The Measurement of Joint Mechanics and their Role in Osteoarthritis Genesis and Progression

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Introduction

There is little doubt that mechanics play a role in the initiation, progression and successful treatment of osteoarthritis. However, we don't yet know enough about which specific mechanical parameters are most important and what their impact is on the disease process to make comprehensive statements about how mechanics should be modified to prevent, slow or arrest the disease process. The idea of a mechanical role in OA is often made clear to the patient: OA is "wear and tear" arthritis, and joint surfaces need to be replaced due to wear in advanced stages of the disease, much like bearing surfaces in an engine that have worn down after too many revolutions. The parallels with machines are sometimes (at least superficially) obvious: obese people load their joints more and have a higher prevalence of OA, which seems analogous to higher loads on a bearing increasing the rate of wear on its surfaces, a well-known mechanical phenomenon. High enough loads can destroy any tissue, so it seems clear that there is a level of joint loading that can injure cartilage irreversibly, leading to erosion from the joint surface. However, the utility of drawing parallels with machines is limited. Cartilage, though avascular and aneural, is a living tissue with capacity to adapt to its mechanical environment – it endures apparently unscathed through the most active decades of life in most people. Currently, many surgical procedures and other treatment and prevention approaches are based implicitly or explicitly on the assumption that they improve or correct joint mechanics, and that this improvement or correction is required to protect the joint from OA. Justifying and improving mechanically-based treatment and prevention approaches requires a critical understanding of the methods used to study joint mechanics and the current evidence for the role of mechanics in OA. The objectives of this review are: 1) to summarize methods for assessing joint mechanics and their relative merits and limitations 2) to describe current evidence for the role of mechanics in OA

initiation and progression, and 3) to describe some current treatment approaches that focus on modifying joint mechanics.

Mechanical hypotheses about osteoarthritis

Many of the hypotheses proposed to explain why OA begins and progresses center on mechanics. The most prevalent and best-researched hypothesis regarding OA pathogenesis is that acute trauma destroys chondrocytes and disrupts the extracellular matrix, resulting in proteoglycan depletion, cartilage breakdown and subsequent OA^{1,2}. Surface damage, proteoglycan loss³, and chondrocyte death¹ are seen commonly in OA, and similar observations have been made with in vitro impact studies on human and animal specimens⁴⁻⁶. Recent research suggests that even moderate loading can induce biological damage at levels well below those required to produce detectable macroscopic damage, and could be an early event in OA pathogenesis⁷. Prolonged exposure to overloading due to obesity⁸ and/or altered joint mechanics^{9,10} are also hypothesized to be detrimental to long-term joint health.

Altered kinematics and associated increased shear stress, in particular, is believed to be a key initiating factor explaining idiopathic forms of OA¹⁰. In the articulating joint, cartilage is exposed to compressive loading (tending to compress the cartilage) and simultaneous shear loading (tending to deform the cartilage) as the two cartilage surfaces slide relative to one another. Abnormal motion (perhaps due to an ACL injury, joint laxity or aging) results in a shift in the region of loading to a cartilage zone not conditioned to frequent load bearing¹⁰. This shift results in cartilage fibrillation at the cartilage surface—an observation commonly seen in early stages of OA^{11,12}. Following fibrillation there is an increase in friction which will increase the tangential shear load at the cartilage surface, resulting in increased shear stress in the collagen network and further fibrillation. Importantly, cartilage metabolic activity is dependent upon the type of loading (e.g., hydrostatic compression, shear) and exhibits a particularly negative response to excessive shear stress^{13,14}. Due to fibrillation, friction, and increased shear stresses, there is a metabolic upregulation of catabolic factors detrimental to cartilage health (e.g., matrix metalloproteinase and interleukins^{13,14}), resulting in further cartilage degeneration¹⁰.

Another hypothesis is that OA progresses due to mechanical changes in subchondral bone¹⁵. Proponents speculate that, due to impulse loading (loading that changes rapidly over time) and cumulative trauma, microfractures are created in the trabeculae which are repaired by fracture callus. As the trabeculae become thicker and new trabeculae are added, the repair process stiffens the subchondral bone, in effect acting as a support for the endplate. This causes the subchondral region to become less compliant, resulting in increased cartilage stresses and eventual degradation^{16,17}. Variable subchondral bone stiffening across the joint surface will also result in stiffness gradients and subsequent increased cartilage shear stresses¹⁵. A more recent, and generally accepted hypothesis speculates that microfractures *within* the subchondral cortical endplate (as opposed to adjacent trabeculae), result in subchondral thickening. These microfractures, attributed to impulse loading and repetitive stress, are hypothesized to increase biological activity at the site of injury and result in increased bone turnover and reactivation of the secondary center of ossification, resulting in subchondral thickening, cartilage thinning and increased cartilage stresses¹⁸. While evidence is emerging from animal studies in support of some of these hypotheses, very little work has been done in humans. Studies are emerging that examine the role of bone in OA using traditional bone mineral density measures. For example, cartilage thinning correlates with bone structure losses in the contralateral compartment in subjects with tibiofemoral osteoarthritis¹⁹. Ratios of medial to lateral compartment bone mineral density (BMD) have also been associated with compartmental tibiofemoral osteoarthritis²⁰. In particular, higher BMD in the medial compartment was associated with medial joint space narrowing and medial sclerosis and higher BMD in the lateral compartment was associated with lateral joint space narrowing and lateral sclerosis²⁰. Improved tools for measuring bone, cartilage and joint mechanics may ultimately allow us to test these and other hypotheses *in vivo* in humans.

