Advanced Medical Imaging with Synchrotron and Compton X-ray Sources
Bologna, 21-22 November 2019

X-ray imaging of the skeleton: a review of clinical and research applications

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X-ray imaging of the skeleton: a review of clinical and research applications

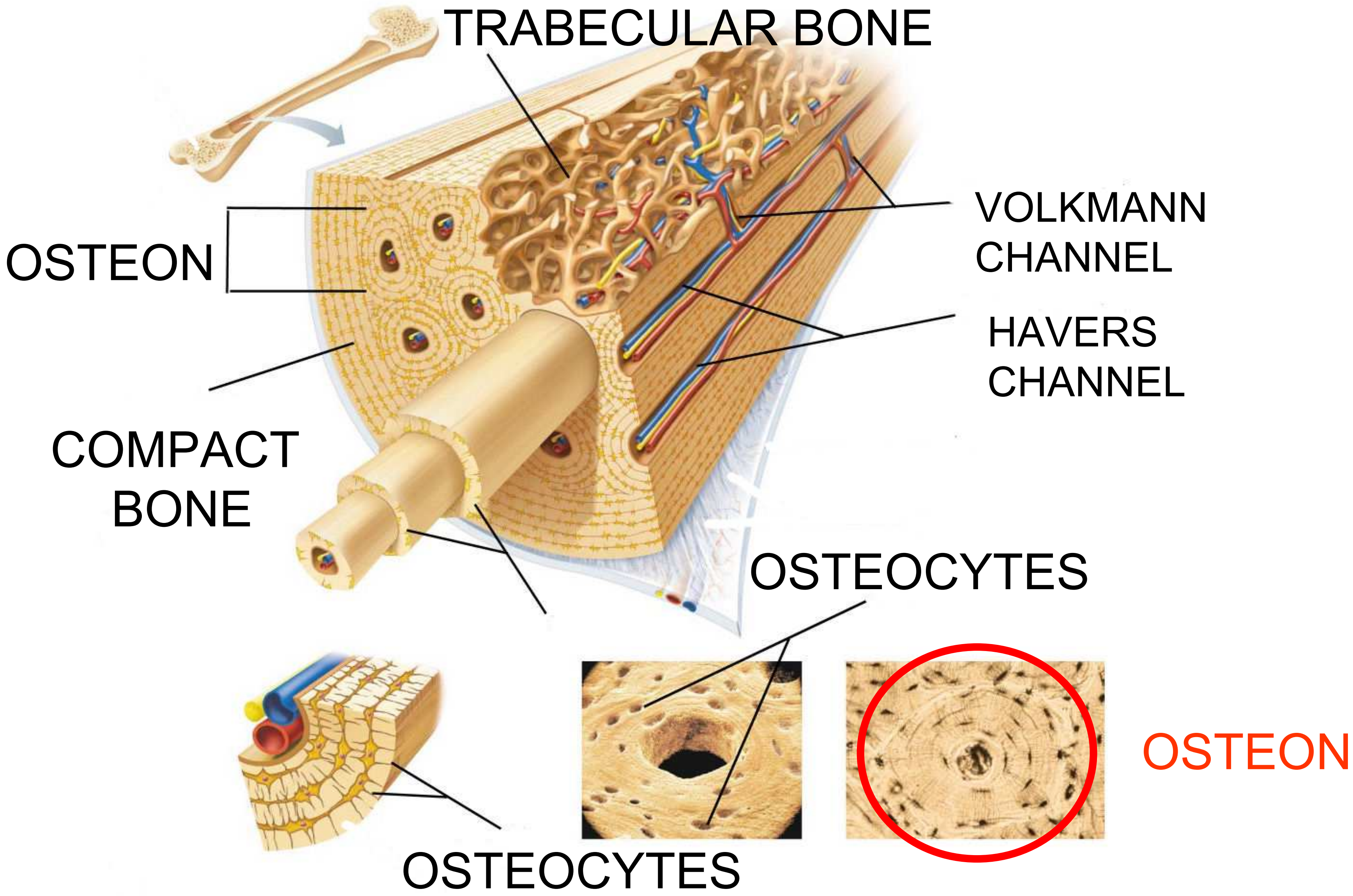
First x-ray taken at the Rizzoli Institute (1899)

AIMS

Clinical and research applications for bone tissue imaging based on:

- CT
- MicroCT
- Synchrotron Radiation (SR)

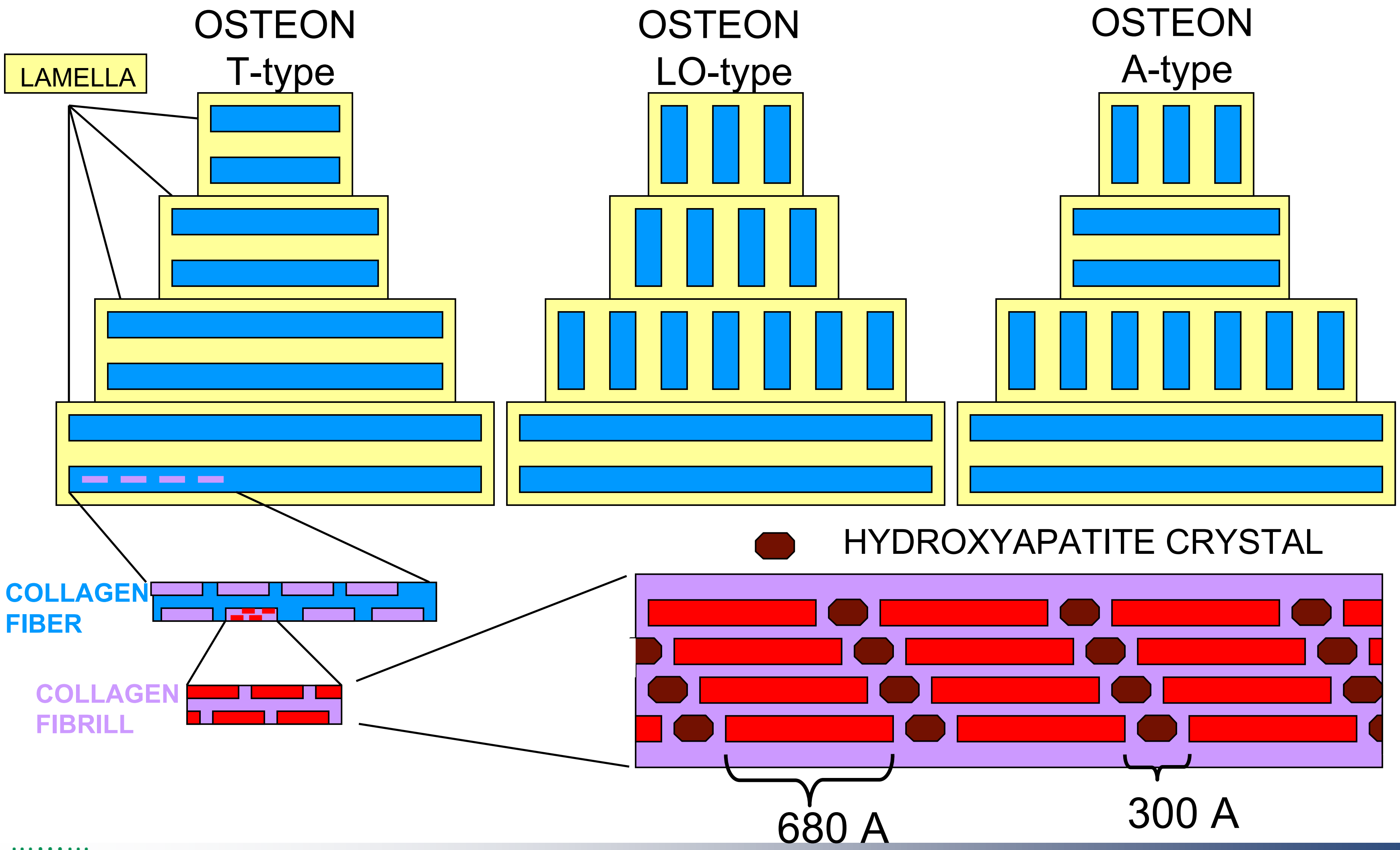
Possible applications for bone imaging from a compact Compton X-ray Source in Bologna (BoCXS)



<u>ORGANIC COMPONENT:</u> Cells, Collagen type I (20% dry weight of matrix)

<u>MINERAL COMPONENT:</u> Hydroxyapatite

The orientation of collagen fibers inside individual osteons and the hierarchical structure that packs collagen and Hydroxyapatite crystals are elements involved in the processes of bone adaptation to mechanical stress



BONE

Is an efficient composite material, adaptable to mechanical stress, but:

accidental overloading

and/or

aging and/or pathological bone remodeling affecting morphology and mineral content

ALTERED RISK OF FRACTURE

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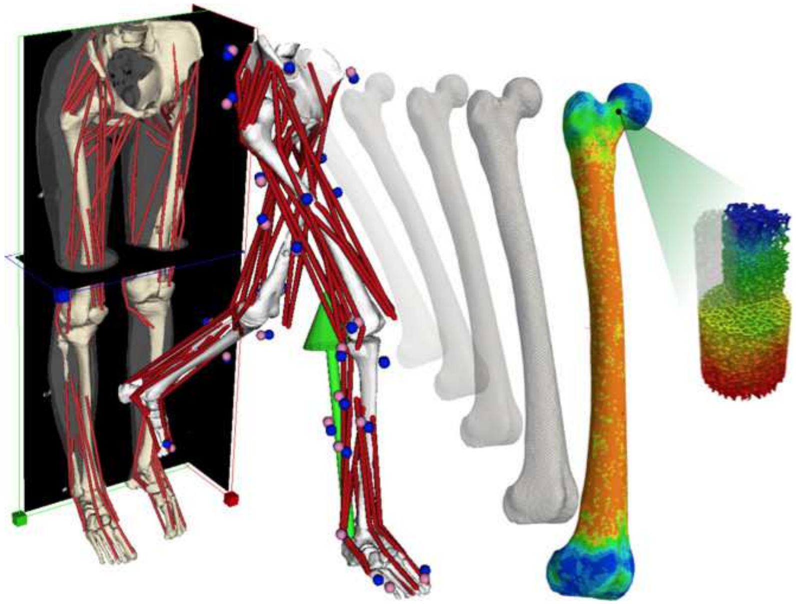


