ADAPTATION OSSEUSE A LA GRAVITE REDUITE OU AUGMENTEE

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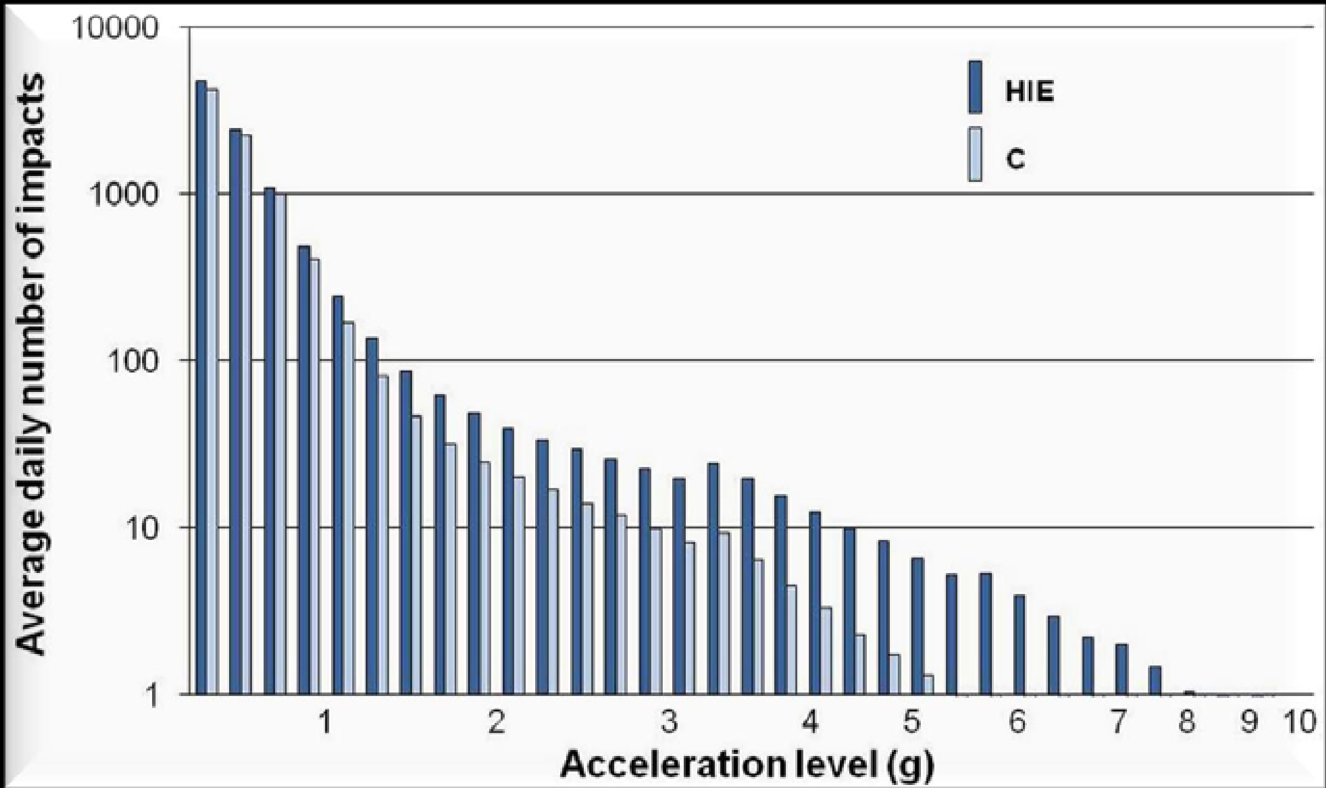
IMPACT QUANTIFICATION AND BONE GAIN

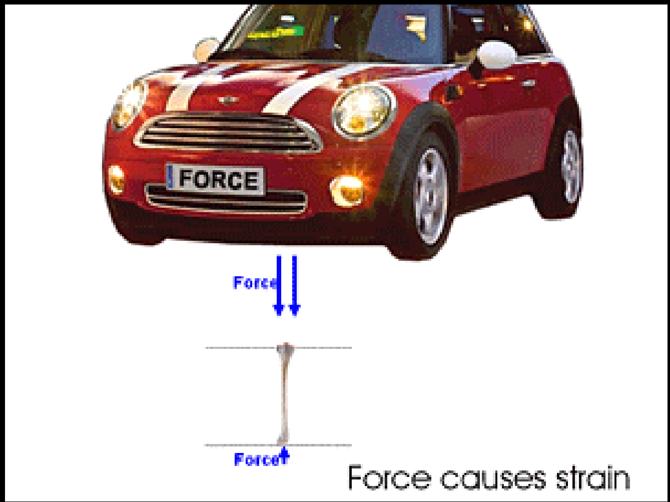


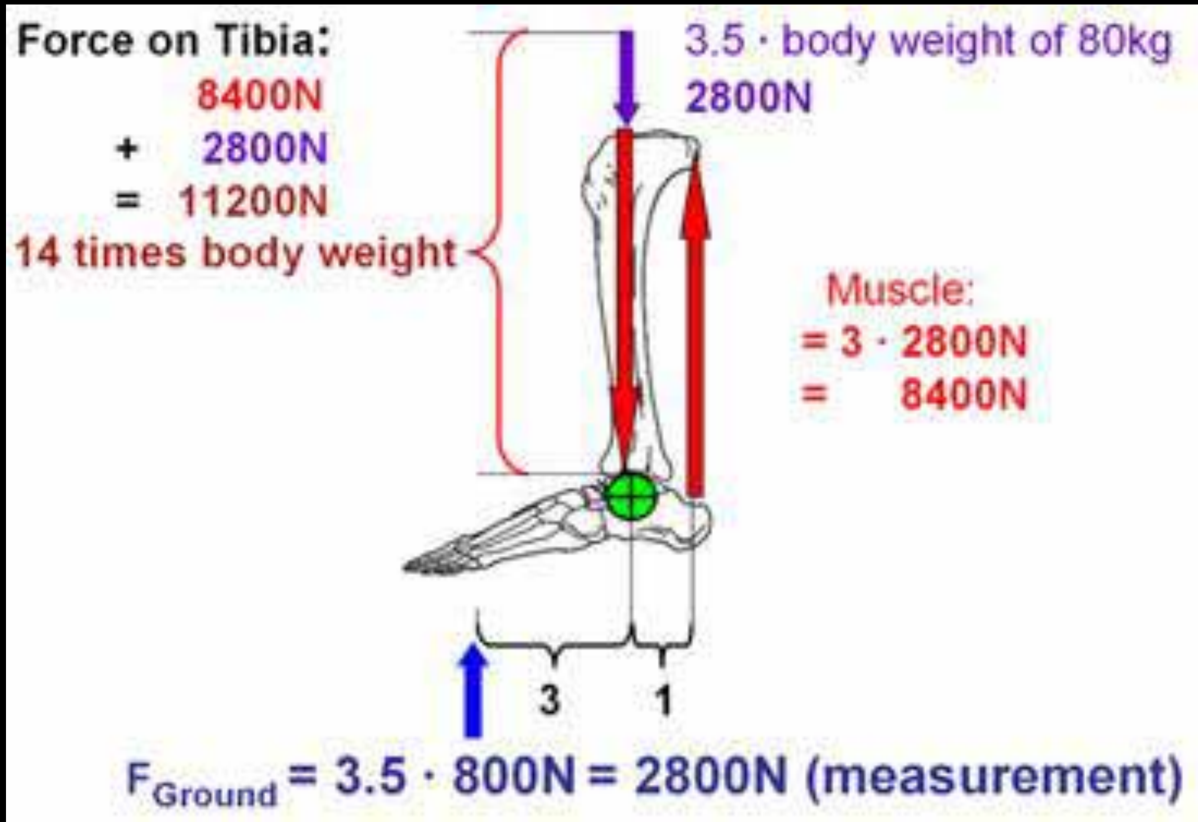
The average daily distribution of impacts during the 12-month high-impact exercise intervention in premenopausal women.
HIE, high-impact exercise group (N =34);
C, control group (N =30).

Changes in hip were threshold dependent, indicating the importance of high-impacts exceeding acceleration of 4g as an osteogenic stimulus. The number of impacts needed was 60/day.

