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Platinum Priority – Editorial

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Platinum Opinion Counterview: The Evidence Base for the Benefit of Magnetic Resonance Imaging-directed Prostate Cancer Diagnosis is Sound

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We read with interest the Platinum Opinion by Vickers et al [1] suggesting that the routine use of magnetic resonance imaging (MRI) for early detection of prostate cancer in patients with elevated serum prostate-specific antigen levels, as advised by the urological guidelines, are misguided and not justified by clinical trials evidence. Their arguments focus on the lack of oncological equivalence of cancers found via MRI-directed biopsies (MRDBs) against systematic 10–12-core biopsies (SBs). Furthermore, they comment on the lack of superiority of MRI approaches for detection of higher-grade (grade group [GG] $\geq$2) cancers.

At the onset, it must be noted that the principal well-validated incremental value of prostate-MRI over SB in biopsy-naïve men is not its noninferiority in ruling in GG $\geq$ 2 disease, but its superiority in ruling out GG $\geq$ 2 cancers [2]. The focus of Vickers et al on the lack of superiority of MRI in ruling in GG $\geq$ 2 cancers therefore misses the point.

Prebiopsy prostate MRI has a negative predictive value of 90.8% for noninvasively ruling out GG $\geq$ 2 cancers, with a narrow 95% confidence interval (88.1–93.1%) [3]. This facilitates biopsy avoidance by at least 30% of men and reduces the rate of detection of low-grade (GG 1) cancer in 18% of men, with downstream reductions in overtreatment, while retaining noninferiority for detection of GG $\geq$ 2 cancers [3]. These are the main benefits of using the MRI pathway for biopsy-naïve men.

In addition, Goldberg et al [4] showed that the ability of MRDB to rule in GG $\geq$ 2 cancers is even slightly superior (5–15%) to that of SB. The MRI pathway also provides higher precision and risk stratification for GG $\geq$ 2 tumours than SB does, using fewer targeted biopsy cores per patient with potentially fewer complications [4–6].

These benefits have all been demonstrated in multiple prospective diagnostic studies with level 1A clinical evidence brought together within systematic reviews and meta-analyses, particularly from the Cochrane project [4,7–12]. Consequently, the European Association of Urology and the American Urological Association advised on the upfront use of MRI in biopsy naïve men [13,14]. The predominant challenge in implementing the MRI pathway remains maintaining quality in clinical practice with robust quality control and quality assurance [15].

Vickers and colleagues challenge the biological relevance of cancers detected using the MRI pathway. They make a theoretical abstraction that targeted biopsy cores through the MRI-visible parts of lesions may lead to more over-grading when compared to SB approaches. The sensitivity of MRDB in detecting GG $\geq$ 2 cancer is achieved via the ability to target sampling needles towards the most aggressive part of cancers, recognised as high cell density on diffusion-weighted images [16]. If only a few targeted cores are obtained per MRI-visible lesion, indeed we will assign more

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lesions to higher grades. However, this claim of grade inflation by MRDB has not been shown to occur in practice, as indicated by the systematic analysis by Goel et al [17] and the prospective 4 M study [12]. Both showed that MRDB is more likely to agree with final pathology at whole-mount prostatectomy than SB. Surely this is the goal of all cancer biopsies, to reflect more precisely the actual disease present.

The authors' assertion that there is a Will Rogers phenomenon from prebiopsy MRI is credible. Risk shifts did occur when pathologists stopped reporting Gleason grades 1 and 2, changed the criteria for assigning pattern 4, and changed the way for assigning the total Gleason score. We will continue to see similar risk shifts and stage migration in diagnosis and staging as more accurate imaging such as prostate MRI and advanced body imaging techniques are introduced into practice [18,19]. This is the mandate of clinical research leading to medical advances to improve patient care. However, risk migration is not an argument to stop using more accurate tests. Instead, it calls for recalibration of our existing risk stratification and staging systems, which were built and validated on cohorts for which less accurate techniques were used. With the use of more accurate tools for disease stratification, we are more likely to be able to validate novel fluid biomarkers and, importantly, we stand a chance of finally finding out what significant versus insignificant disease is. It now behoves the medical community to embrace these advances and integrate the superior test results from MRI to improve patient management. Instead of implying that the MRI pathway should not be used because of its assumed overdiagnosis of irrelevant cancers, we should evaluate how we can use the more precise information obtained using this technique [4,12,17,20] to explore what type of cancer really is present in the prostate.

We conclude that MRI-directed diagnosis of prostate cancer represents a paradigm shift for early detection of clinically relevant prostate cancers based on level 1 evidence. Do we need longitudinal cohort studies that would allow us to validate the better cancer granularity from better MRI-directed biopsies, and thus recalibrate our existing risk stratification categories? The answer is yes, without a doubt. However, while waiting for such studies to deliver their fruits, it is unethical to withhold accurate prostate MRI from patients who can immediately benefit from biopsy avoidance and reduction of overdiagnosis. We consider it our imperative to learn from and value the precise and accurate data resulting from MRI.

Conflicts of interest: The authors have nothing to disclose.

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