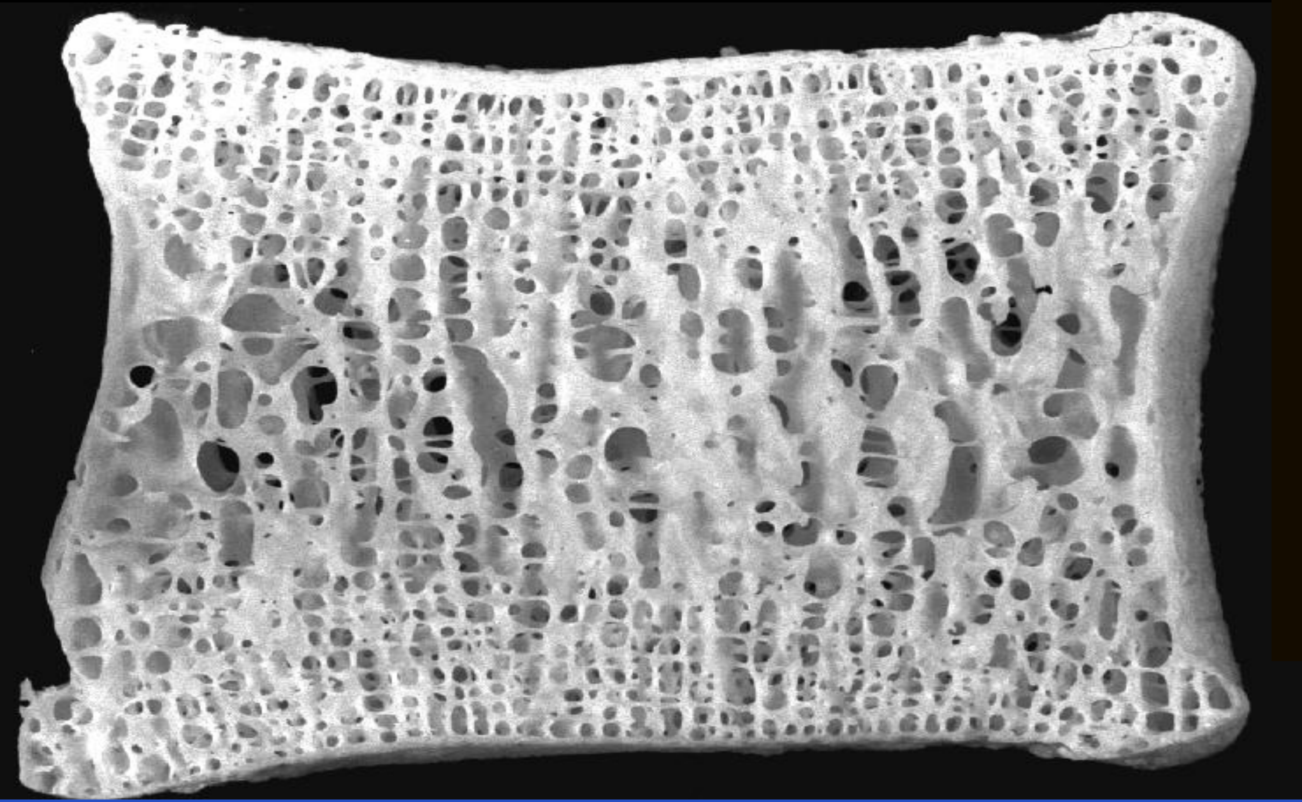
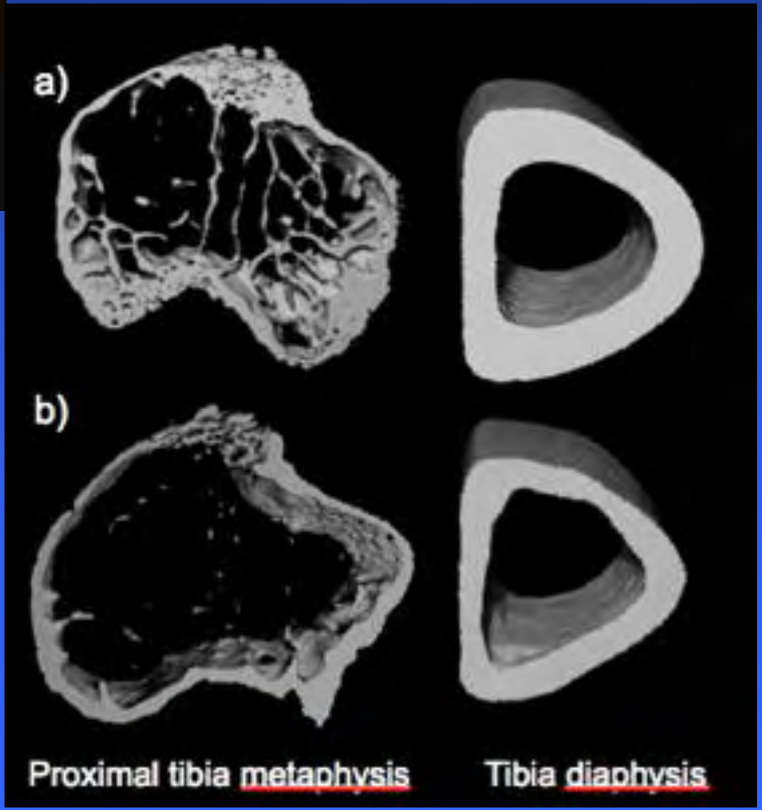
La minéralisation osseuse et la qualité osseuse

Prof P. Ammann

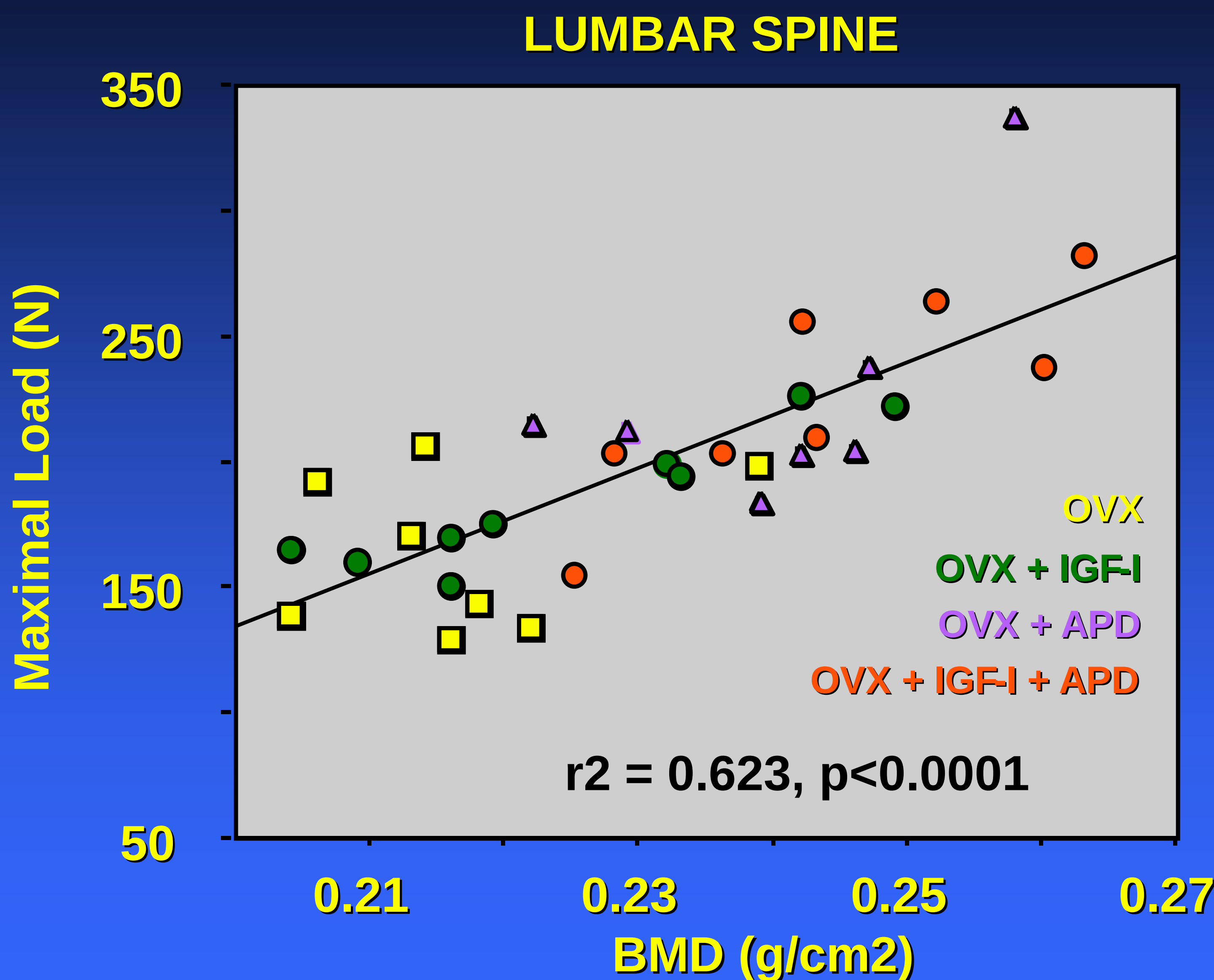
Service des maladies osseuses
Département des spécialitées de médecine

