

■ ANNOTATION

Understanding pain in osteoarthritis

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The majority of patients with osteoarthritis present to orthopaedic surgeons seeking relief of pain and associated restoration of function. Although our understanding of the physiology of pain has improved greatly over the last 25 years there remain a number of unexplained pain-related observations in patients with osteoarthritis. The understanding of pain in osteoarthritis, its modulation and treatment is central to orthopaedic clinical practice and in this annotation we explore some of the current concepts applicable. We also introduce the concept of the 'phantom joint' as a cause for persistent pain after joint replacement.

The majority of patients who present to orthopaedic surgeons do so with pain and loss of function. Musculoskeletal pain is the primary cause of chronic pain worldwide.¹ Commonly, it is the perception of pain which troubles the patient and is the principle reason for seeking redress.² Despite scientific advances in both its understanding and treatment, the burden of musculoskeletal pain is estimated to have increased between two- and fivefold over the last 40 years.³

During this period, research in pain has led to an improved understanding of nociceptive transmission⁴ and how a stimulus is modified as it passes from peripheral detection, to awareness and to behaviour. It is now apparent that the process is rather more complex than the initial theory proposed by Descartes in the 17th century, in which pain sensation was thought to pass, unadulterated, from stimulus to brain (Fig. 1).⁵

From a research perspective, pain associated with osteoarthritis (OA) presents a number of dilemmas that demand further consideration. First, not all OA causes pain and it is not possible to predict with any degree of precision who will experience pain in the presence of joint degeneration. Secondly, the pain associated with OA has been shown to be reduced using techniques of placebo surgery^{6,7}, implying that not all the benefit seen following operations can be attributed to the technical process alone. Finally, more than one in ten patients who undergo joint replacement continue to experience pain attributed to the affected joint.^{8,9}

In 1952, Kellgren and Lawrence¹⁰ quantified the relationship between radiologically-

identified OA and pain in a cohort of coal miners. Only 24% of those with radiologically demonstrable OA of the knee had pain and 8% of 'normal' knees were painful. This poor correlation between radiologically determined OA and pain has subsequently been highlighted by a number of other authors,¹¹⁻¹⁶ one of whom concluded that the epidemiology of OA and the epidemiology of pain in the knee have something, but not much, in common.¹⁶

The reason for this poor correlation is multifactorial, involving the sensitivity of radiographs to quantify the disease, the heterogeneity of the disease process and an individual's interpretation and behaviour towards a potentially painful stimulus. This variation in response to pain has historically been perceived by clinicians as a nuisance, and difficult to assess and quantify.¹⁷

In this annotation, we aim to consider the pathway of transmission of pain, the role of psychosocial factors in the perception of pain and the mechanism of action of the various methods of control of pain employed in arthritis.

Clinical presentation of osteoarthritis

The localised, unilateral pain experienced in patients with OA affecting a single joint is well recognised. More detailed assessments have revealed that joint-specific localisation may be an oversimplification of the clinical picture, as patients with OA of the hip have quantifiable changes in pain perception and skin sensitivity at distant ipsilateral and contralateral sites.¹⁸ Despite this broader morbidity of disorders of the joint, surgical treatment isolated to the joint appears to remove pain at these secondary pain

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Fig. 1

The model proposed by Descartes of pain transmission⁵ showing a single pathway from stimulus to awareness.

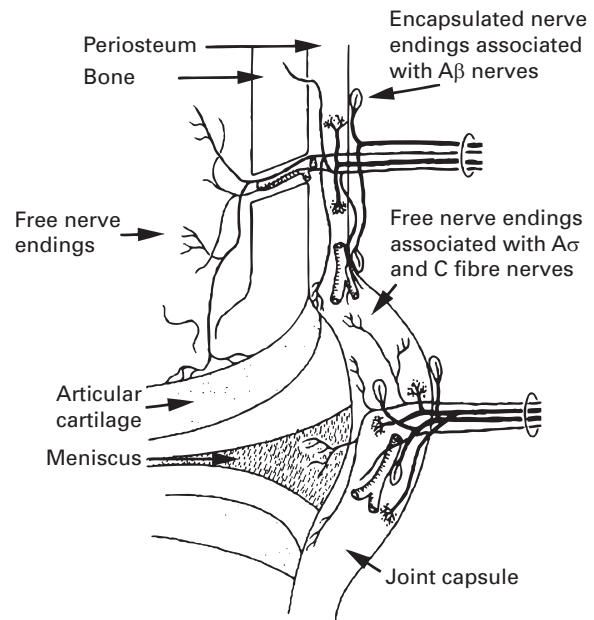


Fig. 2

Diagram showing the neural transmission within the human knee joint. Adapted from Zimmerman.²⁵

sites in addition to the localised joint pain.¹⁸ This suggests that operation has a secondary influence at a central level to produce these distant effects.

