

Guideline #27-2 BEING UPDATED

A Quality Initiative of the
Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Multiparametric Magnetic Resonance Imaging in the Diagnosis of Clinically Significant Prostate Cancer

*M.A. Haider, X. Yao, D.A. Loblaw, A. Finelli, and the MRI in Prostate Cancer Guideline
Development Group*

Report Date: August 5, 2015

CAUTION

As of March 2019, recent evidence indicates that Recommendation 1 requires revision. An updated version of this guideline is in progress.

It is still appropriate for this document to be available while this updating process unfolds. The PEBC has a formal and standardized process to ensure the currency of each document ([PEBC Assessment & Review Protocol](#))

Guideline 27-2 is comprised of 3 sections. You can access the summary and full report here:

<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/281>

Section 1:	Guideline Recommendations
Section 2:	Evidentiary Base
Section 3:	Guideline Development Methods and Review Process

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PEBC Guideline Related Journal Citations:

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Guideline #27-2: Section 1

A Quality Initiative of the Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

Multiparametric Magnetic Resonance Imaging in the Diagnosis of Clinically Significant Prostate Cancer: Guideline Recommendations

*M. A. Haider, X. Yao, D.A. Loblaw, A. Finelli, and the MRI in Prostate Cancer Guideline
Development Group*

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GUIDELINE OBJECTIVES

1. To make recommendations with respect to the use of multiparametric magnetic resonance imaging (MPMRI) in the diagnosis of clinically significant prostate cancer in patients with an elevated risk of clinically significant prostate cancer (according to prostate-specific antigen [PSA] level and/or nomograms) who are biopsy-naïve.
2. To make recommendations with respect to the use of MPMRI in the diagnosis of clinically significant prostate cancer in patients with a growing risk of having clinically significant prostate cancer (e.g., continued rise in PSA) who had a negative transrectal ultrasound-guided (TRUS-guided) systematic biopsy.

TARGET POPULATION

Patients with an elevated risk of clinically significant prostate cancer (according to PSA level and/or nomograms) who are biopsy-naïve or have a prior negative TRUS-guided systematic biopsy.

INTENDED USERS

Radiologists, family physicians, oncologists, urological surgeons, and other clinicians who provide care for patients defined by the target population.

RECOMMENDATIONS, KEY EVIDENCE, AND JUSTIFICATION

Recommendation 1

In patients with an elevated risk of clinically significant prostate cancer (according to PSA level and/or nomograms) who are biopsy-naïve:

- MPMRI followed by targeted biopsy (biopsy directed at cancer-suspicious foci detected with MPMRI) should not be considered the standard of care.
- Data from future research studies are essential and should receive high-impact trial funding to determine the value of MPMRI in this clinical context.

Key evidence and quality

- Eight studies [1-8] that met our preplanned study selection criteria addressed the first objective. The quality of evidence was poor to moderate (for details see Appendices II

and III in Section 2). Meta-analyses of the study results were not feasible because of high clinical heterogeneity among studies using different definitions for clinically significant prostate cancer and for positive MPMRI results, and different MPMRI navigational systems and MPMRI techniques.

- In two studies [4,6] with a prevalence of clinically significant prostate cancer of 21% to 30%, the ranges of sensitivity, specificity, positive predictive value, and negative predictive value of MPMRI to detect clinically significant prostate cancer were 68% to 94%, 21% to 72%, 24% to 50%, and 83% to 94%, respectively.
- Clinically significant prostate cancer detected by MPMRI followed by targeted biopsy but not by TRUS-guided systematic biopsy ranged from 2% to 13% and clinically significant prostate cancer detected by TRUS-guided systematic biopsy but not by MPMRI followed by targeted biopsy ranged from 0% to 7% in five studies with a total of 1388 patients [1,3,5,7,8].
- A randomized controlled trial (RCT) by Park et al [2] found that MPMRI followed by targeted biopsy plus TRUS-guided systematic biopsy identified more clinically significant prostate cancer patients than TRUS-guided systematic biopsy alone in 85 patients (11 of 44 = 25% versus two of 41 = 5%, $p = 0.01$; but 10 of 11 clinically significant prostate cancer patients were detected by TRUS-guided systematic biopsy alone in the combination group of MPMRI followed by targeted biopsy and TRUS-guided systematic biopsy).
- Pokorny et al [8] (using radical prostatectomy for confirmation) reported that four patients (5%) were upgraded to clinically significant prostate cancer category and 11 (15%) were downgraded to non-clinically significant prostate cancer category by MPMRI followed by targeted biopsy; four patients (5%) were upgraded to clinically significant prostate cancer and 18 (24%) were downgraded to non-clinically significant prostate cancer by TRUS-guided systematic biopsy.
- Pokorny et al [8] reported that 0.9% of patients developed urosepsis, and 0.4% required admission for hematuria after TRUS-guided systematic biopsy; and 0.7% experienced a vasovagal episode after MPMRI followed by targeted biopsy.
- No patient outcomes regarding a positive change in patient management or survival were reported.

Justifications (considering and balancing clinical benefits and harms)

The Working Group (the guideline authors) does not recommend MPMRI followed by targeted biopsy as a standard care in Ontario for the target population because of the following reasons:

- The quality of evidence was poor to moderate;
- Specificity and positive predictive value of MPMRI were not high;
- The detection rates from MPMRI followed by targeted biopsy were not consistently higher than TRUS-guided systematic biopsy in the eligible studies;
- Although cost-effectiveness and resource allocation issues are beyond the scope of this Program in Evidence-Based Care (PEBC) guideline, the Working Group was sensitive to the fact that there are limited MRI resources in Ontario and that these recommendations address a large target population: patients with an elevated risk of clinically significant prostate cancer (according to PSA level and/or nomograms) who are biopsy-naïve.