Séminaire “Minéralisation osseuse”
Lyon 26 Mai 2016

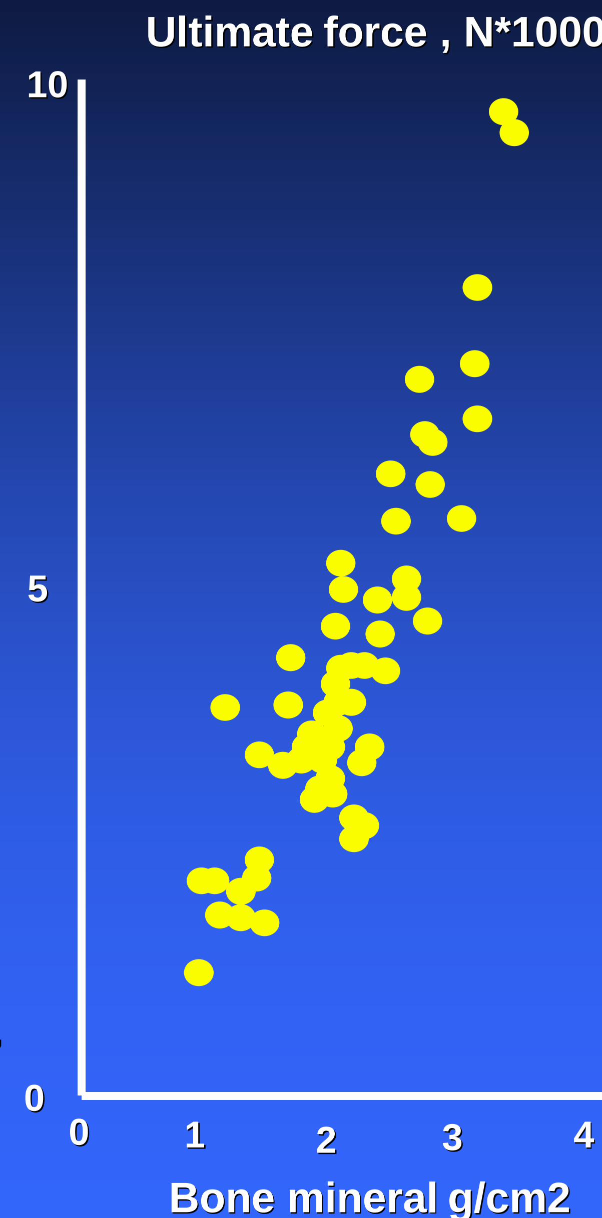



a)
b)
Proximal tibia metaphysis
Tibia diaphysis

Rats Model

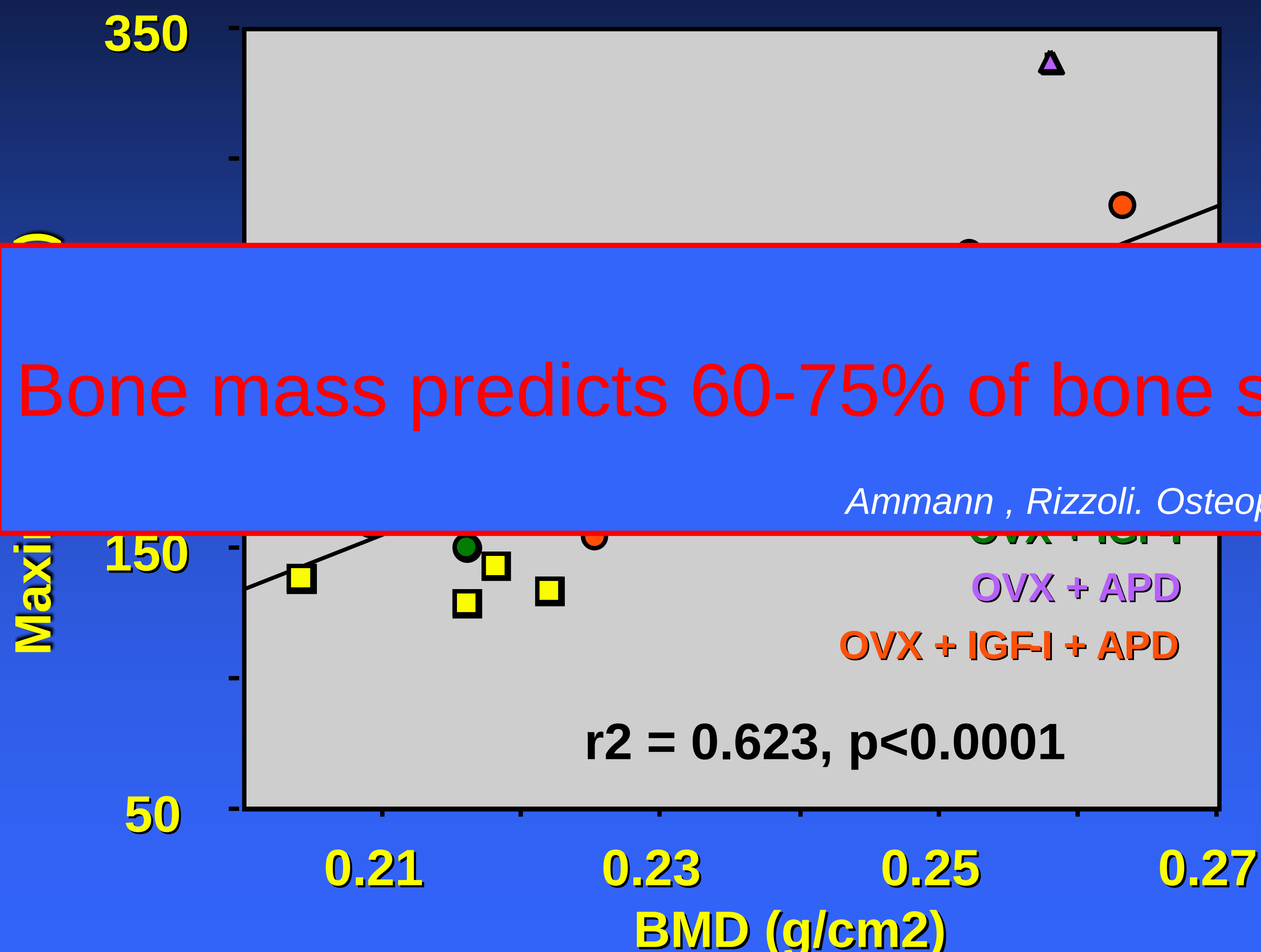


Human



Ammann, Rizzoli, Meyer, Bonjour.Osteoporos Int. 1996;6:219-27.

Rats Model



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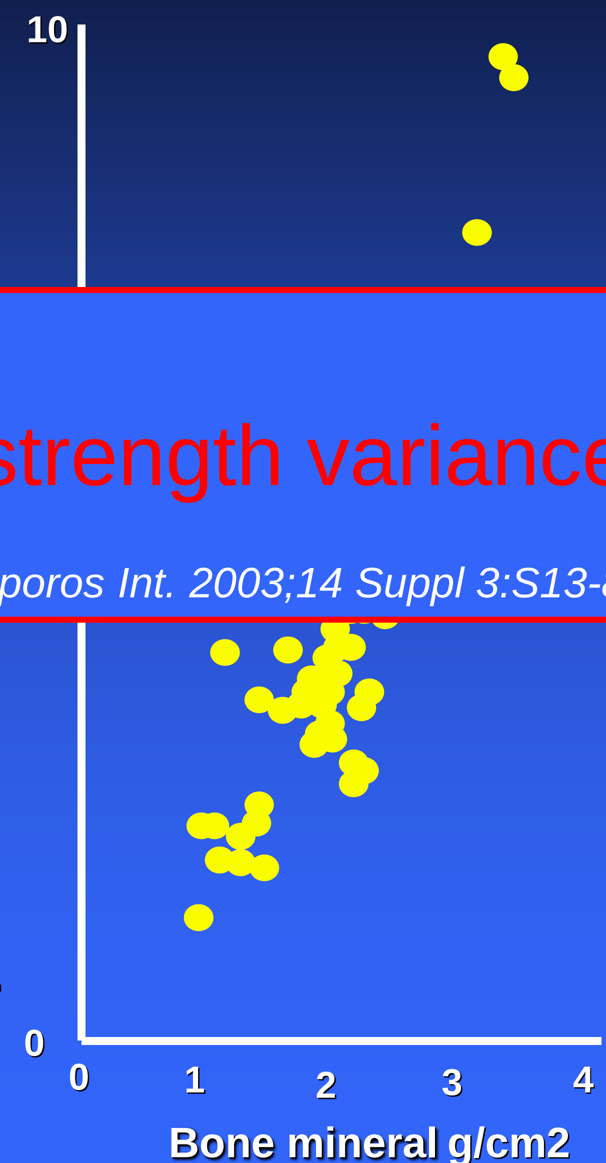
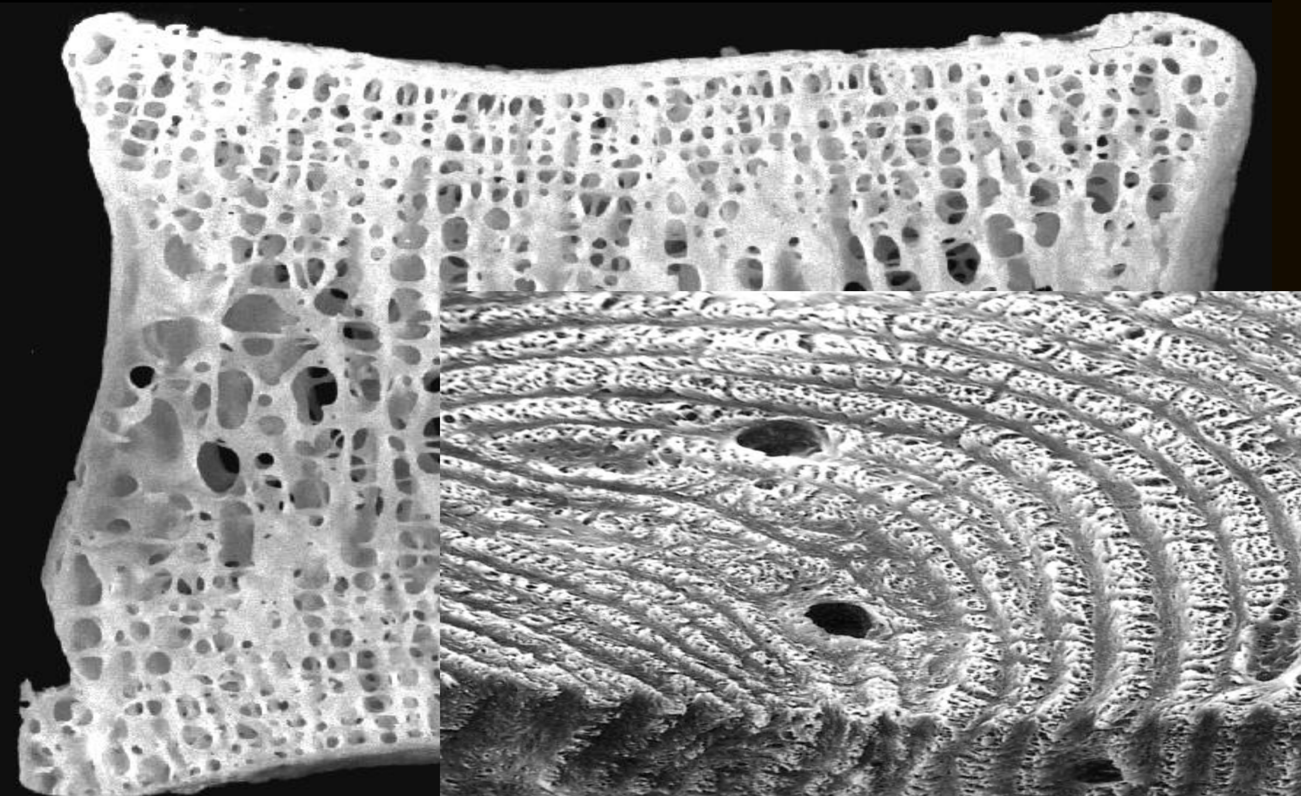
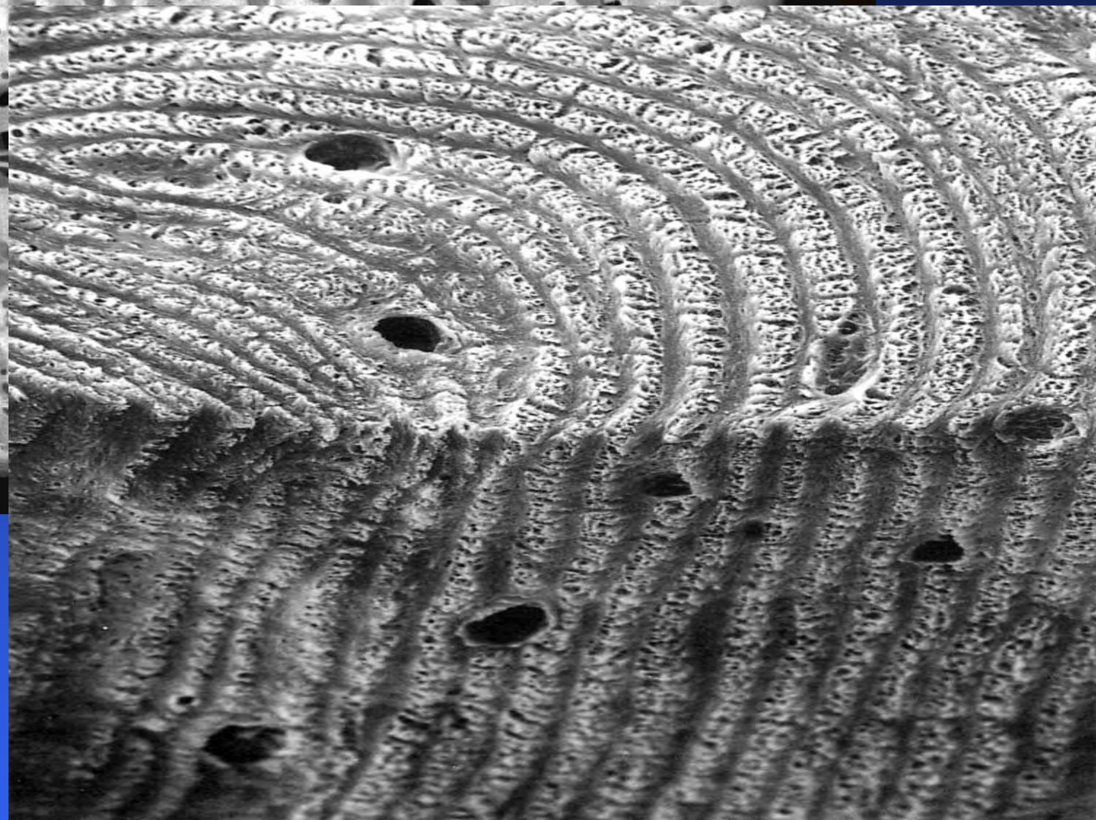
Human



