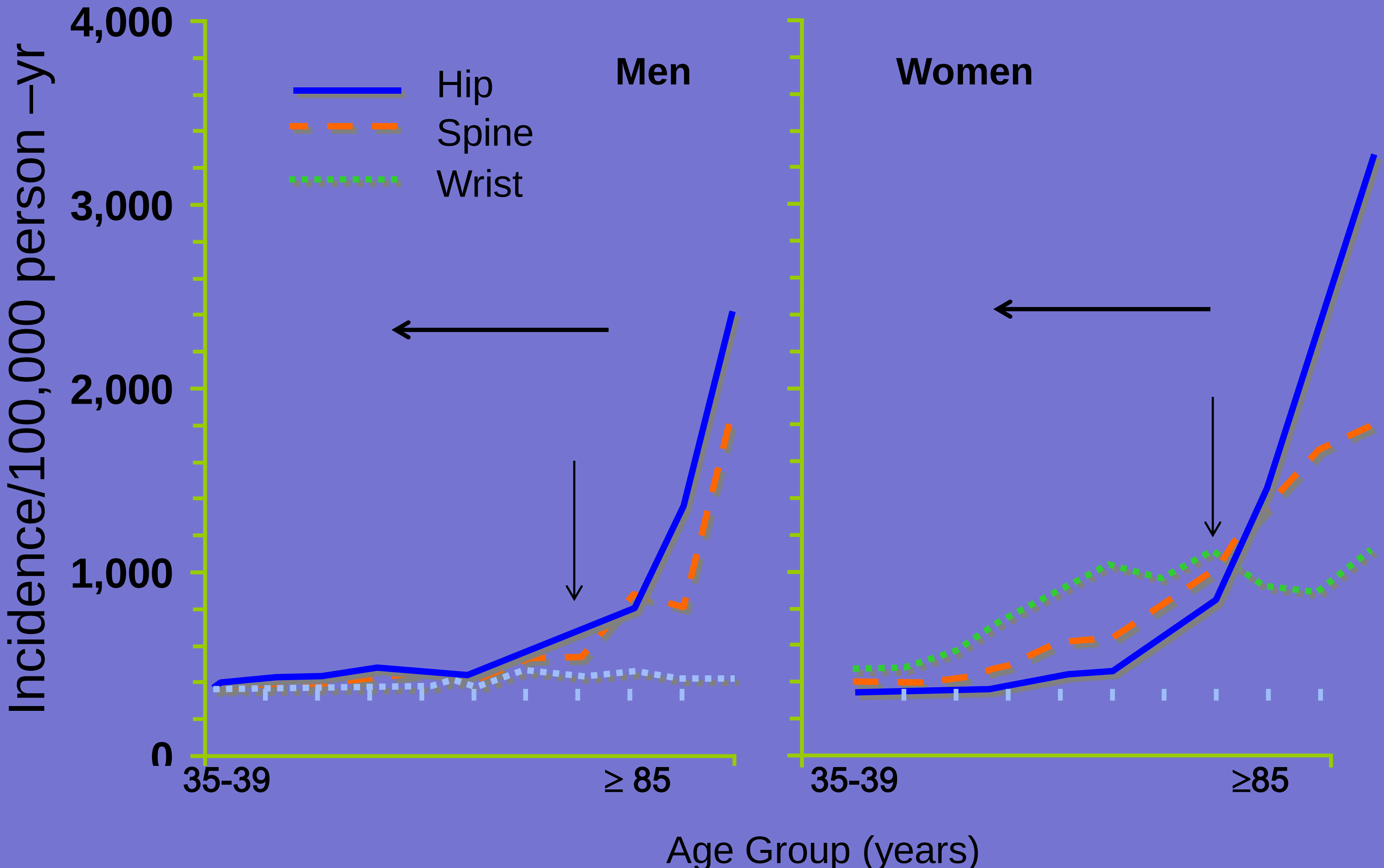
Human

Gain & Loss of Bone Mass with Aging



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

Age-Related Fractures



SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

Cooper and Melton, 1992

History of Bone Imaging in Space

Mercury
1961-63

Gemini
1965-66
- **X-ray densitometry**

Apollo
1968-72
- **SPA heel and wrist**

Skylab
1973-74
- **SPA heel and wrist**

Space Shuttle

Soyuz/Salyut
1974-85
- **SPA**
- **DPA**

Mir
1974-85
- **DXA whole body**
- **CT of lumbar spine BMD**

ISS
2000-present
- **DXA**
- **QCT**
- ***HR3DpQCT (ESA)***

Slide adapted from Dr. Jean Sibonga, NASA JSC

Overview

- Uniqueness of NASA

- Spaceflight Effects:

Out-of-this-World Data

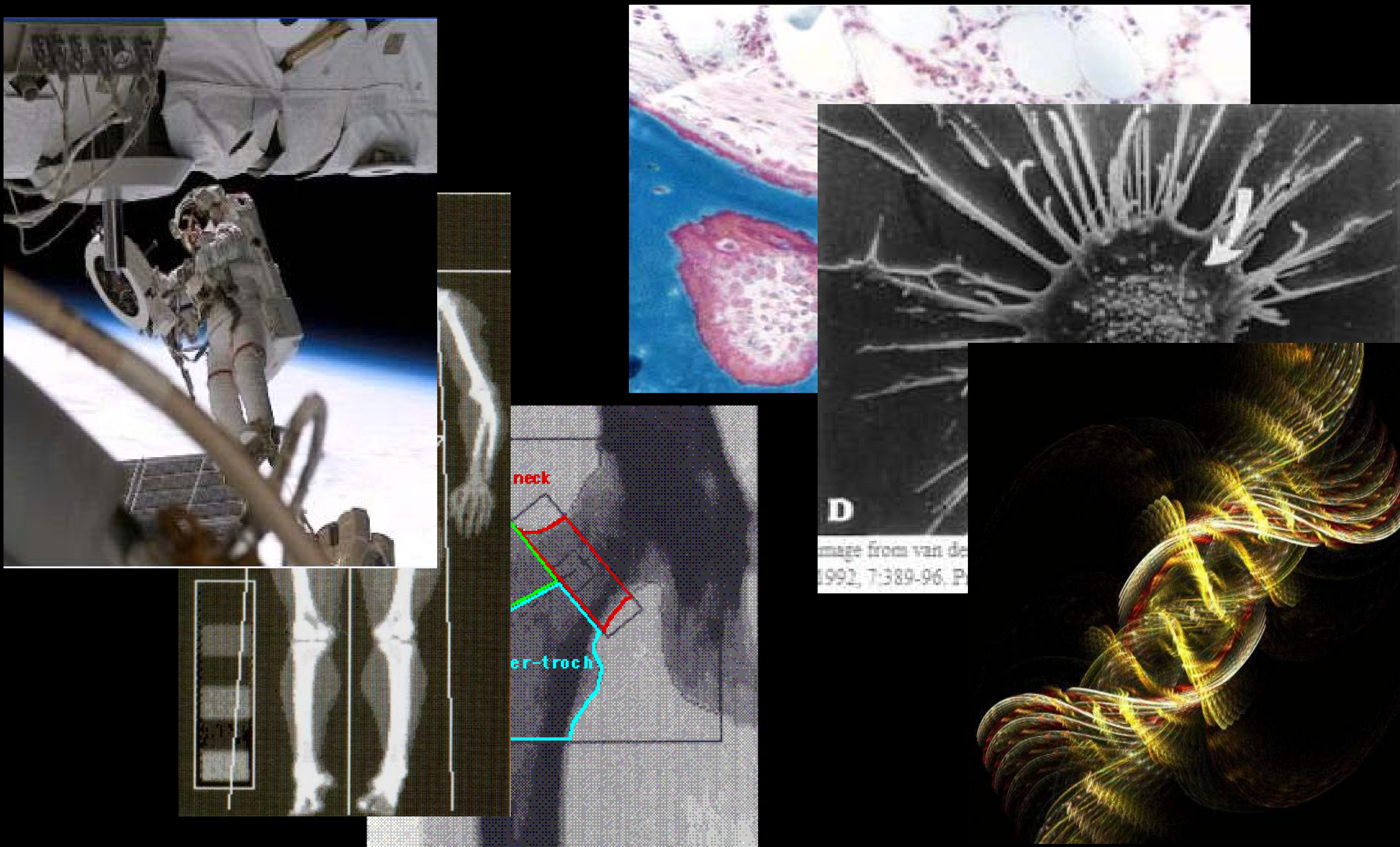
- *Bold* Approaches to

Managing Bone Risk

The Long-duration Astronaut

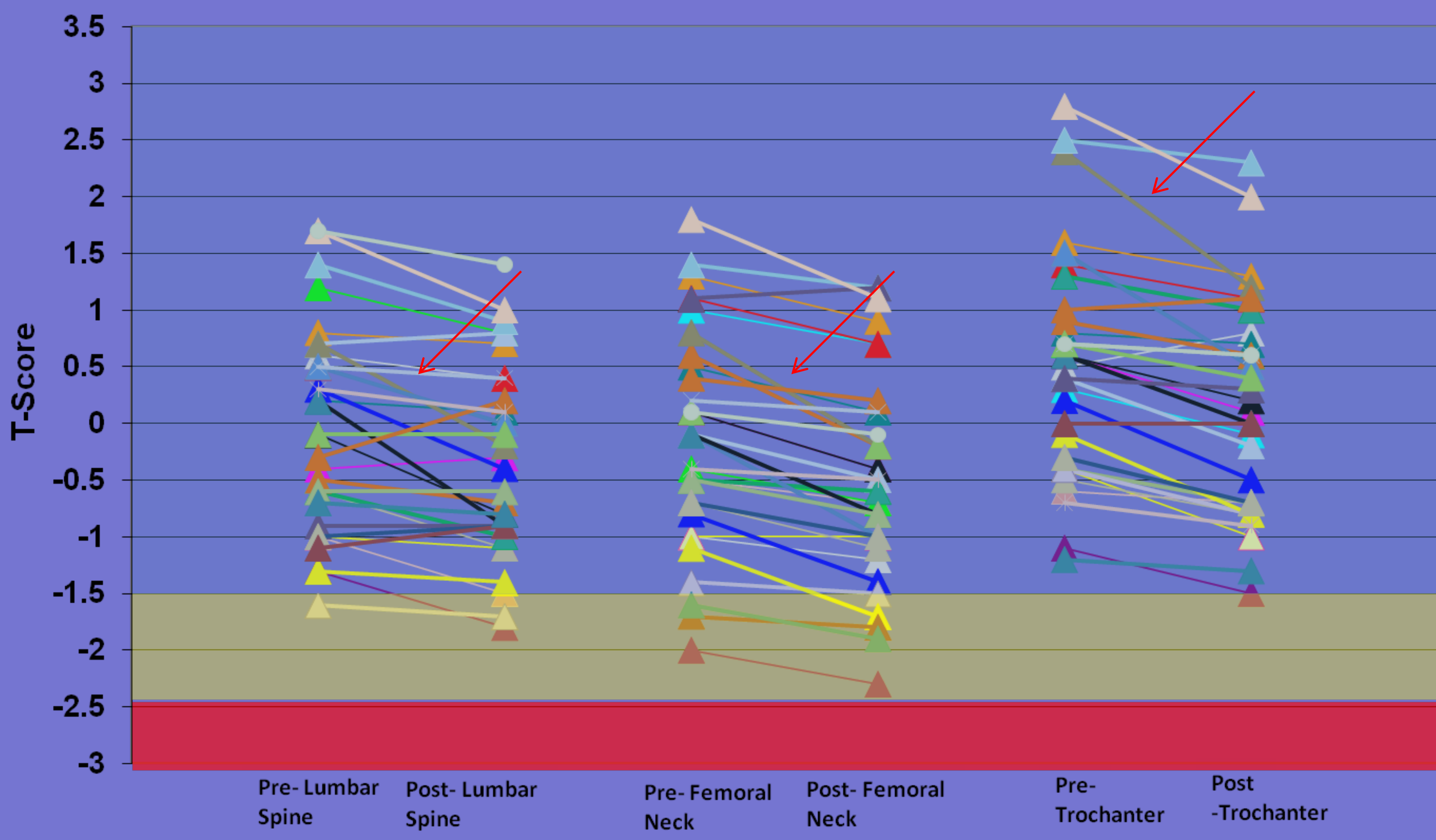
- Typical mission duration – 163 ± 32d (range 90-215d)
- Average Age – 46.5 ± 4.5 y (range 36.8 – 55.3)
- T-score at first* DXA BMD –
- Male to Female Ratio – 3.8 : 1
- Current total number out of total # astronauts in Corps – TBD
- # repeat fliers – 4
- BMI etc– Males 25.9 ± 2.2; Females 22.6 ± 2.2 kg/m^2
- Wt and Ht- Males: 179 ± 20 lbs, 5.8 ± 0.2 ft; Females: 143 ± 15 lbs, 5.6 ± 0.1 ft