Pain mechanisms in the osteoarthritic joint

There are two related but different terms which define pain: nociception and pain. Nociception is a neurophysiological term and describes the activity in a nerve pathway which transmit signals from a potentially noxious stimulus but is not always perceived as painful. The term pain is used to describe the subjective experience that accompanies nociception, but can also arise without a stimulus and includes the cognitive and emotional response.

Detection of peripheral pain

Arthritic pain is the final interpretation of a noxious stimulus within the joint. The innervation of a typical diarthroidal joint offers a number of potential sources for this initial neuronal input. Orthopaedic enquiry into which elements of the synovial joint are responsible for pain dates back to the 19th century.¹⁹

Nociceptors and the spinal cord. A δ fibres and C fibres form the afferent limb of the pain reflex arc and together are responsible for detecting noxious stimuli which damage or threaten the body's integrity, and are therefore termed 'nociceptors'.^{20,21} A δ fibres initiate the sharp pain associated with acute injury while C fibres are responsible for the less well-defined aching pain. The free-ending receptors of this type of nerve may have different sensitivities to chemi-

cal, mechanical and thermal stimuli.²²⁻²⁴ Nociceptor fibres form a plexus which invades the periosteum as well as innervating subchondral bone, joint capsule and fibrocartilagenous structures (Fig. 2).²⁵

Following initiation of nociceptor activity, the first point of integration and modulation of the afferent signal is at the nociceptor synapse of the dorsal horn neurone of the spinal cord. Nociceptor impulses of a sufficient intensity and frequency will produce post-synaptic depolarisation in the spinal neurones.

From the dorsal synapse, either directly or via an interneurone, the nociceptive impulse is transmitted towards the supra-spinal structures via one of four spinal tracts: the contralateral spinothalamic tract, which terminates in the numerous nuclei of the thalamus; the spinoreticular and spinomesencephalic tracts, which transmit to the medulla and brainstem; or the spinohypothalamic tract, which terminates in the hypothalamus (Fig. 3).²⁶

The anatomy of the supraspinal pain matrix. The term 'pain matrix' is used to encompass a number of discoveries and ambiguities in our knowledge of how the supraspinal structures (brain stem, cerebellum, cerebral cortex and cerebral sub-cortical areas) process a nociceptive input. The term matrix offers suitable latitude to account for this constantly developing science and has two inherent foundations. First, that there are numerous regions involved, and secondly that the interpretation of a nociceptive impulse involves neuronal interaction through connections both in parallel and in series.

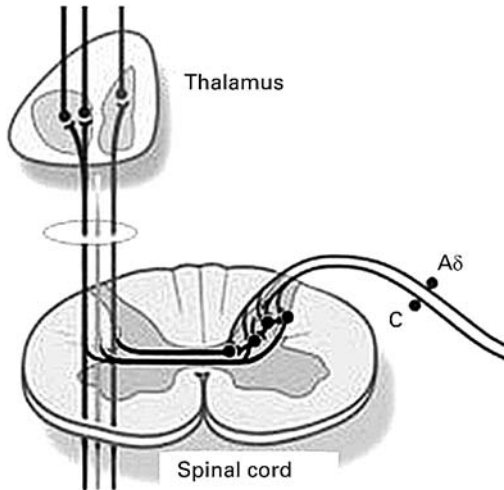


Fig. 3

Typical spinal pathways involved in transmission from the periphery to the brain.