Jämsä T et al., Front Physiol. 2011

AMPLEUR DES DÉFORMATIONS OSSEUSES



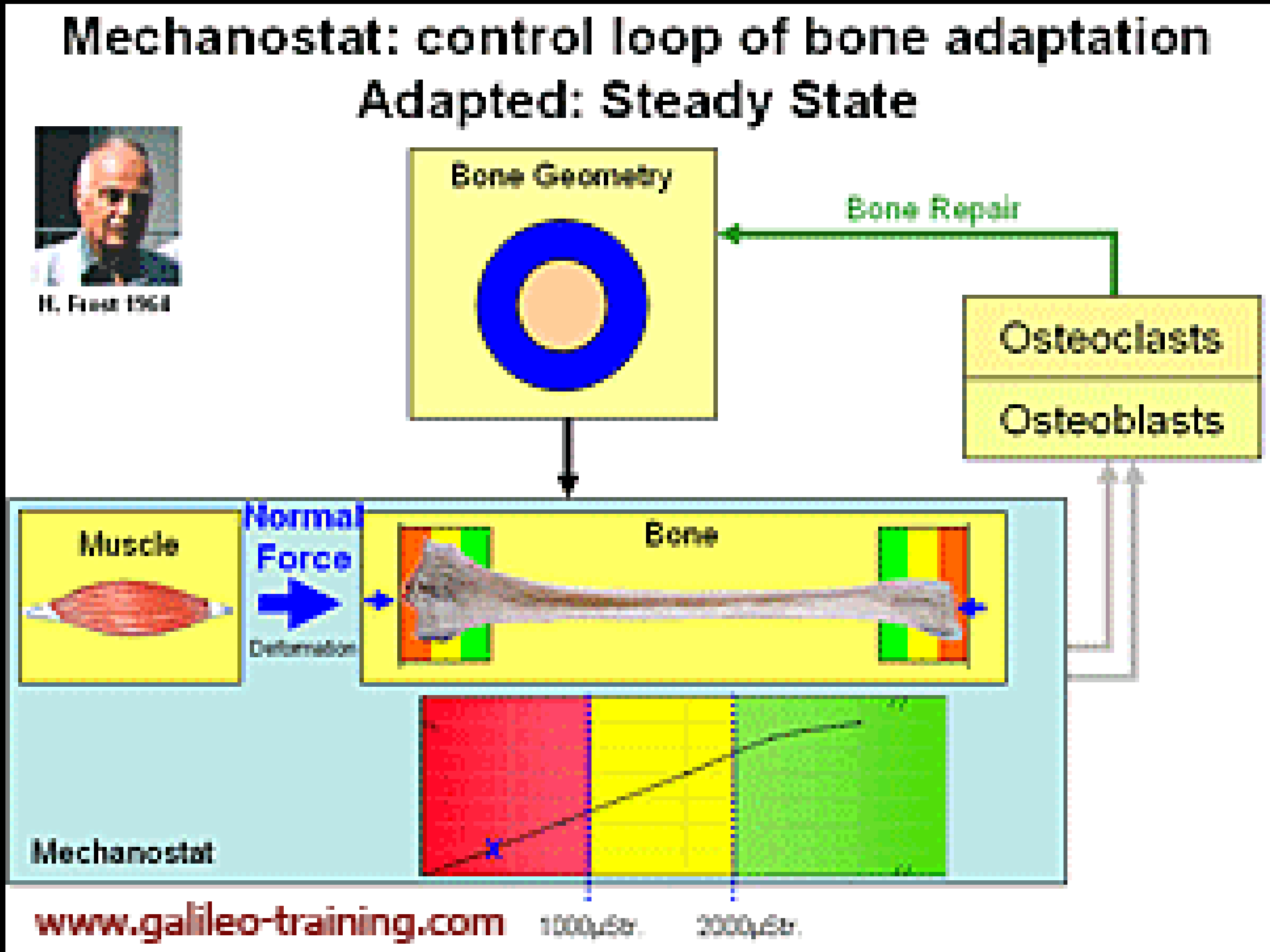


Les pics de force chez un sujet adulte sain engendrent des déformations osseuses de 1000 à 2000 µStrain.

Pour un tibia de 40 cm de long => déformation de 0.4 mm à 0.8 mm.

Déformations mesurées en µStrain (1000 µStrain = 0.1% changement de longueur).

QU'EST-CE QUI GÉNÈRE DES FORCES AU NIVEAU OSSEUX?

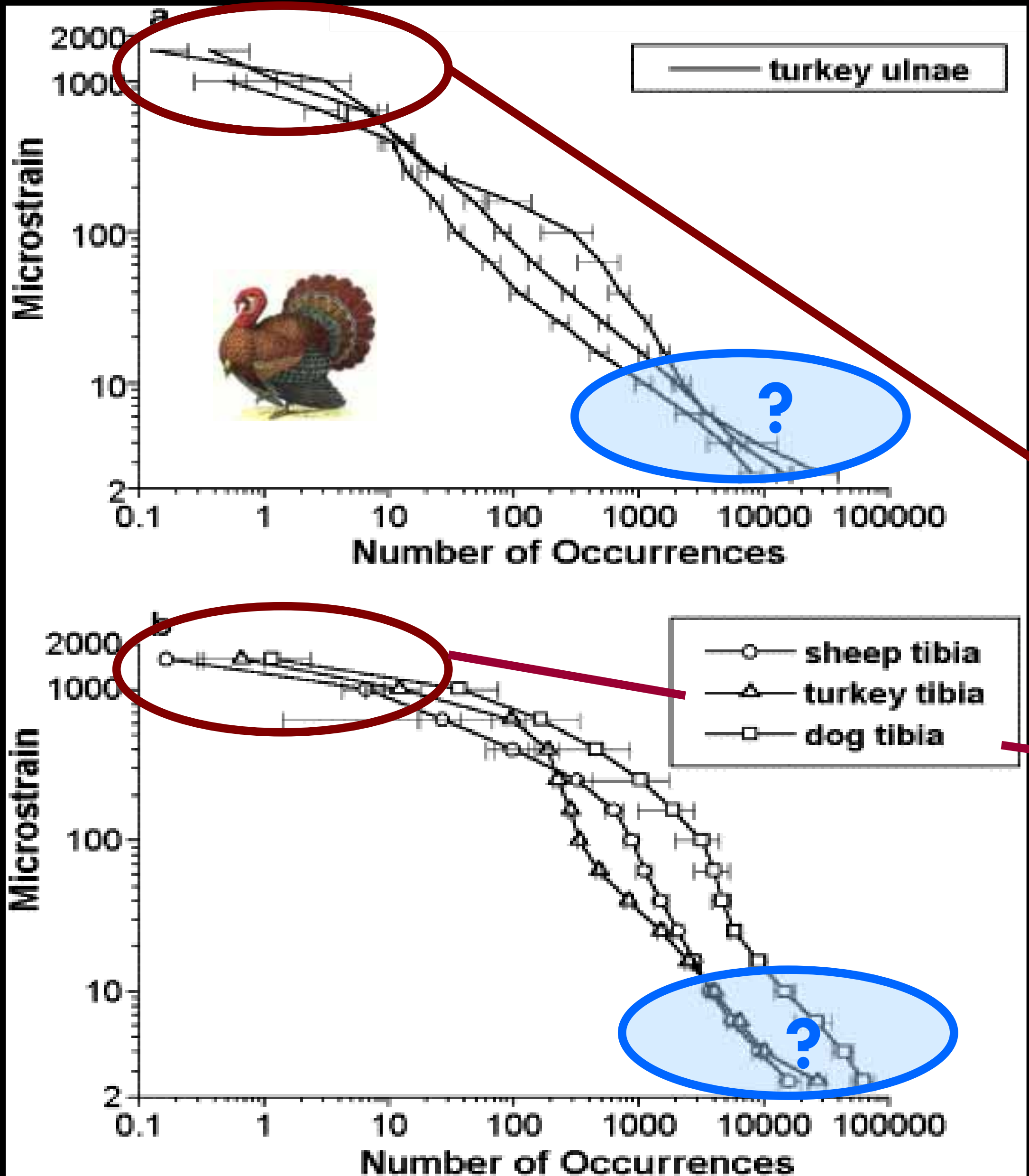


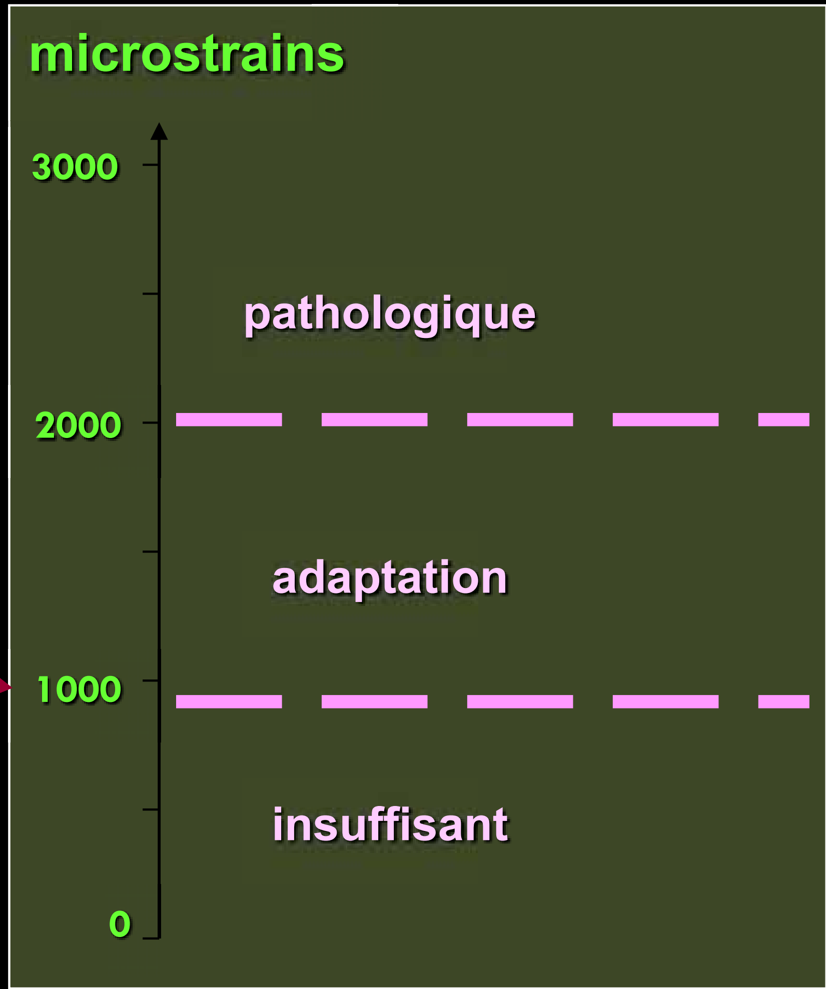
1 - Forces musculaires régionales

2 - Forces gravitationnelles (poids, forces de réaction du sol)

} par l'intermédiaire de la force de réaction du sol et des forces appliquées au niveau des articulations

QUELS SIGNAUX SONT EFFICACES ?

