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Osteoarthritis and Cartilage

Editorial

A special Osteoarthritis and Cartilage issue on imaging in osteoarthritis

Osteoarthritis is a highly prevalent and disabling disease that consequently has a formidable individual and societal impact. At present there are no therapies that have been approved by regulatory authorities to modify the course of the disease. Indeed, the recent failure of a number of phase II and III clinical trials for osteoarthritis structure-modifying drugs has resulted in a considerable decline in the number and size of pharmaceutical company research programs in this area[1]. The reasons for the translational failure of anti-osteoarthritis drugs are likely multifold, but include the poor relationship in individual patients between joint structural pathology (especially joint space narrowing on radiographs) and symptomatic disease, and limited responsiveness of existing approved biomarkers[2]. Instead, we are faced with the current clinical circumstance of "watchful waiting" or steady decline to end-stage joint disease and attendant disablement and loss of quality of life[3]. Further the available symptom-modifying (analgesic) treatments have only moderate long-term effect sizes with the majority of patients dissatisfied with their efficacy[1,4].

This special issue of *Osteoarthritis and Cartilage* focuses on imaging in osteoarthritis. It is entitled "Imaging in Osteoarthritis: The breakthrough decade?" We have been saying this for years, but are we any closer to the pivotal breakthrough? There have been major research advances that have significantly increased our understanding of the molecular pathophysiology of joint destruction and pain in osteoarthritis. 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[1]. Recent disease modification trials[5,6] highlight the fact that we can potentially modify the structural course of OA measured using sophisticated imaging techniques and suggest we are truly on the verge of being able to modify this disease. How has this come about?

A critical first step in modifying disease is the ability to objectively measure response to treatment and natural disease progression. The plethora of imaging research in osteoarthritis over the last 20 years has led to a situation where we can now measure structural change reliably and with greater responsiveness. Time will tell whether regulatory approval follows.

The predominant symptom in most patients presenting with osteoarthritis is pain. Over recent years a number of imaging based studies have narrowed the discord between structural findings on imaging and symptoms[7]. A thoughtful review by Wenham and co-authors examines the role of the commonly used imaging modalities in clinical practice; both in osteoarthritis management and differential diagnosis.

ACL injury is a strong risk factor for premature joint deterioration with osteoarthritic changes being present in 50–70% of the patients at 10–15 years following the injury[8]. Estimates suggest that joint injury accounts for up to 15% of all incident knee OA cases and that this is also eminently preventable. Unfortunately much of what we have learned from preclinical research, especially animal models, has not been immediately translated into improved understanding of the human disease. Kijowski and colleagues review this important area and highlight the importance of imaging in the acute setting but also for the long-term prediction of joint health.

Femoroacetabular impingement, estimated to affect 10–25% of the general population[9,10], is a clinical condition that is commonly associated with anatomical structural changes that may lead to mechanical impingement and hip pain in young active adults. Although untested, the repetitive mechanical impingement in movement and locomotion is believed to lead to labral and chondral stresses that cause irreversible structural pathology. It is also believed that this process may be responsible for the development of a large majority of the cases of hip osteoarthritis[11]. Given the potential role femoroacetabular impingement plays in predisposing to osteoarthritis, the role of imaging in this young active population is crucial to better understand and prevent the later burden of hip osteoarthritis. This is thoughtfully reviewed by Siebelt and colleagues.

There is potentially tremendous value to public health in accelerating the discovery and development processes for OA therapeutics through shorter studies, using validated responsive endpoints. The use, in part, of clinical trial evidence based on biomarker and surrogate endpoint effects (in lieu of morbidity endpoints such as joint replacement or virtual joint replacement[12]) has the potential to revolutionize the osteoarthritis drug development process and to thereby enhance the armamentarium of safe and effective therapeutics. Imaging is a crucial component in clinical trial development and phenotypic characterization of the disease though imaging will likely help in optimizing trial strategies. This is an area of great promise but also pitfalls and is critically reviewed by Eckstein and colleagues.

There are a number of non-osteochondral tissues that can be affected in osteoarthritis including the synovium, menisci in the knee, labrum in the hip, ligaments and muscles. These structures play an important role in maintaining the normal integrity of the joint and pathologic changes can lead to functional limitations and pain.

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Hayashi and colleagues highlight studies that have established a relationship between imaging biomarkers and clinical outcomes. They also provide an excellent overview and recommendations for imaging protocols for assessment of synovium, meniscus in the knee, labrum in the hip, and ligaments, and highlight potential pitfalls in their usage.

There is growing recognition that local perturbation in tissue biomechanics leads to progressive tissue damage and osteoarthritis. The review by Neu discusses emerging functional MRI techniques that complement current MRI methods that provide structural and compositional information. The ability to non-invasively measure tissue strain in the intact joint has potential to address an important knowledge gap between joint kinematics and cellular mechanotransduction which in the future may improve our understanding of mechanical drivers of osteoarthritis.

Improved knowledge of the pathogenesis of osteoarthritis and of its molecular and anatomic pathology and the wealth of information relating biomarkers of disease with clinical outcomes will permit a better means for the assessment of the effects of new therapeutic interventions in OA. Will this decade lead to regulatory approval of disease modifying drugs and widespread clinical use? It is difficult to accurately forecast, but we would be greatly surprised if this did not occur. Given the ubiquity of osteoarthritis and its global burden, ultimately, we will all be the major beneficiaries from the new insights provided into disease risk, characterization and treatment. Assuming we maintain a meaningful motivation with the patient at the forefront of our mind we have an opportunity to make a difference in millions of people's lives.

Readers of this special issue should know that all reviews and original research in this issue were subject to full and impartial peer review, following all procedures that each independently submitted manuscript undergoes. We would like to extend our humble appreciation to the researchers who submitted articles for this issue and to our editorial board and all the reviewers that helped in processing all submitted manuscripts in a limited time frame. We were impressed with the enthusiastic response from the research community by its submission of numerous articles for potential inclusion; they were a pleasure to work with and we are sure you will see from the contents that it reflects wonderful insight and appraisal of a complex and developing field. We hope that this issue will enlighten readers about the current status of imaging research and its application in osteoarthritis.

Author contributions

The manuscript has been read and approved by all the authors, the requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Conflict of interest statement

There are no financial interests, direct or indirect, that might affect the conduct or reporting of the work submitted.

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