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Beyond Cartilage Loss: A Proposed Tissue-Based Classification Framework for Knee Osteoarthritis

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Abstract

Conventional knee osteoarthritis (KOA) grading is dominated by radiographic structural features, particularly osteophytes and joint-space narrowing. These measures are useful for describing structural disease but do not consistently explain pain. Adult articular cartilage is aneural; nociception arises from innervated tissues, including the synovium, infrapatellar fat pad (IPFP), peripheral meniscus and its attachments, subchondral bone, capsule, and ligaments.

This review proposes a simple tissue-based classification framework that complements conventional radiographic grading by identifying the most advanced clinically relevant abnormality in innervated tissues and the mechanical architecture of the knee. A conceptual tissue-based staging framework for KOA was developed based on current understanding of joint innervation, pain generation, mechanical load transfer, and structural disease progression. The framework prioritizes the most advanced clinically relevant abnormality present within innervated tissues and knee mechanical architecture, while recording articular cartilage damage separately. Five classes are proposed: (i) synovial-IPFP involvement; (ii) meniscal/load-transfer failure; (iii) active subchondral bone disease; (iv) compartmental subchondral structural failure; and (v) whole-joint mechanical failure. Articular cartilage damage is documented independently and does not determine the class. Earlier classes are not prerequisites for later classes; instead, the highest class-defining abnormality present determines the overall classification. This framework shifts emphasis from cartilage loss alone to tissue pathology that may better explain pain and mechanical failure in KOA. It is intended as a hypothesis-generating classification and requires expert consensus, operational imaging definitions, reliability testing, and prospective validation before clinical adoption.

Categories: Pain Management, Rheumatology, Orthopedics
Keywords: bone marrow lesion, infrapatellar fat pad, knee osteoarthritis, knee osteoarthritis classification, meniscus, pain, pain-relevant tissue pathology, subchondral bone, synovitis, tissue based classification

Introduction And Background

The knee functions as a whole-joint organ comprising articular cartilage, synovium, menisci, subchondral bone, ligaments, capsule, periarticular muscles, and local adipose tissues, all of which contribute to joint homeostasis, symptom generation, and disease progression (Figure *1*) [1,2]. Knee osteoarthritis (KOA) is a whole-joint disorder in which these tissues interact and undergo pathological changes over time [1,2].

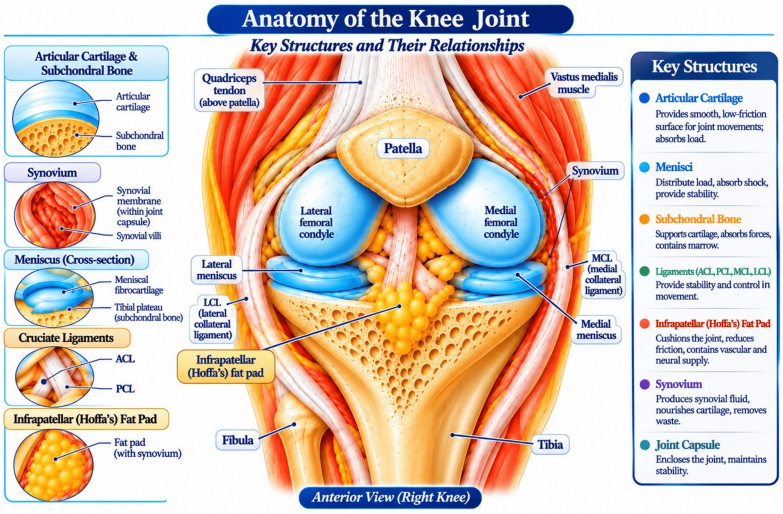


FIGURE 1: Key anatomical structures of the knee joint

Image credit: Figure created using ChatGPT (OpenAI, San Francisco, CA, USA) to generate initial visual concepts; subsequently edited and finalized by the authors using PowerPoint (Microsoft Corporation, Redmond, WA, USA).

