In Vivo Characterization of Trabecular Bone Micro-architecture

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References

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[3] P. K. Saha, B. R. Gomberg, and F. W. Wehrli, "Three-dimensional digital topological characterization of cancellous bone architecture," *International Journal of Imaging Systems and Technology,* vol. 11, pp. 81-90, 2000.

[4] F. W. Wehrli, B. R. Gomberg, P. K. Saha, H. K. Song, S. N. Hwang, and P. J. Snyder, "Digital topological analysis of in vivo magnetic resonance microimages of trabecular bone reveals structural implications of osteoporosis," *Journal of Bone and Mineral Research,* vol. 16, pp. 1520-1531, 2001.

[5] F. W. Wehrli, P. K. Saha, B. R. Gomberg, H. K. Song, P. J. Snyder, M. Benito, A. Wright, and R. Weening, "Role of magnetic resonance for assessing structure and function of trabecular bone," *Topics in Magnetic Resonance Imaging,* vol. 13, pp. 335-355, 2002.

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[7] X. S. Liu, P. Sajda, P. K. Saha, F. W. Wehrli, and X. E. Guo, "Quantification of the roles of trabecular microarchitecture and trabecular type in determining the elastic modulus of human trabecular bone," *Journal of Bone and Mineral Research,* vol. 21, pp. 1608-1617, 2006.

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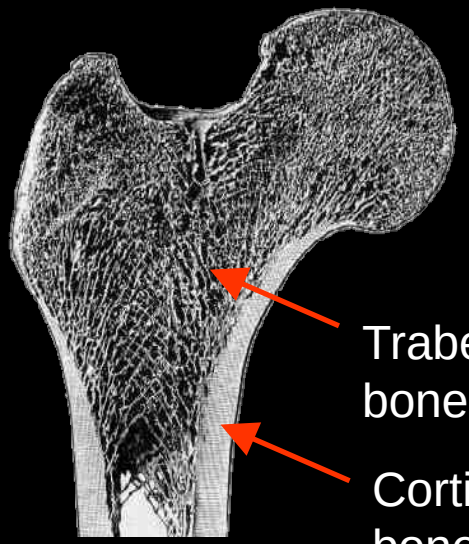
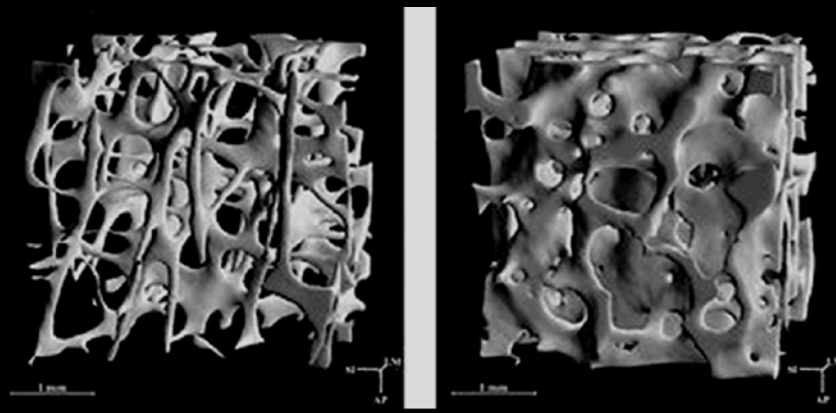
Osteoporosis, Trabecular Bone Micro-Architecture, and Plate-Rod Distribution

- Trabecular bone: network of interconnected plates and rods
- Wolff's law (1892): bone grows/remodels in response to the applied stresses
- Osteoporosis: low bone mineral density and architectural deterioration
- At risk in USA: >40 million
- US health care cost: ~$17B/Y



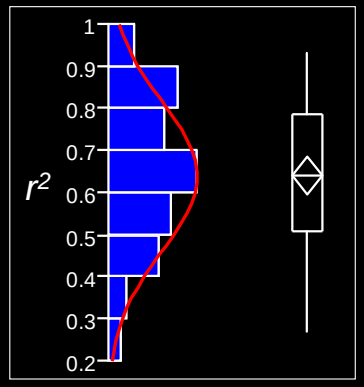
There is histologic evidence confirming the relationship between the gradual conversion of trabeculae from plates to rods and low-trauma fracture risk



Bone Mineral Density (BMD) and Miro-Architecture

How Predictive is BMD of the Bone's Mechanical Behavior?

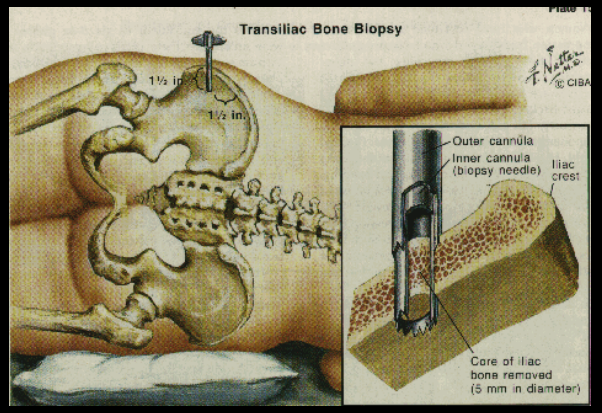
- Meta analysis
- N=38 (1985-2000)
- Various parameters of "strength"
- Mean r^2 = 0.64±0.17



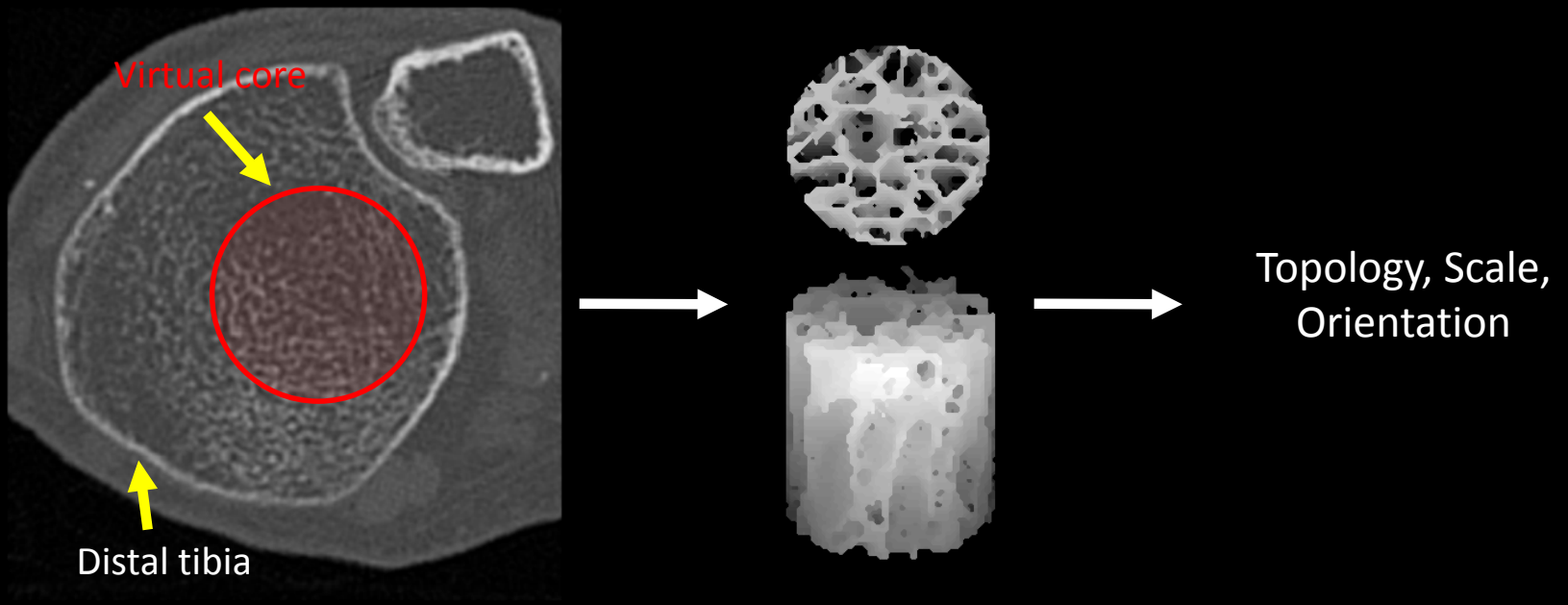
Clinical studies have confirmed the role of plate/rod bone micro-architecture to determine bone strength