Virtual Physiological Human (VPH)
for personalized medicine

AIMS

1) Clinical and research applications for bone tissue imaging based on:

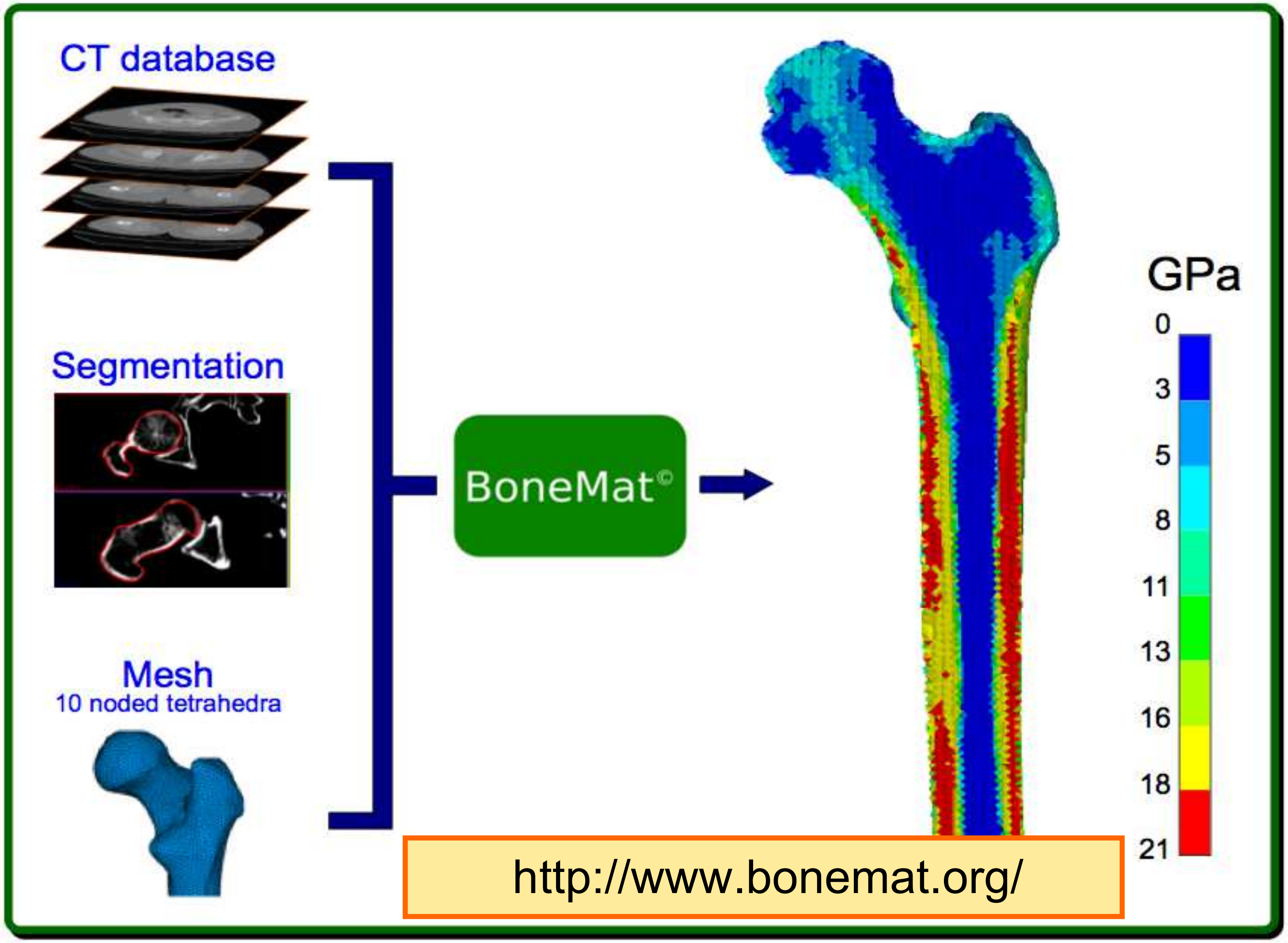
CT

MicroCT

Synchrotron Radiation (SR)

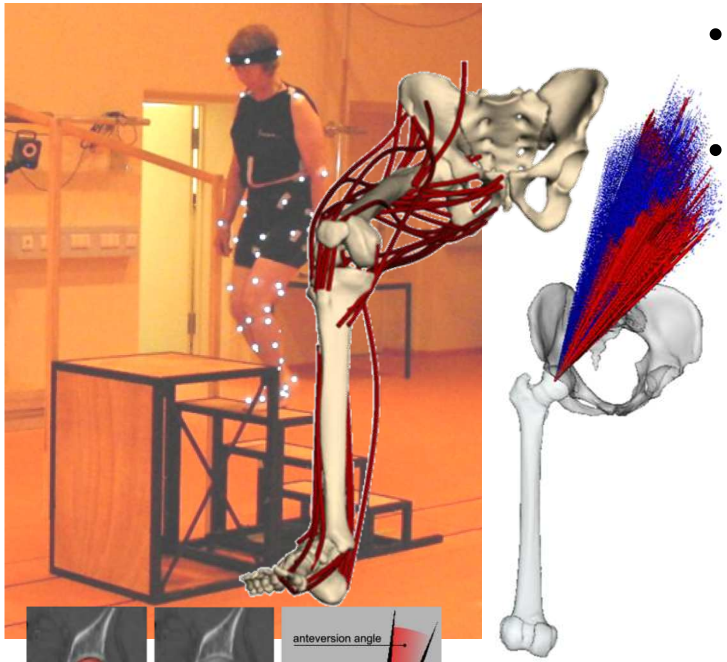
2) Possible applications for bone imaging from a compact Compton X-ray Source in Bologna (BoCXS)

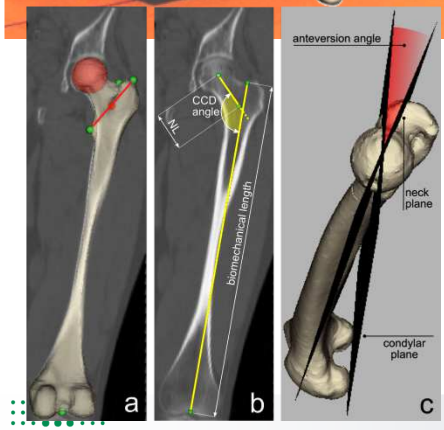
1) Clinical and research applications - CT
Subject-specific Finite Element modeling of mechanical behaviour



http://www.bonemat.org/

Multiscale modeling of the musculoskeletal system



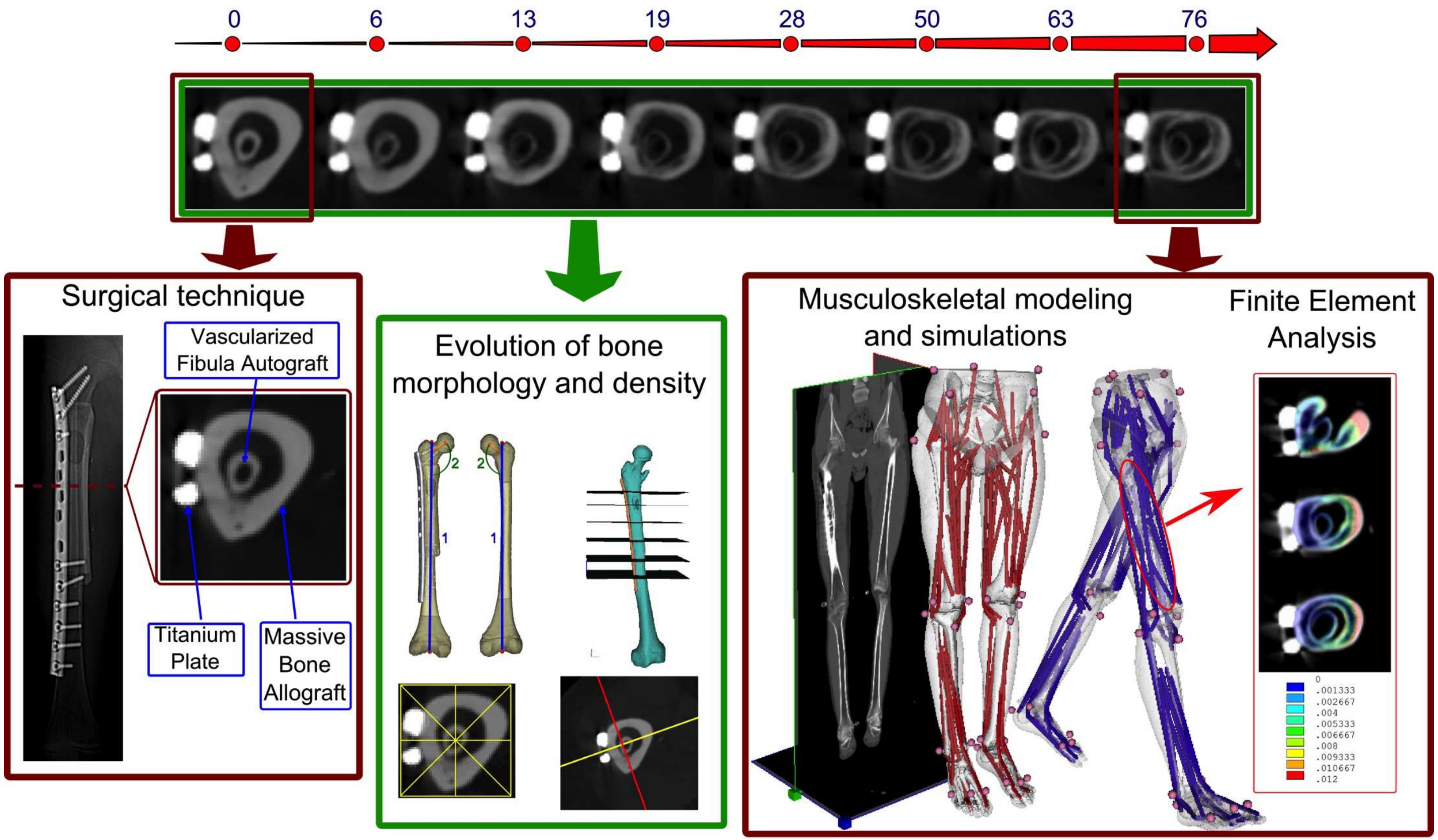


- Subject-specific analysis on 200 subjects
- Simulation of fisiological loading conditions during walking and stair climbing.
- Analysis of the safety factor for the proximal femor in respect of sex, age and bone mineral condition