ACL: Anterior Cruciate Ligament, PCL: Posterior Cruciate Ligament, MCL: Medial Collateral Ligament, LCL: Lateral Collateral Ligament

Radiographic systems such as Kellgren-Lawrence (KL) grading remain valuable for describing structural severity, but radiographic findings and pain show only an imperfect relationship [3,4]. They do not always match the severity of pain, and patients with similar radiographic findings may experience very different symptoms and disease progression. A major biological reason is that adult articular cartilage is aneural and therefore cannot directly generate nociceptive pain. In contrast, the synovium, infrapatellar fat pad (IPFP), peripheral meniscus and meniscal attachments, subchondral bone, capsule, and ligaments are innervated and may become symptomatic when inflamed, mechanically stressed, or structurally damaged [5-9].

The purpose of this article is not to replace any established radiographic or MRI scoring systems. Rather, we propose a complementary, clinically oriented classification framework based on pain-relevant tissue pathology and loss of mechanical architecture. The central question is which innervated tissue is currently abnormal and how far the joint has progressed from potentially active tissue disease to structural failure. Cartilage damage remains an important marker of structural disease, but it is deliberately recorded in parallel rather than used as the staging anchor.

Review

Methodology

Literature Search Strategy

This article is a conceptual narrative review and hypothesis-generating framework proposal rather than a systematic review or clinical practice guideline. A non-systematic literature search was conducted using PubMed/MEDLINE and Google Scholar, supplemented by manual review of reference lists from relevant publications. The literature search focused on studies published through August 2026 related to KOA pain mechanisms, tissue innervation, synovitis, IPFP pathology, meniscal dysfunction, bone marrow lesions (BMLs), subchondral bone pathology, malalignment, and MRI-based assessment of osteoarthritis. Example search terms included “knee osteoarthritis pain,” “synovitis,” “infrapatellar fat pad,” “meniscal extrusion,” “meniscal root tear,” “bone marrow lesion,” “subchondral bone attrition,” “MRI osteoarthritis,” and “knee alignment.”

Evidence Sources and Framework Development

The classification model was developed through review and integration of evidence from human neuroanatomical studies [5,6], reviews of osteoarthritis pain mechanisms [3,4], synovitis and IPFP pathology [7,10], semiquantitative MRI scoring systems [11,12], longitudinal MRI cohort studies [13-16], and literature addressing meniscal dysfunction and altered load transfer [8,17], BMLs and subchondral bone attrition [9,14,18], and malalignment [19]. Evidence relevant to tissue innervation, symptom association, load transfer, imaging appearance, structural progression, and mechanical failure was identified, reviewed, and

discussed collectively by the author group during framework development. Differences in interpretation or proposed category placement were resolved through iterative discussion and consensus among the authors. No formal certainty-of-evidence grading, risk-of-bias assessment, or quantitative weighting process was performed. Accordingly, the proposed hierarchy reflects the authors' interpretation of selected mechanistic, imaging, and longitudinal evidence rather than a formal certainty-of-evidence assessment. Independent expert consensus and prospective empirical validation will be required to determine whether the proposed ordering is reproducible, clinically meaningful, and applicable across diverse patient populations.

Principles for Evidence Integration

Greater weight was assigned to evidence linking specific tissues to nociceptive innervation, pain generation, altered load transfer, biomechanical stress, or structural progression. Emphasis was placed on mechanistic, imaging, and longitudinal studies because these data provide insight into symptom generation and disease progression.

Nature of the Proposed Framework

The proposed hierarchy should therefore be regarded as a hypothesis-generating, evidence-informed, and clinical practice-informed framework rather than a validated classification. Because this work was not designed as a systematic review, no formal study selection process, risk-of-bias assessment, or quantitative evidence synthesis was performed. A future systematic review, formal Delphi consensus process, reliability testing, and prospective validation studies will be required before fixed imaging thresholds, definitions, or clinical recommendations can be established.

Tissue-based classification framework for KOA

Why a Tissue-Based Framework?

Human neurosensory mapping and anatomical studies demonstrate marked differences in pain sensitivity across knee tissues. Synovium and the IPFP are highly pain sensitive; the peripheral meniscus, capsule, and ligamentous structures contain sensory fibers; and subchondral bone is richly innervated and undergoes neurovascular change in osteoarthritis (Figure *2*) [5-9]. By contrast, adult hyaline articular cartilage is aneural. This does not make cartilage unimportant: cartilage loss alters load transmission and is a major structural feature of OA. It does mean, however, that cartilage loss alone is an incomplete explanation for pain.