Quantifying Architecture via Bone Biopsy

- Iliac crest or rib
- Painful, risky, and limited retests
- Not suitable for controls or time-series analysis



In Vivo Imaging Offers an Opportunity for Virtual Bone Biopsy



Features

- Analogous to bone biopsy
- Virtual core is isolated from 3D image data sets.
- Core is subjected to analysis

Challenges

- Reduced resolution
- Limited signal-to-noise ratio

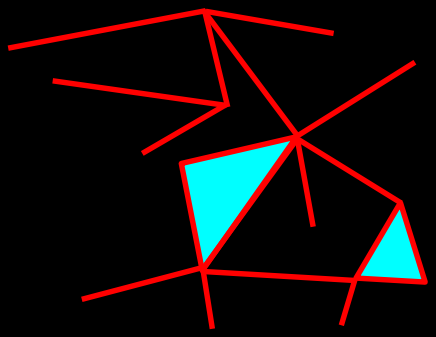
Topology of Trabecular Networks

Topological analysis of line skeletonized structure

3D Euler Poincaré Formula:

χ = objects - tunnels + cavities
= nodes - edges + faces

Connectivity Index = $1 - \chi$



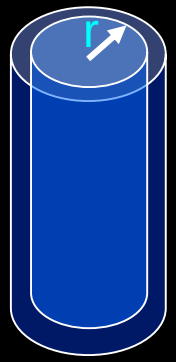
objects: 1
tunnels: 1
cavities: 0

nodes: 17
edges: 19
faces: 2

$\chi = 0$

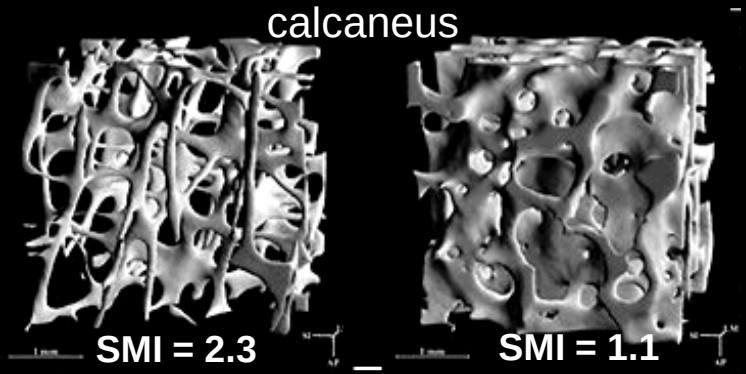
Structure-Model Index (SMI)

SMI μ ($\partial S/\partial r$)



SMI=relative change in surface area (S) upon radial (r) expansion

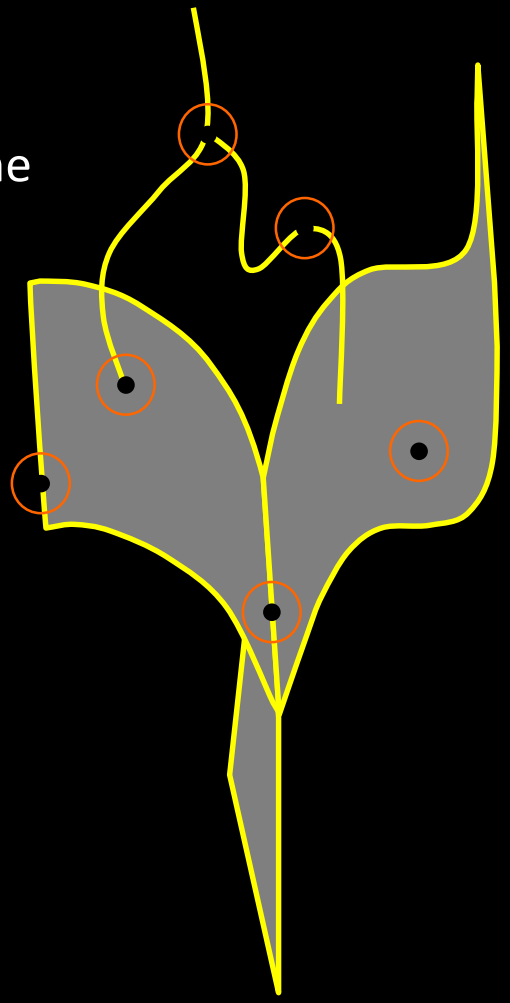
calcaneus



Hildebrand et al, J Bone Miner Res, 1999

Topological Analysis

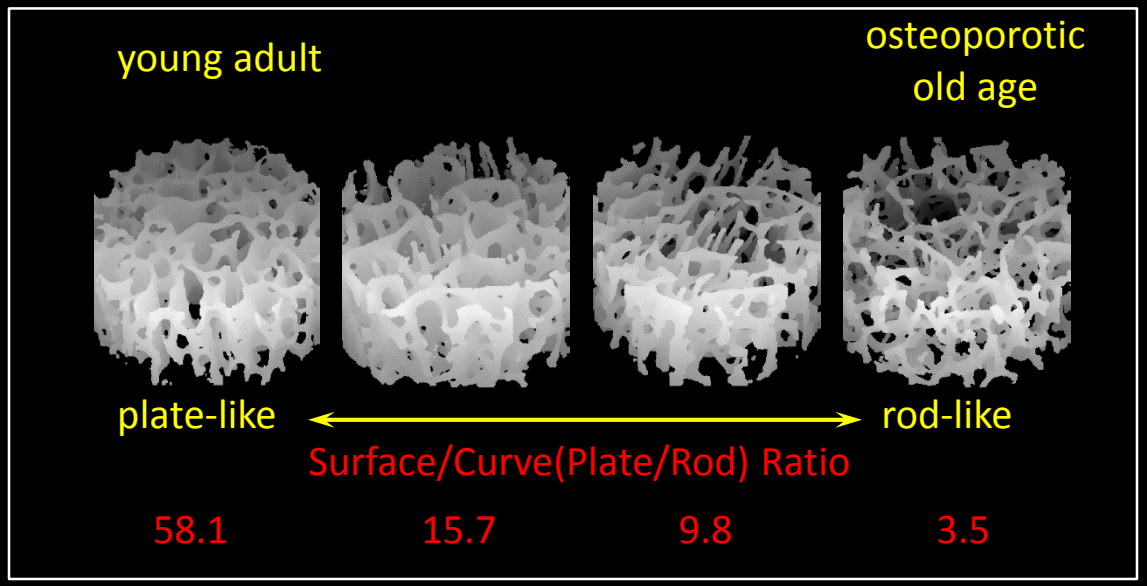
- Topological class (curve, surface junctions) at any location may be unambiguously determined from the topological numbers (#objects (ξ), #tunnels (η), and #cavities (δ))
- Edge: $\xi = 1; \eta = 0; \delta = 0$
- Curve Interior: $\xi = 2; \eta = 0; \delta = 0$
- Surface Interior: $\xi = 1; \eta = 1; \delta = 0$
- Curve-Curve junction: $\xi > 2; \eta = 0; \delta = 0$
- Surface-Curve junction: $\xi > 1; \eta = 1; \delta = 0$
- Surface-Surface junction: $\xi = 1; \eta > 1; \delta = 0$

