Structural correlates of pain in joints with osteoarthritis.

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Word Count: 4476

Keywords: osteoarthritis, imaging, radiography, MRI, pain
Abstract

Objective

To describe the insights on the epidemiology of pain-structure association and the ramifications of these studies for clinical trials.

Design

Narrative review summarizing the pertinent literature in this area, summarizing some of the methodologic challenges inherent and proposing some research initiatives to further understanding of this complex science.

Results

The predominant symptom in most patients presenting with OA is pain. Over recent years a number of imaging based studies have narrowed the discord between structural findings on imaging and symptoms. The interpretation of pain in OA is still enigmatic and difficult to deal with both for clinicians and scientists.

Conclusions

We would envisage that over the next few years many of the pressing questions pertaining to research into the structure pain relationship will continue to be addressed. With this, we can expect clinically appropriate therapeutic advance.
Introduction

Osteoarthritis (OA) is a highly prevalent and disabling disease that consequently has a formidable individual and societal impact. Approximately 10-12% of the adult population have symptomatic OA (1,2). The risk of mobility disability (defined as needing help walking or climbing stairs) attributable to knee OA alone is greater than that due to any other medical condition in people aged 65 and over (3,4). Recent estimates suggest that 250 million people worldwide are burdened by the presence of knee OA (5).

This prevalent and disabling disease is heterogeneous and characterized by failure of the synovial joint organ (6). The disease occurs when the dynamic equilibrium between the breakdown and repair of joint tissues becomes unbalanced, often in a situation where the mechanical loads applied exceed those that can be tolerated by the joint tissues (7). OA is a heterogeneous disease that is characterized by progressive cartilage loss, subchondral bone remodelling, osteophyte formation, and synovial inflammation, with resultant joint pain and increasing disability. Whilst the progressive joint failure may cause pain and disability (4) approximately 50% of persons with structural changes consistent with OA are asymptomatic (8).

In epidemiological investigation, OA is typically defined using conventional radiographs, and less frequently self-report (9). The reported prevalence of OA varies according to the method used to define the disease. The characteristic radiographic features used to define and classify OA severity are osteophytes (osteocartilaginous growths), subchondral sclerosis and joint space narrowing. Symptomatic OA in contrast requires the concomitant presence of pain (usually defined as pain on most days of the last month) and radiographic features. It is the presence of symptomatic OA that is important clinically, not simply the radiographic identification of an osteophyte or self-reported OA (where misclassification is even more problematic than the commonly used radiographic OA definition).

The predominant symptom in most patients presenting with OA is pain. Over recent years a number of imaging based studies have narrowed the discord between structural findings on imaging and symptoms (10,11). This narrative review will summarize these findings and provide insights to the epidemiology of the pain-structure association and the ramifications of these studies for clinical trials especially pertaining to structure modification. We present here a narrative review, supported by a literature search up to January 2013 using Medline as a search engine. This is not a formal systematic review and prior reviews were referenced for their content.

The determinants of pain

The determinants of pain in OA are not well understood, but are believed to involve multiple interactive pathways that are best framed in a biopsychosocial framework (posits that biological, psychological and social factors all play a significant role in pain in OA)
Psychosocial factors that can predispose to symptoms include self-efficacy and pain catastrophizing, and the social context of arthritis (social support, pain communication) are all important considerations in understanding the pain experience.

From a biological perspective, neuronal activity in nociceptive pathways is responsible for the generation of signals that ultimately are interpreted as joint pain. During inflammation or tissue (joint) injury, mediators are released into the joint that sensitize primary afferent nerves such that normally innocuous joint movements (such as increased physical activity, walking on high heeled shoes) may elicit a painful response. This is the neurophysiological basis of allostynia, i.e., the sensation of pain in response to a normally non-painful stimulus such as walking (14). Over time, this increased neuronal activity from the periphery (peripheral sensitization) can contribute to plasticity changes in the central nervous system (central sensitization) (15). In this instance, second order neurons in the spinal cord become more responsive to peripheral input, such as responding to lower-threshold stimuli that would not normally cause the neurons to fire, or an expansion of the receptive field of the dorsal horn neurons such that the transmission of nociceptive information to the somatosensory cortex is enhanced. Central sensitization can intensify the sensation of pain and even lead to pain responses from regions of the body remote from the inflamed joint, i.e., referred pain (14).