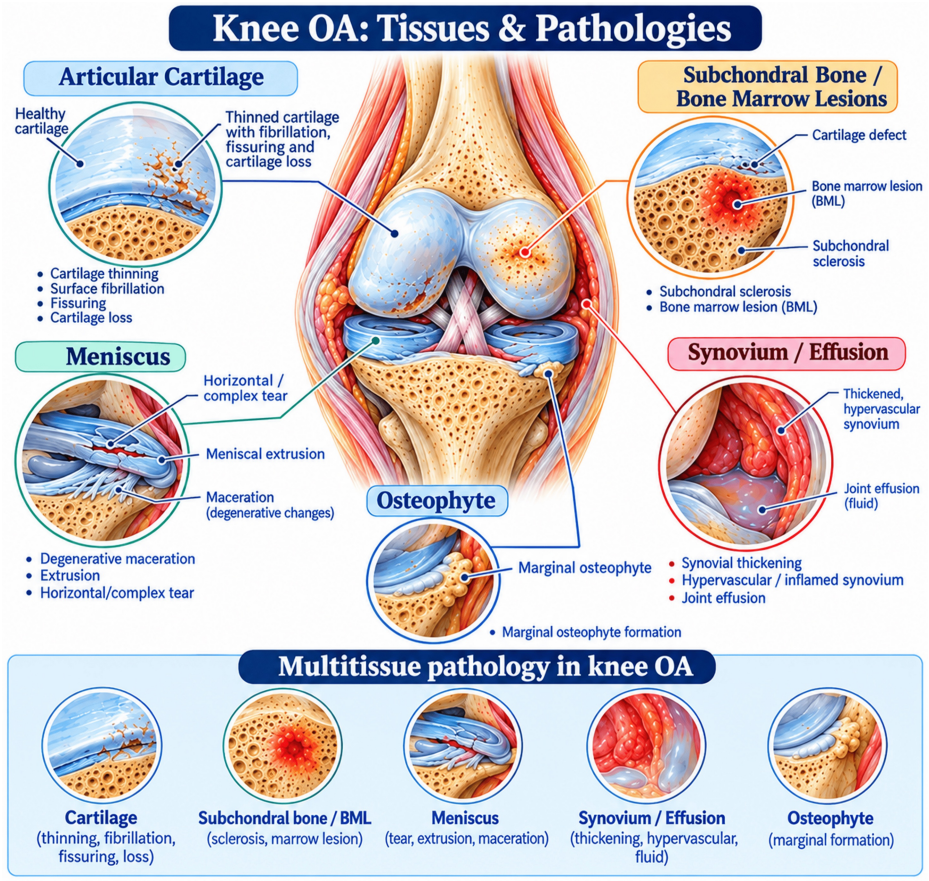


FIGURE 2: Tissue pathologies in knee osteoarthritis

Image credit: Figure created using ChatGPT (OpenAI, San Francisco, CA, USA) to generate initial visual concepts; subsequently edited and finalized by the authors using PowerPoint (Microsoft Corporation, Redmond, WA, USA).

Mechanically evoked pain illustrates this distinction. Pain during standing, walking, or stair climbing may arise when loading stresses a sensitized synovial-IPFP unit, an abnormal peripheral meniscus or root attachment, or diseased subchondral bone. BMLs are associated with knee pain and with subsequent structural deterioration, while meniscal extrusion and root dysfunction alter load distribution across the tibiofemoral joint [13,14,17,18]. Weight-bearing pain should therefore be viewed as a cross-tissue clinical phenotype, not as a cartilage-specific symptom. Table *1* summarizes evidence supporting the biological, nociceptive, or mechanical relevance of individual tissues. It does not validate the placement or ordering of those tissues within the proposed categories. The category assignments represent a provisional conceptual organization that must be evaluated through consensus, reliability testing, construct validation, and longitudinal studies.