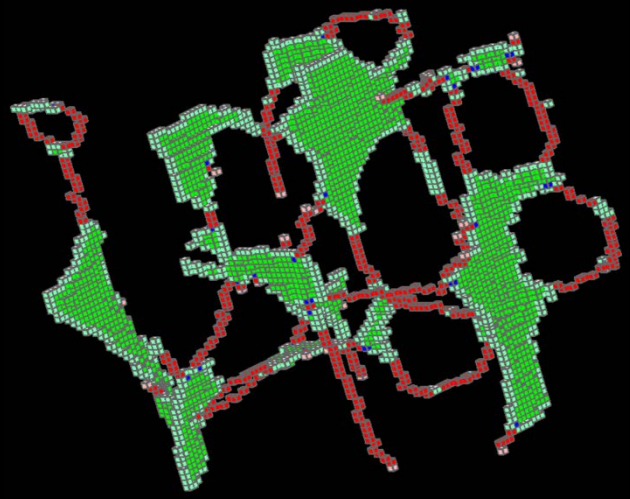


- Saha and Chaudhuri, "3D digital topology under binary transformation with applications," *Comp Vis Imag Und,* **63**:418-429, 1996

Digital Topological Analysis

- Identifies plates/rods and other topological entities
- Able to distinguish between fracture/ non-fracture groups via *in vivo* MRI
- Being used by several leading research groups





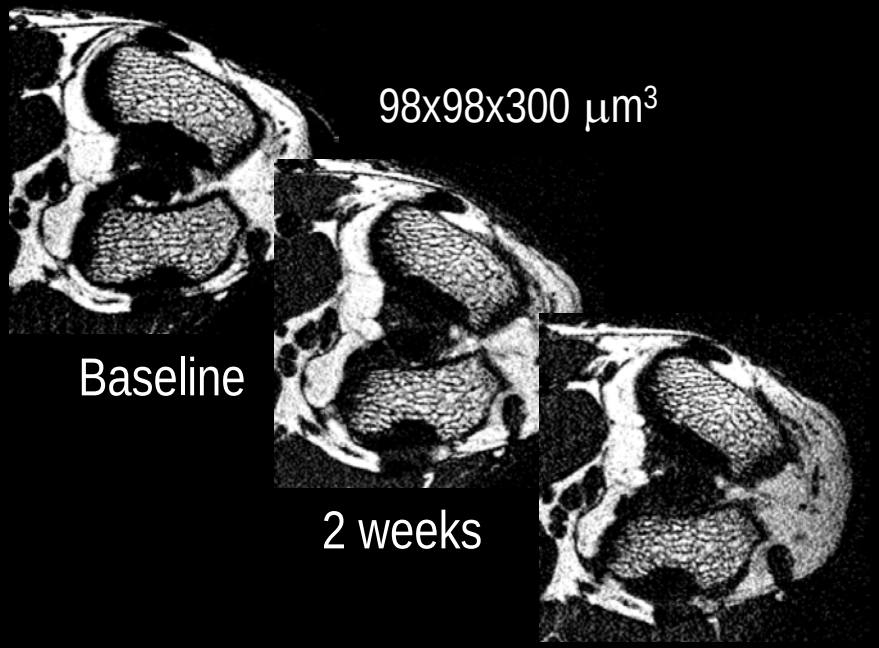
Surface = plate
Rod = curve
Junction

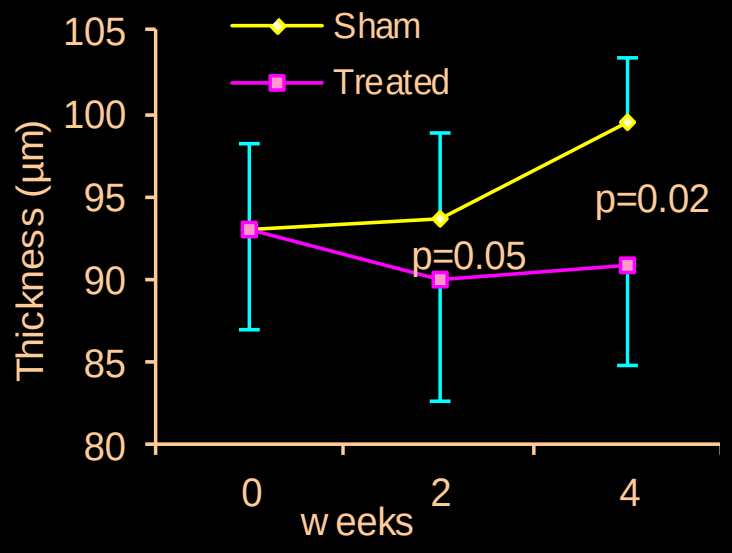
Age and disease-related topological changes

- Saha, Gomberg, Wehrli, "Three-dimensional digital topological characterization of cancellous bone architecture," *Int J Imag Syst Tech*, **11**:81-90, 2000
- Gomberg, Saha, Song, Hwang, Wehrli, "Topological analysis of trabecular bone MR images," *IEEE Trans Med Imag*, **19**:166-174, 2000
- Wehrli, Gomberg, Saha, Song, Hwang, Snyder, "Digital topological analysis of in vivo ….. of trabecular bone ……..," *J Bone Min Res*, **16**:1520-1531, 2001

Measures TB thickness/Spacing at *In Vivo* Resolution using Fuzzy Distance Transform

