### EVIDENCE TABLE

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<tr>
<td>1. Uchio EM, Aslan M, Wells CK, Calderone J, Concato J. Impact of biochemical recurrence in prostate cancer among US veterans, <em>Arch Intern Med.</em> 2010;170(15):1390-1395.</td>
<td>Review/Other-Dx</td>
<td>623 veterans</td>
<td>To describe patterns of BCR and subsequent mortality.</td>
<td>With 5-, 10-, and 15-year follow-up periods, respectively (for all results shown herein), the cumulative incidence of BCR after prostatectomy (n=225) was 34%, 37%, and 37%; PCa mortality among men who failed treatment (n=81) was 3%, 11%, and 21%. Among men receiving RT (n=398), the cumulative incidence of BCR was 35%, 46%, and 48%; PCa mortality among those who failed treatment (n=161) was 11%, 20%, and 42%. Overall, BCR was associated with an increased risk of death from PCa in the study population, but the individual probability of this outcome was relatively low.</td>
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<td>2. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. <em>CA Cancer J Clin.</em> 2016;66(1):7-30</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To estimate the numbers of new cancer cases and deaths that will occur in the United States in the current year and compile the most recent data on cancer incidence, mortality, and survival. Incidence data were collected by the National Cancer Institute (Surveillance, Epidemiology, and End Results [SEER] Program), the Centers for Disease Control and Prevention (National Program of Cancer Registries), and the North American Association of Central Cancer Registries.</td>
<td>In 2016, 1,685,210 new cancer cases and 595,690 cancer deaths are projected to occur in the United States. Overall cancer incidence trends (13 oldest SEER registries) are stable in women, but declining by 3.1% per year in men (from 2009-2012), much of which is because of recent rapid declines in PCa diagnoses. The cancer death rate has dropped by 23% since 1991, translating to more than 1.7 million deaths averted through 2012. Despite this progress, death rates are increasing for cancers of the liver, pancreas, and uterine corpus, and cancer is now the leading cause of death in 21 states, primarily due to exceptionally large reductions in death from heart disease. Among children and adolescents (aged birth-19 years), brain cancer has surpassed leukemia as the leading cause of cancer death because of the dramatic therapeutic advances against leukemia. Accelerating progress against cancer requires both increased national investment in cancer research and the application of existing cancer control knowledge across all segments of the population.</td>
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# Prostate Cancer—Pretreatment Detection, Surveillance, and Staging

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<td>3. Roehrborn CG, Black LK. The economic burden of prostate cancer. <em>BJU Int.</em> 2011;108(6):806-813.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To discuss expenditure on PCa diagnosis, treatment and follow-up and evaluate the cost of PCa and its management in different countries.</td>
<td>A high proportion of the costs are incurred in the first year after diagnosis; in 2006, this amounted to 106.7-179.0 million euros (euro) in the European countries where these data were available (UK, Germany, France, Italy, Spain and the Netherlands). In the USA, the total estimated expenditure on PCa was 9.862 billion US dollars ($) in 2006. The mean annual costs per patient in the USA were $10,612 in the initial phase after diagnosis, $2134 for continuing care and $33,691 in the last year of life. In Canada, hospital and drug expenditure on PCa totaled C$103.1 million in 1998. In Australia, annual costs for PCa care in 1993-1994 were 101.1 million Australian dollars. Variations in costs between countries were attributed to differences in incidence and management practices. Per patient costs depend on cancer stage at diagnosis, survival and choice of treatment. Despite declining mortality rates, costs are expected to rise owing to increased diagnosis, diagnosis at an earlier stage and increased survival.</td>
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<td>4. Evans AJ, Henry PC, Van der Kwast TH, et al. Interobserver variability between expert urologic pathologists for extraprostatic extension and surgical margin status in radical prostatectomy specimens. <em>Am J Surg Pathol.</em> 2008;32(10):1503-1512.</td>
<td>Observational-Dx</td>
<td>200 original hematoxylin and eosin slides.</td>
<td>To report interobserver variability in a group of expert pathologists concerning EPE and surgical margin interpretation for RP specimens.</td>
<td>On the basis of panel diagnoses, as the gold standard, specificity, sensitivity, and accuracy values were high for both EPE (87.5%, 95.0%, and 91.2%) and surgical margin (97.5%, 83.3%, and 90.4%). Overall kappa values for all 60 slides were 0.74 for surgical margin and 0.63 for EPE. The kappa values were higher for slides with definitive gold standard EPE (kappa=0.81) and surgical margin (kappa=0.73) diagnoses when compared with the EPE (kappa=0.29) and surgical margin (kappa=0.62) equivocal slides.</td>
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<td>5. van der Kwast TH, Collette L, Van Poppel H, et al. Impact of pathology review of stage and margin status of radical prostatectomy specimens (EORTC trial 22911). <em>Virchows Arch.</em> 2006;449(4):428-434.</td>
<td>Experimental-Dx</td>
<td>552 patients</td>
<td>To report on the degree of interobserver variation between local pathologists and review pathology (by a single pathologist) for pathological stage, including SVI and EPE, and for surgical margin status. In addition, the prognostic impact of these parameters was analyzed using BCR-free survival (PSA failure after prostatectomy) as outcome parameter.</td>
<td>Although a high concordance between review pathology and local pathologists existed for SVI (94%, kappa=0.83), agreement was much less for EPE (57.5%, kappa=0.33) and for surgical margin status (69.4%, kappa=0.45). Review pathology of surgical margin status was a stronger predictor of biochemical progression-free survival in univariate analysis [HR=2.16 and (P=0.0002)] than local pathology (HR=1.08 and (P&gt;0.1)). The review pathology demonstrated a significant difference between those with and without EPE (HR=1.83 and (P=0.0017)), while local pathology failed to do so (HR=1.05 and (P&gt;0.8)).</td>
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<td>6. Graser A, Heuck A, Sommer B, et al. Per-sextant localization and staging of prostate cancer: correlation of imaging findings with whole-mount step section histopathology. <em>AJR Am J Roentgenol.</em> 2007;188(1):84-90.</td>
<td>Observational-Dx</td>
<td>106 patients</td>
<td>To determine the diagnostic accuracy and interobserver agreement of 1.5-T prostatic MRI for per-sextant tumor localization and staging of PCa as compared with whole-mount step section histopathology.</td>
<td>41 patients had ECE (tumor stage T3), and 65 patients had organ-confined disease (stage T2). Of 636 prostatic sextants, 417 were positive for PCa and 135 were positive for ECE at histopathology. For PCa localization, AUC values ranging from 0.776 +/- 0.023 (SD) to 0.832 +/- 0.027. For the detection of ECE, the AUC values ranged from 0.740 +/- 0.054 to 0.812 +/- 0.045. Interobserver agreement (kappa) ranged from 0.49 to 0.60 for PCa localization and from 0.59 to 0.67 for the detection of ECE.</td>
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<td>7. D'Amico AV, Whittington R, Malkowicz SB, et al. Biochemical outcome after radical prostatectomy, external beam radiation therapy, or interstitial radiation therapy for clinically localized prostate cancer. <em>JAMA.</em> 1998;280(11):969-974.</td>
<td>Observational-Tx</td>
<td>1,872 patients; 888 treated with RP; 218 treated with implant with or without neoadjuvant ADT; 766 treated with RT</td>
<td>To estimate control of PSA after RP, EBRT, or implant with or without neoadjuvant ADT in patients with clinically localized PCa.</td>
<td>The relative risk of PSA failure in low-risk patients (stage T1c, T2a and PSA level ≤10 ng/mL and GS ≤6) treated using RT, implant plus ADT, or implant therapy was 1.1 compared with those patients treated with RP. The addition of ADT to implant therapy did not improve PSA outcome in high-risk patients but resulted in a PSA outcome that was not statistically different compared with the results obtained using RP or RT in intermediate-risk patients. Intermediate- and high-risk patients treated with EBRT or RP fared better than brachytherapy.</td>
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<td>8. Eifler JB, Feng Z, Lin BM, et al. An updated prostate cancer staging nomogram (Partin tables) based on cases from 2006 to 2011. <em>BJU Int.</em> 2013;111(1):22-29.</td>
<td>Review/Other-Dx</td>
<td>5,629 consecutive men</td>
<td>To update the 2007 Partin tables in a contemporary patient population.</td>
<td>The median PSA was 4.9 ng/mL, 63% had GS 6 disease, and 78% of men had T1c disease. 73% of patients had organ-confined disease, 23% had EPE, 3% had SV+ but not LN+, and 1% had LN+ disease. Compared to the previous Partin nomogram, there was no change in the distribution of pathologic state. The risk of LN+ disease was significantly higher for tumors with biopsy GS 9–10 than GS 8 (organ-confined disease 3.2, 95% CI, 1.3–7.6). The c-indexes for EPE vs organ-confined disease, SV+ vs organ-confined disease, and LN+ vs organ-confined disease were 0.702, 0.853, and 0.917, respectively. Men with biopsy GS 4+3 and GS 8 had similar predicted probabilities for all pathologic stages. Most men presenting with GS 6 disease or GS 3+4 disease have &lt;2% risk of harboring LN+ disease and may have lymphadenectomy omitted at RP.</td>
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<td>9. Karakiewicz PI, Bhojani N, Capitanio U, et al. External validation of the updated Partin tables in a cohort of North American men. <em>J Urol.</em> 2008;180(3):898-902; discussion 902-893.</td>
<td>Observational-Dx</td>
<td>1,838 patients</td>
<td>To confirm the accuracy and performance characteristics of Partin tables in an external validation cohort. Three metrics - overall accuracy (AUC), Brier score and calibration plots – were assessed in a large cohort of men.</td>
<td>The rates of EPE, SVI and LN invasion were 26.9%, 5.5% and 1.8%. The accuracy of EPE, SVI and LN invasion prediction was 71%, 80% and 75% according to the AUC method, and 0.176, 0.051 and 0.037 according to the Brier score, respectively. EPE predictions between 0% and 25%, and LN invasion predictions between 0% and 5% correlated well with observed EPE and LN invasion rates, respectively. Conversely a suboptimal correlation was recorded between predicted and observed SVI rates as well as between predicted and observed rates of EPE and LN invasion for predicted EPE and LN invasion values above 25% and 5%, respectively. In this examined validation cohort the overall accuracy of the Partin tables was comparable to results reported in the original 2007 development cohort. However, performance characteristics indicate that predictions within specific probability ranges should be interpreted with caution.</td>
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<td>10. Yu JB, Makarov DV, Sharma R, Peschel RE, Partin AW, Gross CP. Validation of the partin nomogram for prostate cancer in a national sample. <em>J Urol.</em> 2010;183(1):105-111.</td>
<td>Observational-Dx</td>
<td>11,185 patients</td>
<td>To validate the Partin nomogram for PCa in a large, population based sample.</td>
