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Can Biparametric Prostate Magnetic Resonance Imaging Fulfill its PROMIS?

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Recently updated international guidelines recommend a more prominent role for multiparametric magnetic resonance imaging (mpMRI) in the work-up for prostate cancer (PCa) diagnosis [1,2]. However, the benefit of dynamic contrast-enhanced (DCE) MRI for PCa detection and localization is still a matter of debate. Omitting DCE may improve MRI accessibility in response to the increasing demand for this imaging modality. A so-called biparametric MRI (bpMRI) protocol only uses T2-weighted and diffusion-weighted imaging. There are several advantages of using a bpMRI strategy for all biopsy-naïve patients, the most enticing one being time and costs savings [3–5]. Furthermore, the potential side effects of contrast can be avoided [6].

Recent systematic reviews and meta-analyses found similar diagnostic performance for bpMRI and mpMRI, suggesting a transition to bpMRI for biopsy-naïve men could be feasible [7,8]. However, the studies included showed high methodologic heterogeneity in prior biopsy status, MRI equipment, MRI protocol and scoring system, the definition of clinically significant cancer, and (biopsy) reference standard. This undermines the strength of the underlying evidence. Furthermore, the studies included were often from highly experienced prostate centers with 3-T equipment, which somewhat limits the generalizability of these data to general clinical practice [5].

We commend El-Shater Bosaily et al [9] on their study published in this issue of *European Urology*, as it contributes to filling this void in the literature. For the original PROMIS study the intent was to reflect "daily clinical practice" with 1.5-T MRI scanners and multiple readers with varying prostate MRI reading experience [10]. As an additional aim, the value of mpMRI over bpMRI was assessed within the setting of this prospective, multicenter, multireader and paired validation study with template mapping (TMP) biopsies as the reference standard. The diagnostic performance of both techniques in detecting clinically significant disease in 497 biopsy-naïve men was compared using a 5-point Likert scoring system. The authors conclude that the diagnostic accuracy values for mpMRI and bpMRI are similar, suggesting that DCE could be omitted from the MRI diagnostic work-up.

Some issues in the present study by El-Shater Bosaily and colleagues should be critically appraised. First, it is important to realize that the conclusions from this PROMIS study are based on the assumption that targeted biopsies (which were not performed in this study) would achieve similar diagnostic accuracy as TMP biopsy. What is currently lacking, however, is an assessment of the correlation between lesion location on MRI and TMP biopsy to be able to justify the assumption made.

Second, the PROMIS data show a clear difference in the total number of "equivocal" or "uncertain" cases (ie, Likert score of 3 out of 5) for bpMRI and mpMRI (32% vs 27%) compared to studies by Van der Leest et al (the 4M study; 7.8% vs 6.4%) [5] and Zawaideh et al (17% vs 8.3%) [11]. The low percentage of equivocal results in the latter two studies can be explained by the high-quality 3-T images assessed by experienced readers, whereas images from routine 1.5-T scanners were read by radiologists with varying experience

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levels in the PROMIS study. Despite the high number of equivocal cases in the PROMIS study, the reduction in "uncertainty" by using DCE (mpMRI) was only 4.4% (31.8% to 27.4%), while Zawaideh et al reported substantially greater of 8.7% (17% to 8.3%) [11]. Moreover, the suboptimal "blinding" protocol used in the PROMIS study for the bpMRI and mpMRI readings may have resulted in a significant bias.

It is apparent that omitting DCE from prostate MRI would allow a higher throughput and lower costs, would make prostate MRI noninvasive, and would avoid potential contrast-related side-effects. However, suboptimal results because of lower image quality from the use of suboptimal MRI scanners and less experienced radiologists could be mitigated by the use of DCE in mpMRI protocols to decrease uncertainty (ie, decrease scores of 3). Equivocal MRI scores are troublesome for urologists, as they do not give guidance in biopsy decision-making. High numbers of equivocal cases could result in a loss of confidence in the MRI pathway and prompt urologists to lean back towards the systematic biopsy pathway. Previous studies reported that DCE could aid in assessment and decrease uncertainty in reading, especially in settings with suboptimal image quality and non-expert readers [12,13]. Therefore, focusing on high-quality examinations and adequate training for radiologists is crucial.

Thus, before using bpMRI routinely, radiologists should be competent in both bpMRI and mpMRI. In daily practice, we see many radiologists performing bpMRI who are "unaware-incompetent" in this respect. Ideally, prostate MRI radiologists should compare their bpMRI and mpMRI diagnosis with histopathologic outcomes and attend multidisciplinary team meetings to this end. In addition, reading performance should be benchmarked against results from expert centers and the literature. Only if these conditions are fulfilled, we agree with El-Shater Bosaily et al that there is a role for bpMRI as a triage test for the detection of clinically significant PCa, but only in men in whom biopsy avoidance is a clinical priority, such as in early detection of cancer in biopsy-naïve men with a lower risk of clinically significant PCa. For men with high clinical suspicion for significant disease, for whom the clinical priority is cancer detection and not biopsy avoidance, mpMRI is preferred over bpMRI.

