National Aeronautics and Space Administration

Bone *Changes* During Spaceflight: The Path to Risk Reduction

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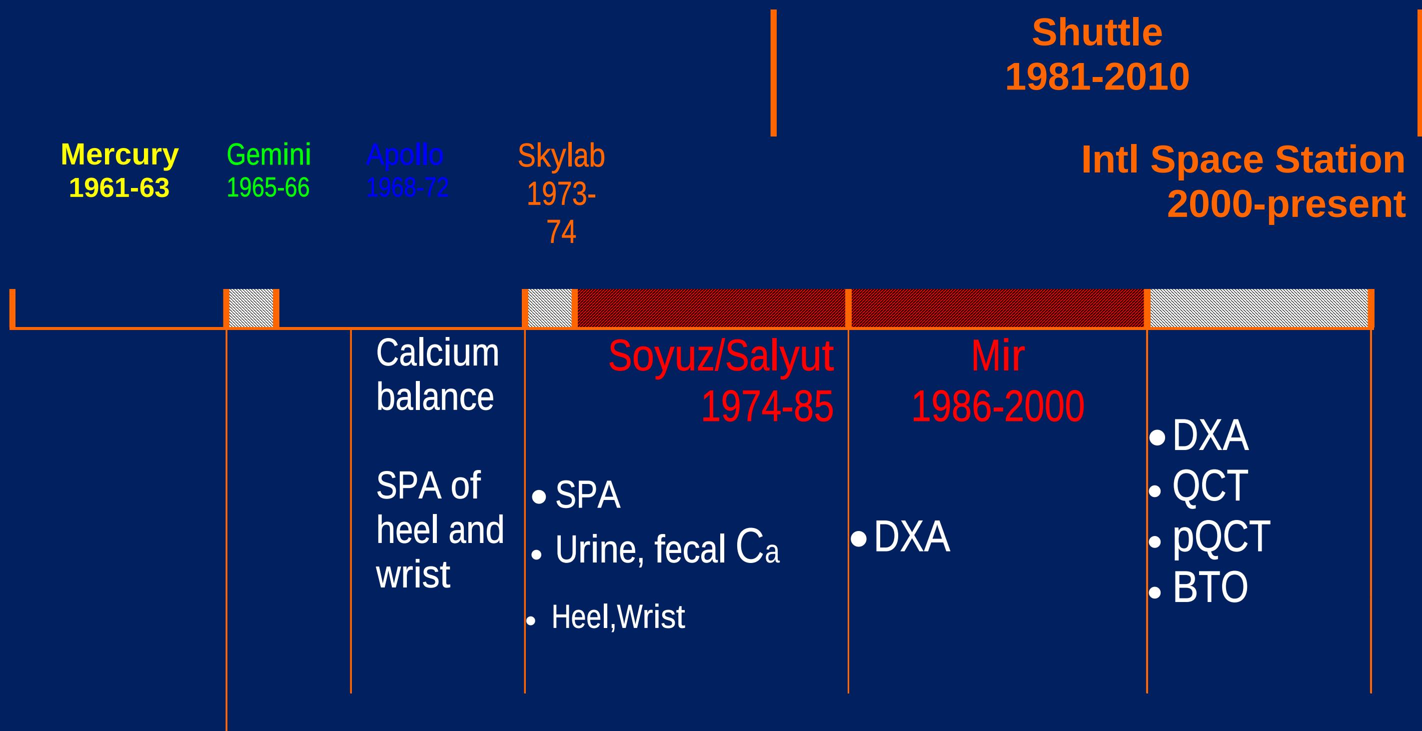
April 8, 2014

At the end of this lecture, you should understand:

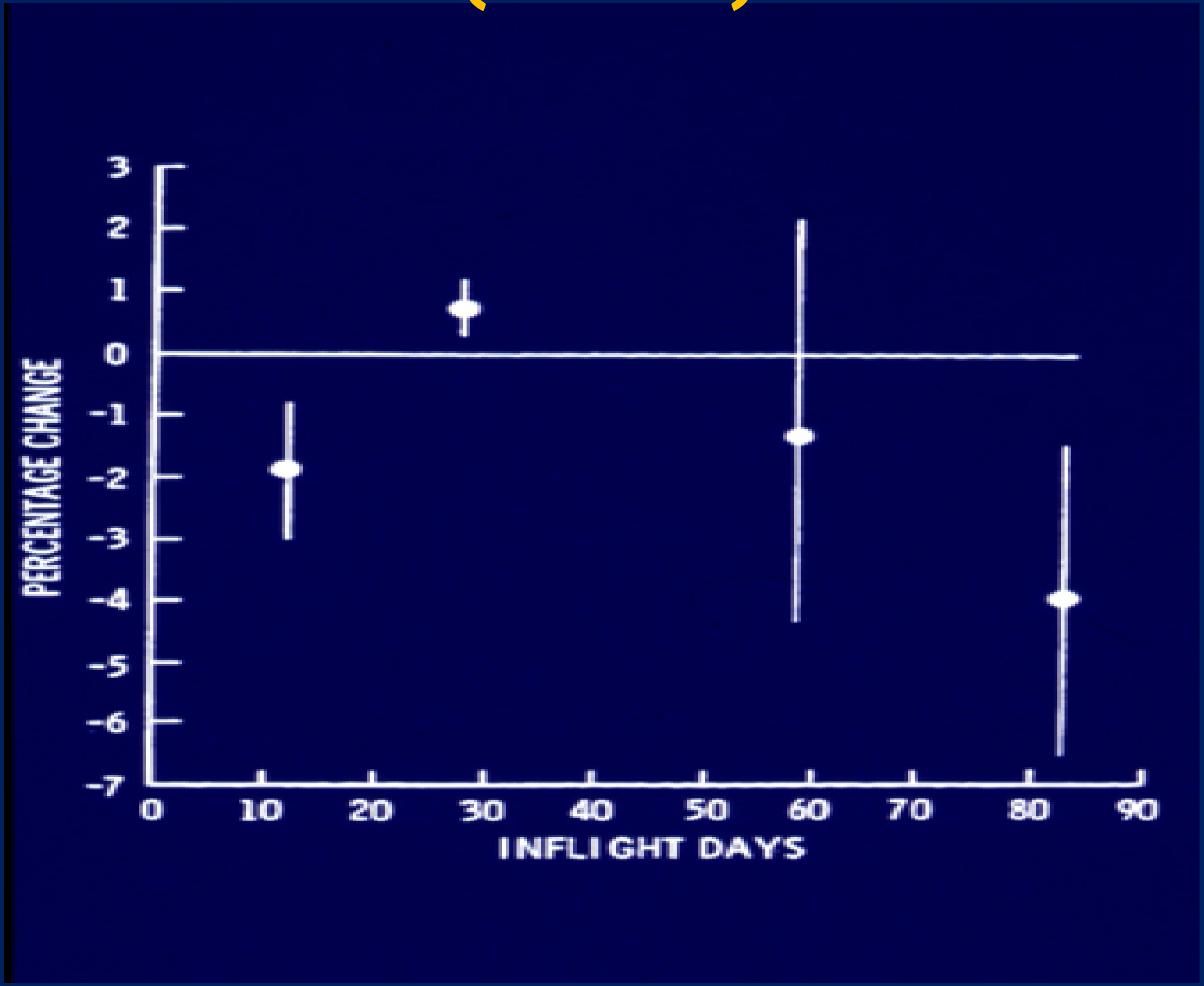
- The progression of bone research on the path to risk reduction for the human system.
- The view of DXA BMD as a surrogate for fracture risk in terrestrial medicine. Why “loss” is not measured by this test.
- Flight data describing the unique effects of spaceflight on skeletal sites at risk for age-related osteoporosis.
- Bold research approaches to a hip fracture surrogate in the context of NASA’s constraints.

Characterizing Bone Changes in Space



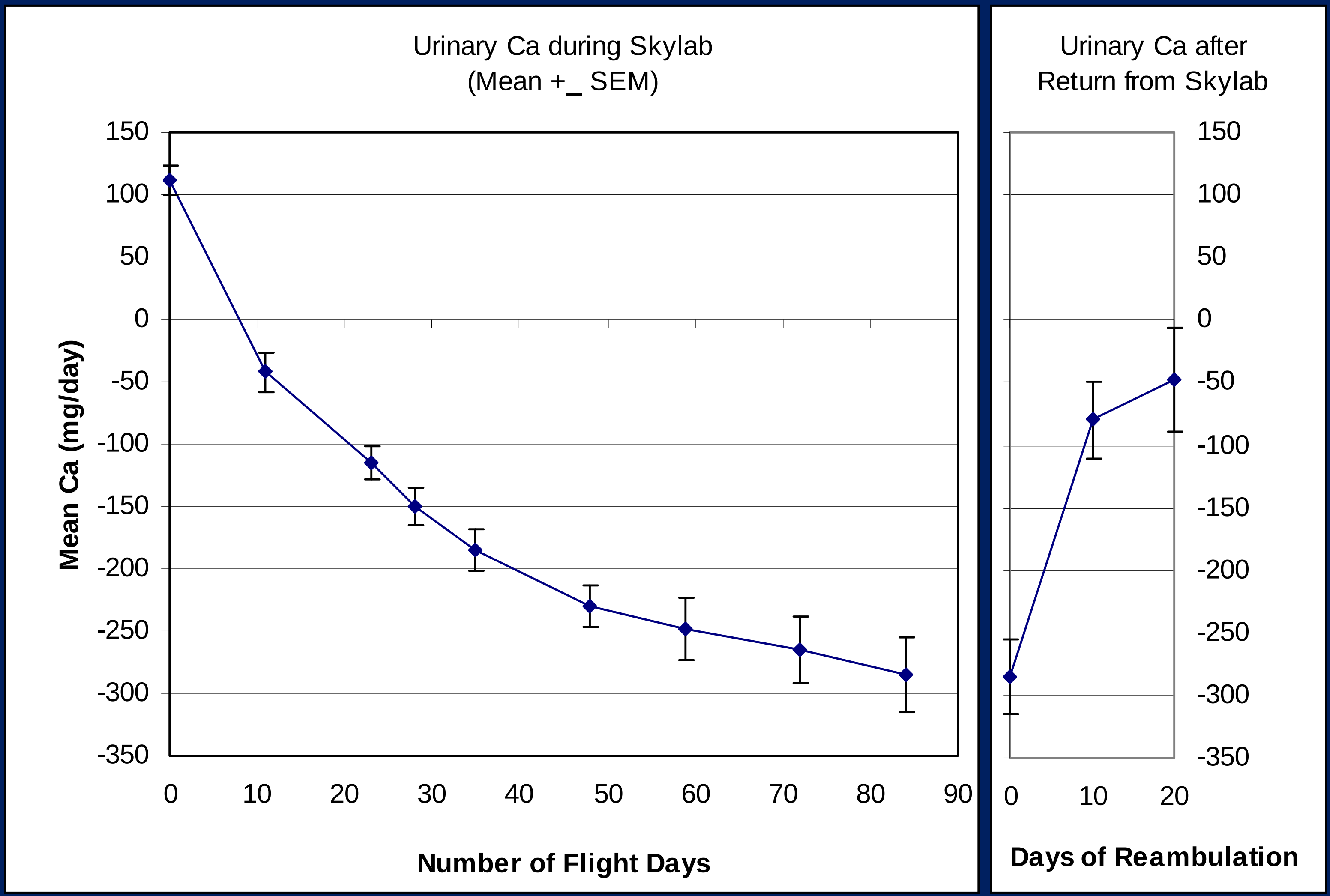
SPA=Single Photon Absorptiometry
DXA=Dual-energy X-ray Absorptiometry
QCT=Quantitative Computed Tomography
pQCT = peripheral QCT
BTO=biochemical markers of bone turnover

Skylab-Bone Mineral Density of Calcaneus (vs. wrist)



Rambaut P, Johnston R. Acta Astronaut. 1979;6:1113-22.

Skylab-Urinary Calcium Excretion



Two Functions of the Skeleton*

- Internal support for the body
- Attachment for muscles / tendons for motion
- Protects vital organs
- Encloses blood-forming elements in marrow
- Mineral reservoir for Calcium (Ca^{2+}) homeostasis

*What potential risks to human health & performance?

Four identified "Bone" health risks for exploration missions.

1. Early Onset Osteoporosis (fragility fractures)
2. Bone Fracture (trauma fractures)
3. Formation of Renal Stones
4. Intervertebral Disc Injury *(or Damage)*

Four Identified "Bone" health risks for exploration missions.

1. Early Onset Osteoporosis

2. Bone Fracture

3. Formation of Renal Stones

4. Intervertebral Disc Injury *(or Damage)*

Journal of Bone & Mineral
June 28(6):1243-1255, 2013

"Bone Summit I – 2010"

REVIEW

JBMR

Skeletal Health in Long-Duration Astronauts: Nature, Assessment, and Management Recommendations from the NASA Bone Summit

Eric S Orwoll,[1] Robert A Adler,[2] Shreyasee Amin,[3] Neil Binkley,[4] E Michael Lewiecki,[5]
Steven M Petak,[6] Sue A Shapses,[7] Mehrsheed Sinaki,[8] Nelson B Watts,[9] and Jean D Sibonga[10]

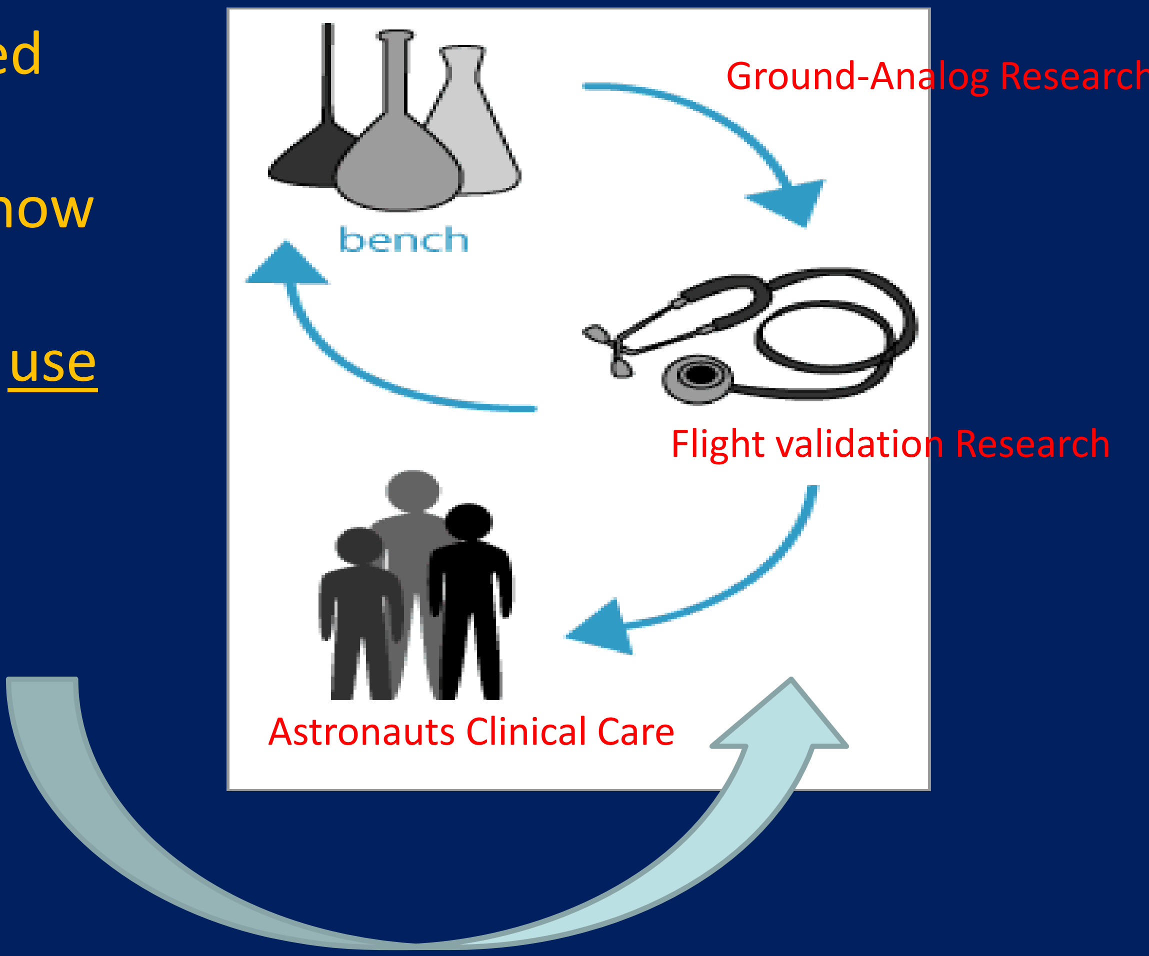
Combined Medical and Research Tests:

Intervention Requirement?, Clinical Triggers?, Surveillance Recommendations

1. What additional measure(s) do we need to monitor?
2. How frequently? For how long?
3. How should Med Ops <u>use research data</u> in its clinical practice?
4. Need specific clinical practice guidelines.

BONE SUMMIT 2010 and 2013

Bone Research @ NASA



Take Home Messages from Bone Summit (2010)

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 tests have limitations.
6. NASA's medical standards for bone health (based upon terrestrial guidelines) are not applicable to long-duration astronauts.
7. *Recommended exploring the transition of research approaches to clinical arena.*

Risk: Different types of fractures

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

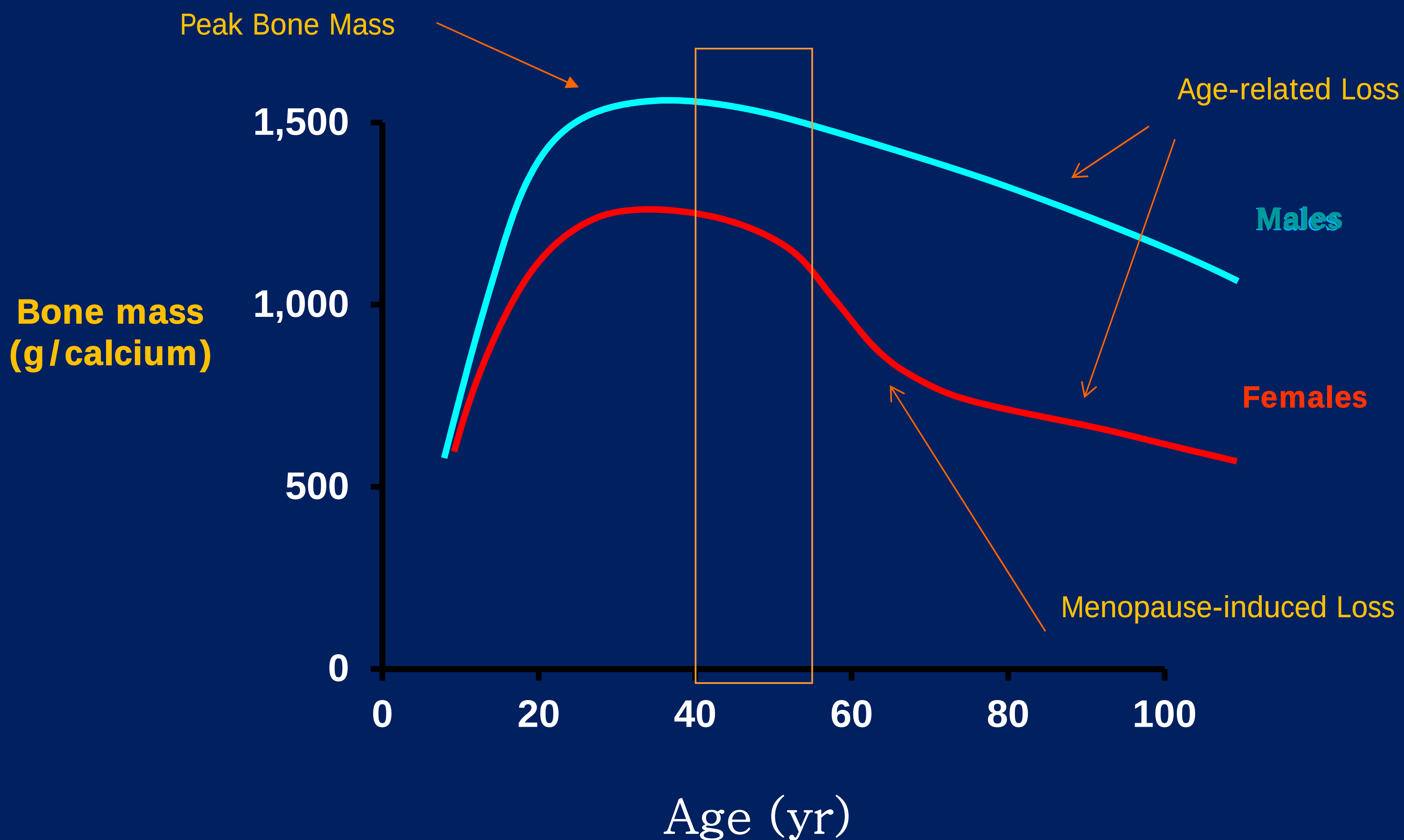
You don't have to be OLD.

