

## COMMENTARY

# Magnetic resonance imaging diagnosis of prostate cancer: promise and caution

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Among solid-organ tumours, prostate cancer is alone in being diagnosed via a nontargeted biopsy approach. Systematic transrectal ultrasonography-guided biopsy has

### KEY POINTS

- Randomized controlled trial evidence supports the introduction of been the standard of care to detect clinically important prostate

magnetic resonance imaging (MRI) for biopsy-naive men with cancer since 1989.<sup>1</sup> Yet modern image acquisition and quantifica-

suspected prostate cancer to improve detection of clinically tion with magnetic resonance imaging (MRI) has recently been shown to delineate prostatic disease accurately, reprodu cibly and noninvasively.<sup>2,3</sup> Is it now time to proceed to widespread use of MRI to diagnose and stage prostate cancer in Canada?

Recently, the PRECISION (PRostate Evaluation for Clinically

important cancer, decrease the overdiagnosis and treatment of clinically unimportant cancer, and avoid biopsy for men at low risk.

- However, poor interobserver reliability and reproducibility, unknown long-term follow-up and natural history of MRI- detected lesions, and current capacity limitations in the Canadian context suggest that caution is warranted in Important Disease: Sampling Using Image-guidance Or Not?) ran-

implementing services. domized controlled trial<sup>2</sup> and the PROMIS (PROstate Magnetic reso-

- Implementation would be challenging within the universally nance Imaging Study) prospective paired validation study<sup>3</sup> investi-

funded Canadian health care system; initially, rollout at high- gated MRI imaging as the first step in evaluating suspected prostate cancer. In the PRECISION trial, 500 men with clinically suspected prostate cancer were randomly allocated across academic and

volume cancer centres would be prudent to ensure appropriate patient selection, image interpretation and accuracy of targeted biopsy, while a robust knowledge translation strategy for primary care and specialist physicians would minimize confusion. community sites to undergo MRI (with or without targeted biopsy, depending on the MRI findings) or systematic biopsy.<sup>2</sup> Magnetic res- onance imaging was found to be noninferior to traditional biopsy in the detection of clinically important prostate cancer (38% v. 26%, 95% confidence interval 4%–20%), with the confidence interval indi- cating superiority of the MRI strategy. Overdiagnosis of clinically unimportant prostate cancer was reduced (9% v. 22%), and biopsy was avoided in 28% of those in the MRI group. In PROMIS, MRI out- per formed systematic biopsy in sensitivity (93% v. 48%), negative predictive value (89% v. 74%) and biopsy avoidance for men at low risk (27%), and showed probable cost-effectiveness.<sup>3</sup> These findings have prompted consideration of funding for MRI diagnosis in biopsy- naive men with suspected prostate cancer, as well as revision of clinical guidelines, in Canada and beyond.<sup>4</sup> However, caution is warranted before considering changing guidelines and health care services. The aforementioned studies included men with higher prostate-specific antigen (PSA) levels (6.8– 7.1 ng/mL), and therefore higher pretest probability of cancer, than those in men in contemporary Canadian biopsy cohorts,<sup>5</sup> which impairs generalizability of the findings. This effect is evident when reviewing the higher rates of detection of clinically important cancer observed in the PRECISION trial versus those at a tertiary Canadian centre (12%/60%/83% v. 6%/33%/64% for stage 3 [intermediate risk], 4 [high risk] and 5 [very high risk] lesions, respectively, using Prostate Imaging-Reporting and

Data System [PI-RADS] version 2).<sup>6</sup>

Furthermore, poor interobserver reliability and reproducibility are concerning. In the PRECISION trial's quality-control group, 24/64 men (38%) had discordant classification in MRI grading between local and central review; of the 24 cases, 14 (58%) would have changed management.<sup>2</sup> Low interrater agreement may impede clinical decision-making, and patients' experience of uncertainty and anxiety may erode their confidence in the health care service.<sup>7</sup> Until the risk of misclassification (particularly the failure to identify high-risk lesions) decreases, we should be cautious in adopting MRI as the standard of diagnosis. Centralized subspecialist review may be necessary.