Tissue	Nociceptive relevance	Typical pathology	Role in Classification framework
Synovium	Rich sensory innervation; inflammatory sensitization [7,10]	Synovitis, effusion	Class 1
Infrapatellar fat pad	Highly innervated and biologically active [7,20]	Inflammatory signal change, fibrosis, impingement	Class 1
Peripheral meniscus/root	Innervated peripheral zone, horns and attachments [8,17]	Degeneration, tear, root dysfunction, extrusion	Class 2
Subchondral bone	Richly innervated; neurovascular remodeling in OA [9,18]	BML/stress response; later attrition or collapse	Class 3-4
Capsule/ligaments	Nociceptors and mechanoreceptors [5,6]	Stretch, instability, failure	Contributes across all the classes; important in Class 5
Articular cartilage	Aneural in adults [3-5]	Focal or diffuse loss	Parallel structural descriptor; not class-defining
Periosteum/ Osteophytes/ Bone spurs	Highly innervated; Periosteal stretch and osteophyte-related impingement may contribute to pain [9]	Osteophyte formation, periosteal remodeling, local impingement	Parallel structural descriptor; may contribute to pain; does not independently determine the class

TABLE 1: Tissue pathology, nociceptive relevance, and their role in the proposed framework

OA: Osteoarthritis

Proposed five-category tissue-based framework for KOA

The framework is cross-sectional. The highest class-defining abnormality present at assessment determines the class; abnormalities assigned to earlier classes are not required. Thus, a patient may present directly at Class 3 or Class 4. The classes describe increasing tissue and architectural involvement, not an obligatory biological sequence (Table *2* and Figure *3*).

Class	Class-defining tissue level	Key criterion	Principal imaging
1	Synovium-IPFP	Synovitis/effusion or concordant IPFP pathology	MRI; targeted US ± Doppler
2	Meniscal/load-transfer apparatus	Concordant peripheral/horn/root pathology, extrusion, or load-transfer failure	MRI; weight-bearing radiographs for consequences
3	Active subchondral bone	BML/stress-remodeling lesion without osseous surface failure	MRI + baseline weight-bearing radiographs
4	Compartmental subchondral structural failure	Attrition, flattening/depression, focal contour loss, or compartmental collapse	Weight-bearing radiographs + MRI; CT selectively
5	Whole-joint mechanical failure	Global architectural failure with substantial malalignment, subluxation/instability, or major combined/multicompartment failure	Long-leg weight-bearing radiograph + MRI; CT selectively

TABLE 2: Proposed tissue-based classification for knee osteoarthritis

IPFP: Infrapatellar Fat Pad, MRI: Magnetic Resonance Imaging, US: Ultrasound, BML: Bone Marrow Lesion, CT: Computed Tomography, OA: Osteoarthritis

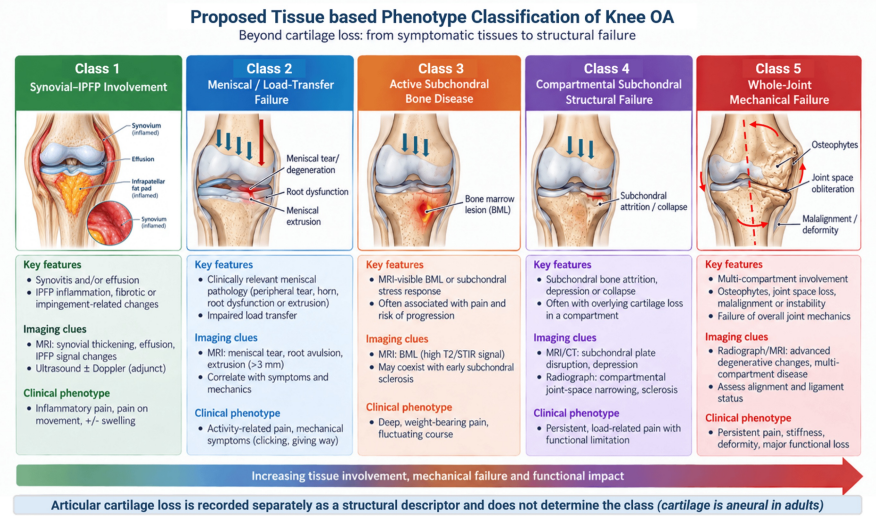


FIGURE 3: Proposed tissue-based phenotype classification of knee osteoarthritis (these classes represent increasing tissue and architectural involvement, but not an obligatory biological sequence)

Image credit: Figure created using Microsoft Copilot (Microsoft Corporation, Redmond, WA, USA) for the generation of the initial visual concept and subsequently edited, refined, and finalized by the authors using PowerPoint (Microsoft Corporation, Redmond, WA, USA).