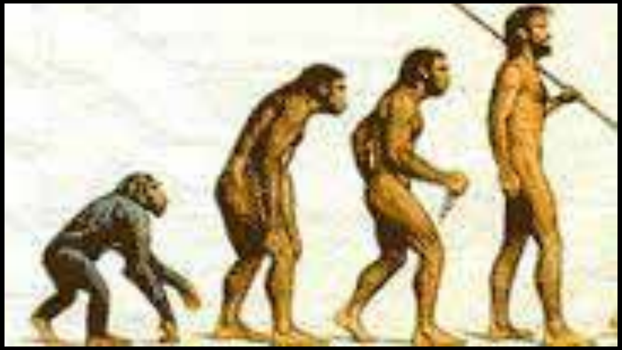


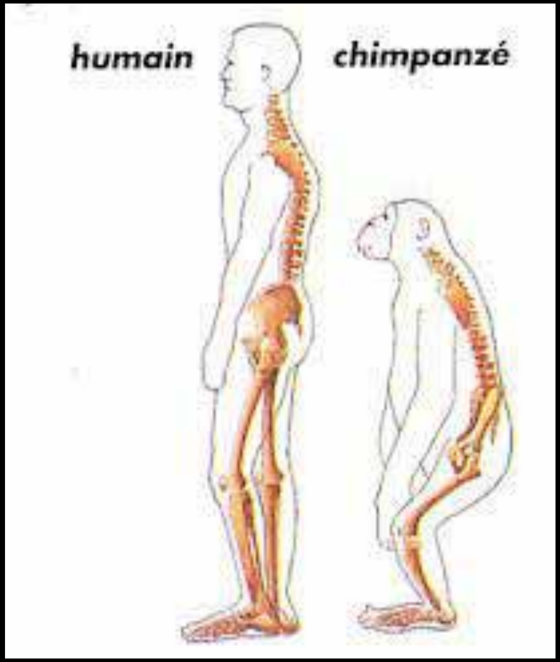


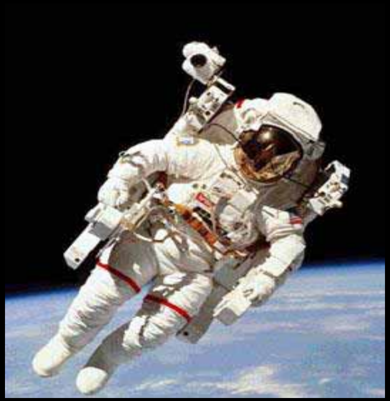
Fritton et al., J Biomech , 2000

LA GRAVITE : SA VARIATION A DES EFFETS MAL CONNUS

1g







Hypogravité
$10^{-4} - 10^{-6}$ g

Hypergravité
2 – 9g

L'ESPACE, PAS QUE LA MICROGRAVITE

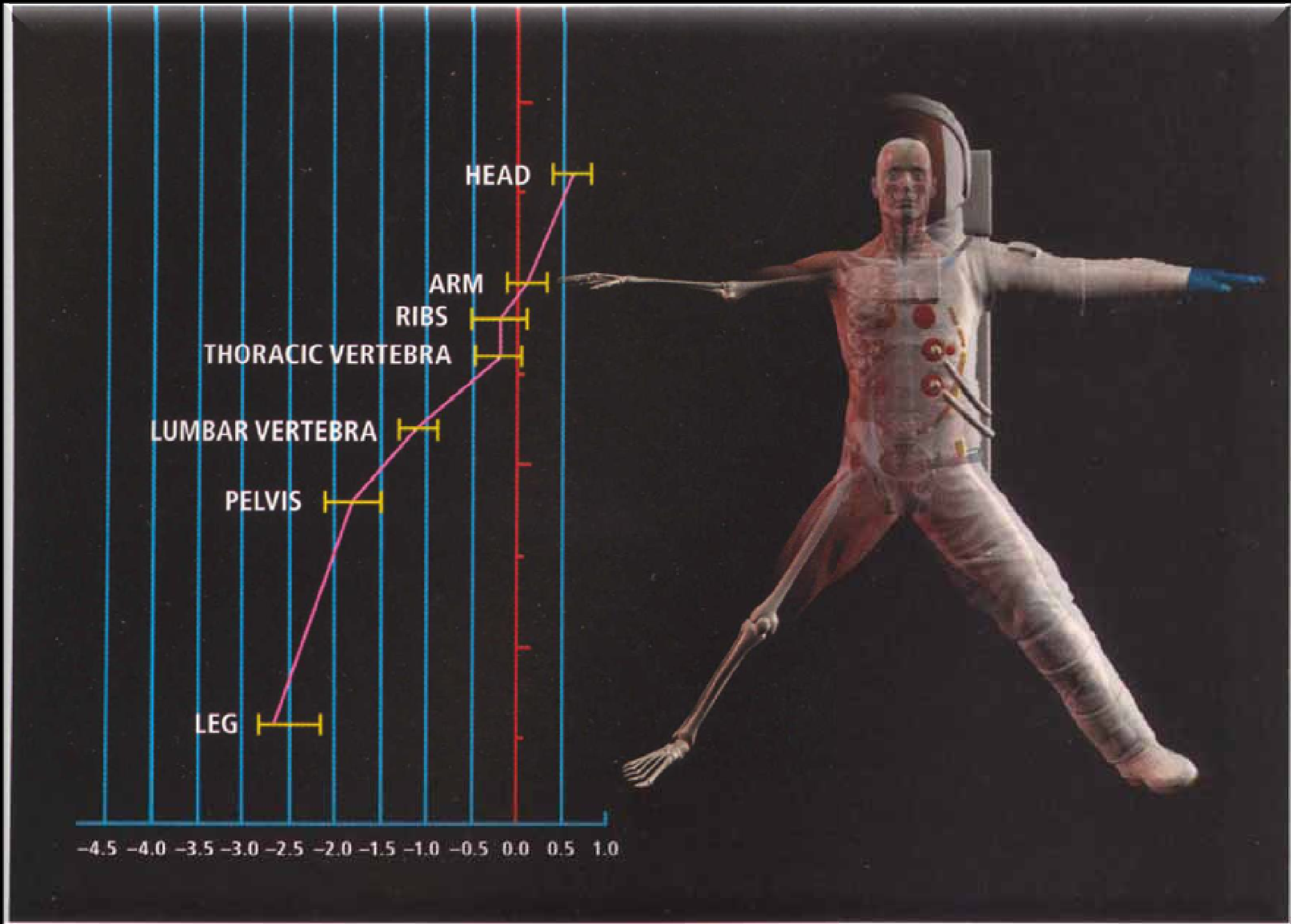
- Microgravity, radiations
- Isolation and confinement
- Social factor
- Chronobiology
- Energy intake
- Reentry

Treadmill

Cycle Ergometer

NASA, resistive exercise

DANS L'ESPACE: REDISTRIBUTION DES MINÉRAUX?



Gradient of bone loss in spaceflights of at most 6-month duration
in % variation (attempt at synthesis, DXA+pQCT)

(Vico, Lancet 2000, Scientific American, 2008)

BECAUSE iRED WAS LIMITED IN THE MAXIMAL LOADS => aRED

Astronaut Edward T. Lu,
Expedition 7 NASA ISS
Interim Resistive Exercise Device (IRED)
Max load (1337 N)

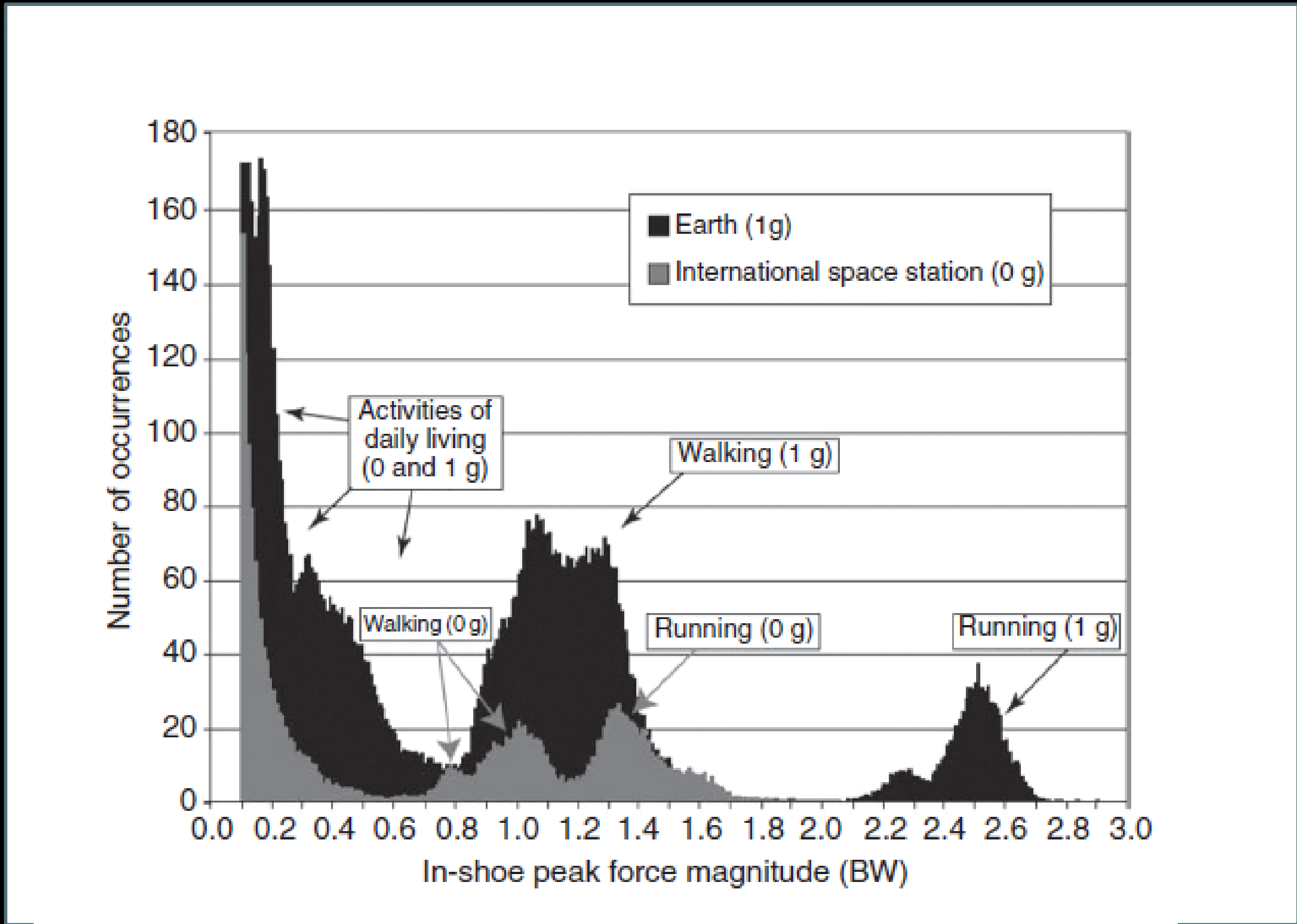
⇩

Failed to affect bone

Steve Lindsey, STS-133, 2011
aRED, Advanced Resistance Exercise Device
Max load (2675 N),