<td>The Partin tables discriminated well between patient groups at risk for positive LNs and SVI (AUC 0.77 and 0.74, respectively). The discrimination of EPE and organ confined disease was more limited (AUC 0.62 and 0.68, respectively). The AUC for positive LNs was 0.78 in white men, 0.73 in black men and 0.83 in Asian/Pacific Islander men (<em>P</em>=0.17). The AUC for positive LNs in men 61 years old or younger was 0.80 vs 0.74 in men older than 61 years (<em>P</em>=0.03). The Partin tables showed excellent discrimination for SVI and positive LNs. Discrimination of EPE and organ confined disease was more limited. The Partin tables performed best in young men.</td>
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<tr>
<td>11. Armatys SA, Koch MO, Bihrle R, Gardner TA, Cheng L. Is it necessary to separate clinical stage T1c from T2 prostate adenocarcinoma? <em>BJU Int.</em> 2005;96(6):777-780.</td>
<td>Observational-Dx</td>
<td>288 patients</td>
<td>To test the hypothesis that PCa patients with clinical stage cT1c and cT2 have similar outcomes and clinicopathological features, and should be grouped together.</td>
<td>Patients with cT2 tumors were more likely to have a higher GS (<em>P</em>=0.04) and final pathological stage (<em>P</em>=0.05) than those with cT1c tumors. There was no significant difference in age (<em>P</em>=0.92), preoperative PSA level (<em>P</em>=0.17), prostate weight (<em>P</em>=0.34), tumor volume (<em>P</em>=0.16), surgical margin status (<em>P</em>=0.86), multifocality (<em>P</em>=0.92), the presence of perineural invasion (<em>P</em>=0.09), or high-grade prostatic intraepithelial neoplasia (<em>P</em>=0.99) between patients with clinical stage cT1c and those with cT2 tumors. There was no difference in PSA recurrence between patients with clinical stage T1c and those with cT2 tumors (<em>P</em>=0.27).</td>
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<td>12. Klaassen Z, Singh AA, Howard LE, et al. Is clinical stage T2c prostate cancer an intermediate- or high-risk disease? <em>Cancer.</em> 2015;121(9):1414-1421.</td>
<td>Observational-Dx</td>
<td>2759 patients</td>
<td>To assess whether cT2c tumors without other high-risk factors (clinical stage T2c, not otherwise specified [cT2c-NOS]) behaved as an intermediate or high risk through an analysis of BCR after RP.</td>
<td>99 men (4%) from SEARCH and 202 men (2%) from JHH had tumors classified as cT2c-NOS. The cT2c-NOS patients had a BCR risk similar to that of the intermediate-risk patients (SEARCH, P=.27; JHH, P=.23) but a significantly lower BCR risk in comparison with the high-risk patients (SEARCH, P&lt;.001; JHH, P&lt;.001). When they were specifically compared with intermediate- and high-risk patients, after adjustments for year and center, cT2c-NOS patients had outcomes comparable to those of intermediate-risk patients (SEARCH, P=.53; JHH, P=.54) but significantly better than those of high-risk patients (SEARCH, P=.003; JHH, P&lt;.001).</td>
<td>4</td>
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<tr>
<td>13. Reese AC, Cooperberg MR, Carroll PR. Minimal impact of clinical stage on prostate cancer prognosis among contemporary patients with clinically localized disease. <em>J Urol.</em> 2010;184(1):114-119.</td>
<td>Observational-Dx</td>
<td>4,899 men</td>
<td>To test whether, in the context of data available from a contemporary biopsy, clinical stage no longer offers meaningful independent prognostic information for clinically localized PCa.</td>
<td>Of the 4,899 men in the study cohort 51.9% were classified as having T1 disease and 48.1% T2 disease. On univariate analysis clinical stages T2b and T2c were associated with pathological outcomes but only stage T2b was associated with BCR. In contrast PSA, biopsy GS and percent of positive biopsy cores were strongly associated with recurrence and adverse pathological outcomes. On multivariable analysis clinical stage was of no use in determining pathological or biochemical outcomes.</td>
<td>3</td>
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<td>14. Reese AC, Sadetsky N, Carroll PR, Cooperberg MR. Inaccuracies in assignment of clinical stage for localized prostate cancer. <em>Cancer.</em> 2011;117(2):283-289.</td>
<td>Observational-Dx</td>
<td>3875 patients</td>
<td>To characterize the prevalence of clinical stage misassignment in a multi-institutional national disease registry and to identify factors influencing staging errors.</td>
<td>Clinical stage was assigned incorrectly in 1370 of 3875 men (35.4%). Errors more commonly resulted in patient downstaging than upstaging (55.1% vs 44.9%; P&lt;.001). Patients with TRUS lesions were more likely to be staged incorrectly than those with abnormal DRE findings (65.8% vs 38.2%; P&lt;.001). Biopsy laterality was found to strongly influence stage assignment. Even after correction of staging errors, there was no association noted between clinical stage and biochemical disease recurrence after RP.</td>
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**Prostate Cancer–Pretreatment Detection, Surveillance, and Staging**

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<td>15. Stephenson AJ, Scardino PT, Eastham JA, et al. Preoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy. <em>J Natl Cancer Inst.</em> 2006;98(10):715-717.</td>
<td>Observational-Dx</td>
<td>1,545 patients</td>
<td>To examine preoperative nomogram predicting the 10-year probability of PCa recurrence after RP.</td>
<td>The nomogram was externally validated on an independent cohort of 1,545 patients with a concordance index of 0.79 and was well calibrated with respect to observed outcome. The inclusion of the number of positive and negative biopsy cores enhanced the predictive accuracy of the model. Thus, a new preoperative nomogram provides robust predictions of PCa recurrence up to 10 years after RP.</td>
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<td>16. Williams SG, Buyyounouski MK, Pickles T, et al. Percentage of biopsy cores positive for malignancy and biochemical failure following prostate cancer radiotherapy in 3,264 men: statistical significance without predictive performance. <em>Int J Radiat Oncol Biol Phys.</em> 2008;70(4):1169-1175.</td>
<td>Observational-Dx</td>
<td>3,264 patients</td>
<td>To retrospectively define and incorporate the impact of the percentage of positive biopsy cores into a predictive model of PCa RT biochemical outcome.</td>
<td>The cohort consisted of 21% low-, 51% intermediate-, and 28% high-risk cancer patients and 30% had with RT. The median percentage of positive biopsy cores was 50% (interquartile range 29%-67%), and median follow-up was 51 months (interquartile range 29-71 months). Percentage of positive biopsy cores displayed an independent association with the risk of biochemical failure ($P=0.01$), as did age, PSA value, GS, clinical stage, ADT duration, and RT dose ($P&lt;0.001$ for all). Including percentage of positive biopsy cores increased the c-index from 0.72 to 0.73 in the overall model. The influence of percentage of positive biopsy cores varied significantly with RT dose and clinical stage ($P=0.02$ for both interactions), with doses &lt;66 Gy and palpable tumors showing the strongest relationship between percentage of positive biopsy cores and biochemical failure. Intermediate-risk patients were poorly discriminated regardless of percentage of positive biopsy cores inclusion (c-index 0.65 for both models). Outcome models incorporating percentage of positive biopsy cores show only minor additional ability to predict biochemical failure beyond those containing standard prognostic factors.</td>
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<td>18. Klein EA, Cooperberg MR, Magi-Galluzzi C, et al. A 17-gene assay to predict prostate cancer aggressiveness in the context of Gleason grade heterogeneity, tumor multifocality, and biopsy undersampling. <em>Eur Urol.</em> 2014;66(3):550-560.</td>
<td>Observational-Dx</td>
<td>441 patients</td>
<td>To identify and validate a biopsy-based gene expression signature that predicts clinical recurrence, PCa death, and adverse pathology.</td>
<td>Of the 732 candidate genes analyzed, 288 (39%) were found to predict clinical recurrence despite heterogeneity and multifocality, and 198 (27%) were predictive of aggressive disease after adjustment for PSA, GS, and clinical stage. Further analysis identified 17 genes representing multiple biological pathways that were combined into the Genomic Prostate Score (GPS) algorithm. In the validation study, GPS predicted high-grade (OR per 20 GPS units: 2.3; 95% CI, 1.5-3.7; <em>P</em>&lt;0.001) and high-stage (OR per 20 GPS units: 1.9; 95% CI, 1.3-3.0; <em>P</em>=0.003) at surgical pathology. GPS predicted high-grade and/or high-stage disease after controlling for established clinical factors (<em>P</em>&lt;0.005) such as an OR of 2.1 (95% CI, 1.4–3.2) when adjusting for Cancer of the Prostate Risk Assessment score. A limitation of the validation study was the inclusion of men with low-volume intermediate-risk PCa (GS 3+4), for whom some providers would not consider AS.</td>
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<td>19. Locke JA, Black PC. Next generation biomarkers in prostate cancer. <em>Front Biosci (Landmark Ed).</em> 2016;21:328-342.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To highlight the potential value of the urine tests PCA3 and Prostarix(TM), especially for their ability to stratify patient risk with previous negative biopsy for occult cancer.</td>
<td>No results stated in abstract.</td>
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<td>21. Andriole GL, Crawford ED, Grubb RL, 3rd, et al.</td>
<td>Observational- Dx</td>
<td>76,693 men</td>
<td>To provides information on prostate-cancer incidence, staging, and mortality in both study groups during the first 7 to 10 years of the study.</td>
<td>In the screening group, rates of compliance were 85% for PSA testing and 86% for DRE. Rates of screening in the control group increased from 40% in the first year to 52% in the sixth year for PSA testing and ranged from 41 to 46% for DRE. After 7 years of follow-up, the incidence of PCa per 10,000 person-years was 116 (2820 cancers) in the screening group and 95 (2322 cancers) in the control group (rate ratio, 1.22; 95% CI, 1.16 to 1.29). The incidence of death per 10,000 person-years was 2.0 (50 deaths) in the screening group and 1.7 (44 deaths) in the control group (rate ratio, 1.13; 95% CI, 0.75 to 1.70). The data at 10 years were 67% complete and consistent with these overall findings.</td>
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<td>22. Schroder FH, Hugosson J, Roobol MJ, et al.</td>
<td>Experimental- Dx</td>
<td>72,891 intervention group and 89,352 control group</td>
<td>To provide updated results of mortality from PCa with follow-up to 2010, with analyses truncated at 9, 11, and 13 years.</td>
<td>With data truncated at 13 years of follow-up, 7408 PCa cases were diagnosed in the intervention group and 6107 cases in the control group. The rate ratio of PCa incidence between the intervention and control groups was 1.91 (95% CI, 1.83-1.99) after 9 years (1.64 [1.58-1.69] including France), 1.66 (1.60-1.73) after 11 years, and 1.57 (1.51-1.62) after 13 years. The rate ratio of PCa mortality was 0.85 (0.70-1.03) after 9 years, 0.78 (0.66-0.91) after 11 years, and 0.79 (0.69-0.91) at 13 years. The absolute risk reduction of death from PCa at 13 years was 0.11 per 1000 person-years or 1.28 per 1000 men randomized, which is equivalent to 1 PCa death averted per 781 (95% CI, 490-1929) men invited for screening or 1 per 27 (17-66) additional PCa detected. After adjustment for nonparticipation, the rate ratio of PCa mortality in men screened was 0.73 (95% CI, 0.61-0.88).</td>