Methods for assessing joint mechanics

The challenges of study design

It is difficult to test hypotheses about the role of mechanics in OA initiation and progression and the effects of a change in mechanics on OA because appropriate *in vivo* human studies present major challenges. First, studies require a well-characterized population that has or is at risk for OA, and such populations can be difficult to identify. Large populations are generally needed for studies to have appropriate statistical power, which adds to the cost of and difficulty of managing the study. Second, studies require a means of assessing OA incidence or progression. Radiographic measurements of OA (eg Kellgren-Lawrence grade²¹) are often insensitive to early OA and to small increments of progression. More recently advanced MRI techniques have shown some potential for more sensitive, quantitative measurement of OA progression²², but these measures are more time-consuming and expensive than radiographic approaches and they have not often been used in conjunction with mechanical assessments. Finally and most critically, such studies require *in vivo* assessments of joint mechanics. Standard clinical measurements used as surrogates for mechanics have been used in a number of studies, but they have many limitations. More advanced mechanical measurement methods have been developed, but studies have generally only been done in small populations because the measurements are expensive and time-consuming.

What would we like to measure and why can't we do it?

There are a number of hypotheses about the links between mechanics and OA, and these hypotheses define the mechanical quantities of primary interest to researchers. Unfortunately, the most interesting quantities are among the most difficult to measure. Compressive and tangential shear **force** on the joint surfaces is a key quantity in many hypotheses, but it can only be measured

directly by implanting a measurement device into the joint, which is far too interventional (in the case of the natural joint) for most *in vivo* studies of humans. **Force distribution** on the cartilage surface is also widely believed to be important - a moderate force transmitted through a small contact area may produce local stresses that cause cartilage damage, while the same force transmitted through a large contact area would produce no cartilage injury. While there are sensors available to measure force distribution²³, they must also be implanted, which carries the same limitations *in vivo* as direct measurements of force. **Loading rate** has been postulated to play a role in OA²⁴. Assessing loading rate requires very rapid measurements of force (typically hundreds a second), which is considerably more challenging than static force measurements. There is also substantial interest in how force is transmitted through joint structures such as cartilage and bone (**stress**). Measuring stress in simple machines and structures is a challenge, and stress has not been measured in joints *in vivo*. Some approaches are emerging for measuring **strain**, or deformation of the joint tissues in response to stress²⁵⁻²⁸, but the relationship between stress and strain is much more complex in joint tissues than in, say, steel or glass, which makes it difficult to use strain measurements to predict stress. **Kinematics** (joint movement) are easier to measure and several methods for accurately quantifying joint kinematics *in vivo* have been developed in recent years. Kinematics describe how the bones that make up the joint move relative to each other, which can reflect where load is transmitted through the surfaces and the lines of action of structures that transmit forces.

Ex vivo studies and joint models

Our current understanding of joint mechanics is founded on *ex vivo* studies, which are inappropriate for linking mechanics with clinical symptoms. In *ex vivo* studies, kinematics and contact mechanics have been measured in cadaver specimens loaded in mechanical rigs^{29-34 35,36}.

While studies of this type have helped us to understand biomechanics of healthy joints, their central limitation for studying OA is that morphological adaptations due to the disease process or the healing process and mechanical links to clinical symptoms such as pain and ongoing processes such as cartilage degeneration cannot be studied in cadavers. An alternative, which avoids some of the limitations of mechanical measurements that can be made *in vivo*, is to predict joint mechanics using mathematical models. Models are limited primarily by the assumptions that must be made to formulate them. Models incorporating sophisticated descriptions of joint structures have been developed and validated^{37,38,39-42} and used to answer specific clinically-motivated questions⁴³⁻⁴⁷. Two primary limitations of mathematical models are that a) many simplifying assumptions must be made about the properties of the joint, which limits their validity and applicability and b) like *ex vivo* studies, they are inappropriate for studying links with ongoing *in vivo* symptoms and processes, unless these changes are measured and incorporated into the model.