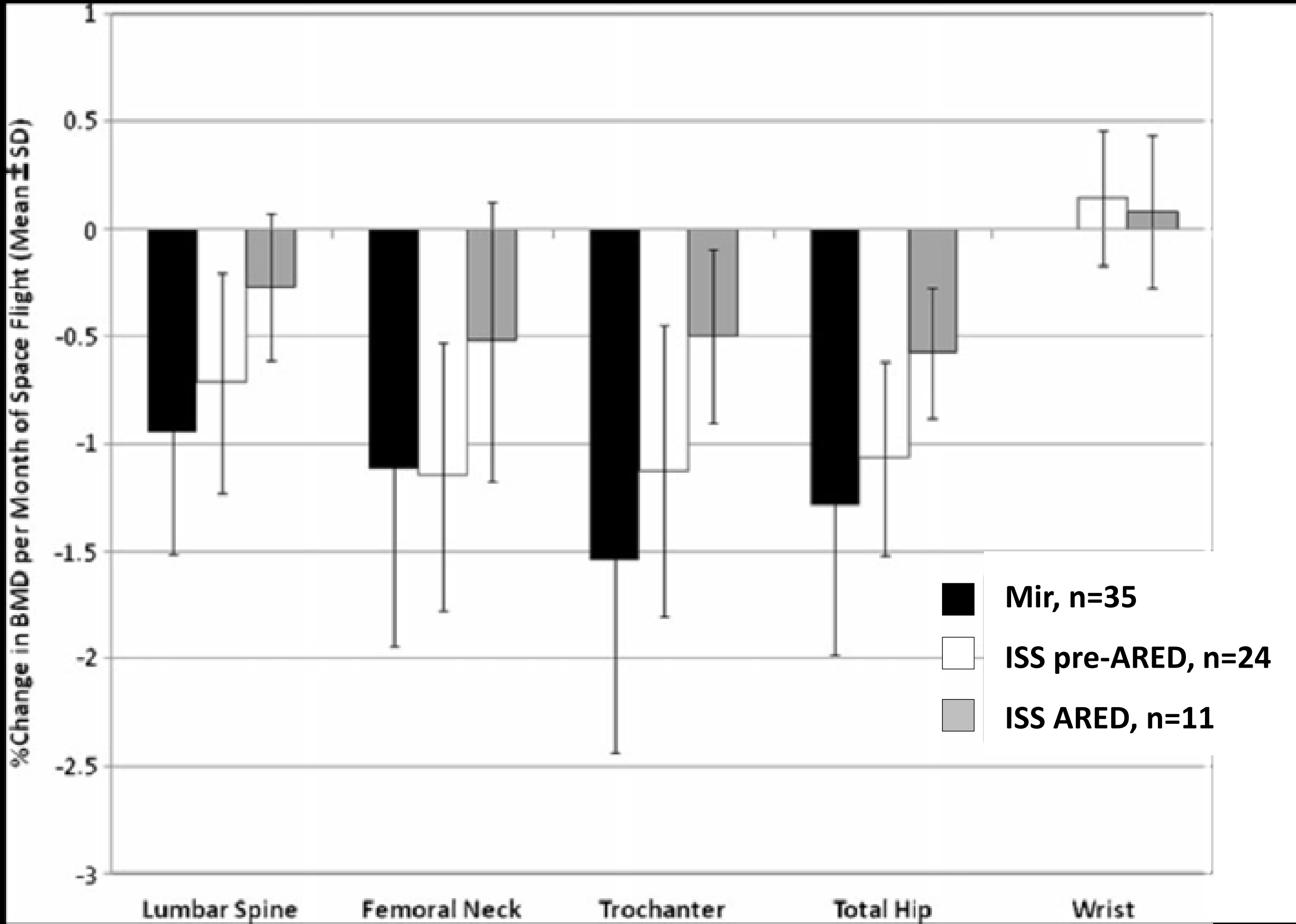
http://spaceflight.nasa.gov/gallery/images/shuttle/sts-133/html/s133e008323.html

FOOT FORCES ABOARD ISS ARE MUCH REDUCED COMPARED TO 1G



In-shoes peak force magnitudes recorded during activities of daily living on Earth and aboard ISS. Both magnitude and frequency of the GRFs observed in 1g are reduced onboard ISS. No GRF's> 2xBW, from Cavanagh et al., 2010

DECLINES IN DXA aBMD IN LONG-DURATION CREWMEMBERS ON MIR AND ISS SPACEFLIGHTS.



% change of preflight aBMD /month [calculated by subtracting the first postflight BMD from the preflight measurement and normalizing by the mission duration (typically 4–6 months)].

Sibonga JD, Curr Osteoporos Rep, 2013

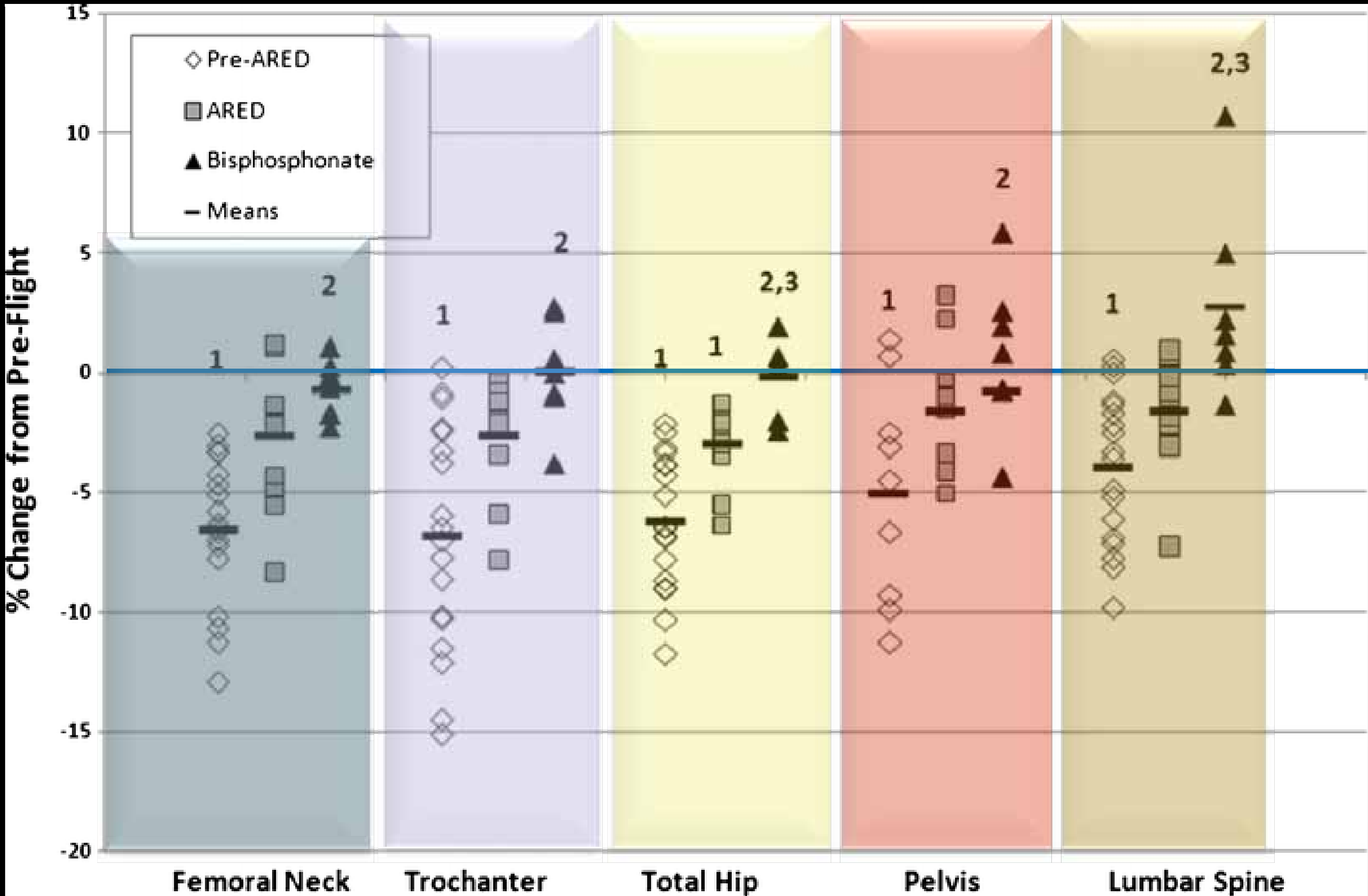
BENEFITS FOR BONE FROM RESISTANCE EXERCISE AND NUTRITION IN LONG-DURATION SPACEFLIGHT: EVIDENCE FROM BIOCHEMISTRY AND DENSITOMETRY