	Normal	Osteopenic	Osteoporotic	Total
Age < 50	**6.07** (1.25) N=18	**5.44** (1.11) N=14	4.02 (0.46) N=2	**5.69** (1.25) N=34
	4.41 (1.24) N=8	[illegible].92 (1.18) N=24	5.29 (2.46) N=2	4.82 (1.24) N=34
50 ≤ Age < 65	5.75 (1.32) N=4	**4.92** (1.[illegible]0) N=28	4.61 (1.42) N=4	**4.98** (1.38) N=36
	6.07 (0.40) N=3	5.21 (1.58) N=15	4.16 (0.81) N=3	5.18 (1.45) N=21
Age ≥ 65	4.28 (0.62) N=2	**5.40** (1.13) N=21	**3.42** (0.76) N=23	**4.37** (1.35) N=46
	7.19 (1.75) N=2	5.01 (1.05) N=19	4.28 (0.89) N=8	4.96 (1.23) N=29
Total	**5.87** (1.29) N=24	**5.20** (1.26) N=63	**3.63** (0.93) N=29	**4.94** (1.43) N=116
	5.22 (1.56) N=13	5.02 (1.24) N=58	4.41 (1.11) N=13	4.96 (1.28) N=84

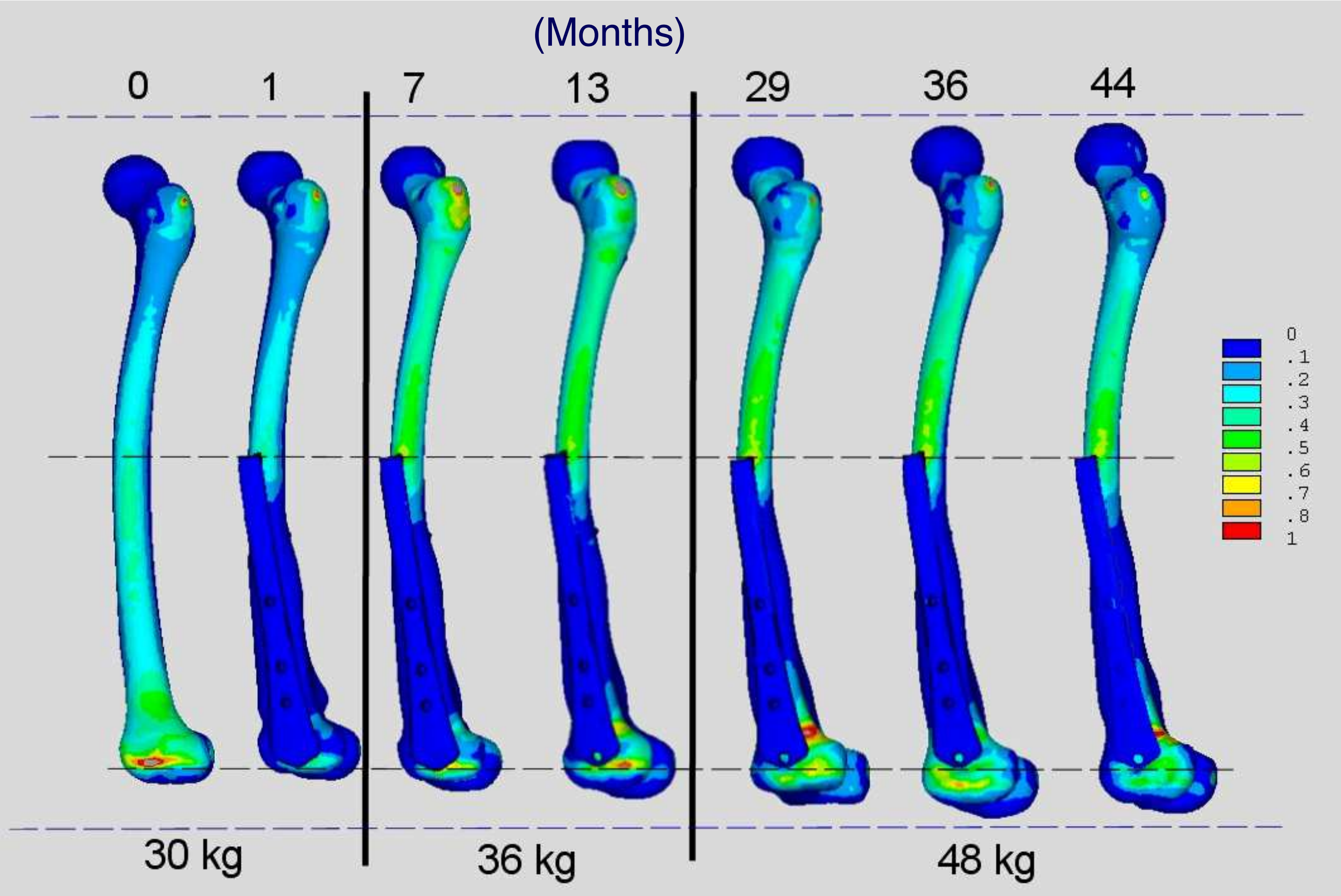
Taddei F., et al. J Biomech. 2014 Nov 7;47(14):3433-40.

Bone adaptation of reconstructed femur after bone tumors resection



Valente G. et al., Skeletal Radiol (2017) 46:1271–1276

Evolution of risk of fracture



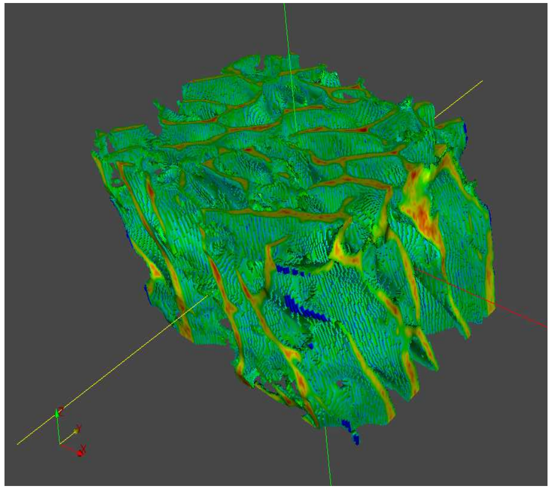
1) Clinical and research applications - CT

New in-vivo CT diagnostic methods are providing imaging close to resolution of trabecular bone:
High Res peripheral QCT (80-150 µm), Cone Beam CT (100-300 µm)

Systems specifications and patient dose considerations limit these diagnostic methods to peripheral arms (HRpQCT) and maxillo-dental (CBCT)

Suitable for large scale

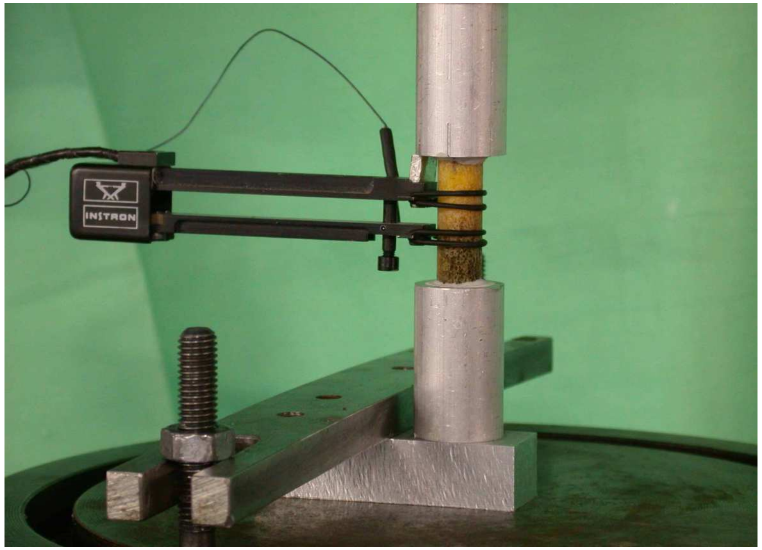
micro FE models?[1]

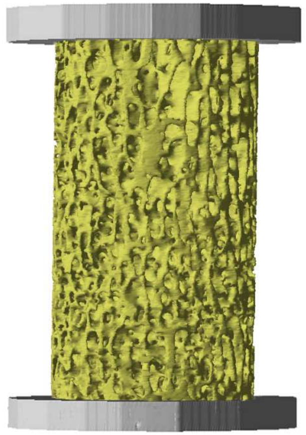


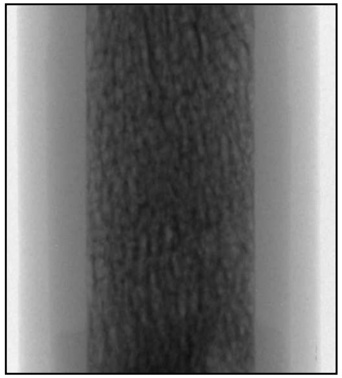
[1] Large-scale finite element analysis of human cancellous bone tissue micro computer tomography data: a convergence study. Chen Y, Pani M, Taddei F, Mazzà C, Li X, Viceconti M. J Biomech Eng. 2014 Oct;136(10)

1) Clinical and research applications - in-vitro microCT

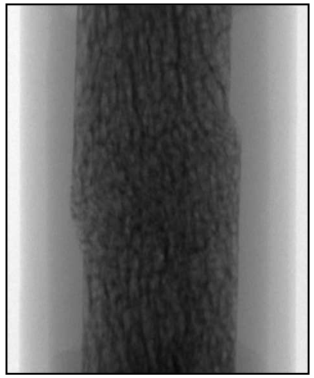
Structural parameters vs. mechanical strength of trabecular bone







