Edwin H.G. Oei, MD, PhD
Radiologist, Assistant Professor of Musculoskeletal Imaging
Department of Radiology
Erasmus MC, University Medical Center Rotterdam, The Netherlands
e.oei@erasmusmc.nl

Clinical Imaging for Engineers and Scientists (MSK): Arthritis

Target audience: MR physicists and scientists with an interest in imaging of (osteo)arthritis.

Outline of lecture

This lecture focuses on advanced MR imaging of osteoarthritis (OA), which is the most common form of arthritis. The significance of OA is stressed by means of a brief overview on the clinical aspects of the disease, including several basic facts and concepts that all researchers in the field of OA, as well as radiologists reporting on OA cases should be aware of. The OA epidemiology, etiology and risk factors, clinical symptoms, and treatment options are discussed, emphasizing the large negative consequences for patients in terms of reduced quality of life as well as the tremendous socio-economic impact because of high costs to health care. These effects are expected to increase even more in the coming decades due ageing of the population combined with growing prevalence of obesity.

With regard to therapy, the only definite treatment still is joint replacement for end-stage OA, despite continuous efforts of the pharmaceutical industry to develop disease-modifying osteoarthritis drugs (DMOADs) that target OA in an early stage. So far, the search for DMOADs has been disappointingly unsuccessful, however, especially when compared to disease-modifying antirheumatic drugs (DMARDs). This is mainly due to the lack of sensitive endpoints for OA research and limited knowledge on the OA pathogenesis and pathways. Advanced radiological imaging techniques for OA have the potential to solve both these issues by providing a sensitive outcome measure for OA research (e.g. clinical trials) and by offering more insight in the pathogenesis of OA.

The pathological and radiological features of OA are discussed next, listing the classic OA features such as osteophytes, cartilage defects/joint space narrowing, subchondral sclerosis and cysts. The current concept of OA is introduced in which OA is considered a “whole joint disease”, implying that all tissues of the joint are affected by OA or are involved in its pathogenesis. This is in contrast to traditional viewpoints (and imaging techniques) applied to OA that focused primarily on articular cartilage and bone. Many of the affected tissues, e.g. synovium, meniscus, and ligaments, can be assessed with MRI as shown in several examples. Novel MRI techniques in this regard include dual echo steady state (DESS) for synovitis and ultrashort echo time (UTE) for meniscus imaging. Other structures and processes believed to play a role in OA, such as subchondral bone structure and blood perfusion, may also be evaluable with novel MRI methods.

To illustrate the advantage of MRI for OA imaging, the "traditional" radiographic method of OA assessment is explained briefly, emphasizing that it only provides an indirect visualization of articular cartilage loss, i.e. joint space narrowing. Next, the "traditional" MRI methods for OA are discussed, starting with an overview of the MRI hardware (field strength and coil) requirements and recommended pulse sequences. The traditional MRI methods rely on morphological cartilage loss – thinning and defects – that represent advanced stage OA. A number of morphological MRI scoring methods for OA exist, of which two are presented, i.e. the Knee Osteoarthritis Scoring System (KOSS) and the more recent MRI Osteoarthritis Knee Score (MOAKS). The complexity and laboriousness of these scoring systems is demonstrated, as well as the fact that all current MRI scoring systems share an important limitation: they all lack a cut-off point and severity grading for OA. Thus, traditional radiographical and MRI methods for OA are unsuitable for use in advanced OA research (e.g. into DMOAD development), because they are too insensitive to OA change, too subjective, and all focus on advanced stages of the disease.

Advanced quantitative MRI techniques to assess cartilage are discussed in the remainder of the lecture. Two different concepts of quantitative MRI of cartilage can be distinguished: quantitative morphometry and quantitative compositional (or biochemical) MRI. Quantitative cartilage morphometry provides a numerical outcome of articular cartilage morphology (e.g. thickness or volume) after manual or automated segmentation. Although this increases the sensitivity compared to visual radiographical and MRI methods and improves intra-observer agreement, these techniques are also very laborious and are incapable of evaluating early stage OA.

Quantitative compositional MRI of cartilage is explained next, enabling visualization of articular cartilage structure and biochemical composition, which can be mapped in various regions of the joint and quantified to provide an objective numerical outcome measure of cartilage quality. By assessing cartilage composition changes rather than morphology alterations, such techniques are sensitive to detect the earliest stages of OA, as it is known that change in cartilage composition occur long before the onset of morphological cartilage loss. The main composites of articular cartilage are type 2 collagen (15%), proteoglycans (glycosaminoglycans) (15%) and water (70%), collectively referred to as the extracellular matrix of cartilage. These components of cartilage can be evaluated with a variety of novel quantitative MRI techniques.

As an example, the delayed gadolinium enhanced MRI of cartilage (dGEMRIC) technique is discussed in detail. dGEMRIC is capable of assessing proteoglycan content in cartilage by making use of an inversed relationship between negatively charged proteoglycan macromolecules and a negatively charged MRI contrast agent administered intravenously. Because of this interaction, contrast agent accumulates in areas with proteoglycan depletion and influences T1 relaxation time proportionally with cartilage quality in terms of proteoglycan content. Two other quantitative compositional MRI techniques for cartilage are explained: T2 mapping (correlating with collagen content) and T1rho (presumably correlating with collagen and proteoglycan content). Other quantitative techniques such as sodium MRI, diffusion weighted MRI, ultrashort TE, and GagCEST are discussed briefly. The method of data acquisition using relaxometry is explained, in which a pulse sequence is applied several times with a varying inversion times, flip angles or echo times depending on the technique after which T1, T2 or T1rho values can be computed using curve fitting algorithms. The post-processing method is demonstrated, illustrating the importance of image registration to improve the accuracy of relaxometry calculations.

All quantitative compositional MRI methods mentioned above are used more and more in a clinical OA research environment, although their correlation with regular MRI features, OA symptoms, and, most importantly, prognosis and clinical outcome is yet to be determined for many of the techniques. In some centers dGEMRIC and T2 mapping are already implemented in clinical patient care as an important factor for therapeutic decision making. Although these advanced imaging techniques are regarded as very promising to play a pivoting role in future OA research by many within the OA community, much research is to be done to properly validate the techniques.

The lecture is concluded with the following take-home messages:

- OA is a common disease with high morbidity and tremendous socio-economic effects.
- OA is a whole joint disease that involves all tissues of the joint.
- Radiography is still first-line diagnostic tool for OA, but it is insensitive to change, early OA, and soft tissue abnormalities.
- Morphological MRI is superior to radiography, but also carries limitations for OA research
- Quantitative (compositional) MRI techniques are promising, but more research is needed to determine their value.

Suggested references

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