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WHOLE JOINT STRUCTURE IN A RAT OSTEOARTHRITIS MODEL FOR SAMPLE-SPECIFIC MECHANICAL EVALUATION

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Introduction

Micro-computed tomography (microCT) allows 3D assessment of calcified tissue structures in the joint, and recent advances use contrast agents to quantify glycosaminoglycan content in cartilage [Palmer 2006], alongside measurement of volume changes [Siebelt 2011]. However, challenges in clearly delineating the cartilage from the surrounding joint space still remain. Solving this would allow more accurate definitions of structural requirements for finite element (FE) studies of mechanical loading, which is an important determinant in the progression of osteoarthritis (OA).

The goal of this work is to provide accurate structural definitions for future FE studies, by clearly delineating the joint tissues using a single imaging modality; i.e. microCT.

Methods

Medial meniscectomy/ACL desmotomy of four 3 month-old male Wistar rats was performed to destabilise the right tibio-femoral joint. Seven non-operated rat joints served as healthy controls. Animals were sacrificed 6 weeks post-op, the knees dissected, and scanned using microCT (SCANCO Medical, Switzerland; 10 μm voxel size). After a pre-scan, the joint space was filled with a contrast agent and immersed overnight in 60% Hexabrix™ (Mallinckrodt, USA), followed by a second scan with the same settings. MicroCT scans were processed and the cartilage was manually segmented. Morphometric analysis was performed to obtain the average 3D cartilage thickness (Cg.Th) for the medial and lateral tibial plateaux. The joints were then sliced and stained with Safranin O. Registration of the bones from histology and microCT allowed identification of the microCT slice corresponding to the histology section (figure 1 a-c). Cartilage was then segmented from both images, and 2D Cg.Th was calculated and correlated (figure 1 d-e).

Results and Discussion

The results show a strong correlation between 2D Cg.Th measured from histology and the registered microCT slices (figure 2a). Correlations were similar for OA-induced and control rat knees, therefore the data was pooled to give a correlation, $R^2 = 0.80$, $p < 0.001$.

The protocol also provided a qualitative 3D assessment of cartilage, as shown in figure 2 (b-c). This allows investigation of patterns of destruction in OA, where the medial tibial plateaux showed cartilage loss and fibrillation compared to both the lateral plateaux and the healthy controls.

Finally, with segmentation of tibio-femoral components, it was also possible to generate an individualised joint model for FE analysis (figure 3); where the interface between tissues can be accurately defined, and sample-specific structural changes can be included.

Conclusions and Outlook

In conclusion, the results clearly show a good correlation with quantitative cartilage measures taken from microCT compared to histomorphometry; which highlights the capacity of microCT to accurately measure cartilage structures. Furthermore, the high-resolution, 3D data obtained with microCT allows whole-joint analysis and imaging of disease-induced changes, and permits investigation of local bone adaptation alongside cartilage degeneration. The validated individual models produced with this technique can be used in future to study load bearing of articulating surfaces, and the role of microstructural changes in the progression of OA. Structural delineation also allows investigation of patterns of destruction in the onset of OA that can be used for individualised FE analysis of a particular joint of interest.