Compressive testing



MicroCT of trabecular bone
from human proximal femur:
- height 20 mm, diameter 10 mm
- 19.5 µm pixel size

Perilli et al. / Bone 41 (2007) 760–768

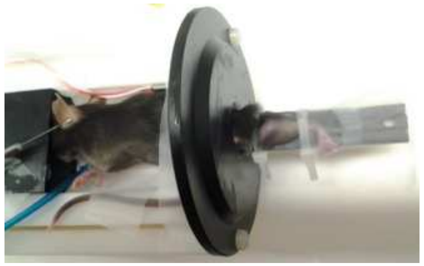
1) Clinical and research applications - in-vivo microCT

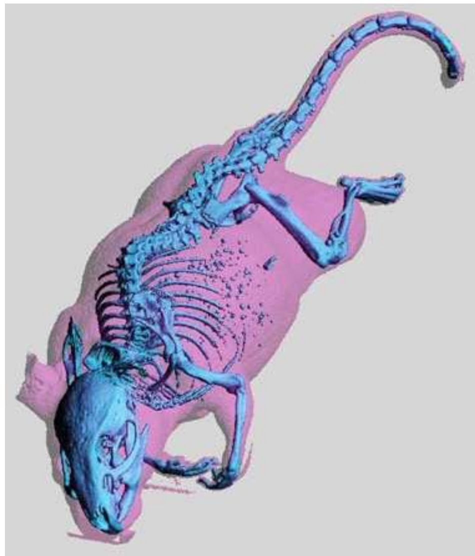
Reduce, Refine, and Replace animal experimentation

Mouse
Virtual Physiological ~~Human~~

Laboratory
In-vivo microCT (1)

Synchrotron Radiation (SR)
In-vivo microCT (2)





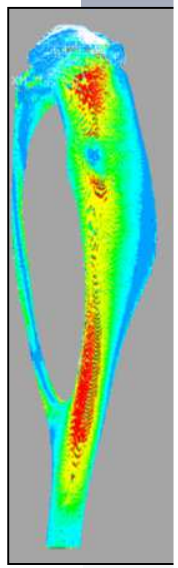


Image courtesy by Insigneo Institute, Sheffield, UK

1) Fini M et al. Clin Exp Metastasis 2013, 30(8):1033-1045; 2) Kinney JH et al., Technol Health Care. 1998 6(5-6):339-50

In-vivo SR MicroCT

WHOLE BODY IN VIVO SCAN (~70μm)

TIBIA IN VIVO SCAN (~10μm)

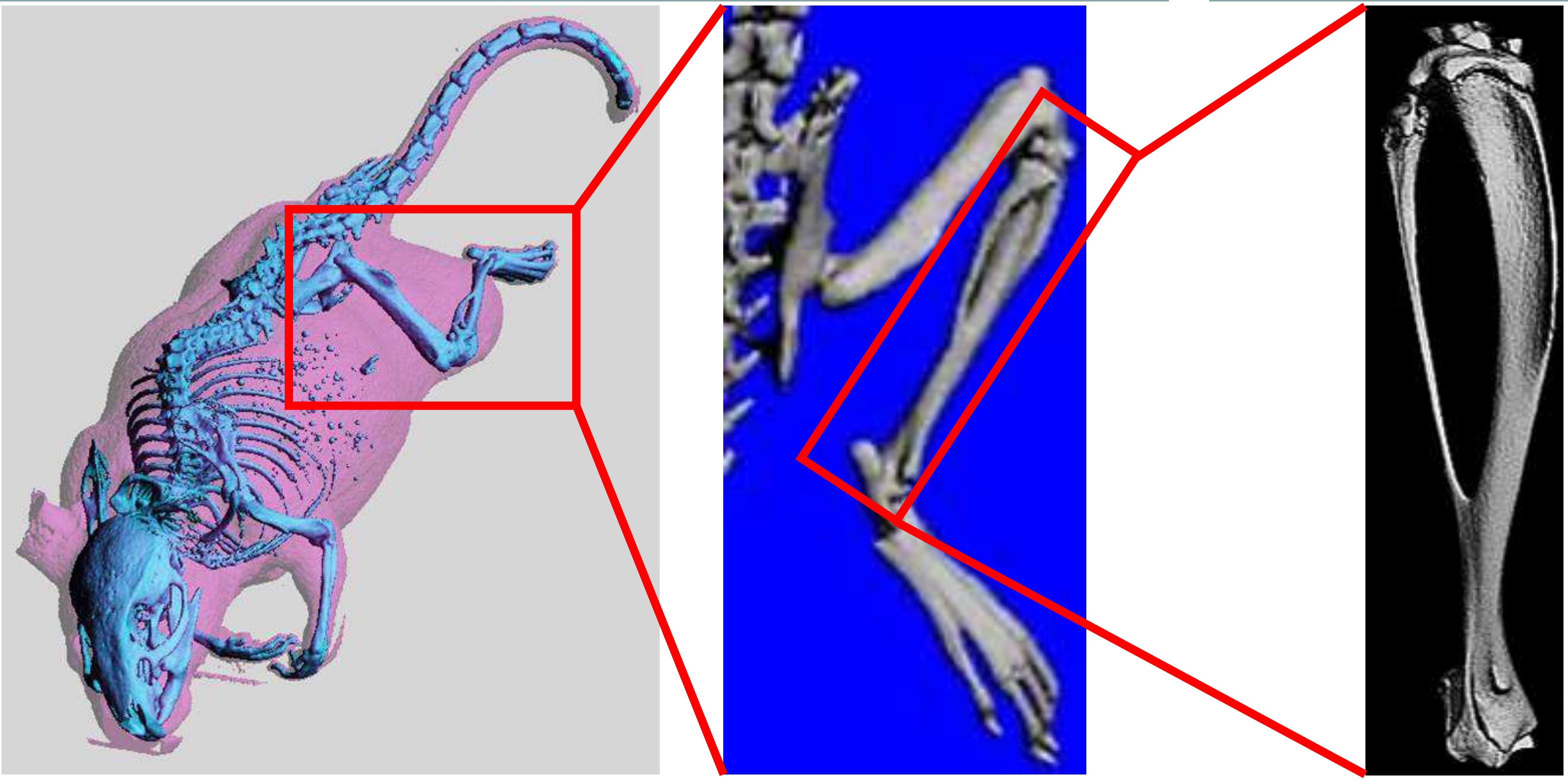
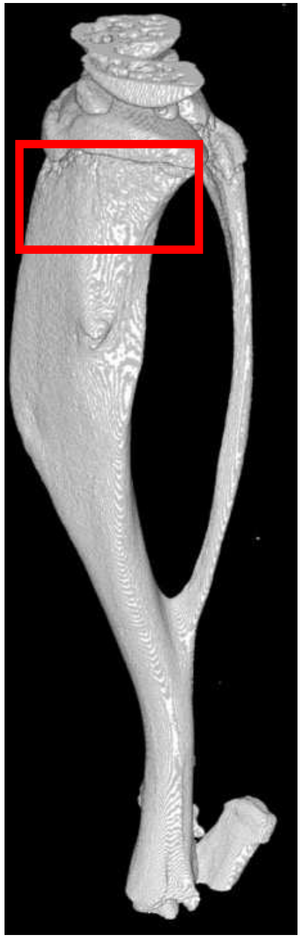
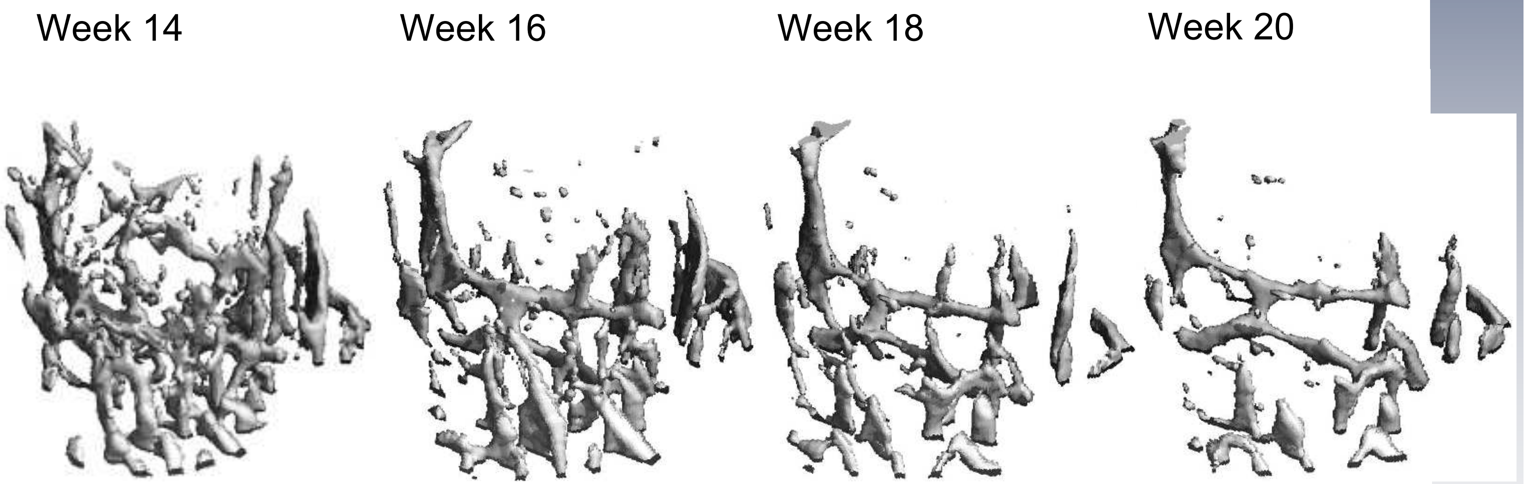


Image courtesy by Insigneo Institute, Sheffield, UK

In-vivo SR MicroCT

LONGITUDINAL MEASUREMENTS:
Proximal Trabecular Bone





Ovariectomized mice
(model of accelerated bone resorption in osteoporosis)