Another important component of the biological contribution to pain comes from the multitude of tissues within the joint that contain nociceptive fibers and these are the likely sources of pain in osteoarthritis. The subchondral bone, periosteum, periarticular ligaments, periarticular muscle and joint capsule including its inner synovial lining are all richly innervated and are the likely source of nociception in OA. However, subjects with the same degree of structural damage experience widely different levels of pain, a phenomenon that is poorly understood (16).

Research into pain is challenging as a result of the multiple risk factors responsible for pain occurrence and pain severity as well as pain being a subjective phenomenon. In population studies there is a significant discordance between radiographically diagnosed OA and knee pain (8). Whilst radiographic evidence of joint damage predisposes to joint pain, the underlying pathologies leading to pain cannot be readily discerned from radiography alone and may require consideration of other factors including function and load (17). Novel study designs are one approach to deal with the so-called structure-symptom discordance. For example, when inter-individual differences influencing the pain experience (e.g., genetics, psychosocial factors, etc.) are adequately accounted for, a strong relationship between radiographic OA and knee pain has been noted (18). In addition, it is important to consider that structural pathology is associated with somatosensory deficits in OA, since the extent of sensory loss directly correlated with the radiographic severity of knee OA, although causality has not been discerned (19). One study applying direct unanesthetized examination of articular tissues in the human knee joint has provided some insight into particular structures that do and do not elicit pain when probed (20). In lieu of such direct examination, utilizing
other imaging modalities such as magnetic resonance imaging (MRI), numerous structural alterations evident on MRI such as subchondral bone marrow lesions (21), subarticular bone attrition (22), synovitis and effusion (23;24) have been related to knee pain. Furthermore, changes in BMLs and synovitis on MRI are associated with fluctuations in knee pain in patients with knee OA (25). These findings were systematically reviewed within the last 2 years (26). Twenty-one studies examined the concurrent relation of MRI findings in OA to symptoms (26). Of these, just over half (13 studies) demonstrated a statistically significant association, defined as P <0.05, indicating that studies to date have found inconsistent associations of structural features to symptoms. Nonetheless, in general, large bone marrow lesions were strongly associated with knee pain, followed by synovitis and effusion, and cartilage volume/ thickness. There was no consistent relation of meniscal tears to the presence of pain. Interpretation of these relationships must be made cautiously as it is not clear as to whether all of these associations are truly causal, or rather are markers of the severity of other structural pathology that may be contributing to the pain experience.

### Table 1. OA structure pain correlation studies

<table>
<thead>
<tr>
<th>Structural feature</th>
<th>Number of supportive studies (references)</th>
<th>Supportive of association</th>
<th>Negative or neutral findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow lesions</td>
<td>5 (22;27-30)</td>
<td></td>
<td>2 (31;32)</td>
</tr>
<tr>
<td>Synovitis</td>
<td>3 (22;23;33)</td>
<td></td>
<td>2 (34;35)</td>
</tr>
<tr>
<td>Effusion</td>
<td>3 (23;27;32)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cartilage</td>
<td>3 (29;31;36)</td>
<td></td>
<td>1 (32)</td>
</tr>
<tr>
<td>Meniscus</td>
<td>1 (22)</td>
<td></td>
<td>4 (31;32;37;38)</td>
</tr>
<tr>
<td>Bone attrition</td>
<td>1 (22)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteophytes</td>
<td>1 (32)</td>
<td></td>
<td>1 (22)</td>
</tr>
<tr>
<td>Peri-articular lesions</td>
<td>1 (39)</td>
<td></td>
<td>1 (32)</td>
</tr>
</tbody>
</table>

The different tissues within the joint and their respective contribution to symptoms are discussed further below.