Load > Bone Strength = FRACTURE

(Key Causality – BIOMECHANICS)

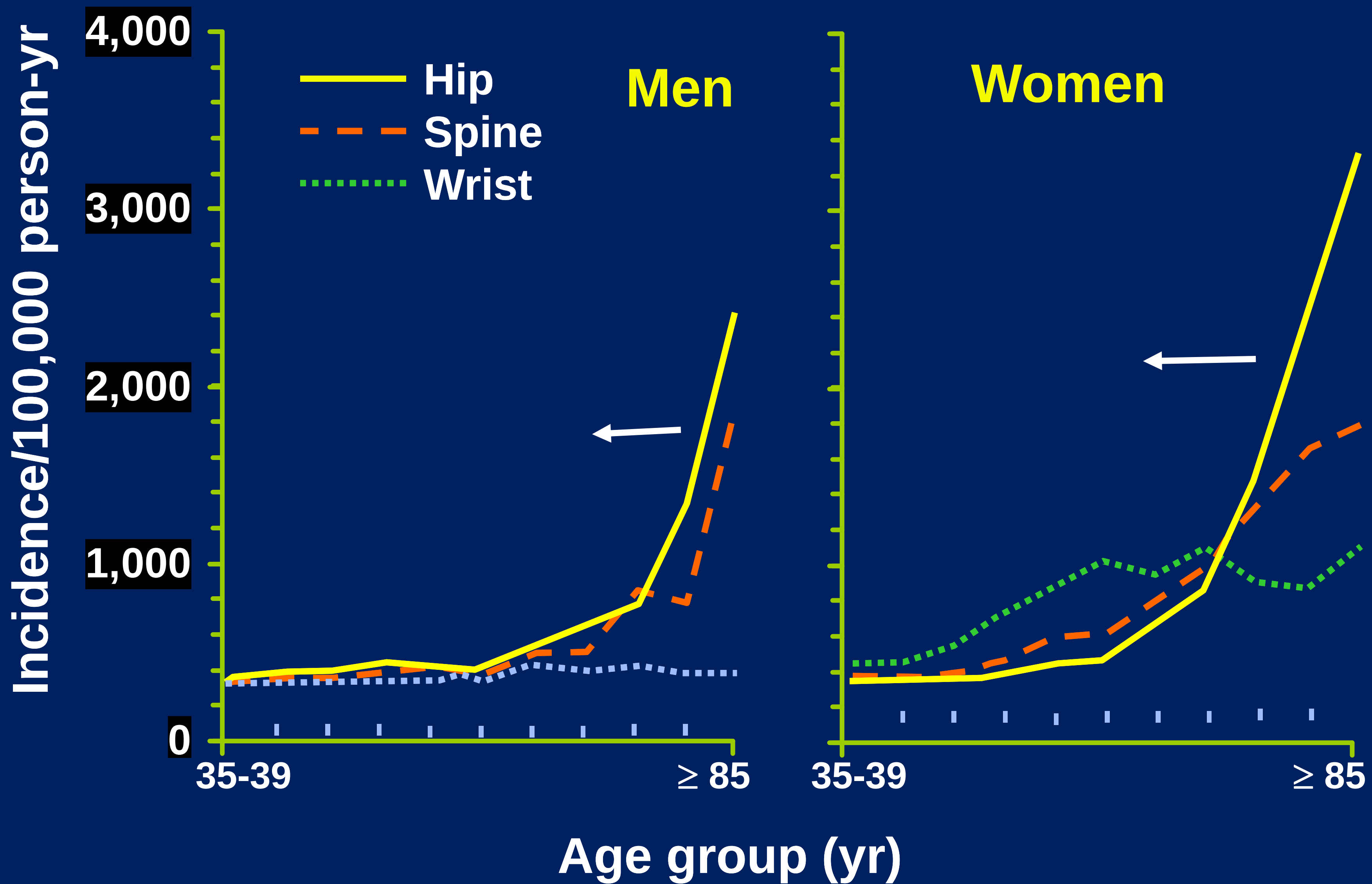
You don't have to have OSTEOPOROSIS.

RISK FOR FRAGILITY FRACTURES: Does spaceflight result in irreversible changes to bone that combine with age-related losses? Then, what do we measure?



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

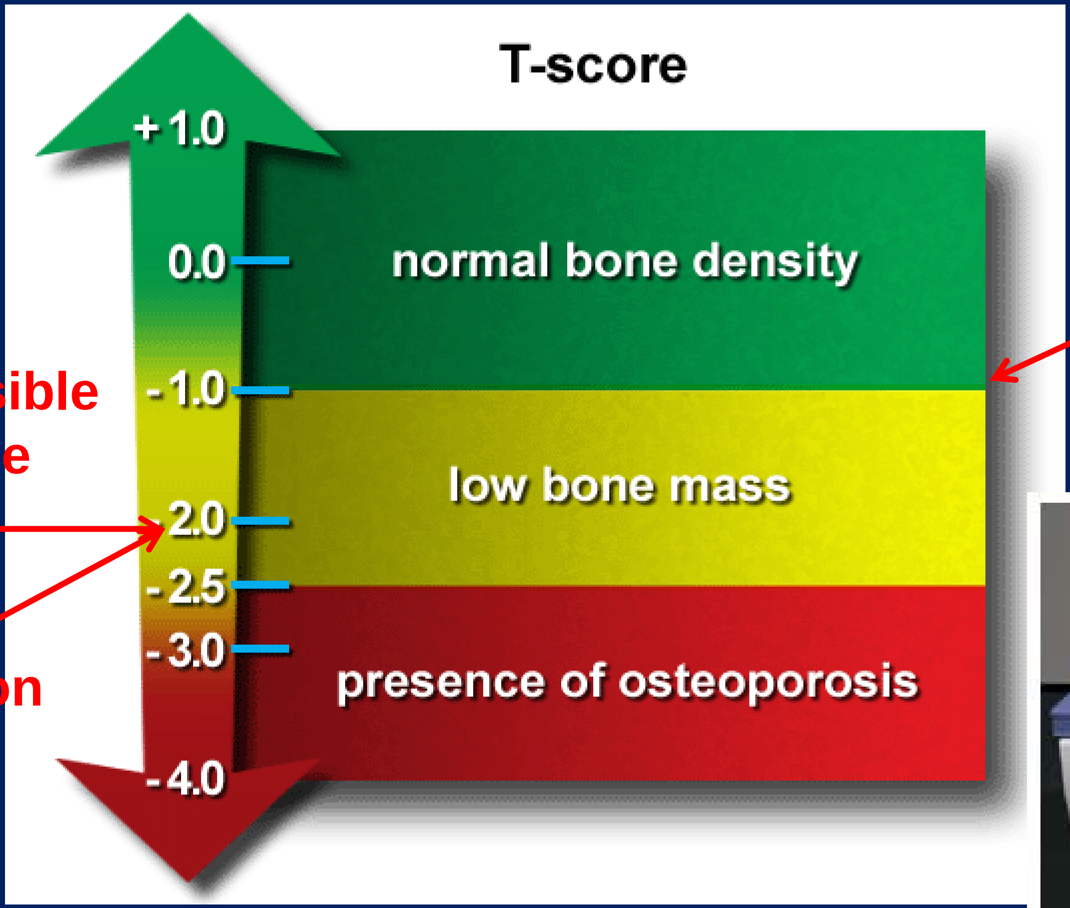
Increased risk in astronauts?
Limited time to count incidence of fractures.



SLIDE COURTESY OF Dr. S. AMIN, Mayo Clinic

Cooper and Melton, 1992

NASA measures Bone Mineral Density [BMD] by DXA as a surrogate for fracture just as clinical world. –T-scores (Not BMD change). circa 2000



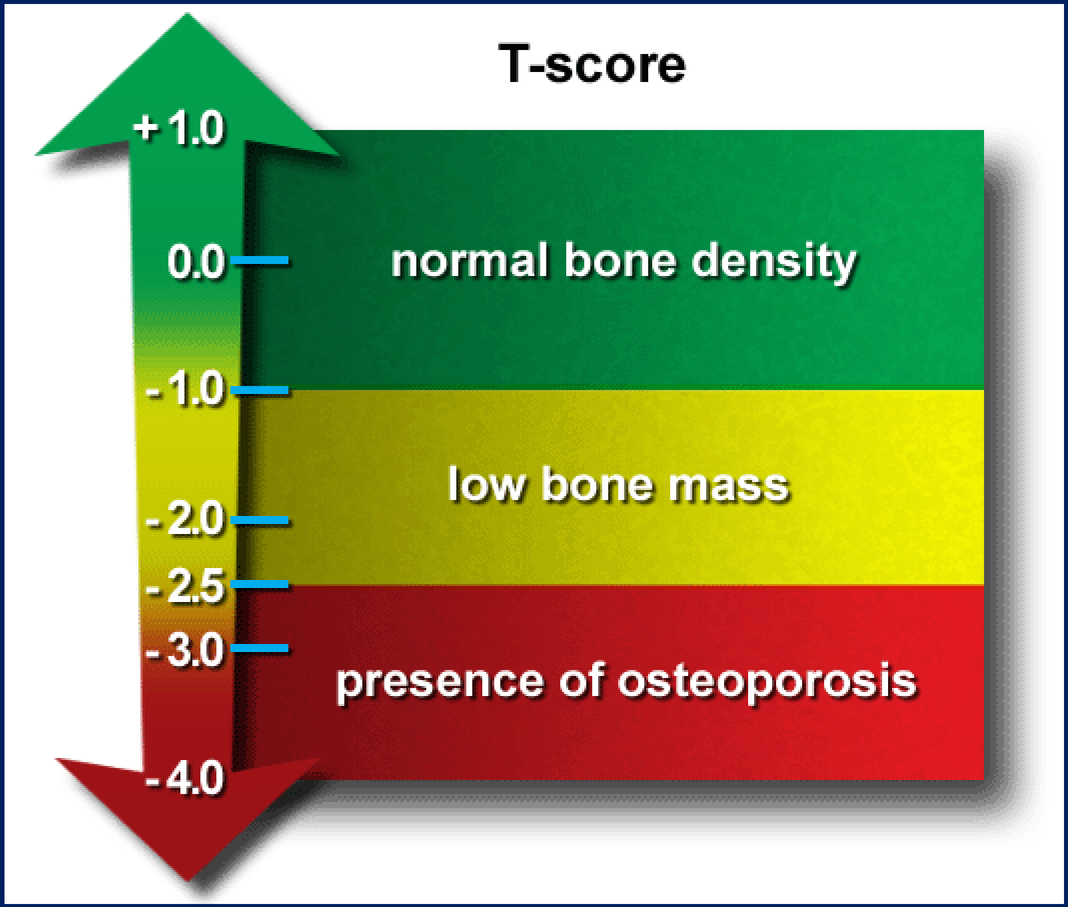
Permissible Outcome Limit

Mitigation Efficacy

Preflight Standard

"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



Disconnects evident In population studies.

FRACTURE CASES

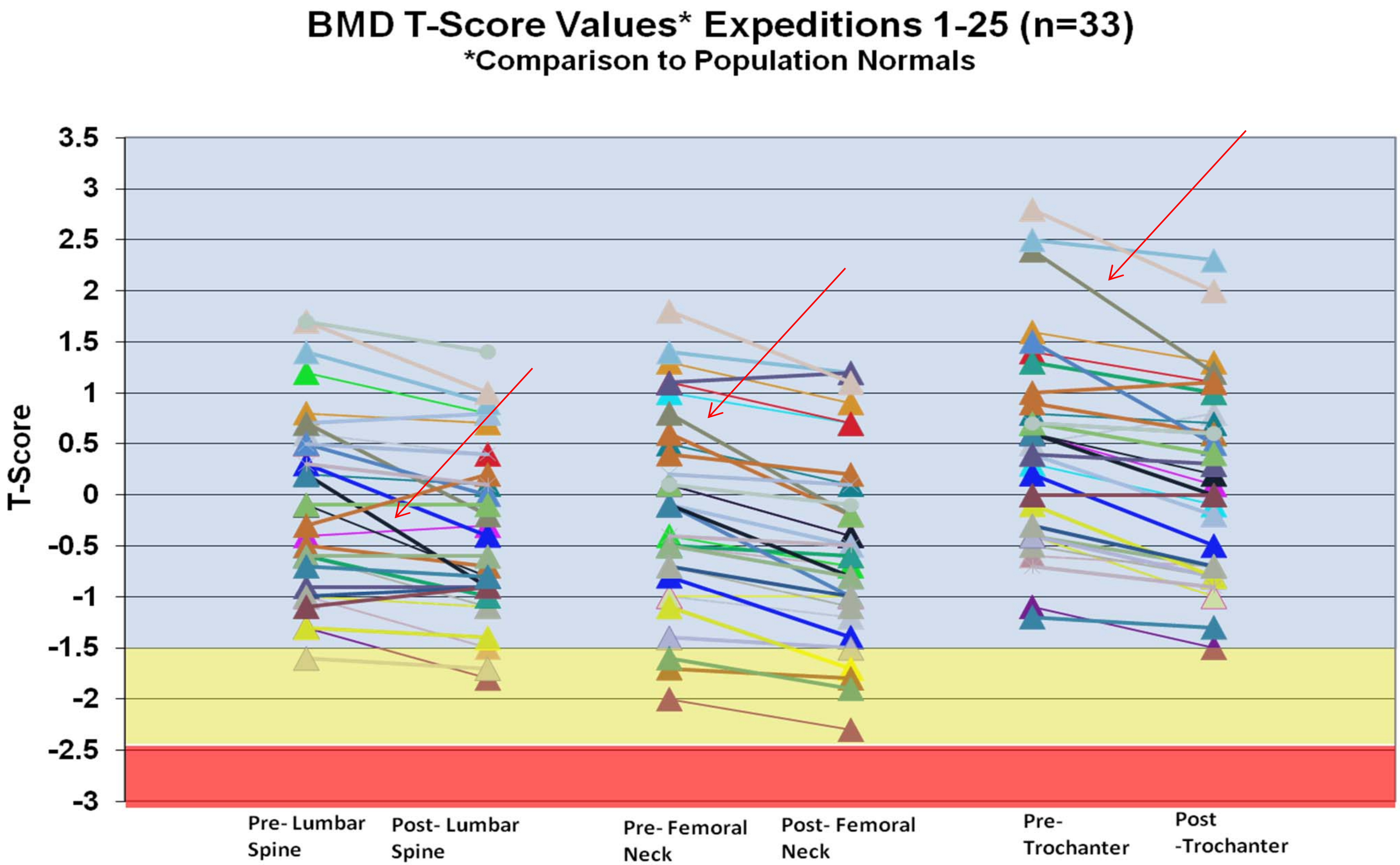
NON FRACTURES

Widely-applied surrogate for fracture

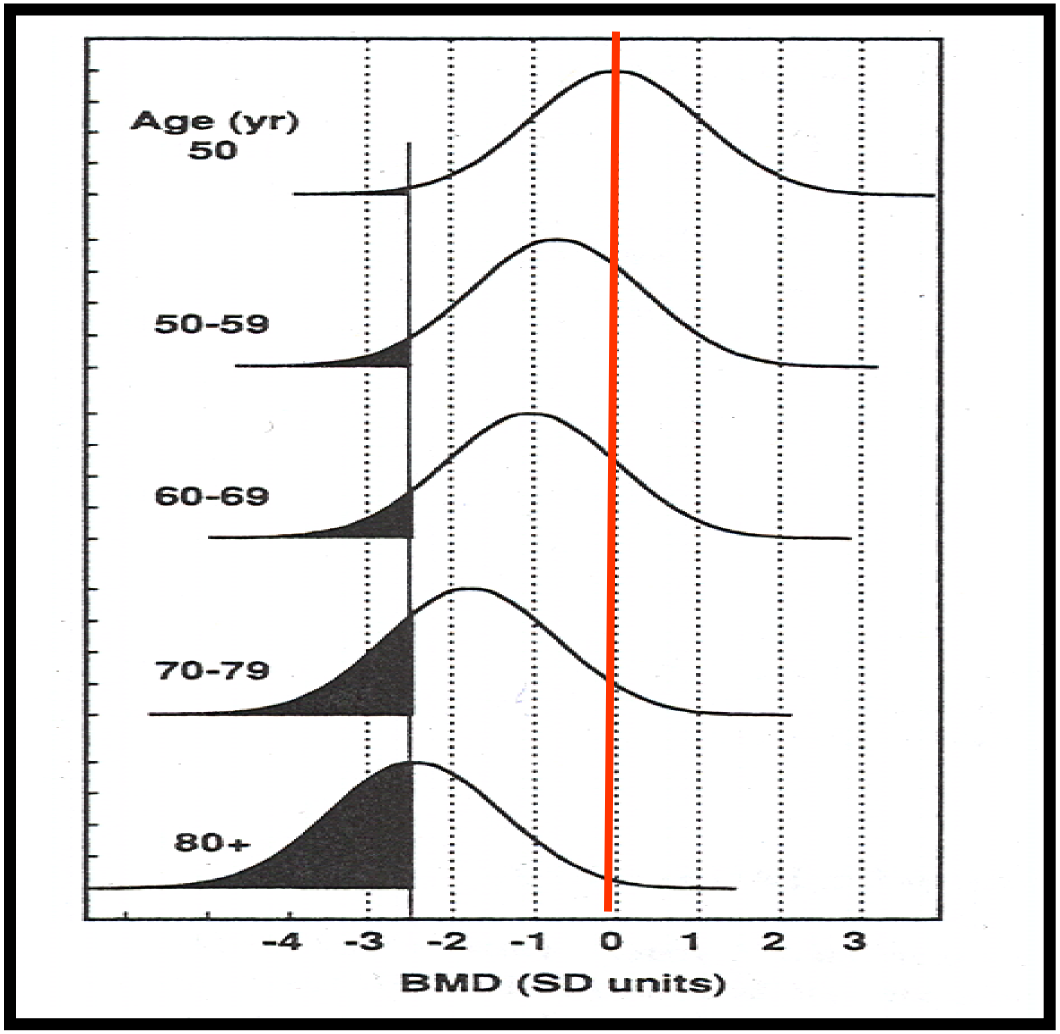
BONE STRENGTH IS INFLUENCED BY ADDITIONAL FACTORS THAT ARE NOT MEASURED BY DXA AREAL BMD.

Diagnostic Guidelines Not Meaningful for Astronauts

for peri- and postmenopausal women and men > 50 years.



Age is important risk factor for bone loss but the utility of BMD for < 50 years not clearly evident .*

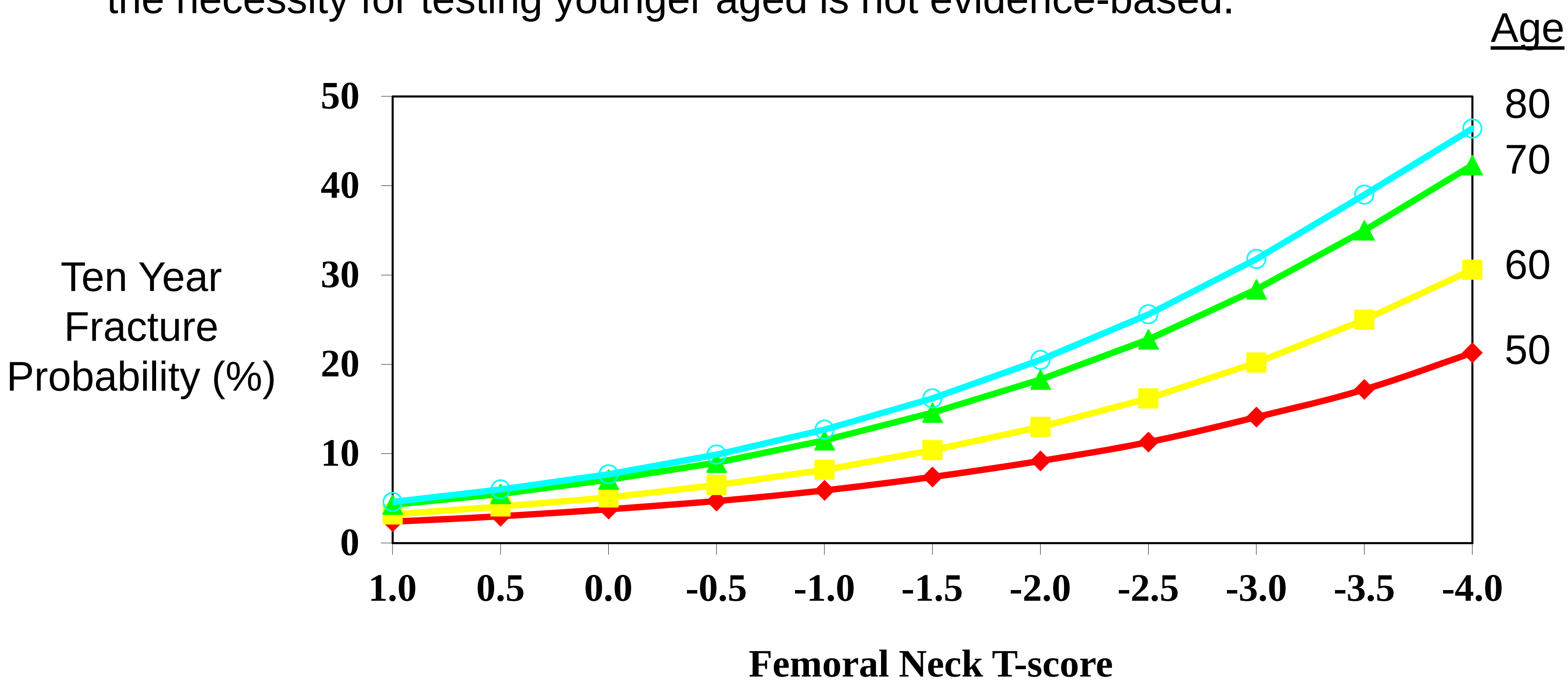


Kanis et al JBMR 9(8):1137, 1994

* The use of DXA BMD for surveillance of active astronauts is a unique application.

Risk for osteoporotic fractures is lower at younger ages.

Given the probability of fracture drives the requirement for interventions, the necessity for testing younger aged is not evidence-based.



Probability of first fracture of hip, distal forearm, proximal humerus, and symptomatic vertebral fracture in women of Malmö, Sweden.

Adapted from:
Kanis JA et al. *Osteoporosis Int*. 2001;12:989-995

Slide Courtesy of S. Petak, MD.

Uncertainty exists. Are the long-duration astronauts at risk?

WHAT COULD BE MEASURED TO DEFINE A RARE RISK IN YOUNGER PERSONS?