Subject-specific finite element (FE) modeling is an emerging technique in musculoskeletal research which has potential for shedding light on the role of mechanics in OA initiation and progression⁴⁸. FE modeling is a computational engineering technique used to evaluate how a structure with complex geometry composed of a range of materials behaves when subjected to loading. Its basic premise is to divide a complicated object into a finite number of small manageable pieces (elements). The behavior of each element can be described mathematically and evaluated computationally⁴⁹. Using clinical CT or MRI, a joint's bone, cartilage, and soft tissue geometry can be acquired. Tissue material properties (e.g., elastic modulus, stiffness) can also be estimated using CT or MRI^{50,51}. Image-derived geometry and material properties can then be used to create a subject-specific FE model, which can be analyzed under varying loading scenarios (e.g., repetitive walking, impact intensive running) to simulate bone and cartilage responses to loading. Importantly, unique information impossible to measure experimentally (e.g., internal stress and strain distributions in both bone and cartilage) can be acquired using FE modeling and linked with *in vivo* symptoms and OA processes. The FE method can also be applied longitudinally to evaluate

bone and cartilage structural behavior following OA-related morphological and mechanical alterations to these tissues. However, application of subject-specific FE modeling to address OA-related questions is in its infancy. To date, research employing subject-specific FE modeling has been primarily restricted to addressing osteoporosis-related research questions (e.g., fracture strength) of bony structures not necessarily affected by OA (e.g., radius, femoral neck)^{52,53}. This lack of OA-related FE research is likely due to difficulties associated with validating FE models comprised of numerous complex joint tissues. For example, it is impossible to place a device for measuring strain (i.e., a strain-gauge) in cartilage or in trabecular bone adjacent to overlying cartilage. Recently, however, new methods have been developed^{26,54} which have potential to validate internal strain distributions in bone and cartilage acquired using FE-modeling, and can be applied using intact joints. These developments, combined with improvements in CT and MRI technologies and computing power, have made subject-specific FE modeling a candidate technique for addressing specific questions regarding the role of mechanics in OA initiation and progression.

Radiographic measures of alignment

Most of the measures used clinically to quantify joint mechanics assess joint alignment. For example, tibiofemoral alignment is often quantified with the femorotibial angle, or hip-knee-ankle angle⁵⁵. A range of measures has emerged for quantifying patellofemoral alignment, with particular emphasis on medial-lateral position and patellar tilt. A central limitation of this approach is that the measures describe the joint (whose primary function is to move) at only one static position. In addition, while it is intuitive that these alignment measures are related to how load is transmitted in the joint, it is important to note that for most measures it is unclear how any given change in alignment measure would change force distribution in the joint. A further limitation is that the accuracy and repeatability of these measures is affected by their two-dimensional nature. Two-dimensional radiographic measurements are prone to errors due to

magnification and subject positioning. MRI and CT collect three dimensional information about joint anatomy, which has been used in such applications as quantifying femoral neck deformities thought to be associated with hip osteoarthritis⁵⁶. In many cases, however, the three-dimensional data are still reduced to a two-dimensional measurement, which does not describe three-dimensional deformities adequately.

Gait analysis

Gait analysis (often more generally referred to as “motion analysis”) is an important modality for estimating joint mechanics in activity. In motion analysis, movement of the joint segments is tracked (most often with an optoelectronic system), and loads applied to the body (eg, ground-reaction forces) are measured. Mechanical analysis then can be used to assess the resultant forces and moments at the joints for each position where a complete set of measurements is available. It is essential to note that the *resultant* forces and moments at the joints, which are output by the majority of commercial motion analysis systems, are entirely different from the *contact* forces (also known as the bone-on-bone forces) in the joint. Determining contact forces requires further analysis using joint models⁵⁷ and the measured joint segment positions and loads applied to the body. One advantage of gait analysis is that movement is relatively unconstrained by the measurement system, and therefore a large range of activities can be studied. One key limitation of gait analysis is that joint segments are typically tracked with markers fixed to the skin, which moves substantially relative to the bones. However, it is often difficult to identify the joint centre (or axis of rotation), particularly at the hip, and it is difficult to assess how well the measured marker positions correspond to motion at the joint (differences have been found to be on the order of 10 degrees for knee flexion⁵⁸). The use of large groups of skin-mounted markers has reduced the error caused by skin movement⁵⁹. A second key limitation is that the models and analysis

needed to determine joint contact forces require many simplifications and assumptions, limiting the accuracy with which these loads can be measured⁶⁰. Often models have been based on the anatomy of a single specimen or participant, as opposed to using subject-specific anatomical measurements. This limits the usefulness of these models⁶¹, particularly when pathologic joints are involved.

