

available at www.sciencedirect.com
journal homepage: www.europeanurology.com



European Association of Urology



Platinum Priority – Editorial and Reply from Authors

Referring to the article published on pp. 986–996 of this issue

Toward the End of Blind Prostate Biopsies?

Bertrand Tombal*

Service d'Urologie, Cliniques universitaires Saint Luc, Université catholique de Louvain, Av. Hippocrate, 10, B-1200 Brussels, Belgium

The diagnosis of prostate cancer (PCa) remains one of the only blind biopsy procedures in cancer and therefore is a source of much discussion and frustration. The indication of a biopsy is almost always driven by an elevated level of prostate-specific antigen (PSA), a nonspecific biomarker, or by an abnormal digital rectal examination. In most cases, we assume that the patient *might* have PCa, and we *sample* the prostate with biopsy cores. As a result, that *shotgun* sampling procedure harvests cancer in only 20–50% and, ironically, detects a lot of indolent cancer that would have better remain silent.

Transrectal ultrasound (TRUS)-guided prostate biopsy (PBx) appeared in the early 1980s, but it took almost a decade and the pivotal study of Hodge et al. for TRUS PBx to replace digitally directed biopsies and so become the accepted standard for PCa diagnosis [1]. The main question after reading the provocative practice-changing paper of Portalez et al. [2] in the present issue of the Platinum Journal, is how many years will it take before magnetic resonance imaging (MRI) supersedes TRUS for PBx guidance?

TRUS PBx is and will remain an inefficient procedure, diagnostically speaking. Its true intrinsic diagnostic accuracy is not known because men with negative biopsy do not undergo radical prostatectomy and thus no confirmation of biopsy findings. In an attempt to overcome that limitation, Haas et al. reported in 2007 the result of a study in which they performed 18-core needle biopsies on autopsy prostates from 164 men who had no history of PCa [3]. Biopsies were taken from the midperipheral, the lateral peripheral, and the central zones. PBx detected cancer in only 25 of the 47 prostates involved with cancer (53%), representing only 34 of the 87 identified tumor foci (39%). That result is scary to some extent because we realize that the technique we trust each day misses half of the cancers.

Instead of investing from the beginning in modern imaging trials, urologists have taken the simplest route of increasing the number of biopsy cores, using apparently organized biopsy schemes only to mask a consistent stochastic approach. So was created the most common flaw in that debate: the conventional wisdom that more extensive sampling may overcome the absence of target identification. This is illustrated by the recent publication by Ploussard et al. demonstrating that incremental expansion from 6 to 12 cores increases the PCa detection rate by 19.4% and from 12 to 21 cores increases the rate by an additional 6.7% [4]. This increase, however, comes with an increased detection of insignificant cancers [4]. This trial suffers, as do many others, from an important verification bias, and the proportion of missed cancers remains unknown. In the Reduction by Dutasteride of Prostate Cancer Events (REDUCE) trial, 17% of the patients had cancer within 2 yr following a 12-core biopsy [5]. Clearly, core escalation and a “needle in a haystack” strategy are not the way to go.

The Dutch humanist Erasmus (1466–1536) once said, “In the country of the blind, the one-eyed man is king.” This is not true for PBx, where the blind still reign. The data are there, but we still have difficulty seeing and accepting them. MRI of the prostate is not a new technique, with the first report dating back to 1982, contemporary with TRUS [6]. Since then, however, it has been a consistent history of the conflict between faith in the standard blind approach and more Cartesian reasoning about the value of MRI. No later than last year, in an editorial comment on the excellent attempt of Dickinson et al. [7] to systematize reading of multiparametric MRI (mp-MRI), Heidenreich [8] concluded that MRI was “not ready for routine use.” The center of the debate is constantly the same: There is a lack of consensus about the reproducibility and the technical parameters for

DOI of original article: <http://dx.doi.org/10.1016/j.eururo.2012.06.044>.

* Tel. +32 2 764 1409.

E-mail address: Bertrand.tombal@uclouvain.be.

MRI, the reporting is not standardized, and there are no randomized trials.