OA: Osteoarthritis, IPFP: Infrapatellar Fat Pad, BML: Bone Marrow Lesion, MRI: Magnetic Resonance Imaging, CT: Computed Tomography

Structural Category Assignment and Symptom Concordance

Structural category assignment and symptom attribution are separate assessments. A category is assigned using prespecified imaging criteria after alternative explanations for the observed abnormality have been considered. Clinical concordance is then documented independently for every category using pain location, provoking activities, examination findings, and the anatomical distribution of imaging abnormalities. A structurally assigned category should not, by itself, be interpreted as identifying the dominant pain generator.

The evidence summarized below supports the relevance of the included tissues to KOA symptoms, load transfer, or structural deterioration. However, evidence supporting the specific ordering of these tissues into five categories is currently limited. Therefore, the proposed category positions and summary rules should be regarded as hypotheses to be tested rather than validated disease classes.

Class 1 - Synovial-IPFP involvement: Category 1 is defined structurally by prespecified imaging evidence of synovitis and/or effusion, or an IPFP abnormality, including inflammatory, fibrotic, or impingement-related changes. The synovium and IPFP are innervated and biologically active tissues that may contribute to inflammatory or movement-provoked pain [7,10,20]. However, the presence of an imaging abnormality does not, by itself, establish that the tissue is the dominant source of symptoms.

MRI serves as the principal tissue-mapping modality. Ultrasound, with or without Doppler, may be used as a targeted adjunct to assess effusion, synovial hypertrophy, hypervascularity, or dynamic periarticular abnormalities. A nonspecific Hoffa-synovitis signal should be interpreted cautiously because it represents a surrogate imaging feature and not histological confirmation of synovitis.

The relationship between the identified structural abnormality and the patient's current symptoms should be assessed and recorded separately using the anatomical distribution of pain, provoking activities, clinical examination findings, and consideration of competing explanations.

Class 2 - Meniscal/load-transfer failure: Category 2 is defined structurally by prespecified imaging evidence of pathology involving the peripheral meniscus, meniscal horns, or root attachments, including root dysfunction, extrusion, or another meniscal abnormality associated with impaired load transfer.

Because meniscal abnormalities are common in asymptomatic individuals, their presence on imaging alone does not establish clinical relevance or symptom causation. Clinical concordance should therefore be

assessed and recorded separately rather than being embedded within the structural category-assignment rule. This assessment should consider the anatomical distribution of symptoms, clinical examination findings, mechanical symptoms where present, and alternative explanations for the patient's presentation.

Meniscal derangement is associated with ipsicompartmental BMLs and structural progression, supporting its proposed role as a mechanical link between meniscal or soft-tissue abnormalities, altered load transfer, and subchondral involvement [17,21,22]. However, these associations do not establish that every meniscal abnormality progresses to subchondral disease or validate Category 2 as an obligatory intermediate step in a sequential disease pathway.

Class 3 - Active subchondral bone disease: Class 3 is defined by an MRI-visible BML or related subchondral stress/remodeling abnormality without established articular-surface attrition, depression, or osseous collapse. BMLs are dynamic lesions that reflect a mixture of fibrosis, necrosis, microdamage, and abnormal remodeling rather than simple marrow oedema. Their association with pain is probabilistic and context-dependent, but longitudinal data link BMLs to cartilage loss and subsequent bone attrition [13,14,18,23]. Class 3 therefore represents active, mechanically stressed subchondral bone, not irreversible collapse.

Class 4 - Compartmental subchondral structural failure: Class 4 is defined by established local loss of subchondral architecture, including attrition, flattening, depression, focal contour loss, insufficiency-related remodeling, or compartmental collapse. The abnormality may remain predominantly confined to one tibiofemoral or patellofemoral compartment. Secondary malalignment may coexist, but the defining feature is local osseous structural failure rather than failure of the entire knee as a mechanical unit.

