Brief Correspondence

Risk Stratification and Artificial Intelligence in Early Magnetic Resonance Imaging–based Detection of Prostate Cancer

Maarten de Rooij a,*, Hendrik van Poppel b, Jelle O. Barentsz a

a Department of Medical Imaging, Radboud University Medical Center, Nijmegen, The Netherlands; b Department of Development and Regeneration, University Hospital KU Leuven, Leuven, Belgium

Abstract

Magnetic resonance imaging (MRI) has transformed the diagnostic pathway for prostate cancer and now plays an upfront role before prostate biopsies. If a suspicious lesion is found on MRI, the subsequent biopsy can be targeted. A sharp increase is expected in the number of men who will undergo prostate MRI. The challenge is to provide good image quality and diagnostic accuracy while meeting the demands of the expected higher workload. A possible solution to this challenge is to include a suitable risk stratification tool before imaging. Other solutions, such as smarter and shorter MRI protocols, need to be explored. For most of these solutions, artificial intelligence (AI) can play an important role. AI applications have the potential to improve the diagnostic quality of the prostate MRI pathway and speed up the work.

Patient summary: The use of prostate magnetic resonance imaging (MRI) for diagnosis of prostate cancer is increasing. Risk stratification of patients before imaging and the use of shorter scan protocols can help in managing MRI resources. Artificial intelligence can also play a role in automating some tasks.

Early detection of prostate cancer

Screening in a formal sense is not used for detection of prostate cancer (PCa). In 2012, the United States Preventive Services Task Force recommended against the use of a serum prostate-specific antigen (PSA)-based screening program for PCa because the expected disadvantages outweigh the possible advantages [1]. Systematic use of a PSA test for men in a certain age group (eg, all men aged >55 yr) would lead to overdiagnosis and thus overtreatment of many indolent tumors and underdiagnosis of some clinically significant PCa, mainly because of the low sensitivity and specificity of the PSA test. In addition, many men would undergo an unnecessary biopsy. Thus, it was advised not to use the PSA test until men are well informed about the expected advantages and disadvantages. Similar recommendations were included in the European Association of Urology (EAU) guidelines [2]. However, these recommendations were based on a conventional diagnostic strategy, in which systematic transrectal ultrasound (TRUS)-guided biopsies were used to find the cause of the elevated PSA without the use of risk stratification tools such as multivariable risk calculators and prostate magnetic resonance imaging (MRI).

In recent years, MRI has transformed the PCa diagnostic pathway on the basis of studies that include the PROMIS
verification trial, the randomized international PRECISION trial, a multicenter Canadian trial, and head-to-head comparisons of systematic versus MRI-directed biopsy [3–9]. Taken together, the evidence indicates that MRI before biopsy can allow one-third of men to avoid an immediate biopsy and can reduce overdiagnoses, with 40% fewer clinically indolent PCa and approximately 15% more clinically significant PCa cases detected. The recent EAU guidelines include MRI in an upfront role before prostate biopsies [10].

Given the changes in the PCa diagnostic pathway, with prostate MRI performed before biopsies, a sharp increase in the number of men who will undergo prostate MRI is expected. Although MRI is not used in a formal screening setting, the increased use of diagnostic tests will lead to challenges in providing good image quality and diagnostic accuracy while meeting the demands of the expected higher workload. Here we provide a brief overview of possible solutions to these challenges. These include better risk stratification before imaging and adaptations of the MRI pathway, with shorter and faster MRI protocols. We also discuss the role that artificial intelligence (AI) might play in this clinical setting.

**Strategies to maintain high diagnostic quality and reduce the workload**

**Better upfront patient selection**

A first step to overcome the above challenges is to use better risk stratification tools before imaging. Van Poppel and colleagues [11–13] proposed a diagnostic pathway with personalized risk stratification for early detection of PCa in well-informed men, called PCa Screening 2.0. It is expected that this pathway could provide a more favorable balance between the harms and benefits of early detection. The initial step is to use a PSA test for well-informed men according to age-based PSA interval testing. In cases of PSA elevation, men will be further stratified using risk calculators [14]. If there is a higher risk of PCa, MRI will be performed. Targeted biopsy is only performed in men with lesions with a Prostate Imaging–Reporting and Data System (PI-RADS) score of 4 or 5, and for PI-RADS 3 lesions with unfavorable clinical characteristics (PSA >10 ng/ml and/or PSA density >0.15 ng/ml/cm³). Although the EAU guidelines recommend both targeted and systematic biopsies in cases with positive MRI findings (PI-RADS 4 or 5), additional grade group ≥2 tumors detected with systematic biopsy are predominantly located on the same side as the region of interest on prostate MRI, which supports a targeted or “focal saturation” approach [15,16]. Increasing evidence shows that systematic biopsies can be avoided in cases of negative (PI-RADS 1 or 2) or equivocal MRI (PI-RADS 3) findings without additional risk factors (PSA level, family history, age, digital rectal examination findings) [17].