Urinary Markers of Bone Turnover and Calcium Status

	preflight	FD15	FD30	FD60	FD120	FD180	R+0	R+30
N								
iRED	**8**	**8**	**8**	**7**	**5**	**4**	**8**	**8**
ARED	**5**	**5**	**5**	**5**	**3**	**2**	**5**	**5**
Calcium, mmol/d								
iRED	**4.4±2.3**	**6.4±3.8**	**6.7±2.7**	**6.0±2.5**	**4.9±2.6**	**4.9±2.1**	**4.3±1.5**	**3.2±1.6**
ARED	**4.4±1.7**	**6.6±2.6**	**6.6±2**	**6.5±2.9**	**5.2±1.5**	**8.0±0.4**	**5.7±2.1**	**4.3±1.4**
CTX, mg/mmol/Cr								
iRED	**135+36**	**248±71**	**272±79**	**289±62**	**302±48**	**238±35**	**252±75**	**154±31**
ARED	**133+44**	**257±132**	**193±82**	**195±107**	**281±150**	**360±27**	**267±118**	**206±125**

Smith et al., JBMR, 2012

BISPHOSPHONATES AS A SUPPLEMENT TO EXERCISE TO PROTECT BONE DURING LONG-DURATION SPACEFLIGHT



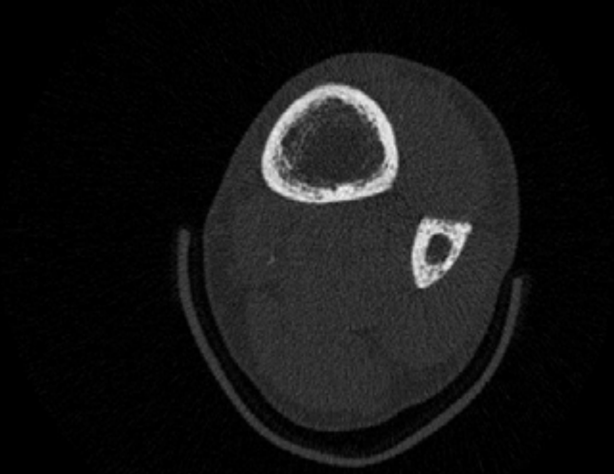
Change in DXA BMD after long-duration space flight. 1 $p < 0.05$, pre vs. post; 2 $p < 0.05$ (bisphosphonate group significantly different from pre-ARED); 3 $p < 0.05$ (bisphosphonate group significantly different from ARED). Pre-ARED (n = 18); ARED (n = 11); bisphosphonate (n = 7).

Leblanc et al., Osteoporosis Int, 2013

pQCT DENSISCAN
RADIUS - TIBIA

distal

proximal



TIBIA : PROFILE OF 11 INDIVIDUAL BMD CHANGES

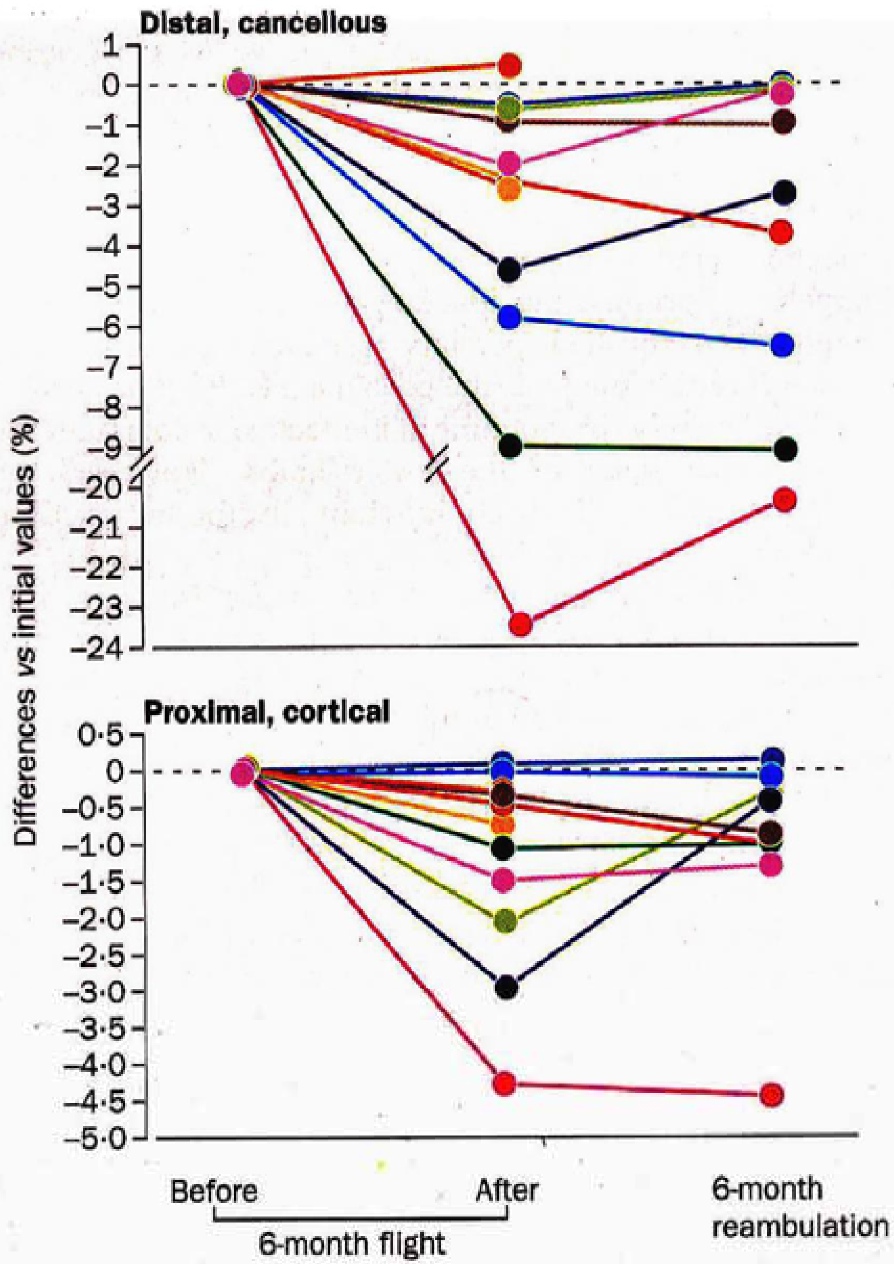


Figure 2: **Profile of 11 individual BMD changes in distal tibia relative to 6-month missions**

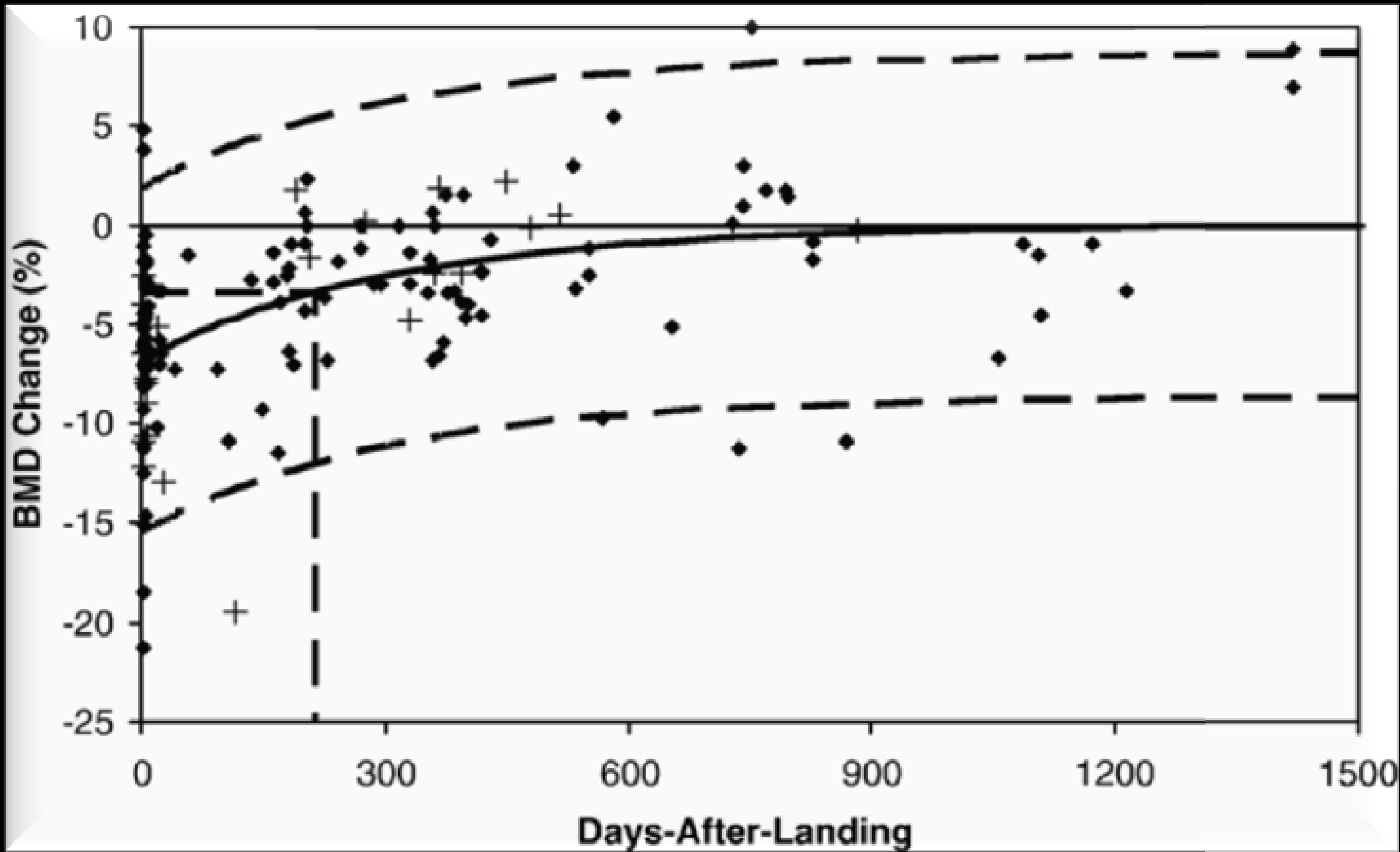
- Cosmonaut 5 (174 days)
- Cosmonaut 7 (0 days)
- Cosmonaut 9 (198 days)
- Cosmonaut 11 (0 days)
- Cosmonaut 13 (0 days)
- Cosmonaut 15 (60 days)
- Cosmonaut 6 (180 days)
- Cosmonaut 8 (0 days)
- Cosmonaut 10 (460 days)
- Cosmonaut 12 (126 days)
- Cosmonaut 14 (0 days)

Figure 1: **Profile of 11 individual BMD changes in distal radius relative to 6-month missions**

Profiles show BMD measured either immediately after flight or after 6-month reambulation period. Values correspond to variations (%) from preflight values (dotted line). Profiles of cosmonauts 12 and 13 end at postflight. Individuals did not undergo postrecovery analysis. Cumulative days spent in space before the present mission are shown in parentheses for each cosmonaut.

