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European Association of Urology

Platinum Priority – Editorial

Referring to the article published on pp. 570–578 of this issue

In-bore Multiparametric Magnetic Resonance Imaging Targeted Biopsy: As Good as it Gets?

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In this issue of *European Urology*, van der Leest et al. [1] present a head-to-head comparison of in-bore magnetic resonance imaging-guided biopsy (MRI-GB) against transrectal ultrasound-guided prostate biopsy (TRUS-GB) in biopsy-naïve men. The authors claim noninferiority for the MRI-GB pathway over the TRUS-GB pathway in detection of clinically significant prostate cancer (csPC; defined as any Gleason grade group $\geq$2), with a concomitant reduction in the number of biopsies performed and of clinically insignificant PCs detected. The most notable features of the study include an impressive level of concordance for mp-MRI (88%), a low rate of equivocal Prostate Imaging-Reporting and Data System (PI-RADS) 3 lesions of 6% (compared with a mean rate of 22% in the literature [2]; Table 1), and a nonsuspicious mpMRI rate of 49%, leading to a marked reduction in men undergoing MRI in-bore biopsy. Undoubtedly, the MRI techniques and reporting described are of an extremely high standard. The real problem lies in trying to determine how effective the targeting strategy was and the implications for routine clinical practice.

The use of in-bore MRI-GB is not widespread in urological or radiological practice. It potentially removes many of the inherent difficulties associated with transferring knowledge of a target identified on mpMRI to TRUS-GB, but brings with it significant logistic challenges. There are few data comparing MRI in-bore biopsy with an adequate reference standard [3] and the approach has little evidence to support it in terms of outcomes or health economics. In this respect the current study has taken us little further; similar rates of csPC identified in the mpMRI pathway (25%) and traditional TRUS-GB group (23%) are at variance with findings from the PROMIS [4] and PRECISION [5] trials. In PROMIS, best-case scenario modelling predicted a 28% increase in detection of csPC for MRI-directed biopsies over TRUS-GB against the reference standard of a transperineal mapping biopsy (TPM). In PRECISION (which was also a noninferiority study) there was an overall 11.7% increase in the diagnosis of csPC on MRI-GB over TRUS-GB, with a similar reduction in the detection of clinically insignificant PC (current study 11% vs PRECISION 13.1%). It is instructive that "perilesional" TRUS-GB in the current study [1] improved the diagnostic yield of the in-bore transrectal MRI biopsies by 7% (21/317 cases). Furthermore, on subsequent review a lesion was identified on mpMRI but not correctly targeted in 20/21 cases, thus bringing into question the efficacy of the biopsy strategy.

The authors suggest that the low prevalence of csPC (30%) in comparison to contemporary cohorts (38–47%) "could contribute to the high number of nonsuspicious MRI scans". Unfortunately, without an adequate reference standard (eg, TPM) the true prevalence of disease in this cohort remains unknown. It is somewhat reassuring that relatively few cases of PC were detected on TRUS-GB in men with bland (PI-RADS 1/2) MRI scans; nevertheless, "blind" TRUS-GB has low sensitivity for PC detection (Table 2) and thus significant disease might have been missed. The choice of a transrectal approach for the in-bore MRI biopsies might well have contributed to a lower than expected PC detection rate, as not all PCs are detected via a transrectal route [6], particularly in the anterior prostate [7], which is where mpMRI has an advantage in providing a targetable lesion [8].

DOI of original article: https://doi.org/10.1016/j.eururo.2018.11.023.
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https://doi.org/10.1016/j.eururo.2018.12.001

Table 1 – Lesion rates by PI-RADS score on multiparametric resonance imaging for men undergoing first biopsy from systematic review [2]