In vivo evidence of Dexamethasone on trabecular bone thickness

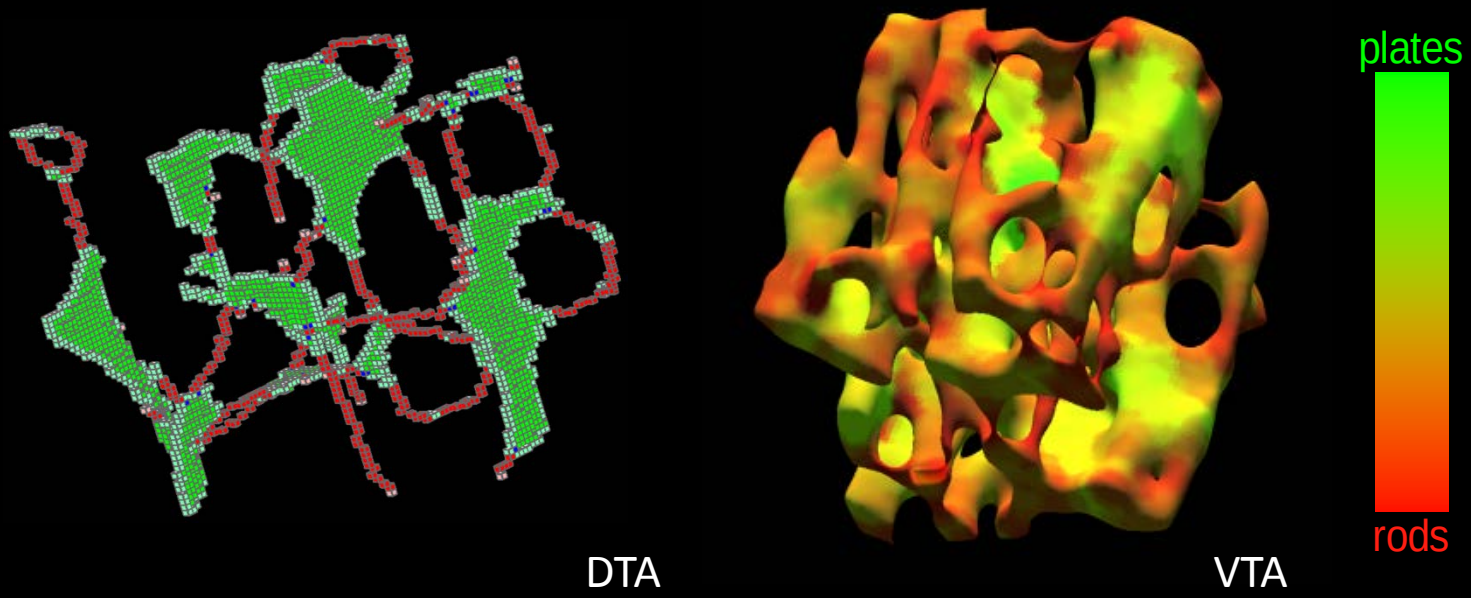




Treatment effect is not visually apparent!

- Saha and Wehrli, "Measurement of trabecular bone thickness in the limited resolution regime of in vivo MRI by fuzzy distance transform," *IEEE Trans Med Imag*, **23**: 53-62, 2004

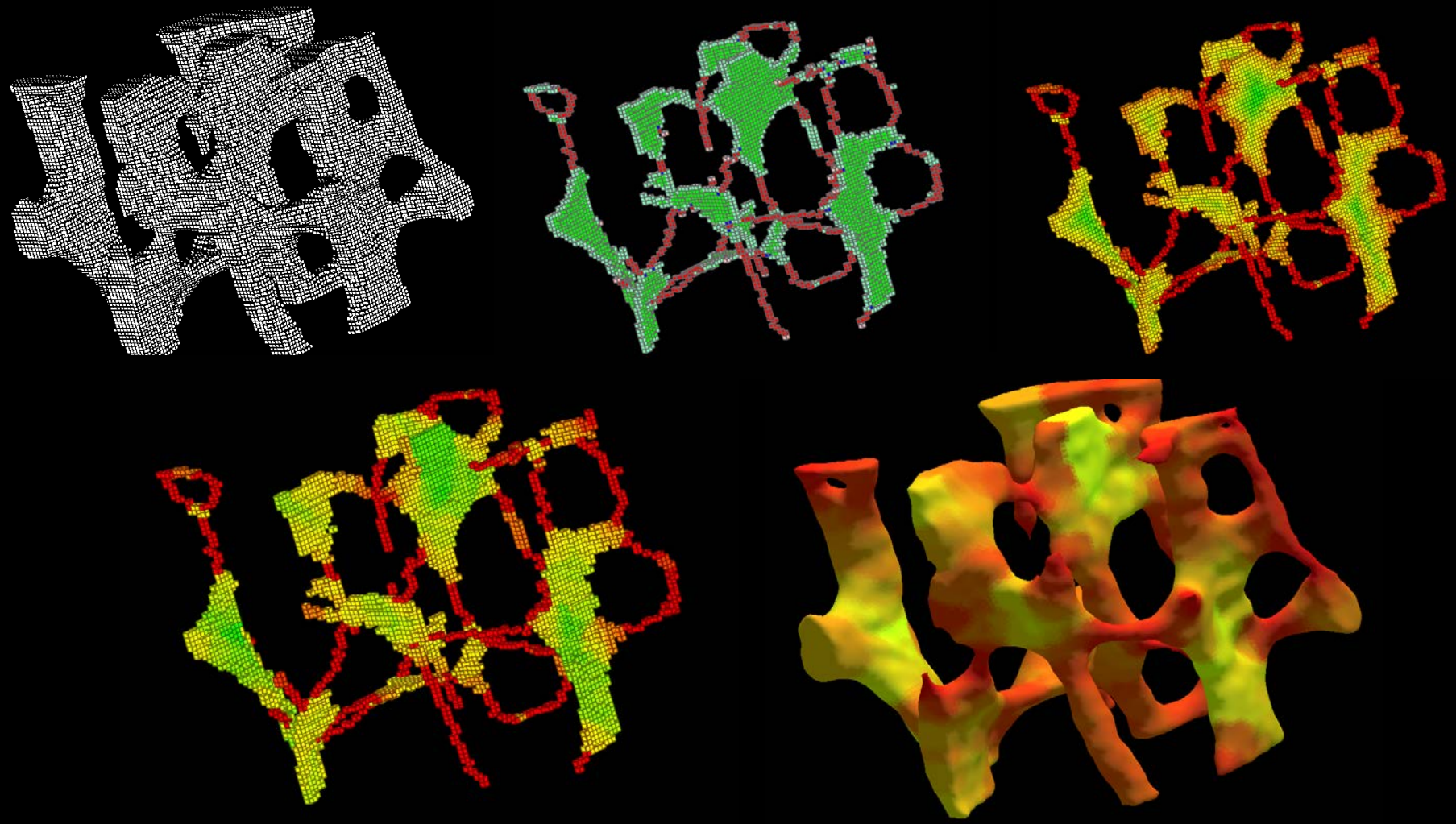
Recent Works: Volumetric Topological Analysis



- Quantify trabecular bone architecture via clinical CT imaging
  - Plateness and rodness on the continuum between perfect plates and perfect rods
  - Local trabecular bone width in the unit of microns

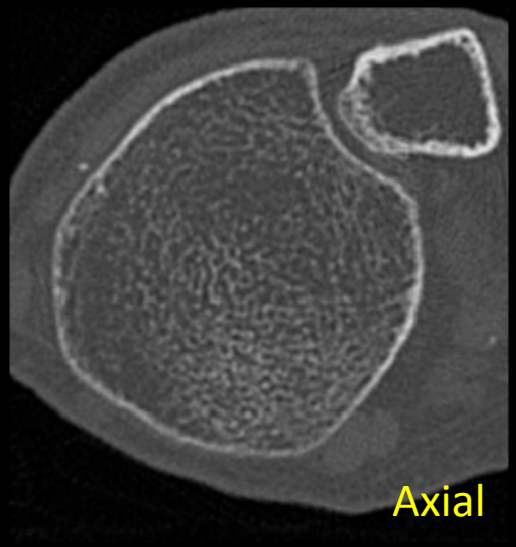
- Saha, Xu, Duan, Heiner, Liang, "Volumetric topological analysis: a novel approach for trabecular bone classification ……..," IEEE Trans Med Imag, **29**:1821-1838, 2010

