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PROSTATE CANCER

Improving diagnosis — can MP-MRI fulfil its PROMIS?

Prostate cancer remains a common cause of death in men. Early diagnosis is perhaps the key to reducing prostate cancer mortality; however, approaches to screening and diagnosis have been beset by problems related to overdiagnosis, on the one hand, and understaging, on the other, leading to the suboptimal treatment of some patients. The PROMIS study was designed to provide level 1 evidence on the utility of multiparametric MRI (MP-MRI) as a triage test to avoid performing unnecessary prostate biopsies and to improve diagnostic accuracy. Results of the study have now been reported.

In the PROMIS study, 576 patients with suspected prostate cancer underwent MP-MRI, with the report locked and blinded, followed by a standard transrectal ultrasonography-guided (TRUS)-biopsy plus template mapping (TPM)-biopsy testing. TRUS–TPM-biopsy sampling was used as the 'gold-standard' reference diagnostic test, as performing radical prostatectomy in all patients was, of course, ethically unacceptable.

The sensitivity of MP-MRI for the detection of 'clinically significant' prostate cancer (Gleason score ≥4 + 3, or cancer core length ≥6 mm) was found to be almost double that of TRUS biopsy (93% versus 48%). The false-positive rate, however, was 49% for MP-MRI, necessitating follow-up biopsy sampling to confirm suspicious findings. Nevertheless, MP-MRI triage for subsequent TRUS-biopsy testing was estimated to enable the detection of 18% of the clinically significant cancers that would have been missed had primary TRUS-biopsy been used in all patients. Moreover, the authors estimated that MP-MRI triage could have avoided TRUS-biopsy testing for 27% of the men and reduced the overdiagnosis of clinically insignificant cancer by 5%. Of note, the false-negative rate with MP-MRI was not insubstantial at 11%, but was 26% with TRUS biopsy as the primary test.

"Further work is needed to evaluate targeting of biopsy sampling based on MRI findings, including the detection rates and cost-effectiveness of the various possible approaches," explains lead author Hashim Ahmed. In addition, "efforts are needed to assess whether serum biomarkers might help identify men at risk of prostate cancer, prior to MP-MRI, in order to reduce the costs and capacity issues that many health-care settings will face." Ahmed concludes, nevertheless, that "this study shows that MP-MRI is clinically beneficial for diagnosis, and patients should ask for such a test before their biopsy; doctors and policy makers need to think that, if they're not doing an MRI before biopsy, they are compromising the diagnosis of cancer in their patients."

Malcolm Mason, a UK expert on prostate cancer, agrees that "MP-MRI could dramatically change the diagnostic pathway: men with elevated PSA levels could undergo MP-MRI, and those with scans suggesting that they are unlikely to have clinically significant prostate cancer could avoid biopsy altogether." He adds, however, that "exactly how such patients should be followed up is another debate, and they would, of course, need to be given adequate information and counselling, as no strategy, this one included, is 100% accurate." Mason concludes: "a substantial amount of work is also needed to look at the resource issues, if MRI is going to be provided on this scale. In the future, although MRI might be used more often, fewer biopsies might be performed, necessitating modelling to evaluate the best strategy for use in health-care systems such as the NHS."

Peter Choyke, a US prostate cancer expert, provides a different perspective: "this study provides support for the use of MRI in biopsy-naive patients, not particularly for sparing them from undergoing a biopsy, but rather to improve the diagnostic effectiveness of image-guided biopsy. The concept that MRI can be used to defer a biopsy remains controversial, and this study will not allay concerns. For some clinicians, the false-negative rate of MRI is unacceptable, and whether or not a lesion is detected, most will perform a random biopsy on the premise that MRI is imperfect." Choyke also emphasizes the importance of completing such studies quickly, before other events overshadow the results: "when conceived, PROMIS was state of the art; however, today, it would be done a bit differently, owing to changing definitions of 'clinically significant' disease, the growing importance of active surveillance, and improvements in MRI–TRUS-targeted biopsy, and in the acquisition and interpretation of MRI data — emphasis has shifted from reducing the number of patients undergoing biopsy on to the optimal management of those diagnosed. These factors conspire to reduce the impact of the PROMIS results."

David Killock

> "… MP-MRI could dramatically change the diagnostic pathway…"

ORIGINAL ARTICLE Ahmed, H. U. *et al.* Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet* http://dx.doi.org/10.1016/S0140-6736(16)32401-1 (2017)