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AUTHOR REPLY.

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precede biopsy.[1,2] In fact, the 14 men who underwent prebiopsy mpMRI in this cohort were excluded from further analysis. The authors acknowledge postbiopsy hemorrhage contributed to disease inconspicuity in approximately one-third of men (2−3/9) with high-grade disease, however, given this well-established phenomenon, this proportion may be higher.[5] As postbiopsy hemorrhage was accepted and incorporated into this study, it is possible that other radiological features (eg, background patchy/diffuse patterns) may have contributed to reduced tumor conspicuity.

In addition to mpMRI quality, other aspects of this study warrant scrutiny. Of note, 45% (15/33) of men had grade reclassification from random 12-core transrectal ultrasound (TRUS)-guided biopsy to radical prostatectomy (18% downgraded, 27% upgraded). This effect may be attributable to an imperfect reference standard (random TRUS-guided biopsy) which demonstrably overlooks significant cancer approximately half the time.[2] Furthermore, while mpMRI were scored according to PI-RADSv2.1 guidelines, it seems unusual that men with "negative" mpMRI had such high prostate specific antigen densities (eg, 1.08, 0.48, and 0.22 ng/mL/mL) which, in other settings, may have raised radiological suspicion. Unfortunately, a number of key details are missing to fully appraise this study including, biopsy core length, tumor size at prostatectomy, age of MRI machines, number of reporting radiologists and their experience in prostate mpMRI reporting (ie, how many prostate MR scans per year), all of which impact upon tumor detection on mpMRI. Lastly, in their discussion, the authors cite the Prostate MRI Study (PROMIS), proposing that a 10% nondetection rate of significant disease by mpMRI is a "considerable risk," however, they do not quote the false negative rate of systematic TRUS-guided biopsy (their own reference standard), which had a nondetection rate of over 50%, in the same study.[2]

Collectively, we should work toward optimal mpMRI-directed pathway delivery, at every juncture, including scan acquisition, reporting, and biopsy. In an attempt to standardize mpMRI quality, the Prostate Imaging Quality (PI-QUAL) score was developed, based on a 1-to-5 Likert scale derived from evaluation of each sequence, against objective quality criteria in line with the PI-RADSv2 recommendations.[4] Work is currently underway to evaluate effects of PI-QUAL on tumor conspicuity, however, we hope that this scheme provides a starting point for centers to evaluate quality of mpMRI delivery. Alanee et al should be congratulated for adding to the mpMRI literature, expounding links between histopathology and radiology, however, we believe their findings should be cautiously interpreted in light of the methodological issues highlighted here. We agree that long-term ramifications of mpMRI conspicuity remain pressing avenues for future research and we eagerly await results of ongoing work.

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AUTHOR REPLY

We thank the authors of this intriguing letter for their significant interest in our work. They raise essential points that we would like to respond to in detail. The authors' first concern was that, contradictory to "guidelines", the magnetic resonance imaging (MRI) studies included in our analysis were done after prostate cancer was diagnosed with a biopsy, causing bleeding and making it harder to visualize the tumor inside the prostate. The patients included in our study were prostate cancer patients receiving MRI for surgical planning. The "guidelines" the authors refer to is for patients with elevated prostate specific antigen (PSA). Besides, our pathology coauthors (2 fellowship-trained genitourinary pathologists) characterized the tumors that were not visible on MRI and did not notice significant bleeding in the areas of interest.

The authors' second concern was that the reference for upgrading was the random 12-core transrectal ultrasound (TRUS) biopsy. We agree with them that a random TRUS biopsy could underestimate the grade of prostate cancer. However, this study's goal was to characterize MRI invisible tumors, not to look into reasons for upgrading from TRUS biopsy on postprostatectomy pathology, which has been examined by many other papers. We also agree with others that TRUS-biopsy has a high nondetection rate, and we are not advocating against MRI of the prostate in favor of TRUS-guided biopsy. In fact, in the editorial comment we wrote to accompany our paper, we state that MRI provides "essential information during prostate cancer management." Still, we call on providers to consider other clinical variables when interpreting MRI results. The authors mention that elevated PSA density would have made the radiologist suspicious that their MRI may be missing significant cancer, which supports paying attention to clinical variables while MRI technology continues to evolve.

Finally, we would like to highlight 2 recent papers that support our conclusions. In a recent report by Ahdoot et al in the *New England Journal of Medicine*, 2103 men with MRI-visible prostate lesions underwent both MRI-targeted and systematic biopsies. A proportion of them then received treatment with radical prostatectomy. Ahdoot et al then showed that MRI-targeted biopsies misclassified 8.8% of clinically significant cancers.[1] Separately, Westphalen et al conducted a retrospective cross-sectional study across 26 centers treating prostate cancer to estimate the positive predictive value (PPV) of PI-RADS to detect high-grade prostate cancer. The authors estimated the PPV to be 35% for PI-RADS $\geq$ 3 and 49% for PI-RADS $\geq$ 4. The interquartile ranges of PPV at these same PI-RADS score thresholds were 27%-44% and 27%-48%, respectively. They then concluded that the PPV of the PI-RADS was low and varied widely across centers.[2]

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