This is not absolutely true anymore, as clearly illustrated by the recent review by Moore et al. on image-guided PBx using MRI-derived targets [9]. That exhaustive meta-analysis concludes that when MRI was applied to men indicated for PBx, 62% had MRI abnormalities. Most important, they show that targeted biopsy was more efficient; fewer men were biopsied overall, and those who had a biopsy required a mean of 3.8 targeted cores compared with 12 standard cores. In the elegantly written accompanying editorial, Edhaie and Shariat noted that “the heterogeneity in patient cohorts, interventions, and outcomes is the major limitation of studies in MRI-guided prostate biopsy.” This comment is interesting, considering that the same can be applied to TRUS PBx, which we use every day. The famous economist John K. Galbraith (1908–2006), father of the conventional wisdom’s concept, explained that in light of persistent doubt, “faced with the choice between changing one’s mind and proving there is no need to do so, almost everyone gets busy on the proof.”

One of the constant criticisms made about MRI has been the lack of a standardized technique and system to characterize and objectively score MRI readings, hampering any development of proper validation trials. That work has been conducted now and has led to the publication of several consensus papers, including the European Society of Urogenital Radiology (ESUR) MRI guidelines [7,10]. The ESUR guidelines is a major leap forward in standardizing prostate imaging. The ESUR guidelines define basic recommendations for mp-MRI, including diffusion, perfusion, and spectroscopic analysis. More interesting, the ESUR prostate working group has developed a structured reporting system called PI-RADS (prostate imaging, reporting, and data system) that allows quantification of MRI abnormalities.

This had remained a purely rhetorical exercise because the PI-RADS system had never been used in a well-conducted trial. This is now done with the paper by Portalez et al. in the present issue of *European Urology* [2]. In a multicentric study, the authors have prospectively validated the ESUR scoring system in 129 consecutive patients referred for mp-MRI after at least one set of negative biopsies. The authors have used a commercially available MRI/three-dimensional (3D) TRUS fusion-guided system, the Koelis urostation system, to target and analyze the biopsy location. To our knowledge, this is the first attempt to validate the ESUR score in a contemporary cohort. The authors report that a threshold of ESUR-S ≥ 9 exhibited sensitivity of 73.5%; specificity of 81.5%; positive

predictive value of 38.2% and, more important, negative predictive value of 95.2%; and accuracy of 80.4%. This is much better than any published risk calculator or available biomarker.

Will it be enough to change the paradigm of blinded biopsies? Unfortunately, and sadly to say, surely not. MRI is still seen by many urologists as costly and difficult to program test. Sophisticated computerized MRI-TRUS registration systems such as Koelis may be commercially available but at a high price. Quality-controlled, precise, modern image-based biopsy is competing with a practice that takes 5 min with a simple ultrasound machine. Change will take more time. As noted by Louis F. Celine (1894–1961), “I think all great innovations are built on rejections.”

Conflicts of interest: The author has nothing to disclose.

References

- [1] Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol* 1989;142:71–4, discussion 74–5.
- [2] Portalez D, Mozer P, Cornud F, et al. Validation of the European Society of Urogenital Radiology scoring system for prostate cancer diagnosis on multiparametric magnetic resonance imaging in a cohort of repeat biopsy patients. *Eur Urol* 2012;62:986–96.
- [3] Haas GP, Delongchamps NB, Jones RF, et al. Needle biopsies on autopsy prostates: sensitivity of cancer detection based on true prevalence. *J Natl Cancer Inst* 2007;99:1484–9.
- [4] Ploussard G, Nicolaiew N, Marchand C, et al. Prospective evaluation of an extended 21-core biopsy scheme as initial prostate cancer diagnostic strategy. *Eur Urol*. In press. <http://dx.doi.org/10.1016/j.eururo.2012.05.049>.
- [5] Andriole GL, Bostwick DG, Brawley OW, et al. Effect of dutasteride on the risk of prostate cancer. *N Engl J Med* 2010;362:1192–202.
- [6] Steyn JH, Smith FW. Nuclear magnetic resonance imaging of the prostate. *Br J Urol* 1982;54:726–8.
- [7] Dickinson L, Ahmed HU, Allen C, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European consensus meeting. *Eur Urol* 2011;59:477–94.
- [8] Heidenreich A. Consensus criteria for the use of magnetic resonance imaging in the diagnosis and staging of prostate cancer: not ready for routine use. *Eur Urol* 2011;59:495–7.
- [9] Moore CM, Robertson NL, Arsanious N, et al. Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. *Eur Urol*. In press. <http://dx.doi.org/10.1016/j.eururo.2012.06.004>.
- [10] Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. *Eur Radiol* 2012;22:746–57.

<http://dx.doi.org/10.1016/j.eururo.2012.07.048>