Longer-term prognosis and natural history of disease following MRI diagnosis and staging are unknown. Strategies and risk calculators are under development. Questions remain regarding the conversion rate over time from negative to positive MRI findings, the evolutionary potential of PI-RADS stage 1 or 2 ("negative") lesions and the necessity of repeat or confirmatory testing following negative findings on MRI. Small retrospective studies show wide variability in the progression or regression of lesions and the appearance or disappearance of new lesions on repeat MRI.<sup>8</sup> Similarly, for patients with positive MRI findings, consensus on the threshold to biopsy has not been reached: many lesions at PI-RADS stage 3 are indeterminate, with low biopsy yields.<sup>2,3</sup>

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In 2018, the Canadian Agency for Drugs and Technologies in Health reviewed the cost-effectiveness of MRI diagnosis in men with suspected prostate cancer.<sup>9</sup> Initially, owing to low availability, MRI was offered by specialized clinicians and cancer centres to a limited number of patients. Data from a prospective study of MRI and targeted biopsy (PI-RADS stage 4–5). Performing tests at high-volume centres would accelerate learning and optimize reliability of interpretation. A randomized trial of active surveillance of prostate cancer showed that the positive predictive value for MRI was 8%–10% at 2 Canadian sites versus 33% at a third, most experienced site.<sup>12</sup> Variability in outcomes depends on both MRI interpretation and targeted biopsy performance: if a lesion is identified from specialized radiologic review, adequate communication of MRI series or image number and lesion location to the biopsy performer must follow. Delivery is optimized at high-volume centres, through use of efficient protocols to reduce cost and waiting time, and quality-assurance programs to ensure acceptable aggregate rates. Finally, given that much confusion already exists around screening using PSA, any introduction of MRI as a diagnostic service will require careful knowledge translation and communication across primary care and specialist physicians.

Prostate cancer is prevalent, and recommendations for wide-spread adoption of MRI diagnosis would need to take into account variability in access to MRI services. Magnetic resonance imaging is an investment-, time- and skill-intensive resource. Waiting times in Ontario for nonurgent MRI currently average 2 months, and MRI is completed within provincial targets less than 29% of the time (Appendix 1, available at [www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.190568/-/DC1](http://www.cmaj.ca/lookup/suppl/doi:10.1503/cmaj.190568/-/DC1)). Introducing MRI as the standard for prostate cancer diagnosis would likely increase wait times for all, and delays in prostate cancer diagnosis could affect treatment outcomes, especially for patients at high risk.<sup>10</sup> If the system is unable to bear an increased demand for MRI diagnosis, core tenets of the *Canada Health Act* — timely care and delivery and accessibility — would be compromised. Uptake of breast MRI has been hampered by similar concerns of high cost, availability and burden to the system, despite evidence of excellent diagnostic accuracy.<sup>11</sup> Magnetic resonance imaging has the potential to revolutionize the way we diagnose and manage prostate cancer.

However, thoughtful integration of MRI into the diagnostic algorithm may be possible using a multipillar framework comprising patient risk stratification, MRI order stratification, high-volume centres, efficient protocols and careful knowledge translation. Judicious consideration of patient appropriateness for MRI would help ease demand for testing and ensure that those who could benefit are given priority. Patients at very high risk (PSA level > 20 ng/mL, palpable extraprostatic extension or cT3+) could proceed straight to biopsy and treatment, as MRI will likely not alter management. Similarly, patients with several comorbidities or life expectancy less than 10 years would be unlikely to benefit. Hence suggests that we can identify and target lesions with increasing accuracy, spare patients unnecessary biopsy, decrease diagnosis and treatment of clinically unimportant cancer, and improve the detection of clinically important cancer. Prebiopsy MRI would help ease demand for testing and ensure that those who suspected prostate cancer is currently under consideration for approval in Canada. However, the long-term impact of this approach remains unknown, and it is not clear that large service changes are currently possible in the Canadian setting. Responsible and practical implementation of MRI diagnosis for prostate cancer in Canada will require patient and MRI order stratification, rollout at

high-volume centres and clear knowledge-translation efforts.

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