History of Bone Imaging in Space

Gemini — Space Shuttle

Mercury — 1961-63

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

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

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

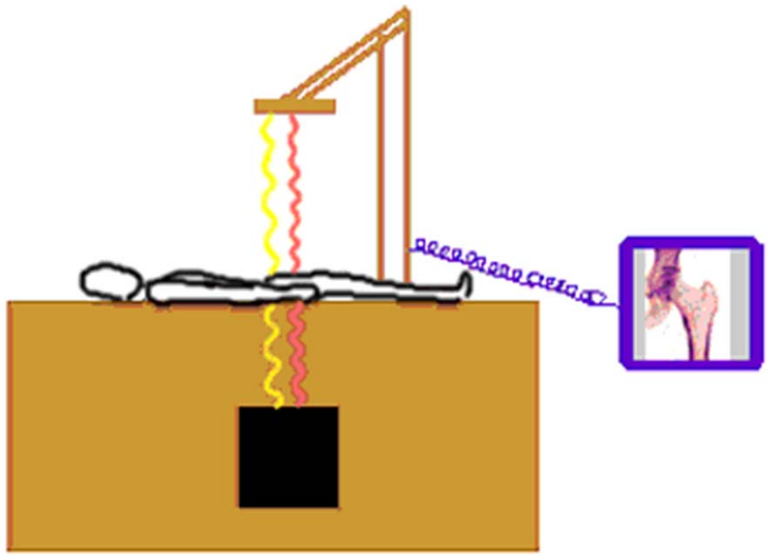
ISS — 2000-present
- **DXA**
- **QCT**
- ***HR3DpQCT (ESA)***

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

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

Slide courtesy of Mayo Clinic adapted from Dr. Jean Sibonga, NASA JSC

Dual-energy X-ray Absorptiometry-DXA



Measurement of bone mineral in 2-d **projection** of bone [BMD_a] g/cm^2

•Improved precision; Low radiation; Shorter scan times; BMD measures over multiple skeletal sites

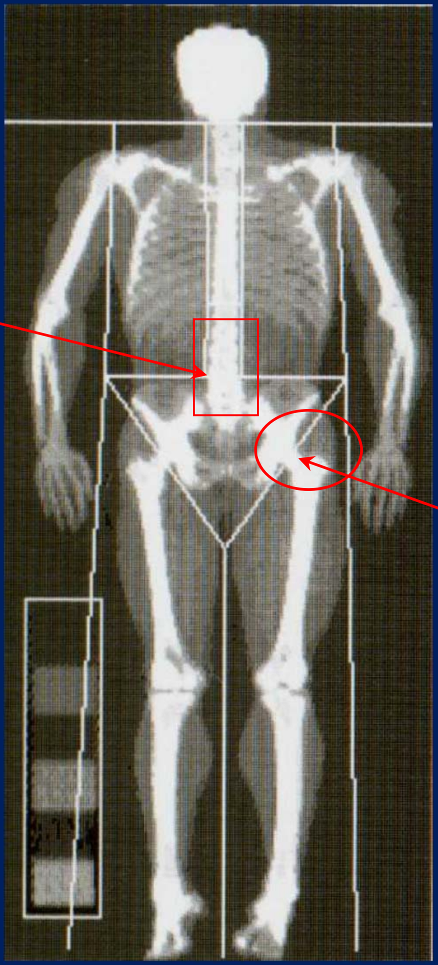
• Validated in numerous population studies for fracture prediction

• Long established, widely-applied surrogate for fracture outcome – become NASA standards, but T-scores give only Relative Risks

DXA: BMD losses are site-specific and rapid

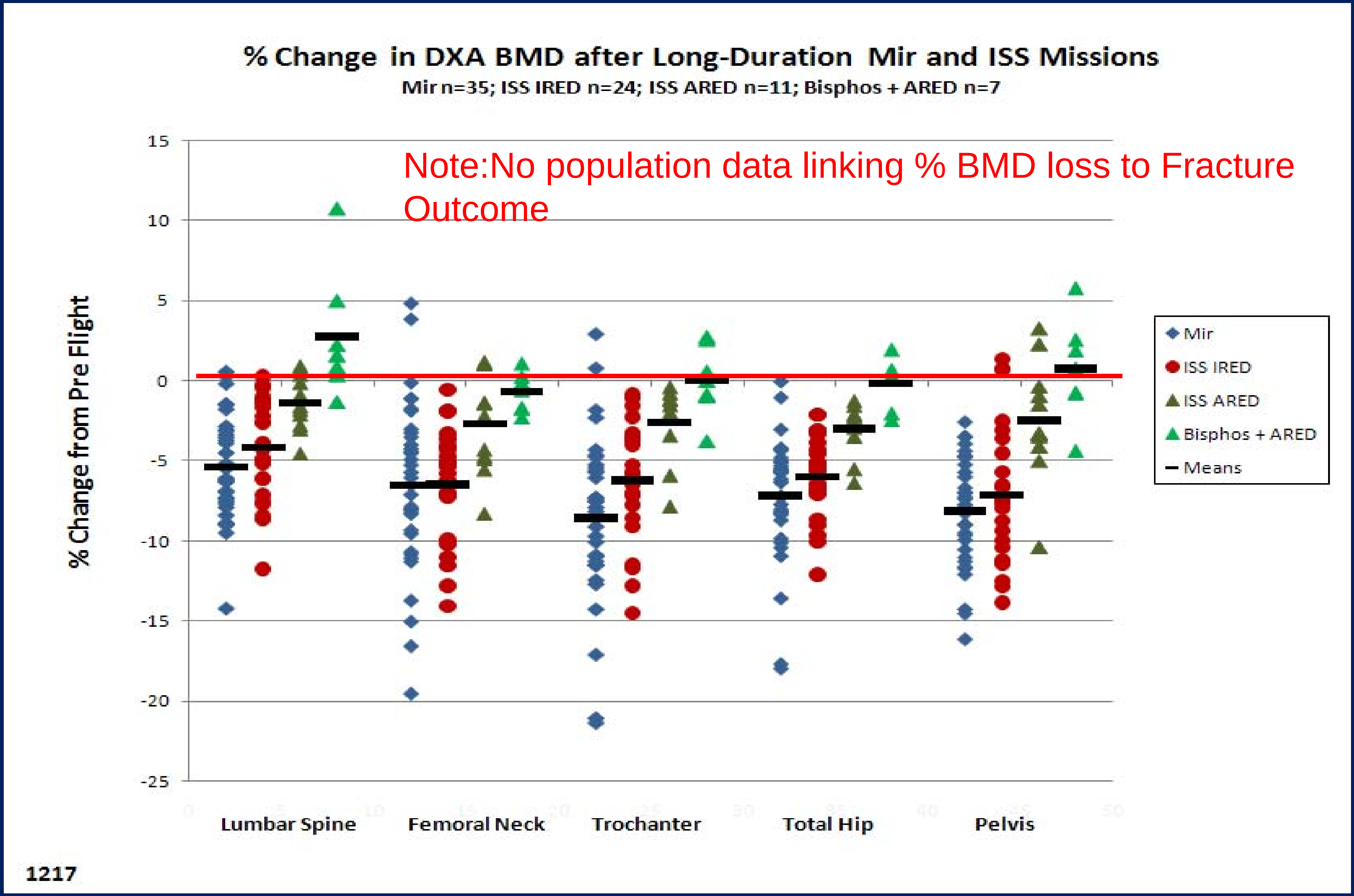
vs. 0.5 – 1.0 % BMD **loss/year** in the aged

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

Effects of exercise regimens described using DXA BMD



* Updated data since 2010 Bone Summit

A Limitation: DXA Cannot distinguish changes in bone size – a contributor to bone strength.

Effect of geometry on long bone strength

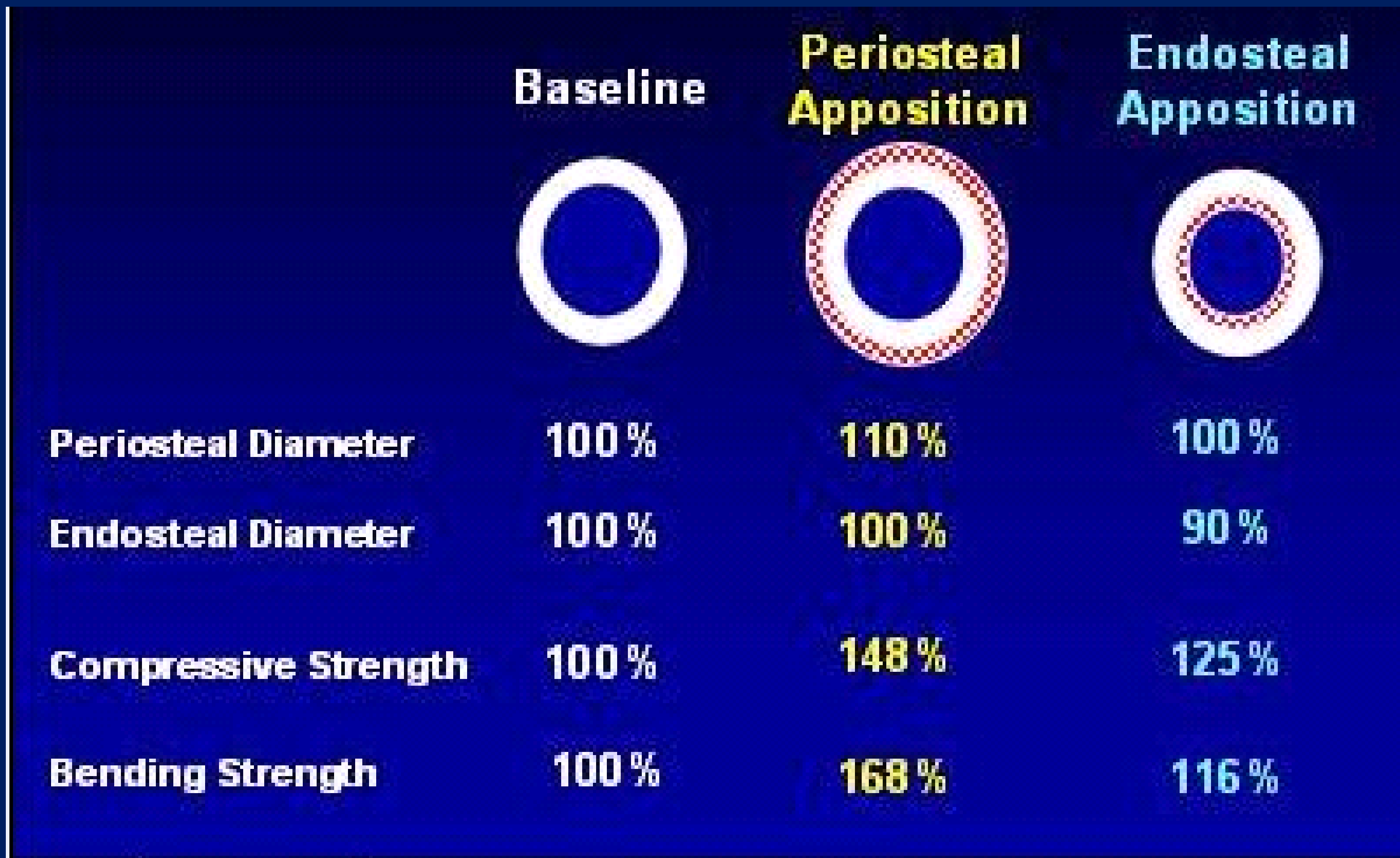
aBMD Areal (g/cm^2)	1	1	1
Compressive Strength	1	1.7	2.3
Bending Strength	1	4	8

Mary Bouxsein, Ph.D. Bone Geometry and Skeletal Fragility, May 2005

Exercise changes <u>geometry</u> of whole bone (adult skeleton)- not detected by DXA.

1. Haapasalo H, Sievanan H, Kannus P, Heinonen A, Oja P, Vuori I. 1996 **<u>Dimensions and estimated mechanical characteristics of the humerus after long-term tennis loading</u>**. J Bone Miner Res. 11:864-872.
2. Adami S, Gatto D, Braga V, Bianchini D, Rossini M. 1999 **<u>Site-specific effects of strength training on bone structure and geometry of ultradistal radius in postmenopausal women.</u>** J Bone Miner Res. 14(1):120-124.
3. Haapasalo H, Kontulainen S, Sievanen H, Kannus P, Jarvinen M, Vuori I. 2000 **<u>Exercise-induced bone gain is due to enlargement in bone size without a change in volumetric bone density: a peripheral quantitative computed tomography study of the upper arms of male tennis players</u>**. Bone 17(3):351-357.
4. Vainionpaa A, Korpelainan R, Sievanen H, Vihriaia E, Leppaluoto J, Jamasa T. 2007 **<u>Effect of impact exercise and its intensity on bone geometry at weight-bearing tibia and femur</u>**. Bone 40(3):604-611.
5. Hind K, Gannon L, Whatley, Cooke C, Truscott J. 2011 **<u>Bone cross-sectional geometry in male runners, gymnasts, swimmers and non-athletic controls: a hip-structural analysis study</u>**. Eur J Appl Physiol . e pub May 24

Changes in size, changes in bone strength.



	Baseline	Periosteal Apposition	Endosteal Apposition
Periosteal Diameter	100 %	110 %	100 %
Endosteal Diameter	100 %	100 %	90 %
Compressive Strength	100 %	148 %	125 %
Bending Strength	100 %	168 %	116 %

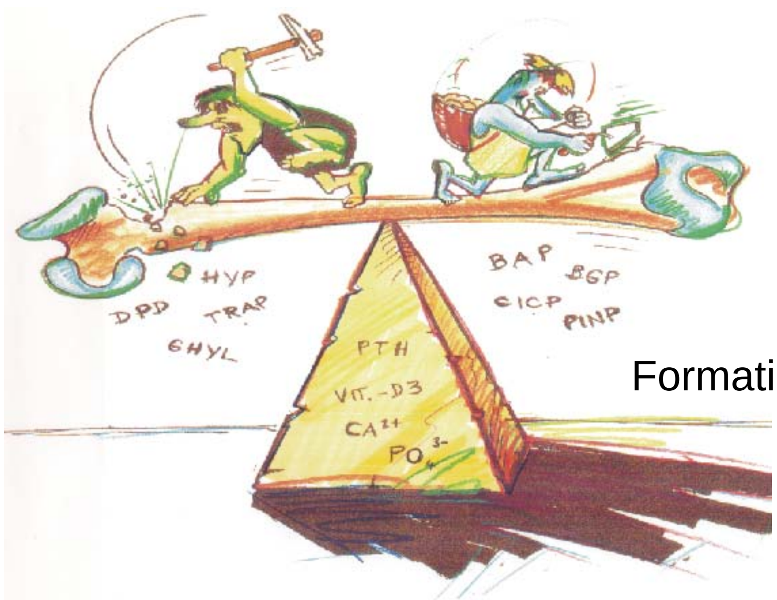
Slide courtesy of M. Bouxsein, PhD

Two Functions of the Skeleton- increasing understanding by biochemistry

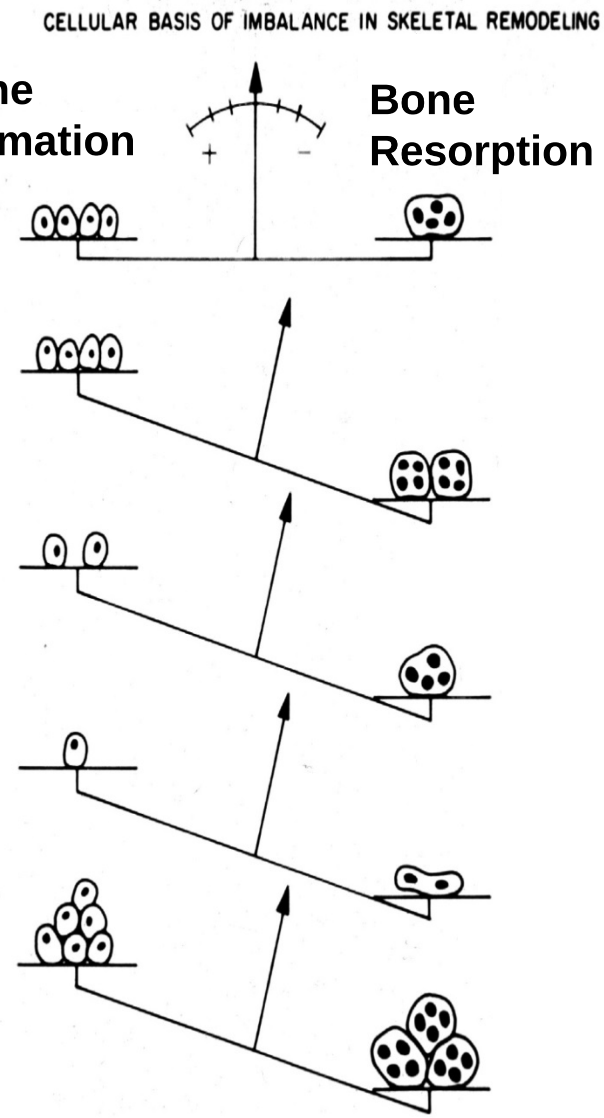
Mineral Reservoir

Structural Framework

Resorption Biochemical Markers



Formation Biochemical Markers



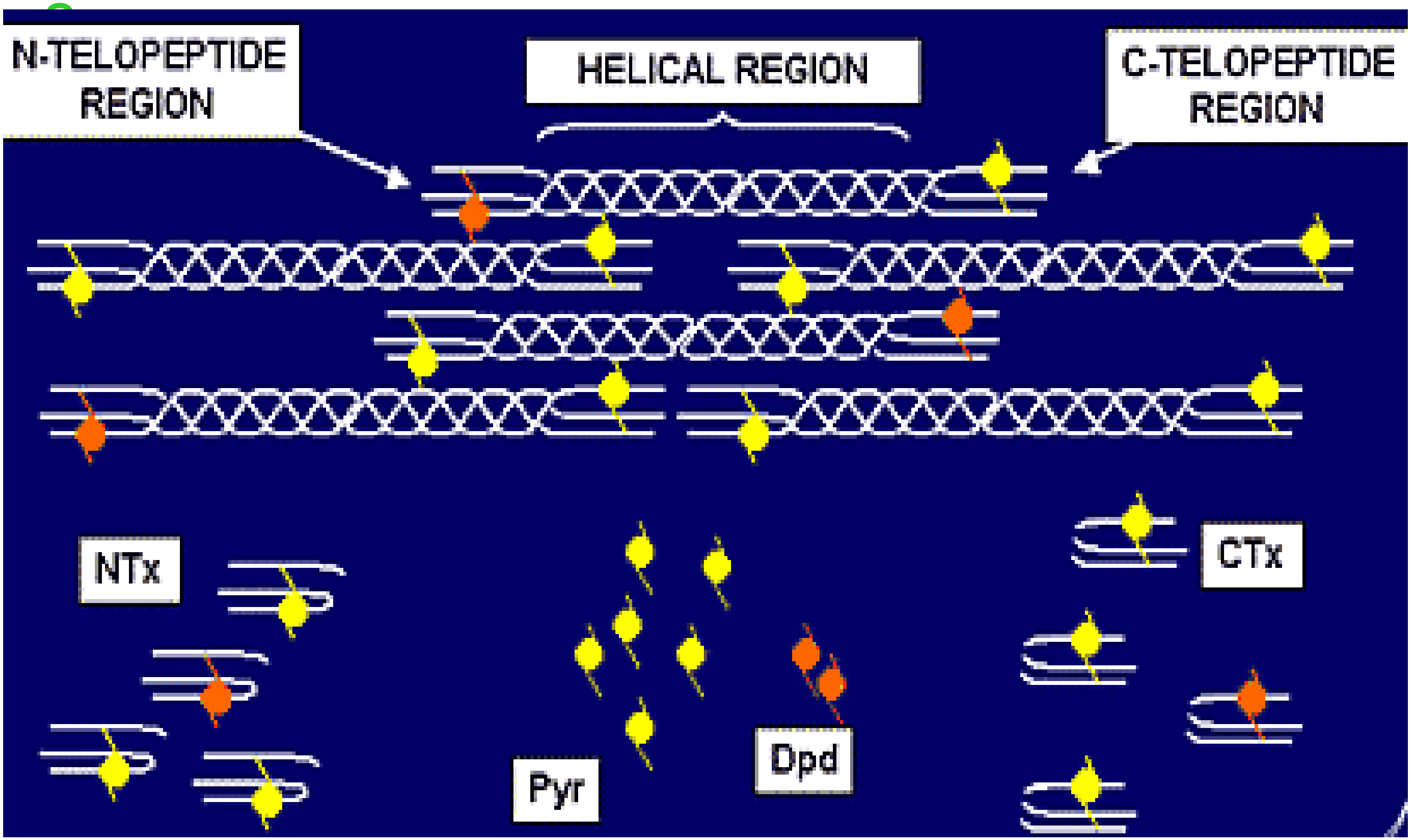
Bone Formation

Bone Resorption

Osteoblasts

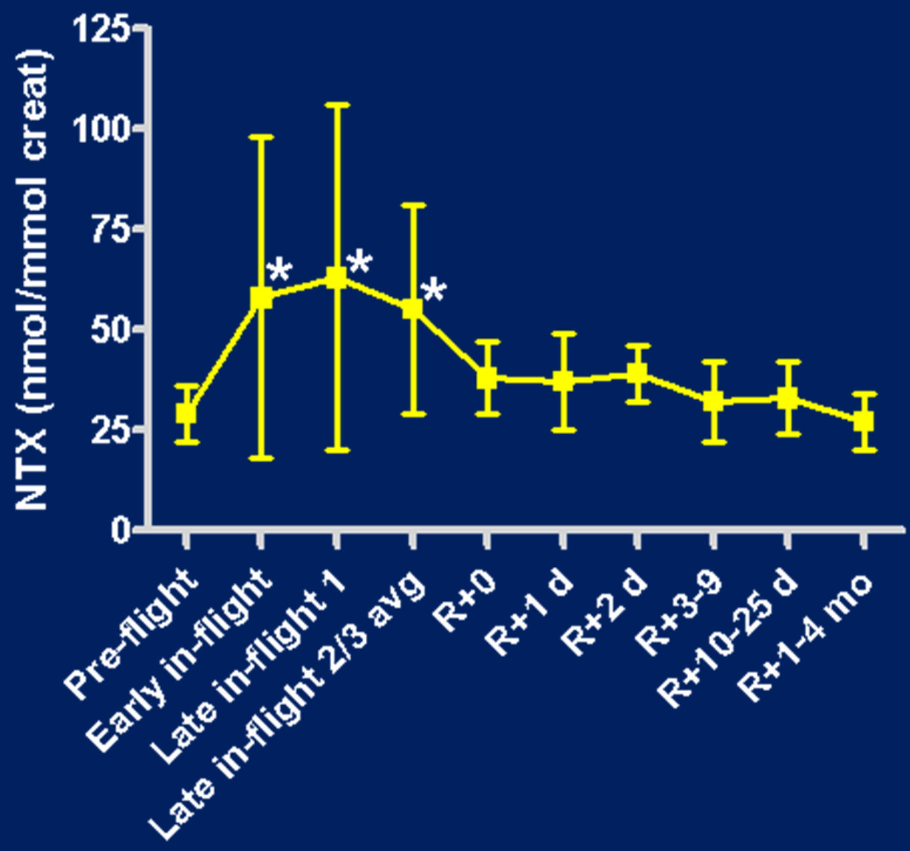
Osteoclasts

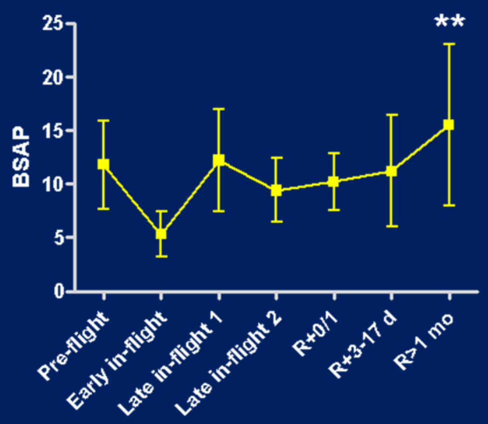
Serum and urinary biomarkers are by-products of bone <u>turnover</u> and bone cell activity.

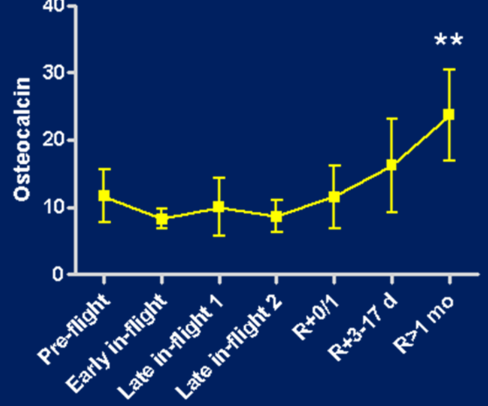


Bone breakdown is increased, formation is uncoupled from resorption, and bone gain and loss are unbalanced*

Reflects changes in bone cells but not where bone mass is lost.