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References

Acknowledge

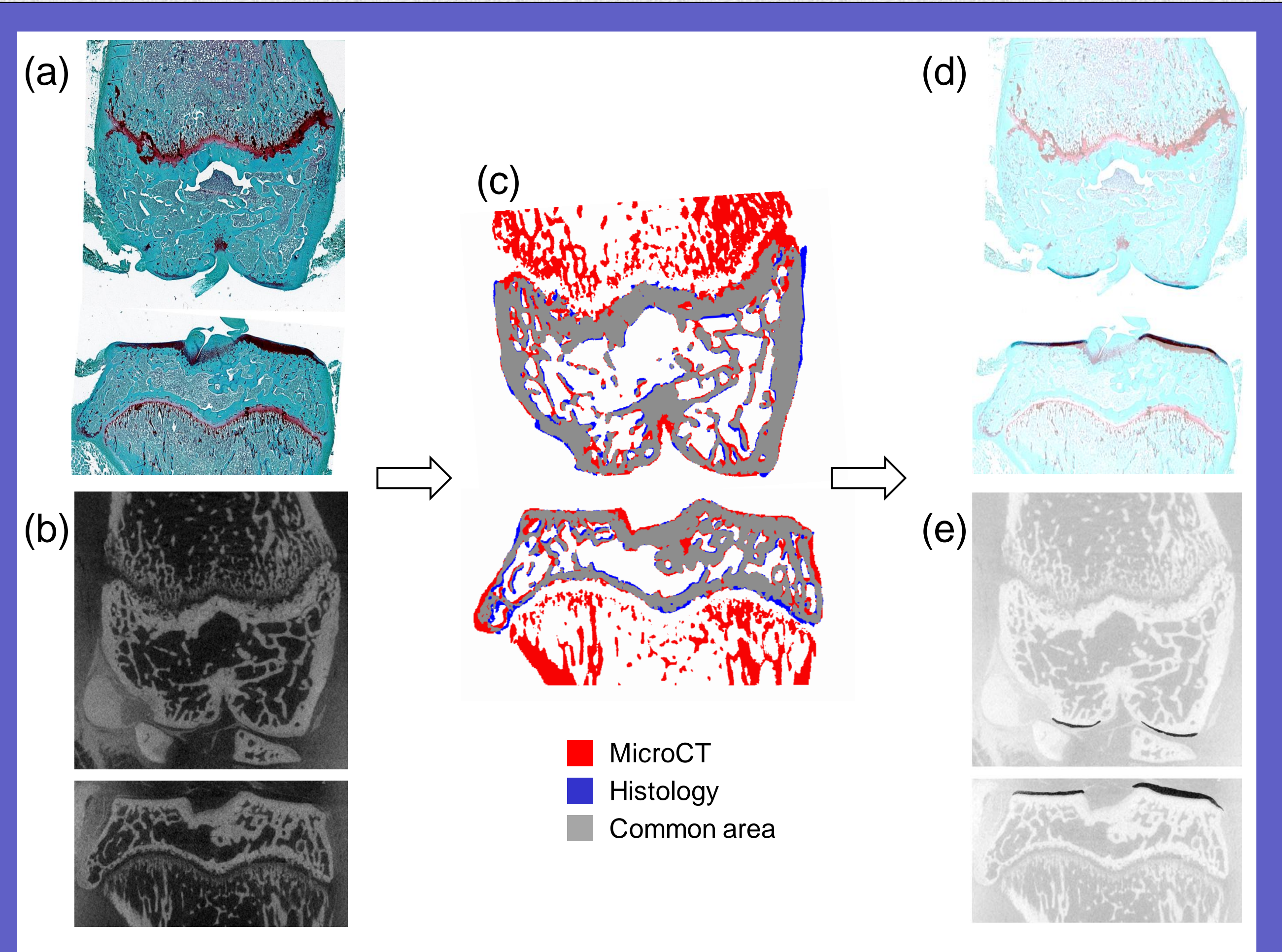


Figure 1: Typical images for (a) histology and (b) microCT. (c) 2D registration of microCT and histology. Manual contours of the cartilage in the corresponding (d) histology and (e) microCT slices.