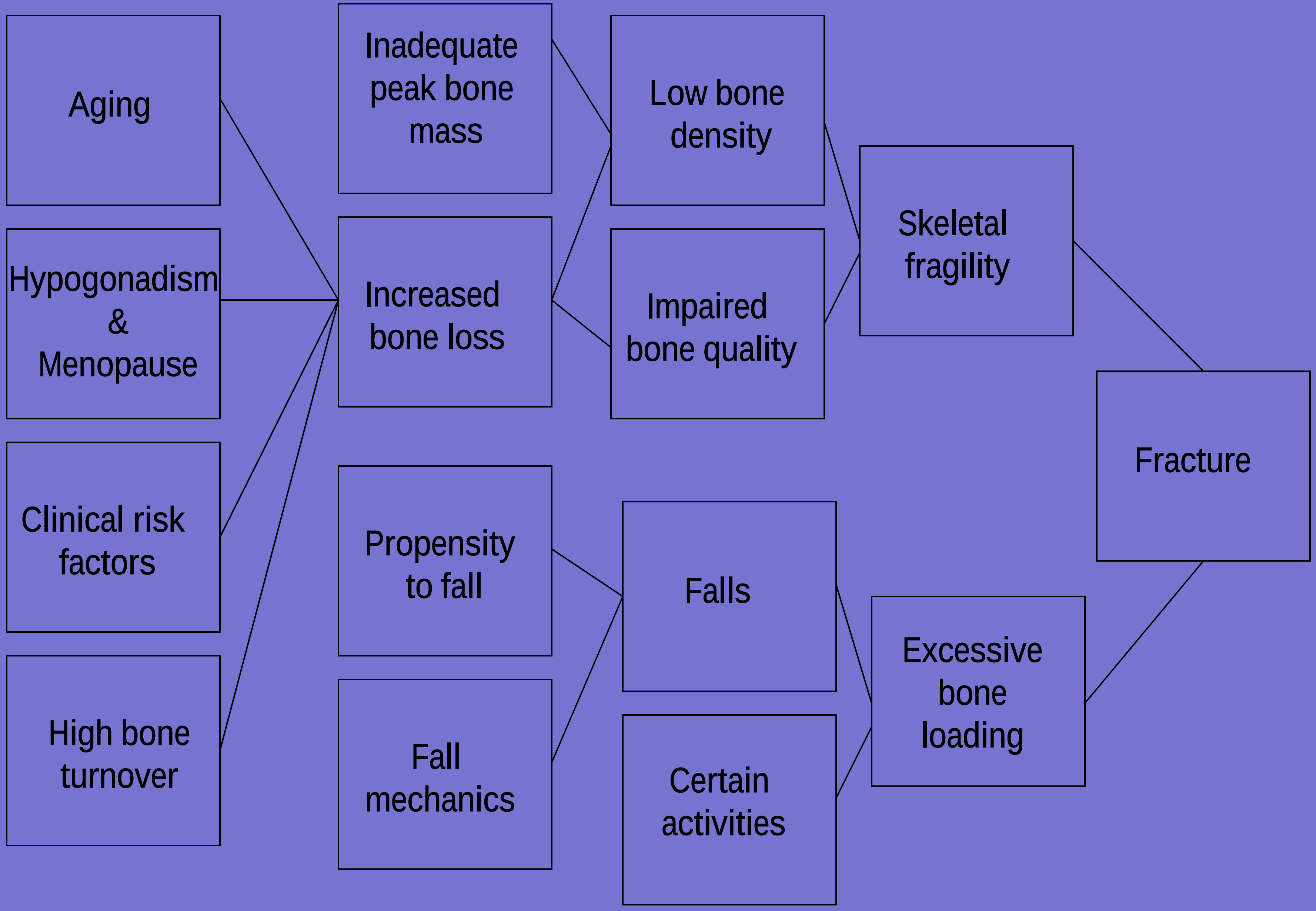
Constraints to Understanding Skeletal Adaptation



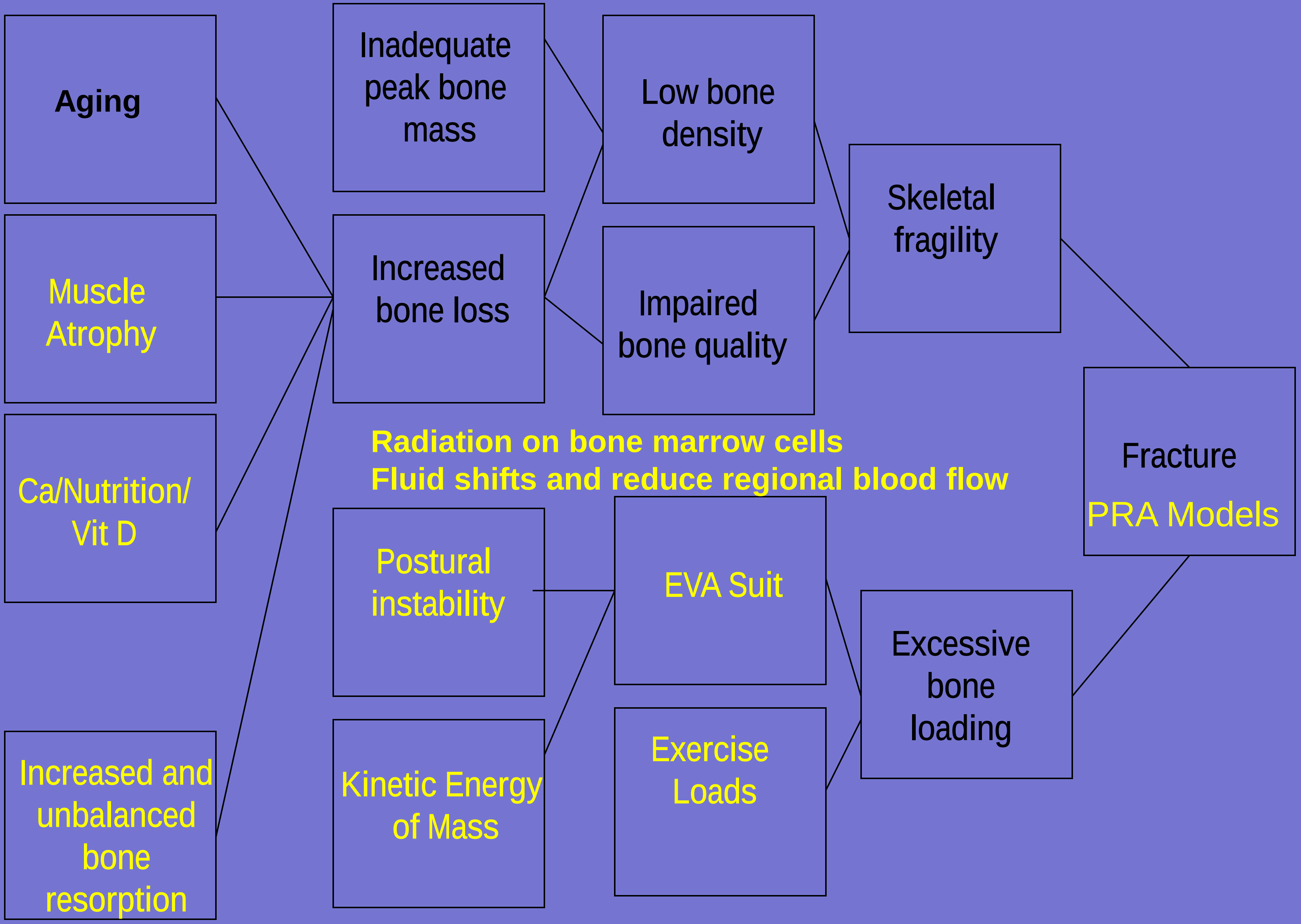
BMD T-Score Values* Expeditions 1-25 (n=33)

