Editorial

Magnetic Resonance Imaging of Articular Cartilage: Toward a Redefinition of "Primary" Knee Osteoarthritis and Its Progression

Assessment of structural damage of the articular cartilage is important for monitoring the progression of osteoarthritis (OA) and evaluating therapeutic response. For years, clinical studies of drug interventions for symptomatic knee OA have focused mainly on clinical variables such as pain and joint function using self-administered questionnaires like the WOMAC[1] but without assessing the effect of treatment on structural changes caused by the disease or the role of treatment in preventing cartilage degradation.

Recently, attempts have been made to evaluate cartilage damage and its progression in OA. Serial radiographs of affected joints appear to be a logical means of documenting the progression of OA over time, providing that a validated, reliable, and easily reproducible technique is used[2]. Although improvements in the standardization and interpretation of radiographs have produced good measures of the joint space width (JSW) and the progression of joint space narrowing[3,4], the sensitivity to change of this measure is such that a minimum followup of 2 years in large numbers of patients are necessary to establish an effect of pharmacological interventions on OA progression. Moreover, measurement of JSW does not capture information on the cartilage changes alone but is also dependent on integrity of surrounding tissue, especially the meniscus. For instance, enucleation of the knee internal meniscus, which may occur during longitudinal studies, can dramatically change the JSW and affect the reliability of such measurement[5], potentially impairing its use in the assessment of cartilage degradation over time. Finally, JSW progression provides only one measurement point, which considerably restricts the statistical power of this technique and gives no indication of cartilage volume and only an approximate measure of the overall thickness of the articular cartilage.

The use of arthroscopy to assess a larger area of cartilage appears reliable and sensitive to change at one year[6]. However, only the cartilage surface can be evaluated; moreover, the method is semiquantitative and, above all, invasive. Large studies are, therefore, difficult to conduct.

Magnetic resonance imaging (MRI) allows precise visualization of joint structures such as cartilage, bone, synovium, ligaments, and meniscus and their pathological changes. MRI acquisitions are noninvasive and nonradiant, providing a clear advantage over arthroscopy and fluoroscopy. Recent advances in this technology have led to significant improvement in spatial resolution and contrast, enabling researchers to evaluate anatomical damage of all these joint structures across both cross-sectional and longitudinal planes. Although anatomical changes can be seen, *quantification* of these changes has long been the real challenge. Initial attempts at quantitative measurement of cartilage were possible only in healthy subjects[7] or in animal models[8]. Recently, improvement in image analysis led to reliable quantitative measurement of cartilage volume and thickness. Methods for measuring cartilage volume for the complete joint (femur and tibia) are now under evaluation for measuring the status of the knee cartilage over time. Research teams are using specific MRI acquisitions combined with semiautomated computer software to obtain valuable information on cartilage volume in healthy subjects and patients with OA[9-11]. Moreover, standard cartilage views can be anatomically segmented, allowing evaluation of cartilage volume and thickness in anatomical subregions and specific focal defects, since OA progression is more likely to be localized to specific areas. Studies are now under way to validate this MRI technology for the assessment of change in cartilage volume of the knee over time in OA patients, and to correlate the changes with standardized radiographic analytic tools and validated clinical variables.

Obviously, the main reason for quantifying cartilage thickness and volume in OA is to evaluate medications that may slow down cartilage degradation, so-called "chondroprotective" agents. However, to be practical in clinical research, such MR technology must be based on conventional MR acquisitions using variables that are easily reproducible by any conventional MR machine. The technology is then exportable to other centers with comparable MR

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facilities and can be used in multicenter trials. Moreover, because of the pain in patients with OA, image acquisition should preferably be completed quickly, but without losing image quality. This is critical for analysis of disease progression over time. MRI should hopefully reduce the number of patients needed, improve retention of these patients, and reduce the overall costs and the length of clinical trials related to OA.

Another advantage, compared with conventional imaging technologies, is the ability of MR images to assess all the joint structure, including the cartilage, menisci, synovial tissue, and ligaments. For example, MRI evaluation of cartilage loss can visualize other structures such as meniscal damage or misalignment. In this issue of *The Journal*[12], Cicuttini, *et al* suggest there was more cartilage loss over time in patients who underwent partial meniscectomy. Their results suggest the strong role of the meniscal apparatus in protecting cartilage, especially in elderly or obese subjects, or those with joint instability. What is not known is whether this is a population at risk that would benefit from the "chondroprotective" agents or whether we should avoid treating a disease course that may be relentless.

The implication of the MRI findings about the cartilage and the surrounding tissues may also influence the definition of "primary" OA in the future. The American College of Rheumatology criteria of the primary OA of the knee[13] are actually based on clinical and/or radiological findings. Since the cartilage is not vascularized or innervated, the pain experienced in OA is likely to originate from bone, synovial capsule, or ligament damage. "Pure" anatomical cartilage loss over time, if considered to define primary OA, may not be reflected by changes in symptoms, may precede radiological changes considerably, and may be accelerated by unsuspected concomitant meniscal damage.

The future of OA research pertaining to anatomical damage and its prevention or repair is similar to the experience in osteoporosis many years ago: significant bone loss was necessary to "see" osteoporosis on plain radiographs. With the advent of osteodensitometry, very small changes of bone mass could be detected. This outcome tool opened the door to clinical research on new therapies to slow or prevent bone mass loss. We know the effect of these medications on osteoporosis today. Similarly, quantification of cartilage loss over time will improve the monitoring of OA and possibly help us develop new interventions to prevent this extremely prevalent disease.

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