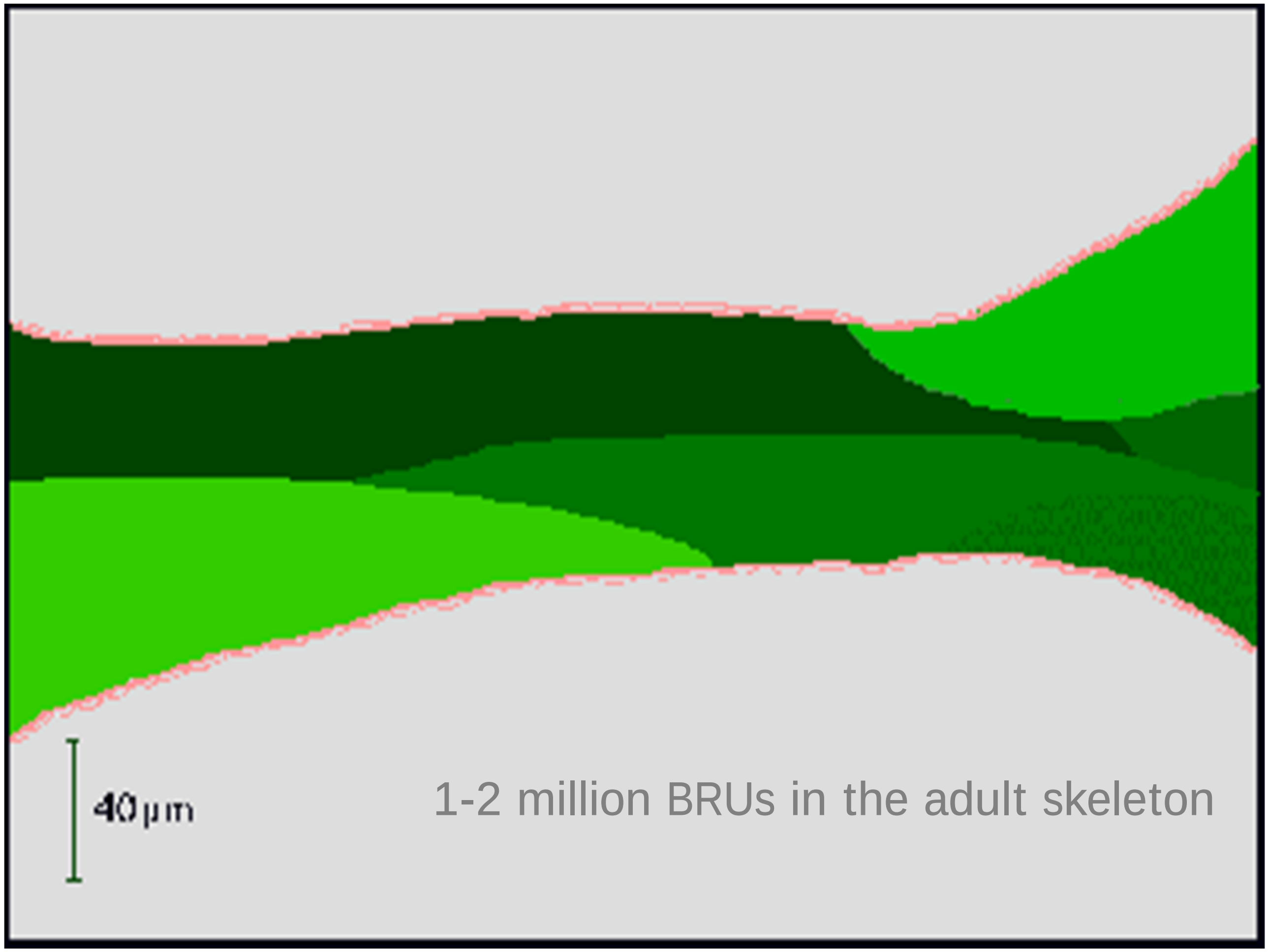


(Smith et al, JBMR 2005); adapted by Sibonga

* Could lead to net bone loss in skeleton.

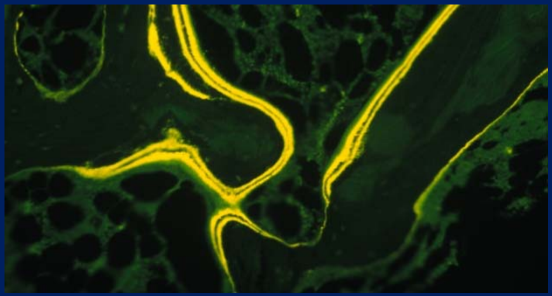
HIGHLY-REGULATED ACTIONS OF BONE CELLS on BONE TURNOVER.

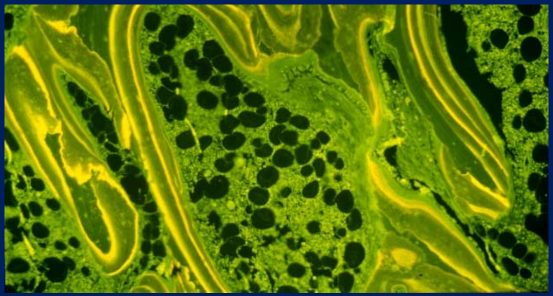
Under-filling, over-filling, balanced filling of the bone remodeling unit [BRU]
Can impact overall structural strength of whole bone (skeletal region).

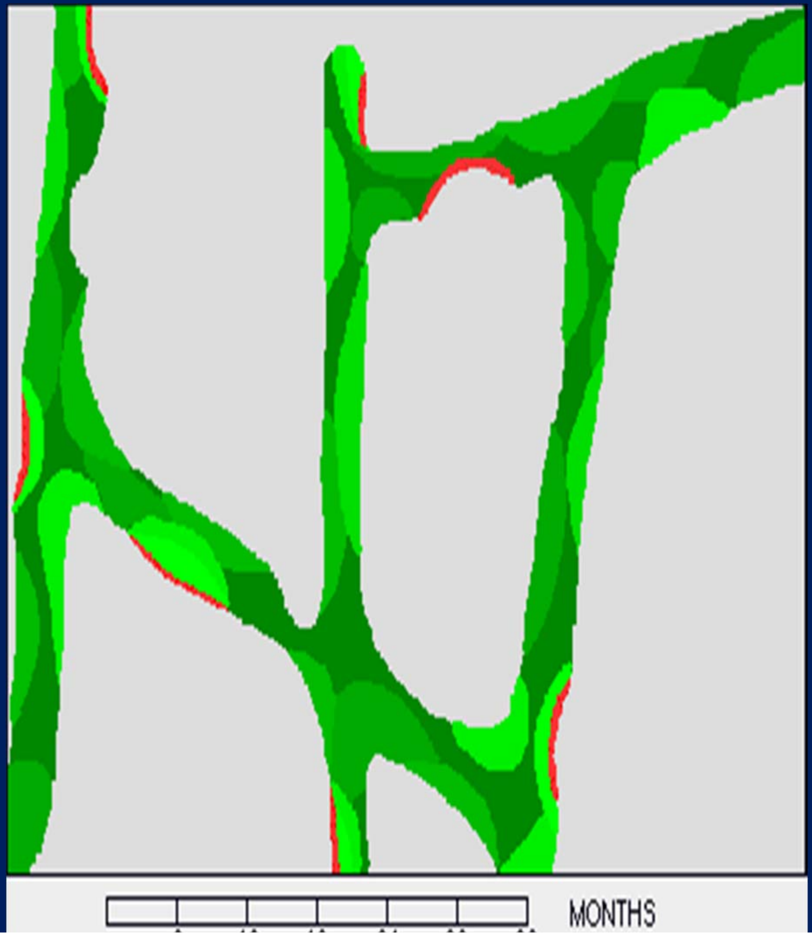


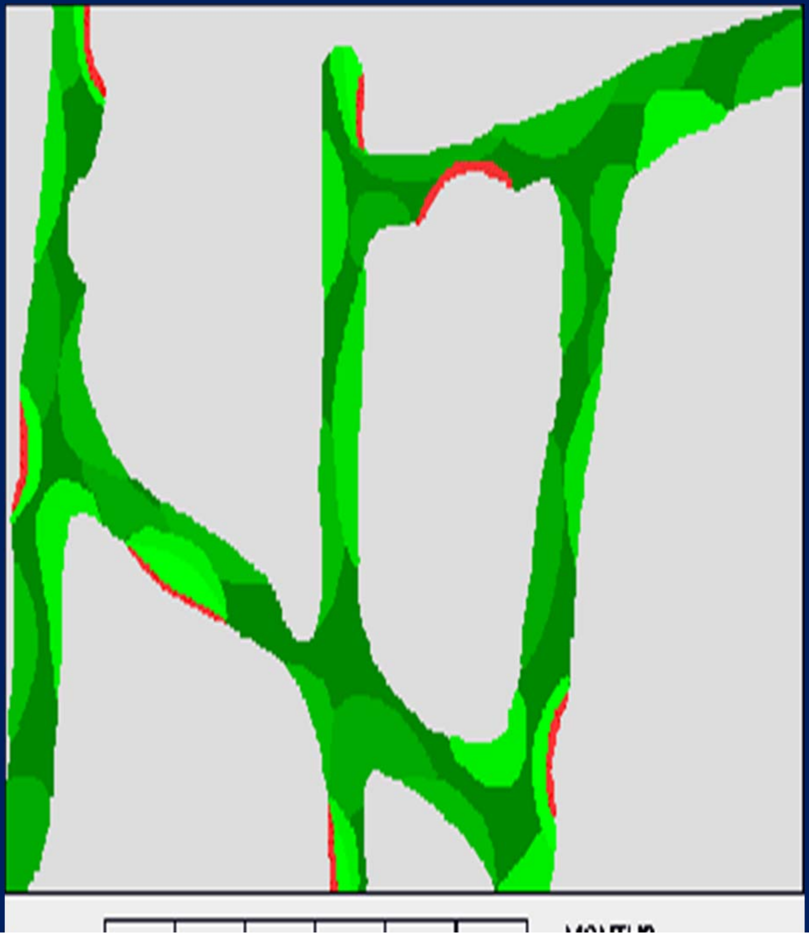
Remodeling of bone at the level of a single “BRU”

Some insight gained by comparison to Earth-based disorders of increased bone resorption.



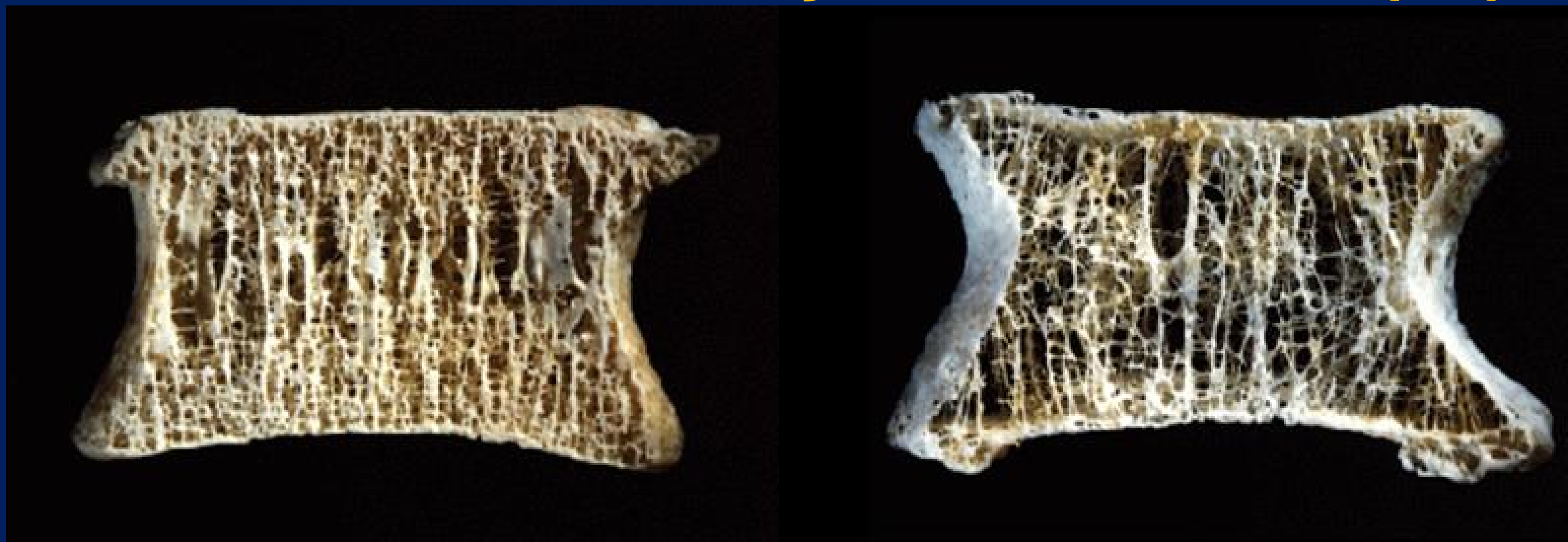


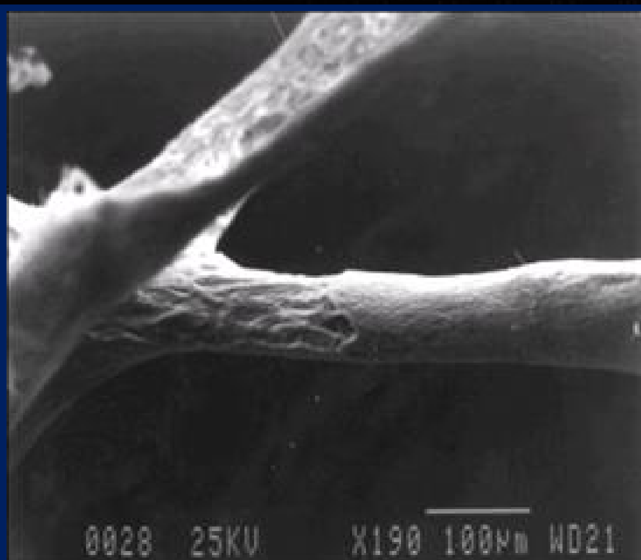




Representative manifestation on bone microarchitecture.

Clinical test not currently available for hip/spine.





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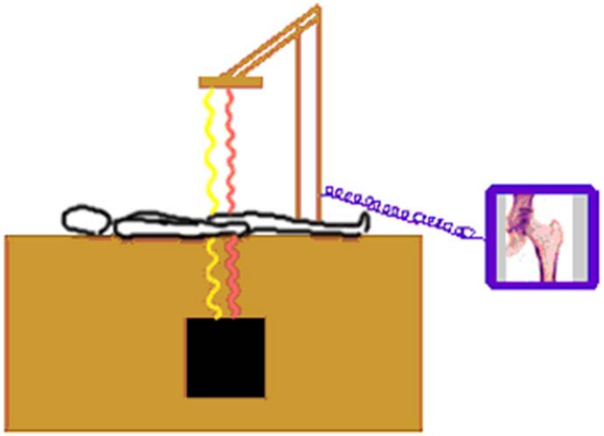
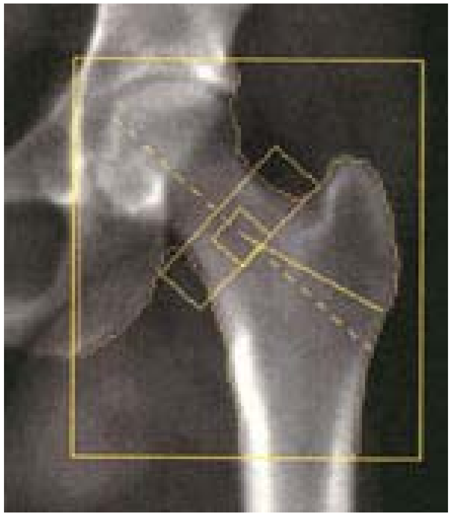
(Mosekilde, 2000; Seeman, 2002; Silva, 1997; Kleerekoper, 1985)

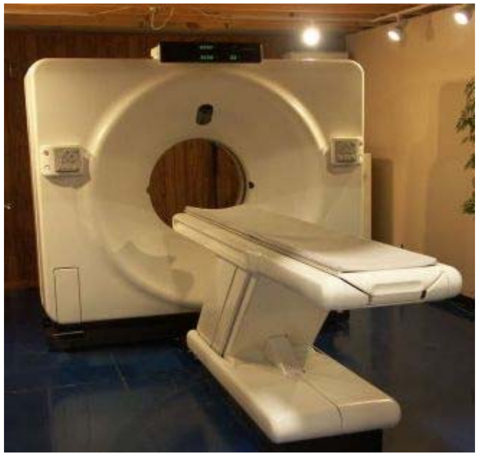
Densitometry & Reported Measurement

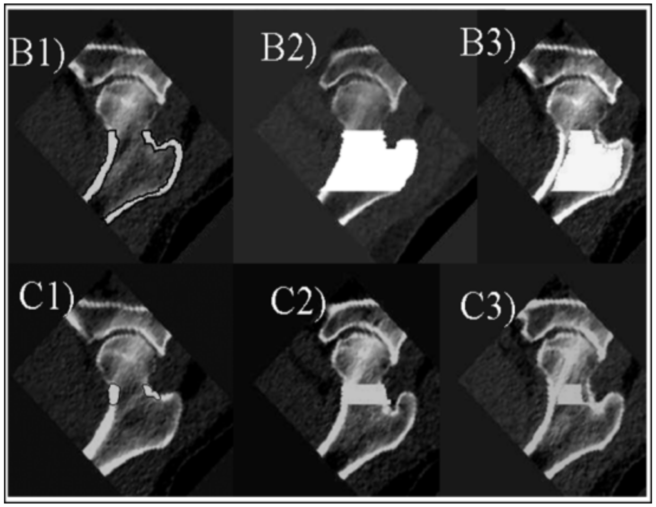




DXA reports areal BMD (aBMD)

g/cm^2 averaged for cortical + trabecular bone

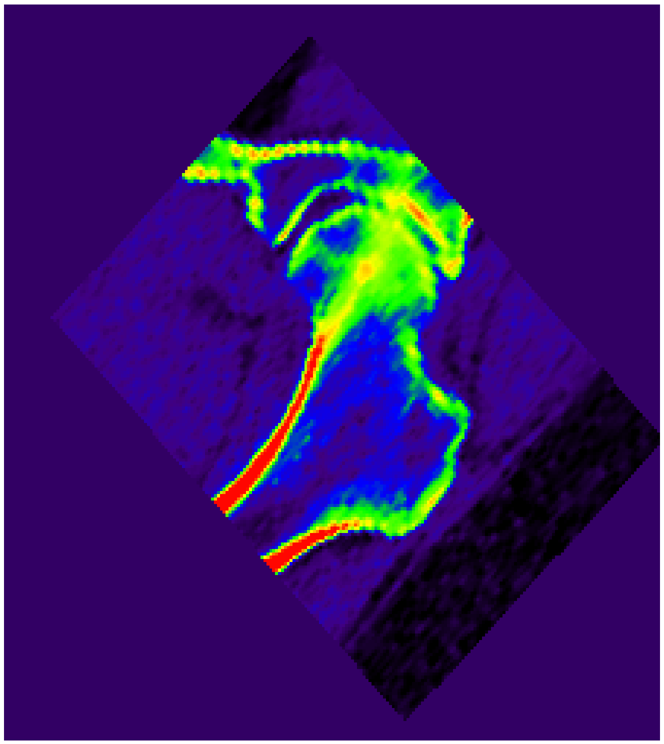




QCT quantifies volumetric BMD

g/cm^3 for separate cortical & trabecular bone

Research: QCT detects different rate of vBMD loss in separate bone compartments of hip. (n=16 ISS volunteers)



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

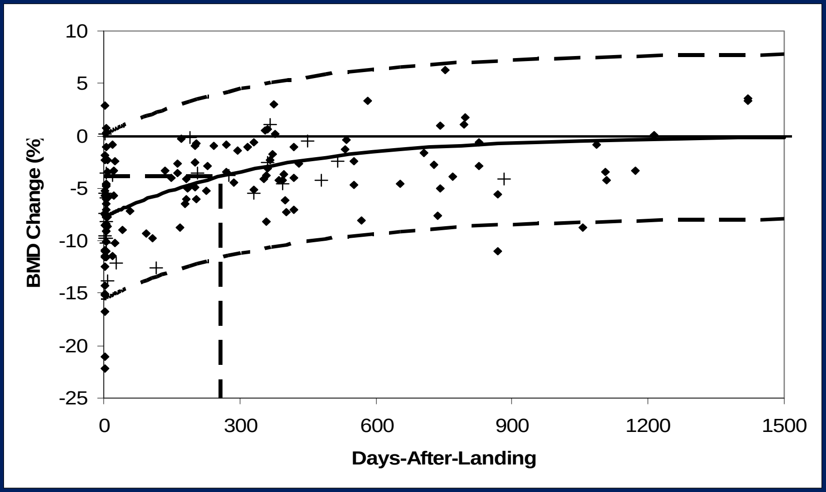
LeBlanc, J Musculoskelet Neuronal Interact. 2000 ;
Lang , J Bone Miner Res, 2004;

Path to Risk Reduction

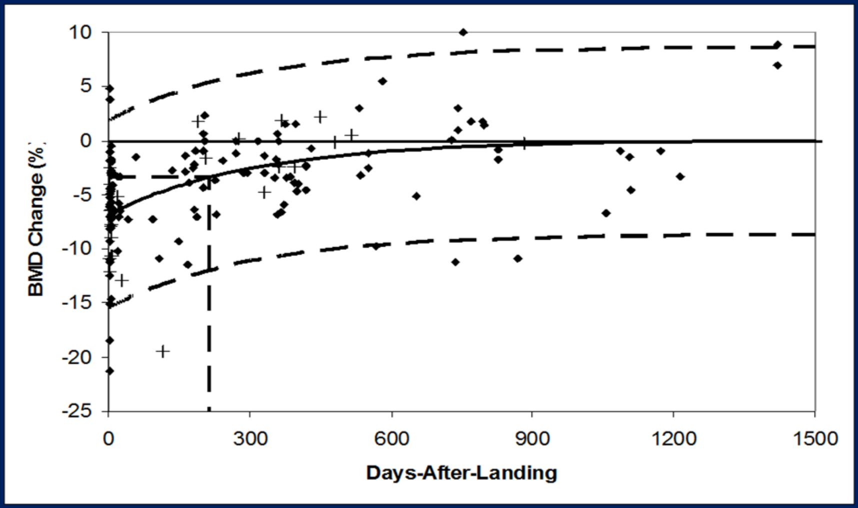
HOW CAN THESE RESEARCH DATA BE USED *CLINICALLY* IN THE ABSENCE OF FRACTURE DATA?

So what?