*Comparison to Population Normals



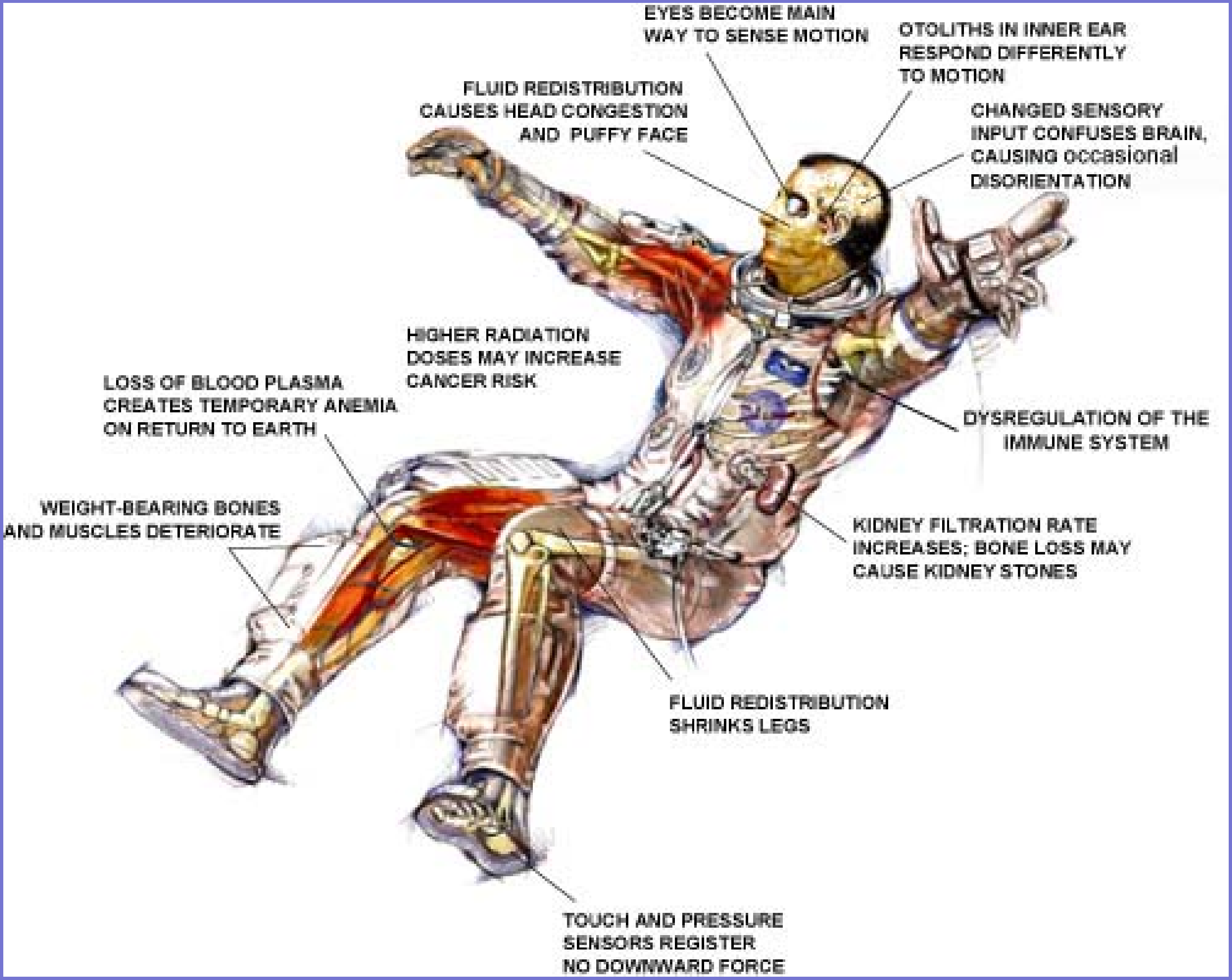


Adapted from: Cooper C, Melton LJ



Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ

Microgravity Effects on the Human Body



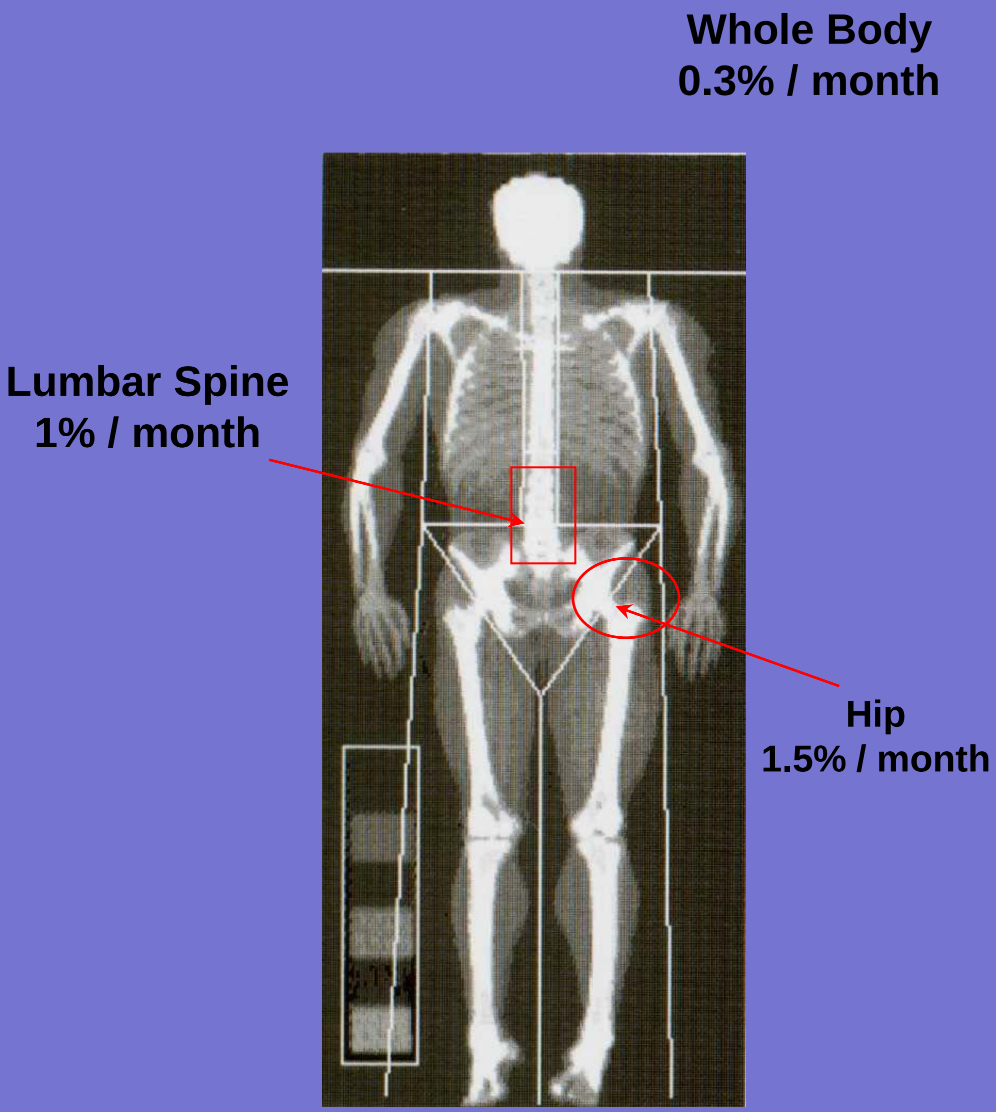
From Scientific American

Overview

- Uniqueness of NASA
- Spaceflight Effects: *Out-of-this-World Data*
- *Bold* Approaches to Managing Bone Risk

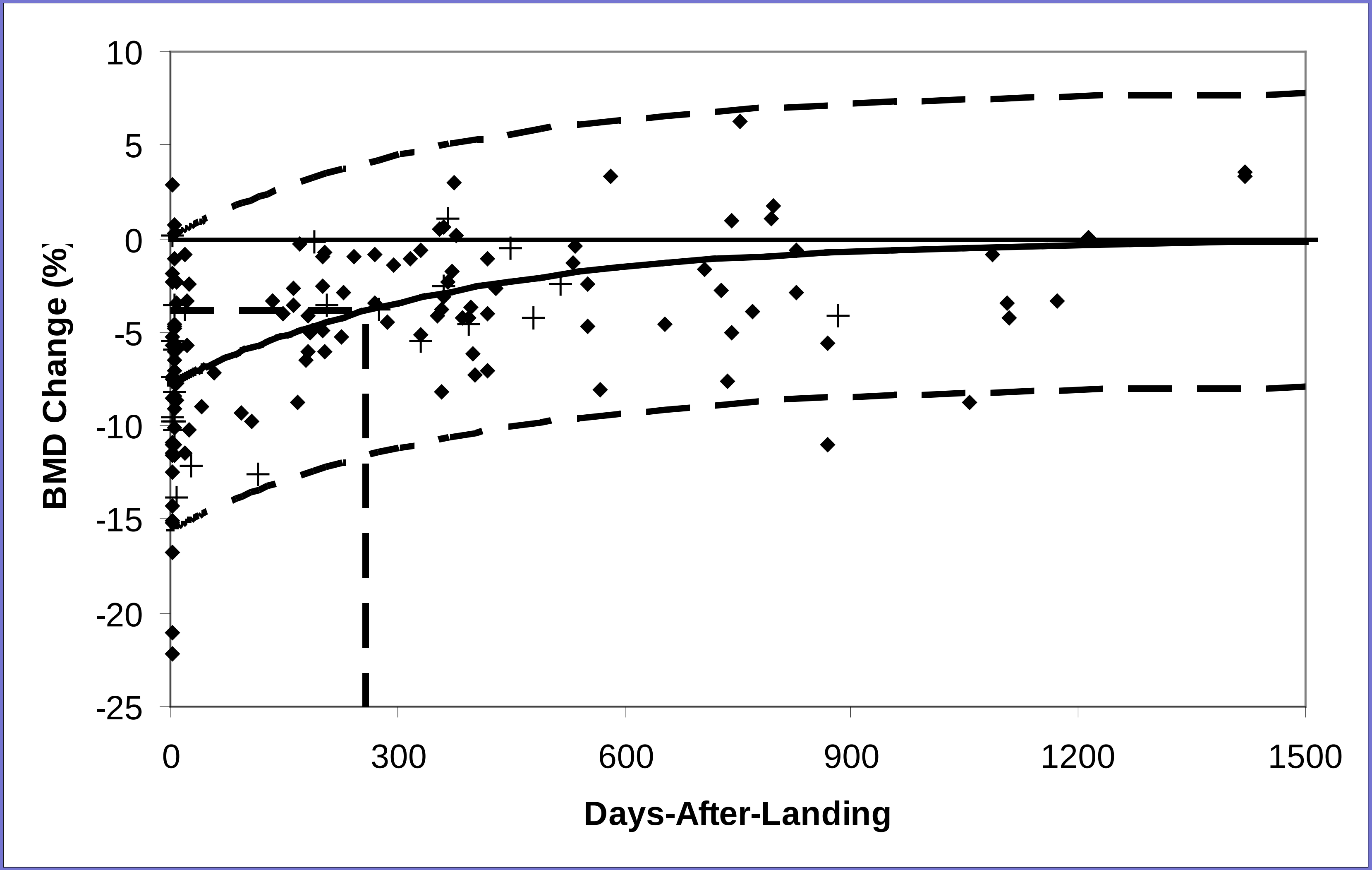
DXA: BMD losses are regional and rapid

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, 2000



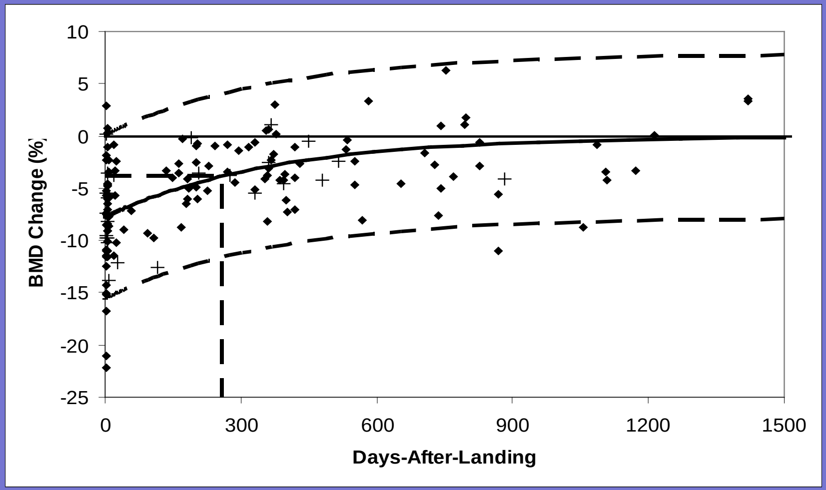
What about recovery?

