The mechanobiology of osteoarthritis

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Abstract. In combining biomechanical investigations with microanatomical studies, the authors have found new evidence suggesting a mechanobiological link between the altered microstructural response of degenerate cartilage to load, and the way in which structural changes develop in the early osteoarthritic joint. This paper presents the data and background for a new hypothesis exploring the initiation and progression of mechanically-driven osteoarthritic processes.

1. Introduction
Osteoarthritis (OA) is a degenerative condition of the joint that results in the structural deterioration of articular cartilage. Macroscopic changes in articular cartilage, either with age or disease, become apparent with the development of superficial fibrillation and shallow fissures or clefts [1,2]. At higher magnification there is increased fibril aggregation in the cartilage general matrix and increased calcification of the osteochondral junction [1-5]. In osteoarthritis (OA), mechanically stimulated biological processes are believed to further degrade cartilage to the extent that is seen in the end-stages of this disease [6,7]. How this disease is initiated and progresses remains a mystery and one important reason is because capturing the early- or pre-OA state of the joint tissue remains a challenge.

2. The influence of tissue degeneration on joint loading
Our experiments investigating the microstructural response of the cartilage matrix to load suggest that any disruption of the tissue continuum by early degenerative structural changes can cause an altered redistribution of load across the joint surface [8]. Such an alteration reduces the overall lateral transmission of forces, increasing instead the radially-directed forces towards the biologically-active cartilage-bone junction (Figure 1).
Figure 1. Differential interference contrast optical microscopic images of the indentation-edge region. Dotted lines are superimposed on chondrocyte alignment, to denote the way forces are transmitted away from the directly loaded region (indenter footprint) and into the non-directly loaded cartilage continuum: (a) intact-healthy tissue, (b) mildly degenerate, (c) moderately degenerate and (d) severely degenerate. The schematics to the right show how degeneration of the cartilage surface layer and matrix alters the magnitude and types of stress that develop in the biologically-sensitive osteochondral junction region.

3. New bone formation in the early osteoarthritic joint

The altered internal mechanical environment resulting from changes in the way the forces are transmitted within a degenerate cartilage matrix may be responsible for some important structural changes that we have revealed using novel micro-imaging techniques. These microstructural studies showed that new bone formation occurs at the cartilage-bone junction, beneath still intact cartilage, but near surface-disrupted sites. The evidence for this new bone formation is the presence of ‘cutting cones’ in the cartilage-bone junction near osteoarthritic lesion sites (Figure 2). These cones are classic morphological features associated with the early stages of primary bone formation. We have very recently established this new bone formation as that indicative of a pre-OA tissue state [9].
Figure 2. EVIDENCE OF NEW BONE FORMATION. Compared with the healthy osteochondral junction shown in (A), the early osteoarthritic junction (B) shows additional and advancing mineralisation fronts (black arrows) and the presence of ‘cutting cones’ (white arrow) shown here are imaged at the osteochondral junction of mild to moderately degenerate cartilage-bone tissue. These cutting cones originate from the underlying bone and develop within the zone of calcified tissue (ZCC). [AC = Articular Cartilage; Scale bar = 50 \mu m]

4. The biomechanical pathway for osteoarthritis
The fact that bone adaptation is related to the presence of mechanical stimuli, and that in the osteoarthritic joint there is new bone formation, allows us to pursue the mechanobiological approach to explain how OA develops. This would involve first defining the mechanical pathway from the macro-level of joint loading through to the micro-level redistribution of load within the tissue structure. A biomechanical framework would then be available for exploring the manner by which mechanical stimuli signal bone development at the crucial cartilage-bone junction in the OA joint.

Such a pathway is illustrated in Figure 3 using both recently acquired experimental evidence and theoretical interpretations, and forms a working hypothesis for our future work.

Figure 3. The theoretical model for OA development is illustrated here showing the important link between the intrinsic structure of the cartilage-bone tissue and the mechanical environment that is a result of load-bearing. The tissue maintenance loop represents the healthy joint that if affected by deviations in structure or mechanical load result in an instability that progressively deteriorates the joint. [Thambyah A 2005]. The challenge is to track tissue microstructural changes that affect and are affected by mechanical stimulus in the environment, and also determine the mechanical load limits (mechanostat) that influence tissue formation and maintenance.
References


[9] Thambyah, A. ‘A hypothesis matrix for studying biomechanical factors associated with the initiation and progression of posttraumatic osteoarthritis.’ Medical Hypotheses 64 (6), 1157-61, 2005