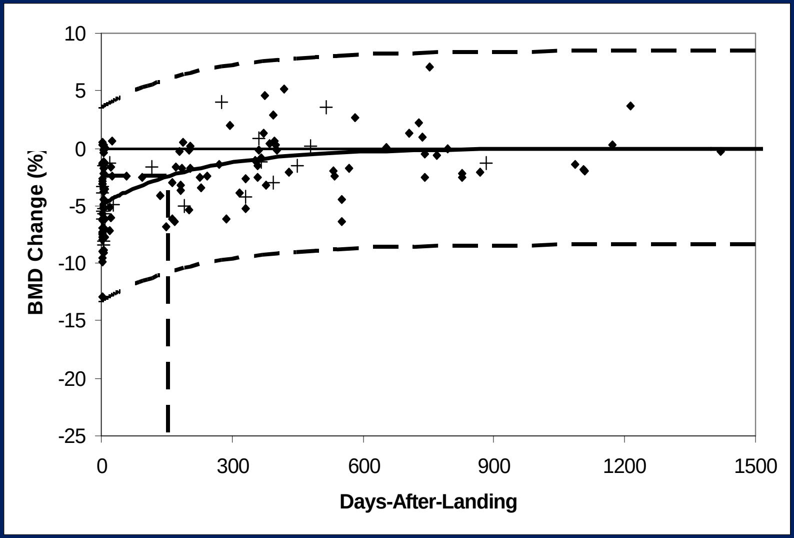
DXA BMD increases in Postflight – but not sufficient to assess recovery of *bone strength*.



Trochanter



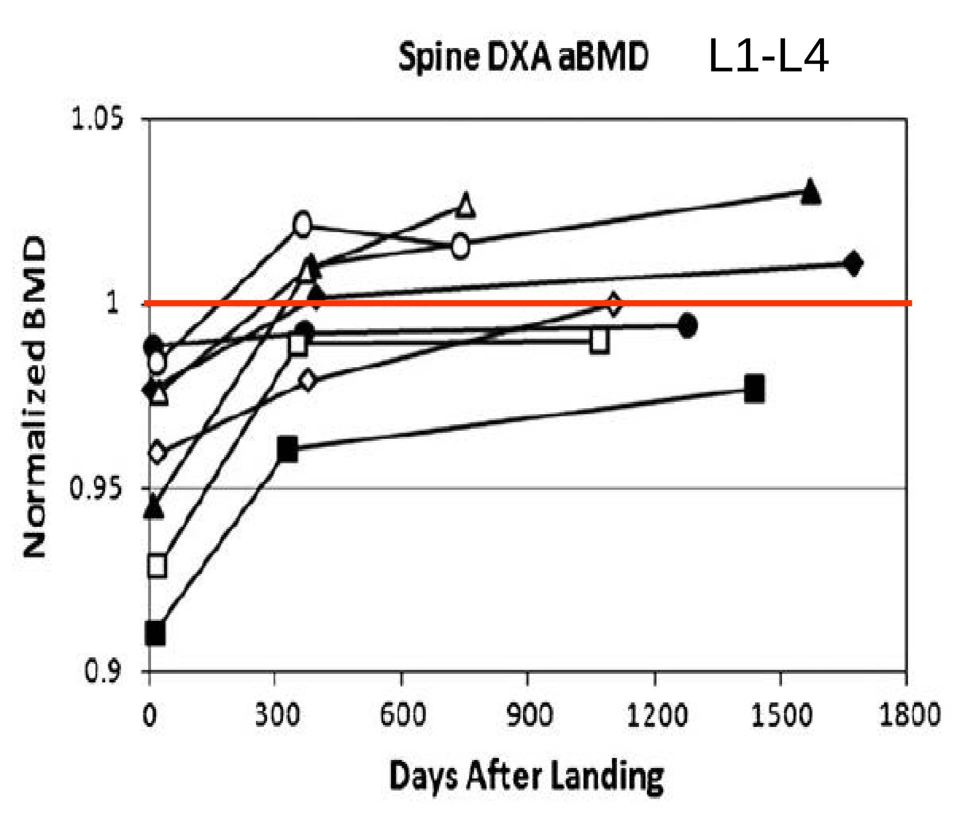
Femoral neck

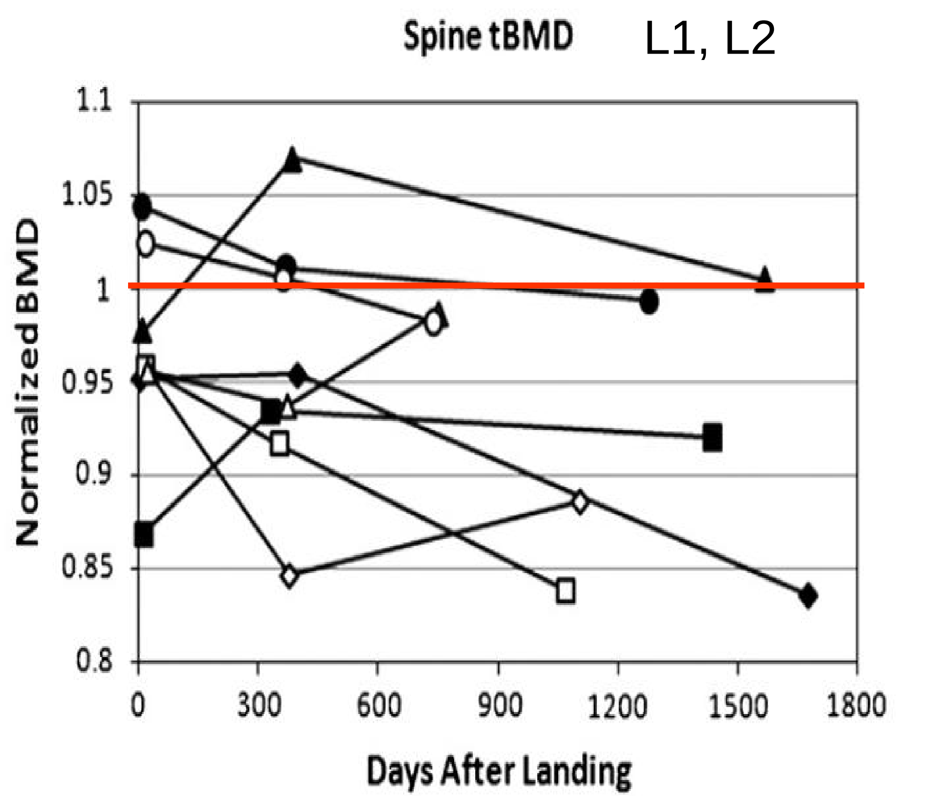


Lumbar Spine

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

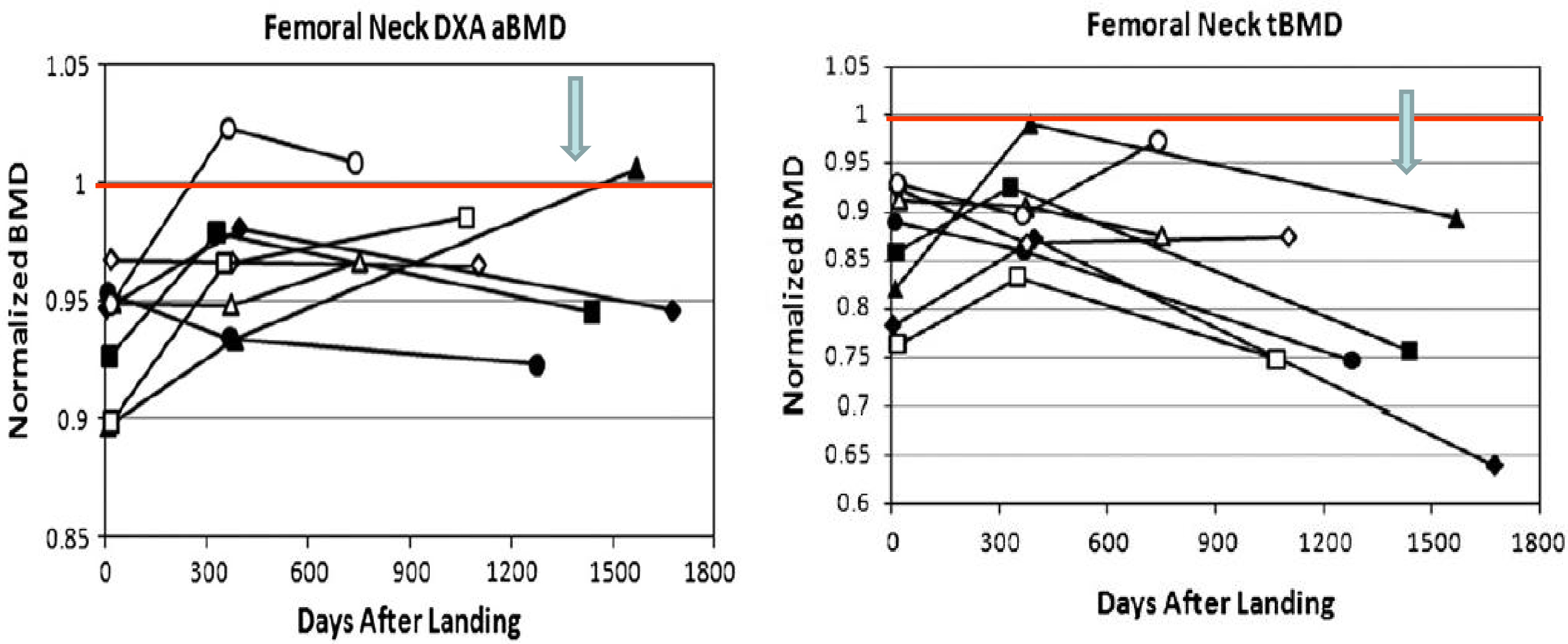
DXA & QCT Spine in 8 ISS astronauts :
Expanding our Understanding of Recovery After Spaceflight





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

DXA & QCT Femoral Neck



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

Clinical Evidence: QCT measures are independent predictors of hip fracture to supplement aBMD.

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

Journal of Bone and Mineral Research
Volume 26, Issue 4, Article first published online: 23 MAR 2011
Abstract | Full Article (HTML) | References | Supporting Information
Cited By

NASA Johnson Space Center

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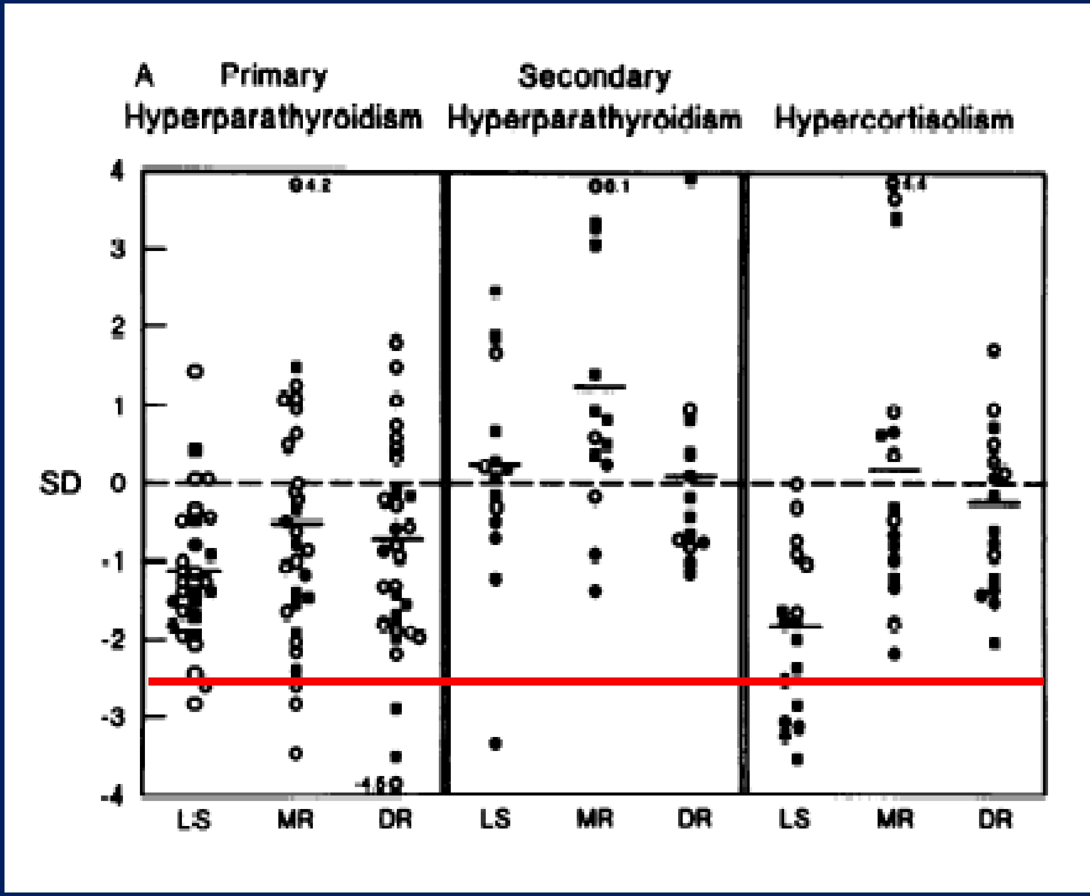
In Vivo Discrimination of Hip Fracture With Quantitative Computed Tomography: Results From the Prospective European Femur Fracture Study (EFFECT)

Valérie Danielle Bousson,[1,2] Judith Adams,[3] Klaus Engelke,[4] Mounir Aout,[5] Martine Cohen-Solal,[6] Catherine Bergot,[2] Didier Haguenauer,[7] Daniele Goldberg,[8] Karine Champion,[9] Redha Aksouh,[1] Eric Vicaut,[5] and Jean-Denis Laredo[1,2]

DXA BMD not as good of predictor of hip fractures for the "complicated patient" i.e., non-age-related bone loss.

- Different patterns of bone "loss" (cortical vs. trabecular) with different metabolic disorders …analogous to spaceflight effects

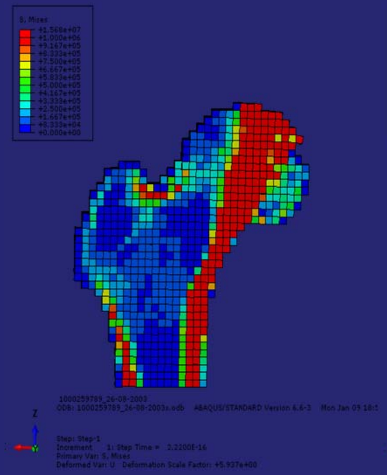


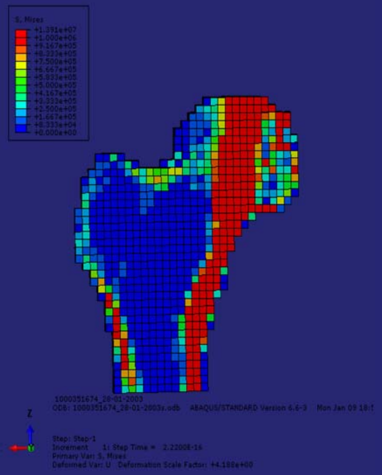
Seeman, JCI 1992
Slide courtesy of Dr. Amin, MD
Dual Photon Absorptiometry (DPA)

Describing changes in hip bone strength with Finite Element Modeling/Analysis: Emerging data from population studies.

- **<u>Male-female differences in prediction of hip fracture during finite element analysis</u>.** Keyak JH, Sigurdsson S, Karlsdottir G, Oskarsdottir D, Sigmarsdottir A, Zhao S, Kornak J, Harris TB, Sigurdsson G, Jonsson BY, Siggeirsdottir K, Eiriksdottir G, Gudnason V, Lang TR. Bone. 2011;48(6):1239-1245.
- **<u>Association of hip strength estimates by finite –element analysis with fractures in women and men</u>**. Amin S,, Kopperdahl DL, Melton LJ 3rd, Achenbach SJ, Therneau TM, Riggs BL, Keaveny TM, Khosla S. J Bone Miner Res. 2011;26(7):1593-1600.
- **<u>Age-dependence of femoral strength in white women and men.</u>** Keaveny TM, Kopperdahl DL, Melton III LJ, Hoffmann PF, Amin S, Riggs BL, Khosla S. J Bone Miner Res. 2010;25(5):994-1001.
- **<u>Osteoporotic Fractures in Med Study Group. Finite element analysis of the proximal femur and hip fracture risk in older men</u>**. Orwoll ES, Marshall LM, Nielson CM, Cummings SR, Lapidus J, Cauley JA, Ensrud K, Lane N, Hoffmann PR, Kopperdahl DL, Keaveny TM J Bone Miner Res. 2009;24(3):475–483.

Finite Element Models of QCT data – "FE modeling" is a computational tool to estimate failure loads ("strength") of complex structures.



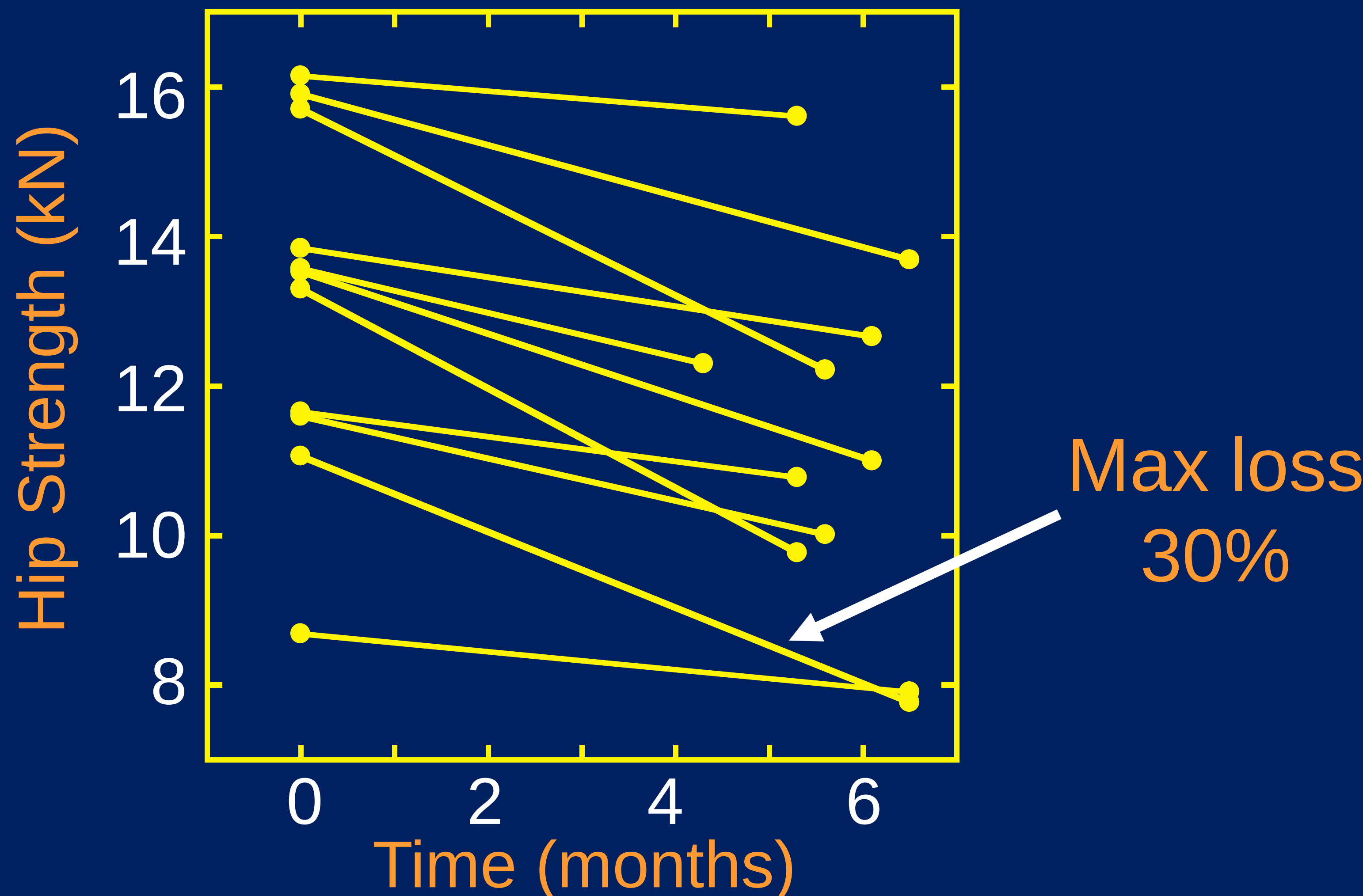


J. Keyak et al, 1998, 2001, 2005

Images courtesy of Dr. J Keyak

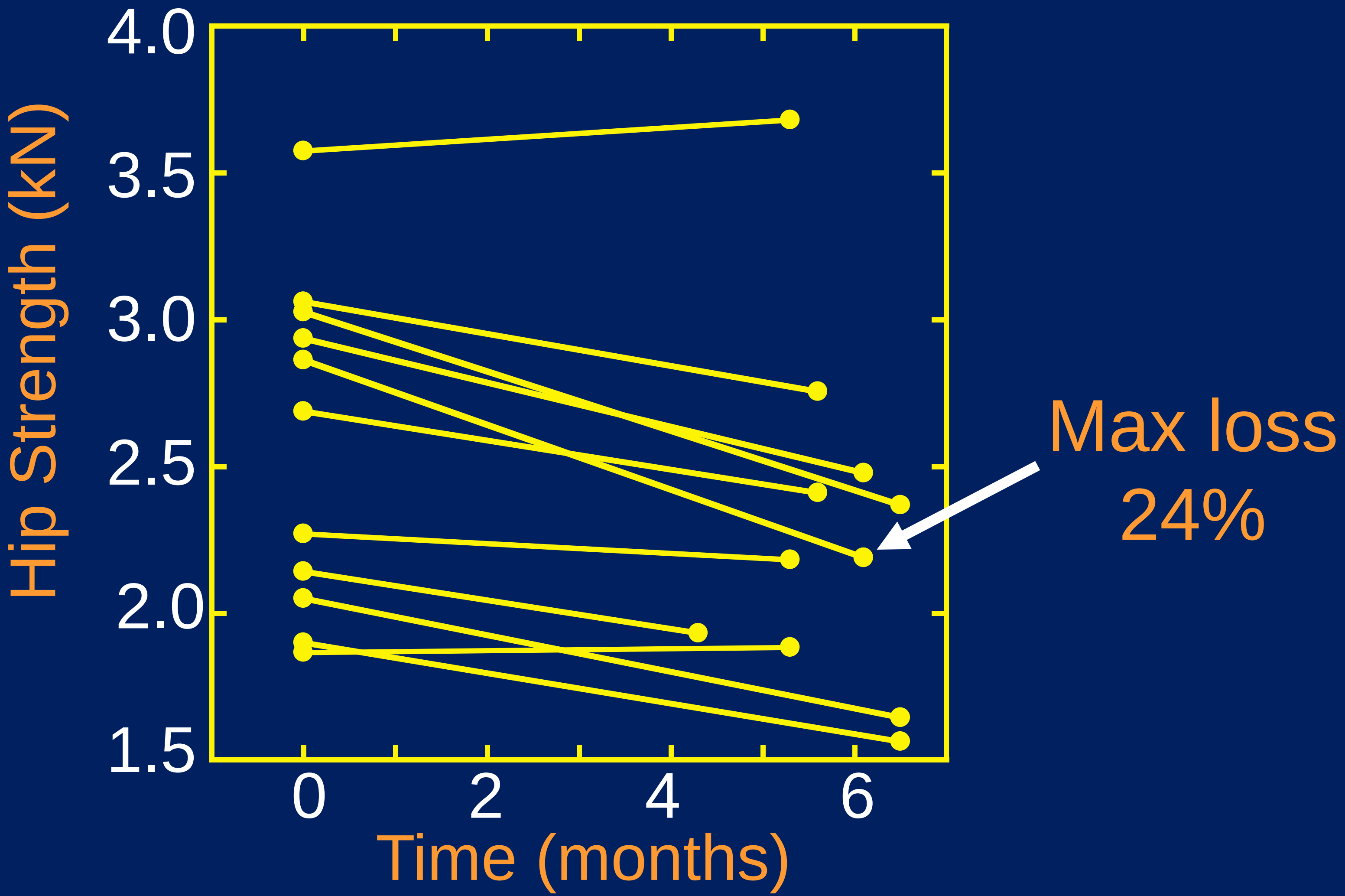
Individual Results

Stance Loading (4 to 30% loss in strength)