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<td>23. Siddiqui MM, Rais-Bahrami S, Truong H, et al. Magnetic resonance imaging/ultrasound-fusion biopsy significantly upgrades prostate cancer versus systematic 12-core transrectal ultrasound biopsy. <em>Eur Urol.</em> 2013;64(5):713-719.</td>
<td>Experimental-Dx</td>
<td>582 patients</td>
<td>To study whether MRI/US fusion results in more accurate biopsies, the correlation was assessed between the GSs detected on MRI/US-fusion biopsy and those found on a standard 12-core TRUS biopsy performed during the same biopsy session.</td>
<td>A diagnosis of PCa was made in 315 (54%) of the patients. Addition of targeted biopsy led to Gleason upgrading in 81 (32%) cases. Targeted biopsy detected 67% more Gleason ≥4+3 tumors than 12-core biopsy alone and missed 36% of Gleason ≤3+4 tumors, thus mitigating the detection of lower-grade disease. Conversely, 12-core biopsy led to upgrading in 67 (26%) cases over targeted biopsy alone but only detected 8% more Gleason ≥4+3 tumors. On multivariate analysis, MP-MRI suspicion was associated with GS upgrading in the targeted lesions (P&lt;0.001). The main limitation of this study was that definitive pathology from RP was not available.</td>
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<td>24. van de Ven WJ, Barentsz JO. Prostate cancer: MRI/US-guided biopsy--a viable alternative to TRUS-guidance. <em>Nat Rev Urol.</em> 2013;10(10):559-560.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To 1) comment on an article by Siddiqui et al and 2) to discuss state of TRUS and MRI/US-fusion guided biopsies.</td>
<td>Implementation of MRI/US-fusion-guided biopsies requires caution: good quality MRIs and image interpretation is required, accurate segmentation and registration is essential for targeting tumor suspicious regions with MRI/US-fusion guidance, and small lesions have a chance of being missed using this technique.</td>
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<td>25. Moore CM, Robertson NL, Arsanious N, et al. Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. <em>Eur Urol.</em> 2013;63(1):125-140.</td>
<td>Review/Other-Dx</td>
<td>50 reports</td>
<td>To systematically review the literature to compare the accuracy of MRI-targeted biopsy with standard transrectal biopsy in the detection of clinically significant PCa.</td>
<td>Evidence synthesis was used to address specific questions. Where MRI was applied to all biopsy-naive men, 62% (374/599) had MRI abnormalities. When subjected to a targeted biopsy, 66% (248/374) had PCa detected. Both targeted and standard biopsy detected clinically significant cancer in 43% (236 or 237 of 555, respectively). Missed clinically significant cancers occurred in 13 men using targeted biopsy and 12 using a standard approach. Targeted biopsy was more efficient. A third fewer men were biopsied overall. Those who had biopsy required a mean of 3.8 targeted cores compared with 12 standard cores. A targeted approach avoided the diagnosis of clinically insignificant cancer in 53/555 (10%) of the presenting population.</td>
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Coakley

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<tr>
<td>26. Schoots IG, Roobol MJ, Nieboer D, Bangma CH, Steyerberg EW, Hunink MG. Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. <em>Eur Urol.</em> 2015;68(3):438-450.</td>
<td>Meta-analysis</td>
<td>16 studies including 1926 men</td>
<td>To systematically evaluate the benefits of MRI-targeted biopsy vs TRUS-biopsy for overall PCa detection (primary objective) and significant vs insignificant PCa detection (secondary objective).</td>
<td>A cumulative total of 1926 men with positive MRI were included, with PCa prevalence of 59%. MRI-targeted biopsy and TRUS-biopsy did not significantly differ in overall PCa detection (sensitivity 0.85, 95% CI, 0.80-0.89, and 0.81, 95% CI, 0.70-0.88, respectively). MRI-targeted biopsy had a higher rate of detection of significant PCa compared to TRUS-biopsy (sensitivity 0.91, 95% CI, 0.87-0.94 vs 0.76, 95% CI, 0.64-0.84) and a lower rate of detection of insignificant PCa (sensitivity 0.44, 95% CI, 0.26-0.64 vs 0.83, 95% CI, 0.77-0.87). Subgroup analysis revealed an improvement in significant PCa detection by MRI-targeted biopsy in men with previous negative biopsy, rather than in men with initial biopsy (relative sensitivity 1.54, 95% CI 1.05-2.57 vs 1.10, 95% CI 1.00-1.22). Because of underlying methodological flaws of MRI-targeted biopsy, the comparison of MRI-targeted biopsy and TRUS-biopsy needs to be regarded with caution.</td>
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<td>27. Bjurlin MA, Rosenkrantz AB, Beltran LS, Raad RA, Taneja SS. Imaging and evaluation of patients with high-risk prostate cancer. <em>Nat Rev Urol.</em> 2015;12(11):617-628.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To describe the various imaging modalities used to evaluate high-risk PCa patients.</td>
<td>While established PCa staging guidelines have increased the appropriate use of imaging, underuse for high-risk PCa remains substantial. Several factors affect the utility of initial diagnostic imaging, including the variable definition of high-risk PCa, variable guideline recommendations, poor accuracy of existing imaging tests, and the difficulty in validating imaging findings. Conventional imaging modalities, including CT and radionuclide bone scan, have been employed for local and metastatic staging, but their performance characteristics have generally been poor. Emerging modalities including mpMRI, PET/CT, and PET/MRI have shown increased diagnostic accuracy and could improve accuracy in staging patients with high-risk PCa.</td>
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<td>29. Smeenge M, de la Rosette JJ, Wijkstra H. Current status of transrectal ultrasound techniques in prostate cancer. Curr Opin Urol. 2012;22(4):297-302.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To present the current status of TRUS imaging in PCa and discuss the latest techniques now under preclinical evaluation.</td>
<td>3D US and quantification techniques are superior to 2D US in visualizing PCa and can be beneficial in staging prior to operation. Doppler-guided biopsies are more likely to yield positive results, especially when high GSs are present. Furthermore, Vardenafil usage strengthens Doppler enhancement and can help in increasing the diagnostic accuracy of Doppler. Multiple studies show elastography to be a promising new addition to the US investigations for detection of PCa. Especially the recently introduced Shear Wave Elastography shows decreased user dependency and increased PCa detection rates. MRI can also aid in the diagnostics of PCa. However, MRI-guided biopsies are more complicated compared to US guidance. MRI/US fusion combines best of both techniques and, although just recently emerged, the studies available show promising PCa detection rates.</td>
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<td>30. Onur R, Littrup PJ, Pontes JE, Bianco FJ, Jr. Contemporary impact of transrectal ultrasound lesions for prostate cancer detection. J Urol. 2004;172(2):512-514.</td>
<td>Observational-Dx</td>
<td>3,912</td>
<td>To study whether the predictability of a biopsy core changes if the tissue comes from an isoechoic vs hypoechoic lesion.</td>
<td>A total of 31,296 cores were obtained from the cohort. Overall 2,642 (68%) cores had at least 1 hypoechoic lesion ultrasonographically. Cancer was detected in 675 (25.5%) and 323 (25.4%) patients with or without hypoechoic lesions (P=0.97). The per core cancer detection was fairly uniform and averaged 9.3% and 10.4% for hypoechoic and isoechoic areas, respectively. The difference was not statistically significant (P=0.3). GSs were less than 7, 7 and greater than 7 in 46%, 34% and 20% of cases, respectively.</td>
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<td>Mitterberger M, Pinggera GM, Horninger W, et al. Comparison of contrast enhanced color Doppler targeted biopsy to conventional systematic biopsy: impact on Gleason score. <em>J Urol.</em> 2007;178(2):464-468; discussion 468.</td>
<td>Observational-Dx</td>
<td>690 men</td>
<td>Prospective randomized study to compare US systematic biopsy with contrast enhanced color Doppler targeted biopsy for the impact on GS findings.</td>
<td>PCa was identified in 221/690 subjects (32%) with a mean PSA of 4.6 ng/ml (range 1.4 to 35.0). PCa was detected in 180/690 subjects (26%) with contrast enhanced color Doppler targeted biopsy and in 166/690 patients (24%) with systematic US biopsy. The GS of all 180 cancers detected on contrast enhanced color Doppler targeted biopsy was 6 or higher (mean 6.8). The GS of all 166 cancers detected on systematic biopsy ranged from 4 to 6 and mean GS was 5.4. Contrast enhanced color Doppler targeted biopsy detected significantly higher GSs compared to systematic biopsy (Wilcoxon rank sum test ( P&lt;0.003 )). Contrast enhanced color Doppler targeted biopsy detected cancers with higher GSs and more cancer than systematic biopsy. Therefore, contrast enhanced color Doppler seems to be helpful in the grading of PCa, which is important for defining prognosis and deciding treatment.</td>
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<td>Mitterberger M, Pinggera GM, Pallwein L, et al. The value of three-dimensional transrectal ultrasonography in staging prostate cancer. <em>BJU Int.</em> 2007;100(1):47-50.</td>
<td>Observational-Dx</td>
<td>180 patients</td>
<td>To use 3D-TRUS to reconstruct the prostate, and thus determine its value in staging clinically localized PCa in a prospective study.</td>
<td>Pathological staging of specimens showed ECE in 69 patients, of whom 53 had pathological capsular perforation and 16 had SVI. 3D-TRUS identified 58 patients with sites of ECE with 84% sensitivity, 96% specificity, 94% PPV, 91% NPV and an overall accuracy of 92%. Of the 16 patients with SVI 14 were identified correctly on 3D-TRUS. Overall the 3D-TRUS staging sensitivity was 84%, specificity 96%, PPV 93%, NPV 91% and accuracy 91%. 3D-TRUS seems to be an accurate technique for staging localized PCa. If 3D-TRUS indicates locally advanced disease, the probability of capsular perforation or SVI is very high.</td>
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<td>33. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. <em>J Urol.</em> 1989;142(1):71-74; discussion 74-75.</td>
<td>Observational-Dx</td>
<td>136 patients</td>
<td>To examine the possibility that random systematic biopsies from the apex to the base in the peripheral and central zones of both prostatic lobes may be a better method to detect posteriorly located cancers than concentrating upon specific hypo-echoic defects.</td>
<td>PCa was diagnosed in 83/136 patients (62%). In 80 of 83 individuals (94%) the cancer was detected by random systematic biopsies alone. Of 57 men in whom random systematic and directed biopsies were obtained the results of biopsy agreed in 86%, while in 9% random systematic biopsies found cancers missed by directed biopsies and in 5% directed biopsies diagnosed cancers missed by random systematic prostate biopsies.</td>
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<td>34. Dominguez-Escrig JL, McCracken SR, Greene D. Beyond diagnosis: evolving prostate biopsy in the era of focal therapy. <em>Prostate Cancer.</em> 2011;2011:386207.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To review the evolution of prostatic biopsy and current controversies.</td>