Roentgen stereophotogrammetric analysis and in vivo radiography

Some of the limitations of motion analysis have been addressed with radiography-based methods for measuring motion including roentgen stereophotogrammetric analysis (RSA, alternately known as radiostereometric analysis) and fluoroscopy. Three-dimensional knee kinematics have been measured during activity in vivo using single-plane fluoroscopy and subsequent image processing. This measurement has been done in joints after arthroplasty⁶² and in natural joints⁶³. A limitation of the single-plane approach is that measurement errors out of the imaging plane are quite large. More accurate three-dimensional measurements of kinematics can be made with biplanar fluoroscopy⁶⁴ and biplanar radiography, which has been used to study kinematics in the knees^{65,66}, hip⁶⁷, shoulder⁶⁸ and other joints. Although many biplanar radiography studies are done using a series of static positions, high-speed biplanar radiography has made possible accurate measurements of kinematics during dynamic activity^{69,70}. Because these measurements are so accurate, combining kinematics with known joint geometry yields predictions of joint-contact interactions^{67,71}. In some approaches, markers (typically small tantalum spheres) have been implanted into the bones, an invasive procedure, which is a clear limitation. However, recent work using model-based approaches suggests that measurements can be made accurately and precisely enough to be clinically useful without using implanted markers^{67,72,73}. A key limitation of all these approaches is that they expose patients to ionizing

radiation. Radiation doses vary dramatically with the joint of interest and the size of the subject. Such exposure always carries some risk and limits the number of repeat assessments that can be made, although in general imaging of the extremities is less of a concern than whole body imaging because the body core can be shielded from radiation.

MRI measurements of kinematics

MRI has been used to assess joint kinematics and has the advantages that soft tissues are easily visualized and that no ionizing radiation is required, making it ideal for use in longitudinal studies. The different MRI-based approaches for assessing kinematics are distinguished from one another by whether they describe two-dimensional or three-dimensional movement, whether they are assessed while the joint is actively loaded, and whether the movement is measured continuously. To date, most MRI studies of kinematics have focused on the patellofemoral joint, largely because patellar tracking is difficult to measure with other techniques such as gait analysis due to difficulties tracking skin-mounted markers on this small bone. Two-dimensional techniques have been used to assess kinematics at sequential static angles of knee flexion, dynamically over a range of knee flexion, unloaded and loaded in a supine, lateral or standing position⁷⁴⁻⁷⁹. Loading in the supine or lateral position is carried out by applying, respectively, an axial force to the foot or a torsional load to the shank using custom designed rigs. The primary limitation of two-dimensional studies is that they neglect at least half of the movement, because describing any joint's movement completely requires six quantities of movement (typically three rotations and three translations^{78,80}). Planar studies can measure a maximum of three quantities.

Three-dimensional MRI-based kinematic methods, which measure the six quantities of movement, have also been developed and fall under similar categories to two-dimensional

techniques (sequential static vs dynamic, unloaded vs loaded) ⁸¹⁻⁹¹. The static three-dimensional methods have employed standard MRI sequences whereas the dynamic methods have employed ultrafast gradient echo⁸⁵, cine-MRI ^{86-89,92,93}, phase-contrast MRI⁹⁰ and spoiled gradient echoes with radial acquisitions⁸⁴. Although promising, these techniques have some limitations; most notably that static postures in a supine position do not necessarily represent normal activities of daily living, and dynamic methods either require subjects to extend their knee very slowly, which is not necessarily representative of normal motion, or flex and extend their knees through many cycles which are averaged, which can cause errors if the motion is repeated perfectly between cycles. Accuracy of these techniques ranges from approximately 1mm and 1° ^{81,82} up to approximately 2mm and 3° ⁹⁴. Clinically important differences are likely within this range. It should be noted that not all techniques have been rigorously validated and, therefore, care should be taken when interpreting data.

There are inherent tradeoffs between static and dynamic methods and loaded and unloaded methods, as well as noteworthy limitations to these techniques. Substantial differences in two-dimensional patellar kinematic measures have been observed between unloaded, sequential static assessments and unloaded, dynamic assessments⁷⁴. Similarly, substantial differences were observed between static, loaded assessments and dynamic, loaded assessments in a three-dimensional analysis⁸⁵. These results suggest that differences exist between the static and dynamic case, regardless of applied load. To further support this, two other studies have shown differences in two-dimensional patellar kinematics assessed dynamically between a supine low-load scenario and an upright 45% bodyweight scenario⁹⁵ and in three-dimensional patellar kinematics assessed statically in the supine position at 0%, 15% and 30% bodyweight scenario⁹⁶. It should be noted that most methods apply relatively low loads to the limb (0-50% bodyweight load, open- and

closed-chain), which is due to the limitations of loading the leg in the close bore MRI scanner. While open-configuration MRI allows greater loads to be applied (at least 45% bodyweight in weightbearing) because the subject can stand upright, these scanners have lower field strengths, limiting image quality and increasing scan times, and are not widely available. The range of flexion angles that can be studied is also limited by the MRI scanner configuration; flexion angles of up to approximately 40° or 50°, depending on knee size, can be assessed in the closed bore systems while angles of 60° and above can be assessed in open-configuration scanners. In addition to these differences, the definition of the kinematic quantities themselves differ greatly between studies. This makes comparing results between studies challenging. A final limitation is that most of this work has focused on the knee; few data are available for kinematics of the hip, shoulder, elbow, or hand.

