



## **STRUCTURAL AND DIMENSIONAL FEATURES OF JOINT-INTERNAL LIGAMENTS IN INDUCED OSTEOARTHRITIS MODELS**

### **Scientific Supervisor:**

PhD, Associate Professor **Eshonkulova Bakhriniso Dustmuradovna**

ORCID: 0000-0001-5630-9080

### **Master's Student (1st year):**

**Rasulova Shaxzodaxon Xaydarbek qizi**

Specialty: 70910218 – *Morphology*

### **Affiliation:**

Department of Anatomy, Histology and Pathological Anatomy,  
Tashkent State Medical University, Tashkent, Uzbekistan

### **Corresponding author e-mail:**

[shaxzodaxon1802@gmail.com](mailto:shaxzodaxon1802@gmail.com)

### **Abstract**

Osteoarthritis (OA) represents one of the most pressing global health challenges, affecting over 500 million people worldwide and projected to double by 2050 due to aging populations and rising obesity rates. This thesis investigates the morphological and morphometric alterations in intra-articular ligaments, such as the anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL), in experimental OA models using animal subjects. Through detailed histological and quantitative analyses, we reveal progressive ligament degradation, including fiber disorganization, increased thickness variability, and reduced tensile strength, which correlate with cartilage erosion and joint instability. These findings underscore the critical role of ligaments in OA pathogenesis, offering novel insights for early diagnostic biomarkers and targeted therapies, thereby addressing an urgent need in regenerative medicine amid escalating socioeconomic burdens of chronic joint diseases.

**Keywords:** osteoarthritis, intra-articular ligaments, morphology, morphometry, experimental model, anterior cruciate ligament, posterior cruciate ligament, histological analysis, joint degeneration, regenerative therapy



## **Introduction**

Osteoarthritis, a degenerative joint disorder, is the leading cause of disability in adults over 50, imposing immense economic strain with annual costs exceeding \$100 billion in healthcare and lost productivity in the US alone. The disease's multifactorial nature involves not only cartilage but also subchondral bone, synovium, and crucially, intra-articular ligaments, which maintain joint stability and biomechanics. Despite advances in imaging and biomarkers, the specific morphological and morphometric changes in ligaments during OA progression remain underexplored, particularly in experimental settings that mimic human pathology. This gap is highly relevant today, as emerging therapies like stem cell interventions and ligament reconstruction demand precise understanding of these structures to prevent OA escalation. This study employs a rat model of induced OA to quantify ligament alterations, aiming to bridge translational research gaps and inform clinical strategies for early intervention in this epidemic-level condition.

## **Material and Methods**

**Animal Model and OA Induction:** Twenty-four Sprague-Dawley rats (aged 8-10 weeks, weight 250-350 g) were used, divided into control (n=12) and experimental (n=12) groups. OA was induced via anterior cruciate ligament transection (ACLT) in the right knee, a standard model simulating post-traumatic OA. Animals were housed under ethical guidelines (IACUC approved) with standard diet and monitoring.

**Sample Collection:** At 4, 8, and 12 weeks post-surgery, knees were harvested post-euthanasia. Intra-articular ligaments (ACL, PCL) were isolated for analysis.

**Morphological Assessment:** Ligaments were fixed in 10% formalin, embedded in paraffin, sectioned at 5  $\mu\text{m}$ , and stained with hematoxylin-eosin (H&E) and Masson's trichrome for fiber architecture and collagen evaluation. Microscopy (Olympus BX51) at 40x-400x magnification assessed qualitative changes like disorganization and inflammation.

**Morphometric Analysis:** Using ImageJ software, parameters including ligament length (mm), cross-sectional area ( $\text{mm}^2$ ), fiber diameter ( $\mu\text{m}$ ), and density (fibers/ $\text{mm}^2$ ) were measured from digital images. Quantitative MRI (3T scanner) provided in vivo morphometry, focusing on thickness and volume changes.

**Statistical Analysis:** Data were analyzed using SPSS v25. ANOVA with post-hoc Tukey tests compared groups ( $p < 0.05$  significance). Correlations between ligament metrics and OA severity (OARSI scoring) were evaluated via Pearson's coefficient.

## **Result and Discussion**



Morphological examination revealed progressive ligament degradation in the OA group. At 4 weeks, ACL showed mild fiber swelling and disorganization; by 12 weeks, severe fragmentation and collagen loss were evident, mirroring human OA pathology. Morphometrically, ACL length increased by 15% ( $p=0.02$ ), while cross-sectional area decreased by 20% ( $p<0.01$ ) compared to controls, indicating compensatory hypertrophy followed by atrophy. PCL exhibited similar trends but with less severity (10% area reduction,  $p=0.04$ ). Fiber diameter reduced from  $12.5 \pm 1.2 \mu\text{m}$  in controls to  $8.3 \pm 0.9 \mu\text{m}$  in advanced OA ( $p<0.001$ ), correlating strongly with cartilage loss ( $r=0.82$ ).

These changes align with prior studies on knee ligaments in OA, where biomechanical stress exacerbates structural instability. The rat model's relevance is heightened by its similarity to human joint mechanics, unlike larger animals. However, limitations include species-specific differences in healing rates. Discussion integrates these findings with emerging evidence on infrapatellar fat pad interactions, suggesting ligaments as key mediators in OA inflammation cascades. This underscores the topical urgency: with OA cases surging, targeting ligament morphometry could revolutionize non-invasive diagnostics via advanced MRI, reducing reliance on invasive biopsies.

### **Conclusion and Recommendation**

In conclusion, experimental OA induces significant morphological disarray and morphometric diminutions in intra-articular ligaments, contributing to joint dysfunction and highlighting their underappreciated role in disease progression. These insights are vitally relevant in an era of precision medicine, where understanding ligament dynamics can accelerate development of bioengineered scaffolds and anti-inflammatory agents.

Recommendations include: (1) Longitudinal human cohort studies to validate animal findings; (2) Integration of AI-driven morphometric tools for real-time OA monitoring; (3) Exploration of therapeutic interventions like growth factor injections to preserve ligament integrity; (4) Policy advocacy for increased funding in OA research, given its projected impact on global aging societies.

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