Class 5 - Whole-joint mechanical failure: Class 5 is defined by loss of overall joint architecture, characterized by a combination of acquired malalignment, subluxation and/or instability, and multicompartment structural involvement. These abnormalities should collectively indicate whole-joint architectural disruption rather than isolated compartmental structural damage. A fixed angular threshold is deliberately avoided because alignment varies with constitutional anatomy and because a clinically meaningful cutoff requires empirical validation. The key distinction is conceptual: Class 4 denotes compartmental failure, whereas Class 5 denotes failure of the knee as an integrated mechanical system.

Cartilage and conventional OA severity as parallel structural descriptors

Cartilage damage should be documented rather than minimized. Its location, surface area, and depth may be recorded using cartilage-specific components of validated MRI instruments such as WORMS or MOAKS, according to the study purpose [11,12]. KL grading may be recorded separately as a composite radiographic measure of overall OA severity [24]. It should not be described as a direct measure of cartilage location, depth, or extent. These parallel measures address questions different from those addressed by the proposed tissue categories and should be retained alongside, rather than replaced by, the proposed classification.

Complete Tissue Profile

In addition to cartilage assessment, each tissue domain should be evaluated and recorded separately to generate a complete tissue profile. The assessed domains should include the synovium and effusion, IPFP, meniscus and meniscal root attachments, subchondral marrow signal, osseous surface architecture, alignment, stability, ligaments, cartilage, osteophytes, and patellofemoral involvement. Where relevant, the anatomical location, compartment, extent, and severity of each abnormality should also be documented.

The complete tissue profile should constitute the primary structural description of the knee. Any overall or summary category should be considered secondary and must not replace or obscure the individual tissue-domain findings. For clinical research reporting, both the complete domain-level profile and the provisional summary category should therefore be presented. The summary category should not be interpreted as identifying the dominant pain generator or as indicating that abnormalities assigned to lower categories are clinically unimportant.

A standardized reporting format proposed as KTP-10 (Knee Tissue Profile-10) may be used as follows (Table *3*):

Code	Tissue domain	Absent	Present	Anatomical location/compartment	Extent/severity	Clinical concordance	Comments
S	Synovium/effusion	□	□			□ Concordant; □ Uncertain; □ Discordant	
I	Infrapatellar fat pad	□	□			□ Concordant; □ Uncertain; □ Discordant	
M	Meniscus/meniscal root attachments	□	□	□ Medial; □ Lateral		□ Concordant; □ Uncertain; □ Discordant	
B	Subchondral marrow signal abnormality	□	□	□ Medial TF; □ Lateral TF; □ PF		□ Concordant; □ Uncertain; □ Discordant	
O	Osseous surface failure	□	□	□ Medial TF; □ Lateral TF; □ PF		□ Concordant; □ Uncertain; □ Discordant	
A	Alignment abnormality	□	□	□ Varus; □ Valgus; □ Other: _____		□ Concordant; □ Uncertain; □ Discordant	
L	Ligamentous abnormality/instability	□	□			□ Concordant; □ Uncertain; □ Discordant	
C	Cartilage damage	□	□	□ Medial TF; □ Lateral TF; □ PF		□ Concordant; □ Uncertain; □ Discordant	
OF	Osteophytes	□	□	_____		□ Concordant; □ Uncertain; □ Discordant	
PF	Patellofemoral involvement	□	□	□ Patella; □ Trochlea; □ Both		□ Concordant; □ Uncertain; □ Discordant	

TABLE 3: KTP-10 reporting format (or) standardized complete tissue profile checklist

KTP-10: Knee Tissue Profile-10, TF: Tibiofemoral, PF: Patellofemoral

The provisional summary category may be recorded as the highest category-defining structural abnormality present, but only alongside the complete tissue profile. Structural findings within each domain should be interpreted together with separately documented clinical concordance and competing explanations. The summary category should not, by itself, be regarded as a measure of overall disease severity, symptom burden, or treatment eligibility.

From subchondral disease to deformity

Hypothesized Relationship Between Subchondral Disease and Structural Failure

In the Multicenter Osteoarthritis Study (MOST) cohort, subchondral BMLs were associated with prevalent bone attrition and predicted incident attrition within the same subregion [14]. These findings support a possible relationship between marrow abnormalities and subsequent osseous-surface damage but do not validate the proposed Class 3-4 boundary, imply inevitable progression, or indicate that all BMLs progress to attrition.