Trochanter: Loss$_0$=7.8% 50% Recovery=255d

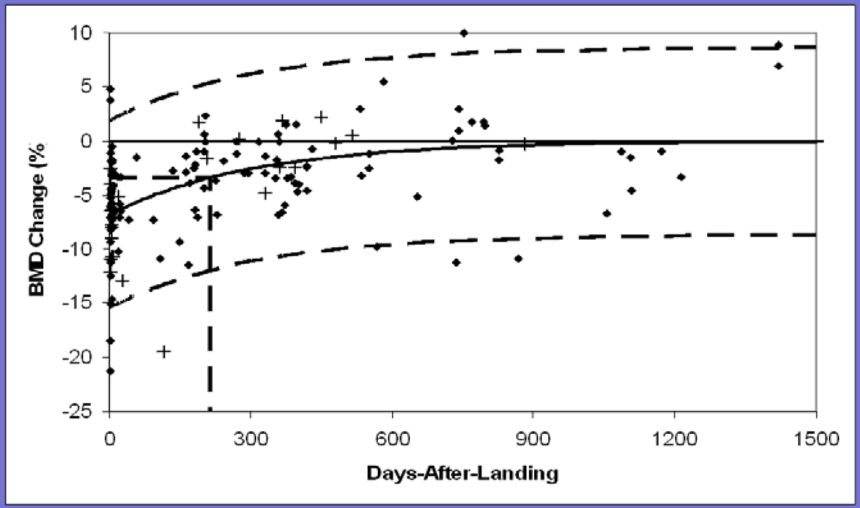


Sibonga et al. BONE 41:973-978, 2007.

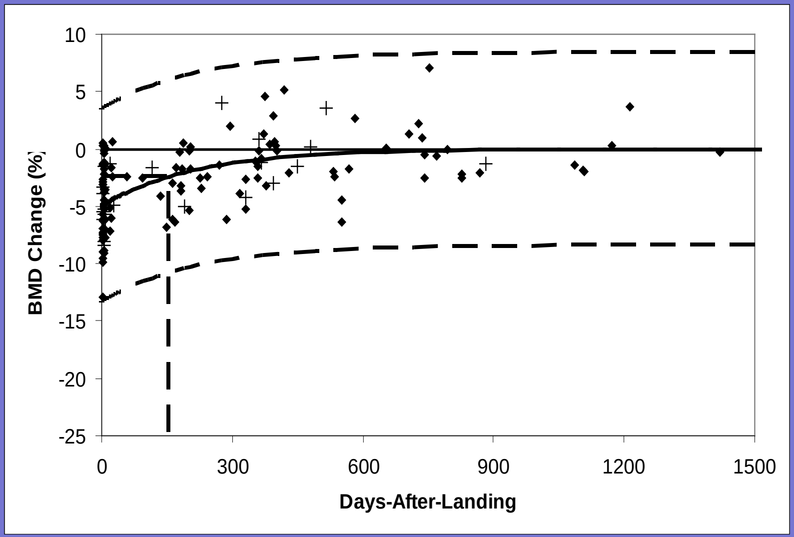
DXA BMD increases in Postflight Period after long-duration flights.



Trochanter



Femoral neck



Lumbar Spine

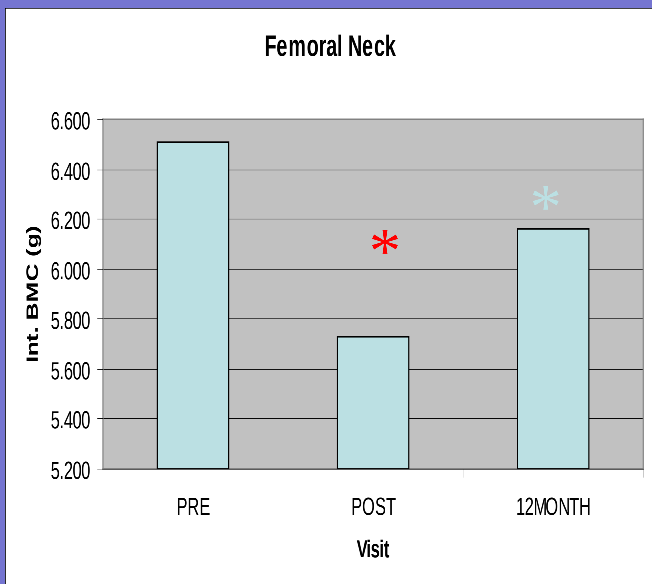
Research Study: QCT measures loss hip vBMD due to spaceflight in trabecular bone compartment (n=16 ISS)

Index DXA	%/Month Change ± SD	Index QCT	%/Month Change ± 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 M Neuron Interact, 2000;
Lang , J Bone Miner Res, 2004;
Vico, The Lancet 2000

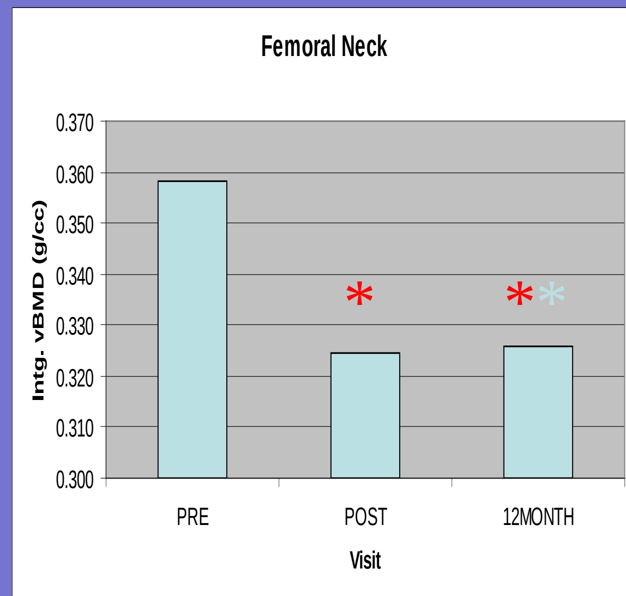
QCT Postflight – Changes in bone mass and structure at Femoral Neck 12 months after return

Bone Mineral Content
(g)



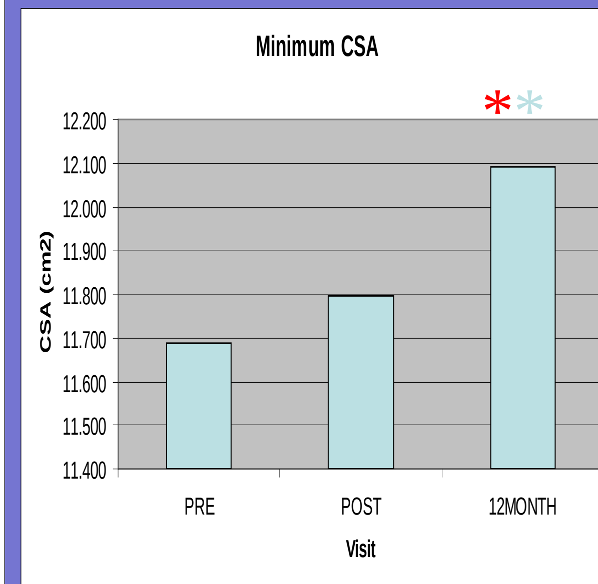
Pre Post 12

Volumetric
Bone Mineral Density
g/cm³



Pre Post 12

Minimum
Cross-sectional Area
cm²

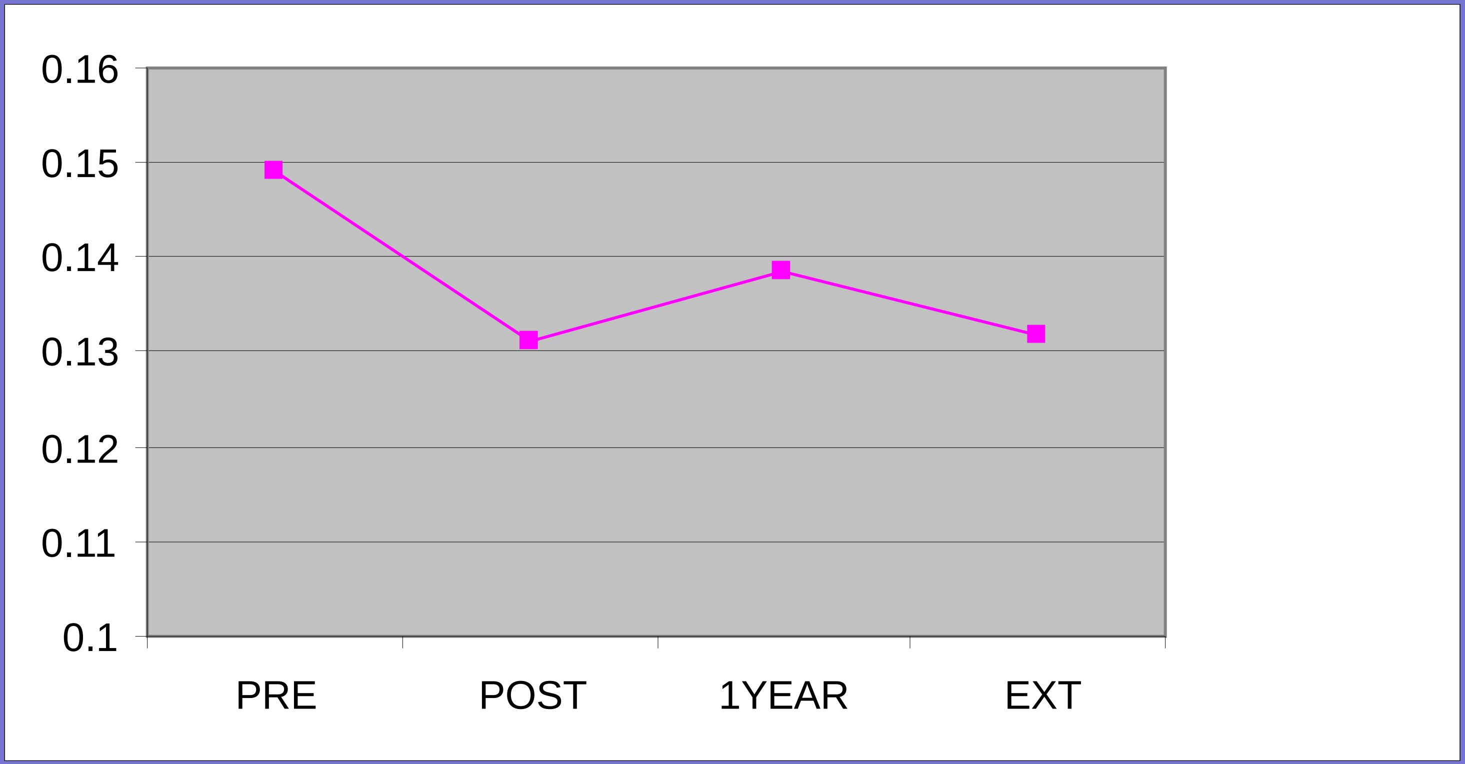


Pre Post 12

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

Slide adapted from T. Lang., JBMR 2006.