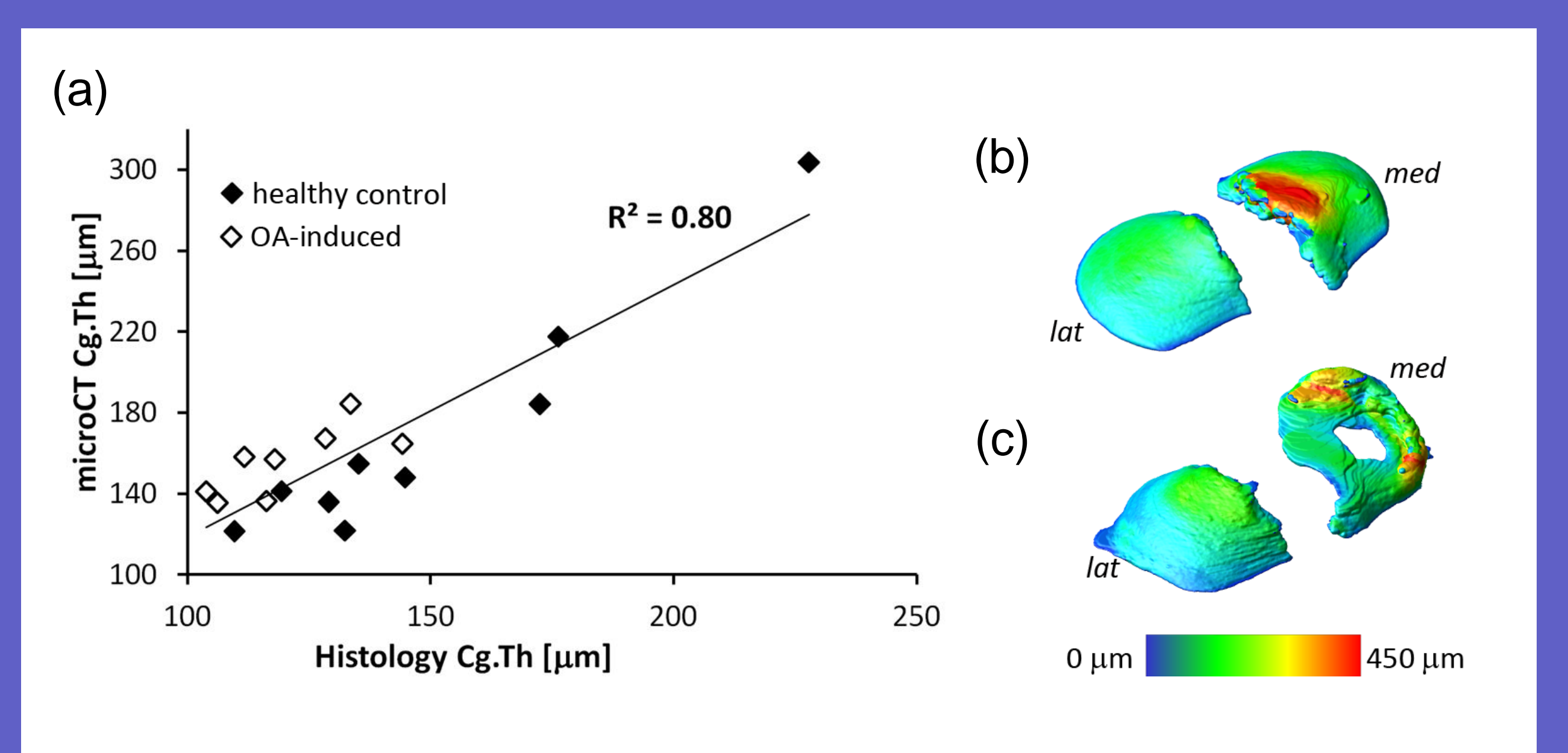


Figure 2: (a) Comparison of 2D Cg.Th measured in histology and microCT ($p < 0.001$). 3D thickness maps from tibial cartilage of (b) a healthy control and (c) an OA-induced animal.