The proposed Class 4-5 boundary reflects a shift from compartmental osseous-surface damage to whole-joint architectural disruption. Bone attrition, meniscal pathology, cartilage loss, ligamentous factors, and instability may collectively contribute to malalignment; therefore, varus deformity should not be attributed to cartilage loss alone [19]. Both boundaries remain hypotheses requiring explicit imaging criteria and prospective validation.

Imaging and clinical assessment

Clinical Concordance

Class assignment should integrate pain location, provoking activities, examination findings, and the anatomical distribution of imaging abnormalities. Night pain, rest pain, morning stiffness, swelling, locking, giving way, and load-related pain may guide clinical assessment but are not class-specific and should not be used alone to assign a structural class. When symptoms are disproportionate to or discordant with knee

findings, neurological and other referred sources should be considered. Persistent knee pain has, for example, been reported in association with cervical spondylotic myelopathy; however, such case evidence supports diagnostic vigilance rather than validation of the proposed classification framework or a specific treatment recommendation.

Diagnostic blocks or targeted injections may occasionally provide mechanistic information, but treatment response should not be used retrospectively as proof of a unique pain generator.

Imaging Assessment

For full tissue classification, weight-bearing radiographs and MRI are the core investigations. Radiographs define gross osseous architecture, joint-space narrowing, attrition, collapse, and alignment; long-leg weight-bearing imaging is added when the mechanical axis is relevant. MRI provides the whole-joint tissue map required for synovium/IPFP, meniscus, BMLs, subchondral architecture, ligaments, and cartilage. Ultrasound ± Doppler is a selective adjunct when synovitis, effusion, or dynamic IPFP pathology is a key clinical question. CT is reserved for situations in which focal bone architecture, collapse, or surgical anatomy is not adequately defined by radiographs and MRI. The practical imaging pathway and role of each modality within the proposed framework are summarized in Table *4*.

Imaging modality	Main role	Use
Weight-bearing radiographs	Osseous architecture, joint-space narrowing, attrition, collapse, alignment	Core
MRI	Whole-joint tissue map: synovium/IPFP, meniscus, BMLs, bone, ligaments, cartilage	Core for full classification
Ultrasound ± Doppler	Effusion/synovitis and selected dynamic IPFP/periarticular assessment	Selective adjunct
CT	Detailed osseous architecture and complex collapse	Selective adjunct

TABLE 4: Practical imaging pathway

MRI: Magnetic Resonance Imaging, IPFP: Infrapatellar Fat Pad, BML: Bone Marrow Lesion, CT: Computed Tomography

Differential diagnosis, referred pain, and coexisting disease

Synovitis, effusion, subchondral marrow signal abnormalities, meniscal pathology, and structural damage are not specific to KOA. Rheumatoid arthritis, spondyloarthritis, crystal arthritis, infection, acute traumatic injury, subchondral insufficiency fracture, osteonecrosis, neoplasm, and other inflammatory or structural disorders should be considered when the history, clinical examination, or imaging pattern is atypical for primary OA.

Extra-articular and referred sources of knee pain should also be assessed when symptoms are disproportionate to, anatomically discordant with, or inadequately explained by the knee findings. Potential sources include hip pathology, lumbar radiculopathy, peripheral neuropathy, cervical myelopathy, vascular disease, and periarticular soft-tissue disorders. Persistent knee pain attributable to cervical spondylotic myelopathy has been described; however, this evidence is derived from a case report and supports diagnostic vigilance rather than validation of the proposed tissue-based classification. Similarly, hip pathology, including femoral-head avascular necrosis, may present with pain radiating toward the knee, emphasizing the need to examine the hip and consider referred pain when symptoms are discordant with knee findings. Such reports should be regarded as diagnostic examples and not as evidence validating the proposed KOA categories.

Laboratory investigations, including erythrocyte sedimentation rate, C-reactive protein, rheumatoid factor, anti-cyclic citrullinated peptide antibodies, and HLA-B27 testing, as well as synovial-fluid analysis, should be performed when clinically indicated rather than routinely or as mandatory assessments for every patient.