We conclude with some points on the use of bpMRI in daily practice that should be considered:

- Only perform bpMRI when image quality and radiological readings are of a high standard.
- Use high-quality bpMRI only for men for whom biopsy avoidance is a clinical priority, such as for early cancer detection in biopsy-naïve men with a lower risk of clinically significant PCa.
- Perform mpMRI as the default for men with a high clinical suspicion for significant disease, where the priority is cancer detection and not biopsy avoidance. Perform mpMRI for men with persisting clinical suspicion after a previous negative biopsy (Fig. 1) or previous negative

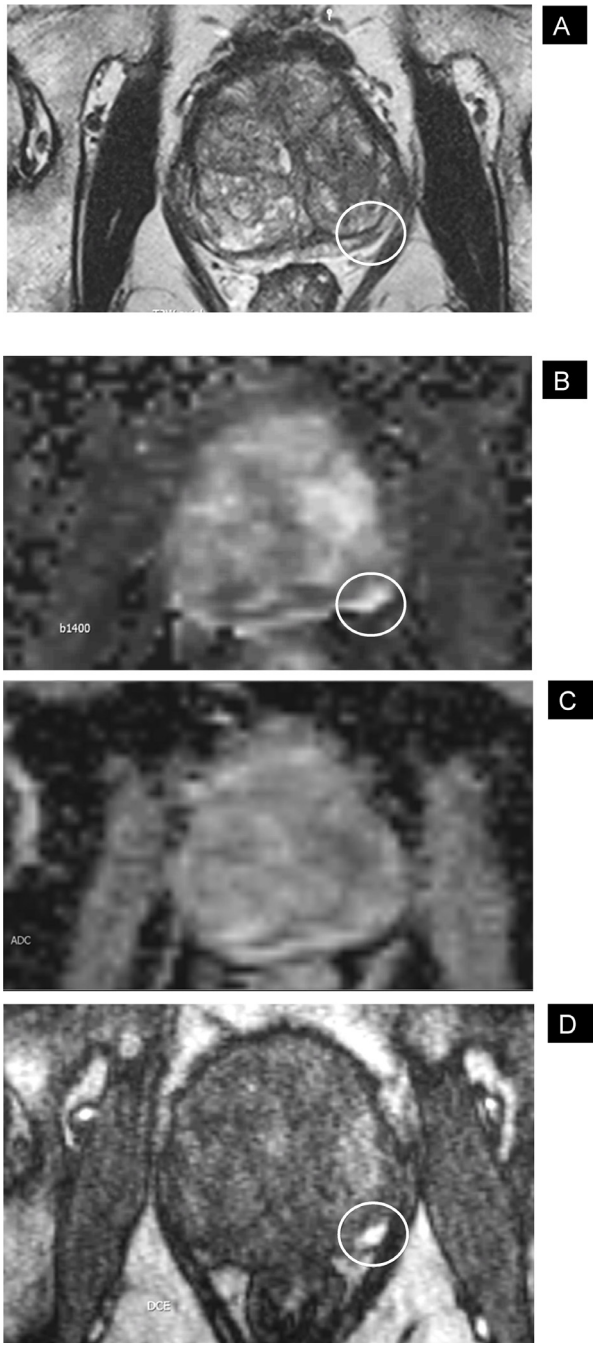

Fig. 1 – High-grade prostate cancer missed on bpMRI. The patient was 74 yr old with prostate-specific antigen of 9.6 ng/mL. Digital rectal examination revealed T0 and the patient had one negative systematic transrectal ultrasound–guided biopsy. bpMRI, consisting of (A) axial T2W, (B) axial DWI b1400, and (C) axial ADC images revealed prospectively no suspicious lesions, only small geographic abnormalities. A PI-RADS score of 2 (T2W/DWI/DCE: 2/2/X) was assigned to the prostate. However, on the (D) "early" DCE image, focal enhancement was identified in the peripheral zone at the 5-o'clock position in the mid-prostate (circle). This focal enhancement was then correlated to focal (A) low T2W and (B) minimal high b1400 signal intensity (circles). The final assessment was PI-RADS 4 (T2W/DWI/DCE: 4/3/+ and upgraded to final score of 4). Transperineal MRI-guided biopsy showed an ISUP grade 4 cancer (Gleason score 4 + 4 = 8). The patient had a successful radical prostatectomy (pT2N0R0, ISUP grade 4). bpMRI = biparametric magnetic resonance imaging; T2W = T2-weighted imaging; DWI = diffusion-weighted imaging; ADC = apparent diffusion coefficient; PI-RADS = Prostate Imaging-Reporting and Data System; DCE = dynamic contrast enhancement; ISUP = International Society of Urological Pathology.

bpMRI, for men with previous prostate treatment, and for men suspected to have cancer recurrence.

This critically appraised PROMIS study represents a great effort. However, additional prospective, randomized or head-to-head multicenter studies using multiple readers and addressing the noninferiority of biopsy yields of MRI-directed biopsies prompted by bpMRI and mpMRI approaches are needed, to confidently recommend bpMRI as the default in PCa diagnosis.

Conflicts of interest: The authors have nothing to disclose.

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