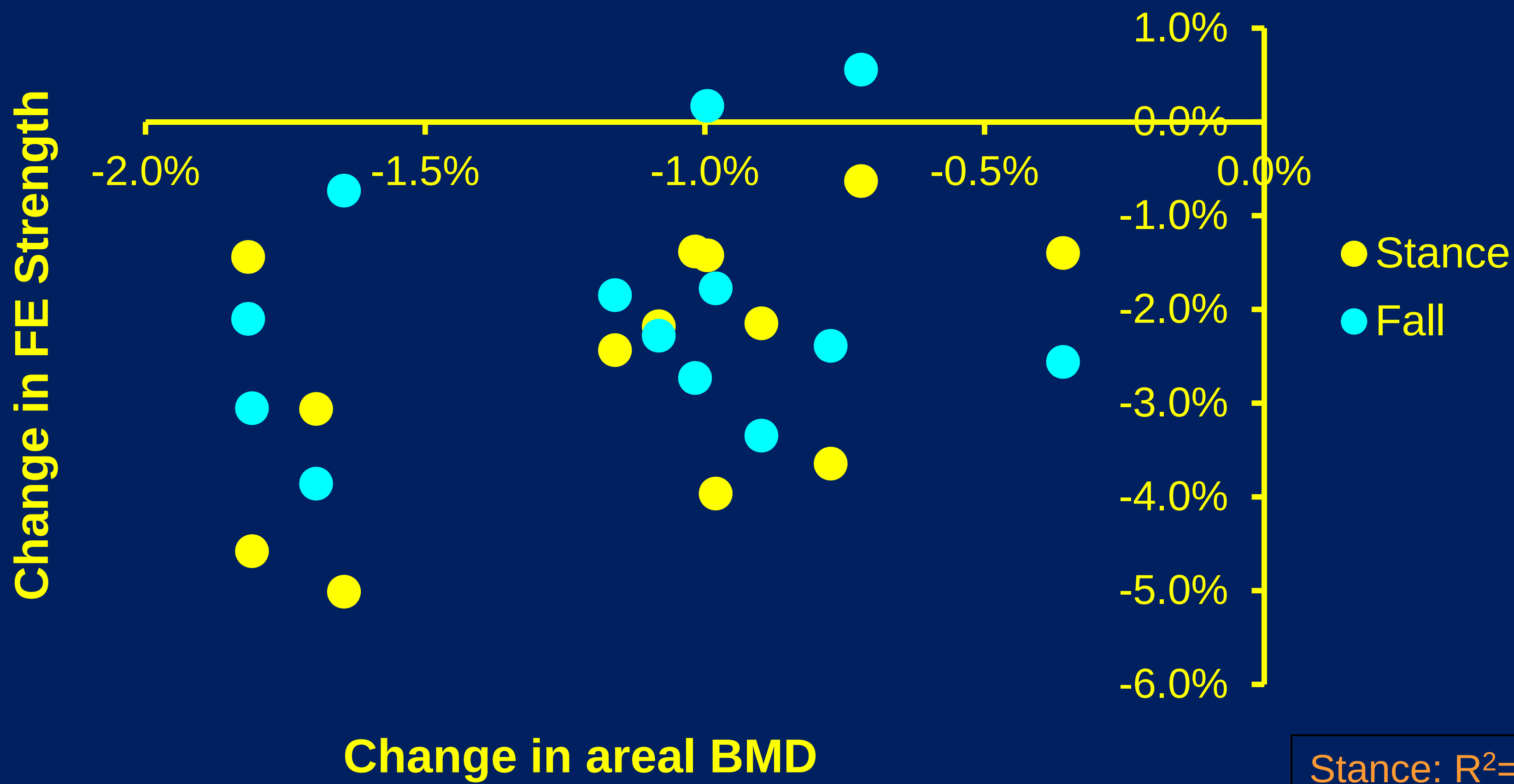


Individual Results

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



Astronaut Data (n=11): Space effects on surrogates of bone strength do not correlate.



Stance: R^2=0.23

Fall: R^2=0.05

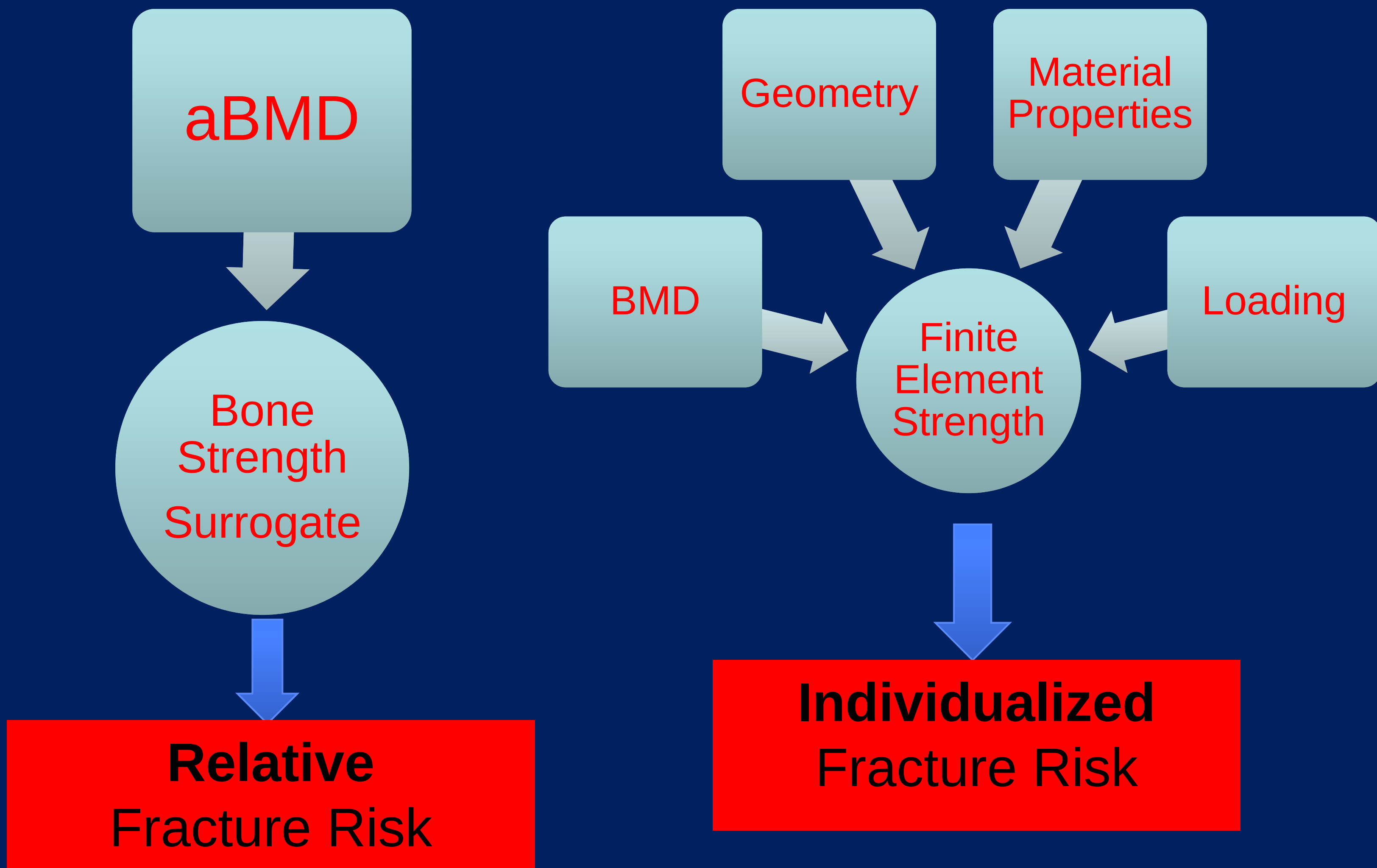
Slides courtesy of J Keyak; Bone. 2009 Mar;44(3):449-53.

Which is better?

Which is better?

Fracture risk by 1 measurement or by > 1 measurement?

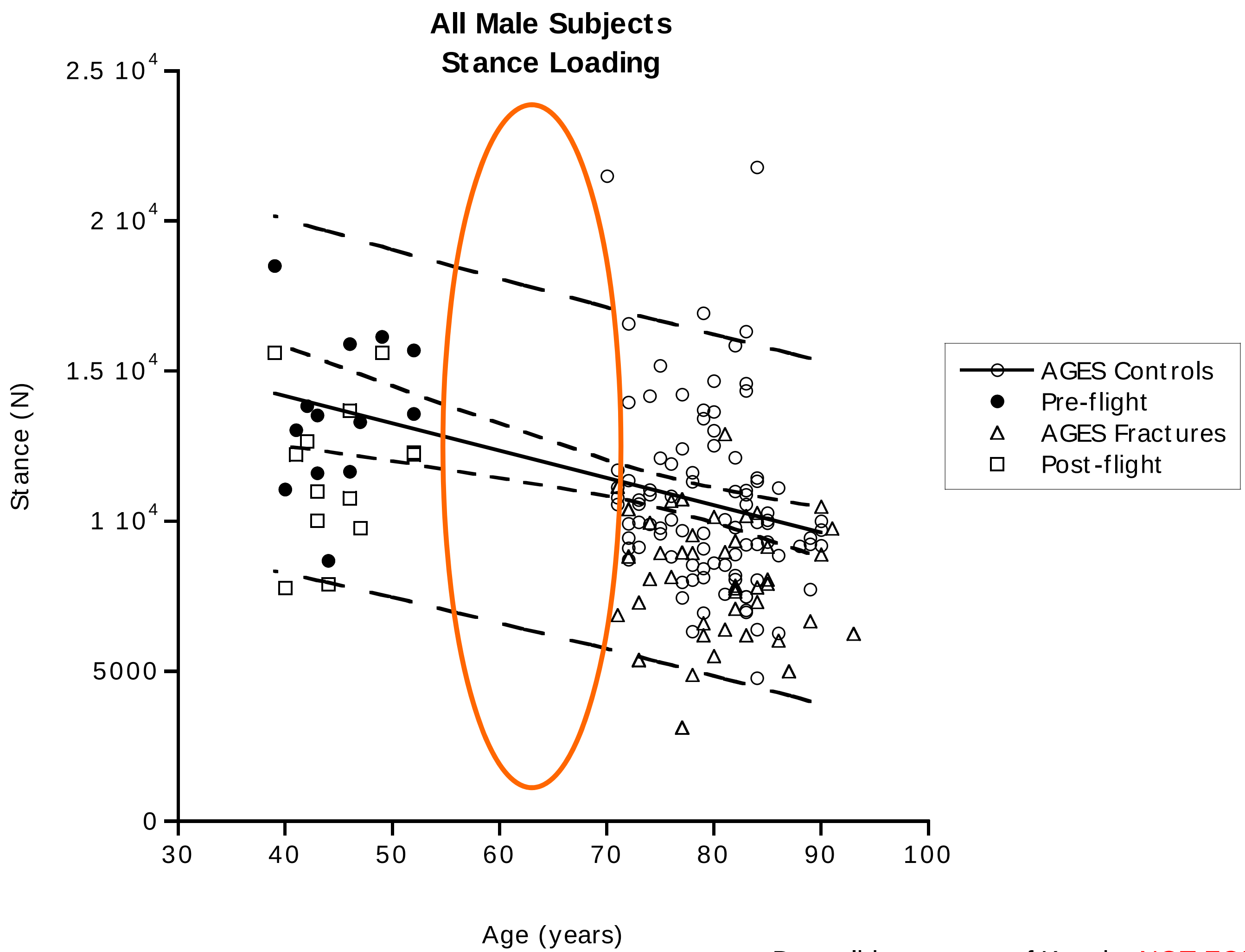
It's not complicated.



Additional cut-points for Bone Health: FE Modeling of QCT Scans from Population Studies

FE Task Group:

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.

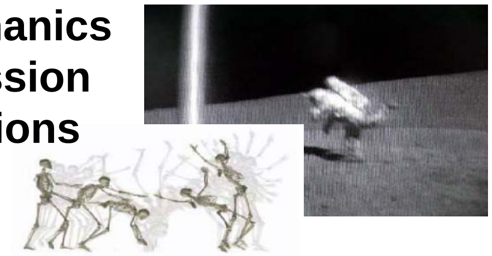


REPRESENTATIVE POPULATION DATA

Data slide courtesy of Keyak. NOT FOR DISTRIBUTION

Probabilistic Risk Assessments for Bone Fracture: NASA's Model for Fracture Likelihood

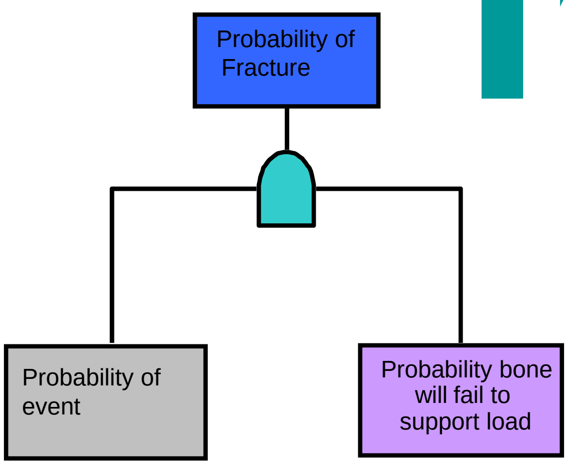
Biomechanics and Mission Operations

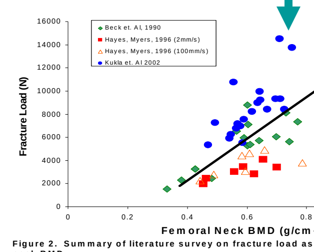


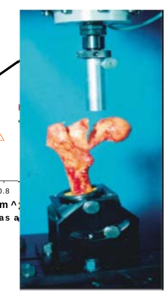
courses.washington .edu/me598rc

Bone Loss in Space

Estimate of Fracture Probability







Clinical and Engineering Characteristics of Bone Strength

Slide courtesy of J Myers; Adapted by Sibonga

For Exploration Class Missions

WHAT IS OUR PATH TO RISK REDUCTION?

Modified Bone Gaps and Expected Deliverables

Risk for Early Onset Osteoporosis

Osteo 1: GUIDED, NEW A new acceptable bone health standard using an improved surrogate for bone strength needs to be defined for the flight environment.

Bone Medical Standards update, Clinical Practice Guidelines [CPG]

Osteo 2: REPHRASED, MERGED What is the incidence & prevalence of early onset osteoporosis or fragility fractures due to exposure to spaceflight?

Surveillance Program to data mine evidence of increased risk for fragility of low trauma fractures.

Osteo 3: GUIDED, MERGED We need a validated, clinically-relevant method for assessing the effect of spaceflight on osteoporosis or fracture risks in long-duration [LD] astronauts.

Data for medical standards; surveillance data for CPG formulation; Clinical trigger; surveillance data

Osteo 4: MERGED 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.

Risk Characterization/Quantification

Osteo 5: REPHRASED We need an in flight capability to monitor bone turnover and bone mass changes during spaceflight.

Prototype In-flight monitoring device for bone mass and for bone biomarkers

Osteo 6: NEW How do skeletal changes due to spaceflight modify the terrestrial risk of osteoporotic fractures?

Risk Characterization: Probabilistic Risk Assessment Model/Tool to generate LxC; Input for clinical practice guidelines

Osteo 7: MERGED We need to identify options for mitigating early onset osteoporosis before, during and after spaceflight.

Integrated suite of countermeasures nutrition, exercise and pharmaceuticals

Schedules: *ISS 2024*

- Standards Update By FY14 End
- Spaceflight Effects Characterized *(as reasonably can be achieved)* ~ FYs 19-20
- Countermeasures (validated efficacy for mitigating risk factors during flight, e.g., declines in BMD, turnover and strength) By FY 23

Summary

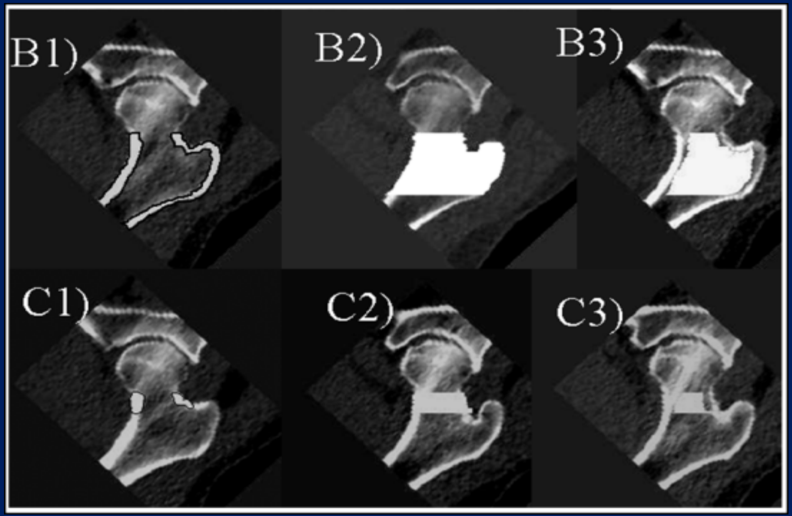
- DXA –widely-applied medical test for terrestrial medicine but may be too limiting for operational and clinical decision-making for bone health of astronauts.
- If skeletal integrity is assessed solely by a <u>surrogate</u> measure of bone strength (DXA –BMD) vs. an <u>estimate</u> of bone strength (e.g., FE modeling), then there may be a risk of underestimating fracture probability and poorly estimating countermeasure efficacy.
- In order to proceed down the path to risk reduction [PRR] , Bone Research needs to take innovative approaches to characterizing risk and countermeasure effects.

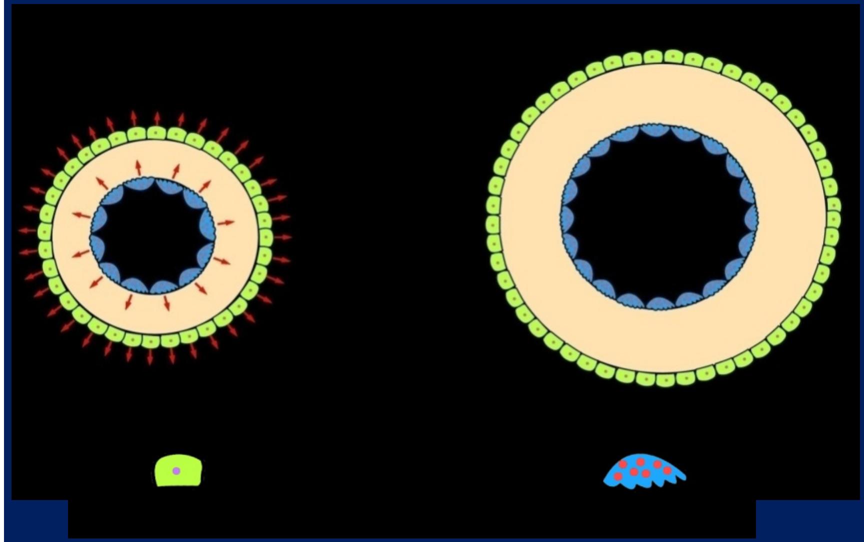
Thank you.

QUESTIONS? COMMENTS?