Centre	Year	Patients (*n*)	PI-RADS 1–2		PI-RADS 3		PI-RADS 4		PI-RADS 5		PI-RADS 4–5	
			n	%	*n*	%	*n*	%	*n*	%	*n*	%
Dresden, Heidelberg, Germany	2017	214	66	31	39	18	71	33	39	18	110	51
Los Angeles, CA, USA	2016	333	60	18	129	39	109	33	35	11	144	43
Cambridge, UK	2016	107	22	21	21	20	23	21	41	38	64	60
Cambridge UK, Heidelberg, Melbourne	2017	807	236	29	153	19	–	–	–	–	418	52
Turku, Finland	2017	161	38	24	24	15	21	13	78	48	99	61
Brisbane, Australia	2014	233	81	35	33	14	–	–	–	–	109	47
Nijmegen, The Netherlands	2017	*184*[a]	–	–	*17*[a]	NA	*67*[a]	NA	*100*[a]	NA	*167*[a]	NA
Total		1855	503	27	399	22	224	27	193	24	944	51

PI-RADS = Prostate Imaging-Data and Reporting System; NA = not applicable.
[a] Numbers in italics are not included in totals.

Table 2 – Sensitivity of mpMRI and TRUS-GB in the detection of prostate cancer compared to the reference standard of template mapping biopsy [4]

Definition of cancer	Men (*n*)	Sensitivity, % (95% CI)	
		mp-MRI	TRUS-GB
GS ≥4 + 3 or cancer core length ≥6 mm	230	93 (88–96)	48 (42–55)
GS ≥ 3 + 4 or cancer core length ≥4 mm	331	87 (83–90)	60 (55–65)
Any GS 7 (≥3 + 4)	308	88 (84–91)	48 (43–54)

mpMRI = multiparametric magnetic resonance imaging; TRUS-GB = transrectal ultrasound-guided biopsy; CI = confidence interval; GS = Gleason score.

An ongoing difficulty with interpreting results from biopsy studies remains the definition of csPC. As highlighted previously [9], the very existence of multiple definitions of clinical significance in the biopsy literature underlines the difficulty in knowing what is truly clinically insignificant; for example, in the current study there was upgrading of Gleason group grade 1 disease (3 + 3) to a higher group grade on radical prostatectomy in 26/45 (58%) and 18/34 (53%) cases identified on TRUS-GB and MRI-GB, respectively (Supplementary Table 9 [1]). In an era in which the management of low-risk and intermediate risk PC via active monitoring is better understood in light of results from the ProtecT study [10], it is possible that concentrating on reducing "overdetection" of so-called "clinically insignificant disease" is perhaps overplayed.

Ultimately we must accept there will always be a level of uncertainty associated with PC diagnostics, but what the clinician and patient want most of all is a strategy that allows a clear management plan to be drawn up, including discharge where appropriate. This seems not to be delivered by the proposed MRI-GB pathway followed in this study; in the 309 men (49%) designated to no initial biopsy because of a negative MRI scan, 73 (24%) were found to have cancer on initial TRUS-GB. In a further 42 men (13.6%), repeat mpMRI scans were carried out (indicating ongoing clinical concern) and 15 (~5%) underwent repeat biopsy within 12 mo; this has clinical and economic implications that need to be borne in mind.

Assuming the excellent technical results for mpMRI (low equivocal rate, high concordance) described by the authors can be reproduced elsewhere, this indeed could be as good as an in-bore approach gets until further technological advances and artificial intelligence come into play for interpretation and targeting. We would now appear to be at a crossroads in the decision as to how best to integrate the results of mpMRI in the diagnostic algorithm for localised PC. On the one hand, mpMRI can be used as a tool in the risk assessment for a man before a decision on whether or not to biopsy; this is certainly achievable and in many urological centres is standard practice, improving on "blind" systematic biopsy by providing a targetable (via cognitive biopsy or fusion technology) lesion, rather than replacing it. Furthermore, such an approach allows choice of the route of biopsy (transperineal for anterior lesions rather than transrectal), which will probably result in a lower false-negative biopsy rate and a lower incidence of infective complications. On the other hand, we could proceed wholesale down the route of contemporaneous in-bore MRI biopsy. This would require substantial investment and represents a fundamental change in the diagnostic pathway. The current publication has shown what is possible, but perhaps not what is necessary.

Conflicts of interest: The authors have nothing to disclose.

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