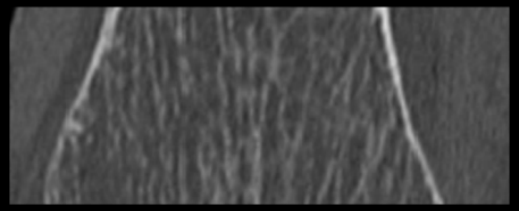
Intermediate Steps

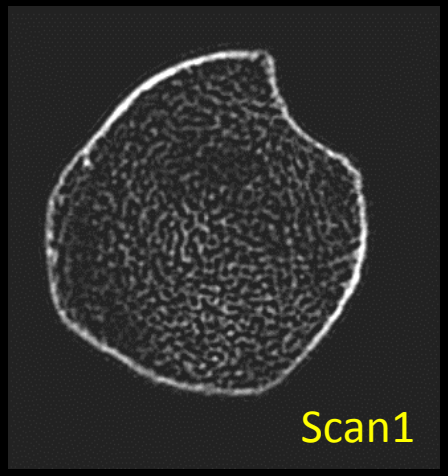


CT Imaging

- 128 slice SOMATOM Definition Siemens Flash scanner
- 120 kV, 200 mAs, pitch: 1.0
- nominal collimation: 16x0.3mm
- scan length: 10 cm
- slice thickness: 300 μm