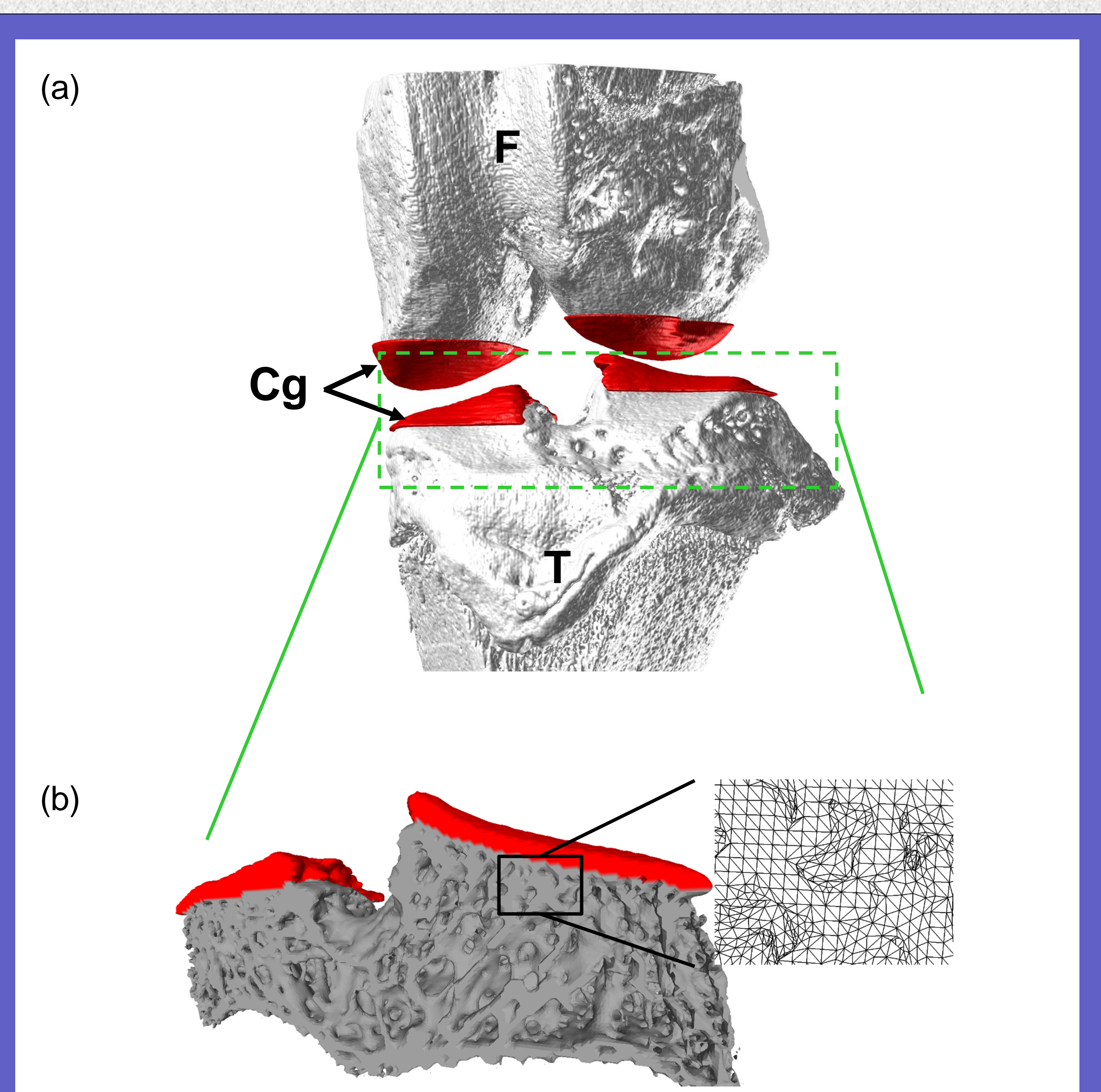


Figure 3: (a) Typical 3D reconstruction of a tibio-femoral joint with delineated structures labelled. (b) Surface mesh of the rat tibia cut in the coronal plane for sample-specific FE analysis. T: tibia, F: femur, Cg: cartilage. Inset: detailed mesh.