**Hyaline articular cartilage**

Articular cartilage is both aneural and avascular. As such, cartilage is incapable of directly generating pain, inflammation, stiffness, or any of the symptoms that patients with OA typically describe, (40) at least early on in the disease course prior to potential neurovascular invasion that may occur in late or end-stage disease (41). During cartilage degradation, substances are released that are capable of inducing inflammation in the joint. Some studies have suggested a relation between cartilage morphometry and lesions and the symptoms of OA (42). It is important to note that this disease of the whole joint concurrently affects other tissues that do contain nociceptors. The studies that have demonstrated a relation of cartilage damage to pain have traditionally investigated the role of cartilage in predisposing to symptoms in isolation from other tissues and as such cannot provide insight into the independent contribution of cartilage pathology to pain. A recent study suggested that areas of denuded cartilage are related to symptoms (43). Again, the
likely mechanism for symptom genesis is through secondary mechanisms such as: 1) exposing the underlying subchondral bone and the inherent symptom genesis (such as exposure of nociceptors) from this structural alteration; (2) vascular congestion of subchondral bone leading to increased intraosseous pressure; (3) synovitis secondary to articular cartilage damage with activation of synovial membrane nociceptors. That is, knees exhibiting denuded areas of cartilage are more likely to have concomitant potentially painful tissue pathology such as synovitis/effusion and BMLs.

Subchondral bone

Periarticular bone changes associated with OA can be segregated into distinct patterns based on the anatomic location and pathogenic mechanisms. These alterations include progressive increase in subchondral plate thickness, alterations in the architecture of subchondral trabecular bone, formation of new bone at the joint margins (osteophytes), development of subchondral bone cysts and advancement of the tidemark associated with vascular invasion of the calcified cartilage.

The osseous changes with the most supportive evidence for a role in symptom genesis are the so-called “bone marrow lesions” (Figure 2). These biomechanically induced lesions in the bone marrow reflecting the histologic changes of fibrosis, trabecular microfractures and other manifestations of bone remodelling play an integral if not pivotal role in the symptoms that emanate from knee OA and its structural progression (28;44). More recently their relation to pain severity (45) and incident pain (46) was also demonstrated. There is conflicting data, albeit from smaller studies with different methods, suggesting no relation of bone marrow lesions to pain (31;32); however the balance of data would support a strong relation of bone marrow lesions to pain (26;47).

Other bone-related causes of pain include periostitis associated with osteophyte formation (48), subchondral microfractures (49), bone attrition (22) and bone angina due to decreased blood flow and elevated intraosseous pressure (50), which are reflected on imaging as bone marrow lesions. Given the strong relationship between bony structural changes, symptoms and structural progression targeting these more selectively would be a major advance in delineating appropriate therapies.

Synovitis, effusion

The synovial reaction in OA includes synovial hyperplasia, fibrosis, thickening of synovial capsule, activated synoviocytes and in some cases lymphocytic infiltrate (B- and T-cells as well as plasma cells) (51). Synovial causes of pain include irritation of sensory nerve endings within the synovium from osteophytes and synovial inflammation that is due, at least in part, to the release of prostaglandins, leukotrienes, proteinases, neuropeptides and cytokines (13;52).

Synovitis and effusion is frequently present in osteoarthritis and correlates with pain and other clinical outcomes (23;27;33). A semi-quantitative measure of synovitis from the
infrapatellar fat pad is associated with pain severity and similarly change in synovitis is associated with change in pain severity (24;26;47) and pain fluctuation (25).

In an important caveat to this analysis a recent study compared non-enhanced proton-density-weighted fat-suppressed (PDFS) sequences with T1-weighted (T1w) fat-suppressed (FS) contrast-enhanced (CE) sequences for semi-quantitative assessment of peripatellar synovitis in OA (53). These data suggested that signal alterations in Hoffa’s fat pad on non-enhanced images do not always represent synovitis as seen on T1w CE images but are a rather non-specific albeit sensitive finding (Figure 3).