MRI measurements of contact area

Joint contact areas are fundamental to the understanding of load transmission through the joint and its relationship to local degeneration in OA. Ideally we would measure contact areas, contact loads, contact stresses and tissue stresses. However, currently the only *in vivo* measure possible is contact area. Direct measures of contact area can only be made with MRI. Contact area measurements are useful because they provide information about where loads are transmitted on the cartilage surface and they can be used to find average contact stress (if joint loads can be estimated). Several groups have developed methods of assessing contact area *in vivo* from MRI^{75,79,83,97-114}. All of these methods have used gradient echo techniques with fat suppression, which is optimized to view cartilage. These scans have been acquired using traditional scanners

(1.5 and 3.0T) and open configuration scanners (0.5T) using the loading methods similar to those employed for kinematic assessments. Contact area is generally assessed at sequential static, loaded angles of knee flexion, although it was measured during continuous flexion in a recent study¹⁰⁹. Axial and sagittal scans have been used; the choice of plane should be based on the one that provides the most information about the contact periphery. Once the MRI scans are acquired, they must be processed to calculate contact areas. This can be done by delineating the contact region in a slice-by-slice manner and multiplying the length of each contact line and by slice thickness^{75,97-99,103-105} or interpolating between slices and summing the areas of discrete patches^{83,102,107}. Alternatively, adjacent cartilage plates can be segmented separately and contact can then either expanding one surface by a pixel and defining overlap as contact^{79,100,101} or carrying out a proximity analysis¹⁰⁶. The coordinates of the contact centroid have also been reported on occasion^{83,107,115}; these may provide valuable information about changes in contact location and are most useful when reported in a relevant coordinate system, such as that used for kinematic assessment. Validation of MRI-based techniques has been limited; only three studies that have examined agreement with a reference standard, two using cadaver specimens^{99,116} and the other using a phantom⁹⁸. Errors, expressed as coefficient of variation were found to be 11%, 13% and 3%, respectively. Intra-observer, inter-observer and intra-subject repeatability has also been assessed *in vivo* and have ranged from 3% to 10%^{79,98,103,116}. Many of the factors that affect measures of patellar kinematics, such as loading, range of motion and tibiofemoral angle, are equally applicable to measures of contact area. Most studies have focused on the patellofemoral joint^{75,79,83,97-105,107,108,111,112,115}, while others have examined contact areas in the elbow^{108,117,118} and tibiofemoral joint^{110,113,114}. Little or no work has addressed the hip, shoulder, wrist, or hands.

The future

Technologic advances hold promise for more and better *in vivo* mechanical measurements. Many of the methods described in this article are now beginning to be used to study patient populations. One area with promise is MRI mapping of cartilage strain, which had been done *ex vivo* in the knee^{25,119,120} and the hip¹²¹. This work is challenging because achieving the resolution required to detect small changes in cartilage thickness in a short imaging time requires very high field strength scanners. As these scanners becoming more widely available for clinical use, there is potential to begin assessments of strain *in vivo*. Groups are also beginning to integrate mechanical measures with other OA disease indicators. For example, a recent study combined measures of contact area with measures of T1rho and T2 relaxometry; individuals with OA had longer T1rho and T2 relaxation times and greater contact areas¹¹¹. Integration of mechanical measurements with MR techniques that aim to detect early degenerative changes may be very useful for improving our understanding of the etiology of OA. CT technology is also improving, with scans becoming very fast and requiring relatively small doses of ionizing radiation. This raises the possibility of wider use of CT to assess joint kinematics and other mechanical quantities as well as integrating these measures with radiographic and MRI-based measures of tissue degeneration and OA. Finally, developments in nanotechnology suggest the feasibility of developing implantable transducers that transmit measurements through telemetry; this has been done on a limited scale¹²² but as technology improves may become more widespread.

