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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.eururo.2018.09.010>.

## References

- [1] Fankhauser CD, Curioni-Fontecedro A, Allmann V, et al. Frequent PD-L1 expression in testicular germ cell tumors. *Br J Cancer* 2015;113:411–3.
- [2] Cierna Z, Mego M, Miskovska V, et al. Prognostic value of programmed-death-1 receptor (PD-1) and its ligand 1 (PD-L1) in testicular germ cell tumors. *Ann Oncol* 2016;27:300–5.
- [3] Necchi A, Bratslavsky G, Corona RJ, et al. Genomic characterization of testicular germ cell tumors relapsing after chemotherapy. *Eur Urol Focus* 2018. <http://dx.doi.org/10.1016/j.euf.2018.07.013>, [Epub ahead of print].
- [4] Adra N, Einhorn LH, Althouse SK, et al. Phase II trial of pembrolizumab in patients with platinum refractory germ-cell tumors: a Hoosier Cancer Research Network study GU14-206. *Ann Oncol* 2018;29:209–14.
- [5] Kato S, Goodman A, Walavalkar V, Barkauskas DA, Sharabi A, Kurzrock R. Hyperprogressors after immunotherapy: an analysis of genomic alterations associated with accelerated growth rate. *Clin Cancer Res* 2017;23:4242–50.

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# A Dedicated Prostate MRI Teaching Course Improves the Ability of the Urologist to Interpret Clinically Significant Prostate Cancer on Multiparametric MRI

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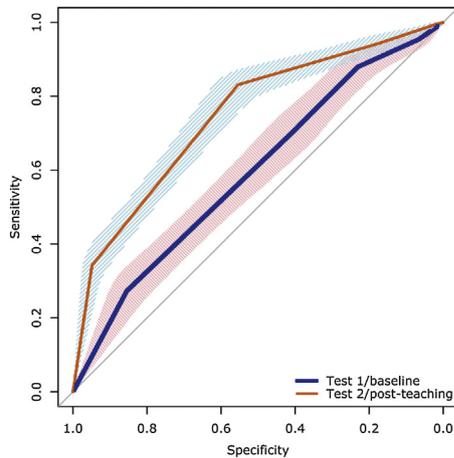
Multiparametric magnetic resonance imaging (MRI) plays an increasingly important role in the diagnosis and treatment of men with prostate cancer. It is important for urologists to be able to interpret prostate MRI to a high standard so that they can perform accurate targeted prostate biopsy and prostate cancer treatments [1]. The objectives of this study were to assess whether the accuracy of urologists in identifying the presence of clinically significant cancer based on a standardised multiparametric MRI set could be improved by completion of a 2-d training course.

A 2-d national training course in prostate MRI for urologists was delivered in September 2016. A total of 25 urologists (17 attendees, 8 residents) independently reported 32 prostate MRI scans under test conditions. Attendees had some prior exposure to prostate MRI; however, this ranged from very limited exposure to more substantial exposure. Scans were chosen at random from men who had previously undergone pre-biopsy MRI, transperineal template, and targeted prostate biopsies at our institution [2]. MRIs included T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences. A test was conducted at the start

of the course where participants, blinded to pathology findings, recorded the likelihood of 16 MRIs harbouring clinically significant cancer (defined as Gleason grade 3 + 4 or greater and/or maximum cancer core length  $\geq 4$  mm) on a 1–5 Likert scale of suspicion. Teaching was then given over 2 d in the form of lectures, practical reporting sessions, and case-based discussions on prostate MRI interpretation. At the end of the course, the participants assessed a different set of 16 randomly chosen scans.

The primary outcome was the cohort's change in average area under the curve (AUC) for detection of clinically significant cancer before and after teaching. Receiver operating characteristic (ROC) curves were based on generalised linear mixed models with random effects on readers and cases. This approach generalises the Obuchowski-Rockette method [3] and is described by Liu et al. [4]. For each ROC curve and AUC value, 95% confidence interval (CI) was computed by stratified bootstrap (B = 50 000 samples) and adjusted percentile.

MRIs were performed in men with no prior biopsy (14/32, 44%) or men with a prior negative biopsy (18/32, 56%).



**Fig. 1** – Average area under the curve (AUC) for detection of clinically significant cancer at baseline (test 1) and post-teaching (test 2) at whole gland level. The shaded areas represent the 95% confidence intervals (CIs) for the AUC. The red line represents the AUC for detection of clinically significant cancer from test 1 at baseline (0.60 [95% CI: 0.55–0.65]). The blue line represents the AUC for detection of clinically significant cancer from test 2, post-teaching (0.77 [95% CI: 0.72–0.82]),  $p < 0.001$ .

Mean age (63 vs 63, respectively), prostate-specific antigen (7.0 vs 7.0, respectively) and baseline characteristics were similar for men in the baseline and post-teaching tests. There was a significant improvement in average urologist AUC for detection of clinically significant cancer from baseline (0.60 [95% CI: 0.55–0.65]) to post-teaching (0.77 [95% CI: 0.72–0.82]; Fig. 1). This was an improvement of 0.17 (95% CI: 0.10–0.24,  $p < 0.0001$ ). Improvement in performance in prostate MRI interpretation following exposure to training has been demonstrated in radiologists previously; however, this is the first time it has been demonstrated in urologists [5]. AUC for the expert radiologist was 0.87 (95% CI: 0.77–0.98) for the baseline test and 0.88 (95% CI: 0.77–0.98) for the post-teaching test. Strengths of the work include the random selection of MRIs and the verification of disease status using detailed transperineal prostate biopsies. Limitations include that it is not known whether the benefits of this training persist.

Whilst we require expert radiologists to report prostate MRI, this study has demonstrated that identification of clinically significant cancer on prostate MRI by urologists is improved following exposure to a 2-d teaching course. These results would support efforts to integrate prostate MRI teaching courses into the training of urologists managing patients with prostate cancer.

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## References

- [1] Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N Engl J Med* 2018;378:1767–77.
- [2] Kasivisvanathan V, Dufour R, Moore CM, et al. Transperineal magnetic resonance image targeted prostate biopsy versus transperineal template prostate biopsy in the detection of clinically significant prostate cancer. *J Urol* 2013;189:860–6.
- [3] Obuchowski NA. Multireader, multimodality receiver operating characteristic curve studies: hypothesis testing and sample size estimation using an analysis of variance approach with dependent observations. *Acad Radiol* 1995;2:S22–9, discussion S57–64, S70–1 pas.
- [4] Liu W, Pantoja-Galicia N, Zhang B, et al. Generalized linear mixed models for multi-reader multi-case studies of diagnostic tests. *Stat Methods Med Res* 2017;26:1373–88.
- [5] Akin O, Riedl CC, Ishill NM, Moskowitz CS, Zhang J, Hricak H. Interactive dedicated training curriculum improves accuracy in the interpretation of MR imaging of prostate cancer. *Eur Radiol* 2010;20:995–1002.

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