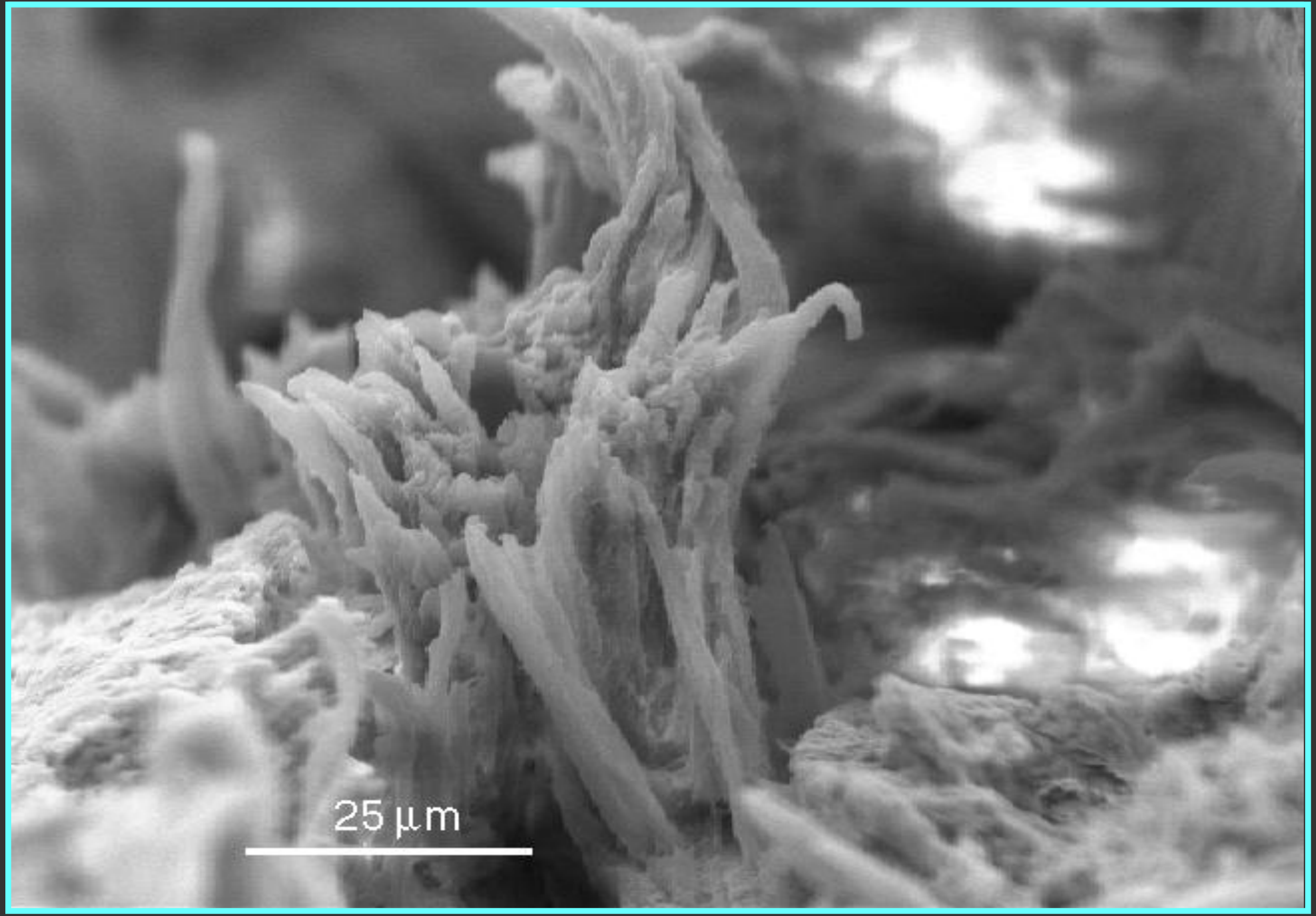
Bone mass predicts 60-75% of bone strength variance

Ammann , Rizzoli. Osteoporos Int. 2003;14 Suppl 3:S13-8.

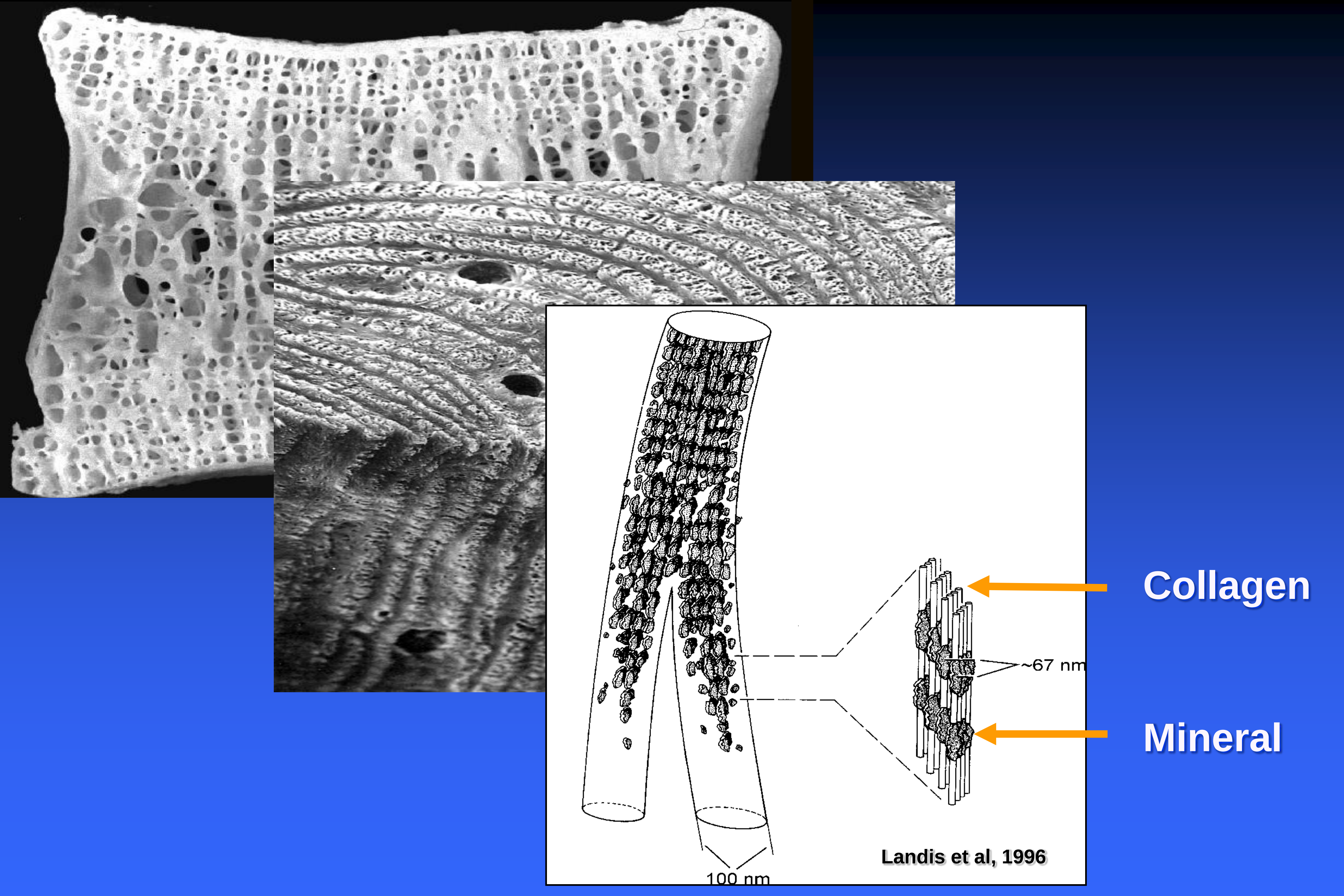



Mineralized Collagen Fibrils

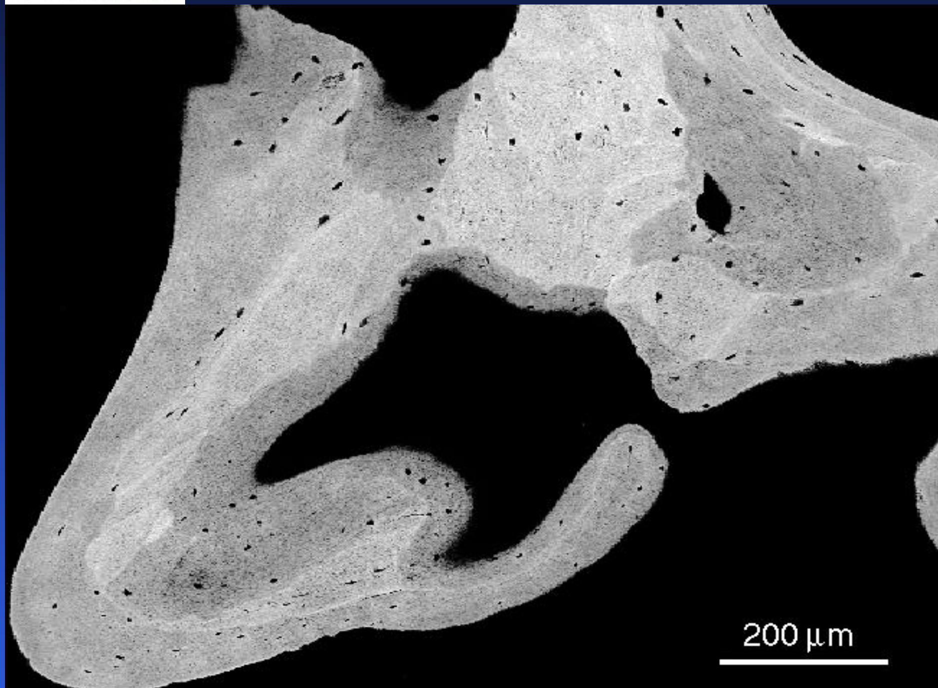
basic building block of bone



SE-image of ruptured bone


~67 nm
100 nm
Landis et al, 1996
Collagen
Mineral

Degree of Mineralisation of Bone



The degree of mineralisation of bone is inversely related to bone turnover

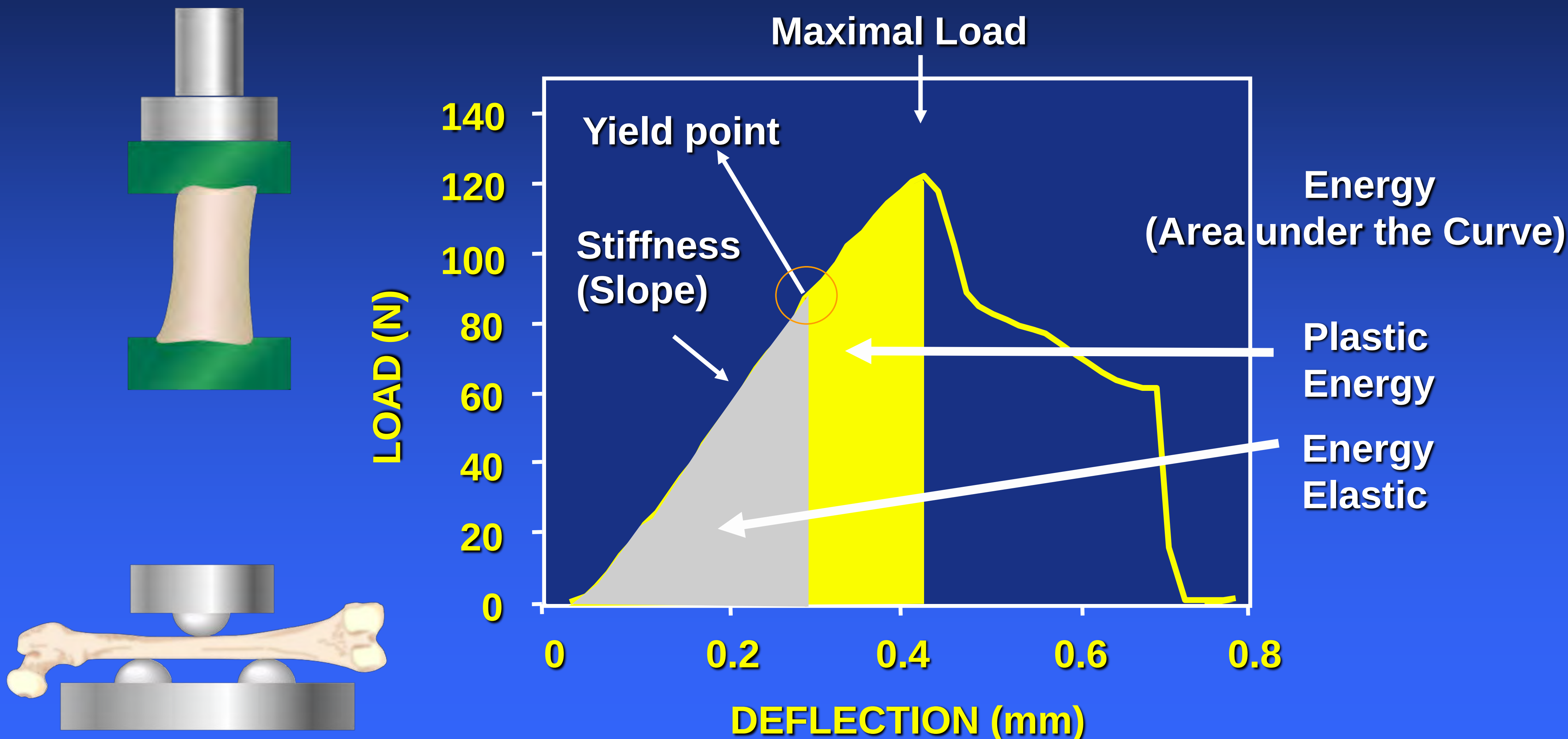
Primary mineralisation:

mineralisation during bone remodelling cycle
(few days, up to 70%)

Secondary mineralisation:

slow and gradual maturation of mineral and increase in its amoun
(months/year scale)

