METHODOLOGICAL FRAMEWORK FOR THE MORPHOLOGICAL AND MORPHOMETRIC ASSESSMENT OF THE JOINT CAPSULE IN EXPERIMENTAL OSTEOARTHRITIS

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Relevance

Osteoarthritis (OA) affected 595 million people in 2020, 7.6 % of the world population, and case numbers have risen by 132.2 % since 1990 (GBD 2021 Osteoarthritis Collaborators, 2023). The disease is no longer regarded as cartilage loss alone: subchondral bone, menisci, ligaments, periarticular tissue and the joint capsule are all involved (Sanchez-Lopez et al., 2022). The fibrous layer of the capsule has nevertheless remained in the background, although its remodelling is what narrows the range of motion and drives contracture (Zhang et al., 2021).

A further obstacle is methodological. Krenn synovitis scores differ by an average of 10.6 % between sampling sites within one joint (Mussawy et al., 2022), and for rodent models a standardised scheme appeared only recently, with the recommendation that lining hyperplasia, cellularity and fibrosis be graded separately rather than summed (Obeidat et al., 2024). Published capsule data therefore remain hard to compare: one study measures lining thickness, another relies on a semi-quantitative score, and few assess the cellular, fibrous and vascular components together.

Aim. To develop and justify a standardised approach to the complex morphological and morphometric assessment of the joint capsule in experimental osteoarthritis.

Materials and methods

The framework is built for 45 sexually mature female outbred albino rats (3–3.5 months, 180–220 g) kept under identical conditions. Animals are allocated to three groups: control (n = 5, intra-articular 0.9 % NaCl, 50 μL), untreated experimental OA (n = 20) and OA with treatment (n = 20). OA is induced by a single intra-articular injection of 50 μL of 40 mg/mL monosodium iodoacetate (2 mg MIA) into the right knee under ketamine–xylazine anaesthesia; the dose follows published dose-response data in rats (Pu et al., 2026). The two OA groups are each divided into four subgroups of five animals, examined on days 14, 21, 30 and 45, and the control animals are examined in parallel. Single-sex groups remove sex as a source of variance, which matters because the synovial response after joint injury is sexually dimorphic (Bergman et al., 2023).

Material is fixed in 10 % neutral buffered formalin, decalcified in 10 % EDTA and sectioned sagittally through the middle of the medial compartment, so that the suprapatellar recess and the posterior compartment of the capsule appear on one slide. Sixteen sections per animal — 720 in total — are stained by haematoxylin and eosin, Van Gieson and Weigert methods, by the PAS reaction, and with Alcian blue and toluidine blue. Measurements are made blind in ImageJ (Fiji) on calibrated images: five sections per animal, five fields in each of the two sites, 50 fields per animal. The animal, not the field, serves as the unit of analysis. Statistical processing is performed in IBM SPSS Statistics with non-parametric tests (Mann-Whitney, Kruskal-Wallis with Dunn post-hoc) and Bonferroni correction.

Results and discussion

The approach rests on four decisions, each with a specific justification. The MIA model was chosen because it requires no arthrotomy: the capsule is not opened and its reaction is not confounded by operative trauma, which is difficult to avoid in surgical models (Zaki et al., 2022). The observation points span the staged course of the model — proliferation of spindle-shaped cells and multilayering of the lining are prominent in the first two weeks and then subside, whereas narrowing of the spaces between collagen bundles appears at weeks four to eight (Takahashi et al., 2017) — so that days 14 and 21 capture the proliferative phase and days 30 and 45 the fibrotic remodelling.

Sampling is fixed to two sites that differ in structure and in mechanical role: the suprapatellar recess, with a well-developed synovial layer that stretches most during movement, and the posterior compartment, with a thick load-bearing fibrous layer. Examining both on one section addresses the site dependence of the synovitis score and reflects evidence that the anterior and posterior capsule form a single tissue system distinct from the other joint tissues (Laneuville et al., 2025).