<td>Despite decades of use as the “gold standard” in the detection of PCa, the optimal biopsy regimen is still not universally agreed upon. While important aspects such as the need for laterally placed biopsies and the importance of apical cancer are known, repeated studies have shown significant patients with cancer on subsequent biopsy when the original biopsy was negative and an ongoing suspicion of cancer remained. Attempts to maximize the effectiveness of repeat biopsies have given rise to the alternate approaches of saturation biopsy and the transperineal approach. Recent interest in focal treatment of PCa has further highlighted the need for accurate detection of PCa, and in response, the introduction of transperineal template-guided biopsy. While the saturation biopsy approach and the transperineal template approach increase the detection rate of cancer in men with a previous negative biopsy and appear to have acceptable morbidity, there is a lack of clinical trials evaluating the different biopsy strategies.</td>
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<td>35. Kvale R, Moller B, Wahlqvist R, et al. Concordance between Gleason scores of needle biopsies and radical prostatectomy specimens: a population-based study. BJU Int. 2009;103(12):1647-1654.</td>
<td>Observational-Dx</td>
<td>1,116 patients</td>
<td>To study the concordance between the GSs of needle biopsies and RP specimens in a population-based registry, to clarify whether the concordance depends on the annual number of RP specimens assessed in the pathology unit, and to identify preoperative clinical factors that predict upgrading from a GS of ≤6 in the biopsy to ≥7 in the RP specimen.</td>
<td>The GSs were identical in biopsy and RP specimens in 591/1116 (53%) patients. The biopsy-based GS more often under-graded (38%) than over-graded (9%) the RP-based GS. Pathology units that examined &gt;40 RP specimens annually had a higher concordance between the GS in the biopsy and RP specimen than did lower-volume units. The rate of upgrading from a GS of ≤6 in the biopsy to ≥7 in the RP specimen increased with increasing preoperative PSA serum levels, and with increasing intervals between biopsy and RP.</td>
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<td>36. Porten SP, Whitson JM, Cowan JE, et al. Changes in prostate cancer grade on serial biopsy in men undergoing active surveillance. J Clin Oncol. 2011;29(20):2795-2800.</td>
<td>Observational-Dx</td>
<td>377</td>
<td>To further characterize the behavior of Gleason grade on serial biopsies over time in men undergoing AS.</td>
<td>377 men met inclusion criteria. Mean age at diagnosis was 61.9 years. 53% of men had PSA of 6 ng/mL or less, and 94% had GS of 6 or less. A majority of men were cT1 (62%), had ≤33% of biopsy cores involved (80%), and were low risk (77%) at diagnosis. Median number of cores taken at diagnostic biopsy was 13, mean time to follow-up was 18.5 months, and 29% of men had 3 or more repeat biopsies. Overall, 34% (129 men) were found to have an increase in Gleason grade. The majority of men who experienced an upgrade (81%) did so by their second repeat biopsy.</td>
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<td>37. Rifkin MD, Zerhouni EA, Gatsonis CA, et al. Comparison of magnetic resonance imaging and ultrasonography in staging early prostate cancer. Results of a multi-institutional cooperative trial. N Engl J Med. 1990;323(10):621-626.</td>
<td>Observational-Dx</td>
<td>230 patients</td>
<td>To compare body coil MRI and TRUS in staging clinically localized cancer.</td>
<td>MRI 57% accurate in staging local cancer; TRUS 46% accurate in staging local cancer. The MRI and US equipment that is currently available is not highly accurate in staging early PCa, mainly because neither technique has the ability to identify microscopic spread of disease. Further evaluation with improved equipment may improve the accuracy of these techniques.</td>
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### EVIDENCE TABLE

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<tr>
<td>38. Tempany CM, Zhou X, Zerhouni EA, et al. Staging of prostate cancer: results of Radiology Diagnostic Oncology Group project comparison of three MR imaging techniques. <em>Radiology.</em> 1994;192(1):47-54.</td>
<td>Observational-Dx</td>
<td>213 patients</td>
<td>To determine the accuracy of endorectal MRI staging and compare with body coil.</td>
<td>Overall accuracy for conventional body-coil, fat-suppressed body-coil, and endorectal-coil MR was 61%, 64%, and 54%, respectively. Overall group accuracy for combinations A and B was 57% and 61%. Considerable inter-reader variability was found for combination A. No technique was highly accurate for staging early PCa. Individual radiologists did achieve a high degree of staging accuracy with the endorectal-coil and body-coil combination.</td>
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<td>39. Weinreb JC, Blume JD, Coakley FV, et al. Prostate cancer: sextant localization at MR imaging and MR spectroscopic imaging before prostatectomy--results of ACRIN prospective multi-institutional clinicopathologic study. <em>Radiology.</em> 2009;251(1):122-133.</td>
<td>Observational-Dx</td>
<td>110 patients with complete data, 8 readers</td>
<td>Prospective, multicenter study to determine the incremental benefit of combined endorectal MRI and MRSI, as compared with endorectal MRI alone, for sextant localization of peripheral zone PCa. Reference standard was presence or absence of cancer at centralized histopathologic evaluation of prostate specimens.</td>
<td>MRI alone and combined MRI-MRSI had similar accuracy in peripheral zone cancer localization. (AUC, 0.60 vs 0.58, respectively; (P&gt;0.05)). AUC for individual readers were 0.57-0.63 for MRI alone and 0.54-0.61 for combined MRI-MRSI. For RP, accuracy of combined 1.5-T endorectal MRI-MRSI for sextant localization of peripheral zone PCa is equal to that of MRI alone.</td>
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<td>40. Engelbrecht MR, Huisman HJ, Laheij RJ, et al. Discrimination of prostate cancer from normal peripheral zone and central gland tissue by using dynamic contrast-enhanced MR imaging. <em>Radiology.</em> 2003;229(1):248-254.</td>
<td>Observational-Dx</td>
<td>36 patients</td>
<td>To evaluate which parameters of dynamic MRI and T2 relaxation rate would result in optimal discrimination of prostatic carcinoma from normal peripheral zone and central gland tissues and to correlate these parameters with tumor stage, GS, patient age, and tumor markers.</td>
<td>Results of multivariate receiver operating characteristic analysis showed that relative peak enhancement demonstrated the highest AUC in the peripheral zone and the central gland (AUC = 0.93, 0.82). Results of multivariate analysis without relative peak enhancement showed that relative peak enhancement in the peripheral zone and washout in the central gland demonstrated the highest AUC (AUC = 0.9, 0.81). Pearson correlation coefficients between the dynamic parameters or T2 relaxation rates in carcinoma and the tumor stage, GS, patient age, and tumor markers ranged between 0.02 and 0.44.</td>
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**Observational-Dx** 20 patients

To compare DCE imaging and T2-weighted imaging using a 3T MR unit for the localization of PCa.

PCa was pathologically detected in 64 (53%) of 120 peripheral zone areas. The sensitivity, specificity, and accuracy for PCa detection were 55%, 88% and 70% for T2-weighted imaging and 73%, 77%, and 75% for DCE imaging, respectively. Three cancer areas were detected only by T2-weighted imaging, 15 only by DCE imaging, and 34 by both T2-weighted imaging and DCE imaging. A fair or excellent degree at depicting tumor border was achieved in 67% by T2-weighted imaging and in 90% by DCE imaging ($P<0.05$).


**Observational-Dx** 33 patients

To investigate the utility of diffusion tensor imaging, quantitative DCE-MRI, and the two techniques combined at 3T in detecting PCa of the peripheral zone.

There were significant differences in the ADC, FA, K(trans), and kep values between cancerous sextants and noncancerous sextants in peripheral zone ($P<0.0001$, $P<0.0001$, $P<0.0001$, and $P<0.0001$ respectively). The AUC for diffusion tensor imaging + DCE-MRI was significantly greater than that for either diffusion tensor imaging (0.93 vs 0.86, $P=0.0017$) or DCE-MRI (0.93 vs 0.84, $P=0.0034$) alone.


**Observational-Dx** 20 patients

To compare utility of T2-weighted MRI and DWI-MRI obtained with and without an endorectal coil at 3T for localizing PCa.

At histopathology 51 cancer foci were present ranging in size from 2 to 60 mm. The sensitivity of the endorectal dual-coil, nonendorectal coil MRIs were 0.76, 0.45, respectively. PPVs for endorectal dual-coil, nonendorectal coil MRI were 0.80, 0.64, respectively. Mean size of detected lesions with nonendorectal coil MRI were larger than those detected by dual-coil MRI (22 mm vs 17.4 mm).
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<td>44. Vargas HA, Akin O, Franiel T, et al. Diffusion-weighted endorectal MR imaging at 3 T for prostate cancer: tumor detection and assessment of aggressiveness. Radiology. 2011;259(3):775-784.</td>
<td>Observational-Dx</td>
<td>51 patients</td>
<td>Retrospective study to assess the incremental value of DWI-MRI over T2-weighted MRI at 3T for PCa detection and to investigate the use of the ADC to characterize tumor aggressiveness, with whole-mount step-section pathologic analysis as the reference standard.</td>
<td>For tumor detection, the AUCs for readers 1 and 2 were 0.79 and 0.76, respectively, for T2-weighted MRI were 0.79 and 0.78, respectively, for T2-weighted MRI plus the ADC map. Mean ADC for both cancerous and healthy prostatic regions were lower when DWI-MRI was performed with a b value of 1000 sec/mm(2) rather than 700 sec/mm(2). Regardless of the b value used, there was a significant difference in the mean ADC between malignant and benign prostate regions. A lower mean ADC was significantly associated with a higher tumor GS (mean ADC of [1.21, 1.10, 0.87, and 0.69] × 10(-3) mm(2)/sec were associated with GS of 3 + 3, 3 + 4, 4 + 3, and 8 or higher, respectively; P=.017). Combined DWI and T2-weighted MRI had similar performance to T2-weighted MRI alone for tumor detection; however, DWI MRI provided additional quantitative information that significantly correlated with PCa aggressiveness.</td>
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<td>45. de Rooij M, Hamoen EH, Witjes JA, Barentsz JO, Rovers MM. Accuracy of Magnetic Resonance Imaging for Local Staging of Prostate Cancer: A Diagnostic Meta-analysis. Eur Urol. 2015;[E-pub ahead of print].</td>
<td>Meta-analysis</td>
<td>75 studies including 9796 patients</td>
<td>To assess the diagnostic accuracy of MRI for local PCa staging and explore the influence of different imaging protocols.</td>
<td>A total of 75 studies (9796 patients) could be analyzed. Pooled data for ECE (45 studies, 5681 patients), SVI (34 studies, 5677 patients), and overall stage T3 detection (38 studies, 4001 patients) showed sensitivity and specificity of 0.57 (95% CI, 0.49-0.64) and 0.91 (95% CI, 0.88-0.93), 0.58 (95% CI, 0.47-0.68) and 0.96 (95% CI, 0.95-0.97), and 0.61 (95% CI, 0.54-0.67) and 0.88 (95% CI, 0.85-0.91), respectively. Functional imaging in addition to T2-weighted imaging and use of higher field strengths (3T) improved sensitivity for ECE and SVI. ECE sensitivity was not improved by endorectal coil use.</td>
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<td>46. Verma S, Turkbey B, Muradyan N, et al. Overview of dynamic contrast-enhanced MRI in prostate cancer diagnosis and management. AJR Am J Roentgenol. 2012;198(6):1277-1288.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To provide a detailed summary of efforts to date in prostate DCE-MRI as well as to present a guide for performing DCE-MRI in patients with known or suspected prostate cancer.</td>