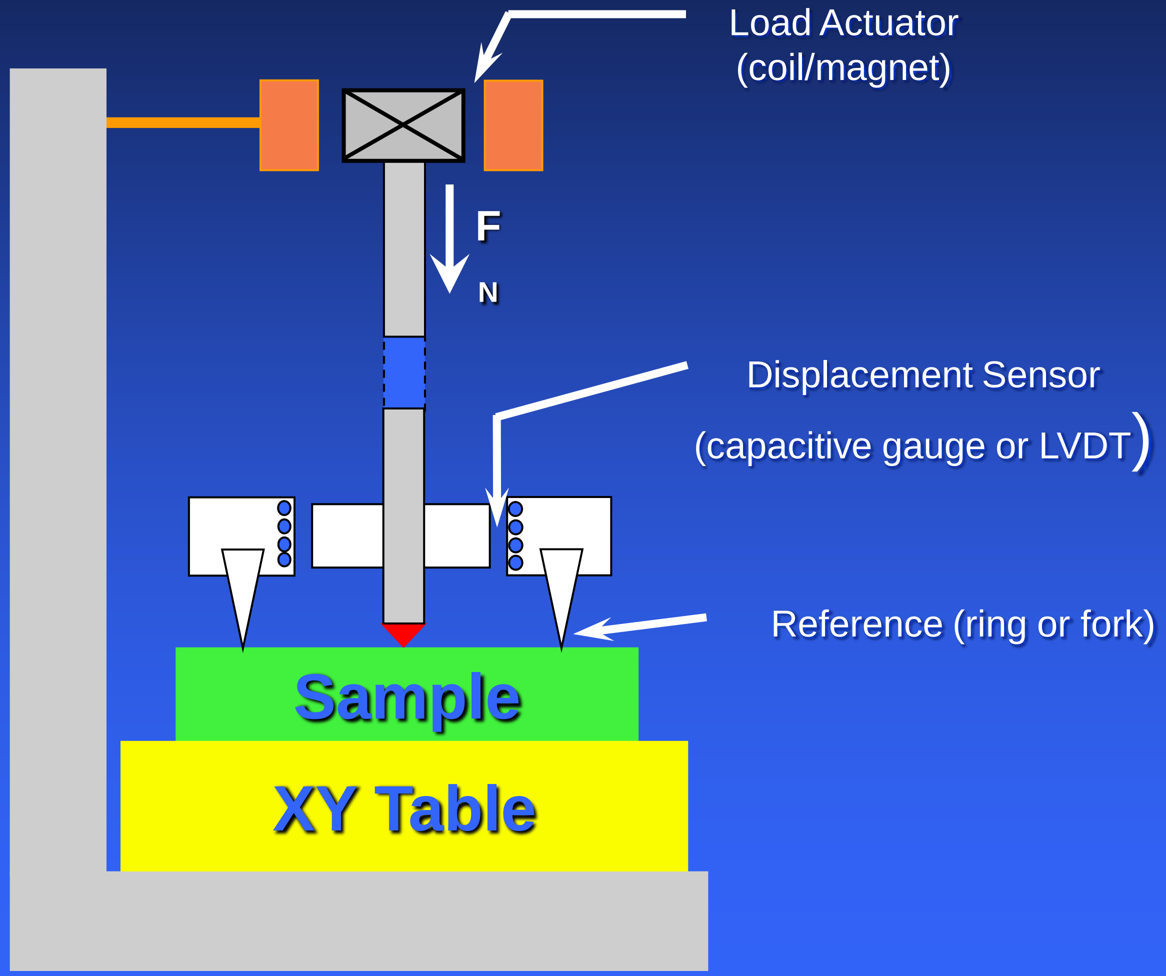
Biomechanics: Load Deflection Curve

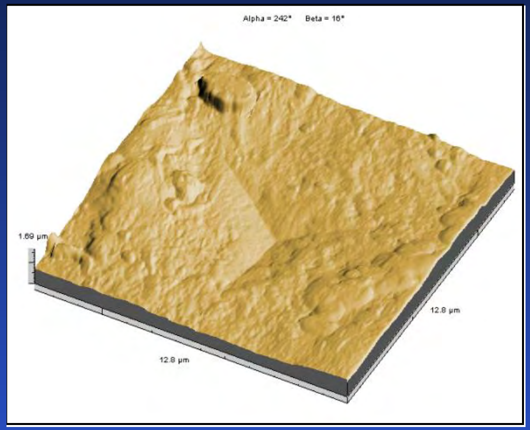


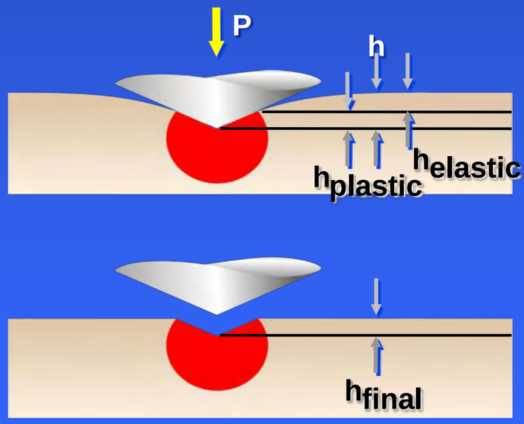
Ammann , Rizzoli. Osteoporos Int. 2003;14 Suppl 3:S13-8.

Instrument of nano-indentation

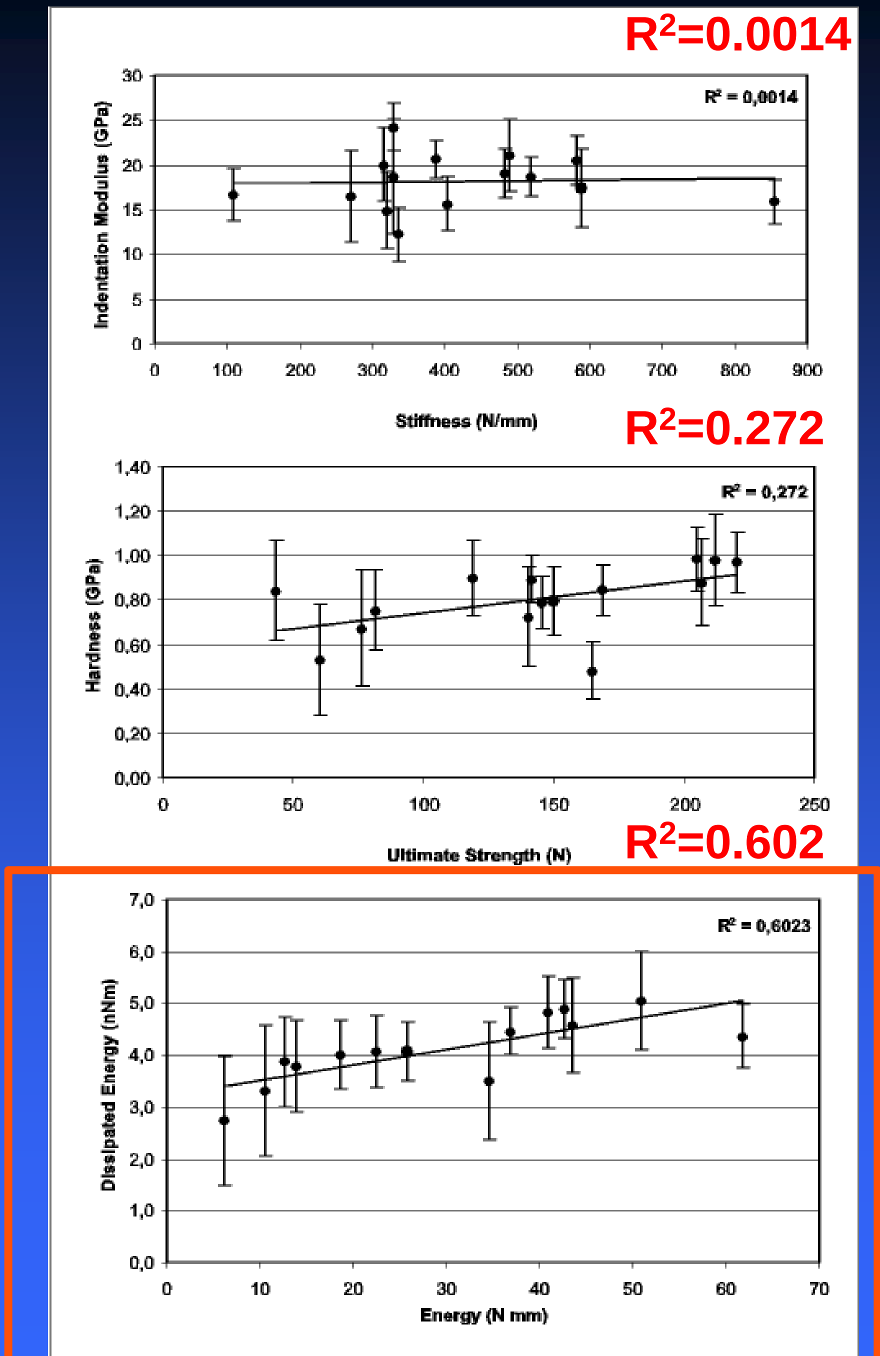
Principle

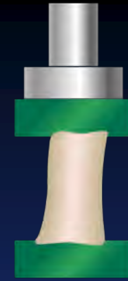




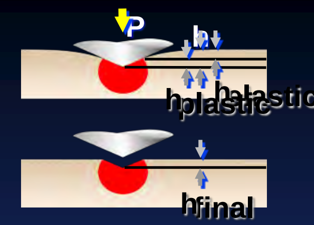


Ammann, Hengsberger , Legros , Rizzoli , Zysset . Bone. 2005;36(1):134-41.





VS



Stiffness vs Modulus

Ultimate strength vs hardness

Energy vs dissipated energy

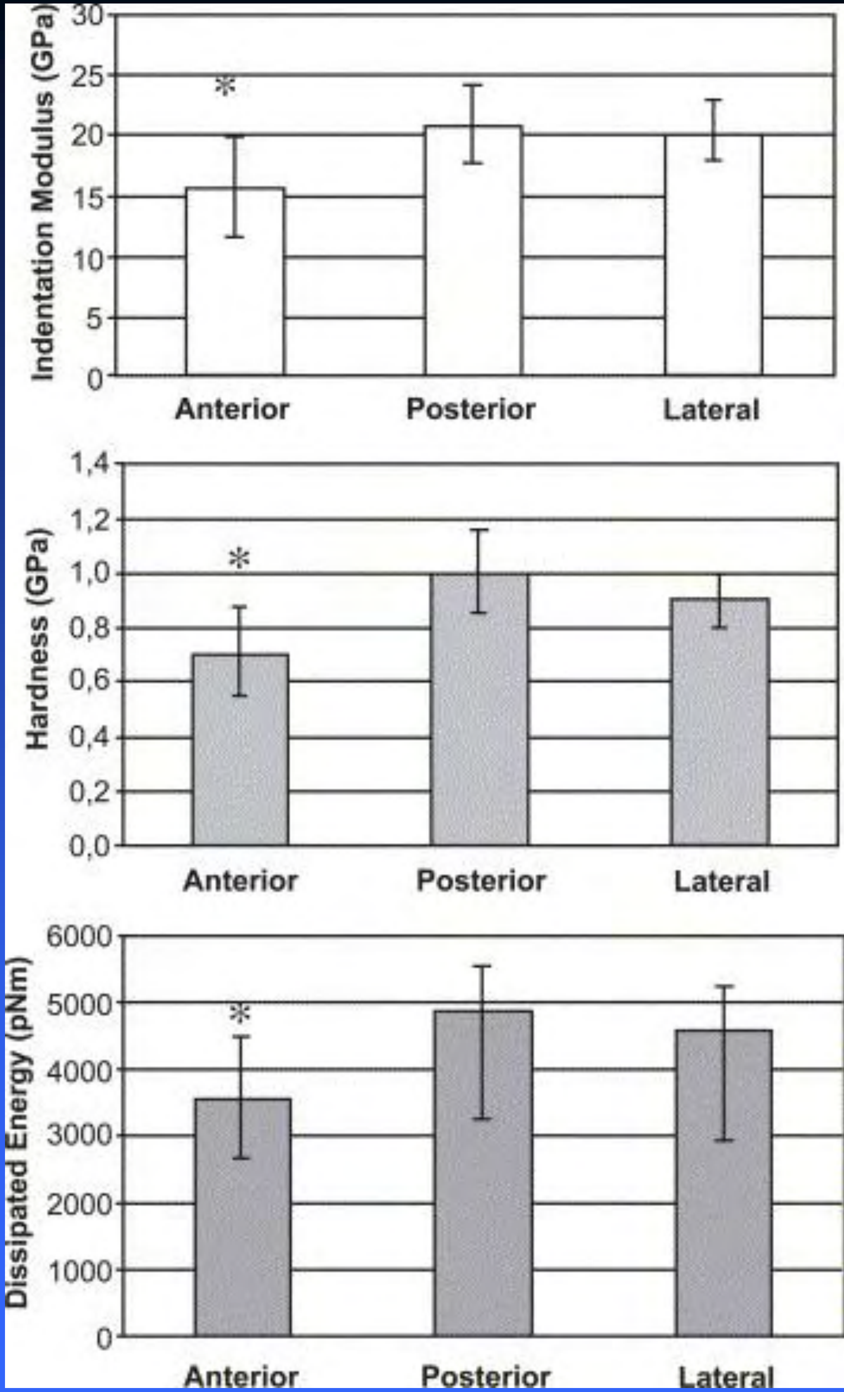
Ammann, Hengsberger , Legros , Rizzoli , Zysset . Bone. 2005;36(1):134-41.