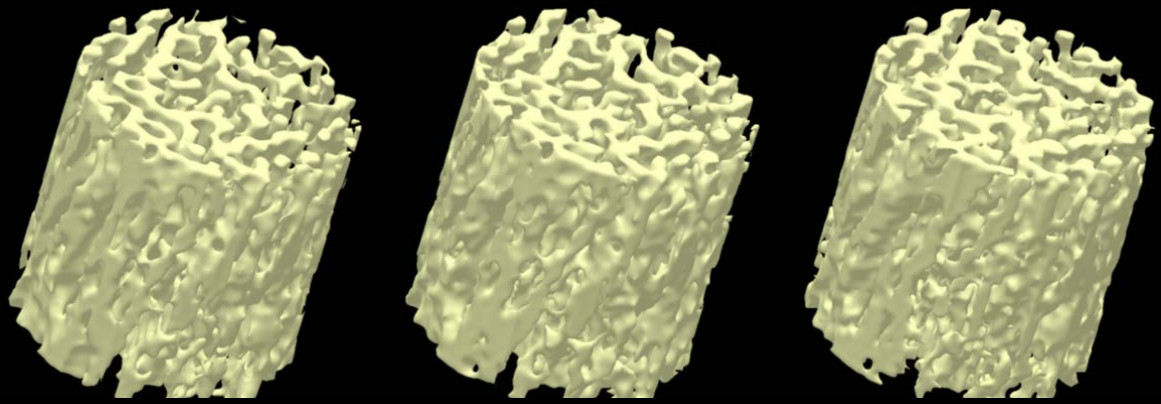




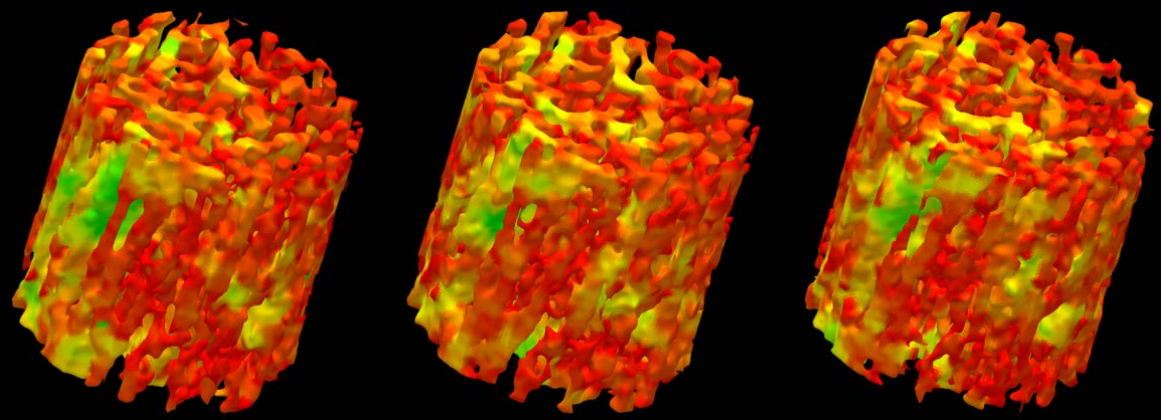


High Intra- and Inter-Modality Reproducibility

Three repeat CT scans

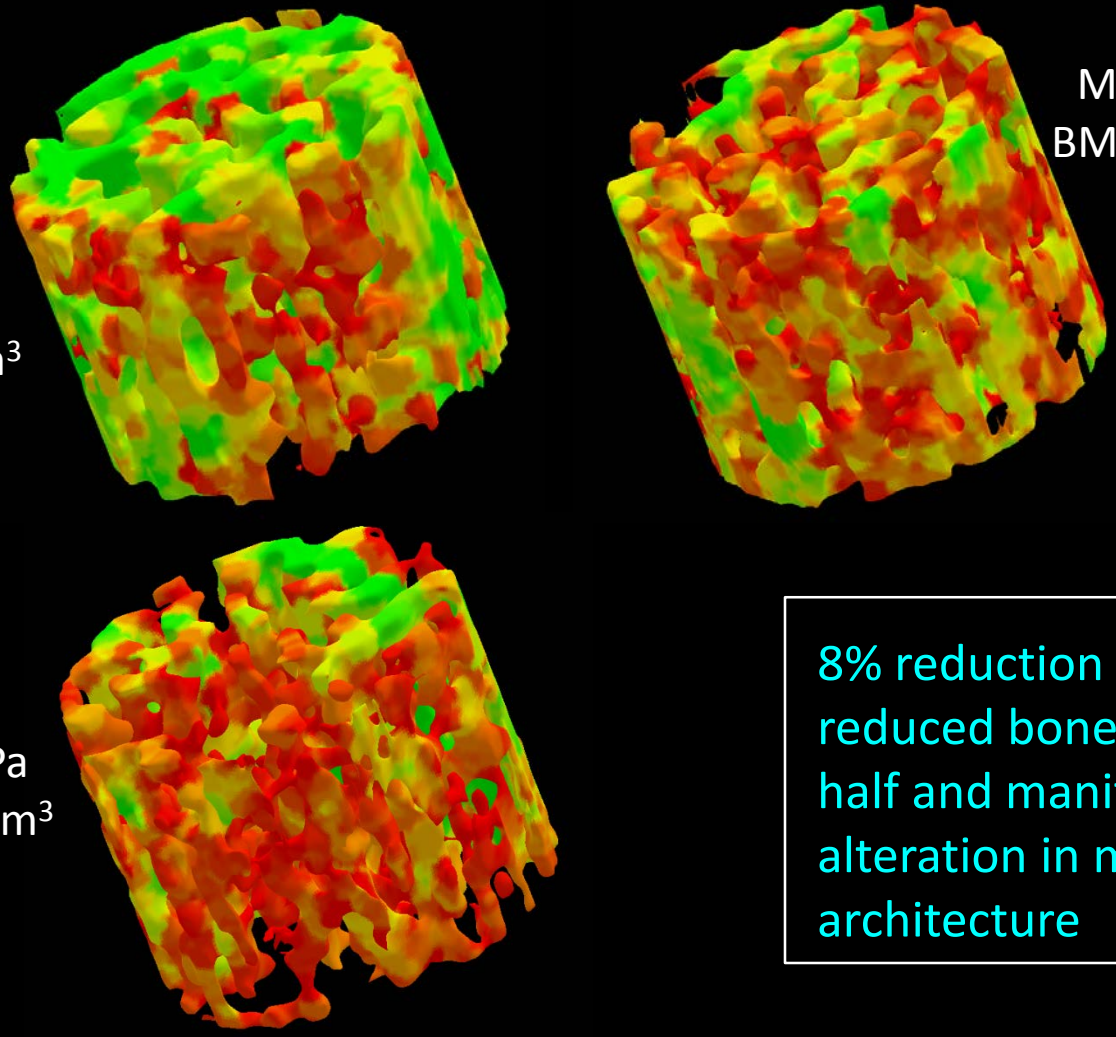


Color-coded results of volumetric topological analysis



Repeat CT scan
ICC: 0.97

VTA Measure for TB with Distinctively Different Strengths



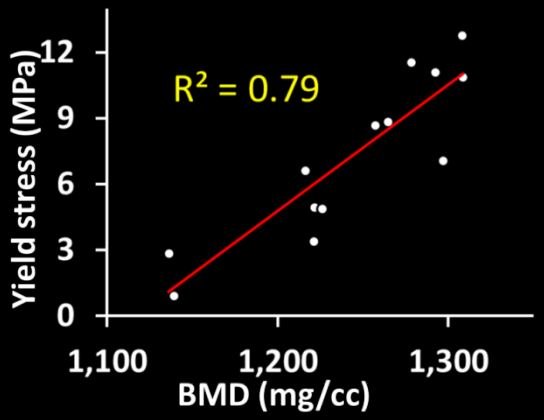
Modulus: 3.3 GPa
BMD: 1.31 gm/cm^3
SW_{VTA}: 464 µm
SCR_{VTA}: 0.58

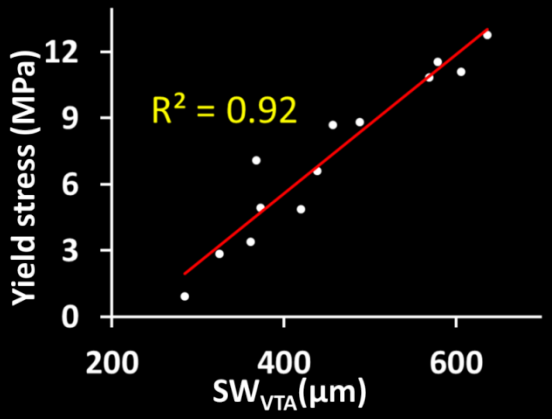
Modulus: 2.2 GPa
BMD: 1.27 gm/cm^3
SW_{VTA}: 385 µm
SCR_{VTA}: 0.38

Modulus: 1.5 GPa
BMD: 1.20 gm/cm^3
SW_{VTA}: 340 µm
SCR_{VTA}: 0.26

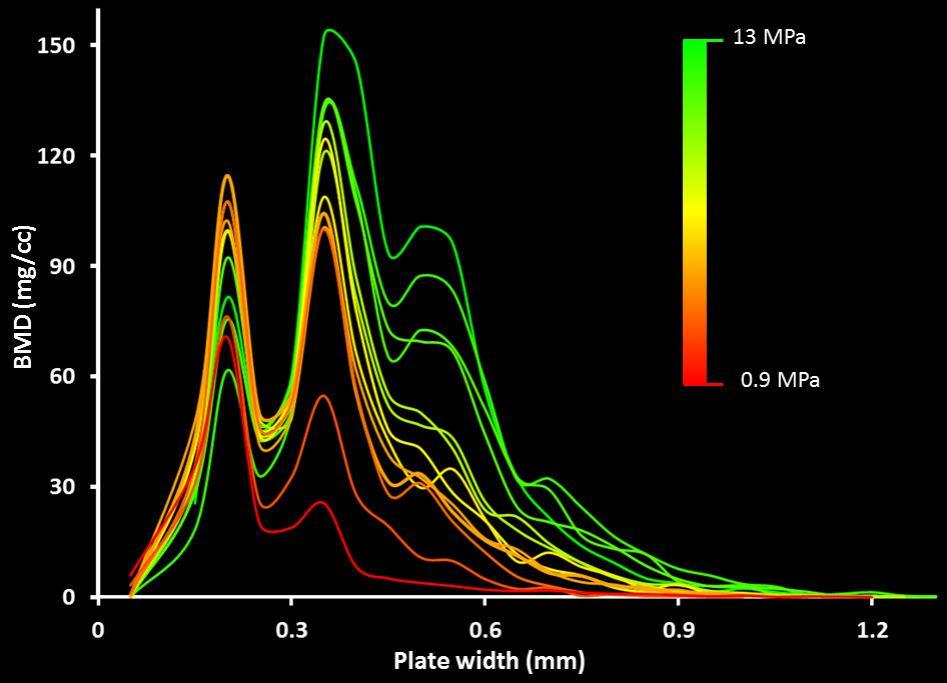
8% reduction in BMD reduced bone strength to half and manifest a 50% alteration in micro-architecture

