MRI-Targeted Biopsy for Prostate-Cancer Diagnosis

TO THE EDITOR: In PRECISION (Prostate Evaluation for Clinically Important Disease: Sampling Using Image Guidance or Not?), a multicenter, randomized, noninferiority trial, Kasivisvanathan et al. (May 10 issue)[1] found that magnetic resonance imaging (MRI)–targeted biopsy was superior to standard transrectal ultrasonography–guided biopsy in men at risk for prostate cancer who had not undergone biopsy previously. Of the 246 patients in the MRI-targeted biopsy group, 62 (25.2%) underwent MRI performed with the use of a 1.5-T scanner and 175 (71.1%) had lesion scores of 3 or greater (combined results from 1.5-T and 3.0-T scanners) according to the Prostate Imaging–Reporting and Data System, version 2 (on a scale from 1 to 5, with higher numbers indicating a greater likelihood of clinically significant cancer). Eight centers had a 1.5-T MRI scanner, and only 1 of them used an endorectal coil, whereas 15 centers had a 3.0-T MRI scanner, and 2 of them used an endorectal coil. We think it would be interesting to know how many of the lesions were detected by an MRI performed with a 1.5-T scanner.

In addition, it could be worthwhile to perform sensitivity analyses to exclude any difference attributable to varying magnetic field strengths. Such analyses (one possibly with an endorectal coil and one without an endorectal coil, if numbers allow that) could also confirm the equivalence of both magnet strengths to detect clinically significant cancer.

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1. Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378:1767-77.

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TO THE EDITOR: Urologists have been performing transrectal ultrasonography–guided prostate biopsies for decades. The results of the PRECISION trial suggest that urologists have not been detecting large numbers of the most aggressive cancers. These cancers are graded according to the Gleason score, which is composed of a primary (most predominant) grade plus a secondary (highest nonpredominant) grade; the range for a primary or secondary grade is from 3 to 5, with the Gleason sum ranging from 6 to 10, and with higher scores indicating a more aggressive form of prostate cancer. The annual incidence of prostate cancer in the United States is 165,000 cases,[1] and approximately 50% of biopsies to detect prostate cancer are positive. Thus, in the PRECISION trial, an absolute risk difference of 5.5 percentage points between the MRI-targeted biopsy group and the standard-biopsy group for cancers of Gleason sum 8 to 10 suggests that urologists have been missing approximately 20,000 such cancers every year for decades.

So where are all the bodies? If transrectal ultrasonography–guided biopsy missed so many of the worst cancers, we would expect that it would be routine for patients in our clinics to present with metastatic disease a few years after a negative biopsy. But such cases are extremely rare. In a Danish Cancer Registry study based on data from men with negative biopsy results and a prostate-specific–antigen level of less than 10 ng per milliliter (the level in the majority of participants in the PRECISION trial), the cumulative incidence of prostate cancer–specific death was 0.7% at 15 years.[2]

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Dr. Vickers reports being named on a patent for a statistical method and apparatus for predicting the risk of prostate cancer and prostate gland volume (US9672329B2, commercialized as the 4Kscore test by OPKO Health) and receiving royalties from and having stock options in OPKO Health. No other potential conflict of interest relevant to this letter was reported.

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2018. CA Cancer J Clin 2018;68:7-30.
2. Klemann N, Røder MA, Helgstrand JT, et al. Risk of prostate cancer diagnosis and mortality in men with a benign initial transrectal ultrasound-guided biopsy set: a population-based study. Lancet Oncol 2017;18:221-9.

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THE AUTHORS REPLY: We agree with Martini et al. that it is useful to know the differences in the performance of 1.5-T and 3.0-T MRI machines. We allowed both coil strengths as part of the pragmatic trial design. Of note, we did not power

the trial to assess for differences in clinically significant cancer in the subgroups with different coil strengths. Eighteen of 62 men in the 1.5-T MRI group (29%; 95% confidence interval [CI], 19 to 41) and 75 of 184 men in the 3.0-T MRI group (41%; 95% CI, 34 to 48) had clinically significant cancer. Since men were not randomly assigned to undergo MRI performed with 1.5-T or 3.0-T scanners, the differences observed may be confounded by other factors. The Prostate MRI Imaging Study (PROMIS), a multicenter study involving 576 men, used only 1.5-T MRI machines and showed that MRI was superior to transrectal ultrasonography–guided prostate biopsy for the detection of clinically significant cancer.[1]

We agree with Vickers and Ehdaie that urologists have been performing transrectal ultrasonography–guided biopsies for decades, but we would assert that tradition alone is an insufficient reason not to change practice in the face of growing scientific evidence. Transrectal ultrasonography–guided biopsy has been shown to miss more than 50% of clinically significant cancers in men.[1] Many men undergo repeat transrectal ultrasonography–guided biopsy, with a 2 to 4% risk of sepsis and costs to health services.[2] The Danish Cancer Registry study cited by Vickers et al. showed that in 17% of men with negative results on transrectal ultrasonography–guided biopsy who underwent repeat biopsy, prostate cancer of Gleason sum 8 was missed.[3] This is undesirable for a diagnostic test. In the PRECISION trial, with the use of the same threshold for clinically significant cancers as described by Vickers et al., MRI with or without targeted biopsy detected 6% (95% CI, 1 to 10) more cancers of Gleason sum 8 or worse than transrectal ultrasonography–guided biopsy. In addition, 13% (95% CI, 7 to 19) fewer men in the MRI-targeted biopsy group than in the standard-biopsy group received a diagnosis of clinically insignificant cancer — a diagnosis that can lead to considerable overtreatment and harm to men. Other studies have also shown that MRI-targeted biopsy detects more clinically significant cancer and less clinically insignificant cancer than transrectal ultrasonography–guided biopsy.[4] We acknowledge that there is uncertainty as to the prognosis of clinically significant cancer identified by MRI-targeted biopsy,[5] although future studies, and not conjecture, may ascertain the risk of death among these patients.

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Since publication of their article, the authors report no further potential conflict of interest.

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5. Robertson NL, Hu Y, Ahmed HU, Freeman A, Barratt D, Emberton M. Prostate cancer risk inflation as a consequence of image-targeted biopsy of the prostate: a computer simulation study. Eur Urol 2014;65:628-34.

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Single-Inhaler Triple versus Dual Therapy in Patients with COPD

TO THE EDITOR: In the randomized Informing the Pathway of COPD Treatment (IMPACT) trial involving more than 10,000 patients with chronic obstructive pulmonary disease (COPD), Lipson and colleagues (May 3 issue)[1] compared a once-daily combination of fluticasone furoate (an inhaled glucocorticoid), umeclidinium (a long-acting muscarinic antagonist [LAMA]), and vilanterol (a long-acting β_2-agonist [LABA]) with an inhaled glucocorticoid–LABA or a LABA–LAMA combination. The primary outcome was the annual rate of moderate or severe COPD exacerbations. Since a large fraction of COPD exacerbations are infectious in origin,[2] we wonder whether there were any differences among the three groups with respect to the proportion of patients who