**Meniscus**

An intact and functional meniscus is important to the preservation of joint integrity and prevention of further joint damage. In contrast, the meniscus plays a much smaller role in symptom genesis. There is some emerging data that incident tears and those involving the red zone (outer rim) of the meniscus may play a limited role in symptom genesis through angiogenesis and associated sensory nerve growth (54). However in clinical practice an unfortunate consequence of the frequent use of MRI in clinical practice is the frequent detection of meniscal tears (55). Degenerative lesions, described as horizontal cleavages, flap (oblique), or complex tears or meniscal maceration or destruction are associated with older age and are almost universal in persons with osteoarthritis (55). In asymptomatic subjects with a mean age of 65 years, a tear was found in 67% using MRI, whereas in patients with symptomatic knee OA, a meniscal tear was found in 91% (56). In the interests of preserving menisci an important cautionary note: meniscal tears are nearly universal in persons with knee OA and are unlikely to be a cause of increased symptoms (56;57). The penchant to remove menisci is to be avoided, unless there are symptoms of locking or extension blockade, at which point surgical treatment often becomes necessary (58).

**The role of other tissues**

Periarticular muscles influence joint loading, and impairments in muscle function have been observed in people with OA (59). Various studies have investigated the role of muscle strength on joint integrity and some have explored the impact on physical functioning. Sharma et al (60) conducted a three-year longitudinal cohort study investigating factors contributing to poor physical functioning in 257 patients with knee OA. They found that in addition to factors such as age, reduced absolute quadriceps and hamstrings strength and poor proprioceptive acuity increased the likelihood of poor physical functioning as measured by the time to perform five repetitions of rising and sitting in a chair. In addition to their exploration in observational studies there is ample evidence from clinical trials demonstrating that muscle strengthening exercises result in improvements in pain, physical function and quality of life in people with knee OA (61;62).

**Epidemiologic insights- Challenges in studying structure-pain relationships**
This section will address some of the important epidemiologic challenges and the insights that have come from imaging on structure-symptom relationships. To date, little is known about the natural history of structural lesions and the clinical signs and symptoms in the development of OA. This makes studying the independent effect of each specific structural lesion on the occurrence of clinical symptoms, such as pain or functional limitations, challenging.

This is especially the case as MRI technology has been more widely used to identify various pathologic changes in the joint. There is a tendency to include all structural lesions in the same statistical model to obtain “independent” associations of various structural lesions and risk of the outcome, such as pain, and to compare the magnitudes of effect of each structural lesion on the outcome of interest. Without knowing the causal pathway and chronology of occurrence of these lesions, standard approaches of automatically mutually adjusting for all factors can not only lead to biased effect estimates (due to selection bias (63)), but the effect estimates for each of the structural lesions are not directly comparable with one another. (64;65). Thus, without improved understanding of the basic pathogenesis of such lesions and more appropriate statistical methods, even with improvements in the quality of image assessment, such approaches will unfortunately be unable to provide valid insights. For example, if one is interested in assessment of the relation of meniscal extrusion and bone marrow lesions to the risk of frequent knee pain, and assuming meniscal extrusion often occurs before BML, any attempt to compare the magnitude of effect of each structural lesion generated from the same regression model is problematic. First, the effect estimate for BML reflects its total effect on risk of frequent knee pain (i.e., all possible means by which BMLs may exert their effects), but the effect estimate for meniscal extrusion represents its direct effect on pain through pathways other than through BMLs. These two effect estimates are not directly comparable. Second, the direct effect of meniscal extrusion may be biased owing to selection bias (i.e., collider-stratification bias) unless appropriate analysis methods are used (66;67).