Ability To Predict Mechanical Properties



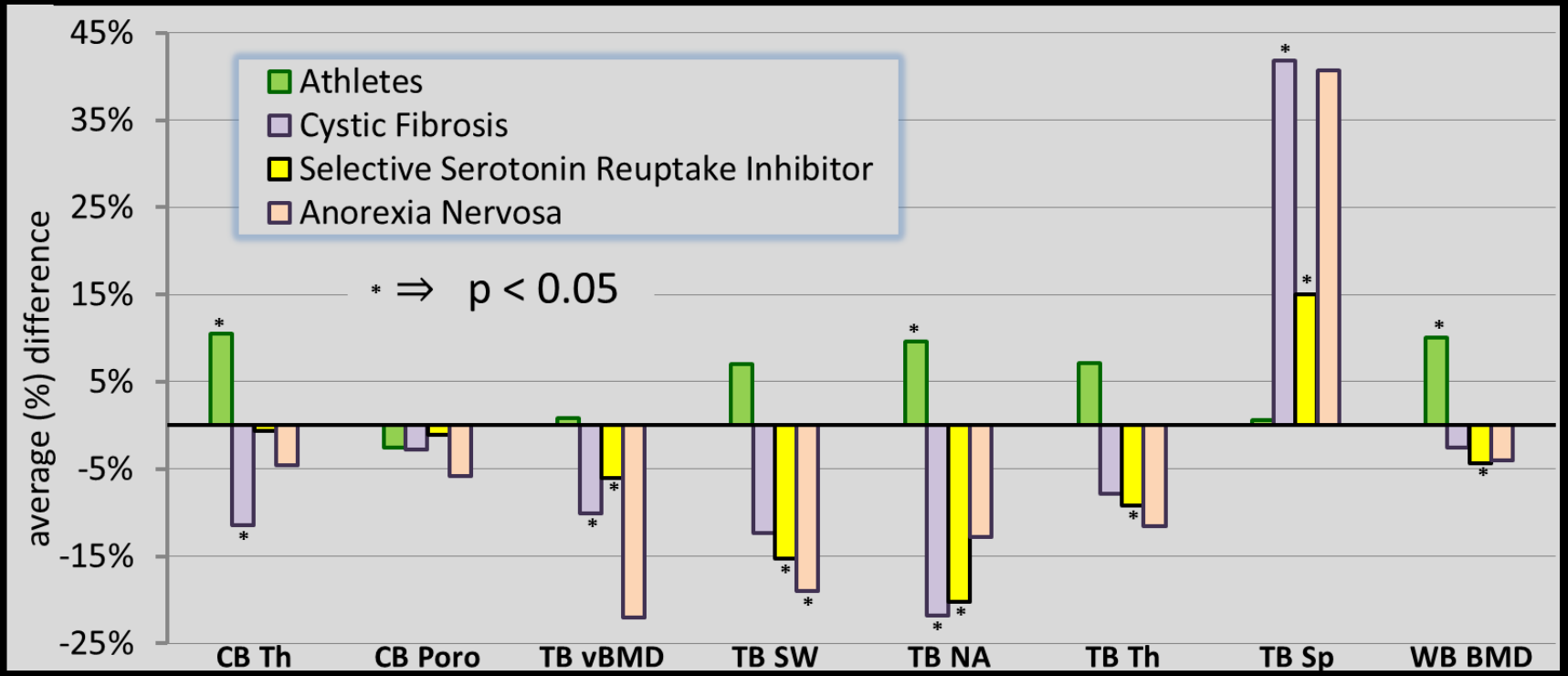


High predictability of experimental biomechanical properties.



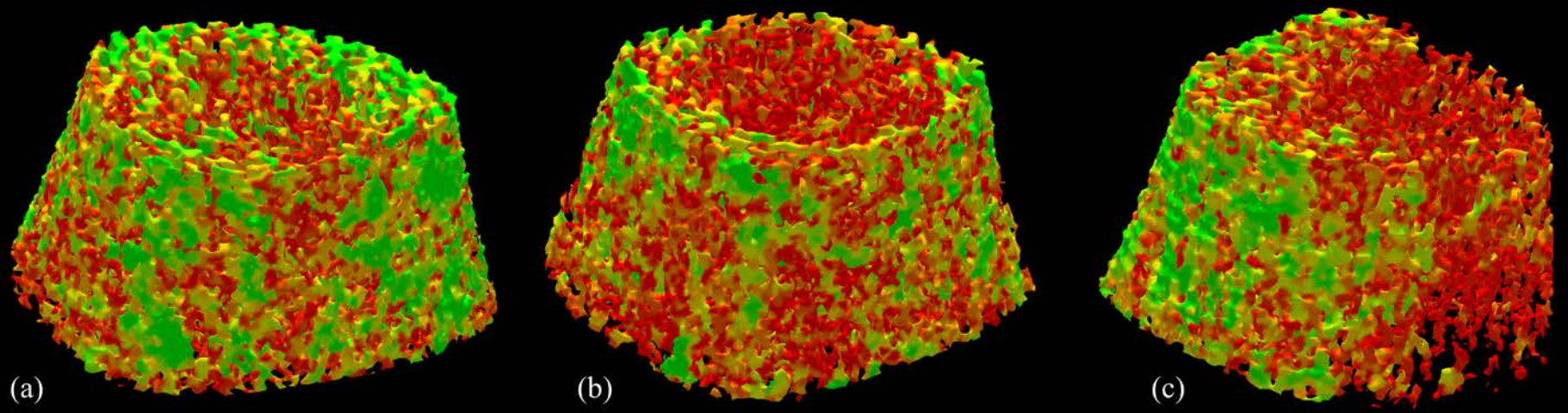
Bone mass distribution at different plate width: a new class of information

Results of a Human Pilot Study



Average differences of bone measures in athlete (N=10), cystic fibrosis (N=11), selective serotonin reuptake inhibitor (N=12), and anorexia nervosa (N=4) groups as compared to age-sex-BMI-similar healthy controls from the Iowa Bone Development Study (N=102). Age-sex-height matching was used for the anorexia nervosa group.

Bone Characterization in Different Human Groups

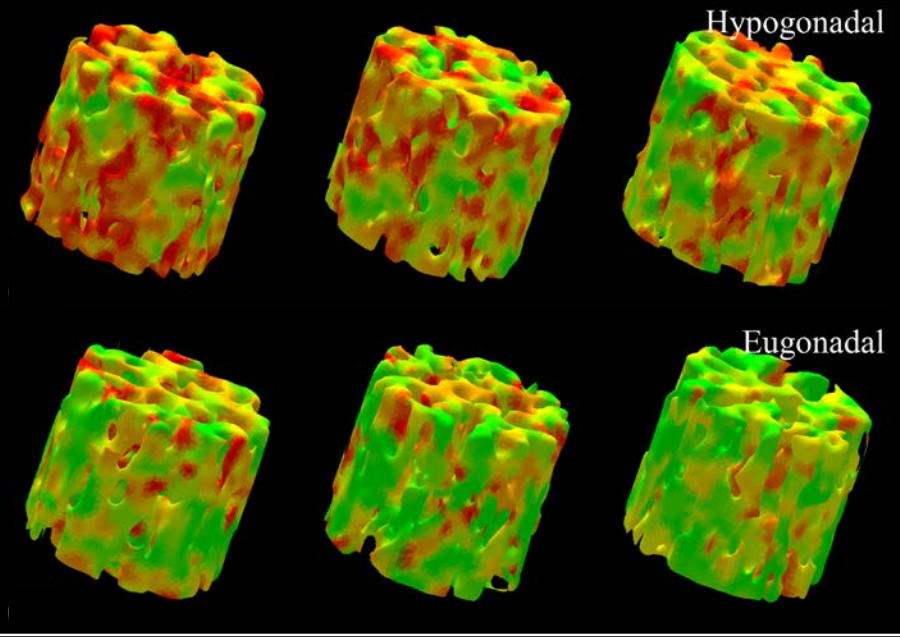


Color-coded illustration of trabecular bone (TB) plate/rod classification for a IBDS female control (a) and an age-similar, sex- and BMI-matched patient on continuous treatment with an SSRI (b), and another age-similar, sex- and BMI-matched patient with confirmed diagnosis of CF (c). The healthy female (a) has more TB plates (green) as compared to the two patient participants. Between the two patients, the CF patient (c) has some signs of heterogeneous bone loss.

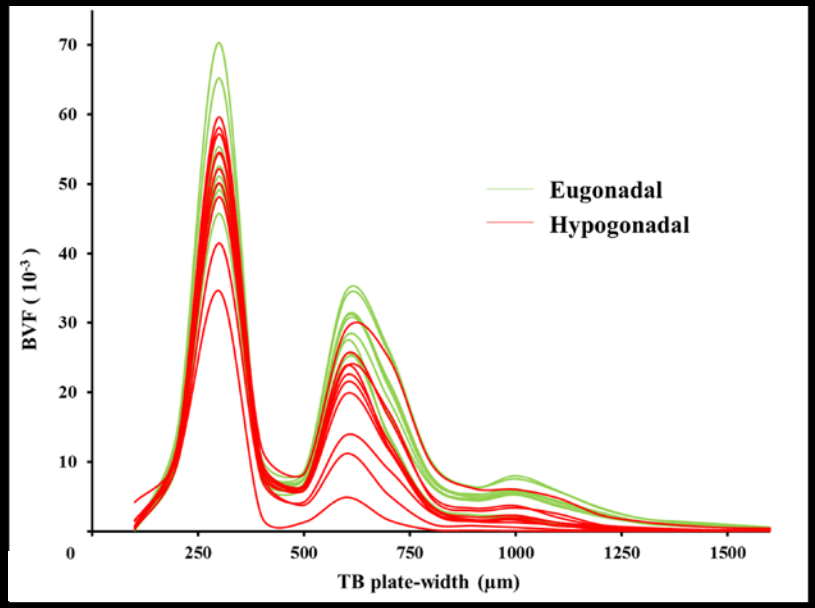
- Saha, Liu, Chen, Jin, Letuchy, Xu, Amelon, Burns, Torner, Levy, "Characterization of trabecular bone plate-rod microarchitecture ….," Med Phy, **42**:5410-5425, 2015