Vico et al., Lancet, 2000

RECOVERY



Changes in BMD at the femoral neck after landing.

Averaged losses of bone mineral after long-duration spaceflight ranged between 2% and 9% across all sites with our recovery model predicting a 50% restoration of bone loss for all sites to be within 9 months.

Sibonga et al., Bone 2007

POINTS CLES

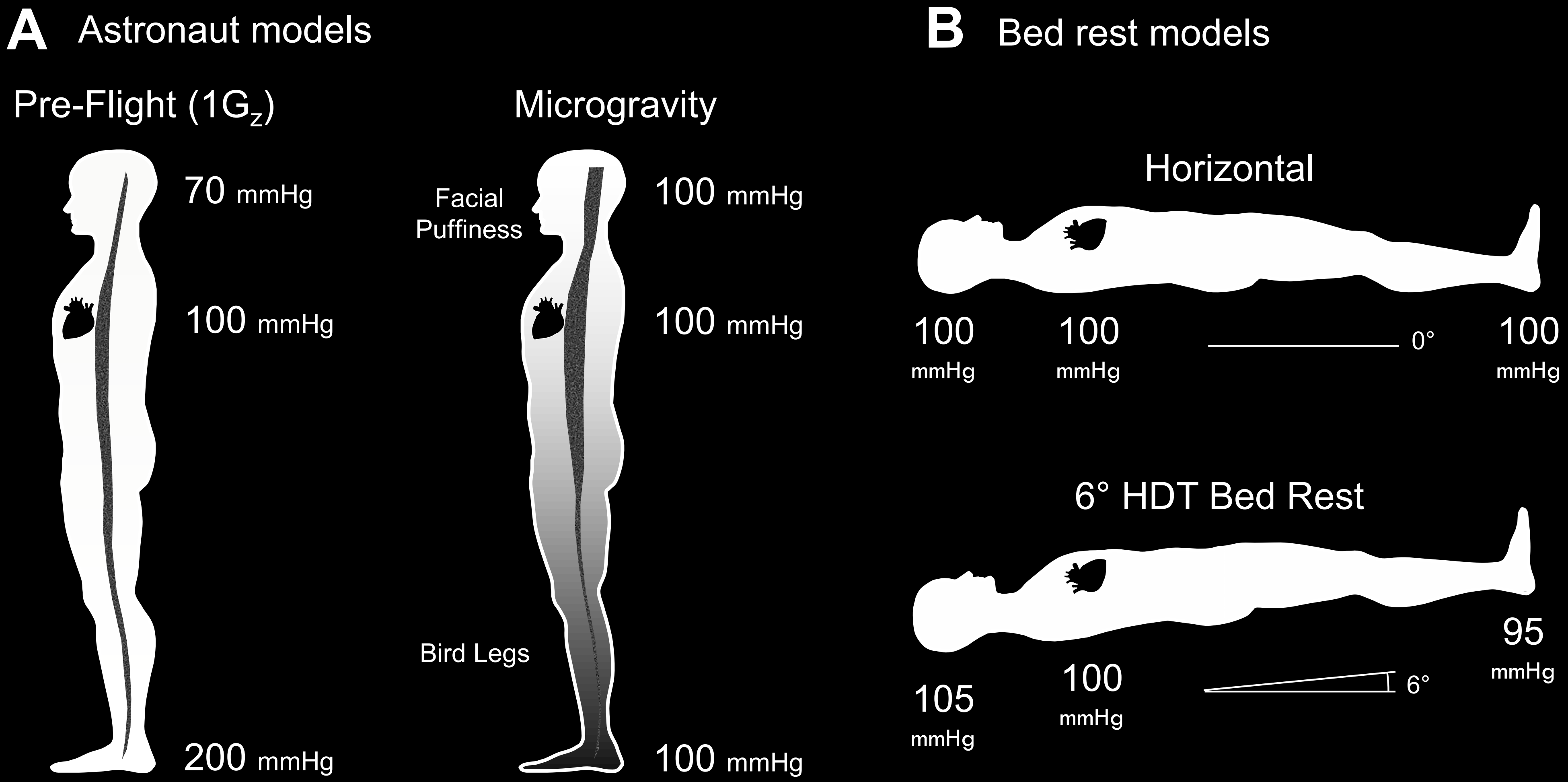
En post-vol immédiat (après des missions de 4-6 mois)

- Perte osseuse au niveau des os porteurs, variation inter-individuelle importante
- Augmentation de la porosité corticale dans os non porteurs
- Remodelage osseux découplé en faveur de la résorption
- Balance calcique négative et altération des hormones phospho-calciques en réponse aux modifications d'activités cellulaires osseuses

En récupération

- Rebond de la formation osseuse et récupération de la résorption (entre 3 et 6 mois) puis diminution au délà de 6 mois.
- Le tibia cortical récupère, pas le trabéculaire à 12 mois
- Le radius conserve une porosité augmentée et montre une fragilité osseuse qui devient significative à 12 mois
- Les paramètres biomécaniques (ultimate load) sont compromis aux deux sites 12 mois après le retour

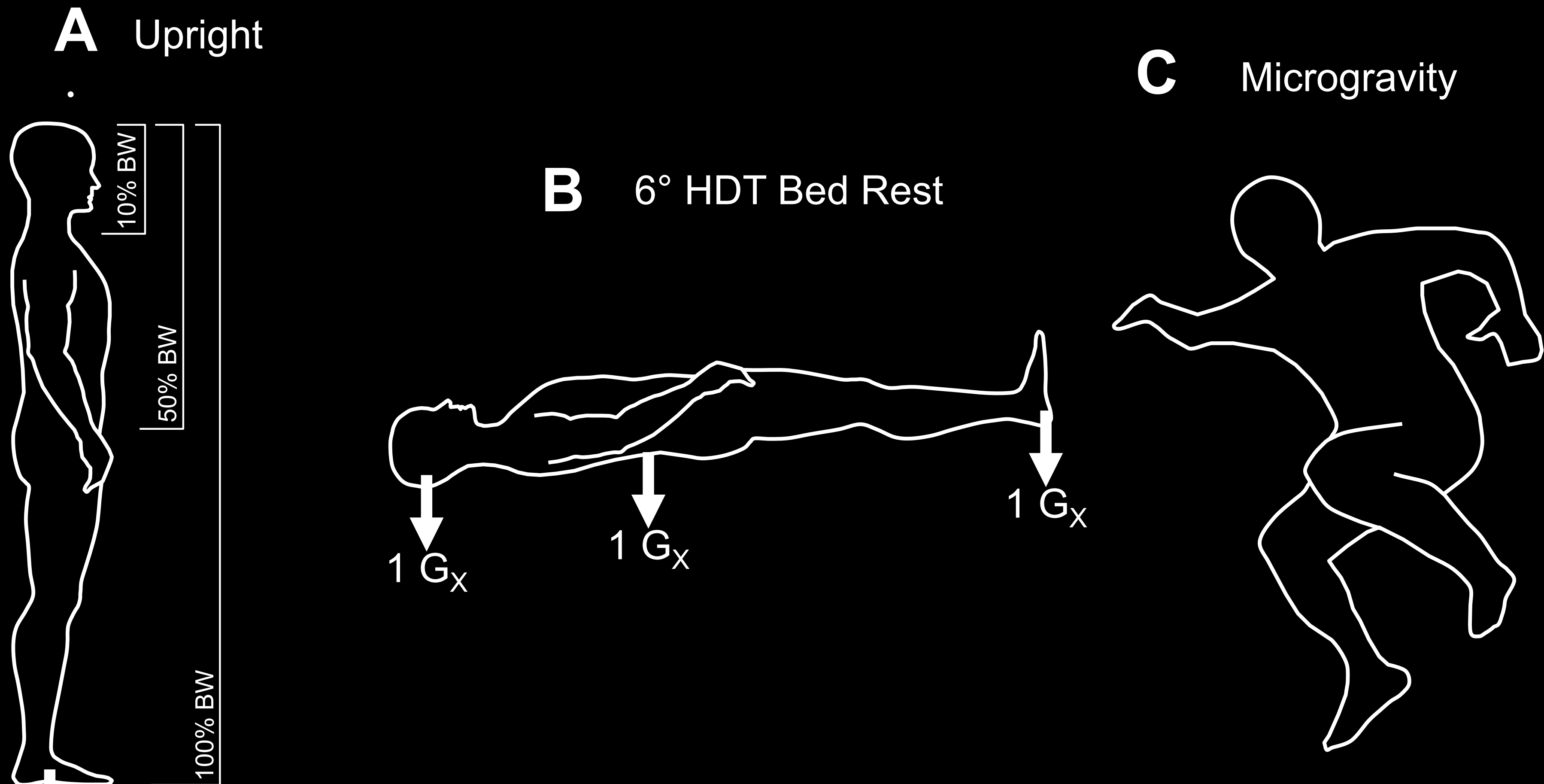
« LES ANALOGUES »



Hypothetical arterial blood pressures (mmHg) and tissue fluid accumulations on Earth and in actual microgravity, horizontal bed rest and 6 degrees head-down-tilt bed rest.