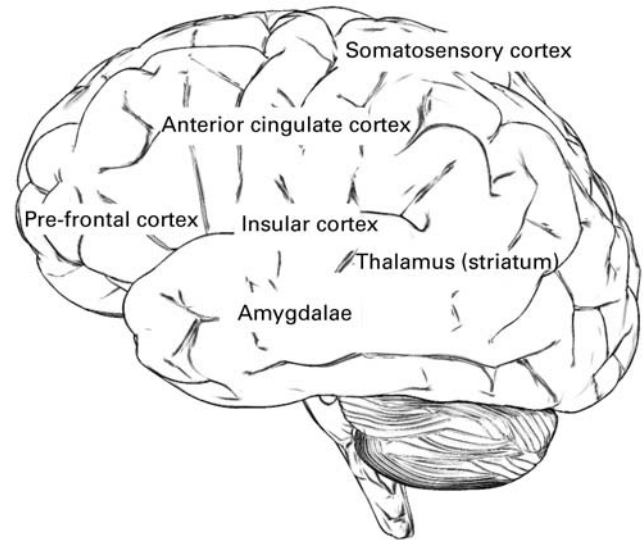


Fig. 4

Brain areas active during perception of pain. Activity in some of these areas is known to correlate to an emotional/affective situation and none is 'pain-specific'.

Imaging modalities such as positive emission tomography and functional MRI have been used to determine the activity of cortical and sub-cortical areas during application of painful stimuli. These techniques detect focal changes in blood flow within the brain following peripheral stimulation and produce a map of brain activity. A detailed account for the use of these techniques is beyond the scope of this annotation but may be found elsewhere.^{27,28}

Correlating the areas of the brain which are active during the perception of pain and those active during unrelated cognitive and physical challenges enables an understanding of the various influences on perception of the pain at the central level. Figure 4 illustrates some of the cortical and sub-cortical areas 'active' during pain awareness.

How these areas connect to each other, the effect of chronic pain on these connections and the absolute activity level within an area are currently under investigation using psychosocial, psychophysical, electrostimulatory and imaging techniques.

The psychosocial influences on arthritic pain

The first recognition of the psychosocial aspects of pain is attributed to the Greek philosopher, Aristotle.²⁹ Since the 1940s, pain in orthopaedic conditions has been acknowledged to be influenced by an individual's personality.^{30,31} Initially, personality 'types' were sought to describe the patient who was felt to magnify the nociceptor input at a cortical level. More recent interest has focused on sub-clinical facets of patient psychology which may predispose to developing chronically painful conditions.

The demonstrable psychological traits associated with variable perception of pain include catastrophising, a situation where the patient has a tendency to focus on pain and negatively evaluate their ability to cope with it; helplessness, the belief that nothing can be done to resolve a problem, characterised by emotional, motivational and cognitive deficits; and self efficacy/coping, a belief that one can achieve specific goals through taking specific action. These, and related psychological states and their effect on pain perception, are illustrated in Figure 5.

These psychological variables have been investigated in patients experiencing painful arthritis^{32,33} and modulation of these traits is a target for therapeutic intervention in early osteoarthritic pain.^{34,35}

Historically, orthopaedic training has not included an appreciation of sub-clinical psychological traits which may influence a patient's response to degenerative changes within a joint. However, it may be suggested that, either implicitly or explicitly, we already perform these assessments as part of our diagnosis and assessment for treatment, potentially exploiting them to gain benefits not directly attributable to the process of surgery itself. Arguably, this process could be further improved.

The assessment of pain

Assessing pain can be as complex or as simple as a clinician wishes. In current practice, clinicians typically make two assessments based on their consultation with a patient estimating the proportion of pain attributable to 'non-organic' factors and how much pain they believe the patient is really experiencing. These assessments, whilst not 'evidence-

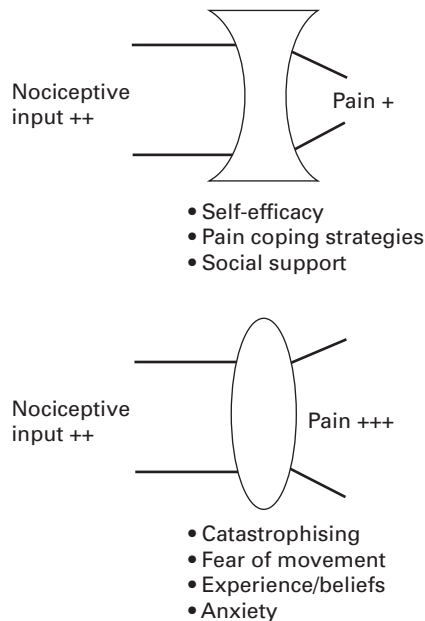


Fig. 5

Psychological states which may act to increase or reduce the perception of osteoarthritic pain.