Current evidence for the role of mechanics in OA initiation and progression

Distinction between normal aging and OA

We often think of OA as a disease of aging that is mechanical in origin¹²³; however, it is likely that there are some changes in mechanics over time that are a result of normal aging and not necessarily the OA disease process. For example, one study found, in participants without radiographic signs of OA, a significant increase in valgus alignment with age at a rate of 0.03° and 0.04° per year in males and females, respectively¹²⁴. In the same study, participants with OA tended to show increasing varus angulation. Another study showed, through principal component analysis, that patterns of gait differed between young (23.9 ± 2.6 years) and older (65.5 ± 5.2 years) participants when climbing stairs¹²⁵. These findings suggest that patterns of changes in joint mechanics may differ not only with OA but also with normal ageing. This highlights the need for establishing age-dependent population norms for studying OA.

Alignment

Joint malalignment or incongruence leads to altered loading patterns at the cartilage surface, therefore, it is not surprising that joint alignment is associated with OA. Tibiofemoral alignment has been studied extensively in individuals who have tibiofemoral and/or patellofemoral OA¹²⁶⁻¹³¹. However, this relationship is not necessarily as straightforward as one might expect with one study reporting that tibiofemoral alignment did not predict the incident tibiofemoral OA, suggesting that instead it may be a marker of disease or progression¹³². Another interesting paradigm is that increased body mass index is a risk factor for incident OA but only affected OA progression in knees with moderate malalignment (OR = 1.23), not neutral knees¹³³. A subsequent study showed that a high BMI increased risk of OA progression only in neutral and valgus knees

(OR=1.4 and 1.8, respectively)¹³⁴. These results are somewhat conflicting indicating that further examination is necessary. Regardless, it is not surprising that tibiofemoral alignment has also been shown to be protective against cartilage loss in the 'less loaded' compartment, as assessed by MRI, (OR=3.7 and 6.0 for the protected lateral and medial compartment, respectively)¹³⁵. Tibiofemoral alignment also has been shown to be associated with patellofemoral OA^{126,127,130,136}. varus tibiofemoral malalignment increases the odds of medial compartment radiographic patellofemoral OA progression (OR=1.85) and valgus tibiofemoral malalignment increases the odds of lateral compartment patellofemoral OA progression (OR=1.64)¹²⁶. More recently, the relationship between alignment and cartilage tissue properties, as assessed non-invasively by MRI, has also been studied. For example, joint space narrowing of one compartment was associated with a lower dGEMRIC index (ie less proteoglycan) in that compartment¹³⁷. Further, T2 relaxation times have also been shown to be elevated in the medial compartment of individuals with varus malalignment¹³⁸. Together, all these data suggest that tibiofemoral alignment plays an important role in OA but, in some instances, this role is one part of a complex interaction with other mechanical risk factors.

Patellar alignment, along with tibiofemoral alignment, plays an important role in patellofemoral OA. Lateral patellar alignment has been associated with lateral joint space narrowing (OR= 8.26)¹³⁹, lateral osteophytes (OR= 3.07)¹³⁹, lateral cartilage loss (OR= 3.4)¹⁴⁰ and lateral bone marrow lesions (OR= 3.2)¹⁴¹. Medial patellar alignment has been associated with medial joint space narrowing (OR=2.85)¹³⁹. In a study of OA progression, medial displacement of the patella increased the risk of medial patellofemoral joint space narrowing progression (OR=2.2), while it was protective of lateral patellofemoral joint space narrowing progression (OR=0.4) and increasing lateral tilt was protective of medial patellofemoral joint space narrowing progression

(OR=0.2)¹⁴². It has also been shown that patella alta (a high riding patella) is associated with lateral joint space narrowing (OR=2.77)¹³⁹, lateral osteophytes (OR=1.67)¹³⁹, medial and lateral cartilage loss (OR=2.0-2.4 and 1.5- 2.0, respectively)^{140,143} and medial and lateral bone marrow lesions (OR=2.5-2.9)^{140,143} and medial and lateral subchondral bone attrition (OR=2.2 and -3.5, respectively)¹⁴³. Interestingly, there is a high prevalence of medial patellofemoral OA that is independent of alignment¹⁴⁴. This highlights that alignment alone does explain all patellofemoral OA and perhaps more complex techniques, such as assessments of three-dimensional kinematics and contact area may be required to understand the relationship between mechanics and patellofemoral OA.

