available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Letter to the Editor

Reply to Roderick C.N. van den Bergh, Olivier Rouvière, and Theodorus van der Kwast's Letter to the Editor re: Andrew Vickers, Sigrid V. Carlsson, Matthew Cooperberg. Routine Use of Magnetic Resonance Imaging for Early Detection of Prostate Cancer Is Not Justified by the Clinical Trial Evidence. Eur Urol. In press. https://doi.org/10.1016/j.eururo.2020.04.016. Prebiopsy MRI: Through the Looking Glass

We would like to thank Dr. van den Bergh and the members of the EAU-EANM-ESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel for their interest in our editorial [1]. They make three main points. First, they correctly assert that while men with negative systematic biopsy have extremely low long-term prostate cancer–specific mortality if prostate-specific antigen (PSA) is moderate, mortality after negative biopsy is dramatically higher for men with higher PSA (eg, >10 ng/ml) [2]. We concur, and indeed this fully supports our argument that although magnetic resonance imaging (MRI) has some clear clinical indications for early detection of prostate cancer, it should not be used routinely before first biopsy. For instance, if a man has negative biopsies at PSA levels of 7 and 12 ng/ml, and now has PSA of 17 ng/ml, it is likely that a systematic biopsy missed an important cancer and we need to carry out MRI to find it. However, longitudinal evidence does not suggest that a man with moderately elevated PSA is at important risk of prostate cancer mortality if a systematic biopsy is negative, and so there is no justification for routine MRI-targeted biopsy in such a man.

Second, the authors point out that MRI may be of value because it has the "potential" to "dramatically decrease" the number of unnecessary biopsies. Again we agree, particularly because of the use of the word "potential". To fulfill that potential, however, further research would need to demonstrate that: first, the reduction in biopsy rates was indeed "dramatic" (in the recent National Cancer Institute study [3] only approximately 20% of men avoided biopsy); second, that MRI had a consistently high negative predictive value (a recent systematic review [4] and multicenter study both showed massive variation between centers [5]); and third, that urologists would forgo systematic biopsy after negative MRI, despite European Association of Urology guidelines that the evidence for doing so is weak [6].

Third, the authors suggest that the problem is not so much to do with MRI but with the associated treatment guidelines: it is not the MRI that is doing the harm by finding indolent grade group 2 cancers that would have been missed by systematic biopsy; the harm is caused by guidelines telling us to treat most of those cancers. Again, we have great sympathy with this argument. However, the point is that treatment guidelines incorporating the method of detection have not been written and it is unclear what the current evidence would be for such guidelines. The authors state that "the urological community should adapt risk classification in order to correctly separate the wheat from the chaff in the MRI era". Our point is that this has not been done yet and we are not actually sure how to do it.

In sum, neither the clear and obvious value of MRI in certain clinical indications, such as persistently elevated or rising PSA after a negative biopsy, the "potential" of MRI to reduce unnecessary biopsy, nor the possibility that MRI could mitigate overtreatment (pending changes in guidelines) warrants the routine use of prebiopsy MRI at the current time.

Conflicts of interest: Andrew Vickers is named on a patent for a statistical method to detect prostate cancer that has been commercialized by OPKO Health and receives royalties from sales of the test and has stock options in OPKO Health. Sigrid Carlsson has received a lecture honorarium and travel support from Astellas Pharma (unrelated to the current study). Matthew Cooperberg has nothing to disclose.

Acknowledgments: This work was supported in part by the National Institutes of Health/National Cancer Institute (NIH/NCI) via a Cancer Center Support Grant to Memorial Sloan Kettering Cancer Center (P30 CA008748), a SPORE grant in Prostate Cancer to Dr. H. Scher (P50-CA92629), the Sidney Kimmel Center for Prostate and Urologic Cancers, and David H. Koch through the Prostate Cancer Foundation.

References

[1] Vickers A, Carlsson SV, Cooperberg M. Routine use of magnetic resonance imaging for early detection of prostate cancer is not justified by the clinical trial evidence. Eur Urol. In press. https://doi.org/10.1016/j.eururo.2020.04.016.

DOIs of original articles: https://doi.org/10.1016/j.eururo.2020.05.038, https://doi.org/10.1016/j.eururo.2020.06.023.
https://doi.org/10.1016/j.eururo.2020.06.059

[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.
[3] Ahdoot M, Wilbur AR, Reese SE, et al. MRI-targeted, systematic, and combined biopsy for prostate cancer diagnosis. N Engl J Med 2020;382:917–28.
[4] Sathianathen NJ, Omer A, Harriss E, et al. Negative predictive value of multiparametric magnetic resonance imaging in the detection of clinically significant prostate cancer in the Prostate Imaging Reporting and Data System era: a systematic review and meta-analysis. Eur Urol. In press. https://doi.org/10.1016/j.eururo.2020.03.048.
[5] Westphalen AC, McCulloch CE, Anaokar JM, et al. Variability of the positive predictive value of PI-RADS for prostate MRI across 26 centers: experience of the Society of Abdominal Radiology Prostate Cancer Disease-focused Panel. Radiology. In press. https://doi.org/10.1148/radiol.2020190646.
[6] Mottet N, Bellmunt J, Briers E, et al. EAU-ESTRO-ESUR-SIOG guidelines on prostate cancer. Arnhem, The Netherlands: European Association of Urology; 2020.

Andrew Vickers[a,*]
Sigrid V. Carlsson[a,b,c]
Matthew Cooperberg[d]

[a]*Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, New York, NY, USA*
[b]*Urology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA*
[c]*Department of Urology, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*
[d]*Department of Urology, University of California—San Francisco, San Francisco, CA, USA*

*Corresponding author. Department of Epidemiology and Biostatistics, Memorial Sloan Kettering Cancer Center, 485 Lexington Avenue, New York, NY 10065, USA. Tel.: +1 646 8888233; Fax: +1 929 3211516.
E-mail address: vickersa@mskcc.org (A. Vickers).

June 24, 2020