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Reply to Erik Rud and Eduard Baco's Letter to the Editor re: Re: Jeffrey C. Weinreb, Jelle O. Barentsz, Peter L. Choyke, et al. PI-RADS Prostate Imaging – Reporting and Data System: 2015, Version 2. *Eur Urol* 2016;69:16–40

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Letter to the Editor

We are grateful for the letter from Rud and Baco as it raises an important and somewhat contentious issue concerning the role of dynamic contrast enhancement (DCE) in PI-RADS v.2 assessment of prostate multiparametric magnetic resonance imaging (mpMRI).

PI-RADS v.2 states:

The added value of DCE is not firmly established, and most published data show that the added value of DCE over and above the combination of T2W and DWI is modest. Thus, although DCE is an essential component of the mpMRI prostate examination, its role in determination of PIRADS™ v2 Assessment Category is secondary to T2W and DWI.

Importantly, PI-RADS v.2 only addresses the detection of significant prostate cancer (PCa) in patients with clinical suspicion for PCa in the prebiopsy or postbiopsy setting. It does not address the use of MRI for detection of suspected recurrent PCa following therapy, for which DCE is thought to be important, or of progression during active surveillance.

A major goal of PI-RADS v.2 was to simplify the acquisition, interpretation, and reporting of prostate mpMRI data. In their letter, Rud and Baco question the necessity for inclusion of DCE in routine mpMRI for the detection of clinically significant PCa. As they point out,

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omission of DCE would not only simplify and shorten the examination but also eliminate the cost and potential risk of injection of a gadolinium-based contrast agent. In fact, DCE was among the most challenging issues for members of the PI-RADS Steering Committee that built PI-RADS v.2 over 3 yr, and it reflects in part the challenge of making any recommendation in the face of changing and evolving knowledge. An explanation is certainly warranted.

In 2012, when the PI-RADS Steering Committee began its work, DCE was almost universally considered to play a critical role in prostate mpMRI. On the basis of past experience and peer-reviewed scientific publications, most leading centers were routinely using T2, DCE, and diffusion-weighted imaging (DWI), and a few were also using magnetic resonance spectroscopy imaging (MRSI). Only a few studies attempted to isolate the relative benefits of each of these techniques in various combinations. In this context the burden of proof fell more on evidence to safely eliminate sequences, but high-quality trials on which to base this decision were, and still are, lacking. The need for simplification and practicality drove two major decisions by the PI-RADS Steering Committee: (1) eliminate MRSI given its technical challenges and lack of support in a multi-institutional trial; and (2) minimize the role of DCE given its complexity in scoring and interpretation. There was a strong sense that as published data on the value of DWI continued to accrue, the incremental benefit of DCE was small. Nevertheless, because of both published studies and individual personal experience, there was reluctance to eliminate it entirely from the routine mpMRI examination.

We agree with Rud and Baco that in the detection of significant PCa according to PI-RADS, DWI forms a key sequence and outperforms DCE. However, in some instances DWI is technically compromised for part or all of the prostate (ie, assessment category X) by susceptibility artifacts such as distortion from bowel gas, hip prostheses, and inadequate signal-to-noise ratios. It was felt that the DCE sequence in these scenarios would add confidence to interpretation. In addition, Vos et al [1] showed that quantitative and semi-quantitative DCE parameters at 3 T have the potential to discriminate between low-grade and intermediate- plus high-grade PCa in the peripheral zone. Therefore, we decided to include DCE to upgrade PI-RADS 3 lesions. Future studies that include DCE need to show if this is a correct approach.

There is currently a paucity of data supporting elimination of DCE in every setting in which PI-RADS v.2 is being used and explored. In our view, meta-analysis of retrospective data does not suffice for clinical applications selected by the PI-RADS Steering Committee. Meta-analysis may be flawed in selecting patient groups and addressing scientific questions. More specifically, Rud and Baco base their comments on just two meta-analyses by Tan et al [2] and Haghighi et al [3] that only included papers up to 2013 and for which the studies included are limited and heterogeneous. In addition, Tan et al [2] and Haghighi et al [3] did not validate the papers used by applying the QUADAS 2 criteria. Finally, they are also much more careful in their conclusions than Rud and Baco, and we agree with their conclusion that “larger studies with uniform methodology are warranted to further understand the relative merit of DCE.”

In summary, elimination of DCE from some of the common indications for prostate MRI is a logical next step in the incremental development of guidelines for mpMRI, especially in the “screening” prebiopsy situation. The great merit of PI-RADS v.2 is that it will allow multiple institutions to combine their data so that future meta-analyses will provide enhanced information that may help to address whether DCE omission is warranted and to guide the development of PI-RADS v.3. We look forward to further evidence to support these decisions.

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