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



PRE: n= 16 POST: n= 16 1 YEAR: n=16 EXT: n=8

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

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

http://depts.washington.edu/bonebio/ASBMRed/structure.html

Photo by Paul Crompton

And what has happened to bone microarchitecture of hip?

L Mosekilde

Overview

- Uniqueness of NASA

- Spaceflight Effects:

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- *Bold* Approaches to

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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 that uses QCT data to estimate hip bone strength

QCT estimates fracture loads better than DXA

QCT + FEM has superior capabilities for estimating fracture loads

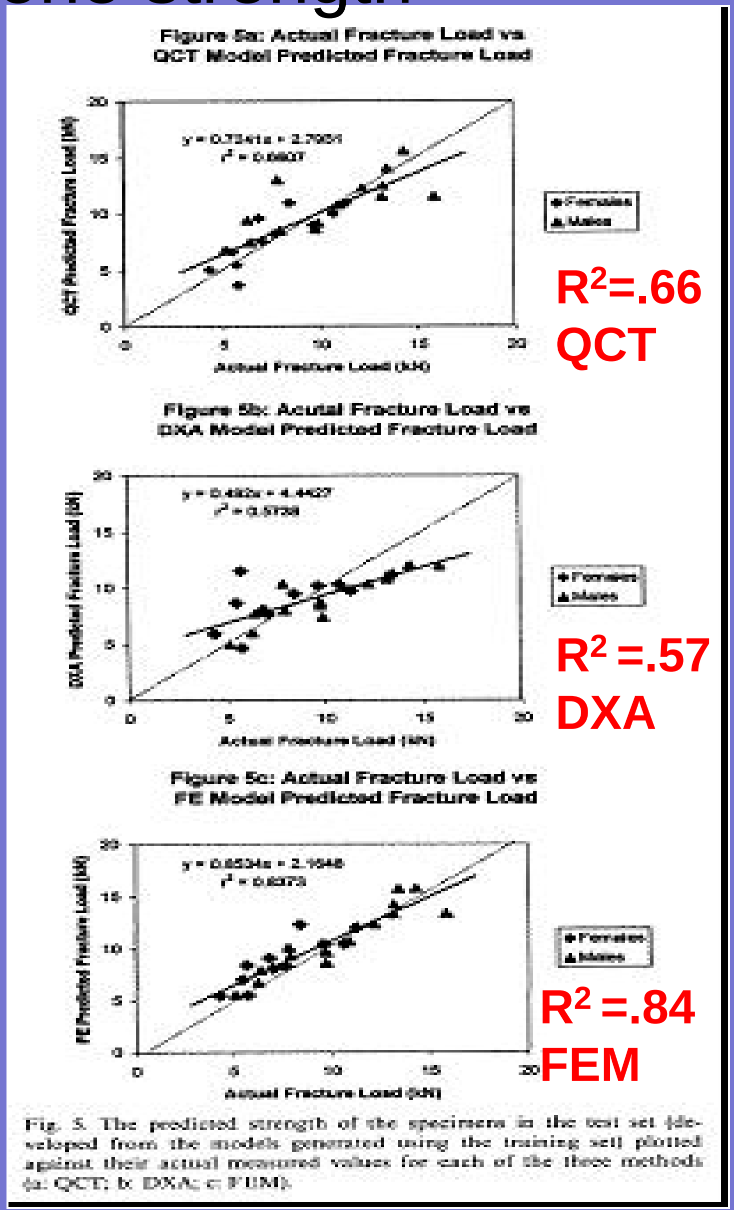
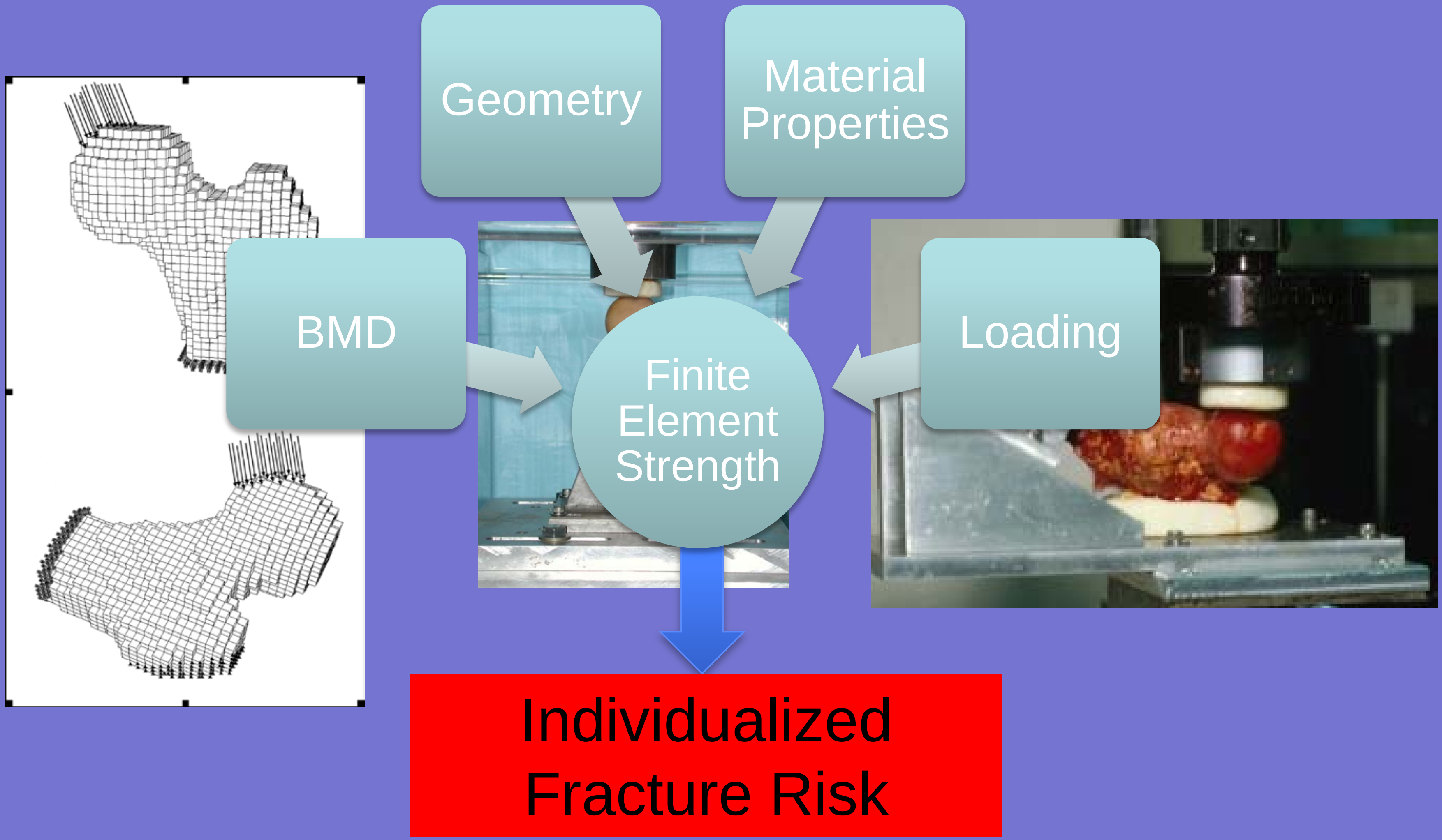


Fig. 5. The predicted strength of the specimens in the test set (developed from the models generated using the training set) plotted against their actual measured values for each of the three methods (a: QCT; b: DXA; c: FEM).

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

FEM to estimate changes to hip bone strength after spaceflight.