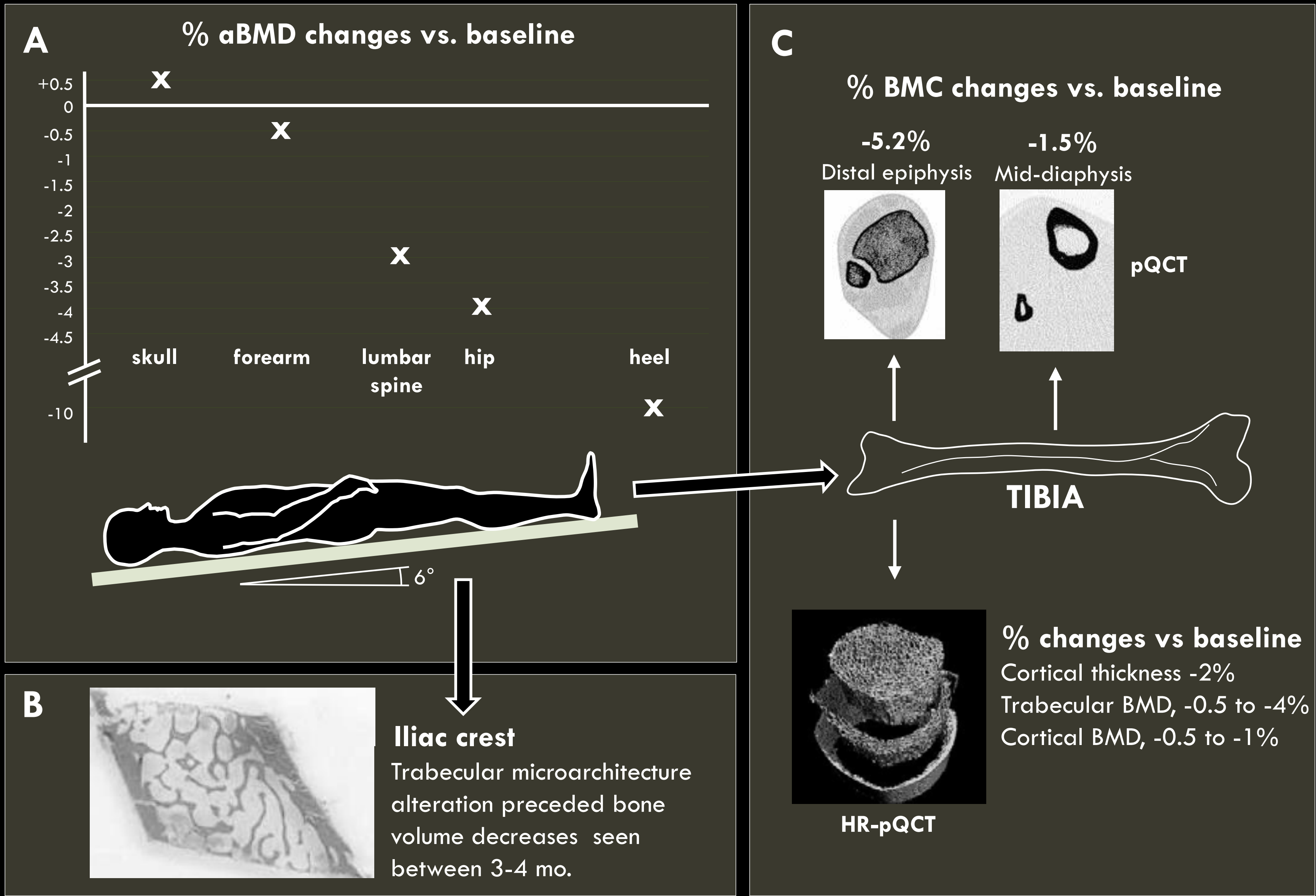
Hargens and Vico JAPPL, 2016

GRAVITY VECTORS



A: upright posture on Earth provides a 1 Gz vector from head to feet.
B: in 6 degrees headdown- tilt bed rest, the Gz vector is mostly lost, so that the body adapts to a Gx vector from anterior to posterior when supine.
C: astronauts experience no significant gravity vector

Hargens and Vico JAPPL, 2016



Attempt at synthesis of bone changes after 2-3 months bed rest duration (except when precised)

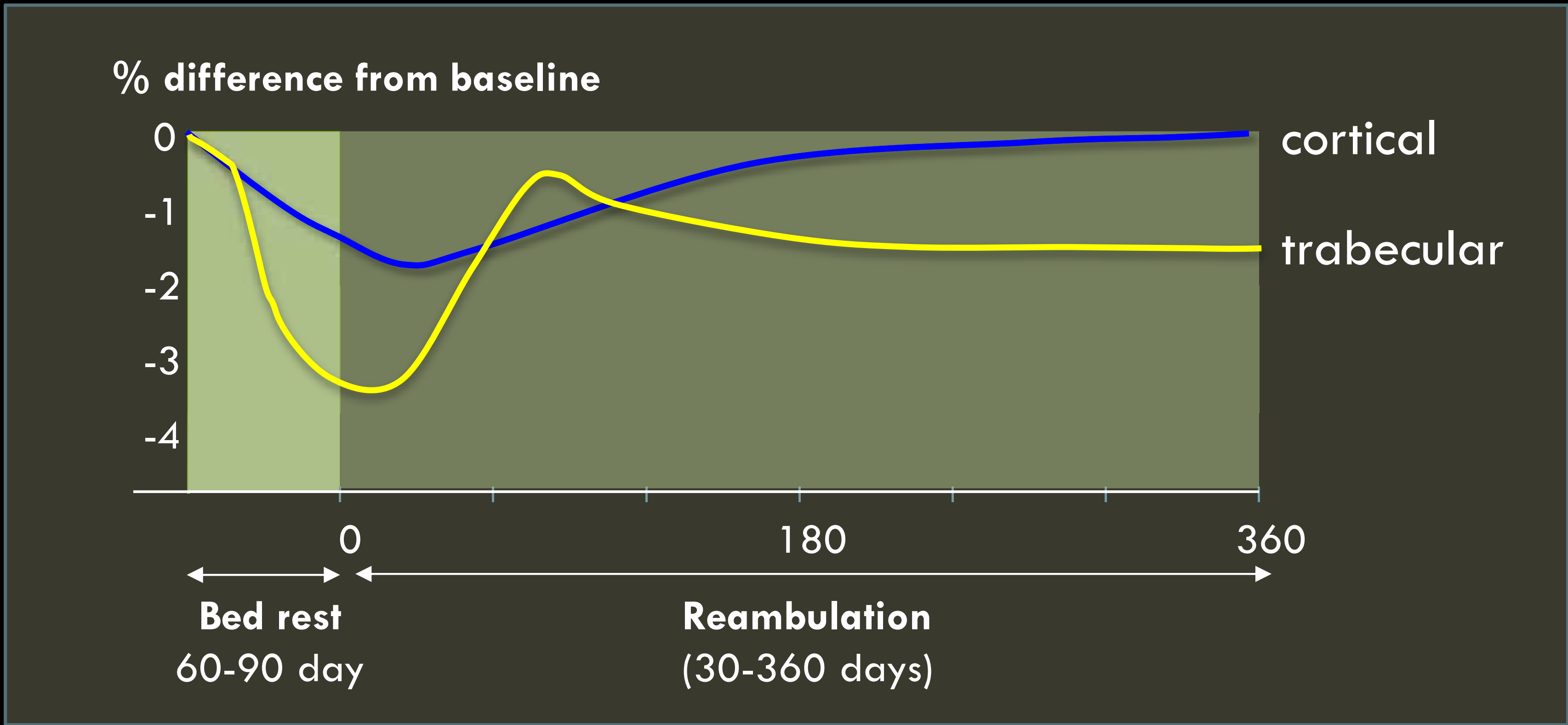
A) DXA areal bone mineral density (aBMD, mg/cm^2) changes vs. baseline

B) Histomorphometry main features from iliac crest biopsies

C) Quantitative computed tomography, peripheral (pQCT, BMC in mg) upper part; high resolution –pQCT (HR-pQCT, BMD, bone mineral density in mg/cm^3) lower part