At what cost will the use of risk calculators reduce the number of negative MRI scans? Risk stratification will never be perfect and has the consequence of clinically significant PCa being missed [18]. There are similar challenges when using next-generation biomarkers such as the SelectMDx test. This test can also reduce the number of negative MRI findings, but with comparable concerns regarding clinically significant tumors being missed [19]. It is a challenge to find the optimal balance between a more costly pathway with a higher MRI burden and a more affordable pathway with fewer MRI scans and fewer unnecessary biopsies, at the cost of missing a few more significant cancers. Cost-effectiveness analyses might be helpful for stakeholders such as policy-makers and clinicians in making well-informed decisions on the best diagnostic strategies [20]. When using risk calculators, it must be noted that the results depend heavily on the prevalence of the disease. Therefore, a good risk calculator should be carefully calibrated to match the target population.

**Better radiology workflow**

It is evident that with the changing guidelines there will be an increase in the number of men who will have to undergo a prostate MRI. This will lead to increased pressure especially on the regular radiology program. One of the solutions is to shorten and simplify prostate MRI-protocols. Optimal multiparametric MRI of the prostate consists of three different sequence types [21]: a T2-weighted sequence in a minimum of two planes, a diffusion-weighted sequence, and a dynamic contrast-enhanced (DCE) sequence. The omission of DCE in so-called biparametric MRI (bpMRI) results in shorter scan times and can thus reduce capacity problems. Most importantly, a noncontrast protocol can be performed without a radiologist outside of office hours. In addition, the examination without contrast is less invasive, as it does not require intravenous access or contrast injection. But is this possible without being accompanied by lower accuracy? Emerging evidence shows that omission of contrast series does not necessarily lead to missing of clinically significant PCa [22]. This is especially true in an expert setting when investigating a rather low-risk biopsy-naïve population [23]. A shorter protocol could even lead to fewer false-positive MRI findings and could thus reduce unnecessary biopsies without missing clinically significant tumors in a screening population [24]. Various meta-analyses underline these findings, with no significant difference observed between the shorter (bpMRI) and longer (multiparametric) protocols [25,26]. The most important caveats for the bpMRI protocol are that the studies to date were carried out in expert centers with high-quality scans. In centers with less experience in bpMRI, avoidance of DCE could lead to a higher degree of equivocal lesions (PI-RADS 3). Therefore, especially for less experienced readers, DCE can be of added value, as it reduces uncertainty and detects more significant cancers and can serve as an additional “safety net” [26]. When using bpMRI, it is important that centers adhere to the technical MRI recommendations. They must also be aware of the consensus-based recommendations of expert radiologists and urologists on image acquisition, MRI reporting, and training of radiologists and technicians to avoid downstream effects on the final quality of the entire MRI pathway [20,27].

**The role of AI in the PCa diagnostic pathway**

AI can potentially improve diagnostic quality and reduce the workload for PCa diagnosis. AI is a rapidly emerging technology and has attracted massive interest in medical imaging research, mainly in a preclinical setting [27,28]. In what parts of the PCa diagnostic pathway could AI play a role? AI not only has the potential to improve the
detection of clinically significant PCa, which is generally considered the most obvious benefit, but can also play a role in other steps in the diagnostic pathway, from MRI acquisition to generating the radiology report (Fig. 1).

**Image acquisition**

MRI is generally considered to be a relatively long and time-consuming technique in comparison to computed tomography, for example. However, advantages of MRI include its excellent soft-tissue contrast and the lack of ionizing radiation. Several studies have shown that AI can speed up MRI acquisition and thus can potentially help in solving capacity problems. To date, there are no AI solutions for prostate MRI acquisition that can be directly implemented into clinical workflows, but there are research examples for other body parts. For example, in the field of musculoskeletal radiology, knee MRI scans can be acquired almost twice as fast using AI in comparison to conventional acquisition techniques, with similar or even better image quality [29]. Similar AI solutions for prostate MRI are expected in the future.