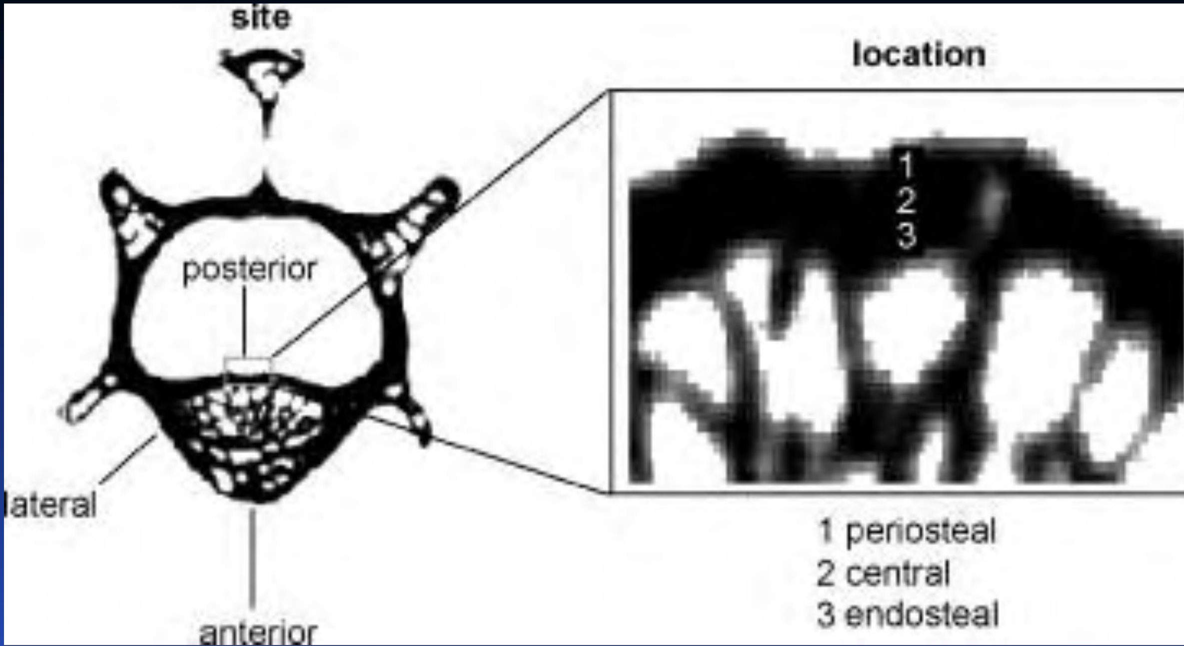
Intrinsic Trabecular Bone Quality : Nano Indentation

Dry Conditions	Control	Strontium ranelate 900 mg/kg/d
Modulus	19.35 ± 0.39	19.33 ± 0.40
Hardness	849 ± 21	887 ± 21
Working Energy	5318 ± 149	5254 ± 173

Physiological	Control	Strontium ranelate 900 mg/kg/d
Modulus	12.37 ± 0.34	14.24 ± 0.37 *
Hardness	457 ± 18	510 ± 19 *
Dissipated Energy	4142 ± 146	4677 ± 160 *

Ammann, Badoud, Barraud, Dayer, Rizzoli. J Bone Miner Res. 2007 Sep;22(9):1419-25.





Ammann, Hengsberger , Legros , Rizzoli , Zysset . Bone. 2005;36(1):134-41.

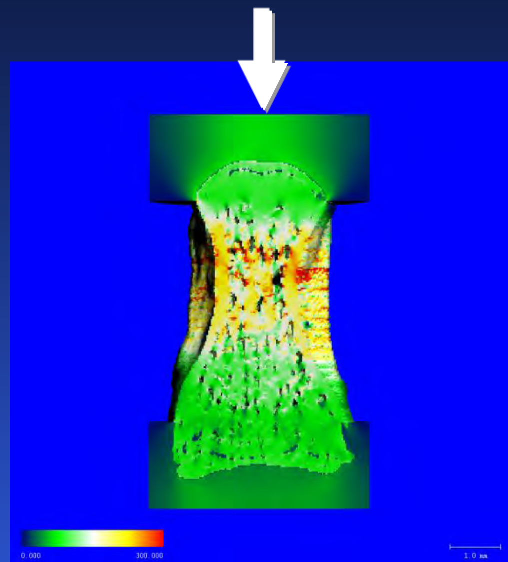
Stepwise regression: Ultimate Strength

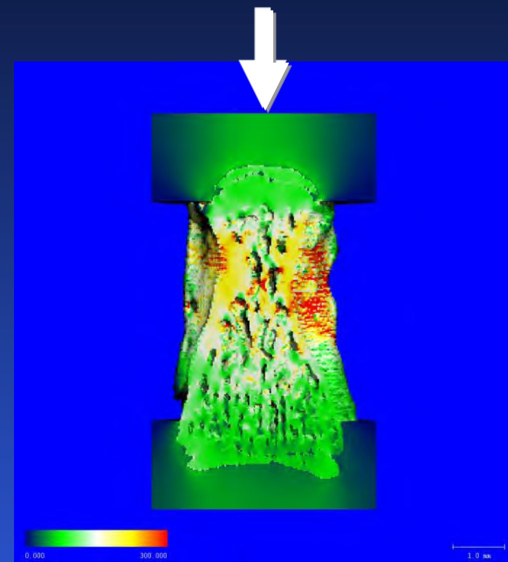
	Parameter introduced	Prediction of bone strength variance
Bone Mass	BMD	60 %
Bone Material Level Properties	Elasticity	71 %
	Hardness	95 %

Ammann, Hengsberger , Legros , Rizzoli , Zysset . Bone. 2005;36(1):134-41.

FE analysis integrating two important determinants of bone strength bone **microarchitecture** and **intrinsic tissue quality**.

Strontium Ranelate





Control

- **Bone microarchitecture and intrinsic tissue quality can explain independently bone strength**

- **When augmented intrinsic tissue quality was taken into account in the FE models,**
  - **the stiffness was estimated to be +31% (compared to +22%)**
  - **the failure load was estimated to be +48% (compared to +29%).**

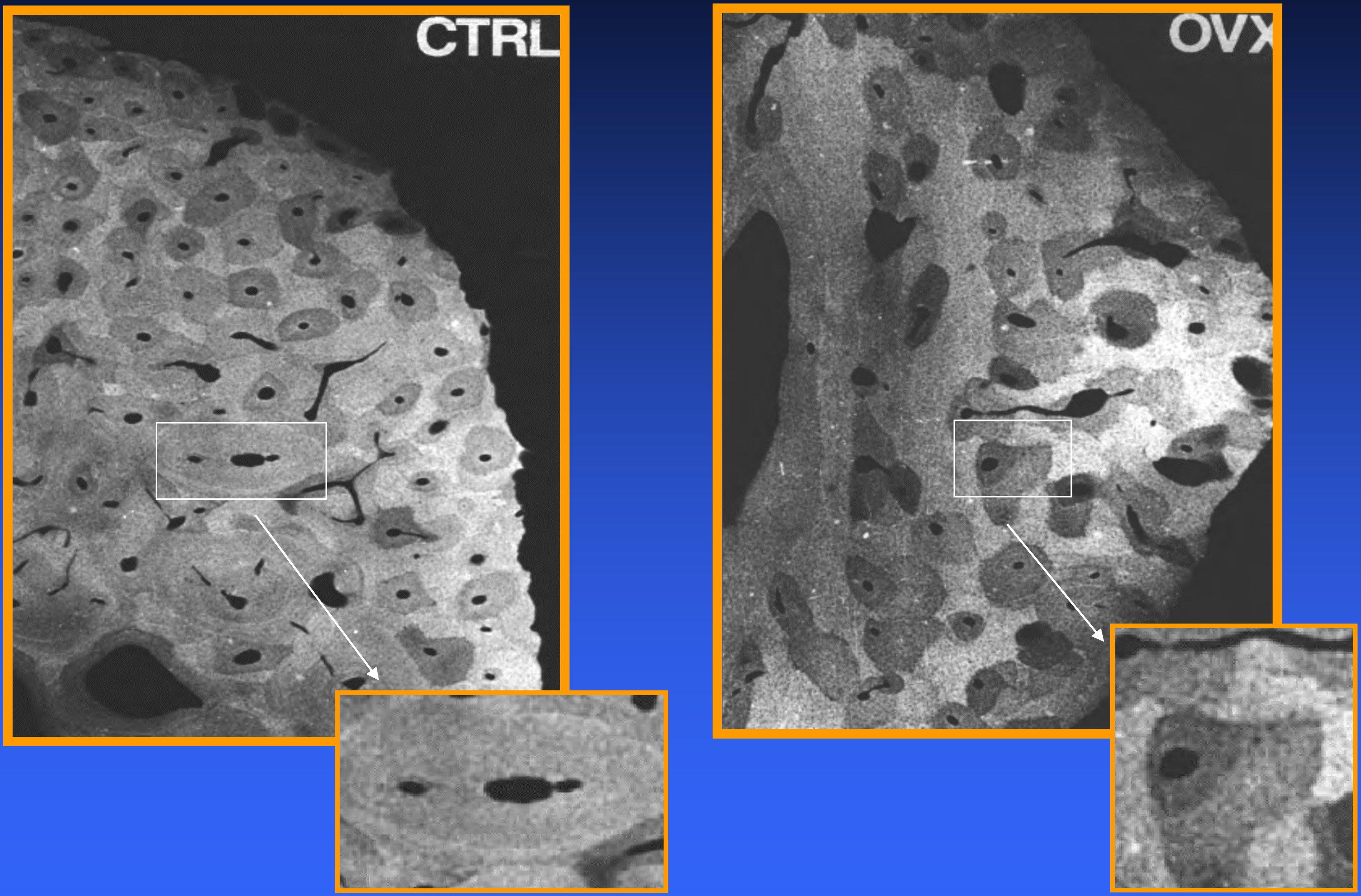
SK Boyd, E Szabo, P. Ammann (BONE 2011)

Effects of anticatabolic and anabolic agents on determinants of bone strength

	Ovariectomized rats			
	Controls	Pamidronate	Raloxifen	Teriparatid
MAXIMAL LOAD	↓	↑	↑	↑↑
BONE MASS & MICRO-ARCHITECTURE	↓			
BONE MATERIAL QUALITY	↓			
BONE TURNOVER	↑			