based' are potentially robust and have historically formed a cornerstone of clinical practice. This clinical pain assessment is subtly different to pain measurement. The measurement of pain distils all contributory components of the pain pathway into the end result, the perceived pain level, whereas assessment of pain attempts to break down these components and quantifies each facet as a separate entity. For the orthopaedic surgeon, the quantification of pain measurement facilitates outcome research and may guide the provision of healthcare. On an individual basis, it provides a tool for diagnosis and treatment, and helps to predict outcome. A truly objective measure for assessing musculoskeletal pain still eludes us.²⁹ Various options are available to the clinician and researcher including numerical scoring systems, and pain-specific, multi-dimensional disability, and arthritis specific questionnaires. During the 1980s, there was a move to standardise the assessment of arthritic symptoms to enable comparison of research output between institutions. Composite scoring assessments of pain, function and disability have been introduced. Osteoarthritis of the hip and knee were the first to have widely-accepted assessment tools, although arthritic symptoms in other joints have now been measured in this way and validated.^{36,37}

The Western Ontario and McMaster University Osteoarthritis Index (WOMAC),³⁸⁻⁴² the Harris hip score⁴³ and the Oxford Scores for the hip,⁴⁴ shoulder,⁴⁵ and knees,⁴⁶ when combined with examination and radiological findings, are thought to be valuable in documenting the longi-

tudinal progress of both treated and untreated individuals with arthritis.

When assessing pain, the extent of enquiry will clearly be context-specific. In many orthopaedic situations such as acute injury, a purely biomedical approach may be sufficient,⁴⁷ although for chronic pain, a more holistic model is preferable. This latter model of pain assessment requires time, continuity of care and a high level of doctor-patient interaction. It may be difficult to achieve with the trend towards team-care, diagnostic treatment centres and non-resident surgical teams. Despite our increasing understanding of the complexity of pain and the importance of addressing the multi-faceted components of an individual's pain paradigm, there is a risk of regression into measurement rather than assessment of pain.

Potential confounders to pain assessment in orthopaedics

The influence of the placebo-effect in surgery has been highlighted in a recent randomised control trial of knee arthroscopy for OA in which a sham procedure was one of the treatment arms.⁶ Placebo-controlled studies illustrate the potential influence on outcomes when a patient has a positive perception of the potential physical and functional benefits to be gained from surgery. Conversely, other groups of patients may benefit socially or financially from a minimal response to operation. Meta-analysis of orthopaedic surgical outcomes has shown that the pursuit of workers' compensation and medicolegal claims significantly influences a patient's predicted response.⁴⁸ There is currently no way of quantifying these influences although there have been attempts to identify patients in whom a significant non-organic component to their pain exists through clinical examination.⁴⁹ It has been highlighted that these behavioural signs are not a test of credibility or 'faking'⁵⁰ but act as a reminder to the clinician to consider non-organic influences on the patients presentation, and their potential response to surgery.

Persistent pain after arthroplasty and the concept of the 'phantom joint'

More than one in ten patients undergoing hip and knee replacement continue to experience pain in the operated joint. Although there is often biomechanical, pathological or iatrogenic reasons for this continuing pain, as discussed by Mandalia et al,⁵¹ there continue to be patients who feel disabling pain despite a technically successful, uncomplicated procedure.

For these patients, there may be two, potentially related, influences driving their persistent pain. First, it has been suggested that the development of chronic pain after joint replacement is influenced by genetic and psychosocial factors. It has been observed more commonly in women than men.⁸ It has also been shown that the expectations of the patient affect the functional outcomes and satisfaction following knee replacement⁵² and the presence of good

social support for patients pre-operatively improves the pain-relieving benefit from joint replacement surgery.⁵³ There is also growing evidence that the central nervous system may set up mechanisms which may continue to drive pain after the removal of nociceptive input, in this instance, the joint. This may be thought of as similar to the well described phenomenon of phantom limb pain after amputation for a chronically painful condition.⁵⁴

In these circumstances, the chronic input from the arthritic joint, potentially influenced by the genetic and psychosocial profile of the patient, sets up 'plastic' mechanisms of sensitisation within the central nervous system. The potential effect of these alterations in pain perception may correlate to, and potentially underly, the pain seen after arthroplasty that has recently been highlighted.⁵⁵ Removal of the joint may not reverse these central pathways and thus the patient continues to experience pain which appears to arise from a joint which no longer exists. Investigation of the role of central sensitisation and the development of a phantom joint is important in our understanding of this challenging cohort of patients.