**Image quality assurance and quality control**

Image quality assurance and quality control represent another potential application of AI. An international panel of radiological and urological experts in prostate MRI considers it mandatory for radiologists to assess the image quality of each prostate MRI examination and mention this in the report [30]. To this end, Prostate Image Quality (PI-QUAL) criteria for evaluation of prostate MRI are under development [31,32]. Radiologists must evaluate the technical parameters and subjectively score the image quality for different MRI sequences. AI may help in generation of a more objective score and in automatic evaluation of image quality during scanning so that technicians can repeat any sequence with inferior quality.

**PCa detection and characterization**

The most obvious application for AI is in improving the workflow for radiological reporting. Numerous AI algorithms are currently being evaluated [33]. Many studies have been performed to classify pre-annotated lesions as insignificant versus significant cancer or benign versus malignant lesions [34]. More advanced algorithms have been used to test automated detection and classification of PCa lesions, with promising results reported. However, it should be noted that most studies involve small cohorts, often without external validation, and they have not been validated prospectively in a clinical workflow. Several applications are now commercially available for prostate MRI (www.AIforRadiology.com) that focus on the reporting workflow. For example, the prostate is automatically segmented, and the prostate volume (and PSA density) is calculated and automatically integrated into the report. Thus, an AI-improved user interface may make annotation and scoring of lesions easier. One of the commercially available applications can also automatically detect clinically significant lesions and provide a PI-RADS score. Initial studies with a prototype of this product in a controlled reader environment showed an improvement in the diagnostic accuracy for detection of clinically significant PCa, with lower inter-reader variability and a shorter reading time in comparison to readers without AI assistance [35,36].

**Other potential applications**

Other AI applications that are of interest are those that allow automated detection of “normal” prostate or obvious frequent conditions such as benign prostate hyperplasia and prostatitis. There has been research on this topic for breast imaging, for which AI in a screening population seems to be able to automatically filter out noncancerous conditions with a high degree of accuracy [37]. Furthermore, AI as a “second reader” could potentially improve the sensitivity of results reported by radiologists, which is of particular interest to less experienced radiologists.

**Future perspectives**

Future applications of AI based on combinations of different (non-imaging) biomarkers may be able to predict which patients will benefit the most from imaging. AI could also predict which patients have a high chance of developing extracapsular extension, recurrence, and/or metastasis, and could thus allow for more personalized treatment. Ideally, when AI is implemented in a clinical setting, a feedback

---

Please cite this article as: M. de Rooij, H. van Poppel and J.O. Barentsz, Risk Stratification and Artificial Intelligence in Early Magnetic Resonance Imaging–Based Detection of Prostate Cancer, Eur Urol Focus (2021), https://doi.org/10.1016/j.euf.2021.11.005
loop with false-positive and false-negative findings could allow the algorithm to learn from its “mistakes” and provide more accurate predictions in the future.

To summarize, the expected rise in the number of prostate MRIs requires solutions that come from different directions. A suitable risk stratification tool (eg, PCA Screening 2.0) is one such solution, but other solutions such as smarter and shorter MRI protocols also need to be explored. For most of these solutions, AI can play an important role. In this respect, the above-mentioned AI applications have the potential to improve the diagnostic quality of the prostate MRI pathway and speed up the workload. However, clinical validation of these tools is needed before their potential can be fully exploited.

**Author contributions:** Maarten de Rooij had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: de Rooij, van Poppel, Barentsz. Acquisition of data: de Rooij, van Poppel, Barentsz. Analysis and interpretation of data: de Rooij, van Poppel, Barentsz. Drafting of the manuscript: de Rooij, van Poppel, Barentsz. Critical revision of the manuscript for important intellectual content: de Rooij, van Poppel, Barentsz. Statistical analysis: None. Obtaining funding: None. Administrative, technical, or material support: None. Supervision: van Poppel, Barentsz. Other: None.

**Financial disclosures:** Maarten de Rooij certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

**Funding/Support and role of the sponsor:** None.

**References**