T Brennan, R Rizzoli, P Ammann JBMR 2009

Bone Mineralization



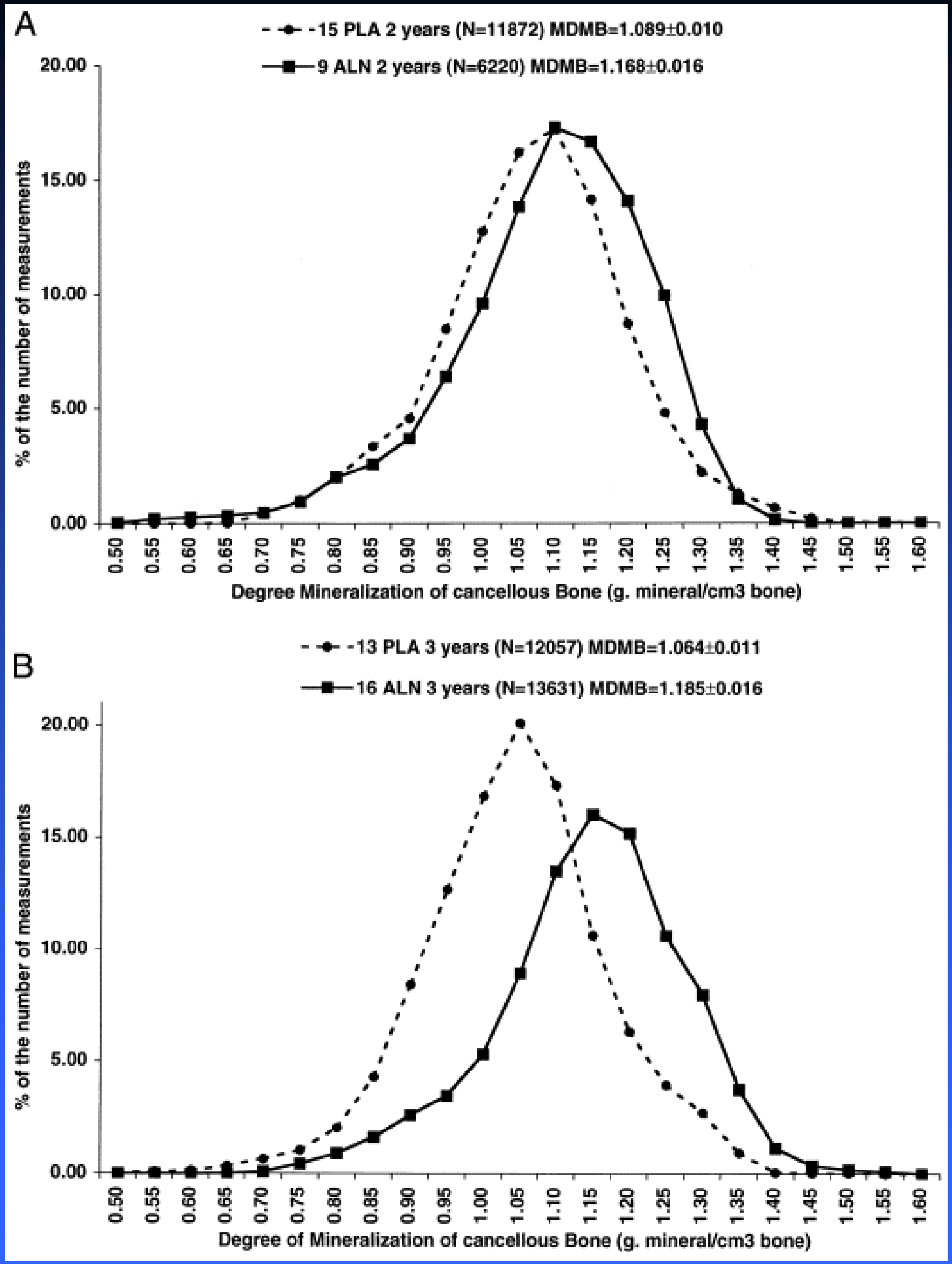
Meunier and Boivin, 1997

Effects of anticatabolic and anabolic agents on determinants of bone strength

Ovariectomized rats

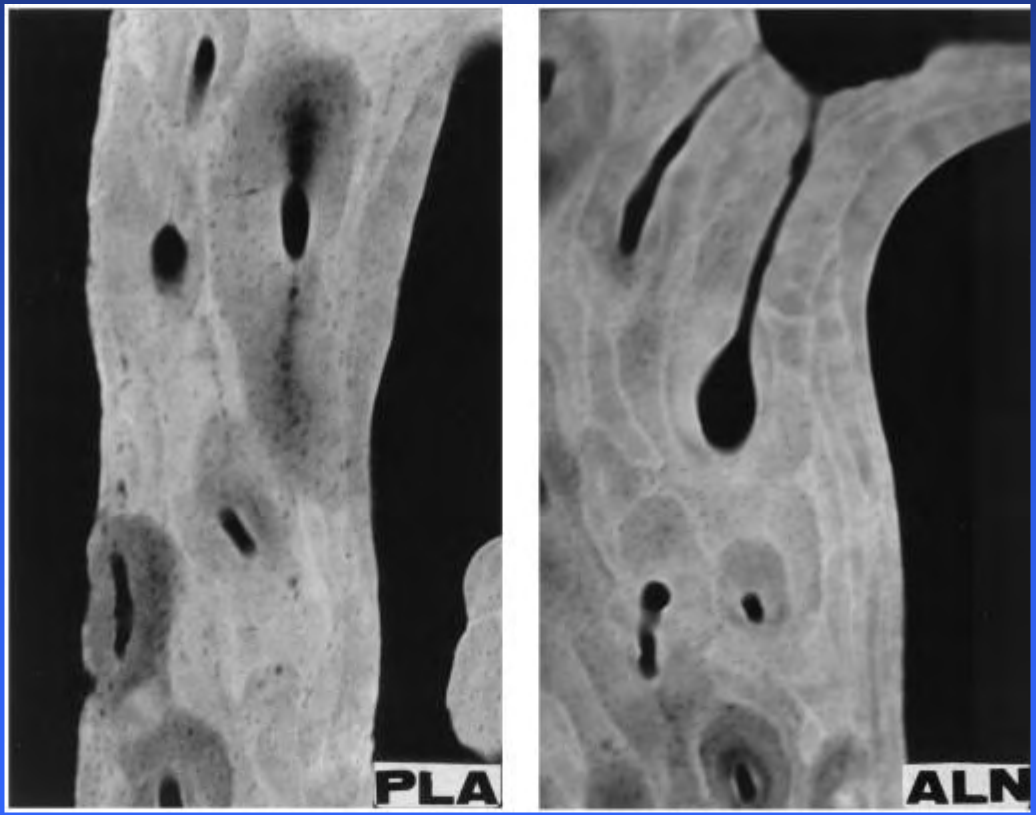
	Controls	Pamidronate	Raloxifen	Teriparatid
MAXIMAL LOAD	↓	↑	↑	↑↑
BONE MASS & MICRO-ARCHITECTURE	↓	↔	↔	
BONE MATERIAL QUALITY	↓	↑	↑	
BONE TURNOVER	↑	↓	↓	

T Brennan, R Rizzoli, P Ammann JBMR 2009



Alendronate increases bone strength by increasing the mean degree of mineralization of bone tissue in osteoporotic women

Boivin, Chavassieux, Santora, Yates, Meunier Bone 2000



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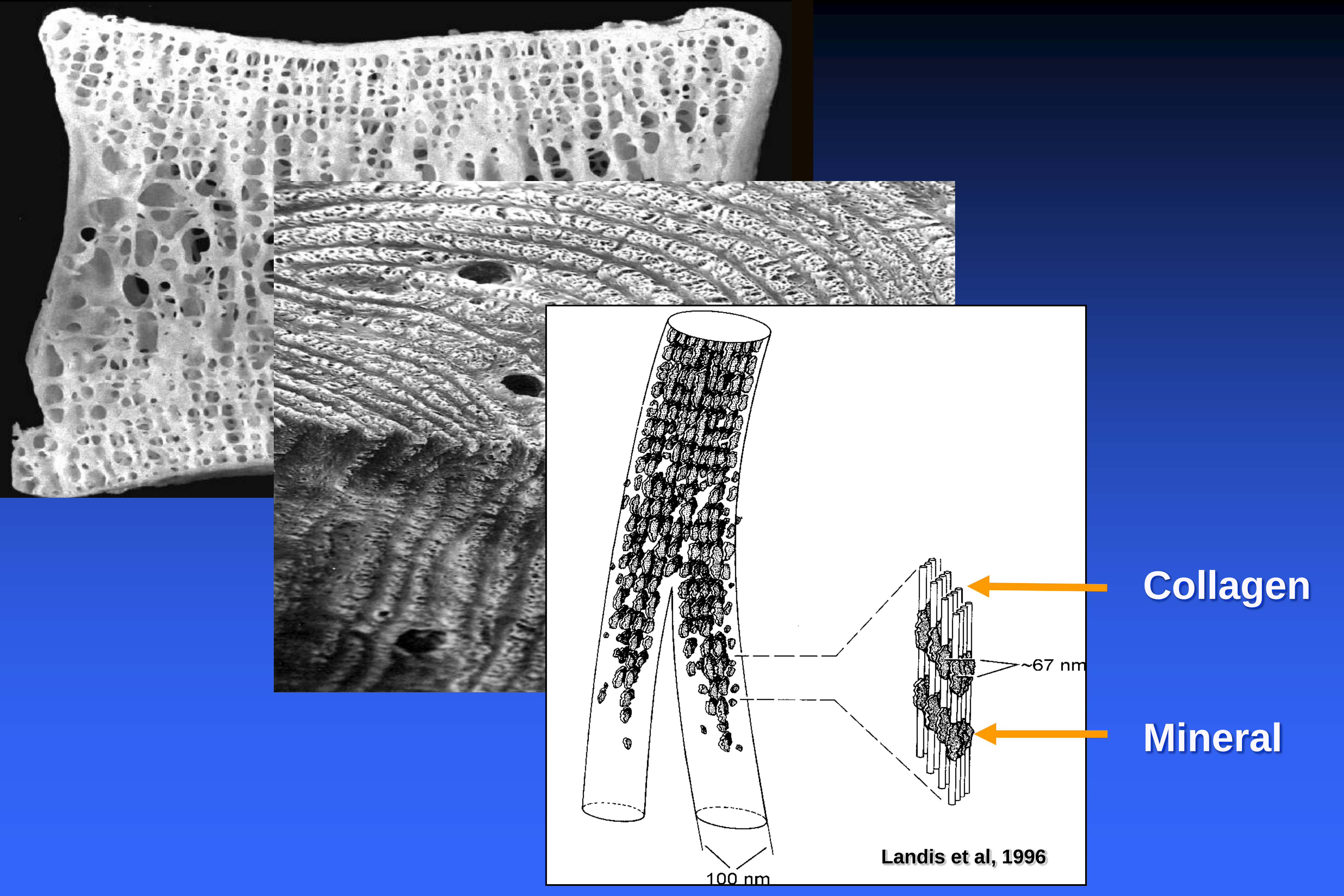
BONE MASS & MICRO-ARCHITECTURE	↓	↔	↔	↑
BONE MATERIAL QUALITY	↓	↑	↑	↓
BONE TURNOVER	↑	↓	↓	↑

T Brennan, R Rizzoli, P Ammann JBMR 2009

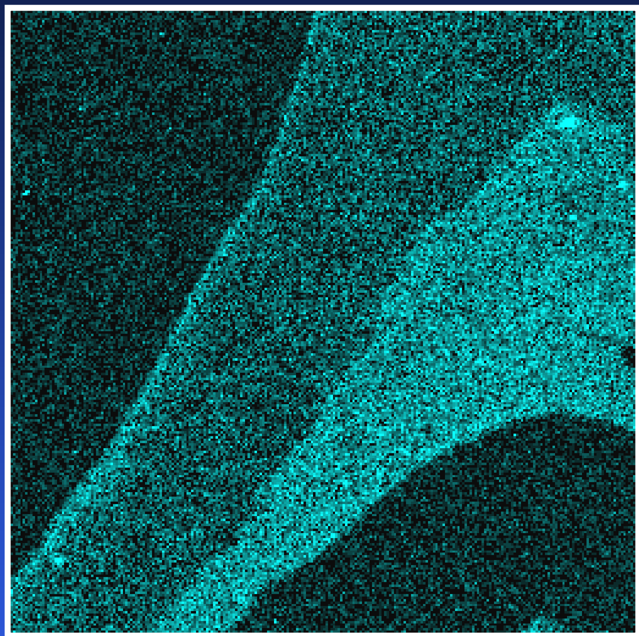

~67 nm
100 nm
Landis et al, 1996
Collagen
Mineral

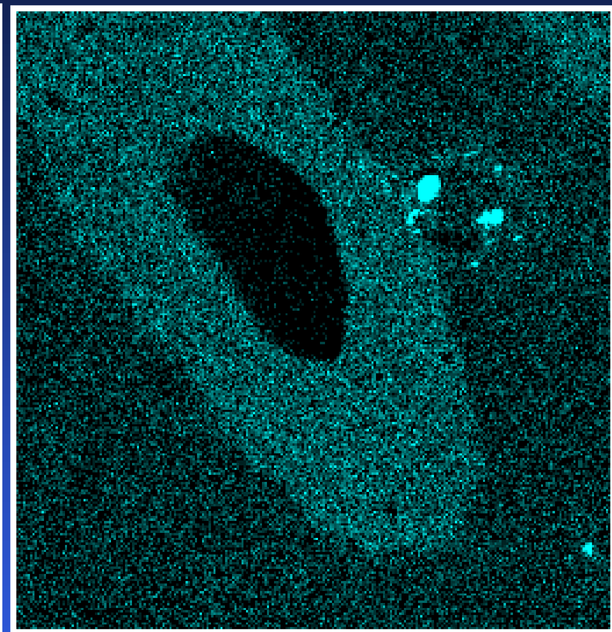
Effects of anticatabolic and anabolic agents on determinants of bone strength

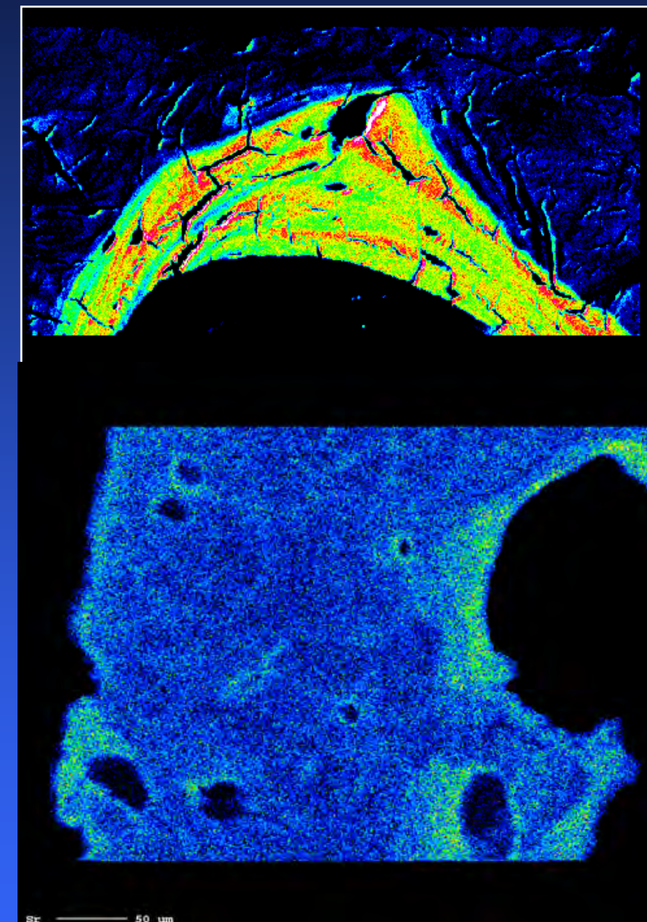
	Ovariectomized rats				
	Controls	Pamidronate	Raloxifen	Teriparatid	SR
MAXIMAL LOAD	↓	↑	↑	↑↑	↑
BONE MASS & MICRO-ARCHITECTURE	↓	↔	↔	↑	↔
BONE MATERIAL QUALITY	↓	↑	↑	↓	↑
BONE TURNOVER	↑	↓	↓	↑	↔