Image courtesy by Insigneo Institute, Sheffield, UK

LTM
Laboratorio di Tecnologia Medica

In-vivo SR MicroCT

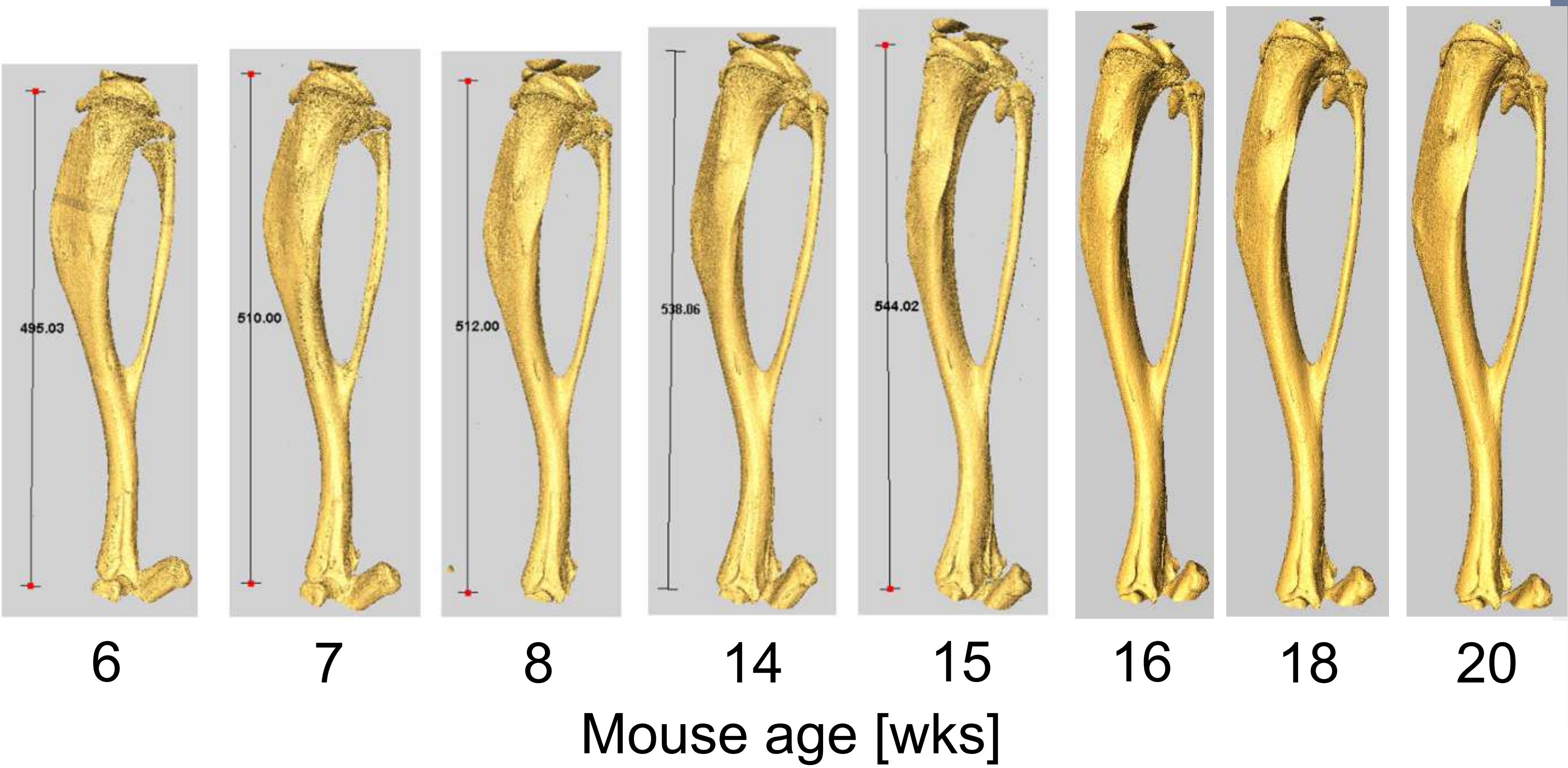
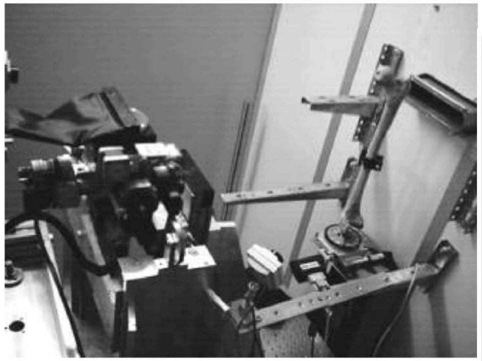
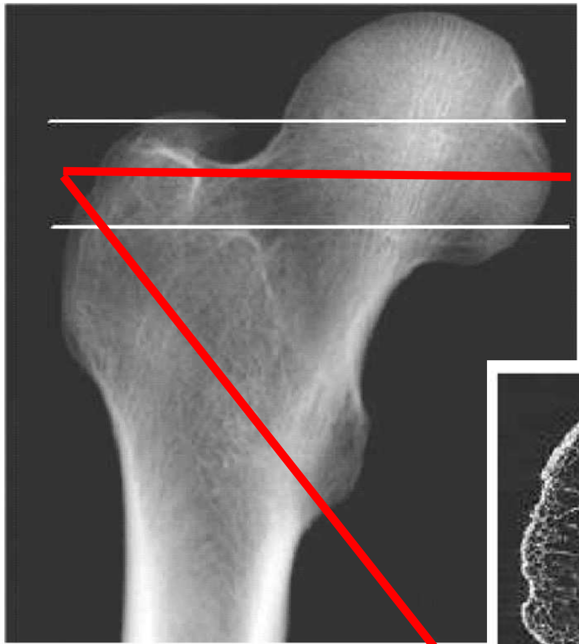


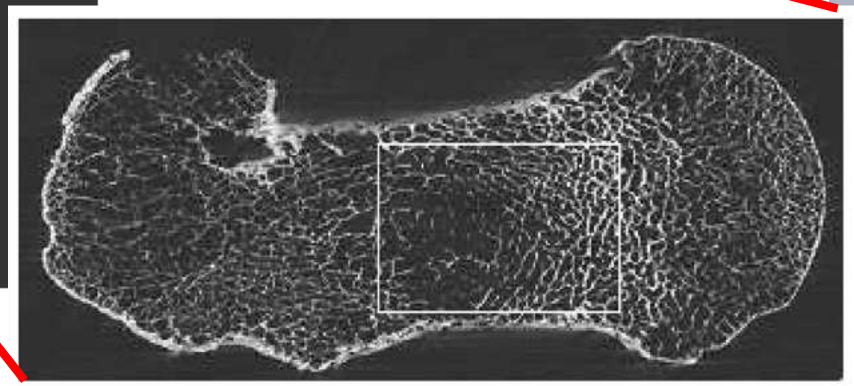
Image courtesy by Insigneo Institute, Sheffield, UK

1) Clinical and research applications - SR microCT





SR microCT
of large
bone structures



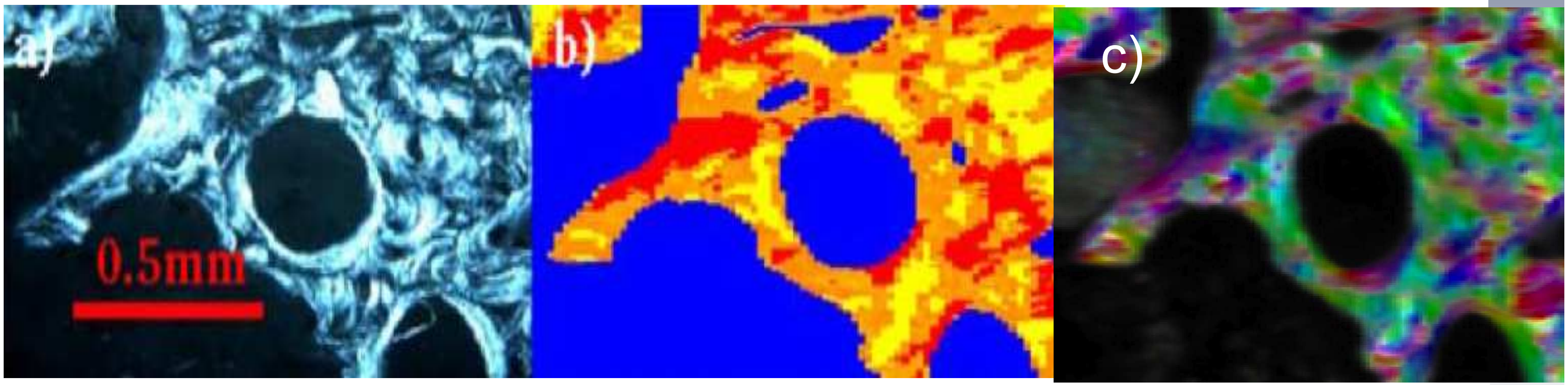
Reconstructed tomographic slice pixel size 22.5 um
FOV 130 mm x 1 mm

Baruffaldi et al. An Innovative CCD-Based High-Resolution CT System for Analysis of Trabecular Bone TissueIEEE Trans Nuc Scien Vol 53 N 5 (2006)

1) Clinical and research applications - SR scattering

SR based x-ray scattering of mineral orientation at micro and nano scale

Small Angle and Wide Angle X-ray scattering (SAXS-WAXS) are effective techniques to investigate at the molecular scale the packing of collagen and mineral phase



Bone biopsy: a) polarized light microscopy; b) WAXS image of collagen orientation in the osteons; c) SAXS imaging of mineral c-axis orientation and collagen fibril orientation

Giannini et al. / Sci. Rep. 2, 435; (2012)