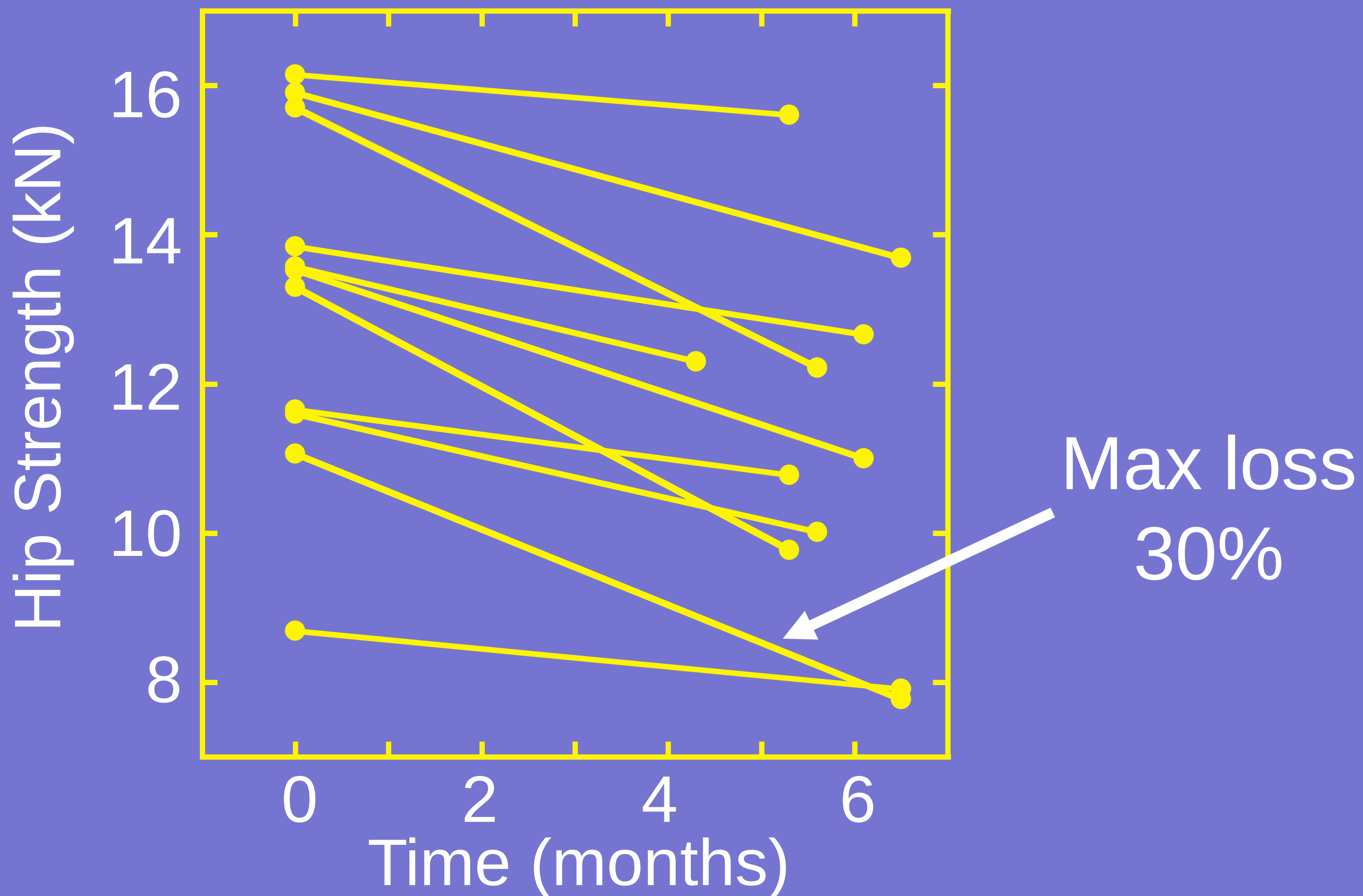


Slide courtesy of P. Truszkowski

Images courtesy of Dr. J Keyak

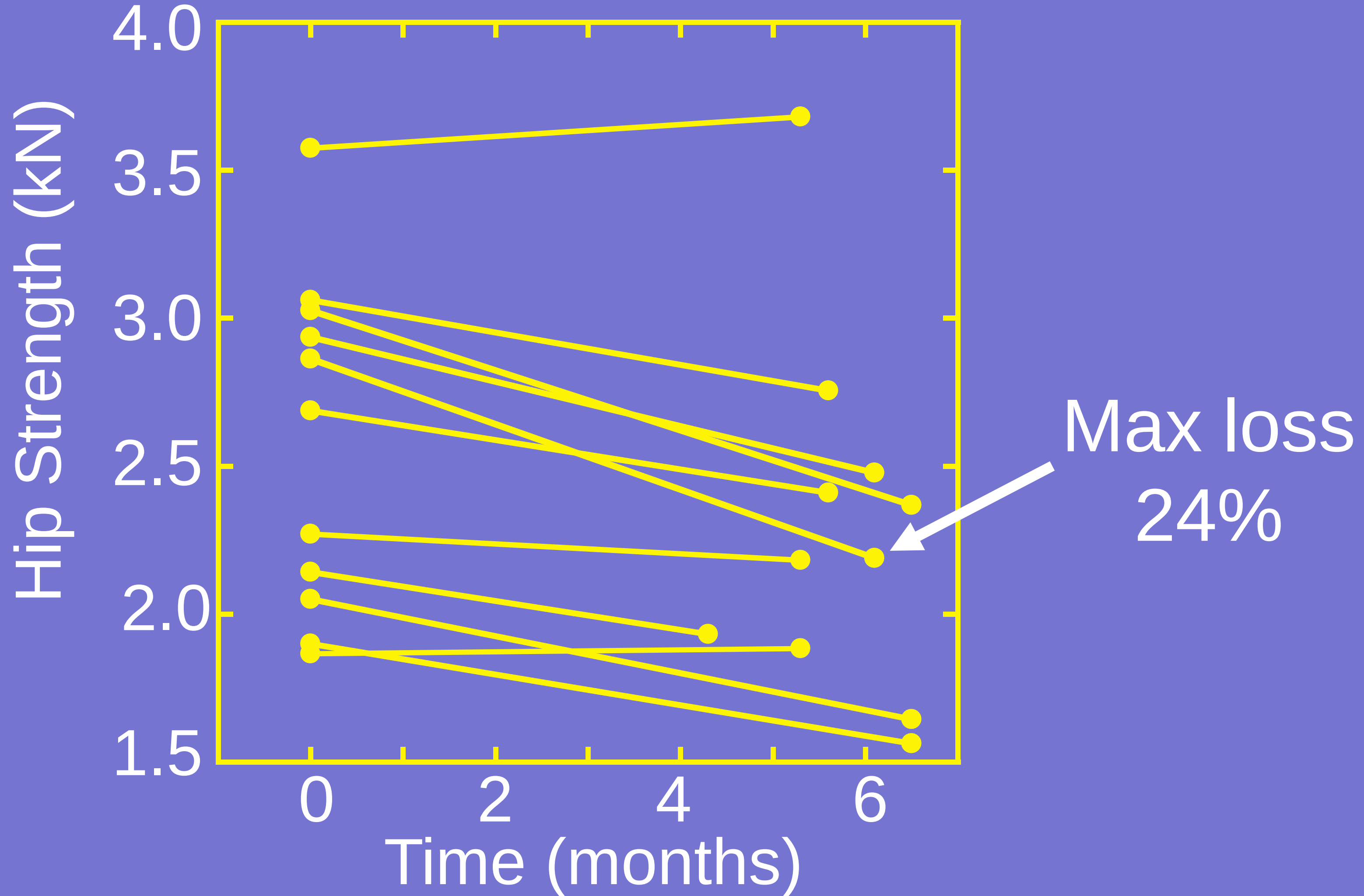
Individual Results

Stance Loading (4 to 30% loss in strength)

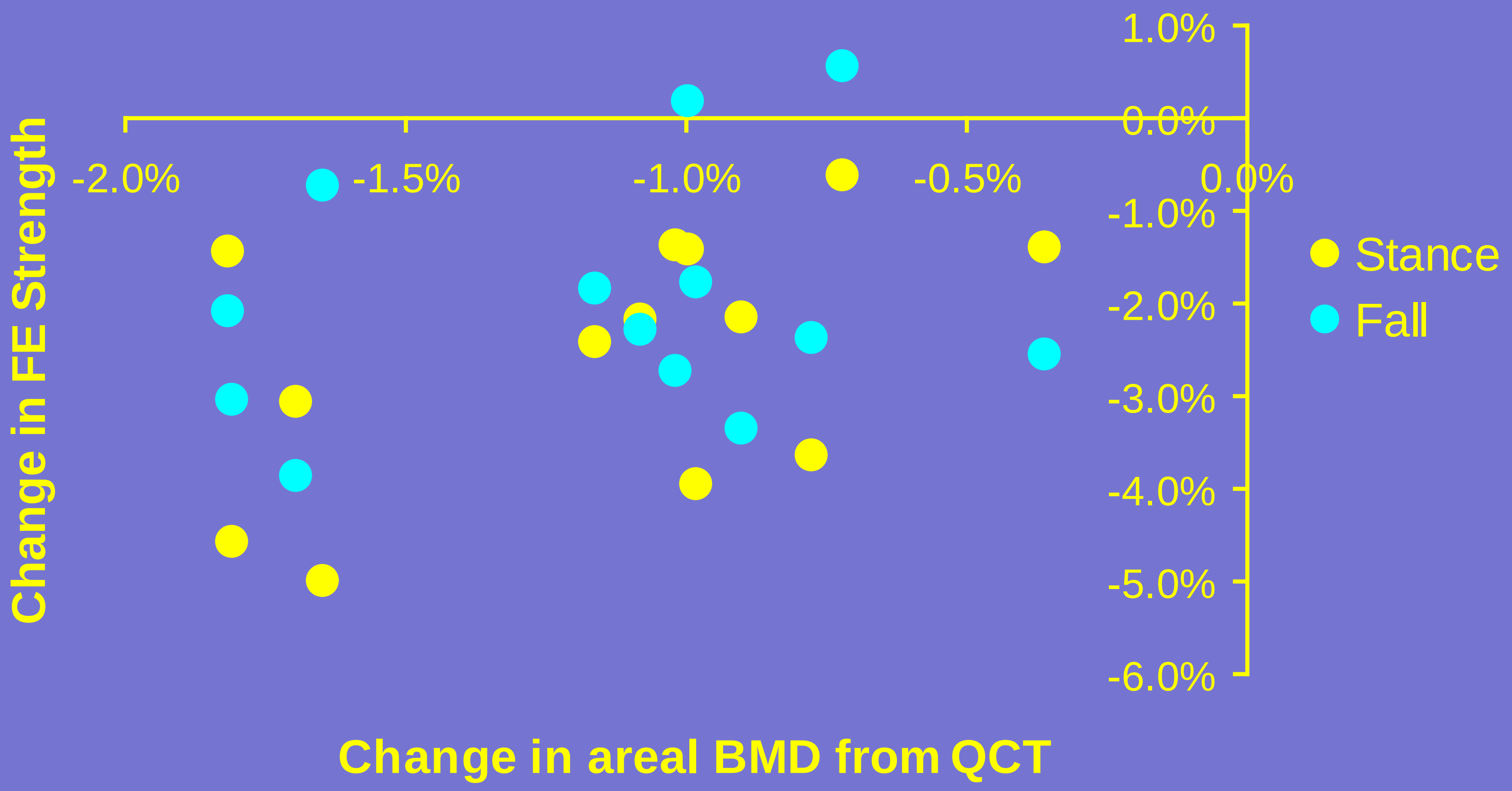


Individual Results

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



Surrogates of bone strength do not correlate.



Stance: R^2=0.23

Fall: R^2=0.05

Slide courtesy of J Keyak

Summary

- Unique <u>cohort</u>, unique <u>environment</u>, unique <u>changes</u> in bone structure during long-duration missions in microgravity

- QCT – added measures of bone that increase our knowledge about how spaceflight affects bone structure – changes that may combine with aging effects

- FE estimates of strength – an improved surrogate for NASA by individualizing the estimates of hip bone strength per astronaut.

Final Comments

- Clinical goal: Prevention of fractures by identifying those at highest risk – risk factors to enhance DXA predictive capabilities

- NASA goal: To reduce the uncertainty of fracture risks (fragility and traumatic fractures) during a mission, after a mission and as the astronaut ages by employing the best technologies and analyses available.

Thank you!