Bone Micro-Architecture among Eugonadal and Hypogonadal Men

N = 20 MRI Study



Trabecular bone plate-rod micro-architecture among hypogonadal and eugonadal men

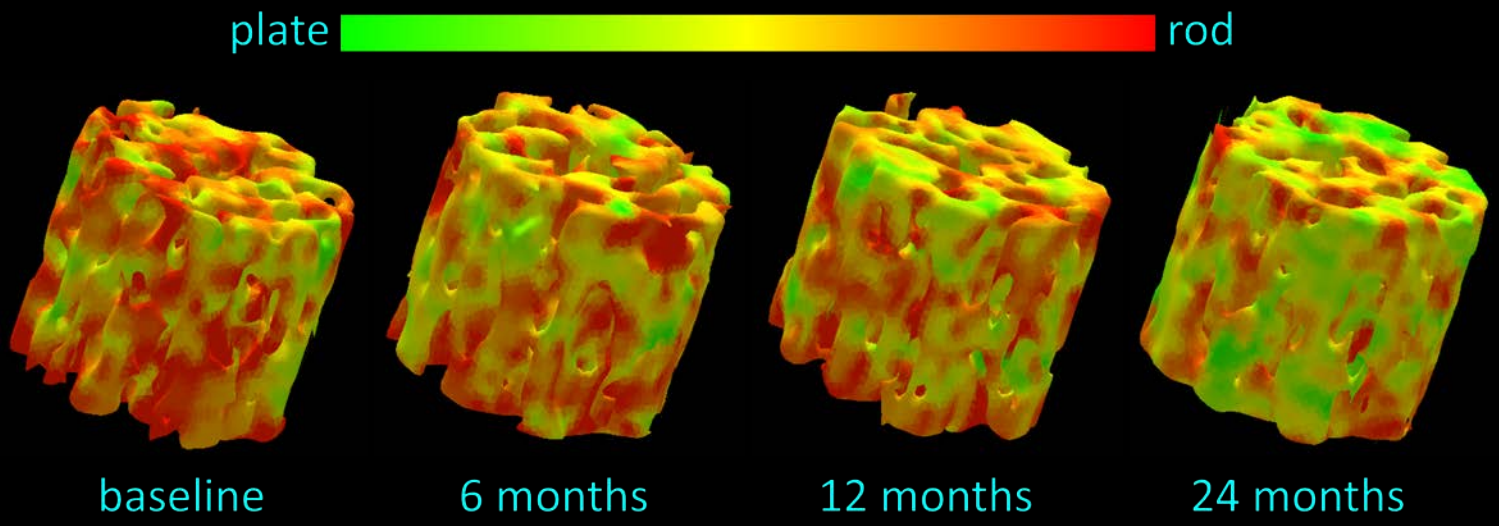


Bone mass distribution at different plate width: a new class of information

- 44 % (p = 0.001) reduction in trabecular bone plate volume
- No significant difference in rod volume

Treatment Effects Hypogonadal Men

N = 10 Two year follow-up MRI study

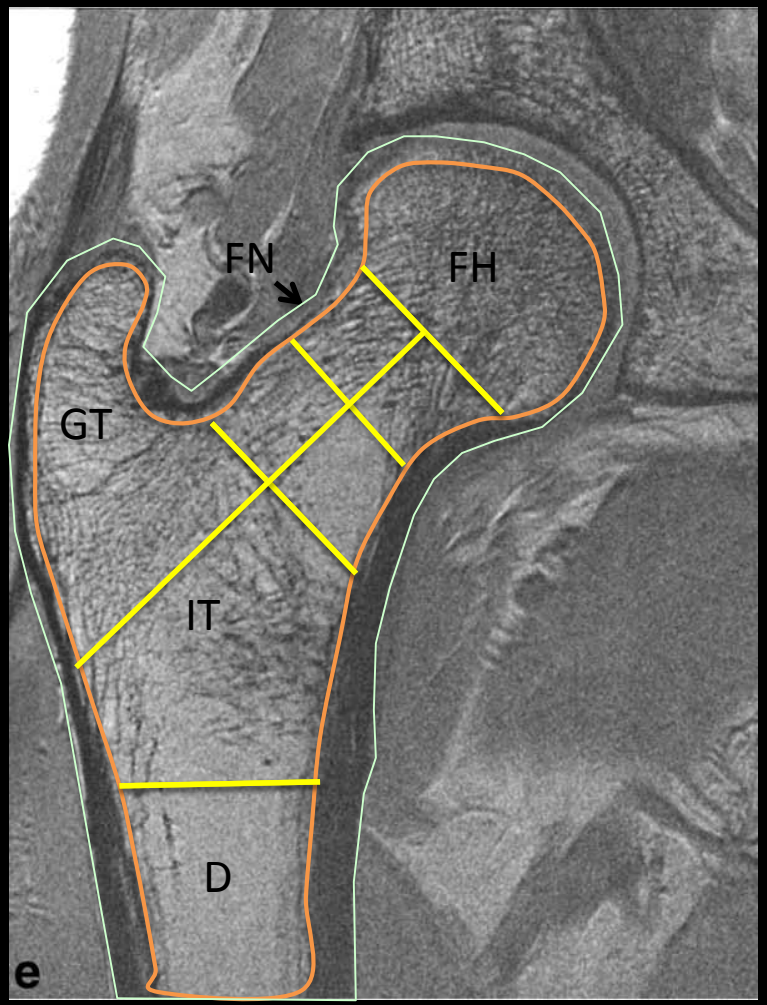


Treatment effects in trabecular bone plate-rod micro-architecture in hypogonadal men

- 6.5 % (p = 0.06) increase in trabecular bone plate volume after 6 months
- 16.2 % (p = 0.003) increase in trabecular bone plate volume after 24 months
- No significant difference in rod volume even after 24 months of treatment

MRI of Proximal Femur Microarchitecture as a Biomarker of Bone Quality

- Periosteal border = green (already drawn)
- The trabecular analysis (orange and yellow lines) should capture the subregional variation in microarchitecture in the common fracture sites:
  - FH = femoral head
  - FN = femoral neck
    - Divided into different subregions
  - GT = greater trochanter
  - IT = intertrochanteric
  - D = diaphysis
- Because the cortex can be very thin at the femoral head, I would err on the side of slightly overestimating the femoral head cortical thickness.



Summary

- CT-based *Virtual Bone Biopsy (VBB)* is a new method that provides detailed quantitative information on cortical and trabecular bone architecture noninvasively.
- Applicable to various anatomic sites, including load-bearing sites.
- VBB structural parameters are highly reproducible and are strongly associated with bone strength.
- Method provides a sensitive tool to assess effects of diseases and therapeutic intervention.
- Technology is more demanding than bone densitometry.
- Method has potential to supplant Dual Energy X-ray Absorptiometry (DAX) based bone densitometry.