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Re: Magnetic Resonance Imaging Guided Prostate Biopsy in Men With Repeat Negative Biopsies and Increased Prostate Specific Antigen

Hambroek T, Somford DM, Hoeks C, et al

J Urol 2010;183:520–8

Experts' summary:

In this analysis, the authors report their results of multimodal 3-T magnetic resonance (MR) imaging and subsequent MR-guided biopsy of suspicious regions if detected ($n = 68$) in 71 men with at least two negative previous biopsies and prostate-specific antigen (PSA) >4.0 ng/ml. Mean age was 63 yr, median PSA was 13.0 ng/ml, and median prostate volume was 48.0 cm³.

With a median of four cores, the tumor-detection rate was 59% (40 of 68 cases), with the principal tumor location in the most ventral aspect of the transition zone (57%). Furthermore, the authors conclude that in 37 of 40 patients (93%), significant tumors were found (Gleason grade 4 or 5 in biopsy or prostatectomy specimen, pT3 or volume >0.5 cm³ after surgery, PSA >10 ng/ml, PSA density >0.15 ng/ml per cubic centimeter in patients without subsequent prostatectomy). In addition, the findings were compared with a matched series of men with transrectal ultrasound (TRUS)-guided biopsies, revealing a significant higher detection rate for MR-guided biopsy.

Experts' comments:

The authors have to be congratulated for the largest series regarding MR-guided prostate biopsy to date. Their findings are quite remarkable, even though considering the retrospective, matched comparison to TRUS-guided cases with 8–10 cores is a weak argument (emphasized in an editorial comment by Schilling and Stenzl). In contrast, a comparison of the whole-mount specimens in those who underwent surgery would have been very interesting.

The most interesting result is the high rate of cancer detection at 59%! Based on a cancer-detection rate of 25% for a standard first-time TRUS biopsy set and about 10–15% in rebiopsy (total: 35%), the majority of men with elevated PSA

have no tumor detection after two sets of random biopsy [1]. Finding tumors in 59% of this large cohort would add another 39% of men with cancer to the initial 35%. This would imply that up to 74% of men with PSA >4 ng/ml (inclusion criterion in the current study) have prostate cancer!

Bearing in mind the major problem of overdiagnosis and overtreatment in prostate cancer, the most important question regarding this specific topic (re-rebiopsy) is whether or not we really want to detect all of these tumors. Even though the authors of this study described a “significant” tumor in 93%, after prostatectomy, 50% had a Gleason score <7 and 50% had a tumor volume <0.5 cm³.

Perhaps the most important aspect to consider when applying new techniques for cancer detection is that we should be aware that the tumors we find may have different behavior than tumors we currently treat after random-biopsy protocols. In fact, our treatment algorithms (eg, when to propose active surveillance or not) are very much dependent on and adjusted to standard ultrasound random biopsies [2].

Conflicts of interest: The authors have nothing to disclose.

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Re: Prostate Cancer Antigen 3 Score Accurately Predicts Tumour Volume and Might Help in Selecting Prostate Cancer Patients for Active Surveillance

Ploussard G, Durand X, Xylinas E, et al

Eur Urol 2011;59:422–9

Expert's summary:

This study investigated whether the urinary prostate cancer antigen 3 (PCA3) can help select good candidates for active surveillance (AS) in addition to the current AS criteria. The study subjects were 106 low-risk prostate cancer (PCa) patients who underwent the urinary PCA3 test before radical

prostatectomy. Performance of biopsy criteria, prostate-specific antigen (PSA) density, magnetic resonance imaging findings, and PCA3 score was examined in predicting bad news in prostatectomy specimens. Multivariate analysis demonstrated strong predictability of the urinary PCA3 score (<25) for tumour volume (<0.5 cm³) and insignificance (no Gleason pattern 4 or 5, no capsular penetration, tumour volume <0.5 cm³) of PCa.

Expert's comments:

AS for low-risk PCa has become an important treatment strategy because it could compensate the risks of overdiagnosis brought about by PSA screening. However, performance of the currently used criteria for patients' selection is far from satisfactory mainly due to the underestimation of the initial biopsy. Our Japanese prospective AS study demonstrated deviation from the selection criteria (the Epstein biopsy criteria) in 33% of patients at 1-yr rebiopsy [1] and frequent unfavourable pathologic findings in prostatectomy specimens during AS [2]. Prediction of indolent PCa at the initial diagnosis even using a nomogram specifically developed for AS seems imperfect (eg, the receiver operating characteristic curves ranged from 0.64 to 0.79 by a nomogram by Kattan et al) [3]. Repeated biopsy has therefore become an important part of follow-up protocol in current AS programmes. From a practical viewpoint, however, both patients and physicians are reluctant to perform repeated biopsy during AS.

Under these circumstances, additional parameters including new biomarkers have long been awaited to predict the significance of PCa. PCA3 is a noncoding RNA specifically secreted from PCa. Clinical studies have demonstrated the usefulness of urinary PCA3 for the diagnosis of PCa, although the function of PCA3 remains to be elucidated. This study showed a strong correlation between urinary PCA3 score and tumour volume in the prostatectomy specimens, and the PCA3 test helped select better candidates for AS. The results seem reasonable because PCA3 is only overexpressed in PCa cells. The study, however, does not yet demonstrate a direct association of the urine PCA3 score with malignant potentials such as high Gleason grade and extracapsular extension. The recommended sample collection method for urinary PCA3

test is three strokes during the digital rectal examination (DRE) to both lobes before the collection of voided urine. One concern is whether such a complicated way of sample collection affects the levels of PCA3 in urine. Engrailed-2 (EN2) protein, a transcriptional factor secreted by PCa, is another candidate urine biomarker for PCa. EN2 is measured without DRE and seems to have a high predictability for PCa [4]. It still remains unclear how PCa cells emerge in voided urine. Nevertheless, urine biomarkers are ideal in the light of noninvasiveness. Urine is still an untapped resource of biomarkers for the diagnosis of PCa. Volatile organic compounds in urine have recently been proposed as cancer biomarkers. The French study demonstrated in a very sophisticated way that trained dogs can detect PCa by sniffing human urine [5].

Conflicts of interest: The author has nothing to disclose.

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Re: Predictors of Androgen Deprivation Therapy Efficacy Combined with Prostatic Irradiation: The Central Role of Tumor Stage and Radiation Dose

Williams S, Buyyounouski M, Kestin L, Duchesne G, Pickles T

Int J Radiat Oncol Biol Phys 2011;79:724–31

Expert's summary:

What is the optimum duration of androgen-deprivation therapy (ADT) when it is given as an adjuvant to radiotherapy for prostate cancer? In this study, data from 3666 patients with prostate cancer from four institutions treated with external-beam radiation therapy (EBRT), with or without ADT, were analysed. The end point was biochemical failure, and the results showed a 38% reduction in risk after only 6 mo of ADT. Thereafter, the risks of biochemical failure continued to fall: The risk

reduction was 58% and 66% after 12 and 24 mo of ADT, respectively. However, there was no discernible reduction in risk for durations of ADT beyond 24 mo. These estimates could be further refined by consideration of other parameters such as radiation dose (smaller benefit of ADT with higher radiation doses) and clinical T category, but in each instance the greatest impact of ADT on risk reduction was in the first year.

Expert's comments:

Randomised trials tell us unequivocally that EBRT should be combined with ADT, at least for patients with locally advanced disease or lower doses of radiotherapy [1–4]. Trials that define the optimum schedule and duration of ADT have tended to favour longer term therapy for patients with high-risk disease [4,5] but still do not tell us precisely how long to continue for