Patterns of Cartilage Deterioration in Human Femoral Condyles: Implications for Mechanobiological Regulation

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Introduction: The deterioration of articular cartilage with aging and osteoarthritis (OA) occurs in distinct spatial patterns consistent with regulation by mechanical loading1-2. However, the way in which in vivo loading may influence the progression of cartilage deterioration is difficult to assess clinically due to the limited resolution of non-destructive cartilage analysis methods and the need for follow-up. An alternative approach is to elucidate the “sequential signatures,” imparted by a lifetime of loading, via detailed analysis of cadaveric samples. We hypothesized that high-resolution mapping of proteoglycan depletion and tissue erosion would reveal spatially-varying patterns indicative of mechanically-induced cartilage deterioration. The objectives of this study were to (1) delineate for cadaveric human femoral condyles the profiles of surface erosion and proteoglycan depletion using microCT, and (2) determine the depth-dependent correlation between proteoglycan content and cartilage thickness in normal to mildly eroded knees.

Methods: Medial (MFC) and lateral (LFC) femoral condyles were obtained from 17 cadaveric adult human knees obtained from tissue banks. Sagittal osteochondral samples (~5mm wide) were cut from the central region of each MFC and LFC. Samples were categorized macroscopically based on regions of erosion (healthy, anterior, posterior, widespread). mCT Scanning. Samples were scanned with air contrast in a sealed container at (35 μm)3 resolution (Skyscan 1076), and then again after equilibration with 20% Hexabrix contrast agent (Hex). Erosion and Hexabrix Profiles. Sagittal slices through the center of each MFC slab were exported into MATLAB for further processing. Cartilage and bone contours were segmented from images by Gaussian fits of the image histogram. Bone contours were aligned by rigid transformation, and an average contour was calculated for each condyle. Cartilage thickness was normalized to that of the average contour based on non-eroded regions (Fig. 1). Relative fixed charge density (FCD) was expressed in terms of % Hex bath concentration and normalized to that of deep zone control cartilage. All measurements were determined at specific A-P angles defined from the averaged bone contour. Statistical Analyses. The relationship between thickness (erosion) and FCD (depletion) was assessed in the subset of samples displaying healthy or mildly-eroded tissue (n=4 each for MFC and LFC) by linear regressions to various FCD depths.

Results: Cartilage thickness was generally higher in the LFC than MFC (2.32±0.21 mm vs. 1.56±0.34 mm, p=0.001). For extensively eroded samples, deterioration was more severe in the MFC (83±14% erosion) than the LFC (41±5% erosion).

Uptake of Hex in normal samples was depth-dependent (Fig.1A, B, i). Joints with anterior or posterior fibrillations showed local increases in [Hex] in corresponding regions (Fig.1B,iii). Areas of visible erosion had corresponding increased average [Hex] in the cartilage (Fig.1C,ii). Surface regions of cartilage up to 300 μm deep in and surrounding the erosion area showed elevated [Hex] (lower FCD), while deep regions of cartilage were unaffected (Fig.1C,iii,iv).

In mildly degenerate joints, normalized cartilage thicknesses showed a weak correlation with [Hex] (MFC, r²=0.33; LFC, r²=0.30, Fig.2A,B). MFC [Hex] in the superficial regions of cartilage were more closely correlated to normalized thickness than was [Hex] averaged over the full thickness of cartilage (Fig.2A,C). Superficial regions (Fig.2C-H) exhibited two clusters of points corresponding to healthy (thick, high FCD) tissue and mildly degenerate (thinner, lower FCD) tissue. The depth-varying distribution of FCD in cartilage was evident in lower [Hex] values of the deep regions (Fig.2J,K), which had low correlation with cartilage erosion.

Discussion: This study provides a novel quantitative method of mapping two metrics of cartilage degeneration, surface erosion and FCD, at specific sites in the joint. The data delineate the extent to which loss of proteoglycan precedes macroscopic erosion; loss of FCD is evident primarily within the superficial regions of affected and adjacent tissue. High-resolution mapping of FCD with depth and site may be useful as a descriptor or predictor of the health and degenerative state of the knee.

References: 1 Arokoski+, SMSS, ’00. 2 Guilak+ CORR,’04. Acknowledgements: NSF, HHMI, NIH.