Biochemical cartilage changes based on MRI-defined T2 relaxation times do not equal OA detection

Frank W. Roemer[a,b,1] and Ali Guermazi[a,c]

We read, with great interest, the recent PNAS publication by Kundu et al. (1). We wish to comment on several aspects of this research.

The abstract states that subjects included were free of symptoms. However, figure 7 in ref. 1 shows that the inclusion definition was a total Western Ontario and McMaster Universities Arthritis Index (WOMAC) score of <10 but not 0. The definition of incident symptomatic knee osteoarthritis (OA) at the 3 year follow-up visit was based on an increase in total WOMAC score of >10. The overall WOMAC score range is from 0 to 96 (on a 0 to 4 Likert scale) and determined by summing scores across three dimensions (2). Assuming the authors used the Likert format, an increase of 10 or more likely does not fulfill the definition of symptomatic OA, particularly as no data on radiographic OA status at 3 years are presented. The arbitrary definition of OA incidence the authors suggest differs widely from the accepted definition of clinical knee OA according to the American College of Rheumatology (3). In addition, the authors state that they present "an approach that enables sensitive OA detection in presymptomatic individuals." However, the content of the paper is diagnostic performance regarding a clinical outcome 3 years later. Thus, diagnostic performance to predict later case status is assessed, but not OA detection, that is, diagnosis of disease.

The authors (1) state that subjects included were free of visual signs of disease on imaging. However, not only knees without any signs of radiographic OA were included but also those fulfilling criteria of Kellgren–Lawrence 1 (KL1), that is, at least exhibiting an equivocal osteophyte. Several authors have stated that KL1, in light of accompanying symptoms, should be regarded as early disease (4–6).

Concerning the detailed baseline Whole-Organ Magnetic Resonance Imaging Score (WORMS), data including different OA structural features are not shown. Thus, it remains unclear whether these knees were free of visual signs on imaging as stated in the abstract. Based on data from a large population-based study, more than 95% of knees without radiographic OA show signs of MRI tissue damage (7). Furthermore, multidimensional ordinal grading schemes likely should not be used as summed scores unless the clinical relevance of the different features has been shown. It has not been clarified that a total score, that is, of six based on six observations of a grade 1 lesion or on one single observation of a grade 6 lesion, means the same regarding structural severity or future outcomes. The statement that semiquantitative scoring systems have not been validated to diagnose knee OA is not correct. A definition of knee OA on MRI exists and has been validated (8, 9).

The fact that visual inspection appears to be insensitive to subtle biochemical changes (as referred to in figure 1 of ref. 1) is not surprising. Color-coded T2 maps are not applied for visual inspection or diagnosis but represent extracted T2 values based on segmentation (10).

In summary, our understanding of OA incidence and progression is rapidly increasing, and the field of radiomics and feature extraction will hopefully help improve prediction of disease incidence and progression of OA, in the future.

[a]Quantitative Imaging Center, Department of Radiology, Boston University School of Medicine, Boston, MA 02118; [b]Department of Radiology, Friedrich-Alexander University Erlangen-Nürnberg and Universitätsklinikum Erlangen, 91054 Erlangen, Germany; and [c]Department of Radiology, Veterans Affairs Boston Healthcare System, West Roxbury, MA 02132

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[1]To whom correspondence may be addressed. Email: frank.roemer@uk-erlangen.de.

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