At present we do not know how much of the variance in pain is accounted for by structural change and in addition, assessing the causal contributions of the various pathologic features in OA to the pain experience has been, and remains difficult. One reason for this difficulty is that the general approach to studying the pathologic features in OA occurs late in the disease process when numerous pathologic changes are already commonly present. In fact, abnormalities on MRI are common even in knees that are considered to be radiographically “normal” (Kellgren and Lawrence (KL) grade 0). For example, using data from a population-based sample of adults aged 50 and over unselected for knee pain or knee OA, 89% of knees that were KL=0 had at least one type of abnormality, with the three most common findings being osteophytes (74%), cartilage damage (69%), and bone marrow lesions (52%), and MRI-detected abnormalities were equally highly prevalent in both those with (91%) and without (88%) knee pain (68).
Another reason for difficulty in discerning the relation of pathologic OA features to pain is because other potential confounders are often not adequately accounted for in observational studies. As discussed above, a number of factors, including genetics, sensitization, mood, coping, catastrophizing, and the social context, among others, influence the pain experience. Unless such factors are appropriately controlled for, the true magnitude of effect of structural pathology on pain cannot be validly determined. Using a within-person knee-matched approach to control for such between-person differences, radiographic severity has been demonstrated to have a strong dose-response relationship with presence of pain, pain severity, and incident (new onset) pain (18). Using a different within-person knee-matched approach, Zhang et al. demonstrated the relationship of changes in bone marrow lesions and in synovitis/effusion with changes in pain presence and severity (25), demonstrating that fluctuation in pain can be linked to fluctuation in structural pathology. More specifically, changes in BML and synovitis were both associated with knee pain fluctuation and pain severity (25).

**Insights for intervention studies**

Unfortunately at present there is no OA equivalent to measuring high lipid levels, atherosclerosis, hypertension, or high glucose and glucose tolerance, for example, as we have for cardiovascular disease and diabetes, where one can detect and treat the disease precursors pre-emptively before the associated processes lead to end-organ failure. In addition in OA, even if we had such a biomarker, there are no therapies proven to reduce the risk of progression to OA. Instead, the “watchful waiting” of steady decline to end-stage joint disease is a major cause of disablement and loss of quality of life (10).

Recent advances in other prevalent rheumatic diseases has resulted in diseases that were associated with inexorable decline, be treated proactively with associated preservation of structure and function. The advance of biologic therapy in rheumatoid arthritis has seen dramatic shifts in preservation of structure and discussion of a new classification of disease remission. Recent evolution in medical care for osteoporosis has seen a marked reduction in fracture rates with their associated morbidity, with the appropriate institution of anti-resorptive therapy. Unfortunately, we don’t have this proactive stance available in OA, and with current structural definitions and measurement strategies that is unlikely to change. We need to focus on earlier disease where changes may be reversible (Figure 4), if we are not to continue current therapeutic approaches that are largely palliative.

A number of obstacles exist to revising the status of OA care, amongst these is our penchant to utilize radiography to diagnose and study OA (69). This penchant is reinforced by the regulatory hurdles that have led to promulgation of a suboptimal imaging modality in OA studies. Utilizing radiography as a means of defining disease serves to limit itself to a disease window that evaluates only some of the synovial joint features affected by OA, and this evaluation may reflect only the later stages of disease evolution. Other technologies such as
magnetic resonance imaging (MRI) may be more sensitive to early pathologic changes (70). Efforts to modify the course of the disease may not be successful if we focus on late disease when the mechanical derangements overwhelm any reparative potential (71). It is akin to studying and intervening upon an end-stage organ. If non-surgical interventions as a single therapy are to be trialled effectively, selecting those with earlier disease, prior to the development of marked aberrant mechanics, is a preferable solution. In the recent iNOS trial (72) there may have been an effect in KL=2 knees, supporting the perspective about needing to intervene earlier when biomechanical effects may not be as difficult to overcome. The fact that the effects were lost over the longer term suggests that perhaps targeting a single pathway even in milder disease may be insufficient.