Backup Slides

Study on Risk Surveillance: Hip QCT



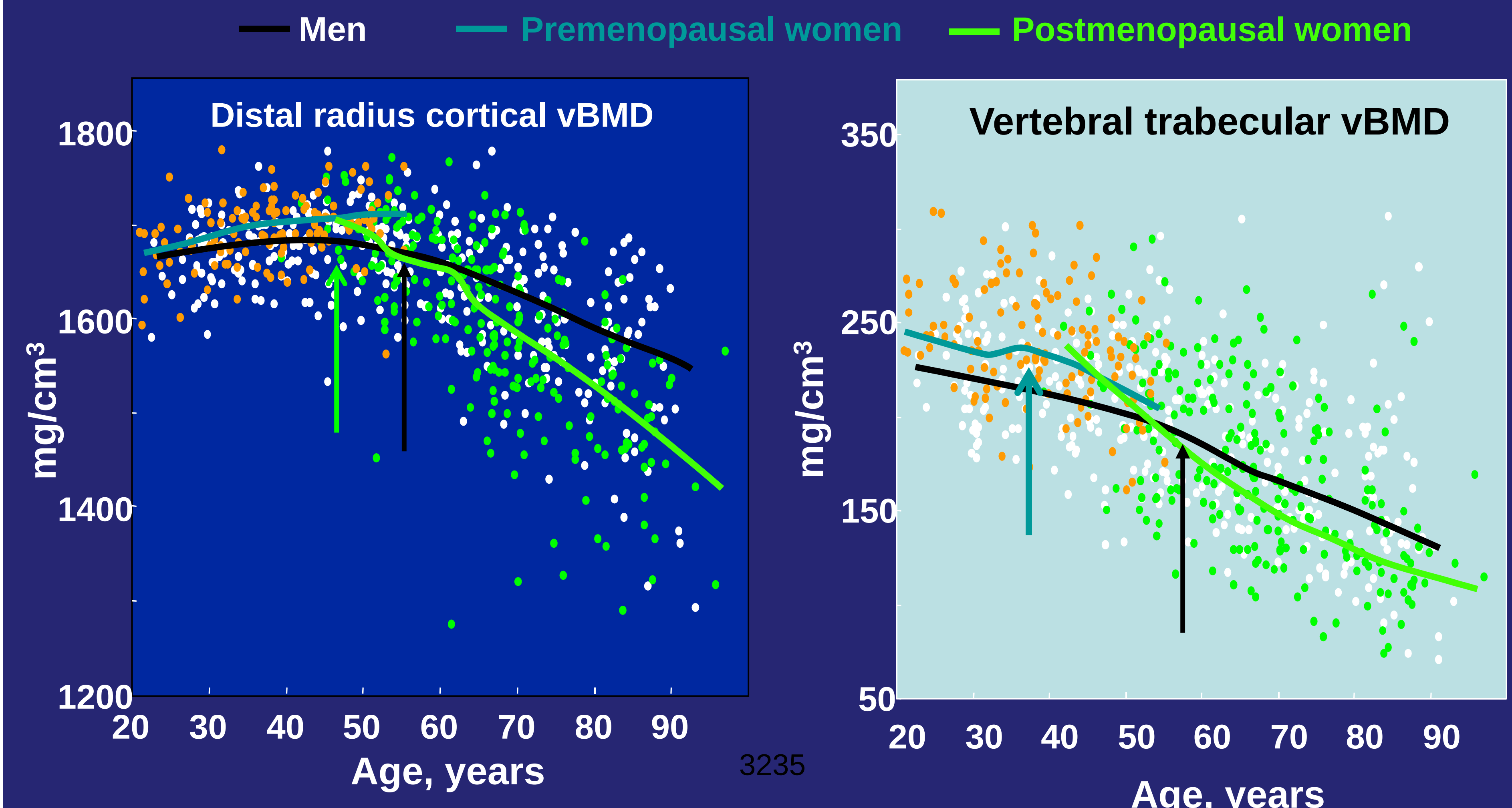


- Test feasibility of QCT protocol for surveillance of clinical trigger.
- Accumulate surveillance data for development of clinical practice guidelines (QCT and FEM)
- **Research**: Demonstrate how QCT can delineate biochemical from mechanical countermeasures. “Proof of Concept” Pilot Study

Figures courtesy of T. Lang (UCSF) and D. Carter (Stanford U)

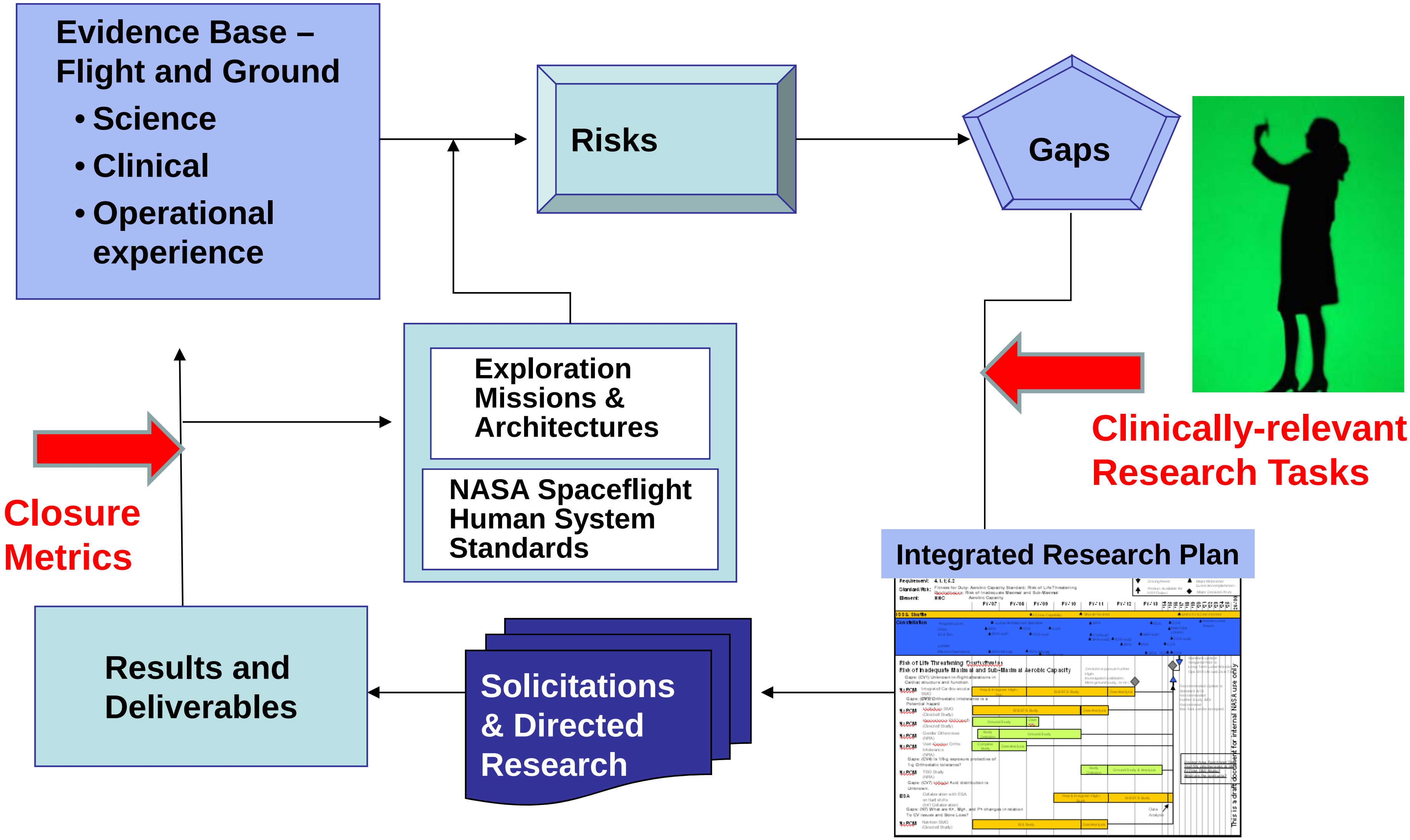
AGE-REGRESSIONS: Trabecular bone loss occurs at earlier age than expected.

Riggs et al. JBMR19:1945, 2004.

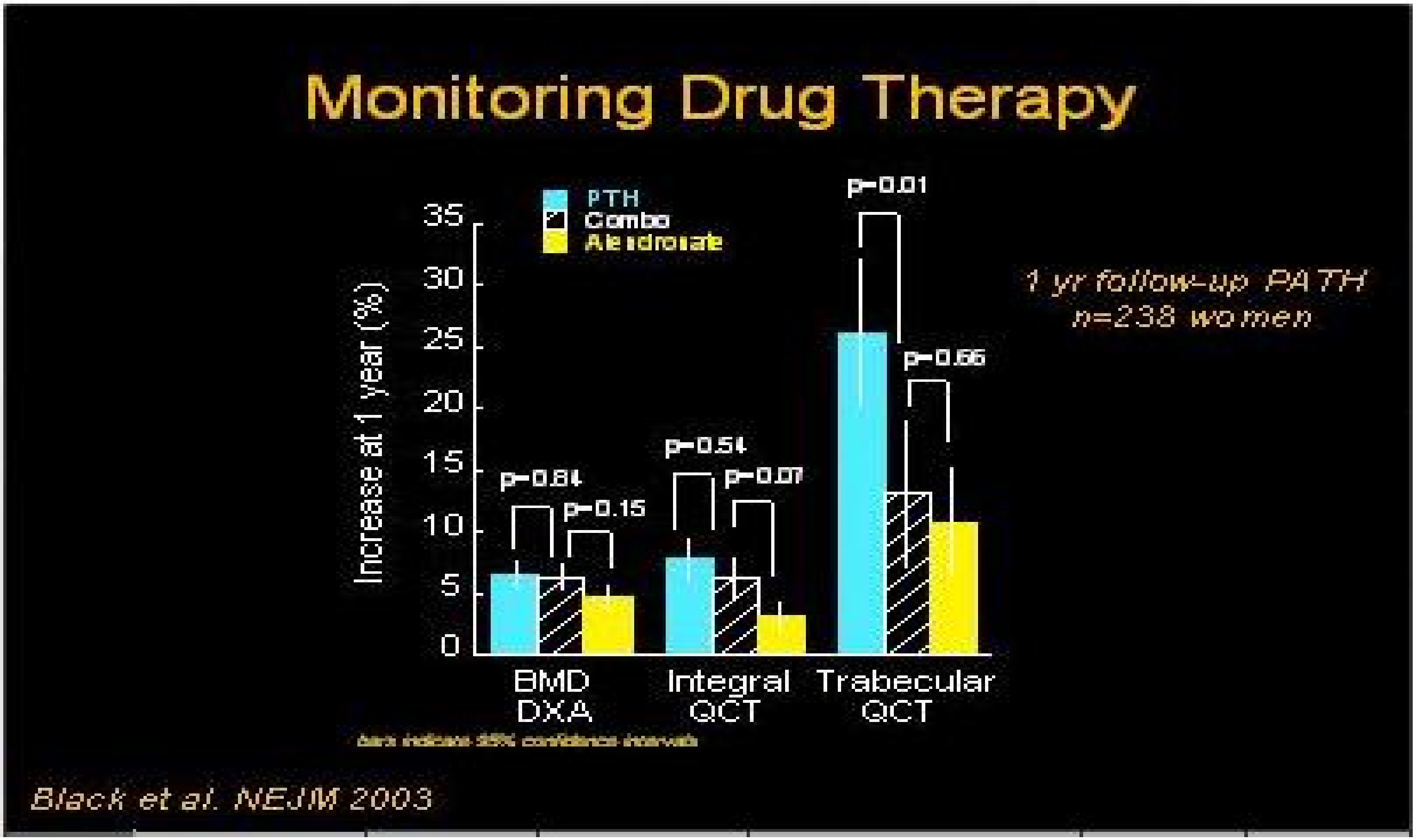


Slide courtesy S. Khosla, adapted by Sibonga

Use of Osteoporosis Policy-makers help to translate research data to CPGs in absence of fracture data.



Effects on Different Compartments of Bone (cortical vs. trabecular BMDs)



QCT + FEM has superior capabilities for estimating mechanical strength of ex-vivo specimens.

QCT estimates fracture loads better than DXA

QCT + FEM has superior capabilities for estimating fracture loads

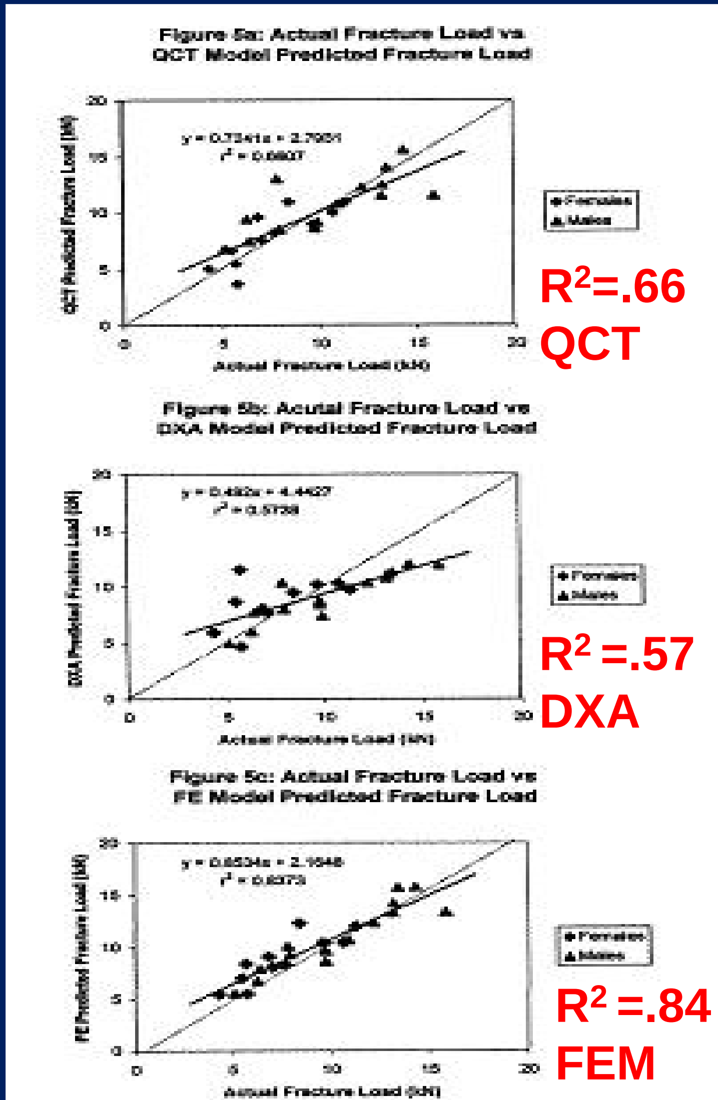
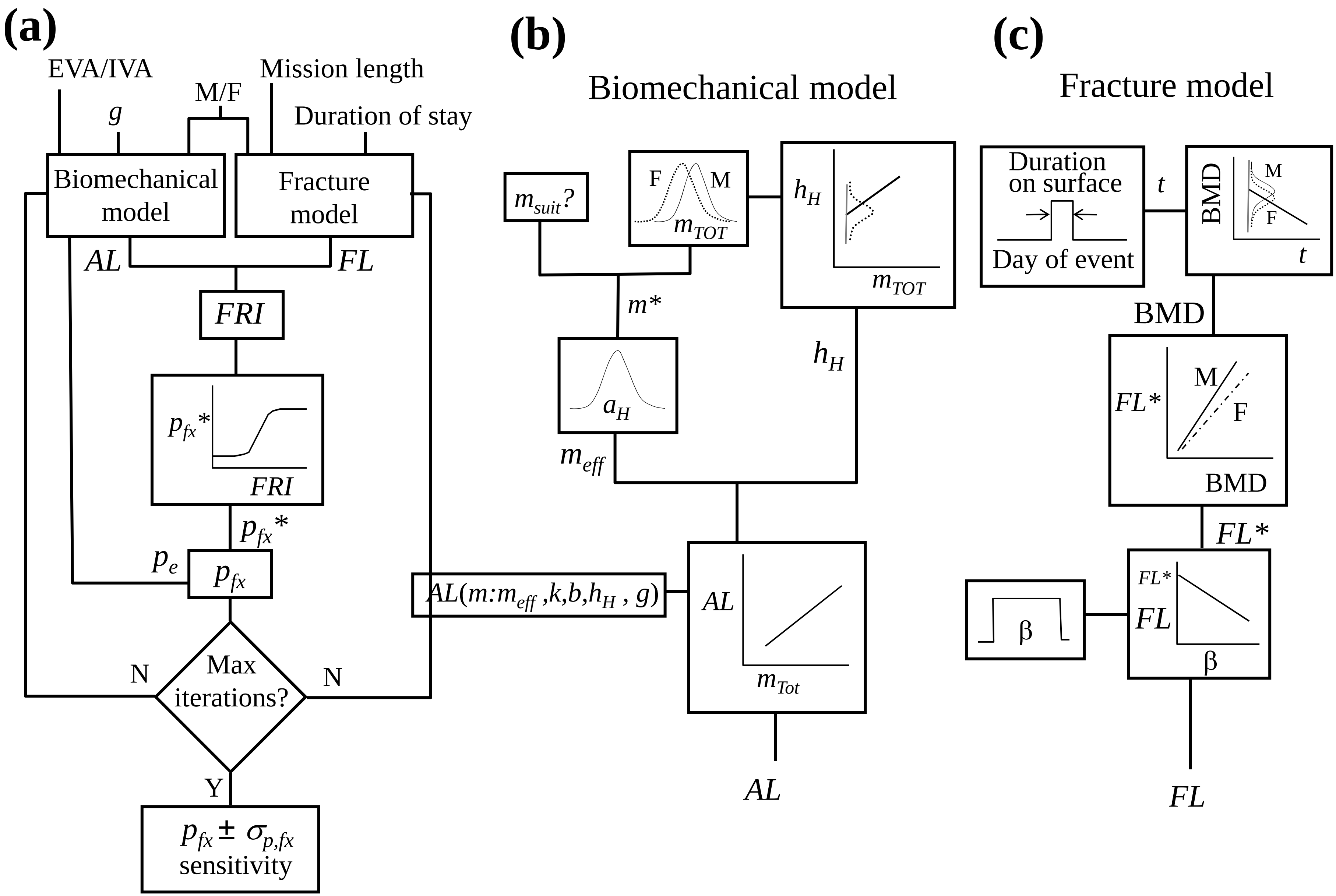


Fig. 5. The predicted strength of the specimens in the test set (developed from the models generated using the training set) plotted against their actual measured values for each of the three methods (a: QCT; b: DXA; c: FEM).

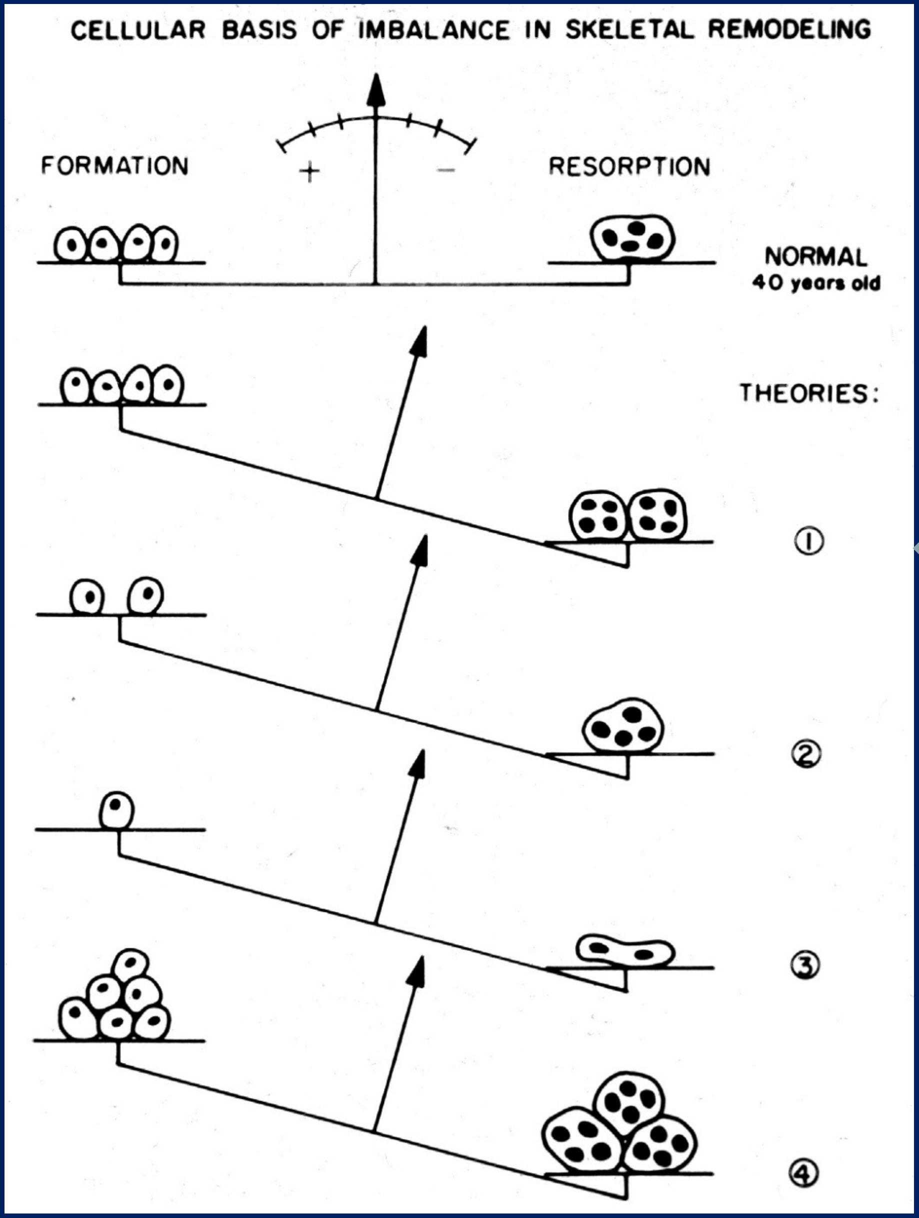
DD Cody: Femoral strength is better predicted by finite element models than QCT and DXA. J Biomechanics 32:1013 1999.



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.

Different ways to unbalance remodeling at bone surface.



Different levels of cell number and cell activities ending in deficit of bone at the BRU.

Space?

QCT provides useful information re: causation of hip fracture, evaluation of hip fracture risk and possible targets for intervention.

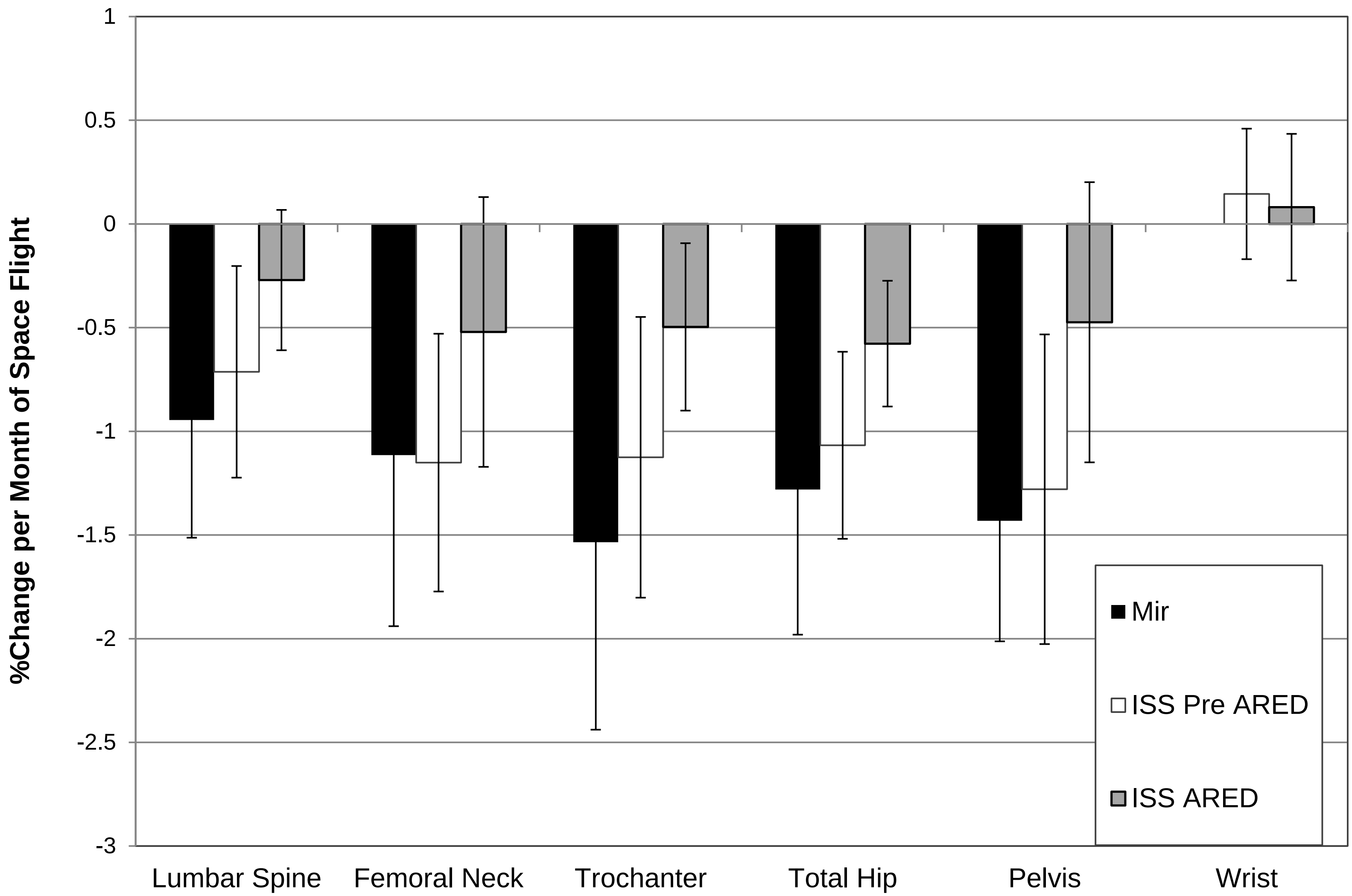
TABLE 4. HRs OF MULTIVARIATE MODELS OF SKELETAL PARAMETERS AT THE FEMORAL NECK FOR HIP FRACTURE ADJUSTED FOR CLINIC SITE, AGE, AND BODY MASS INDEX

	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.