T Brennan, R Rizzoli, P Ammann JBMR 2009

Strontium Integration in cortical and trabecular Bone : Human and Rat Biopsies







Osteoporosis
Cancelous Bone
SR 2g/day
during 2 years

Osteoporosis
Cortical Bone
SR 2g/day
during 2 years

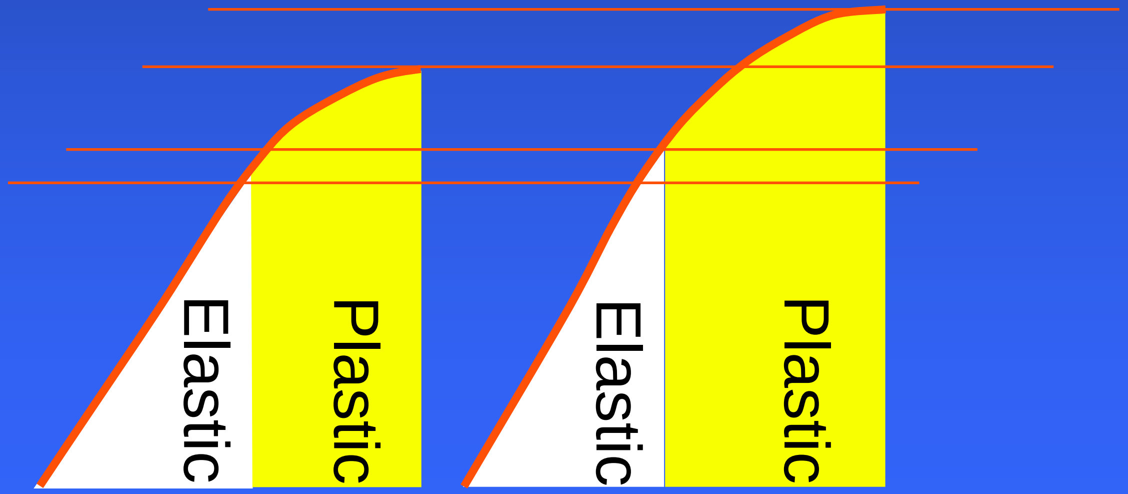
STRATOS Study, transiliac biopsies obtained in Women treated with SR 2g/Day for 2 years.

Boivin et al. 2003

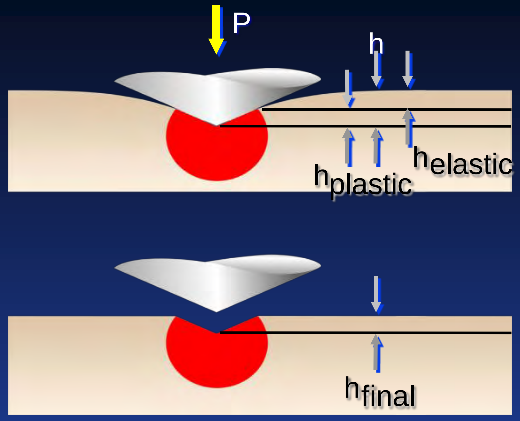
F. Bussy UNIL
P. Ammann UNIGE

Effects of strontium ranelate on bone strength of the vertebra

	Control	SR-900
E	01.8±7.9	157.3±15.0*
E elastic	68.9±5.9	86.6±10.1
E plastic	30.0±3.3	70.7±10.0**
Yield	242.3±10.1	274.4±17.0



Ammann P, Shen V, Robin B, Mauras Y, Bonjour JP, Rizzoli R. J Bone Miner Res. 2004;19(12):2012-20.

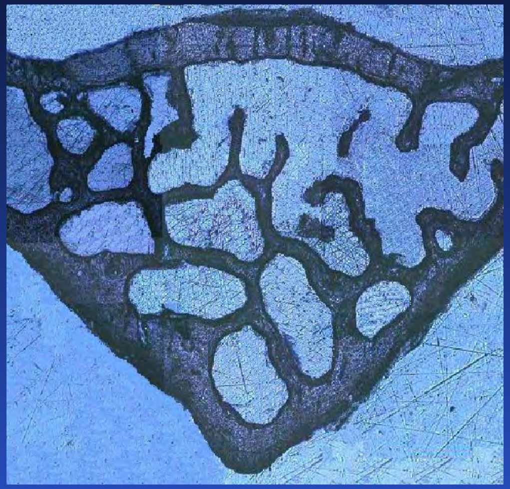


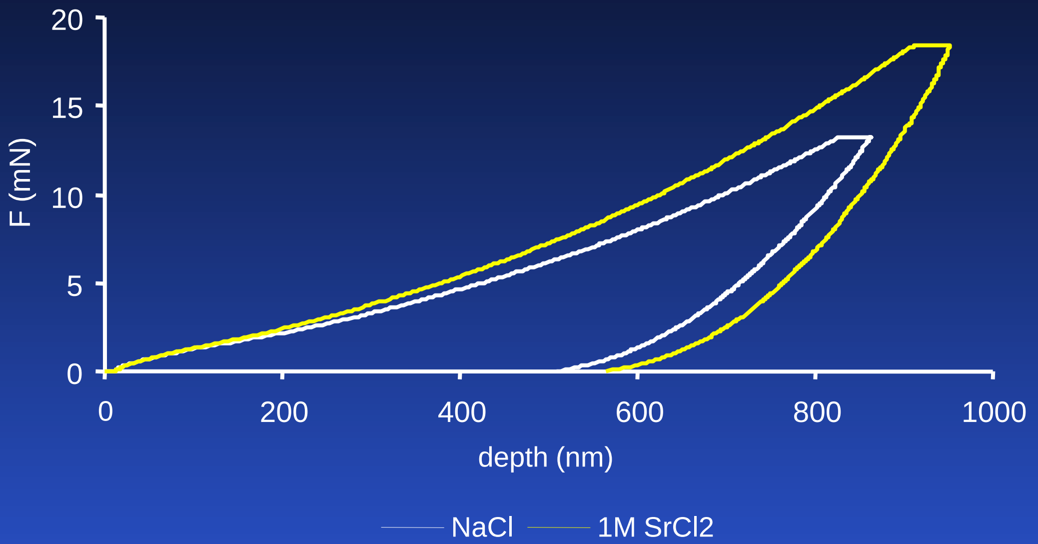
Improvement of intrinsic bone tissue quality und Strontium Ranelate treatment : Trabecular Bone

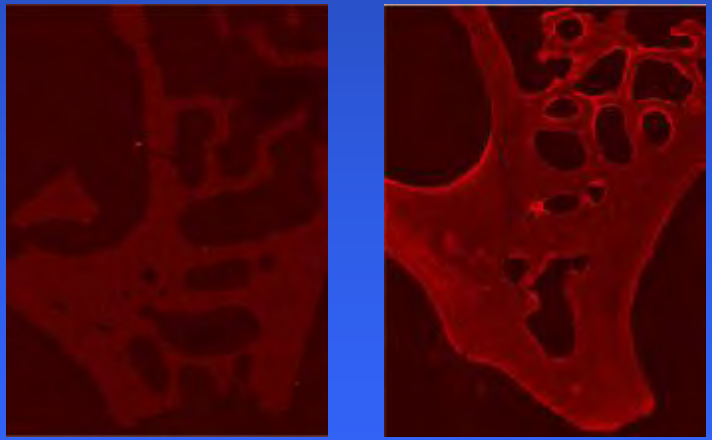
	Sham	OVX	OVX RS 125	OVX RS 250	OVX RS 625
Modulus	14.07±0.38	13.23±0.38	14.40±0.51	15.33±0.44	14.35±0.48
Hardness	562±27	487±23°	590±28*	660±25*°	566±21*
Working Energy	3268±135	3069±175	3596±110*	3634±70*°	3508±103*

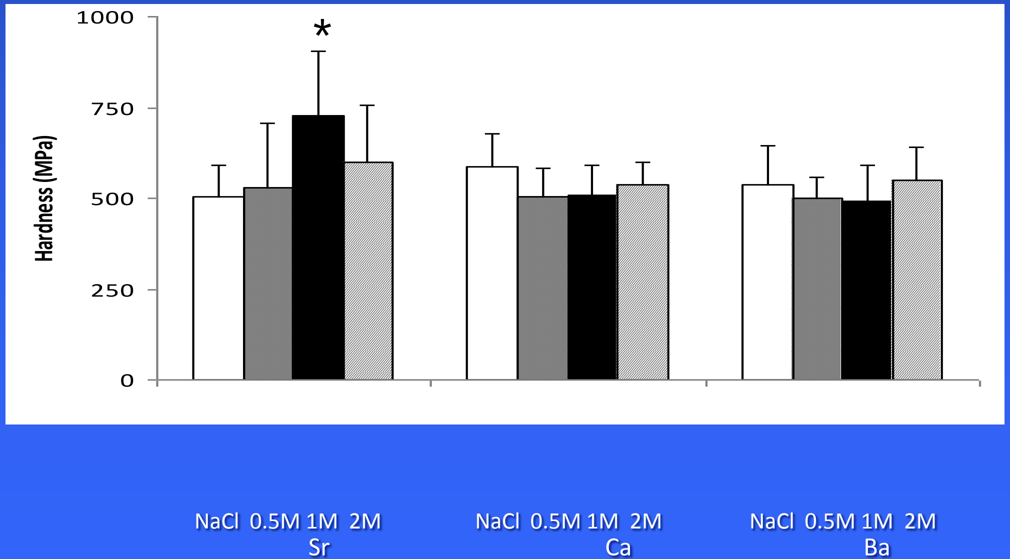
Ammann, Badoud, Barraud, Dayer, Rizzoli. J Bone Miner Res. 2007 Sep;22(9):1419-25.