The denudation of hyaline cartilage (subchondral bone exposed) is not reversible and by the time persons develop radiographic OA, the overwhelming majority of persons have areas of denuded cartilage (73). MRI studies provide strong evidence that ascertainment of disease on radiographs only provides insights into late stage disease (74;75). Further we need to identify and target the tissue that leads to the cascade of events we describe as joint failure. Preclinical studies with varying levels of efficacy suggest that a wide array of agents including glucosamine sulfate, chondroitin sulfate, sodium hyaluronan, doxycycline, MMP inhibitors, bisphosphonates, calcitonin, diacerein and avocado-soybean unsaponifiables can modify disease progression (76). At this point however there is no pharmacologic agent that has been approved by regulatory authorities for disease modification in OA. It may be a while before a disease-modifying drug is available as current trial strategies remain neglectful of some simple fundamentals and or hampered by outdated regulatory requirements. Our current paradigm of studying persons with end-stage irreversible disease needs to change if we are to identify a stage of the disease where the structural changes may be reversible. There are promising therapies being developed for new OA targets for both symptoms and structure, but we need to pay heed to the lessons we have learned and consider the obstacles to development if they are to be effective (77).

Given the bulk of the evidence supporting an important relation of synovitis/effusion and bone marrow lesions to pain in OA, these appear, at present, to be the most promising targets for symptom modification. Intra-articular glucocorticoid injections, which presumably target inflammation related to synovitis/effusion, have been demonstrated to be superior to placebo in the short-term, but long-term benefits have not been found (78). Nonetheless, because of the important role inflammatory mediators play in sensitization of nociceptors and therefore contribute to the pain experience, appropriate targeting of inflammatory cytokines (e.g., TNF-α, IL-1β) would be theoretically expected to modulate symptoms.

A recent randomized trial of intravenous zoledronic acid vs. placebo demonstrated significant bone marrow lesion area reduction as well as pain reduction at 6 months, suggesting the possibility of symptom modification by targeting of bone marrow lesions
(79). Similar promising findings have also occurred for strontium ranelate and calcitonin. However, since OA is a multifactorial disease, targeting single lesions may not be successful unless other factors are also addressed (e.g., abnormal biomechanics) and/or intervention occurs early in the process when a particular pathway (e.g., inflammation) may be the predominant driving mechanism. The challenge lies in identifying that point in the preclinical disease state for early intervention prior to a multitude of pathologic pathways working in concert leading to end-stage disease.

Further, it is possible that structure modification itself would not necessarily have major or beneficial effects on symptoms. First, positive symptom effects may not be detectable in the time-frame that is typically feasible for the conduct of randomized trials if structure modification may lead to prevention of symptoms only in the long-term. Second, while structural pathology in the joint undoubtedly contributes to pain in OA, as discussed above, other factors also contribute to the pain experience. As an extreme example, approximately 20-30% of patients report poor long-term pain outcomes post-knee replacement, which is presumably a definitive means of structure modification (80). Third, we must bear in mind that nociception plays an important protective role, and therefore complete ablation of nociception should not be a therapeutic goal.

Other imaging modalities may also facilitate insights into the relation of structure to symptoms (81). For example, functional MR imaging has shown early promise in depicting the central alterations consistent with the pain experience.

Research opportunities

Because the experience of pain in OA differs between individuals for the same degree of joint pathology, additional research efforts are needed beyond solely structure modification for a more comprehensive approach to symptom modification in OA. Means of addressing poor coping skills and catastrophizing exist through cognitive behavioural therapy, but are under-recognized issues and such therapies are underutilized. Research focusing on addressing these important aspects of the pain experience would improve pain management in OA.