For initial validation studies, active inflammatory arthropathy, infection, primary osteonecrosis, neoplasm, and acute or unhealed subchondral insufficiency fracture should be excluded. Healed subchondral insufficiency fractures with residual structural abnormalities should be documented separately and evaluated within a predefined secondary or stratified cohort. In routine clinical practice, coexisting diseases and alternative sources of symptoms should be recorded separately and should not be incorporated into, or used to determine, the proposed OA category.

Proposed population for initial validation

Initial validation studies should primarily enrol adults with symptomatic primary KOA defined using prespecified clinical and imaging criteria. Individuals with asymptomatic structural OA may be included as a separate comparator group to examine the distinction between structural category assignment and symptom concordance. Isolated patellofemoral OA may be included if the affected compartment and applicable category-defining features are recorded prospectively and analyzed separately.

Post-traumatic OA, prior ligament reconstruction, meniscal repair or resection, osteotomy, cartilage-restoration procedures, fracture fixation, and other joint-preserving operations may alter anatomy and imaging interpretation. Such knees should therefore be excluded from the initial primary validation cohort or enrolled in separately stratified cohorts. Knees with partial or total arthroplasty should be excluded. Active inflammatory arthropathy, infection, crystal arthritis, primary osteonecrosis, neoplasm, and an acute or unhealed subchondral insufficiency fracture should also be excluded from the initial primary OA validation cohort. A healed insufficiency fracture with residual structural change should be documented separately and analyzed in a predefined secondary cohort rather than automatically classified as primary KOA.

Potential applications of the framework

Clinico-Radiological Communication

The framework shifts attention from cartilage loss alone to the dominant tissue abnormality potentially contributing to symptoms, thereby complementing conventional radiographic grading.

Research Stratification

The classification system may facilitate identification of tissue-defined subgroups for studies evaluating anti-inflammatory, meniscal, bone-targeted, biomechanical, regenerative, or pain-focused interventions.

Longitudinal Modeling

The proposed classes generate testable hypotheses regarding transitions between tissue pathology, structural failure, and whole-joint mechanical failure.

Patient Communication

The framework may help explain why patients with similar radiographic findings can experience substantially different symptoms and why severe pain may occur without advanced cartilage loss.

Imaging Interpretation

Encourages whole-joint assessment beyond cartilage loss, integrating synovial, meniscal, subchondral bone, and mechanical abnormalities.

Importantly, these applications are conceptual and hypothesis-generating. The framework should not be used for treatment selection or clinical decision-making until its reliability, validity, and clinical utility have been established in prospective studies.

Limitations and validation priorities

The proposed classes are a conceptual hierarchy, not a proven natural-history sequence. Imaging abnormalities are not synonymous with pain generators; clinical concordance is essential. The relative ordering of synovial/IPFP and meniscal abnormalities may differ among OA phenotypes. No validated threshold currently separates compartmental failure from whole-joint failure; fixed deformity cutoffs should be derived rather than assumed. Central sensitization, nociplastic pain, neuropathic mechanisms, referred pain, muscle dysfunction, and psychosocial contributors are not captured by structural tissue classes. The framework does not yet demonstrate superior prognostic or treatment-selection performance compared with existing classifications.

Validation should proceed through expert Delphi consensus, explicit imaging definitions, inter- and intra-rater reliability testing, cross-sectional construct validation against pain and function, longitudinal assessment of structural progression and arthroplasty risk, and ultimately trials testing whether tissue-informed treatment selection improves outcomes.

Conclusions

This proposed tissue-based framework reframes KOA classification around innervated tissue pathology and

mechanical failure rather than cartilage loss alone. The five classes move from synovial-IPFP involvement, through meniscal load-transfer failure and active subchondral bone disease, to compartmental osseous failure and whole-joint mechanical failure. Cartilage remains an important parallel structural descriptor. The framework is intentionally simple and cross-sectional: the highest class-defining abnormality present determines the class, and earlier classes are not prerequisites. Its clinical value remains to be established through consensus and prospective validation.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Drafting of the manuscript: Krishna Shriram Dhanasekaran, Gautam Das, Sushpa Das, Prashant Jotiram Palkar

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Critical review of the manuscript for important intellectual content: Gautam Das, Samarjit Dey, Sanjay Khanna, Sushpa Das, Smruti Rekha Hota, Shirish Prasad Amatya

Supervision: Gautam Das

Disclosures

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