Ex vivo Sr exposure



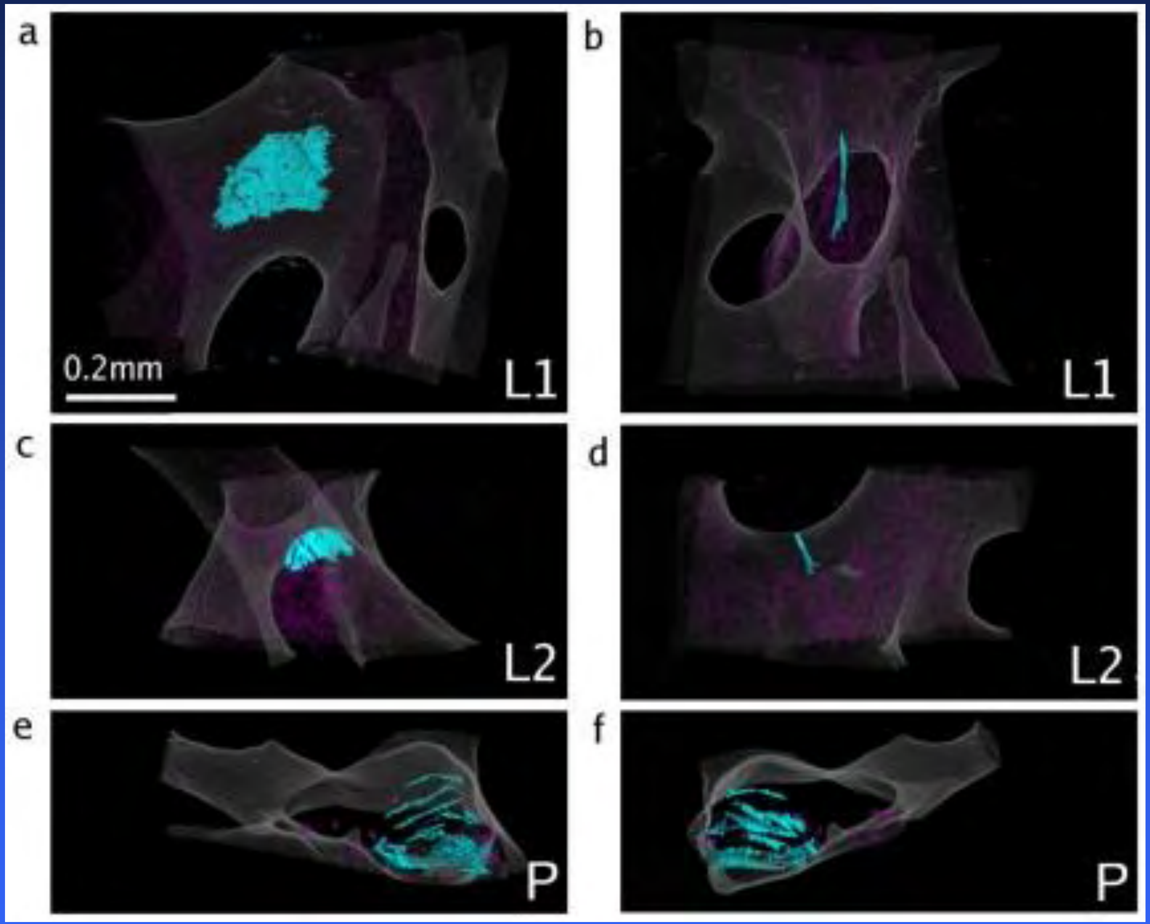






M. Cattani, R. Rizzoli, P. Ammann, Acta biomaterialia 2013

Bone with Cracks and Microcracks



Larrue, Rattner, Peter, Olivier, Vico; Peyrin PLoS One 2011

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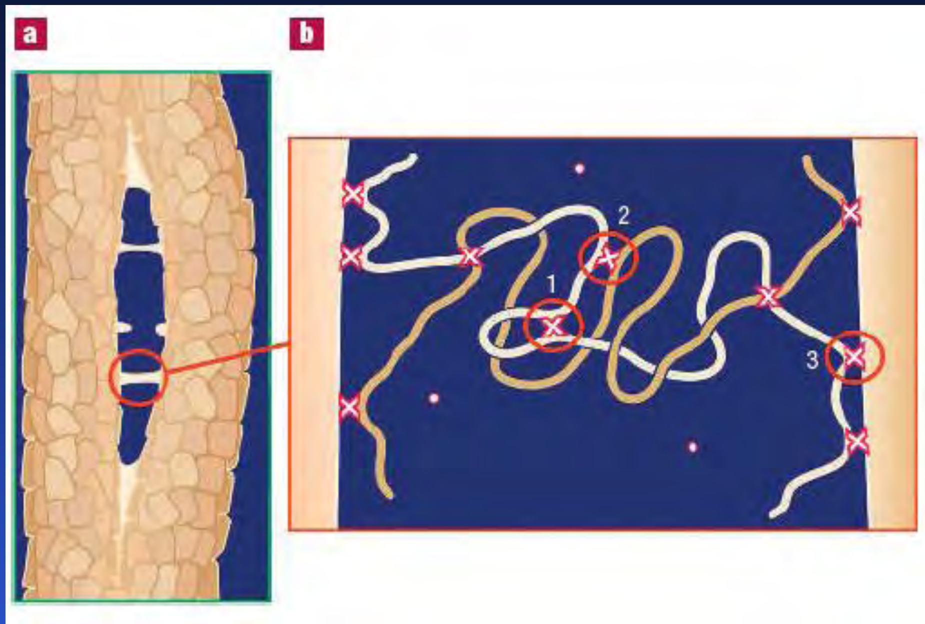
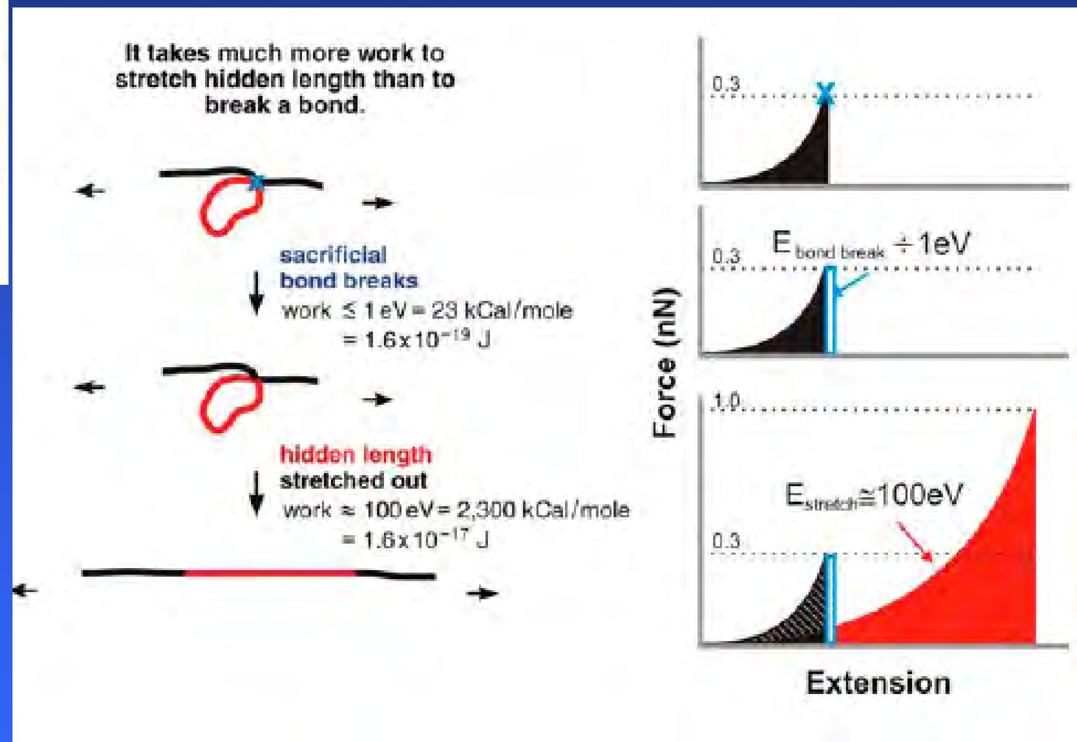
Ammann, Badoud, Barraud, Dayer, Rizzoli. J Bone Miner Res. 2007 Sep;22(9):1419-25.

« Sacrificial bonds »



Fantner et al. (2005)



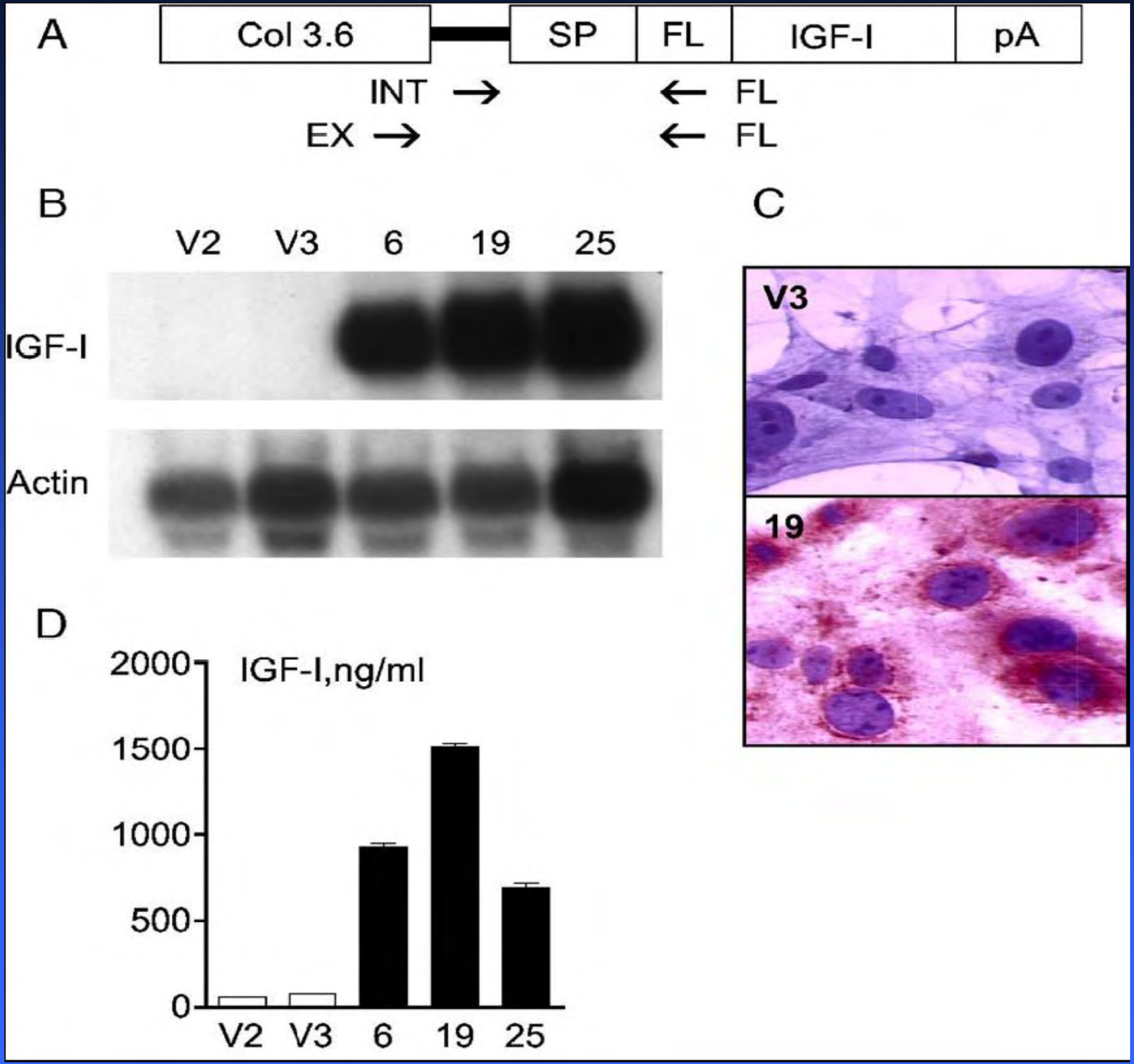
Fantner et al. (2006)

Rat colla1 promotor part of the first exon

Signal Peptide of IGF-1

FLAG Epitope

Bovine GH Poly-adenylation site



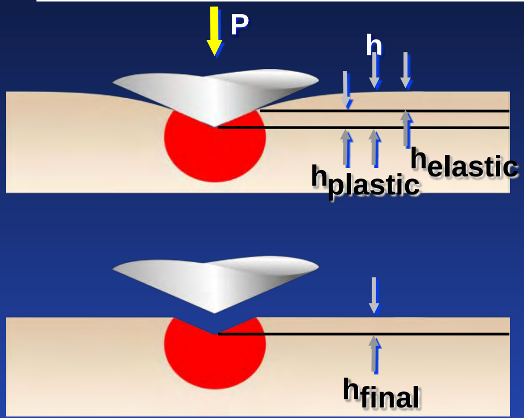
Transgenic mice with osteoblast-targeted insulin-like growth factor-I show increased bone remodeling

J.Jiang,…,B Kream

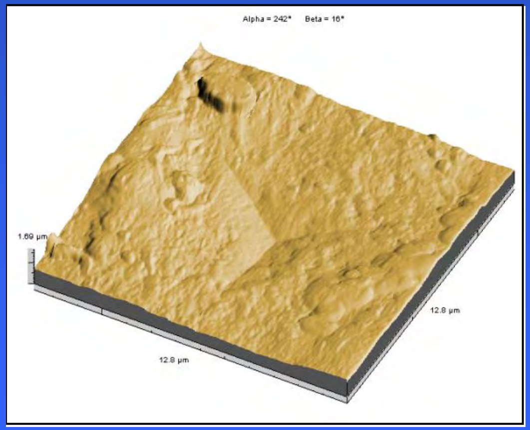
Bone 39 2006, 494-504

Effect of low protein intake and over expression of IGF-I in bone

Nano Indentation of Vertebra



	Modulus (gPa)	Hardness (mPa)
WT 15%	16.40± 0.60	719.20 ± 30.61
WT 2.5%	13.71± 0.43*	601.69 ± 29.19*



Brennan-Speranza, Rizzoli, Kream, Rosen, Ammann; Bone. 2011;49:1073-9.

Effect of low protein intake and over expression of IGF-I in bone

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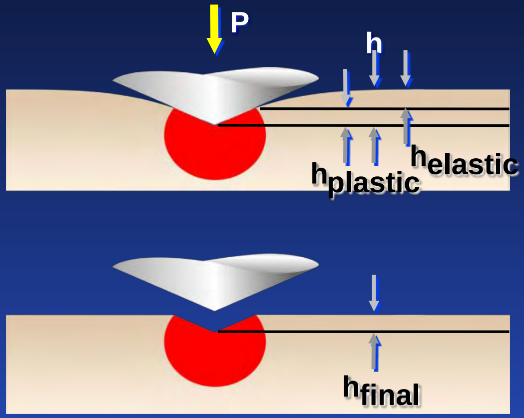

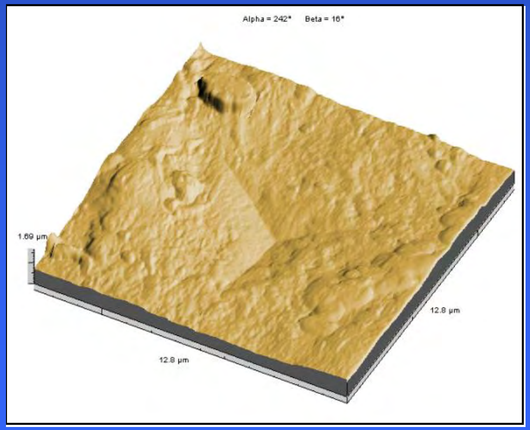

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WT 15%	16.40± 0.60	719.20 ± 30.61
WT 2.5%	13.71± 0.43*	601.69 ± 29.19*
TG 15%	15.33± 0.49	708.71 ± 26.52
TG 2.5%	16.46± 0.40	704.29 ± 29.54

Brennan-Speranza, Rizzoli, Kream, Rosen, Ammann; Bone. 2011;49:1073-9.

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BONE MASS & MICRO-ARCHITECTURE	↓	↔	↔	↑
BONE MATERIAL QUALITY	↓	↑	↑	↓
BONE TURNOVER	↑	↓	↓	↑

T Brennan, R Rizzoli, P Ammann JBMR 2009

HUG Hôpitaux Universitaires Genève