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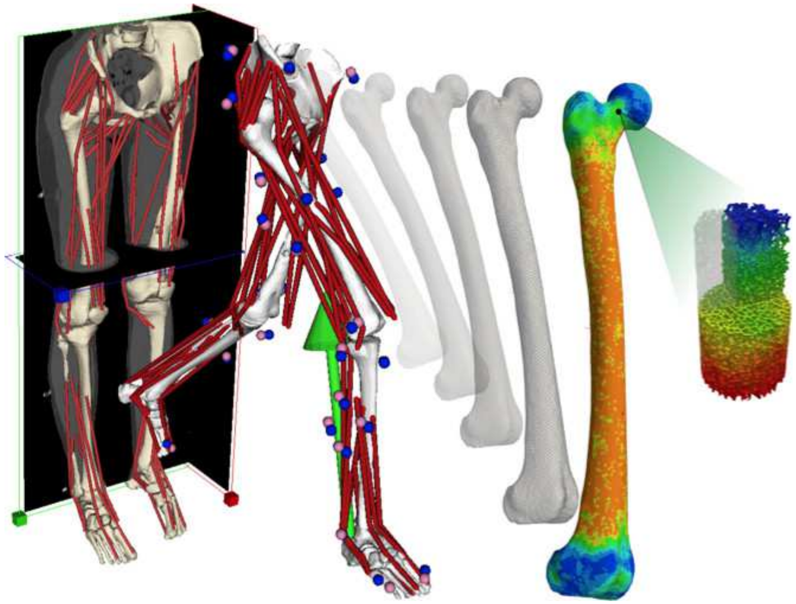


Virtual Physiological Human (VPH) for personalized medicine

<u>AIMS</u>

1) Clinical and research applications for bone tissue imaging based on:

   CT

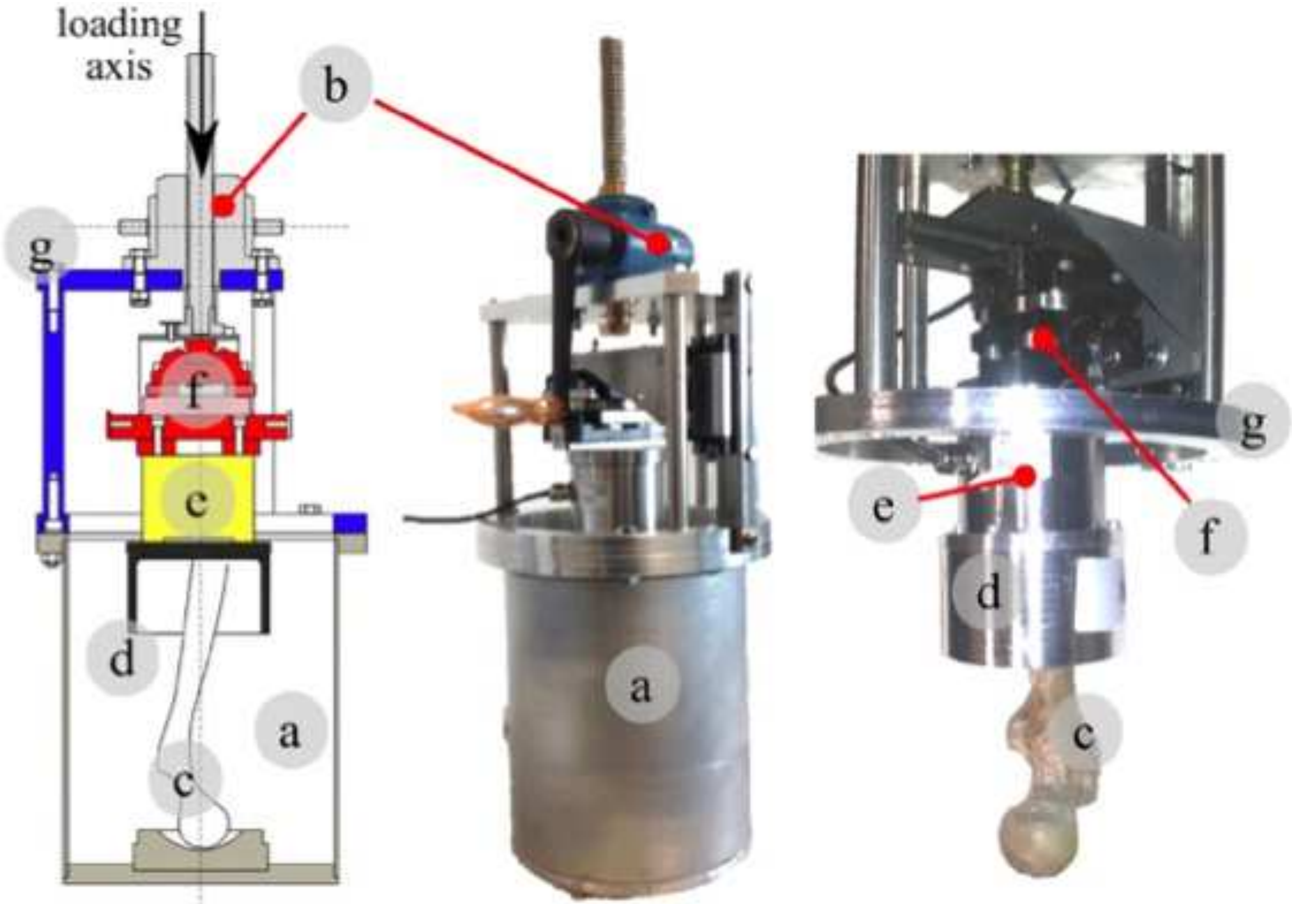
   MicroCT

   Synchrotron light

2) Possible applications for bone imaging from a compact Compton X-ray Source in Bologna (BoCXS)

2) Possible applications for bone imaging from BoCXS

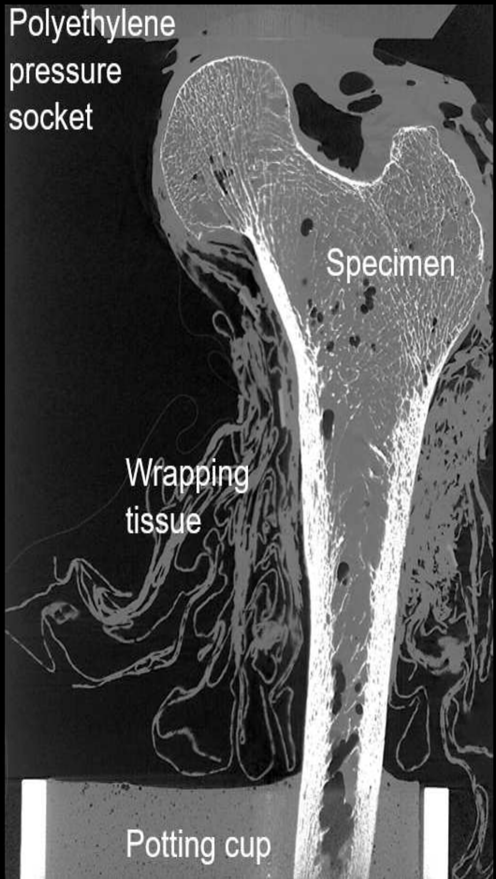
2.1) high resolution 3D/4D analysis on large samples
Time-elapsed SR microstructural imaging of femoral neck fracture



S. Martelli, E. Perilli J. Mech Behav Biomed Mat 84 (2018) 265–272

The sequence to fracture

Pixel size: 29.81 μm;
533 GB disk space (32 bits, tiff)



Flinders University
The Medical Device Research Institute

Video courtesy by the author S. Martelli
Flinders University, South Australia

The μFE mesh

3D mesh (full resolution)

- 1.5 mm thick
- ~ 50M nodes
- Linear hexahedrons
- E = 17000 MPa
- Interpolated DVC displacements (~ 2000 nodes)