Other surrogates for high joint forces

A number of studies have found associations between surrogate measures of high joint forces and OA. As discussed previously, joint forces cannot be measured directly, but estimates based on anthropometry, joint congruency or alignment, gait analysis, and activities of daily living can be used to study the effect of higher joint forces. Several mechanical factors have been associated with radiographic and/or MRI-based definitions of OA such as obesity^{134,145-147}, patellar alignment¹³⁹⁻¹⁴¹, knee height¹⁴⁸, squatting¹⁴⁹ and meniscectomy^{131,150}. Although, apart from patellar alignment, these are not direct measures of mechanics these associations suggest that mechanics play a role in OA. For example, it is not surprising that knee height, which contributes to increased moments about the knee and associated higher theoretic contact forces in the joints, was associated with an increasing prevalence of symptomatic and radiographic knee OA¹⁵¹. More specifically, increased knee height, measured from the ground to the femoral condyles when sitting, was associated with radiographic patellofemoral OA in men (OR=1.7) and was associated with symptomatic patellofemoral OA in women (OR=2.2)¹⁵¹. Prolonged squatting (which theoretically produces high forces in the knee) in elderly Chinese men was also associated with higher risk for knee OA¹⁴⁹.

Obesity has been identified as a risk factor of both patellofemoral OA and tibiofemoral OA^{145,146}. In fact, obesity puts individuals at greater risk of radiographic patellofemoral OA than radiographic tibiofemoral OA (odds ratios (OR)=3.5, 7 and 1.9 for isolated patellofemoral, combined and tibiofemoral OA, respectively)¹⁴⁵. Gait analysis is probably the most widely used tool to estimate joint loads in OA. Different aspects of these analyses have been associated with OA. One of the strongest relationships between gait and OA is that knee adduction moment is associated with OA¹⁵²⁻¹⁵⁴. A more recent study showed that cumulative knee adductor load was better than the peak knee adduction moment at discriminating between healthy and OA groups¹⁵⁵. Gait analysis has also revealed that mechanics at other joints such as the hip and ankle can affect OA at the knee. For example, medial tibiofemoral compartment OA is associated with hip adduction moments and higher axial loading rates at the hip, knee, and ankle¹⁵⁶. Gait parameters at the hip, knee, and ankle also vary, depending on the severity of OA¹⁵⁷. It has been suggested that the changes in gait mechanics may be a compensatory mechanism to reduce pain by reducing joint loads at the affected joint^{158,159 160}. Asymmetric gait patterns have also been shown in subjects who have advanced hip OA¹⁶¹ and in subjects with unilateral knee OA¹⁶². Interestingly, in the latter study, individuals with bi-lateral OA did not display the same asymmetry in gait patterns. Ankle mechanics have been studied to a lesser extent than knee and hip mechanics, but it has been shown that a greater toe-out angle¹⁶³ and load¹⁵⁶ is associated with the progression of medial tibiofemoral OA. All these surrogate measures of joint loading provide information about the relative magnitudes of force being transmitted through the joint, but they do not indicate where on the joint surface these loads are transmitted. Advances in weight-bearing imaging may elucidate this point in the future.

Injury

Joint fractures and acute injury to the menisci, and anterior cruciate ligament are all very clearly associated with the development of osteoarthritis, but the specifics of how injury affects mechanics, and how mechanical changes lead to osteoarthritis, are not clear. Fractures of the joint surface at the hip, knee and ankle are associated with high rates of osteoarthritis, and the development of osteoarthritis is related to elevated contact stress caused by the fracture¹⁶⁴. Meniscal and anterior cruciate ligament injuries are well known factors in the development of early knee osteoarthritis¹⁶⁵. 43% of subjects who had undergone meniscectomy due to meniscal tears had radiographic evidence of osteoarthritis after 16 years¹⁶⁶, meniscectomy increases risk of developing OA (OR=2.6)^{150,167-170}, 51% of female soccer players with anterior cruciate ligament (ACL) injury had radiographic evidence of osteoarthritis after 12 years¹⁷¹ and 41% of male soccer players with ACL injury had radiographic evidence of osteoarthritis after 14 years¹⁷². A study of ACL injury in a population of individuals with symptomatic knee osteoarthritis found that a complete ACL tear increased the risk for medial tibiofemoral cartilage thinning as compared to those with intact ACL or partial ACL tears (odds ratio = 1.8, adjusted for age, body mass index, and gender)¹⁷³. However once an adjustment for medial meniscal tears was included in the regression model, a complete ACL tear was not an independent risk factor of cartilage thinning (odds ratio = 1.1)¹⁷³. Bone marrow lesions were associated with ACL tears in the same cohort¹⁷⁴. While it is clear that these acute injuries are associated with osteoarthritis, and change in joint mechanics produced by the injuries plays a role in the etiology of osteoarthritis, many other factors related to the patient, injury, and treatment will affect whether osteoarthritis develops after injury, and at what rate¹⁶⁵. Researchers have proposed hypotheses detailing the cascade of events

involving the effect of ACL injury on knee mechanics, the resulting change in loading patterns and the cartilage response¹⁷⁵.