<td>No results stated in abstract.</td>
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<td>47. Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS Prostate Imaging - Reporting and Data System: Version 2. <em>Eur Urol.</em> 2016;69(1):16-40.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To promote global standardization and diminish variation in the acquisition, interpretation, and reporting of prostate mpMRI examination, and it is based on the best available evidence and expert consensus opinion.</td>
<td>No results stated in abstract.</td>
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<td>48. Romero G, Foster BR, Pettersson DR, Fung AW, Guimaraes AR, Coakley FV. Endorectal multiparametric MRI of the prostate: incremental effect of perfusion imaging on biopsy target identification. <em>Clin Imaging.</em> 2016;40(3):553-557.</td>
<td>Observational-Dx</td>
<td>52 patients</td>
<td>To evaluate the incremental effect of perfusion imaging on biopsy target identification at endorectal mpMRI.</td>
<td>Reader 1 identified 36 targets without and 39 targets with perfusion imaging (P&gt;.05). The corresponding numbers for reader 2 were 38 and 38, respectively (P=.5).</td>
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<td>49. Klein EA. Prostate cancer: MR-TRUS fusion biopsy−defining a new standard. <em>Nat Rev Clin Oncol.</em> 2015;12(5):253-254.</td>
<td>Observational-Dx</td>
<td>N/A</td>
<td>To 1) comment on a study published by Siddiqui et al and 2) explain how MR-TRUS fusion can address the shortcomings of current biopsy schemes.</td>
<td>The widespread use of PSA screening and TRUS-guided prostate biopsy has resulted in an epidemic of overdetection and overtreatment of PCa. The use of targeted MR and US fusion guided prostate biopsy promises to improve the detection rate of high-risk PCa—reducing the issue of overdetection and overtreatment.</td>
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<td>50. Cool DW, Zhang X, Romagnoli C, Izawa JI, Romano WM, Fenster A. Evaluation of MRI-TRUS fusion versus cognitive registration accuracy for MRI-targeted, TRUS-guided prostate biopsy. <em>AJR Am J Roentgenol.</em> 2015;204(1):83-91.</td>
<td>Observational-Dx</td>
<td>100 patients</td>
<td>To compare TRUS biopsy accuracies of operators with different levels of prostate MRI experience using cognitive registration vs MRI-TRUS fusion to assess the preferred method of TRUS prostate biopsy for MRI-identified lesions.</td>
<td>2D and 3D TRUS sampled only 48% and 45% of clinically significant PCa MRI lesions, respectively, compared with 100% with MRI-TRUS fusion. Lesion sampling accuracy did not statistically significantly vary according to operator experience or tumor volume. MRI-TRUS fusion-naive operators showed consistent errors in targeting of the apex, midgland, and anterior targets, suggesting that there is biased error in cognitive registration. The MRI-TRUS fusion expert correctly targeted the prostate apex; however, his midgland and anterior mistargeting was similar to that of the less-experienced operators.</td>
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<td>51.</td>
<td>Observational-Dx</td>
<td>50 patients</td>
<td>To obtain pilot data on the diagnostic ability of visually directed targeted biopsy vs software-based targeted biopsy, considering transperineal template mapping biopsy as the reference test.</td>
<td>Median age was 68 (interquartile range: 63-73); median PSA level was 7.9ng/mL (6.4-10.2). A total of 79 targets were detected with a mean of 1.6 targets per patient. Of these, 27 (34%), 28 (35%), and 24 (31%) were scored 3, 4, and 5, respectively. At a patient level, the detection rate was 32 (64%), 34 (68%), and 38 (76%) for visually directed targeted, software-based biopsy, and transperineal template mapping, respectively. Combining the 2 targeted strategies would have led to detection rate of 39 (78%). At a patient level and at a target level, software-based targeted biopsy found more clinically significant diseases than did visually directed targeted biopsy, although this was not statistically significant (22% vs 14%, ( P=0.48 ); 51.9% vs 44.3%, ( P=0.24 )). Secondary analysis showed similar results. Based on these findings, a paired cohort study enrolling at least 257 men would verify whether this difference is statistically significant.</td>
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<td>52.</td>
<td>Experimental-Dx</td>
<td>125 men</td>
<td>To prospectively compare targeted biopsy outcomes between MRI-US fusion and visual targeting.</td>
<td>Among 172 targets, fusion biopsy detected 55 (32.0%) cancers and 35 (20.3%) Gleason sum ( \geq 7 ) cancers compared with 46 (26.7%) and 26 (15.1%), respectively, using visual targeting (( P=0.1374, P=0.0523 )). Fusion biopsy provided informative nonbenign histology in 77 targets compared with 60 by visual (( P=0.0104 )). Targeted biopsy detected 75.0% of all clinically significant cancers and 86.4% of Gleason sum ( \geq 7 ) cancers detected on standard biopsy. On multivariate analysis, fusion performed best among smaller targets. The study is limited by lack of comparison with whole-gland specimens and sample size. Furthermore, cancer detection on visual targeting is likely higher than in community settings, where experience with this technique may be limited.</td>
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<tr>
<td>53. Hoeks CM, Schouten MG, Bomers JG, et al. Three-Tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative, random, systematic, transrectal ultrasound biopsies: detection of clinically significant prostate cancers. <em>Eur Urol.</em> 2012;62(5):902-909.</td>
<td>Observational-Dx</td>
<td>438 consecutive patients, MR-guided biopsy performed in 265 patients</td>
<td>To determine the detection rate of (clinically significant) high PCa for MR-guided biopsy of cancer-suspicious regions on 3-T mpMRI in patients with elevated PSA and one or more negative TRUS-biopsy sessions.</td>
<td>In a total of 117 patients, cancer was detected with MR-guided biopsy (n=108) or after negative MR-guided biopsy (n=9). PCa was detected in 108/438 patients (25%) and in 41% (108/265) of MR-guided biopsy patients. The majority of detected cancers (87%) were clinically significant. Clinically significant cancers were detected in 7/9 (78%) negative MR-guided biopsy patients in whom PCa was detected during follow-up. Sensitivity analysis resulted in increased cancer detection (47%-56%). Complications occurred in 0.2% of patients (5/265). In patients with elevated PSA and 1 or more negative TRUS-biopsy sessions, MR-guided biopsy of mpMRI cancer-suspicious regions had a PCa-detection rate of 41%. The majority of detected cancers were clinically significant (87%).</td>
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<td>54. Mendhiratta N, Rosenkrantz AB, Meng X, et al. Magnetic Resonance Imaging-Ultrasound Fusion Targeted Prostate Biopsy in a Consecutive Cohort of Men with No Previous Biopsy: Reduction of Over Detection through Improved Risk Stratification. <em>J Urol.</em> 2015;194(6):1601-1606.</td>
<td>Observational-Dx</td>
<td>382 patients</td>
<td>We report clinical outcomes of 12-core systematic biopsy and MRF-TB in men who presented for primary biopsy and further describe pathological characteristics of cancers detected by systematic biopsy and not by MRF-TB.</td>
<td>PCa was detected in 207/382 men (54.2%) with a mean+/−SD age of 64+/−8.5 years and mean+/−SEM PSA 6.8+/−0.3 ng/ml who met study inclusion criteria. The cancer detection rate of systematic biopsy and MRF-TB was 49.2% and 43.5%, respectively (P=0.006). MRF-TB detected more GS 7 or greater cancers than systematic biopsy (117/132 or 88.6% vs 102/132 or 77.3%, P=0.037). Of 41 cancers detected by systematic biopsy but not by MRF-TB 34 (82.9%) demonstrated Gleason 6 disease, and 26 (63.4%) and 34 (82.9%) were clinically insignificant by Epstein criteria and a UCSF CAPRA (University of California-San Francisco-Cancer of the Prostate Risk Assessment) score of 2 or less, respectively.</td>
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<td>55. Nassiri N, Natarajan S, Margolis DJ, Marks LS. Targeted Prostate Biopsy: Lessons Learned Midst the Evolution of a Disruptive Technology. Urology. 2015;86(3):432-438.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To report lessons learned during a 6-year experience with more than 1200 patients undergoing targeted prostate biopsy via MRI/US fusion.</td>
<td>1) the procedure is safe and efficient, requiring some 15-20 minutes in an office setting; 2) MRI is best performed by a radiologist with specialized training, using a transabdominal multiparametric approach and preferably a 3T magnet; 3) grade of MRI suspicion is the most powerful predictor of biopsy results, eg, Grade 5 usually represents cancer; 4) some potentially important cancers (15%-30%) are MRI-invisible; 5) targeted biopsies provide &gt;80% concordance with whole-organ pathology. Early enthusiasm notwithstanding, cost-effectiveness is yet to be resolved, and the technologies remain in evolution.</td>
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<td>56. Jia JB, Houshyar R, Verma S, Uchio E, Lall C. Prostate cancer on computed tomography: A direct comparison with multi-parametric magnetic resonance imaging and tissue pathology. Eur J Radiol. 2016;85(1):261-267.</td>
<td>Observational-Dx</td>
<td>27 patients</td>
<td>To prove that areas of focal mass-like enhancement on CT imaging directly correlate with prostate neoplasms as revealed on multi-parametric MRI and follow-up targeted biopsy.</td>
<td>CT results were directly compared to multi-parametric MRI findings and biopsy results. The overall agreement of MRI and CT is 85.19% (95% CI: 67.52%-94.08%). The positive percent agreement is 78.95% (95% CI: 54.43%-93.95%) and the negative percent agreement is 100.0% (95% CI: 63.06%-100.0%). When CT results are directly compared to biopsy results, sensitivity and specificity of CT are 63.64% (95% CI: 30.79%-89.07%) and 100.0% (95% CI: 47.82%-100.0%). The PPV is 100.0% (95% CI: 59.04%-100.0%) and the NPV is 55.56% (95% CI: 21.2%-86.3%). When compared to MRI, CT has a lower sensitivity and a higher specificity, as well as a higher PPV and NPV. Logistic regression analysis did not show a significant relationship between concordance of MRI and CT and GS, time between studies, age, and PSA level.</td>
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<td>57. Hovels AM, Heesakkers RA, Adang EM, et al. The diagnostic accuracy of CT and MRI in the staging of pelvic lymph nodes in patients with prostate cancer: a meta-analysis. Clin Radiol. 2008;63(4):387-395.</td>
<td>Meta-analysis</td>
<td>24 studies</td>
<td>To compare the diagnostic accuracy of CT and MRI in the diagnosis of LN metastases in PCa.</td>
<td>A total of 24 studies were included. For CT, pooled sensitivity was 0.42 (0.26-0.56, 95% CI) and pooled specificity was 0.82 (0.8-0.83, 95% CI). For MRI, the pooled sensitivity was 0.39 (0.22-0.56, 95% CI) and pooled specificity was 0.82 (0.79-0.83, 95% CI). The differences in performance of CT and MRI were not statistically significant.</td>
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<td>58. Briganti A, Abdollah F, Nini A, et al. Performance characteristics of computed tomography in detecting lymph node metastases in contemporary patients with prostate cancer treated with extended pelvic lymph node dissection. <em>Eur Urol.</em> 2012;61(6):1132-1138.</td>
<td>Observational-Dx</td>
<td>1,541 patients</td>