Insights into specific factors leading to peripheral and central sensitization in OA would provide opportunities for therapeutic targeting to reduce pain and potentially reduce the transition from acute to chronic pain. For example, the relation of joint structural alterations to peripheral sensitization remains unexamined. The transition from acute, activity-related pain to chronic, persistent pain is not well-understood, and is the source of most of the morbidity related to OA. If targeting inflammation, for example, prevents sensitization and transition to chronic persistent pain, it would have tremendous public health impact. It is possible that one of the reasons for the success of TNF-α agents in rheumatoid arthritis is not just the effects on synovial inflammation, but also on sensitization as pain is so markedly improved (82). Because pain sensitization is likely an important component of the pain...
experience in OA, further development and testing of centrally-acting agents that may specifically target pain mechanisms at play in OA is warranted. Management of OA pain ideally needs to shift to a mechanism-based approach for more optimal symptom modification. Structural modification alone is likely to be insufficient in bringing about adequate and comprehensive pain management in this complex disease.

As discussed previously, at present we still do not have a clear understanding of how common are the various structural changes and how they account for the community prevalence of knee pain. Similarly the variance of pain explained both by independent structural changes (e.g., BMLs vs. synovitis vs. effusion) as well as their sum total remain poorly defined.

**Conclusion**

There are many challenges in the assessment of pain etiology as well as methodological hurdles to overcome. Nevertheless, in recent years many insights have been gleaned which has narrowed what was previously a large discord between structural change and the symptom experience. We would envisage that this gap will continue to narrow as we pay greater heed to some of the methodologic challenges highlighted in this review. With greater understanding we can anticipate that this will lead to therapeutic breakthroughs by virtue of targeting therapies towards lesions earlier in the disease cascade and more closely linked to the symptom experience and future structural progression.
Author contributions
All authors were involved in collecting data, reviewing the literature and drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published.

Acknowledgements
Dr Hunter is funded by an Australian Research Council Future Fellowship.

Disclosure
This is a narrative review and the comments and editorial expressed herein represent those of the author/s and do not reflect those of any official scientific role or institution that the author/s may be hold or be affiliated with. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.
Legends to Figures:

**Figure 1.** Biospsychosocial model depicting the relation of structural pathology to the experience of pain

**Figure 2:**

Anteroposterior knee x-ray (1a) shows mild medial tibiofemoral joint space narrowing, tibial and femoral osteophytes (arrowheads) and faint calcifications of both medial and lateral menisci (arrows) in keeping with meniscocalcinosi. Coronal proton density-weighted fat-suppressed MRI (1b) confirms the tibial and femoral ospteophytes (arrowheads) and demonstrates an extensive loss of medial tibial femoral cartilage with denuded bone contrasting with mild medial tibiofemoral joint space narrowing on x-ray. The MRI also discloses large subchondral medial tibial and femoral bone marrow lesions (thick arrows) and moderate size tibial subspinous bone marrow lesion at the ACL insertion (thin arrows). The medial meniscus is partially macerated and extruded. Coronal proton density-weighted MRI (1c) shows a posterior root tear of the medial meniscus (arrow).
Figure 3:

3a

Axial proton density-weighted fat-suppressed MRI (2a) shows homogeneous moderate size knee joint effusion (arrow). The axial T1-weighted contrast-enhanced fat-suppressed MRI (2b) differentiates between the true joint effusion which does not enhance after contrast administration (arrow) and true synovitis which does show enhancement after contrast administration (arrowheads).
Figure 4. The natural history of osteoarthritis and the purported roles of biomarkers during the disease process. Original attributed to V Kraus (originally presented at OARSI Congress 2009: Kraus, VB. 2009. Clinical perspective on the role of biomarkers and the diagnosis and monitoring of OA. Osteoarthritis Cartilage Sept 17 (Suppl 1): S1.) can also be found in (83).

Initiation of Disease Process

? Onset Clinical Symptoms?

- Serologically Detectable

- Clinically Detectable

MOLECULAR

PRERADIOGRAPHIC

RADIOGRAPHIC

JOINT REPLACEMENT

Biomarkers reflecting change in composition of joint tissues

MRI

Ultrasound

Bone Scan

Structural changes in bone, cartilage, and other soft tissues

Joint Failure

Structural changes in bone

Joint Death (rebirth)

End-stage disease
Reference List


Ref Type: Abstract


Ref Type: Abstract


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