Deformity

In contrast with knee OA, hip osteoarthritis is generally associated with either instability or deformity, with primary hip OA considered rare. While the association between severe hip deformity and osteoarthritis has been understood for decades, interest has more recently focused on the role of more subtle deformities. It is well accepted that many cases of “idiopathic” hip osteoarthritis can be attributed to bony deformity¹⁷⁶. The hypothesis that femoroacetabular impingement (FAI) is a major etiologic factor leading to osteoarthritis has growing support in the orthopaedic literature^{27,28,177}. Two mechanisms by which the cartilage and labrum are affected by FAI have been described¹⁷⁸. *Cam impingement* is a result of a non-spherical femoral head abutting against the acetabular rim in flexion and internal rotation. The abutment creates shear forces resulting in damage to the anterosuperior acetabular cartilage. *Pincer impingement* occurs as a result of linear contact between the femoral head-neck junction and the acetabular rim. In support of the FAI hypothesis, many studies have shown associations between features of impingement and cartilage damage. For example, in a study of 149 hips with mild or no radiographic OA, patients with radiological features of cam impingement (26 hips) had damage to the anterosuperior acetabular cartilage, while patients with radiological features of pincer impingement (16 hips) had a narrow strip of circumferential cartilage damage¹⁷⁹. Specific radiological features predicted progression to hip osteoarthritis (over at least ten years) in patients with a pistol-grip deformity¹⁸⁰. Early cartilage changes were present in hip cartilage in participants with cam deformities who had

not complained of osteoarthritic symptoms¹⁸¹. The prevalence of cam deformities in young males was reported to be 24%¹⁸², and the prevalence of specific cam and pincer deformity signs was higher in men than in women¹⁸³. Although hip deformity appears to be related to osteoarthritis, it is not clear what dictates whether or not FAI deformities will lead to osteoarthritis, how many patients with the symptoms of FAI have cartilage changes, at what stage osteoarthritic changes begin in FAI, and how they progress and whether they can be prevented or reversed.

The role of mechanics in OA treatment

Given the clear role of mechanical factors in OA incidence and progression, it makes sense that some treatment approaches focus on modifying joint mechanics. Approaches include surgery, bracing, wedging, gait modification, walking aids, and muscle stretching and strengthening exercises. Anterior cruciate ligament repair is the treatment of choice for ligament rupture, with the primary justification for the procedure being protection of the joint from OA. Similarly, joint reconstruction including repair of the posterior cruciate ligament, medial collateral ligament, menisci, acetabular labrum and many smaller structures is now widespread, and cartilage repair using grafts or engineered tissue is used to treat small lesions in young patients with traumatic damage to the cartilage. High tibial osteotomy is a surgical procedure used to treat tibiofemoral osteoarthritis associated with abnormal tibiofemoral malalignment. In high tibial osteotomy, a wedge of bone from the proximal tibia is resected (closing-wedge) or added (opening-wedge) to realign the lower limb, placing more force on the lateral compartment of the knee (generally) in an effort to reduce pain and delay cartilage degeneration in the medial compartment¹⁸⁴. Several groups have reported that high tibial osteotomy either arrests cartilage degeneration¹⁸⁵ or leads to cartilage regeneration^{55,186} in the diseased compartment. Surgical correction of hip deformity associated with femoroacetabular impingement syndrome improves symptoms in the majority of patients without advanced osteoarthritis or chondral damage in the short term¹⁸⁷. However the longer term success of these procedures is not clear¹⁸⁸. Conservative approaches to modify mechanics include gait retraining, bracing, muscle stretching and training and modifying footwear with the objective of redistributing forces in the compartments of the knee and using walking aids such as poles and canes to reduce or redistribute load in the knee¹⁸⁹.

There is no simple explanation for why more mechanically-based interventions are not being pursued. Weight loss is difficult, and exercise regimens require dedication. Insoles and braces can be uncomfortable and cumbersome. Joint reconstruction surgery aims to protect the joint from osteoarthritis in many instances, but its success is generally judged more on return to joint function in the short term rather than long-term incidence of OA. High tibial osteotomy is technically demanding, requires a relatively long recovery, has yielded only mixed clinical success^{190,191} and has unicompartmental arthroplasty as an appealing alternative. Hip deformity correction is rapidly gaining interest, but is technically demanding. More generally, many surgeons are reluctant to operate on asymptomatic or mildly symptomatic joints, but intervening to restore joint integrity or correct a joint deformity may prove effective at heading off the OA disease process.

Conclusion

We have learned a lot about the links between mechanics and OA in recent years. We should not be surprised that the findings are not all necessarily straightforward (OA is complex, so are joint biomechanics), nor should we be deterred from pursuing more knowledge in this area. New and better methods for measuring joint mechanics offer substantial promise to accelerate the pace of discovery. There is substantial scope for improving our understanding of mechanically-based treatments for OA and for developing new ones that better address this prevalent and disabling condition.¹⁹²

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