Hargens and Vico JAPPL, 2016

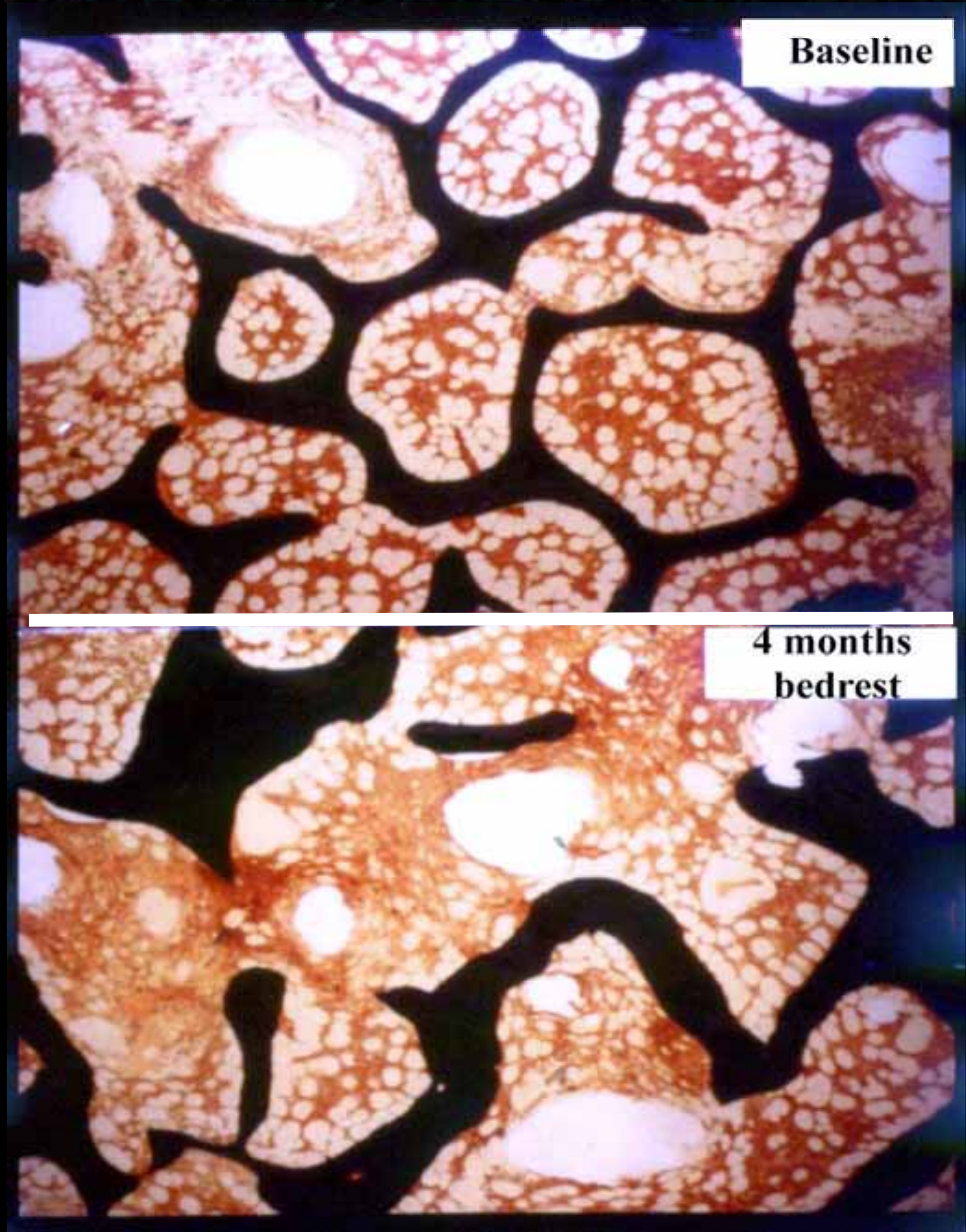
ONE YEAR RECOVERY OF TIBIAL CORTICAL AND TRABECULAR (DISTAL END) BONE AFTER 60 TO 90 DAY BEDREST



It seems that bone loss continues during the first month of reambulation then both compartments revert their slope, cortical bone eventually normalizes, but not trabecular bone.

Hargens and Vico JAPPL, 2016

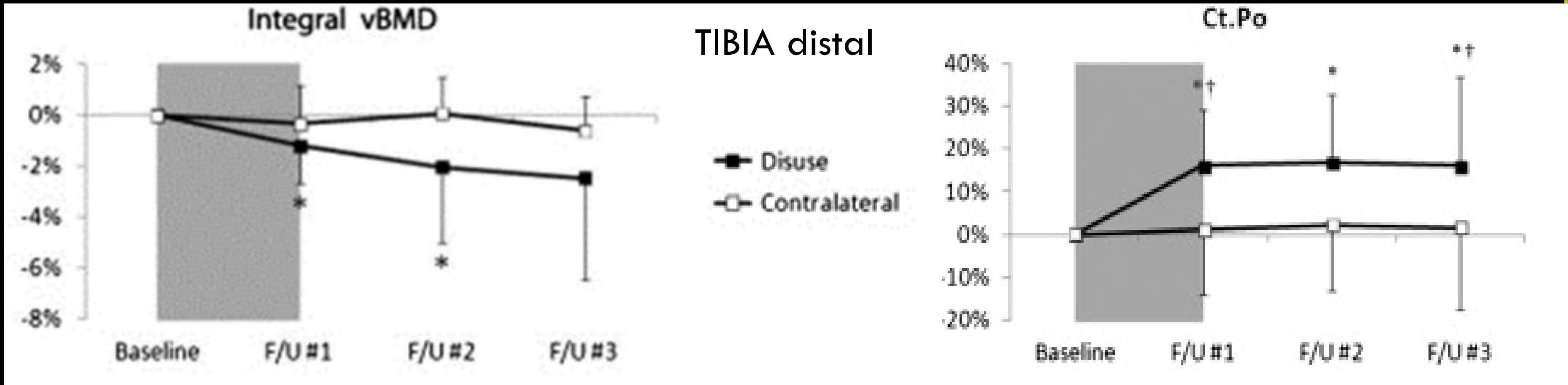
BONE ILIAC CREST 4-MONTH ANTIORTHOSTATIC BEDREST



Palle S, Calcif Tissue Int. 1992

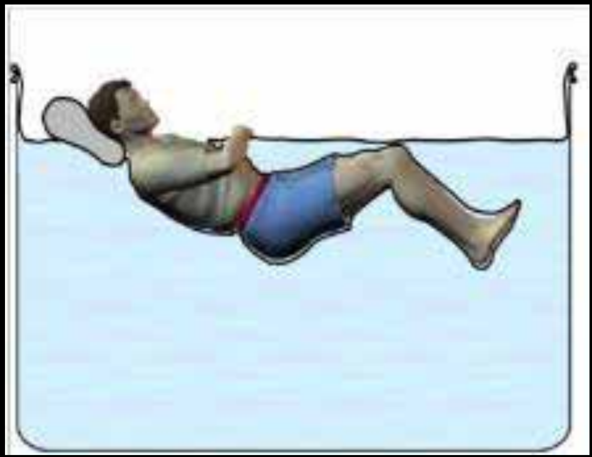
EFFETS DE L'IMMOBILISATION

Marche avec béquilles pendant 6 sem. + suivi à 6 et 13 sem, 12 patients (chirurgie du genou, du plateau tibial, du fémur)



Kazakia GJ et al., Bone, 2014

IMMERSION SECHE



L'atout le plus important de l'immersion sèche est l'absence de support.

température de l'eau entre 32°C et 34,5°C

HYPERGRAVITÉ

Options to apply artificial gravity during spaceflights:

- To rotate a complete module of the spacecraft
- To use a short arm human centrifuge → less complex and expensive, but feasibility must be proven

PROOFS OF CONCEPT : RODENT MODELS

Continuous hypergravity

2 and 3g exposure, 21 days,
male C57BL6/J, 7 wks-old

2g continuous

µCT

BV/TV: +24%
Tb.N: +18%
Conn.D: +36%

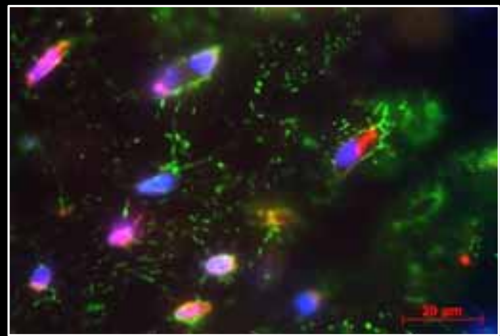
Histo

Formation:
Os/BS: +33%
dLS/BS: +31%
Resorption:
Oc.S/BS: -41%

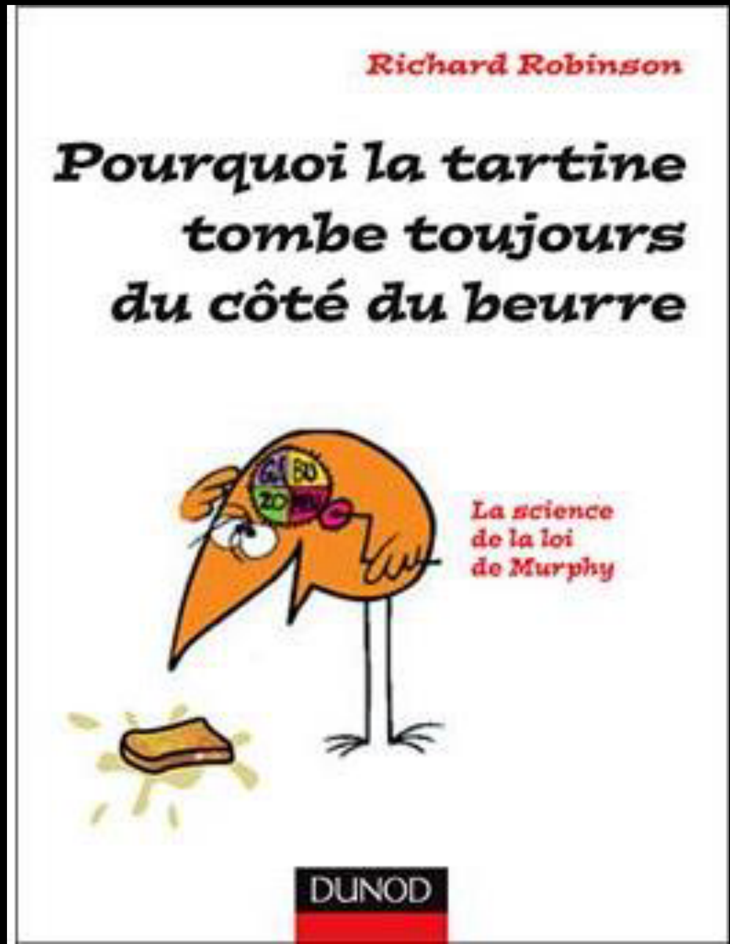
Vessels

Ves.Num: +22%
Ves.Area+44%

Osteocytes
Sclerostine: ↓
DMP1: ↑



MERCI !



A. HELD and P. YODZIS «On the Einstein-Murphy Interaction» General Relativity and Gravitation, Vol. 13, No. 9, 1981