Although an RCT [2] reported that MPMRI followed by targeted biopsy plus TRUS-guided systematic biopsy detected a statistically significant higher rate of clinically significant prostate cancer than TRUS-guided systematic biopsy alone, the study quality was low (no details of randomization methods, no expected effect, power, and sample size calculation, etc.) and TRUS-guided systematic biopsy alone in the combination group detected

significantly more patients with clinically significant prostate cancer than the TRUS-guided systematic biopsy group. The Working Group was therefore concerned regarding reproducibility of these data until another properly designed and powered RCT was to be completed.

Other consideration

Patient preference: The patients should be informed of the possibility of false-negative results from TRUS-guided systematic biopsy, and the potential complications from biopsy.

Recommendation 2

In patients who had a prior negative TRUS-guided systematic biopsy and demonstrate a growing risk of having clinically significant prostate cancer (e.g., continued rise in PSA levels):

- MPMRI followed by targeted biopsy may be considered to help in detecting more clinically significant prostate cancer patients compared with repeated TRUS-guided systematic biopsy.

Key evidence and quality

- Seven studies [9-15] that met our preplanned study selection criteria addressed the second objective. The quality of evidence was poor to moderate (for details see Appendix II in Section 2). Meta-analyses of the study results were not feasible because of high clinical heterogeneity among studies using different definitions for clinically significant prostate cancer and for positive MRI results, and different MRI navigational systems and MRI techniques.
- In three studies (n = 570) [9,13,14] with a prevalence of clinically significant prostate cancer of 18% to 34%, the ranges of sensitivity, specificity, positive predictive value, and negative predictive value of MPMRI to detect clinically significant prostate cancer were 68% to 100%, 41% to 91%, 29% to 87%, and 79% to 100%, respectively.
- MPMRI followed by targeted biopsy detected more clinically significant prostate cancer patients than repeated TRUS-guided systematic biopsy in all four studies with total 516 patients [10-12,15], but only one small sample size study reached a statistically significant difference [12] (n = 38) (24% versus 5%, p = 0.02). Clinically significant prostate cancer detected by MPMRI followed by targeted biopsy but not by repeated TRUS-guided systematic biopsy ranged from 2% to 21% and clinically significant prostate cancer detected by repeated TRUS-guided systematic biopsy but not by MPMRI followed by targeted biopsy ranged from 0% to 5% in four studies.
- The Hoeks et al 2012 study [9] stated 0.4% of patients had sepsis and 1.5% experienced a vasovagal reaction after MRI-guided targeted biopsy. No patients had significant complications that needed hospital admission from saturation biopsy in the Pepe et al 2013 study [13].
- No patient outcomes regarding positively changing patient management or survival outcomes were reported.

Justifications (considering and balancing clinical benefits and harms)

For patients who had a prior negative TRUS-guided systematic biopsy and continue to have a growing risk of clinically significant prostate cancer, although the quality of evidence was poor to moderate and specificity and positive predictive value of MPMRI were not high, all the eligible studies supported the notion that MPMRI followed by targeted biopsy detected a higher number of clinically significant prostate cancer when compared with repeated TRUS-guided systematic biopsy. However, most studies did not reach a statistical difference. Furthermore, the variability in definitions of MPMRI-positive results and clinically significant prostate cancer, and the variability of MPMRI techniques (including different magnet

strength, sequences, MPMRI navigational system, etc.) and radiologists' clinical experience, added more uncertainty to using MRI in the diagnosis of clinically significant prostate cancer. Thus, the Working Group members recommend that MPMRI followed by targeted biopsy may be considered to aid in detecting more clinically significant prostate cancer patients compared with repeated TRUS-guided systematic biopsy in the target population, but should not be a reflexive next step in this population. It should be considered only for those patients who demonstrate a growing risk over time after the first negative biopsy.

Other considerations

Patient preference: Patients and their care providers are faced at times with a rising PSA level and a previous negative biopsy(s). Clinicians together with patients should decide whether MPMRI followed by targeted biopsy should be offered in conjunction with re-TRUS-guided systematic biopsy after weighing the potential benefit of improved detection rates of clinically significant prostate cancer against the extra cost and potential side effects associated with more biopsy cores than re-TRUS-guided systematic biopsy or MPMRI followed by targeted biopsy alone. Patients should be informed of the possibility of false-negative and false-positive results with MPMRI followed by targeted biopsy and/or repeated TRUS-guided systematic biopsy, and the potential complications of prostate biopsy.

Resource use: Cost-effectiveness is beyond the scope of the PEBC guideline; the Working Group leaves resource consideration to other decision makers.

Before MRMRI is used in the clinical practice, diagnostic performance in each centre should be assessed and physicians should be familiar with current international prostate MRI performing and reporting standards [16].

RELATED PEBC GUIDELINES

1. #17-9 Active surveillance for the management of localized prostate cancer (<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/2286>)
2. #27-3 Magnetic resonance imaging in staging for prostate cancer (<https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/606>)

UPDATING

All PEBC documents are maintained and updated through an annual assessment and subsequent review process. This is described in the PEBC Document Assessment and Review Protocol, available on the CCO website at: <https://www.cancercareontario.ca/sites/ccocancercare/files/assets/CCOPEBCDARP.pdf?redirect=true>

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