Orthopaedic surgeons as pain managers

Surgeons have unique skills in the management of pain in OA. However, surgical options are not always the most appropriate as illustrated by the adage, "A good surgeon knows how to operate. A great surgeon knows when to operate".⁵⁶ Avoiding surgery may be appropriate when the level of pain appears disproportionate to the disorder and/or there is evidence of catastrophising, helplessness or failure to cope. Indeed it is reported that between 15% and 30% of patients who undergo total joint replacement are dissatisfied with the outcome.^{57,58} The finding of sub-optimal outcomes following joint replacement has become more widely acknowledged since the application of patient related outcome measures of joint surgery such as the Oxford hip and knee scores.^{44,46} Studies using these measures have shown that patient dissatisfaction post-operatively is related to ongoing pain in the affected joint.⁵⁹ Persistent pain, and hence dissatisfaction, following joint replacement suggests that at least a proportion of patients may have extra-articular components to their pain, which perpetuates it despite a well conducted operation.

These situations draw into question the concept of illness-disease syllogism, on which much of our practice is based. This logic has been attributed to Sydenham, who in the 1700s, described illness in terms of symptoms and signs, which in turn are symbolic of an underlying pathoanatomical disorder, the disease.⁶⁰ This leads to the view that surgically removing disease or tissue will therefore remove illness. Despite the validity of this presumption in certain situations, we still manage a challenging cohort of patients who present with a history of pain but inconsistent pathology. In this small but significant group it is important to remember that we are managing pain behaviour and distress, rather than a pure nociceptor stimulus.⁶¹ Central to

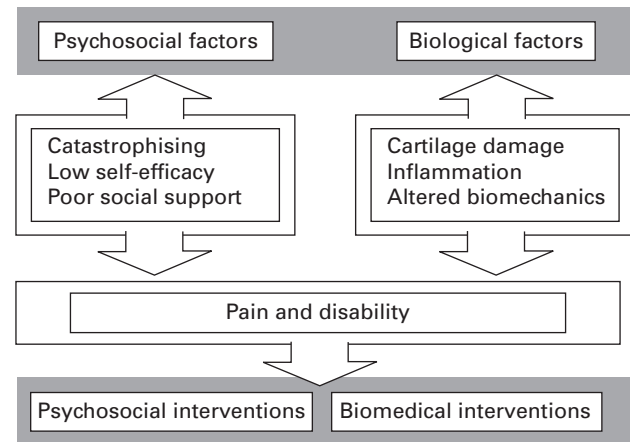


Fig. 6

The treatment options in arthritic disease based on the relative contribution of physical and psychosocial factors (adapted from Keefe et al³⁴). Psychosocial approaches to managing arthritic pain include educational programmes, coping skills, training and cognitive behavioural therapy.

the management of this group of patients is an assessment of their pain, its facets and the sites which may be amenable to intervention. From this assessment a biomedical, psychosocial or combined treatment regime may offer the greatest chance of success, whilst minimising potential morbidity, mortality and disappointment (Fig. 6).

Using psychological interventions in painful OA has been found to decrease distress and reduce pain, at least in the short term.³⁵ Such management may represent a useful adjunct in the non-surgical treatment of patients with pain and associated disability from OA, although the cost-effectiveness and acceptability to both patients and clinicians has yet to be established.

Treatments for osteoarthritic pain and their potential sites of action

Table I⁶²⁻⁷⁶ identifies potential treatment modalities for patients presenting with pain in the knee secondary to OA and their proposed site of action along the pain pathway from nociceptor to awareness.⁶²⁻⁶⁴

Conclusion

It is widely regarded that radiological changes do not correlate with cartilage damage and neither radiographs nor cartilage damage correlate with the pain experienced by patients with OA. The OA model of pain exemplifies its complex nature and demands detailed knowledge of the transmission of a painful stimulus from the periphery to consciousness. The key to understanding the pain experienced by a patient with OA is to remain aware of the potential confounders for which there are no physical cues. The influence of a patient's psychological state, social situation and past experiences will all influence the pain displayed,

Table I. Potential treatments for patients presenting with pain in the knee secondary to osteoarthritis

