MICROMECHANICAL CHARACTERISATION OF OSTEOARTHRITIC SUBCHONDRAL BONE BY MICROPILLAR COMPRESSION

Samuel McPhee (1), Lekha Koria (2), Marlène Mengoni (2), Marta Peña Fernández (1), Rainer Beck (3), Jonathan D. Shephard (3), Claire Brockett (4), Uwe Wolfram (1)

1. Institute of Mechanical, Process and Energy Engineering, Heriot-Watt University, UK. 2. Institute of Medical and Biological Engineering, University of Leeds, UK. 3. Institute of Photonics and Quantum Sciences, Heriot-Watt University, UK. 4. INSIGNEO Institute for in silico Medicine, University of Sheffield, UK

Introduction

Osteoarthritis (OA) is a multifaceted joint disease primarily characterised by the degeneration of articular cartilage. The clinical manifestation is one of pain and loss of mobility [1]. The heterogeneous pathophysiology of OA limits the efficacy of pharmacological and non-surgical interventions. To improve clinical outcomes, further insight into the complex pathogenesis of OA is required. Aside from cartilaginous changes, subchondral bone alterations are both a cause and effect of OA progression [2]. While the macrostructural alterations such as sclerosis and bone plate thickening are well documented, few studies have investigated the microscale mechanical properties of the underlying constituent tissue. Our aim was therefore to investigate whether microscale non-linear mechanical and compositional properties of OA subchondral bone differ from healthy bone.

Methods

Bone specimens from the distal tibia of 3 cadaveric donors (HC) and 2 arthroplasty patients (OA) were sectioned, embedded, and polished. A total of 227 micropillars were extracted via picosecond laser ablation by modifying our previous micromanufacturing protocol [3]. Micropillars (HC = 135; OA = 92) were extracted in arrays located in the subchondral bone plate (SCBP) and subjacent trabeculae (SCTB) (Figure 1a-b). Raman spectroscopy was performed following [4] and quantitative backscattered electron microscopy (FEI Quanta 650) were used to assess whether any relative differences in tissue composition could be explanatory of any differing mechanical properties [5]. Specimens were rehydrated for 24 h by submerging in Hank's buffered saline solution and remained submerged throughout testing. Micropillars were compressed uniaxially to a depth of 15 µm with a cyclic profile of 1 µm loading followed by 0.25 µm unloading using a custom-made indenter (Alemnis AG). We used non-linear finite element analyses to back-calculate the elastic and strength properties from the load-displacement data of each micropillar as done previously [3].

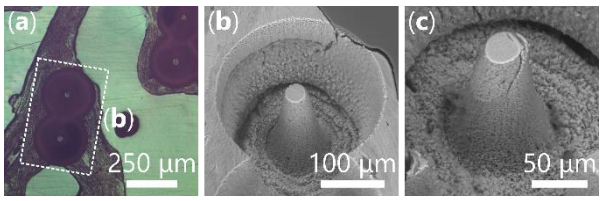

Figure 1: (a) Light microscope image and (b) SEM image of micropillars located in trabeculae. (c) Example of a micropillar exhibiting a shear failure mode.

Results

The micropillars exhibited average surface and base diameters of 32.2 µm and 93.3 µm, respectively. The average height was 143.1 µm and the average taper angle was 12.3°. Evaluation of the force-displacement curves shows that the pillar stiffness (K) and yield force (F_y) were significantly higher in the SCBP compared to the SCTB in the control sample, whereas the converse is realised in OA samples. The OA pillar stiffness and yield force is significantly higher than the HC in only the trabecular bone (Figure 2). Raman spectroscopy revealed no significant differences in the mineral to matrix ratio between pillar location or disease state (Figure 2).

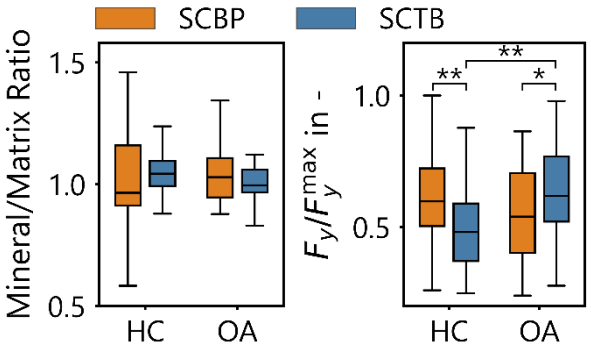

*Figure 2: Box plots of mineral to matrix ratio (left) and normalised yield force (F_y; right). Orange and blue represent subchondral bone plate (SCBP) and subchondral trabecular bone (SCTB). * $p<0.05$, ** $p<0.01$.*

Discussion

Results of our micropillar tests suggest that the morphological alterations to the subchondral bone that occur in progressive OA are accompanied by changes to the underlying tissue. This contrasts our Raman results which indicate no significant changes in the mineral to matrix ratio. Next steps focus on the analysis of other markers that may explain the increased strength observed in OA trabecular bone. The results we show here may help developing targeted therapies that prevent OA progression.

References

1. Vina & Kwoh. Curr. Opin. Rheumatol., 30:160-167, 2018
2. Burr & Gallant, Nat. Rev. Rheumatol., 8:665-673, 2012
3. Wolfram et al, Sci. Rep., 12:1-17, 2022
4. Mirzaali et al. Bone 93:196-211, 2016
5. Kochetkova et al, JMBBM, 134:105405, 2022

Acknowledgements

This research is supported by EPSRC under Grant No. EP/P005756/1. The authors would like to thank the donors and their families.