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NASA

Backup Slides

QCT does not outperform DXA-BMD for fracture prediction but provides extra information that DXA does not

TABLE 4. HRs OF MULTIVARIATE MODELS OF SKELETAL PARAMETERS AT THE FEMORAL NECK FOR HIP FRACTURE ADJUSTED FOR CLINIC SITE, AGE, AND BODY MASS INDEX

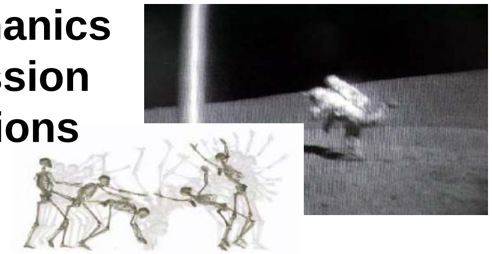
	Model A (HR per SD decrease)			*Model B (HR per SD decrease)*			*Model C (HR per SD decrease)*		
	HR	*95% CI*	*p*	*HR*	*95% CI*	*p*	*HR*	*95% CI*	*p*
Trabecular bone, volumetric BMD (g/cm^3)	—			1.65	1.15, 2.37	0.007	1.29	0.84, 1.98	0.250
Percent cortical volume	—			3.19	2.23, 4.57	<0.001	2.42	1.56, 3.76	<0.001
Minimum cross-sectional area (cm^2)	—			1.59	1.24, 2.05	<0.001	1.48	1.14, 1.94	0.004
Areal BMD from DXA (g/cm^2)	4.13	2.67, 6.38	<0.001	—			1.91	1.06, 3.46	0.033

Area under the ROC curve for Models A, B, and C were 0.853, 0.855, and 0.860, respectively.

Black, et al.: Proximal Femoral Structure and the Prediction of Hip Fracture in Men: A Large Prospective Study Using QCT. J Bone Miner Res 23(8):1326, 2008.

Bone Fracture Risk Module (BFxRM)

Biomechanics and Mission Operations



courses.washington
.edu/me598rc

Bone Loss in Space

Estimate of Fracture Probability

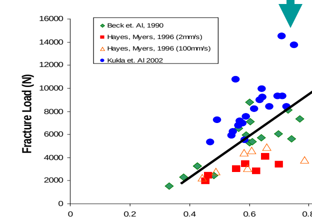


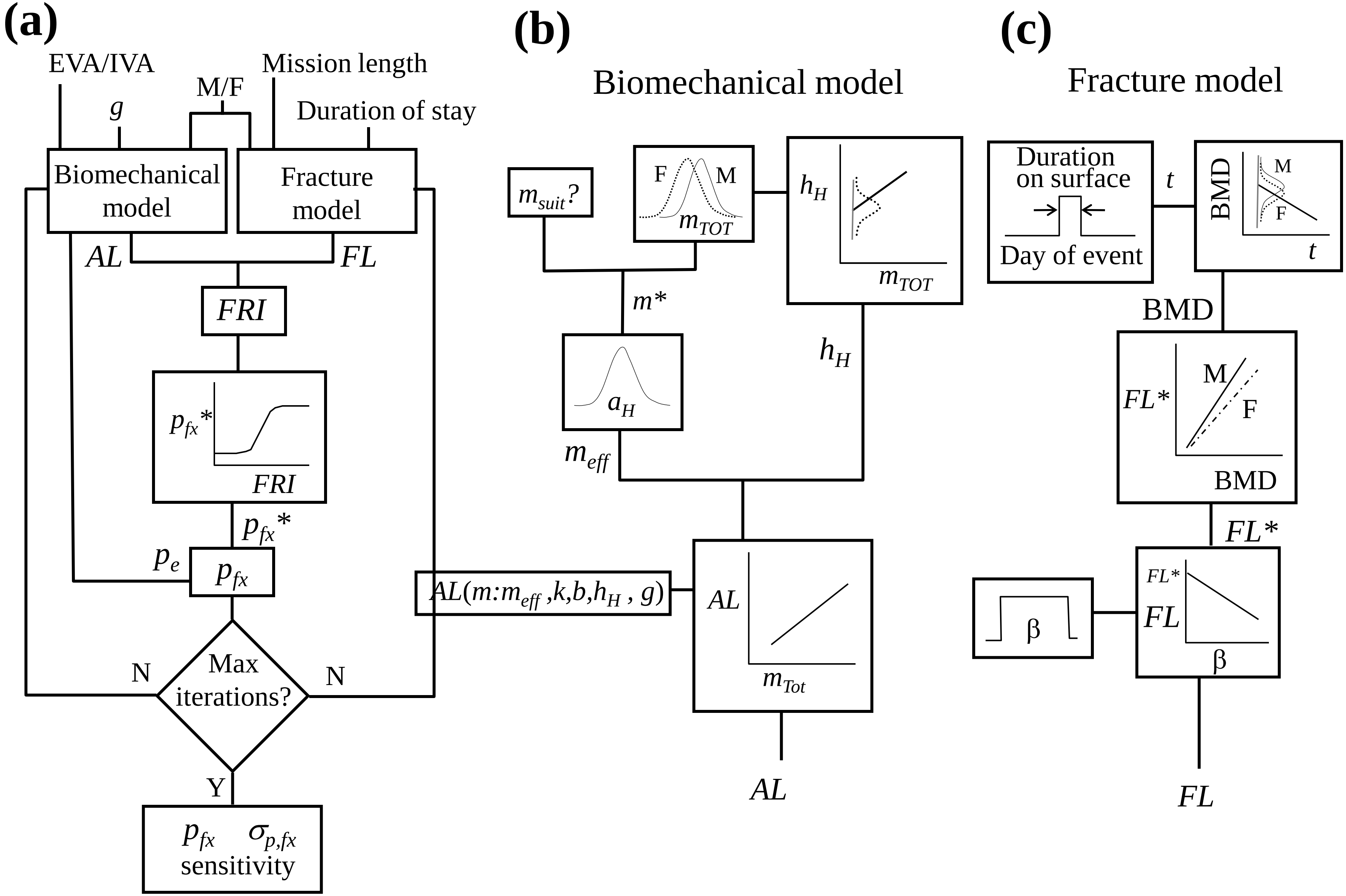
Figure 2. Summary of literature survey on fracture load as a
neck BMD

Clinical and Engineering Characteristics of Bone Strength

Probability of Fracture

Probability of event

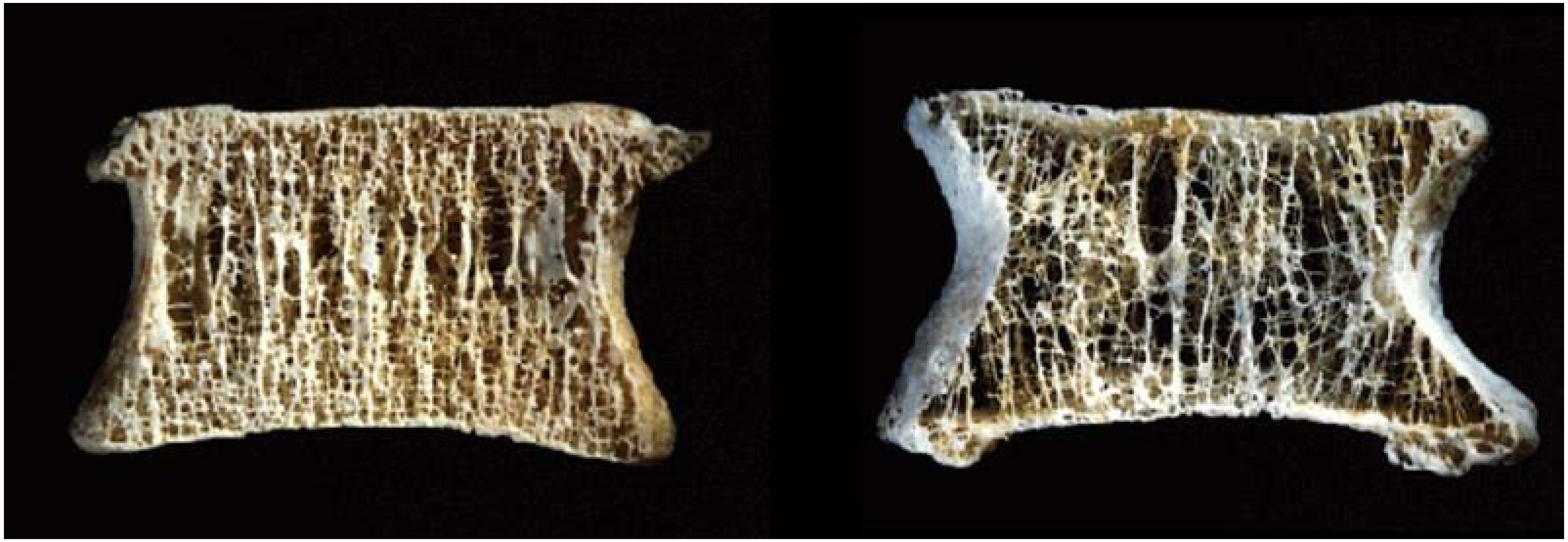
Probability bone will fail to support load



ES Nelson et al. Development and validation of a predictive bone fracture risk model for astronauts NASA Glenn Research Center, Cleveland, OH

Ann Biomed Eng, 37(11), 2009, pg. 2337 - 2359.

What is the impact of Trabecular Bone Loss on bone microarchitecture?



- Impact on HIPmicroarchitecture UNKNOWN*
- Knowledge base: Vertebral trabecular bone loss with <u>menopause.</u>
- Loss of horizontal trabecular struts and directionality , perforation of trabeculae*, reduction in mechanical strength, and increase in fracture risk (Mosekilde, 2000; Seeman, 2002, Silva 1997; Kleerekoper 1985)

