Extensive efforts are currently underway to understand the earliest pathologic changes in synovial joint tissues. These efforts are motivated in part by a desire to understand the pathophysiologic alterations that occur in diseases of the joint. However, in large part the efforts are promoted by the necessity to develop agents to modify structural changes that occur with disease, and the parallel requirement that we have imaging methods to measure these structural changes that are valid, responsive and clinically relevant. Historically we have relied upon plain radiography to depict disease severity in osteoarthritis (OA) and to ascertain progression by determining changes in joint space. With the acknowledged limitations of these methods, development of methods to directly visualize and measure joint tissues including magnetic resonance imaging (MRI) have been pursued. Much of this focus has been on measurement of methods to directly visualize and measure joint tissues including magnetic resonance imaging (MRI) have been pursued. Much of this focus has been on measurement of articular cartilage morphometry. Measurement of morphometry appears to correlate well with the ex vivo assessments of cartilage volume (striped away from bone), in addition to possessing adequate precision and sensitivity to change. Recent MRI studies, however, have observed small rates of change (−1.3% loss per year) and standardized response means of −0.3−0.5% per year.

Possibly more importantly these measures of quantitative cartilage morphometry appear most useful (sensitive to change) in persons with late stage disease (such as in those with established JSN or extensive areas of denuded cartilage). If the pathological changes of cartilage loss are irreversible, and we focus especially on those at the end stage of the disease, we may not be able to accomplish our goal of modifying the progress of the condition as a drug may not produce cartilage in an already denuded area.

Thus, despite inherent advantages much of the potential of MRI to measure structural changes remains to be realized. While quantitative measurement of morphology can be used to monitor loss of cartilage tissue, there is extensive interest in using MRI to detect changes that precede gross tissue degradation that may occur in early disease. Applications of parametric mapping techniques to image compositional changes that may be sensitive to early cartilage damage including T2 mapping, delayed Gadolinium Enhanced MRI of Cartilage (dGEMRIC) and T1rho have been extensively reviewed elsewhere. Intuitively, compositional measures may have a great role to play in examining changes that occur in early disease before gross defects are apparent, whereas morphologic measures—both semi-quantitative and quantitative—may have a greater role in later stages of disease.

One of the most widely used measures is dGEMRIC, which relies on intravenous injection of a negatively charged MR contrast agent and the acquisition of a T1 map after equilibration of the contrast agent in the cartilage, to estimate the glycosaminoglycan distribution within cartilage. The manuscript in this issue of Osteoarthritis and Cartilage by Multanen et al provides an important advance in our knowledge of this technique. They examine the reproducibility of this measure and demonstrate that the root-mean-square average coefficient of variation (CVRMS) ranged between 4.7 and 12.9% and the intraclass correlation coefficient (ICC) ranged between 0.45 and 0.98. For the major regions of the knee the reproducibility was good to excellent; the CVRMS and ICC for bulk dGEMRIC were 4.2% and 0.95 for femur, 5.5% and 0.87 for tibia, and 4.8% and 0.97 for patella. The availability of these performance metrics is helpful when establishing the measurement characteristics (precision, accuracy, validity) of a specific marker and are helpful in future study planning.

There are a number of important limitations to his study, particularly pertaining to generalizing the study findings, that remain worthy of further investigation. Most importantly the population studied does not have OA, and are young (mean age 32 years) and not obese. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA. It is very likely that if a population with OA were studied there would be greater variability and hence less precision and thus the same study needs to be repeated in a population that reflects the characteristic disease of OA.

The CVs and ICCs presented in this study do not compare favorably to other measures including joint space narrowing, cartilage morphometry and BMD measures on DEXA. Precision in measurement science can be influenced by biological variability (for example the influence that would be expected for example from diurnal change in cartilage hydration), technical variability (for example what would be expected from differences in knee position when the scan was acquired) and reproducibility (for example inconsistency introduced in manually processing the imaging data by observers who may select slightly different segmented regions). The investigators have tried to limit the biological variability (by reducing the diurnal variation when scans were obtained) and the technical variability (by using well trained and calibrated technicians and a clearly stated
Thus the current study is but one small step in the direction towards improved knowledge of the performance metrics of markers that are useful in OA clinical studies. Of immediate greatest import for supposedly “early” changes of OA, the natural course of these changes and the relationship with clinical outcome remains to be established. At present there is limited data on the longitudinal assessment of compositional measures in comparison with the clinical constructs. Further assessment of the psychometrics of MRI measures is greatly needed to facilitate further application in clinical trials.

Conflict of interest

There are no financial interests, direct or indirect, that might affect the conduct or reporting of the work submitted. The manuscript has been read and approved by the author, the requirements for authorship have been met, and the author believes that the manuscript represents honest work. This is an original manuscript that has not been reported elsewhere.

References