What is the Role of Diffusion-weighted Imaging in Ileocolonic Crohn's Disease?

To the Editor:

We read with great interest the article by Kim et al,[1] published in the January issue of *Inflammatory Bowel Diseases*. The study design, excluding most of colonic segments (transverse, descending, and sigmoid colons) and operated patients from their statistical analysis, led difficult to draw any conclusion regarding the role of diffusion-weighted magnetic resonance imaging (DW-MRI), in ileocolonic Crohn's disease (CD). We agree partially with the authors concerning the fact that there is no real additional value in performing DW-MRI to increase the detection of ileocolonic CD lesions using qualitative analysis, i.e., diffusion-weighted imaging hyperintensity. Most of the authors focused on the qualitative parameter of DW-MRI to detect and assess inflammatory lesions. Accordingly, Kim et al confirmed that the accuracy of diffusion-weighted imaging hyperintensity is similar to the performances of injected sequences and could also be a marker of severity.[1] Additional studies are warranted to confirm previous data showing that diffusion-weighted sequences could be an alternative to injected sequences to limit side effects and patients' discomfort.[2]

We consider that the quantitative analysis using the apparent diffusion coefficient (ADC) is the main strength of DW-MRI performed with no bowel cleansing and no rectal enema in CD. Our team and others previously showed that the Clermont score[3] is highly correlated to the Magnetic Resonance Index of Activity[4] and to the simplified endoscopic score for CD[5] in the terminal ileum. In addition, we reported that segmental ADC is highly correlated to the Magnetic Resonance Index of Activity in colonic segments,[2] which could mean that ADC use could decrease the number of false positives. We will present at the European Crohn's and Colitis Organization congress, the preliminary results of a prospective study showing that ADC and Clermont score were highly effective in detecting endoscopic ulcerations in the colon and the terminal ileum, respectively. The conclusion of Kim et al[1] should not be misinterpreted and should not discourage IBD physicians to conduct further studies interesting in DW-MRI in CD. DW-MRI is a well-tolerated, reproducible, and non–time-consuming tool, which could be repeated to monitor CD activity both in daily practice and in clinical trials. Further investigations should be performed to confirm that the quantitative parameters (ADC and Clermont score) are able to assess therapeutic response and that DW-MRI could be generalized for the management of patients with CD.

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Reply:

The potential of diffusion-weighted magnetic resonance imaging (DW-MRI) as an imaging biomarker of bowel inflammation in Crohn's disease (CD) has been proposed by multiple research studies, including our own.[1] Currently, there seems to be a general consensus on its diagnostic potential. However, as Dr. Buisson indicates, more research studies to further clarify the clinical role of DW-MRI in the evaluation of CD are needed. One area that merits particular attention is understanding how quantitative parameters derived from DW-MRI, namely apparent diffusion coefficient (ADC), can be used as a biomarker of bowel inflammation of CD. We believe that Dr. Buisson's statement that quantitative analysis of DW-MRI is a reproducible tool for monitoring CD activity is premature. Although there have been several studies that investigated observer agreement in measuring ADC values from DW-MRI images acquired in patients with CD, it should be noted that reproducibility/reliability of any imaging index goes far beyond mere observer reproducibility. In fact, the limited reproducibility of ADC in various applications in the abdomen is well known.[2–7] ADC values can vary substantially even when the same subject is scanned repeatedly using the same scanner and same scanning methods (i.e., within scanner variability). Similarly, interscanner variability is significant. Multiple technical factors, including the b-factor, number of b-factors used to estimate ADC values, and whether perfusion effect is accounted for in the calculation of

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ADC are known to impact ADC. In addition, method of ADC measurement, including the size of region of interest, position of the region of interest, and selection of representative ADC value (i.e., lowest ADC value, mean ADC value, or else) would create additional sources of variability. Such large potential for variability requires particular caution in clinical use of ADC and obviates widespread implementation of quantitative ADC in clinical practice. In fact, recognizing these problems, QIBA (Quantitative Imaging Biomarkers Alliance) was formed to understand and reduce variability of quantitative imaging biomarkers across research studies and practices (see https://www.rsna.org/QIBA.aspx; for DW-MRI and ADC, refer to http://qibawiki.rsna.org/index.php?title=Perfusion%2C_Diffusion_and_Flow-MRI_tech_ctte). It should also be noted that any quantitative diagnostic cutoff values of imaging biomarkers reported in research studies, which are typically derived using the receiver operating characteristic curve analysis, are often subject to spectrum bias. As a result, even if the conceptual conclusions of research studies quantitatively investigating ADC values are generalizable, the numerical ADC values or values of any quantitative parameters derived from ADC are often individual study-specific and not truly generalizable. To our knowledge, the aforementioned issues have yet to be addressed in research studies of DW-MRI in CD and require attention in future studies before ADC, or any quantitative parameters derived from it are adopted in clinical practice or future clinical trials evaluating bowel inflammation in patients with CD.

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