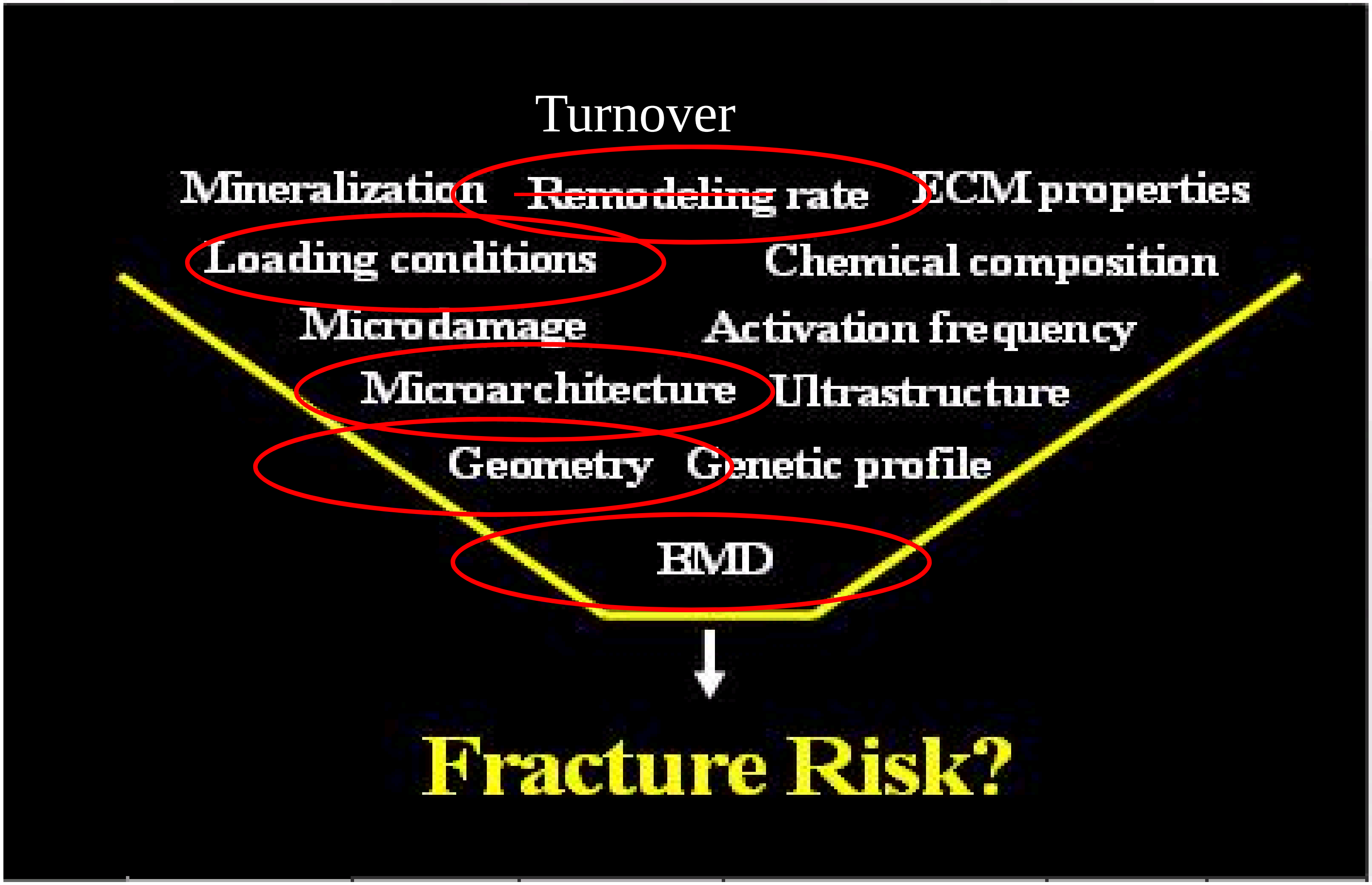
ARED exercise appears to mitigate decline in areal BMD.

(J Bone Mineral Research. Smith et al 2012) * *this is not ref for figure*.



FE Standards Combine Aging and Spaceflight Changes to Hip Strength and used together with DXA BMD Standards.

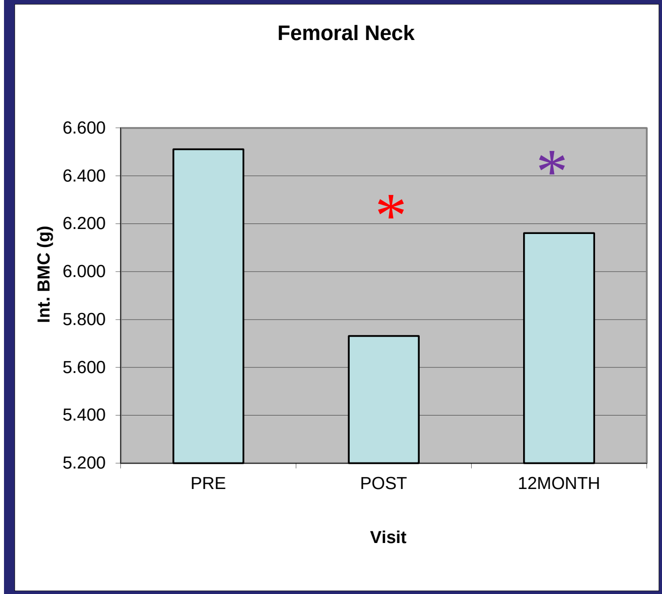
	Minimum FE strength for Bone Health	**“Go”**
	Minimum Permissible Outcome	**“Wait”**
		“No Go”



Steven Goldstein, Ph.D.
“Bone Quality: A Biomechanical Perspective”

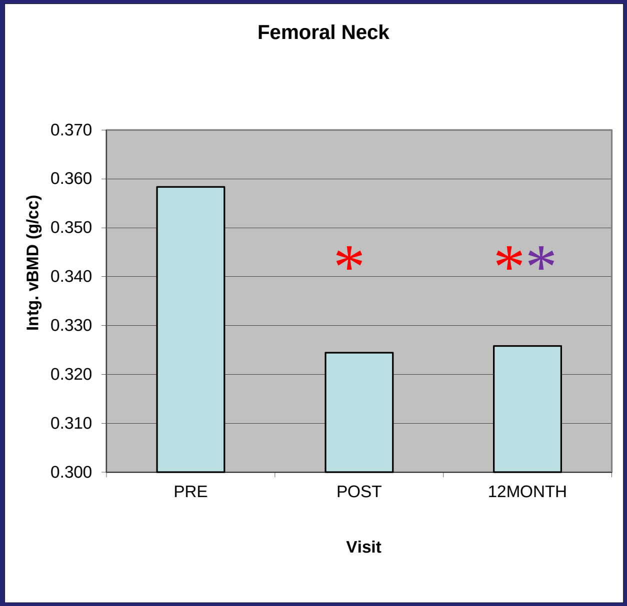
QCT Postflight – Changes in Femoral Neck structure detected 12 months after return

Bone Mineral Content (g)



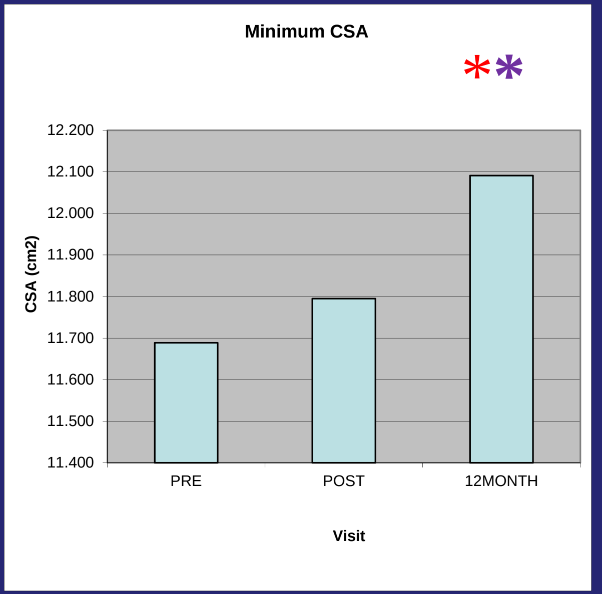
Pre Post 12

Volumetric Bone Mineral Density g/cm^3



Pre Post 12

Minimum Cross-sectional Area cm^2



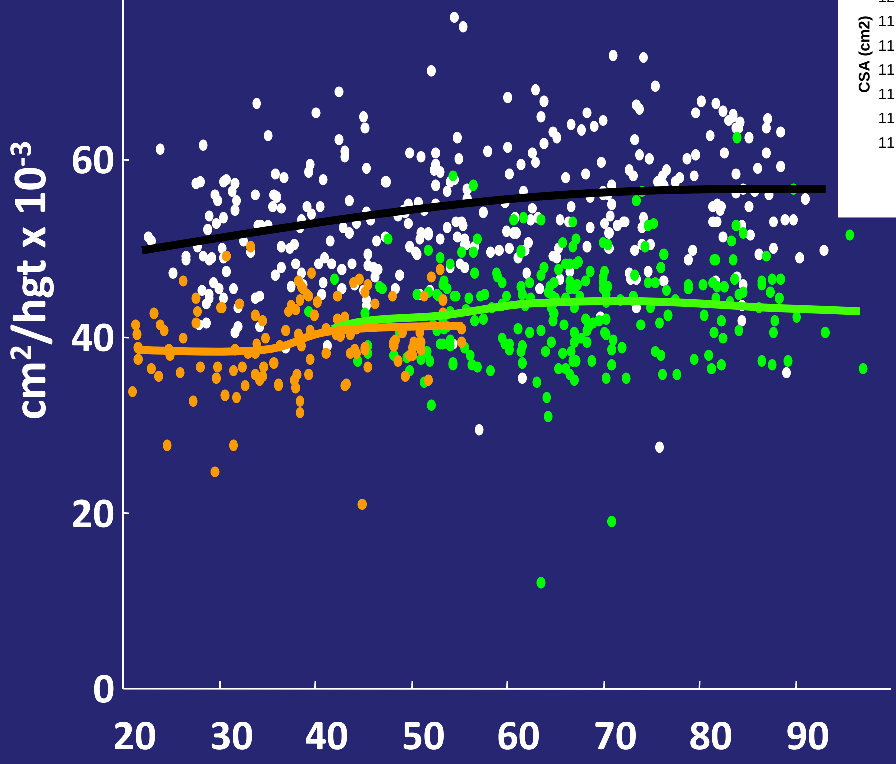
Pre Post 12

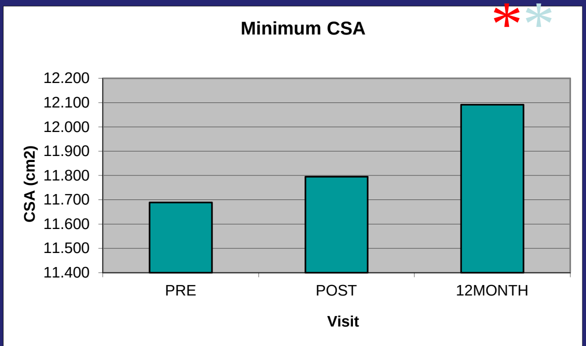
$P < 0.05$ with respect to preflight*, **postflight***

Slide adapted from T. Lang., JBMR 2006.

QCT in Population Study: Age-related Changes

Suggests that femoral neck total area increases by outward displacement when cortex thins with age



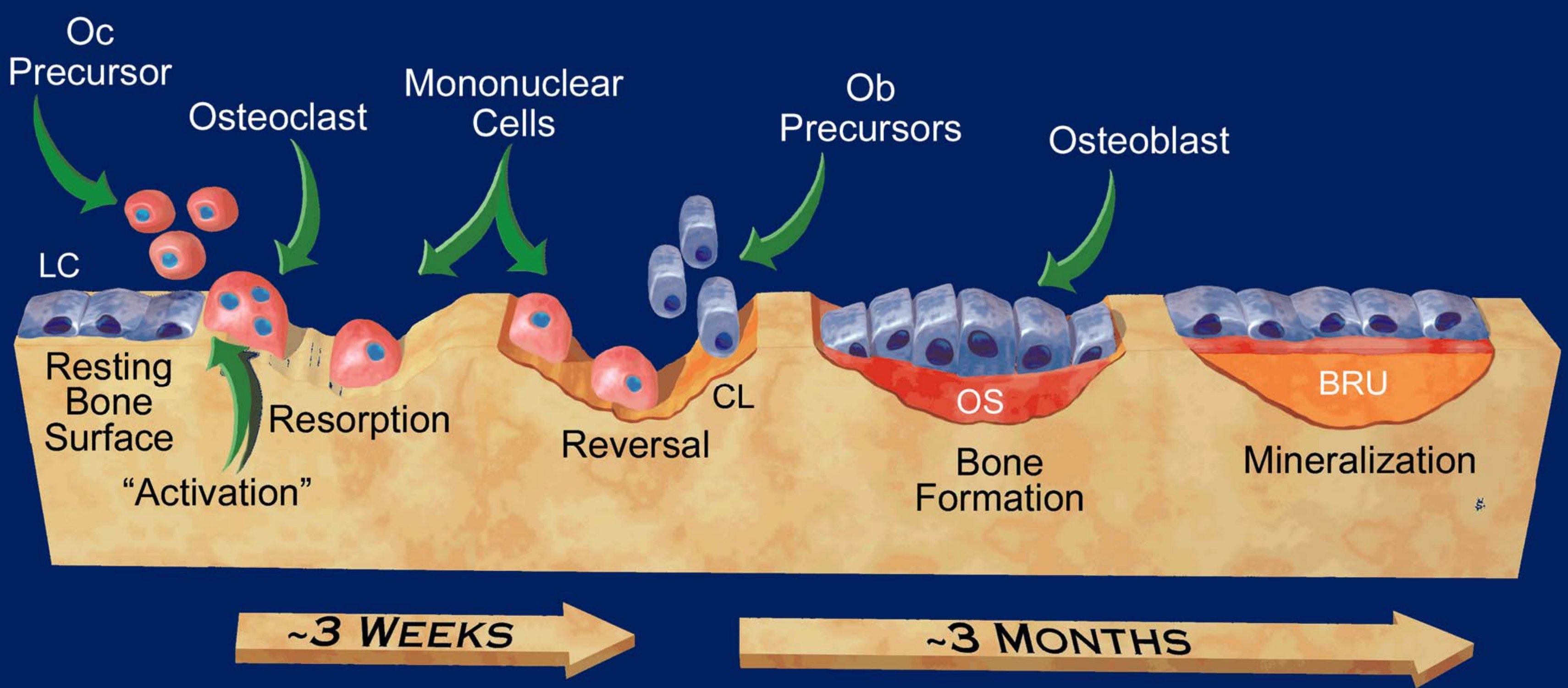


Riggs et al. JBMR19:1945, 2004.

The long-duration astronaut – not typical subject to evaluate osteoporosis (2/2013).

- Typical space mission duration – 162 ± 36d (range 58-215d)
- Average Age – 47 ± 5 y (range 37 – 55)
- Male to Female Ratio – 4.8 : 1
- Current total # per astronauts in corps – 55 of 331
- # repeat fliers – 5
- BMI – Male BMI 25.8 ± 2.0 (range 21.2 to 30.7); Female BMI 23.4 ± 2.4 (range 20.4 to 25.9)
- Wt and Ht- Males: Males: 80 ± 6 (63 to 97); 176 ± 6 (163 to 185)
- Females: 67 ± 8 (57 to 82), 170 ± 4 (165 to 178)
- % Body Fat: Males 20 ± 4 (9 to 27); Females 27 ± 8 (19 to 41)

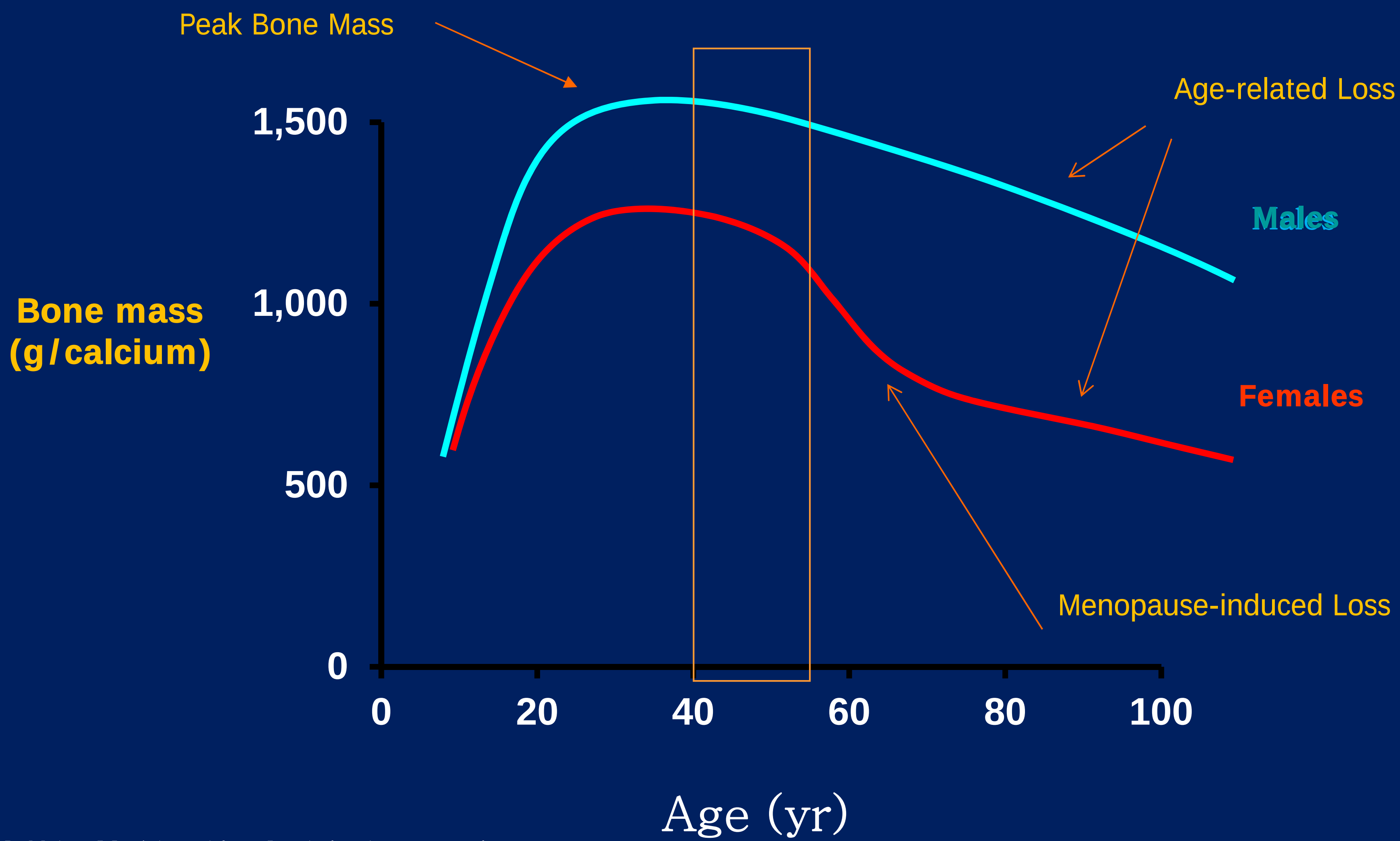
Bone Remodeling Sequence



LC = Lining Cells CL = Cement Line OS = Osteoid BRU = Bone Remodeling Unit

Slide courtesy of Dr. R. Wermers, Mayo Clinic

Risk for fragility fractures: 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

HRP Deliverables as Category

Osteo #	Category	Subcategory	Customers	Deliverables
1	**Standards**	New	OCHMO; Space & Clinical Operations; Human Health Countermeasures [HHC]	Bone *Health* Standards update, Clinical Practice Guidelines
2	**Knowledge Gap: Risk** Characterization	Evidence	OCHMO; Space & Clinical Operations	Evidence of increased risk for fragility of low trauma fractures.
3	**Technology Gap Methodology & bone measurements**	Clinical care; medical informatics	OCHMO; Space & Clinical Operations; HHC	Data for medical standards (including index of countermeasure efficacy); Clinical trigger; surveillance data for Space Normal;
4	**Knowledge Gap: Data, phenomenon, mechanism**	Risk Factor	HHC, Biomed Research Div; Technology & Engineering Division	Risk Characterization/Quantification-
5	Mitigation Gap- detect,monitor, treat	Prototype Hardware	Med Operations; Human Health Countermeasures; Systems Engineering	Prototype In-flight monitoring device for bone mass and for bone biomarkers
6	**Mitigation- surveillance**	Computational models, software	OCHMO; Space & Clinical Operations; HHC	Risk Characterization: Probabilistic Risk Assessment Model/Tool to generate LxC; Input for clinical practice guidelines
7	**Mitigation Prevention & Treatment**	Prescription(s)	Bone Summit-like Panel; Med Operations; OCHMO	Exercise prescription, metabolic countermeasures; validated pharm agent prescription; risk factor modifications; Recommended medical intervention.
		Protocol	Med Operations; OCHMO; HHC	Integrated suite of countermeasures nutrition, exercise and pharmaceuticals