Results in Astronauts – Hip Strength

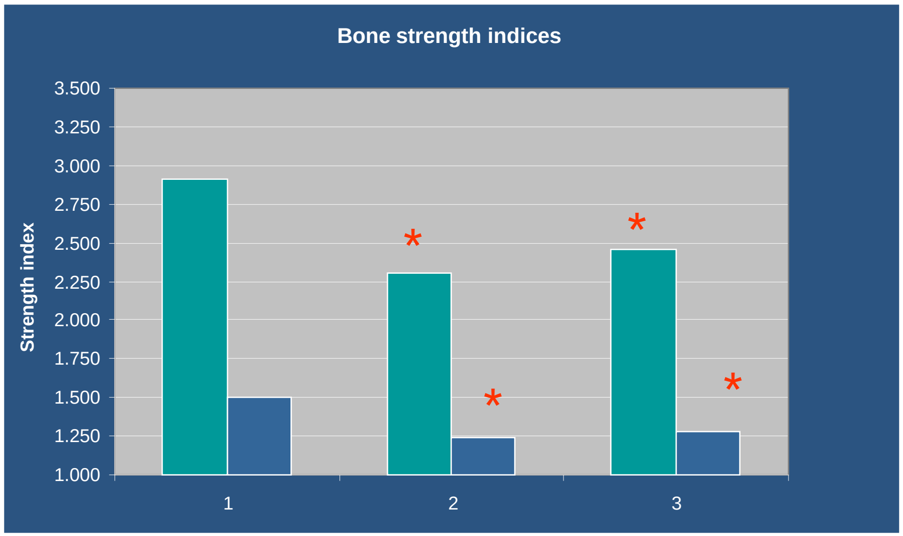
N=11 crewmembers

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

QCT Postflight: Structural changes do not reflect a restoration of bone strength

Bone Strength Indices



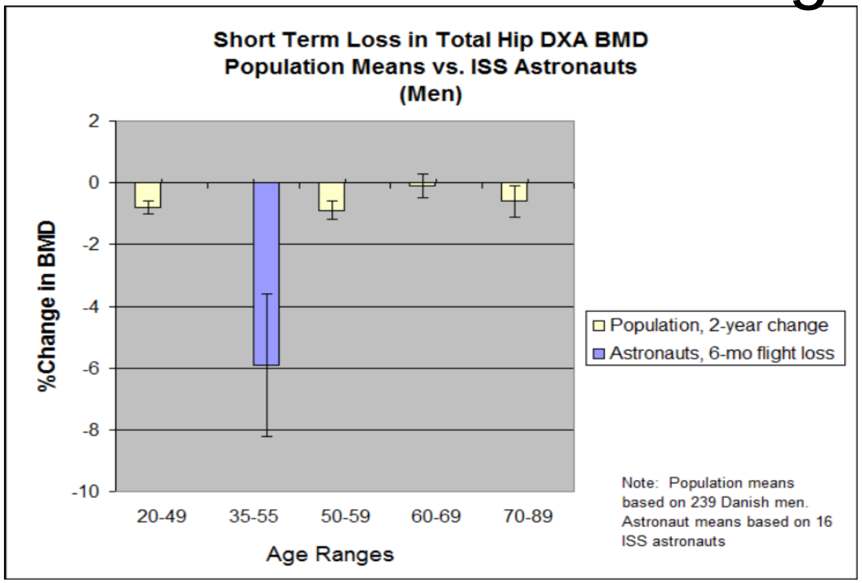
Pre Post 12

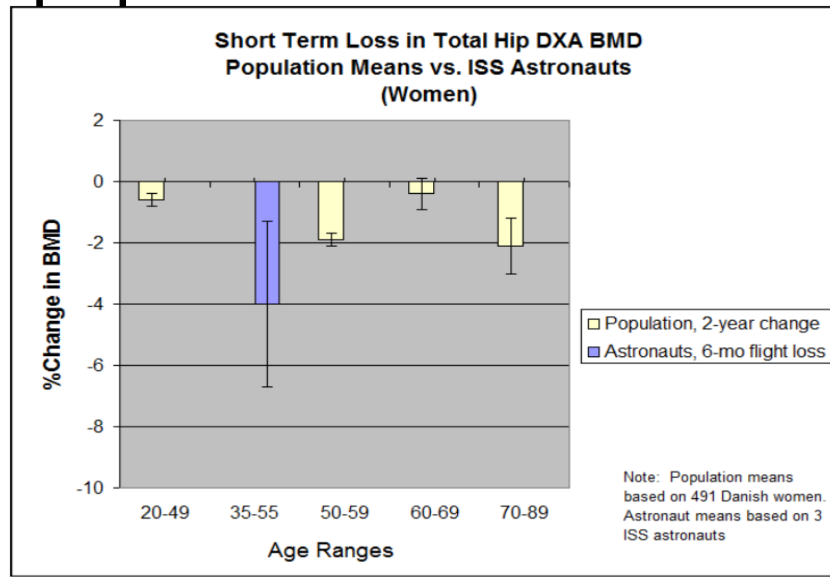
bending (cm3)
compressive (g2/cm4)

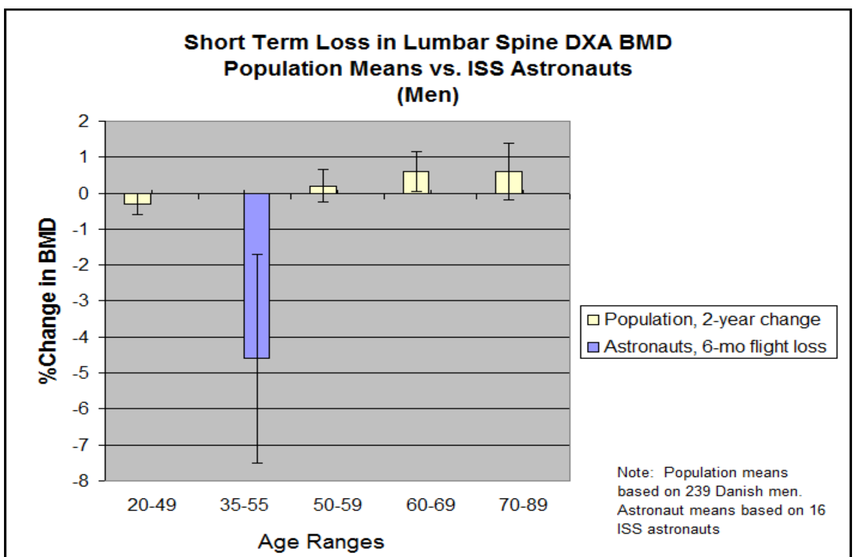
*: $p<0.05$ with respect to preflight

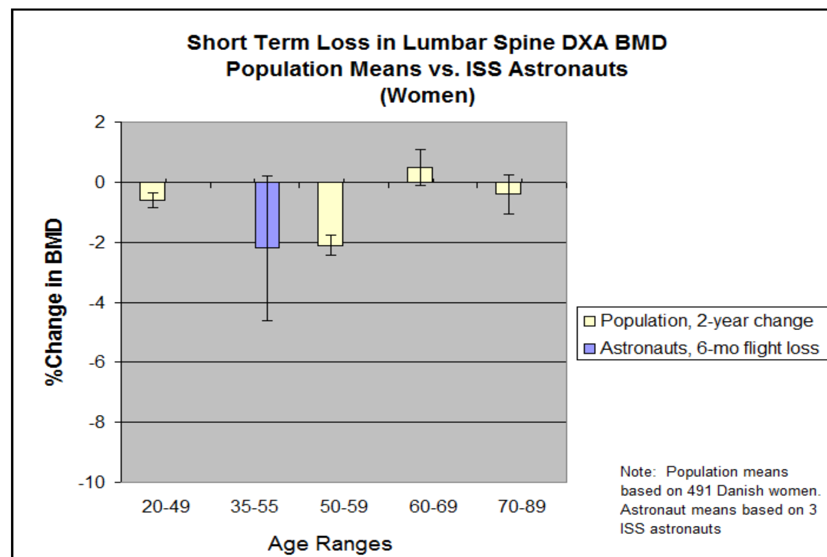
T. Lang et al., JBMR, 2004, 2006.

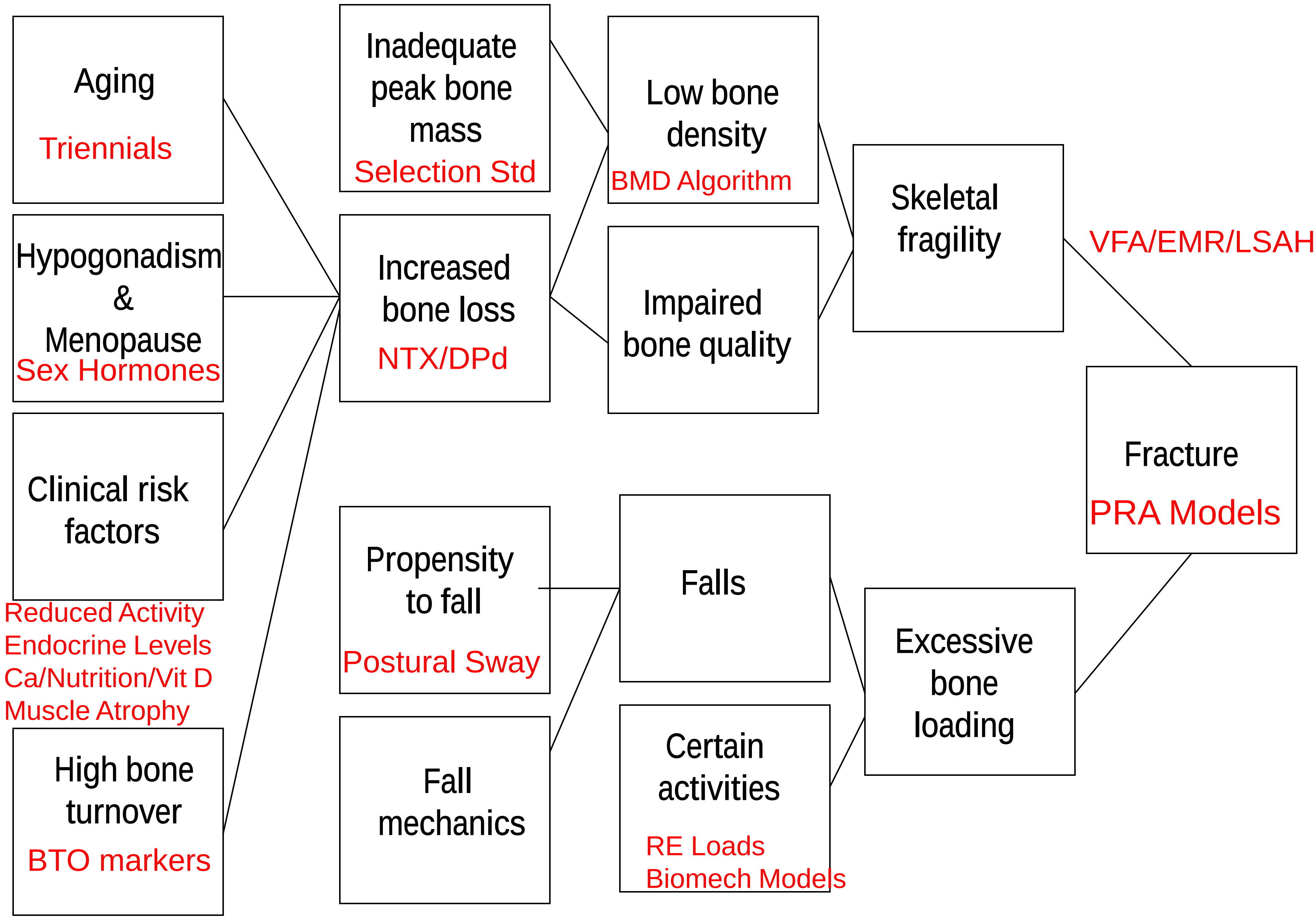
DXA: Losses at total hip and spine after ~6 months in space exceed 2-year losses on Earth in similar–aged population











Adapted from: Pathogenesis of Osteoporosis-Related Fractures (NOF) Cooper C, Melton LJ

Percentage Reduction in Hip Strength