Treatment	Proposed primary effect	Site of action along pain transmission pathway	Comments/references
Weight loss	Mechanical	Decreased nociceptor stimulation	Weight loss has more effect on disability than pain ⁶⁵
Physiotherapy	Mechanical stabilisation	Decreased nociceptor stimulation	Insufficient data to determine optimum exercise or frequency ⁶²
Glucosamine	Suggested increased articular cartilage synthesis Possible 'anti-inflammatory effect' - not via cyclo-oxygenase system	Decreased nociceptor stimulation	Glucosamine is a glycoprotein derived from marine exoskeletons or produced synthetically. ⁶⁶
Chondroitin sulphate	Suggested increased articular cartilage synthesis	Decreased nociceptor stimulation	Chondroitin is manufactured from natural sources, such as shark and bovine cartilage. ⁶⁶
Transcutaneous electrical nerve stimulation	Acts by 'blocking' nociceptor input to spinal cord	Dorsal horn synapse of spinal cord	A β fibre input 'closes the gate' to painful A δ and C fibre transmission ⁶⁷
Acupuncture	Activation of a gate control system Stimulation of the release of neurochemicals in the central nervous system Placebo	Dorsal horn synapse of spinal cord and supraspinal nuclei	Western view of mechanism. Original view is interaction with Qi energy flow ⁶²
Psychological therapy	Alters supraspinal modulation of incoming nociceptive input	Supraspinal nuclei	34,68,69
Paracetamol	Selective inhibition of the enzyme COX-3 in the brain and spinal cord Paracetamol is converted to N-arachidonoylphenolamine, a compound already known as an endogenous cannabinoid	Spinal cord synapse and supra-spinal nuclei	70,71
Non-steroidal anti-inflammatory drugs	Cyclo-oxygenase-2 inhibitors	Decrease peripheral sensitisation of nociceptors by reducing localised inflammatory mediators	63
Opiates	Agonists/partial agonists of the endogenous opiate system	Spinal cord synapse and supra-spinal nuclei	64
Intra-articular steroid injection	Decrease sensitisation of joint nociceptors by decreasing local inflammatory mediators	Decreased nociceptor stimulation	72,73
Synthetic synovial fluid replacement	Temporary restoration of lubricating and shock-absorbing effects of synovial fluid	Decreased nociceptor stimulation	74 Whether hyaluronan ameliorates or modifies disease progression has not been determined and remains the subject of speculation
Arthroscopic washout/debridement	1) Removal of particulate debris 2) Removal of degenerative enzymes and inflammatory mediators 3) Reduced distension of capsule 4) Placebo	(1, 2 and 3) Decreased nociceptor stimulation 4) supraspinal nuclei	75
Arthroplasty	Removes degenerate joint and associated neural structures	Decreased nociceptor stimulation Decreased central sensitisation	Arthroplasty decreases pain both within the affected joint and at distant site ⁷⁶

and identifying the importance of these factors requires a detailed assessment of the patient and their pain. Sometimes it may be appropriate to utilise validated questionnaires to assist in this process. Using this approach may increase the percentage of people who experience significant improvements in pain and function either by identifying them as potentially benefiting from non-surgical options or by suggesting more involved neo-adjuvant treatment in the form of increased support from the medical team or more formal psychological assessment.

If patient management based on surgical syllogism alone is adopted, then the specialty risks demotion to the role of technician with encompassing patient care being the realm of physicians and non-medical specialists who prescribe surgery as part of their treatment plan.

There is little doubt that some patients 'feel' pain more than others. As we move towards the ability to quantitatively assess an individual's sensitivity to pain there is the potential to predict the pain-relieving effect of surgical intervention, enabling us both to rationalise our treatments and to provide more fully informed consent. In order to understand these patients fully, we need to investigate the validity of the 'phantom joint' concept and its influence on the population whom we treat with ongoing pain after arthroplasty. Ultimately, this may help us reduce the proportion of patients who continue to feel pain after joint replacement for no apparent technical or pathological reasons. Even with the potential development of image-based quantification of pain we shall continue to rely on clinical assessment, acumen and validated assessment tools in order to understand the pain experienced by a patient with OA. An appreciation of the multi-dimensional nature of the perception of pain will enable the surgeon to apply a more robust pre-operative assessment of a patient's suitability for surgery.

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