学位論文内容の要旨
（Summary of Dissertation）

博士の専攻分野の名称　　博士（医　学）　　氏 名　Liang Dawei
（Degree conferred: Doctor of Philosophy）　　（Name　Liang Dawei）

学 位 論 文 題 名
（Dissertation Title）

Quantification of cartilage degeneration by surface curvature using 3D scanning in a rabbit model

(3D スキャン技術を応用した表面曲率変化による ウサギ軟骨変性の定量化の試み)

【Background and Objectives】Osteoarthritis (OA) is the most common cause of disability in the elderly. Accurate analysis to quantify cartilage morphology is critical for evaluating degenerative conditions in osteoarthritis (OA). Conventionally, histology and India ink staining are the main tools to assess the health of articular cartilage semi-quantitatively in animal models. However, both of them cannot provide three-dimensional (3D) analysis. Magnetic resonance imaging (MRI) and computed tomography (CT) have provided 3D imaging to assess cartilage surface roughness, but due to the partial volume artifact, it is difficult to extract cartilage profiles perfectly. Arthroscopic methods rely on direct visual inspection without invading the joint surface, but they are subjective evaluations by scoring systems and do not provide stereoscopic information to the surgeon.

3D optical scanning technology has evolved over the last several years and can capture millions of points per second to create point cloud data. 3D scanning does not have a partial volume artifact, because the surface evaluation does not involve the separation of the cartilage layer. Surface curvature analysis quantitatively evaluates how uneven a surface is and is sensitive to abrupt variations in elevation. Therefore, applying curvature analysis to 3D optical scanning data of joint surfaces may enable objective and quantitative evaluation of degenerated cartilage.

Our purpose was to validate a 3D method for evaluating spatiotemporal alterations in degenerative cartilage in a rabbit OA model by analyzing their curvatures at various stages of progression.

【Materials and Methods】Twelve male Japanese white rabbits were divided into 4 groups: 4w control, 4w OA, 8w control, and 8w OA. Anterior cruciate ligament transection (ACLT) was performed on the left knees, and right knees were used as controls. The distal femurs were collected at 4 and 8 weeks postoperatively. 3D scanning, India ink staining, and histological assessments were performed in all groups. In 3D data, the surfaces of the condyles were divided into 8 areas. The standard deviations (SD) of mean curvatures from all vertices of condylar surfaces and subareas were calculated by MeshLab software. The sensitivity test of 3D scanner was performed on 3 different grades of sandpapers. One cartilage sample was scanned for 3 times to test the precision of 3D method. The data are presented as means with 95% confidence intervals (CIs). Statistical significance was determined by one-way ANOVA with Tukey's post-test. Correlations were determined by Spearman's rank correlation coefficient. P values smaller than 0.05 were considered statistically significant.

【Results】The sensitivity test showed that the 3D scanner has no difficulty to distinguish different grades of roughness using sandpapers. The precision test showed a good reproducibility for quantifying cartilage surface roughness. Regarding the site of OA change, 3D evaluation was consistent with India ink staining. The SD of mean curvature correlated strongly with the India ink Osteoarthritis Research Society International (OARSI) score ($r_s = 0.9537$, $P < 0.0001$). In curvature histograms, the curvature distribution in OA groups was more scattered than in control groups, and the amount of extreme curvature values in 4- and 8-week groups was also more than in control groups. Of the 8 areas, significant OA progression in the posterolateral part of the lateral condyle (L-PL) was observed at 4 weeks after surgery. Over time, OA degeneration started to be observed in the anterolateral parts of medial condyles (M-AL), the posteromedial parts of medial condyles (M-PM), and the posterolateral parts of medial condyles (M-PL). The histology was consistent with the 3D evaluation in terms of representative section. Correlation analysis showed that the OARSI score correlated with the SD of mean curvature, but not strongly ($r_s = 0.7930$, $P < 0.0001$).

【Discussion】Our results showed that the variation in mean curvature of the surface was proportional to the severity of cartilage degeneration assessed using other analytical techniques. In addition, the posterolateral part of the lateral condyle is the region that undergoes degenerative changes first in the rabbit ACLT model. These results indicate that 3D scanning and curvature analysis can be reproducible imaging modalities for quantifying OA severity and clarifying pathological mechanisms.

Comparing the conventional evaluation methods with curvature analysis, our results were highly consistent with those of India ink, which verified the accuracy of the 3D technique, whereas they were moderately correlated with the histology OARSI score. The OARSI score is composed of four components: staining, structure, chondrocyte density, and clusters, while 3D scanning is a method of quantifying macrostructural alterations on the joint surface. This difference is possibly why the SD of mean curvature was not strongly correlated with the histology OARSI score.

The principle is that ink particles are trapped in fissures on the cartilage. Early OA stage cartilage sometimes undergoes thickening before tissue peeling, which can be detected by curvature analysis instead of India ink staining. In addition, the 3D curvature visualization is rendered in a vector graphics format. Obtained 3D images can be magnified to show tiny surface texture changes without distortion.

Our results of subarea analysis showed that OA changes first occurred on the lateral femoral condyle in the early stages and subsequently bilaterally. To our knowledge, the present study is the first to focus on the lesions of rabbits in early OA by 3D scanning.

【Conclusion】This study demonstrated that 3D scanning with curvature analysis can quantify the severity of cartilage degeneration objectively during the progression of OA. Furthermore, the L-PL was found to be the initial area where OA degeneration occurred in the rabbit ACLT mode