<td>To assess the value of CT in predicting LN invasion in contemporary PCa patients treated with extended pelvic LN dissection.</td>
<td>Overall, a CT scan that suggested LN invasion was found in 73 patients (4.7%). Of them, only 24 patients (32.8%) had histologically proven LN invasion at extended pelvic LN dissection. Overall, sensitivity, specificity, and accuracy of CT scan were 13%, 96.0%, and 54.6%, respectively. In patients with low-, intermediate-, or high-risk PCa according to NCCN classification, sensitivity was 8.3%, 96.3%, and 52.3%, respectively; specificity was 3.6%, 97.3%, and 50.5%, respectively; and accuracy was 17.9%, 94.3%, and 56.1%, respectively. Similarly, in patients with a nomogram-derived LN invasion risk ≥50%, sensitivity, specificity, and accuracy were only 23.9%, 94.7%, and 59.3%, respectively. At multivariable analyses, inclusion of CT scan findings did not improve the accuracy of LN invasion prediction (81.4% compared with 81.3%; P=0.8). Lack of a central scan review represents the main limitation of our study. In contemporary patients with PCa, the accuracy of CT scan as a preoperative nodal-staging procedure is poor, even in patients with high LN invasion risk. Therefore, the need for and the extent of pelvic LN dissection should not be based on the results obtained by CT scan.</td>
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<td>59. Gabriele D, Collura D, Oderda M, et al. Is there still a role for computed tomography and bone scintigraphy in prostate cancer staging? An analysis from the EUREKA-1 database. <em>World J Urol.</em> 2016;34(4):517-523.</td>
<td>Observational-Dx</td>
<td>1,145 patients</td>
<td>To evaluate whether bone scintigraphy and CT still have a role in PCa staging.</td>
<td>CT scan showed a sensitivity and specificity in predicting LNI of 8.8% and 98%; subgroup analysis disclosed a significant association only for the high-risk subgroup of 334 patients ($P=0.009$) with a sensitivity of 11.8% and PPV of 44.4%. However, logistic multivariate regression analysis including preoperative risk factors excluded any additional predictive ability of CT even in the high-risk group ($P=0.40$). These data are confirmed by receiver-operator characteristic curve analysis, showing a low AUC of 54% for CT, compared with 69% for Partin tables and 80% for Briganti nomogram. Bone scintigraphy showed some positivity in 74 cases, only 4 of whom progressed, while 49 patients with negative bone scintigraphy progressed during their follow-up, 6 of them immediately after surgery.</td>
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<td>60. Heidenreich A, Bastian PJ, Bellmunt J, et al. EAU guidelines on prostate cancer. part 1: screening, diagnosis, and local treatment with curative intent-update 2013. <em>Eur Urol.</em> 2014;65(1):124-137.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To present a summary of the 2013 version of the EAU guidelines on screening, diagnosis, and local treatment with curative intent of clinically organ-confined PCa.</td>
<td>Current evidence is insufficient to warrant widespread population-based screening by PSA for PCa. Systematic prostate biopsies under US guidance and local anesthesia are the preferred diagnostic method. AS represents a viable option in men with low-risk PCa and a long life expectancy. A biopsy progression indicates the need for active intervention, whereas the role of PSA doubling time is controversial. In men with locally advanced PCa for whom local therapy is not mandatory, watchful waiting is a treatment alternative to ADT, with equivalent oncologic efficacy. Active treatment is recommended mostly for patients with localized disease and a long life expectancy, with RP shown to be superior to watchful waiting in prospective randomized trials. Nerve-sparing RP is the approach of choice in organ-confined disease, while neoadjuvant ADT provides no improvement in outcome variables. RT should be performed with ≥74 Gy in low-risk PCa and 78 Gy in intermediate- or high-risk PCa. For locally advanced disease, adjuvant ADT for 3 year results in superior rates for disease-specific and OS and is the treatment of choice. Follow-up after local therapy is largely based on PSA and a disease-specific history, with imaging indicated only when symptoms occur.</td>
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<td>61. Shen G, Deng H, Hu S, Jia Z. Comparison of choline-PET/CT, MRI, SPECT, and bone scintigraphy in the diagnosis of bone metastases in patients with prostate cancer: a meta-analysis. <em>Skeletal Radiol.</em> 2014;43(11):1503-1513.</td>
<td>Meta-analysis</td>
<td>16 articles consisting of 27 studies were included in the analysis</td>
<td>To perform a comprehensive meta-analysis to compare the diagnostic performance of choline-PET/CT, MRI, bone SPECT, and bone scintigraphy in detecting bone metastases in parents with PCa.</td>
<td>On a per-patient basis, the pooled sensitivities by using choline PET/CT, MRI, and bone scintigraphy were 0.91 [95% CI: 0.83-0.96], 0.97 (95% CI: 0.91-0.99), 0.79 (95% CI: 0.73-0.83), respectively. The pooled specificities for detection of bone metastases using choline PET/CT, MRI, and bone scintigraphy, were 0.99 (95% CI: 0.93-1.00), 0.95 (95% CI: 0.90-0.97), and 0.82 (95% CI: 0.78-0.85), respectively. On a per-lesion basis, the pooled sensitivities of choline PET/CT, bone SPECT, and bone scintigraphy were 0.84 (95% CI: 0.81-0.87), 0.90 (95% CI: 0.86-0.93), 0.59 (95% CI: 0.55-0.63), respectively. The pooled specificities were 0.93 (95% CI: 0.89-0.96) for choline PET/CT, 0.85 (95% CI: 0.80-0.90) for bone SPECT, and 0.75 (95% CI: 0.71-0.79) for bone scintigraphy. This meta-analysis indicated that MRI was better than choline PET/CT and bone scintigraphy on a per-patient basis. On a per-lesion analysis, choline PET/CT with the highest diagnostic OR and Q* was better than bone SPECT and bone scintigraphy for detecting bone metastases from PCa.</td>
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<td>62. Sandhu GS, Andriole GL. Overdiagnosis of prostate cancer. <em>J Natl Cancer Inst Monogr.</em> 2012;2012(45):146-151.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To address issues relevant to PCa over-diagnosis.</td>
<td>No results stated in abstract.</td>
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<td>63. Pokorny MR, de Rooij M, Duncan E, et al. Prospective study of diagnostic accuracy comparing prostate cancer detection by transrectal ultrasound-guided biopsy versus magnetic resonance (MR) imaging with subsequent MR-guided biopsy in men without previous prostate biopsies. <em>Eur Urol.</em> 2014;66(1):22-29.</td>
<td>Observational-Dx</td>
<td>223 patients</td>
<td>To compare the diagnostic efficacy of the MRI pathway with TRUS-guided biopsy.</td>
<td>Of 223 men, 142 (63.7%) had PCa. TRUS-guided biopsy detected 126 cases of PCa in 223 men (56.5%) including 47 (37.3%) classed as low risk. MRI-guided biopsy detected 99 cases of PCa in 142 men (69.7%) with equivocal or suspicious mpMRI, of which 6 (6.1%) were low risk. The MRI-guided biopsy pathway reduced the need for biopsy by 51%, decreased the diagnosis of low-risk PCa by 89.4%, and increased the detection of intermediate/high-risk PCa by 17.7%. The estimated NPVs of TRUS-guided biopsy and MRI-guided biopsy for intermediate/high-risk disease were 71.9% and 96.9%, respectively. The main limitation is the lack of long follow-up.</td>
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<td>64. Keetch DW, Catalona WJ, Smith DS. Serial prostatic biopsies in men with persistently elevated serum prostate specific antigen values. <em>J Urol.</em> 1994;151(6):1571-1574.</td>
<td>Observational-Dx</td>
<td>1,136 patients</td>
<td>To determine the need for repeat prostatic biopsies in men whose initial biopsy results revealed no evidence of cancer or atypia.</td>
<td>Of 427 men who had negative initial biopsy results, a persistent serum PSA level of &gt;4.0 ng/mL and abnormal rectal or US examination findings 82 (19%) had cancer on biopsy 2. Of 203 men with persistent abnormalities 16 (8%) had cancer on biopsy 3 and 6 of 91 (7%) had cancer on biopsy 4 or later. Thus, 96% of the cancers were detected through either biopsy 1 or 2. The median initial PSA level, follow-up PSA levels and the yearly rate of change in PSA were significantly greater in men whose cancer was detected compared with those of men whose cancer was not detected (6.4 vs 5.4 ng/mL, 7.4 vs 6.6 ng/mL and 1.1 vs 0.7 ng/mL per year, respectively). There was a trend for a higher percentage of tumors detected through serial screening to be pathologically organ confined with those detected through initial screening (73% vs 62%, P=0.07).</td>
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<td>65. Ploussard G, Nicolaiew N, Marchand C, et al. Risk of repeat biopsy and prostate cancer detection after an initial extended negative biopsy: longitudinal follow-up from a prospective trial. BJU Int. 2013;111(6):988-996.</td>
<td>Observational-Dx</td>
<td>617 men</td>
<td>To assess prospectively the time-varying risk of rebiopsy and of PCa detection after an initial negative biopsy protocol.</td>
<td>A total of 617 men (31%) underwent at least 1 rebiopsy after a mean follow-up of 19 months. PCa detection rates during second, third, and fourth sets of biopsies were 16.7%, 16.9%, and 12.5%, respectively. The overall rate of detected PCa was 7.0%. The 5-year rebiopsy-free and PCa-free survival rates were 65.9% and 92.5%, respectively. Indications for rebiopsy were more frequently reported in patients having a high PSA level ($P=0.006$) or a high PSA density ($P&lt;0.001$) and in younger patients ($P=0.008$). The risk of PCa on rebiopsies was not correlated with age, but significantly increased more than twofold in cases of PSA &gt;6 ng/mL, PSA density &gt;0.15 ng/mL/g, free-to-total PSA ratio &lt;15, and/or prostate volume &lt;50 mL. Time-dependent analyses were in line with these findings. The main study limitation was the lack of control of the absence of PCa and PSA kinetics in men not rebiopsied.</td>
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<td>66. Roehl KA, Antenor JA, Catalona WJ. Serial biopsy results in prostate cancer screening study. J Urol. 2002;167(6):2435-2439.</td>
<td>Review/Other-Dx</td>
<td>2,526</td>
<td>To evaluate prostate biopsy results in men with elevated PSA levels and/or suspicious DRE whose initial biopsies did not reveal cancer.</td>
<td>Of the men who underwent up to 10 biopsy procedures the serial cancer detection rates were 29%, 17%, 14%, 11%, 9% and 7%, respectively, on biopsy procedures 1 through 6. No significant difference in the yield of cancer on serial biopsies was observed between the groups using the greater than 4.0 ng/mL and greater than 2.5 ng/mL cutoff. There was a trend for more cancers detected through serial screening to be organ confined compared with those detected on initial screening (78% vs 69%, $P=0.05$). Also, more cancers detected using the greater than 2.5 ng/mL cutoff were organ confined (80% vs 66%, $P=0.004$). Only approximately 1% of the cancers fulfilled the published criteria for clinically insignificant tumors.</td>
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<td>67. Vencalek O, Facevicova K, Furst T, Grepl M. When less is more: a simple predictive model for repeated prostate biopsy outcomes. Cancer Epidemiol. 2013;37(6):864-869.</td>
<td>Observational- Dx</td>
<td>221 patients</td>
<td>To present a new predictive model for repeated prostate biopsy outcomes.</td>
<td>Of the 221 patients, 29 (13%) were diagnosed with PCa on the repeated biopsy. The final model includes the PSA level and the transitory zone volume as predictors. Its accuracy is 76.4%. The cut-off point of 0.0687 in the predicted positive repeated biopsy outcome assures 95% sensitivity and prevents 42% of unnecessary biopsies.</td>