The morphometric programme comprises 21 quantitative parameters distributed across the four components of the capsule — four for the synovial lining, five for the subintimal layer, four for the fibrous layer and eight for the vascular bed — together with the Krenn synovitis scale and a four-point fibrosis scale. The vascular bed carries the largest number of parameters because its response changes in both early inflammation and late fibrosis, and no single measure captures wall thickening, luminal narrowing, venous congestion and perivascular infiltration at once. Treatment effect is expressed as a correction index, $CI = (M(OA) - M(treated)) / (M(OA) - M(control)) \times 100\ \%$, which places parameters measured in different units on one comparable scale: zero means no effect, 100 % a return to the control level.

Conclusion

A design combining a non-surgical model, four observation points from day 14 to day 45, two fixed sampling sites on a single sagittal section, a six-stain panel and 21 quantitative parameters makes it possible to assess the cellular, fibrous and vascular components of the joint capsule together and under identical conditions. The correction index adds a common scale for comparing treatment effects across parameters of different dimensions. Such standardisation is a precondition for comparing capsule morphometry between studies.

References

1. Bergman, R. F., Lammlin, L., Junginger, L., Farrell, E., Goldman, S., Darcy, R., Rasner, C., Obeidat, A. M., Malfait, A.-M., Miller, R. E., & Maerz, T. (2023). Sexual dimorphism of the synovial transcriptome underpins greater PTOA disease severity in male mice following joint injury. Osteoarthritis and Cartilage, 32(2), 140–151.

2. GBD 2021 Osteoarthritis Collaborators. (2023). Global, regional, and national burden of osteoarthritis, 1990–2020 and projections to 2050. The Lancet Rheumatology, 5(9), e508–e522. https://doi.org/10.1016/S2665-9913(23)00163-7

3. Laneuville, O., Stratis, D., Trudel, G., Feibel, R., & Campbell, T. M. (2025). Transcriptomic characterization of posterior capsule, anterior capsule, and femoral condylar tissue highlights tissue-specific microenvironments in knee osteoarthritis. Genes & Diseases, 101530. https://doi.org/10.1016/j.gendis.2025.101530

4. Mussawy, H., Zustin, J., Luebke, A. M., Strahl, A., Krenn, V., Rüther, W., & Rolvien, T. (2022). The histopathological synovitis score is influenced by biopsy

location in patients with knee osteoarthritis. Archives of Orthopaedic and Trauma Surgery, 142(11), 2991–2997. https://doi.org/10.1007/s00402-021-03889-x

5. Obeidat, A. M., Kim, S. Y., Burt, K. G., Hu, B., Li, J., Ishihara, S., Xiao, R., Miller, R. E., Little, C., Malfait, A.-M., & Scanzello, C. R. (2024). A standardized approach to evaluation and reporting of synovial histopathology in two surgically induced murine models of osteoarthritis. Osteoarthritis and Cartilage, 32(10), 1273–1282. https://doi.org/10.1016/j.joca.2024.05.006

6. Pu, W., Liu, Q., Xue, S., Li, S., Nan, N., Liu, Y., & Hao, H. (2026). Time- and dose-related pathological changes in knee osteoarthritis rat model induced by monosodium iodoacetate. Animal Models and Experimental Medicine, 9(1), 21–30. https://doi.org/10.1002/ame2.70037

7. Sanchez-Lopez, E., Coras, R., Torres, A., Lane, N. E., & Guma, M. (2022). Synovial inflammation in osteoarthritis progression. Nature Reviews Rheumatology, 18(5), 258–275.

8. Takahashi, I., Matsuzaki, T., & Hoso, M. (2017). Long-term histopathological developments in knee-joint components in a rat model of osteoarthritis induced by monosodium iodoacetate. Journal of Physical Therapy Science, 29(4), 590–597.

9. Zaki, S., Blaker, C. L., & Little, C. B. (2022). OA foundations — experimental models of osteoarthritis. Osteoarthritis and Cartilage, 30(3), 357–380.

10. Zhang, L., Xing, R., Huang, Z., Ding, L., Zhang, L., Li, M., Li, X., Wang, P., & Mao, J. (2021). Synovial fibrosis involvement in osteoarthritis. Frontiers in Medicine, 8, 684389. https://doi.org/10.3389/fmed.2021.684389