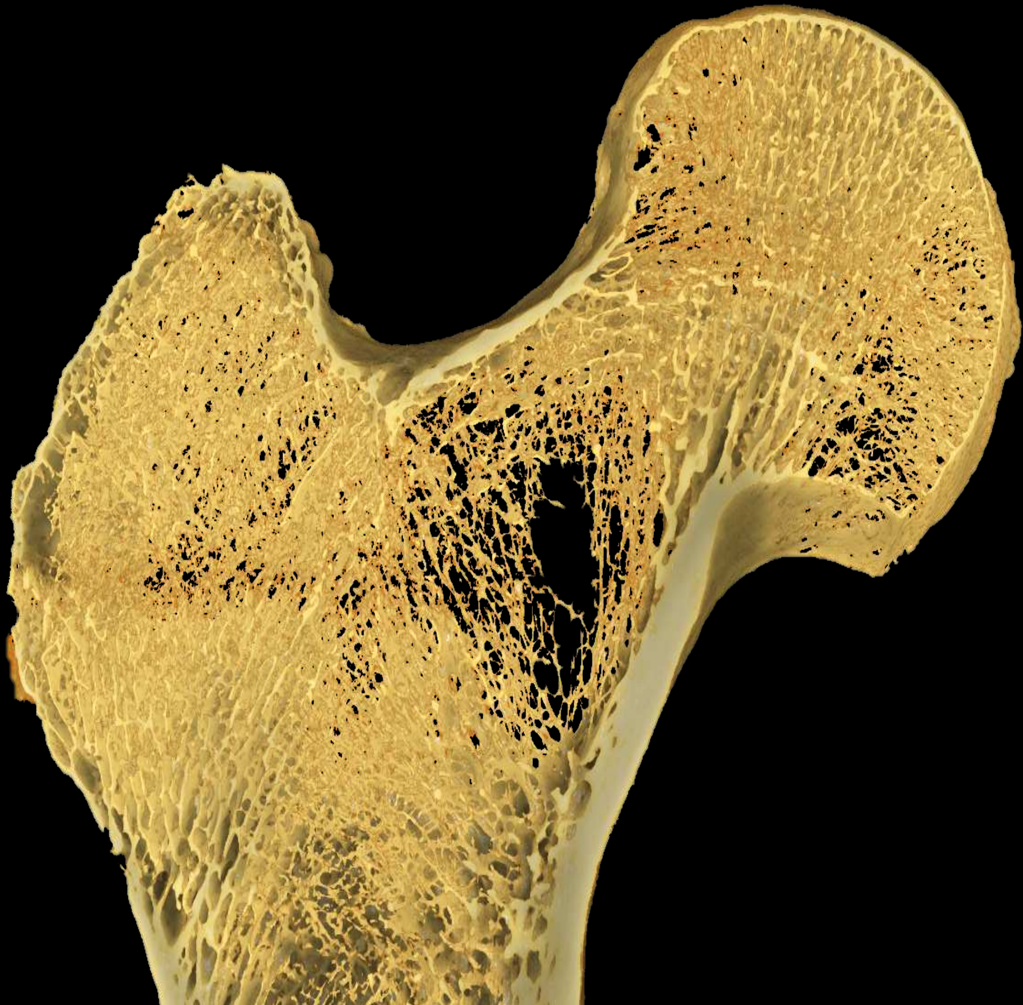
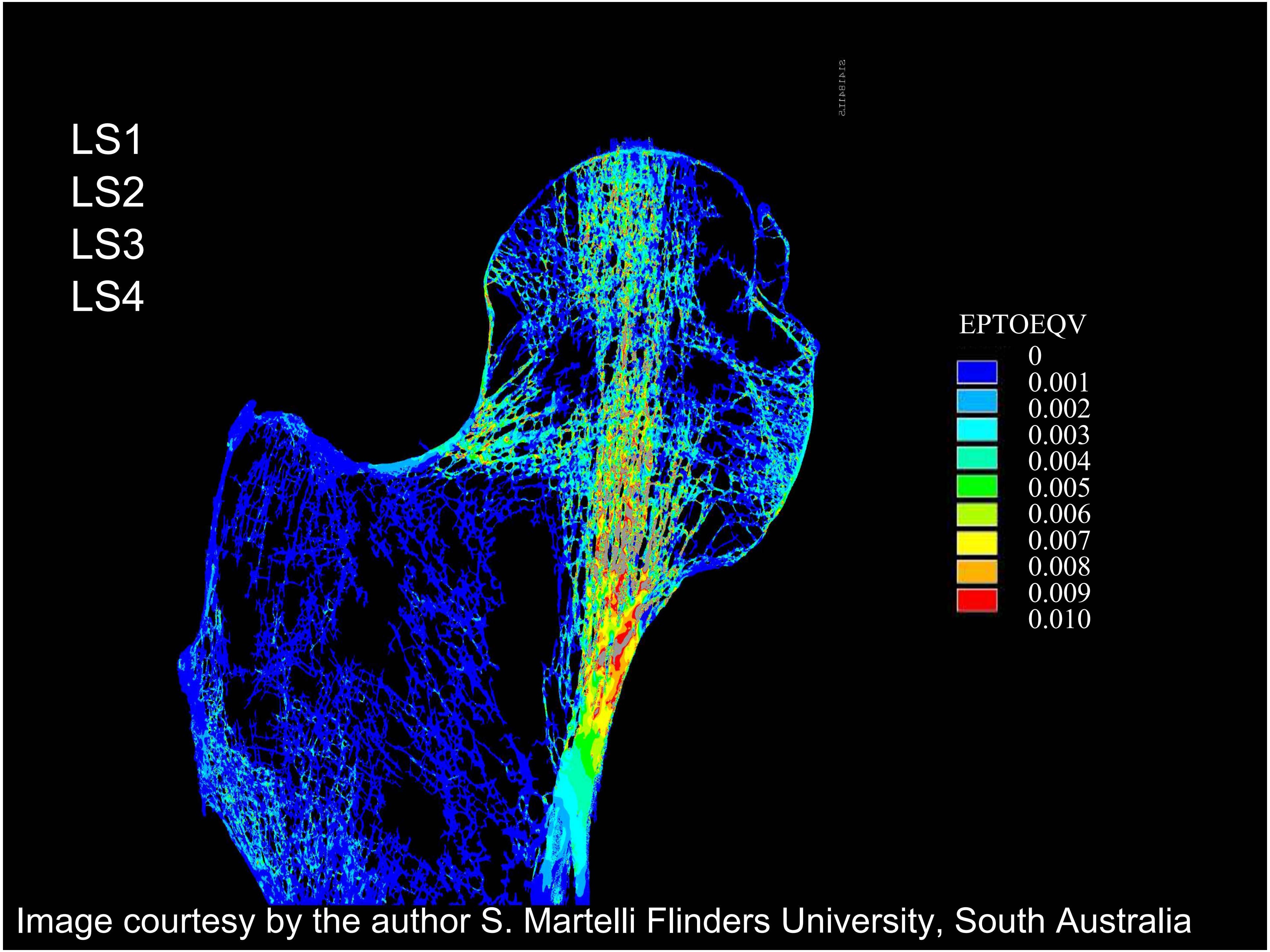
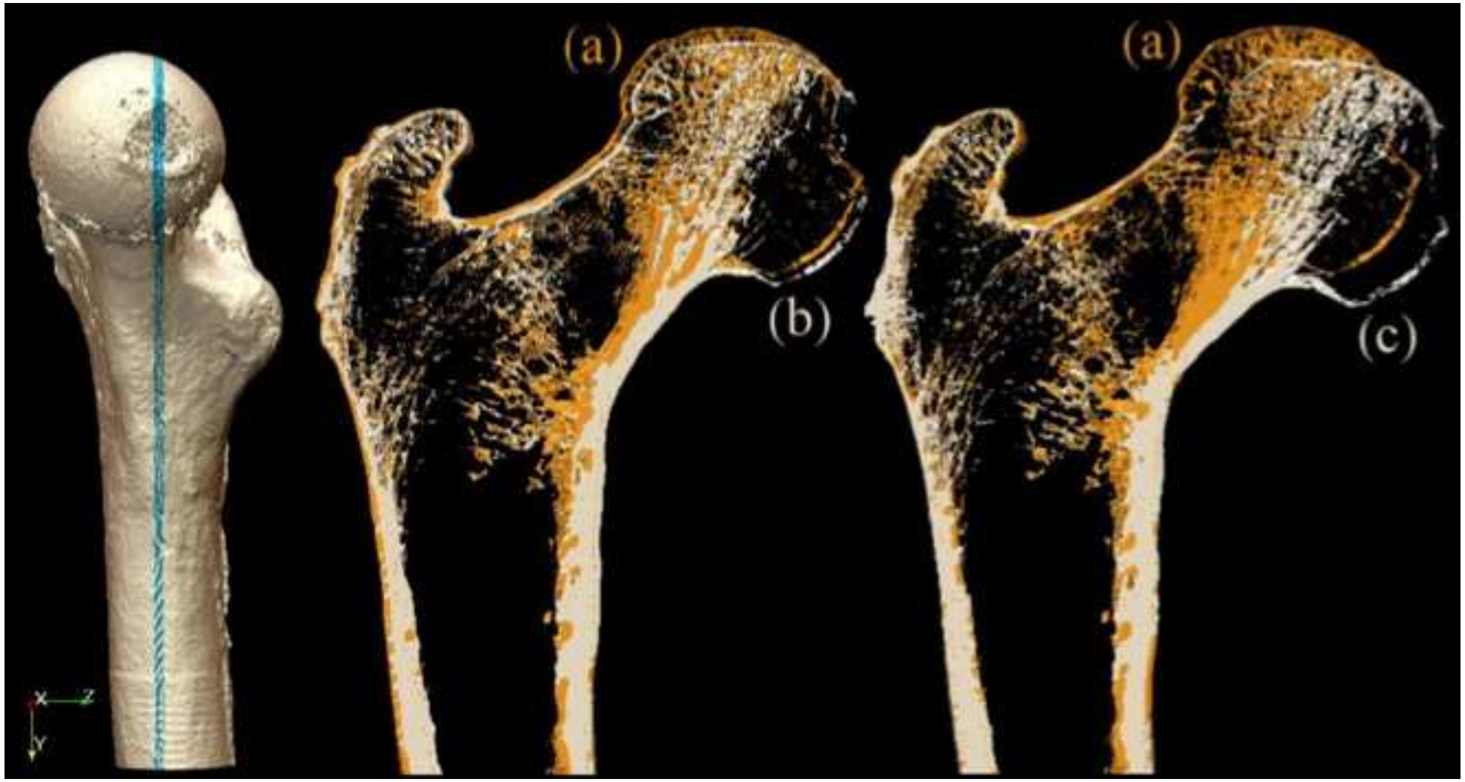


Image courtesy by the author S. Martelli Flinders University, South Australia


LS1
LS2
LS3
LS4
EPTOEQV
0
0.001
0.002
0.003
0.004
0.005
0.006
0.007
0.008
0.009
0.010
Image courtesy by the author S. Martelli Flinders University, South Australia

Digital Volume Correlation for the validation of µFE modeling

The availability of high resolution 3D maps before (a) and after loading (b and c) makes applicable a new experimental method to measure local displacements and strains: the Digital Volume Correlation (DVC)



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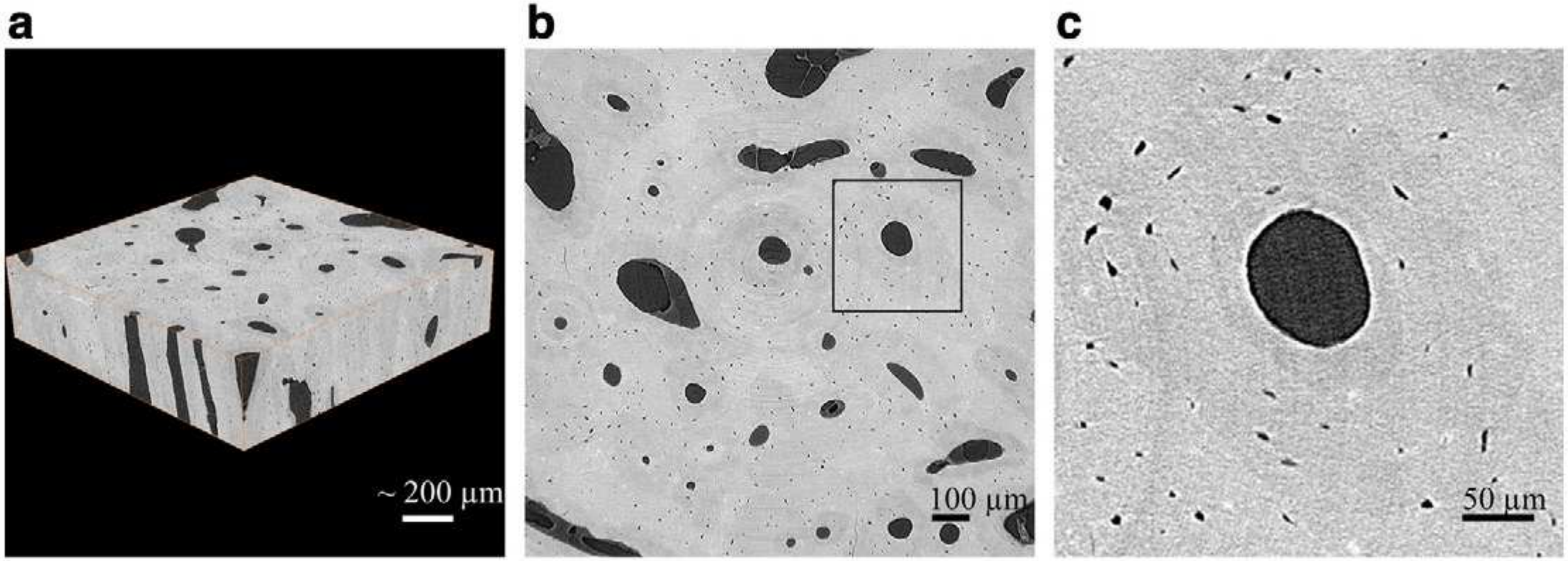
2) Possible applications for bone imaging from BoCXS