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<td>68. Zaytoun OM, Stephenson AJ, Fareed K, et al. When serial prostate biopsy is recommended: most cancers detected are clinically insignificant. BJU Int. 2012;110(7):987-992.</td>
<td>Observational- Dx</td>
<td>749 patients</td>
<td>To investigate the total rate of cancer detection in serial biopsy and how many of these were deemed clinically insignificant.</td>
<td>PCa was detected in 15.9% of 749 serial biopsies, representing a cumulative PCa detection rate of 24.8% (119/479 patients). The sPBx group had a significantly higher detection rate per biopsy session (18.6% vs 12.7%, P=0.026). Nevertheless, most positive biopsies 75/119 (63%) revealed clinically insignificant cancer, including 74.6% of cancers detected by sPBx.</td>
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<td>69. Sonn GA, Chang E, Natarajan S, et al. Value of targeted prostate biopsy using magnetic resonance-ultrasound fusion in men with prior negative biopsy and elevated prostate-specific antigen. Eur Urol. 2014;65(4):809-815.</td>
<td>Observational- Dx</td>
<td>105 patients</td>
<td>To determine whether use of MRI-US fusion biopsy results in improved detection of PCa compared to repeat conventional biopsy.</td>
<td>Fusion biopsy revealed PCa in 36/105 men (34%; 95% CI, 25-45). 72% of men with PCa had clinically significant disease; 21/23 men (91%) with PCa on targeted biopsy had significant cancer compared to 15/28 (54%) with systematic biopsy. Degree of suspicion on MRI was the most powerful predictor of significant cancer on multivariate analysis. 12/14 (86%) subjects with a highly suspicious MRI target were diagnosed with clinically significant cancer.</td>
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<td>70. Meng X, Rosenkrantz AB, Mendhiratta N, et al. Relationship Between Prebiopsy Multiparametric Magnetic Resonance Imaging (MRI), Biopsy Indication, and MRI-ultrasound Fusion-targeted Prostate Biopsy Outcomes. <em>Eur Urol.</em> 2016;69(3):512-517.</td>
<td>Observational-Dx</td>
<td>601 patients</td>
<td>To compare MRF-TB and systematic 12-core biopsy results and investigate the relationship between biopsy outcomes and prebiopsy MRI.</td>
<td>MRF-TB detected fewer GS 6 PCa (75 vs 121; (P&lt;0.001)) and more GS ≥7 PCa (158 vs 117; (P&lt;0.001)) than systematic 12-core biopsy. Higher MRI suspicion score was associated with higher detection of GS ≥7 PCa (P&lt;0.001) but was not correlated with detection of GS 6 PCa. Prediction of GS ≥7 disease by MRI suspicion score varied according to biopsy history. Compared to systematic 12-core biopsy, MRF-TB identified more GS ≥7 PCas in men with no prior biopsy (88 vs 72; (P=0.012)), in men with a prior negative biopsy (28 vs 16; (P=0.010)), and in men with a prior cancer diagnosis (42 vs 29; (P=0.043)). MRF-TB detected fewer GS 6 PCa in men with no prior biopsy (32 vs 60; (P&lt;0.001)) and men with prior cancer (30 vs 46; (P=0.034)).</td>
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<td>71. Jung AJ, Coakley FV, Shinohara K, et al. Local staging of prostate cancer: comparative accuracy of T2-weighted endorectal MR imaging and transrectal ultrasound. <em>Clin Imaging.</em> 2012;36(5):547-552.</td>
<td>Observational-Dx</td>
<td>101 patients</td>
<td>To compare the accuracy of T2-weighted MRI and TRUS for staging of PCa.</td>
<td>Staging accuracy was not significantly different between MRI (A(z) = 0.69-0.70) and TRUS (A(z) = 0.81, (P&gt;0.05)).</td>
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<td>72. Bokhorst LP, Alberts AR, Rammikko A, et al. Compliance Rates with the Prostate Cancer Research International Active Surveillance (PRIAS) Protocol and Disease Reclassification in Noncompliers. <em>Eur Urol.</em> 2015;68(5):814-821.</td>
<td>Review/Other-Dx</td>
<td>4,547 patients</td>
<td>To determine the number of noncompliers and disease reclassification rates in men not complying with the follow-up protocol of the Prostate Cancer Research International Active Surveillance (PRIAS) study.</td>
<td>The compliance rate for PSA visits was 91%. By contrast, the compliance rate for standard repeat biopsies decreased over time (81%, 60%, 53%, and 33% at 1, 4, 7, and 10 year after diagnosis, respectively). Yearly repeat biopsies in men with faster rising PSA (PSA-DT 3-10 year) was low at &lt;30%, although these men had higher upgrading rates at repeat biopsy (25%-30% vs 16%). PSA-DT of 0-3 year was the most common recommendation for discontinuation, but 71% continued on AS. Men with PSA-DT of 0-3 year were at higher risk of upgrading on repeat biopsy (HR 2.02, 95% CI, 1.36-3.00) compared to men without fast rising PSA.</td>
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<td>7 studies provided the diagnostic data on MRI and AS of PCa, comprising 1028 patients. The pooled estimates of MRI on disease reclassification among AS candidates were as follows: sensitivity, 0.69 (95% CI, 0.44-0.86); specificity, 0.78 (95% CI, 0.53-0.91); positive likelihood ratio, 3.1 (95% CI, 1.6-6.0); negative likelihood ratio, 0.40 (95% CI, 0.23-0.70); and diagnostic OR, 8 (95% CI, 4-16). The P-value for heterogeneity was &lt;0.001. We found that the summary receiver operating characteristic curve is positioned toward the desirable upper left corner of the curve, and the AUC was 0.79 (95% CI, 0.76-0.83). For a pretest probability of 0.20, the corresponding PPV was 0.44 and the NPV was 0.91. MRI may reveal an unrecognized significant lesion in 33.27% of patients, and biopsy of these areas reclassified 14.59% of cases as no longer fulfilling the criteria for AS. In addition, when no suspicious disease progression (66.34%) was identified on MRI, the chance of reclassification on repeat biopsy was extremely low at 6.13%.</td>
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<td>74. Abdi H, Pourmalek F, Zargar H, et al. Multiparametric magnetic resonance imaging enhances detection of significant tumor in patients on active surveillance for prostate cancer. Urology. 2015;85(2):423-428.</td>
<td>Observational-Dx</td>
<td>70 patients</td>
<td>To determine whether mpMRI of the prostate combined with MRI fusion technology during TRUS-guided biopsy can enhance the detection of significant disease in patients with apparent low-risk PCa on AS. mpMRI detected 118 suspicious lesions in 70 patients (63%). Of these, 42 patients (60%) had lesions with Prostate Imaging, Reporting, and Data System (PIRADS) score 3, and 28 patients (40%) had PIRADS score 4 or 5 lesions. AS was terminated in 27 (24.3%) of the 111 patients who underwent mpMRI. 17 patients stopped AS based on mpMRI findings including 16 for pathologic progression in target biopsies and 1 for lesion size increase, whereas the other 10 stopped AS because of pathologic progression in the standard cores (n = 6) or other reasons (n = 4). Use of mpMRI increased the rate of AS termination (27 vs 10; P=.002). On multivariate analysis, PIRADS score 4-5 (vs 3) was the only significant predictor of AS termination (P=.015).</td>
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<tr>
<td>75. Da Rosa MR, Milot L, Sugar L, et al. A prospective comparison of MRI-US fused targeted biopsy versus systematic ultrasound-guided biopsy for detecting clinically significant prostate cancer in patients on active surveillance. <em>J Magn Reson Imaging</em>. 2015;41(1):220-225.</td>
<td>Observational-Dx</td>
<td>72 patients</td>
<td>In AS patients: (i) To compare the ability of a mpMRI-US biopsy system to detect clinically significant PCa with systematic 12-core biopsy, and (ii) To assess the predictive value of mpMRI with biopsy as the reference standard.</td>
<td>Clinically significant 7 cancers were found in 19/72 (26%), 7 (37%) identified by UroNavBx alone, 2 (11%) by R-TRUSBx alone (<em>P</em>=0.182). UroNav targeted biopsy was 6.3x more likely to yield a core positive for CS7 cancer compared with R-TRUSBx (25% of 141 vs 4% of 874, <em>P</em>&lt;0.001). Upgrading of GS occurred in 15/72 patients (21%), 13 (87%) detected by UroNavBx and 10 (67%) by R-TRUSBx. The NPV of mpMRI for clinically significant 7 cancer was 100%. MRI suspicion level significantly predicted clinically significant cancer on multivariate analysis (OR 3.6, <em>P</em>&lt;0.001).</td>
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<td>76. Fradet V, Kurhanewicz J, Cowan JE, et al. Prostate cancer managed with active surveillance: role of anatomic MR imaging and MR spectroscopic imaging. <em>Radiology</em>. 2010;256(1):176-183.</td>
<td>Observational-Dx</td>
<td>114 patients</td>
<td>To determine the role that MRI and MRSI findings obtained at the time of diagnosis play in the progression of disease in patients whose PCa is being managed with AS and to compare the role of these findings with the role of TRUS findings.</td>
<td>The final cohort included 114 patients with a median follow-up of 59 months. Patients with a lesion that was suggestive of cancer at MRI had a greater risk of the GS being upgraded at subsequent biopsy (HR, 4.0; 95% CI: 1.1, 14.9) than did patients without such a lesion. Neither MRSI nor TRUS could be used to predict cancer progression.</td>
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<td>77. Park BH, Jeon HG, Choo SH, et al. Role of multiparametric 3.0-Tesla magnetic resonance imaging in patients with prostate cancer eligible for active surveillance. <em>BJU Int</em>. 2014;113(6):864-870.</td>
<td>Observational-Dx</td>
<td>298 patients</td>
<td>To evaluate predictors of more aggressive disease and the role of 3.0-T mpMRI in selecting patients with PCa for AS.</td>
<td>In 35 (11.7%) patients, no discrete cancer was visible on MRI, while in the remaining 263 (88.3%) patients, a discrete cancer was visible. Pathological examination of RP specimens resulted in upstaging (&gt;T2) in 21 (7%) patients, upgrading (GS &gt;6) in 136 (45.6%), and a diagnosis of unfavourable disease in 142 (47.7%) patients. The 263 patients (88.3%) with visible cancer on imaging were more likely to have their cancer status upgraded (49.8% vs 14.3%) and be diagnosed with unfavourable disease (52.1% vs 14.3%) than the 35 patients (11.7%) with no cancer visible upon imaging, and these differences were statistically significant (<em>P</em>&lt;0.001 for all). A visible cancer lesion on MRI, PSAD, and patient age were found to be predictors of unfavourable disease in multivariate analysis.</td>
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<tr>
<td>78. Margel D, Yap SA, Lawrentschuk N, et al. Impact of multiparametric endorectal coil prostate magnetic resonance imaging on disease reclassification among active surveillance candidates: a prospective cohort study. <em>J Urol</em>. 2012;187(4):1247-1252.</td>
<td>Observational-Dx</td>
<td>60 consecutive patients</td>
<td>A report on MRI findings among unselected men with low risk PCa before AS. Men with low grade, low risk, and localized PCa were prospectively enrolled.</td>
<td>MRI did not detect cancer in 23 cases (38%) while MRI and initial biopsy were concordant in 24 (40%). MRI detected a 1 cm or larger lesion in 13 patients (22%). Of the cases 18 (32.14%) were reclassified. When no cancer was identified on MRI, only 2 cases (3.5%) were reclassified. The PPV and NPV for MRI predicting reclassification were 83% (95% CI, 73-93) and 81% (95% CI, 71-91), respectively. PSA density was increased in patients with lesions &gt;1 cm on MRI compared to those with no cancer on imaging (median 0.15 vs 0.07 ng/ml/cc, <em>P</em>=0.016). MRI appears to have a high yield for predicting reclassification among men who elect AS. Upon confirmation of these results MRI may be used to better select and guide patients before AS.</td>