2.2) very high resolution 3D/4D analysis on small samples

3D analysis of osteocyte lacunar morphometric properties and distributions in human femoral cortical bone by SR-microCT

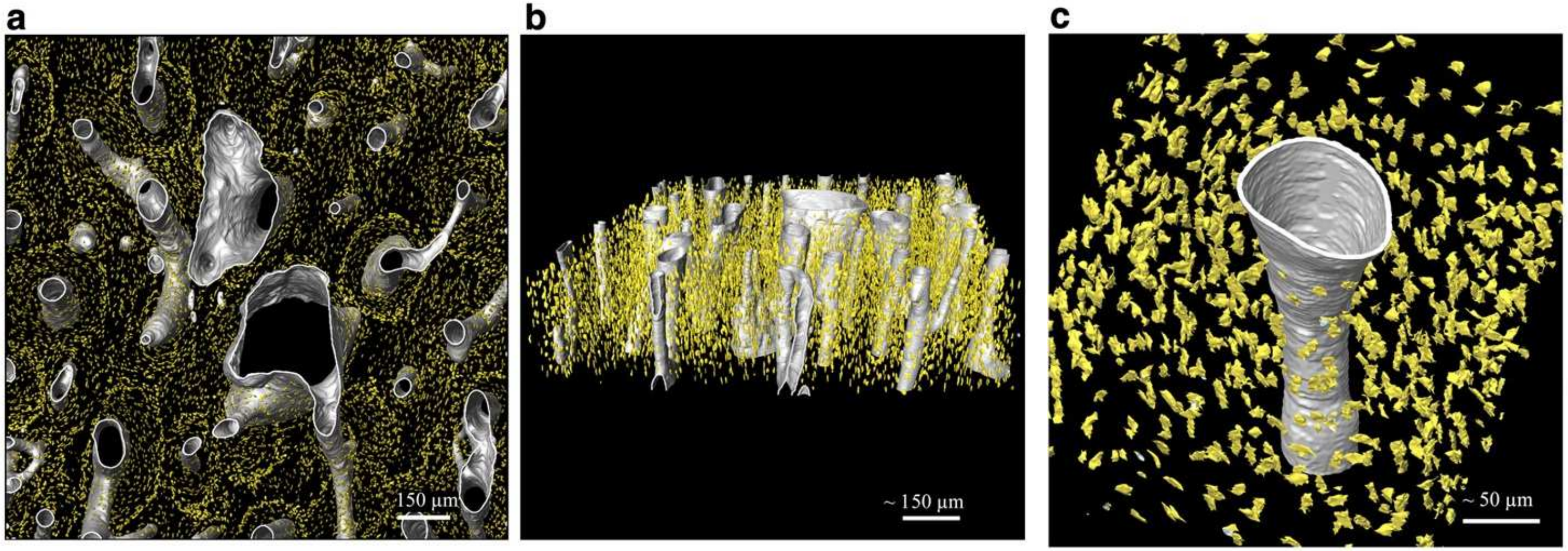


a) 3D rendering; b) Single slice, voxel resolution of 1.4 um; c) Zoom around a Haversian canal

P. Dong et al. / Bone 60 (2014) 172–185

2) Possible applications for bone imaging from BoCXS

2.2) very high resolution 3D/4D analysis on small samples



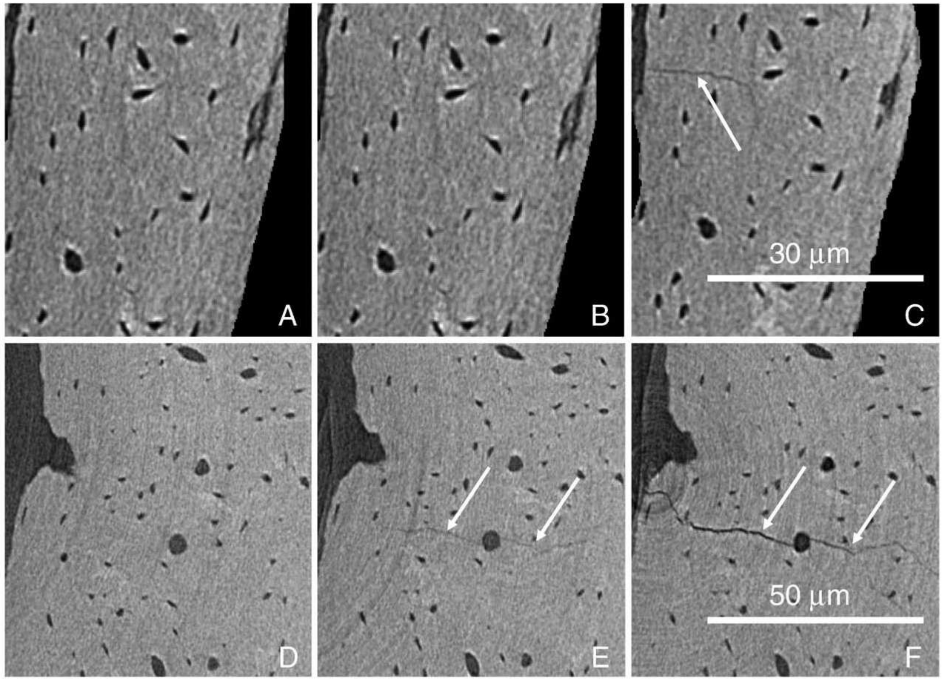
Harversian canal (white) is surrounded by
osteocyte lacunae (yellow): a) Top view; b) side view; c) 3D rendering

P. Dong et al. / Bone 60 (2014) 172–185

2) Possible applications for bone imaging from BoCXS

2.2) very high resolution 3D/4D analysis on small samples

Time-lapsed assessment of microcrack initiation and propagation in murine cortical bone at submicrometer resolution



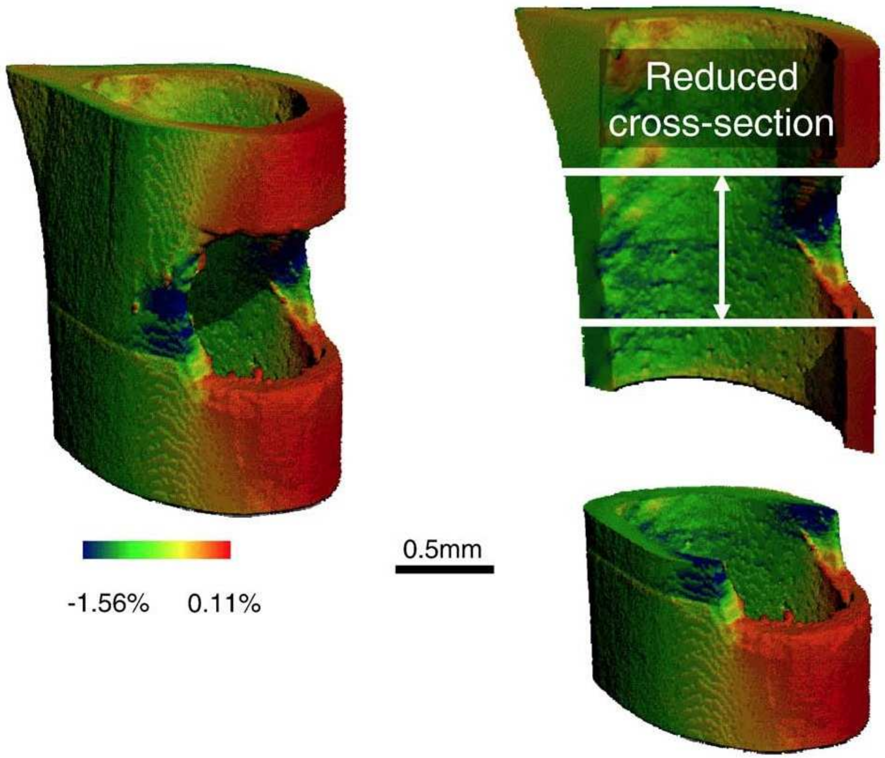
Microcrack initiation and propagation in the femoral mid diaphyseal reduced cross-section using SR microCT at 700 nm nominal resolution

R. Voide et al. / Bone 45 (2009) 164–173

2) Possible applications for bone imaging from BoCXS

2.2) very high resolution 3D/4D analysis on small samples

Time-lapsed assessment of microcrack initiation and propagation in murine cortical bone at submicrometer resolution



Micro-finite element (μFE) modeling within the femoral mid-diaphysis including the reduced cross-section

R. Voide et al. / Bone 45 (2009) 164–173

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Conclusions

CT, microCT and Synchrotron Radiation based applications have a long tradition in bone imaging for clinical and research aims.

The availability of a compact Compton X-ray Source in Bologna (BoCXS) would open new potential research lines in the area of:

high resolution analysis on large bone samples (voxel size 10-30 um, on a FOV of about 100-150 mm)

very high resolution analysis on small bone samples (voxel size <1 um, on a FOV of about 1-2 mm)

possibly joined with time-lapsed microstructural 4D imaging of fracture, with FE modeling validated by Digital Volume Correlation (DVC) method, to better understand the biomechanical behaviour of bone tissue.

Thank you!

First surgery at the Rizzoli Institute (1896)