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<td>79. Hu JC, Chang E, Natarajan S, et al. Targeted prostate biopsy in select men for active surveillance: do the Epstein criteria still apply? <em>J Urol</em>. 2014;192(2):385-390.</td>
<td>Observational-Dx</td>
<td>113 men</td>
<td>To examine the usefulness of mpMRI-US confirmatory biopsy in men initially diagnosed with PCa who were eligible for active surveillance, that is they met the Epstein criteria.</td>
<td>Confirmatory fusion biopsy resulted in reclassification in 41 men (36%), including 26 (23%) due to Gleason grade 6 or greater and 15 (13%) due to high volume Gleason 6 disease. When stratified by suspicion on mpMRI-US fusion, the likelihood of reclassification was 24% to 29% for target grade 0 to 3, 45% for grade 4 and 100% for grade 5 (<em>P</em>=0.001). Men with grade 4 and 5 vs lower grade targets were greater than 3 times more likely to be reclassified (OR 3.2, 95% CI 1.4–7.1, <em>P</em>=0.006).</td>
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<tr>
<td>80. Schoots IG, Petrides N, Giganti F, et al. Magnetic resonance imaging in active surveillance of prostate cancer: a systematic review. <em>Eur Urol.</em> 2015;67(4):627-636.</td>
<td>Review/Other-Dx</td>
<td>19 studies</td>
<td>To systematically review evidence regarding the use of MRI in men with low- or intermediate-risk PCa suitable for AS.</td>
<td>A lesion on MRI suspicious for PCa (positive MRI) is seen in two-thirds of men otherwise suitable for AS. A positive MRI makes the identification of clinically significant disease at repeat biopsy more likely, especially when biopsies are targeted to suspicious MRI lesions. RP data show that positive MRI is more likely to be associated with upgrading (GS&gt;3+3) than a negative MRI (43% vs 27%). A positive MRI is not significantly more likely to be associated with upstaging at RP (&gt;T2) than a negative MRI (10% vs 8%). Although MRI is of interest in the monitoring of men on AS, robust data on the use of repeat MRI in AS are lacking. Prospective studies with clear definitions of radiological significance and progression are needed before this approach can be adopted. MRI is useful for detection of clinically significant disease at initial assessment of men considering AS. To use MRI as a monitoring tool in surveillance, it will be necessary to define both radiological significance and radiological progression.</td>
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<td>81. Cooperberg MR, Cowan JE, Hilton JF, et al. Outcomes of active surveillance for men with intermediate-risk prostate cancer. <em>J Clin Oncol.</em> 2011;29(2):228-234.</td>
<td>Review/Other-Dx</td>
<td>540 men</td>
<td>To determine the extent to which low- and intermediate-risk men differ in terms of risk factors for progression, and whether the rate of cancer progression is in fact higher among the men at intermediate risk.</td>
<td>Compared to men with low-risk tumors, those with intermediate-risk tumors were older (mean, 64.9 v 62.3 years) with higher mean PSA values (10.9 v 5.1 ng/mL), and more tumor involvement (mean, 20.4% v 15.3% positive biopsy cores; all ( P&lt;.01 )). Within 4 years of the first positive biopsy, the clinical risk group did not differ in terms of the proportions experiencing progression-free survival, (low [54%] v intermediate [61%]; log-rank ( P=.22 )) or the proportions who underwent active treatment (low [30%] v intermediate [35%]; log-rank ( P=.88 )). Among men undergoing surgery, none were node positive and none had BCR within 3 years.</td>
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<tr>
<td>82. Raldow AC, Zhang D, Chen MH, Braccioforte MH, Moran BJ, D’Amico AV. Risk Group and Death From Prostate Cancer: Implications for Active Surveillance in Men With Favorable Intermediate-Risk Prostate Cancer. <em>JAMA Oncol.</em> 2015;1(3):334-340.</td>
<td>Observational-Dx</td>
<td>5,580 patients</td>
<td>To estimate and compare the risk of PCa-specific mortality and all-cause mortality following brachytherapy among men with low and favorable intermediate-risk PCa.</td>
<td>After median follow-up of 7.69 years, 605 men had died (10.84% of total cohort), 34 of PCa (5.62% of total deaths). Men with favorable intermediate-risk PCa did not have significantly increased risk of PCa-specific mortality and all-cause mortality compared with men with low-risk PC (adjusted HR, 1.64; 95% CI, 0.76-3.53; <em>P</em>=.21 for PCa-specific mortality; adjusted HR, 1.11; 95% CI, 0.88-1.39; <em>P</em>=.38 for all-cause mortality). 8-year adjusted point estimates for PCa-specific mortality were low: 0.48% (95% CI, 0.23%-0.93%) and 0.33% (95% CI, 0.19%-0.56%) for men with favorable intermediate-risk PC and low-risk PC, respectively. The respective estimates for all-cause mortality were 10.45% (95% CI, 8.91%-12.12%) and 8.68% (95% CI, 7.80%-9.61%).</td>
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<td>83. Anwar M, Westphalen AC, Jung AJ, et al. Role of endorectal MR imaging and MR spectroscopic imaging in defining treatable intraprostatic tumor foci in prostate cancer: quantitative analysis of imaging contour compared to whole-mount histopathology. <em>Radiother Oncol.</em> 2014;110(2):303-308.</td>
<td>Observational-Dx</td>
<td>20 patients</td>
<td>To investigate the role of endorectal MRI and MRSI in defining the contour of treatable intraprostatic tumor foci in PCa, since targeted therapy requires accurate target volume definition.</td>
<td>Histopathology showed 17 treatable tumor foci in 16 patients, of which 8 were correctly identified by both readers and an additional 2 were correctly identified by reader 2. For all correctly identified lesions, both readers accurately identified that tumor contacted the prostatic capsule, with no error in contour identification. On the noncapsular border, the median distance between the imaging and histopathological contour was 1.4mm (range, 0-12). Expanding the contour by 5mm at the noncapsular margin included 95% of tumor volume not initially covered within the MR contour.</td>
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<td>84. Hricak H, Wang L, Wei DC, et al. The role of preoperative endorectal magnetic resonance imaging in the decision regarding whether to preserve or resect neurovascular bundles during radical retropubic prostatectomy. <em>Cancer.</em> 2004;100(12):2655-2663.</td>
<td>Observational-Dx</td>
<td>135 patients</td>
<td>To evaluate endorectal MRI in the decision regarding whether to preserve or resect NVBs during radical radical RP.</td>
<td>MRI findings suggested altering the surgical plan in 39% of NVB (106/270 NVB). When the surgeon judged that the NVB resection was definitely not necessary (165 NVB), MRI confirmed that decision in 138 NVB (84%). The concordant decision was correct in 96% of the cases (133/138 NVB). In 36 high-risk patients (≥75% probability of ECE), MRI findings changed the surgical plan for 28 NVB (78%); the change was found to be appropriate in 26 cases (93%). MRI was found to significantly improve the surgeon’s decision to preserve or resect the NVBs during RP.</td>
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<td>85. Muglia VF, Westphalen AC, Wang ZJ, Kurhanewicz J, Carroll PR, Coakley FV. Endorectal MRI of prostate cancer: incremental prognostic importance of gross locally advanced disease. <em>AJR Am J Roentgenol.</em> 2011;197(6):1369-1374.</td>
<td>Observational-Dx</td>
<td>66 patients with gross locally advanced disease and 65 controls.</td>
<td>The purpose of this study was to determine the frequency and incremental prognostic importance of gross locally advanced disease seen at endorectal MRI in patients with PCa.</td>
<td>66 of 1777 (3.7%) patients had gross locally advanced disease. 1 of 1085 (0.1%) patients had low-risk disease, 25 of 489 (5.1%) had intermediate-risk disease, and 40 of 203 (19.7%) had high-risk disease. Follow-up data were available for 44 of these 66 patients. During a median follow-up period of 79 months, biochemical failure and metastasis had developed in 17 and 6 of these 44 patients compared with 9 and none of the 65 patients in the control group (<em>P</em>&lt;0.001).</td>
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<td>86. Roethke MC, Lichy MP, Kniess M, et al. Accuracy of preoperative endorectal MRI in predicting extracapsular extension and influence on neurovascular bundle sparing in radical prostatectomy. <em>World J Urol.</em> 2013;31(5):1111-1116.</td>
<td>Observational-Dx</td>
<td>385 patients</td>
<td>To evaluate the accuracy of presurgical endorectal MRI for local staging before RP and its influence on NVB resection during RP.</td>
<td>In 294 (76.4%) patients, pathological stage was correctly predicted, 69 patients (17.9%) were understaged and 22 (5.7%) overstaged. Overall sensitivity, specificity, negative and PPV for predicting ECE were 41.5%, 91.8%, 78.0%, and 69.0%, respectively. 152 (48.4%) of the patients classified as stage cT2 by endorectal MRI underwent bilateral NVB sparing, whereas 14 (19.7%) patients with reported ECE underwent bilateral NVB sparing (<em>P</em>&lt;0.01). Overall positive surgical margin rate was 14.8%. Sensitivity of predicting ECE and PPV were lower in the low-risk group than in the intermediate and high-risk group.</td>
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**Prostate Cancer—Pretreatment Detection, Surveillance, and Staging**

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<td>87. Merdan S, Womble PR, Miller DC, et al. Toward better use of bone scans among men with early-stage prostate cancer. <em>Urology</em>. 2014;84(4):793-798.</td>
<td>Observational-Dx</td>
<td>416 men</td>
<td>To evaluate the performance of published guidelines compared with that of current practice for radiographic staging of men with newly diagnosed PCa.</td>
<td>Among 416 men who received a bone scan, 48 (11.5%) had evidence of bone metastases. Patients with bone metastases were older, with higher PSA levels and GS (all (P&lt;.05)). In multivariate analyses, PSA ((P&lt;.001)) and GS ((P=.004)) were the only independent predictors of positive bone scan. Guidelines from the American Urological Association and the National Comprehensive Cancer Network demonstrated similar performance in detecting bone metastases in our population, with fewer negative study results than those of the European Association of Urology guideline. Applying the American Urological Association recommendations (ie, image when PSA level &gt;20 ng/mL or GS ≥8) to current clinical practice, we estimate that &lt;1% of positive study results would be missed, whereas the number of negative study results would be reduced by 38%.</td>
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<tr>
<td>88. Edge SB, American Joint Committee on Cancer. <em>AJCC cancer staging manual</em>. 7th ed. New York: Springer; 2010.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
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<td>89. Gleave ME, Coupland D, Drachenberg D, et al. Ability of serum prostate-specific antigen levels to predict normal bone scans in patients with newly diagnosed prostate cancer. <em>Urology</em>. 1996;47(5):708-712.</td>
<td>Observational-Dx</td>
<td>683 patients</td>
<td>To determine whether pretreatment serum PSA levels in newly diagnosed PCa patients can identify a group with a low probability of osseous metastasis and safely eliminate the need for a bone scan as a routine part of the staging evaluation.</td>
<td>Only 6% of 490 evaluable patients had a positive bone scan on initial evaluation. Scans were positive in 0/290 (0%) with PSA levels below 10 micrograms/L, 4/88 (4.5%) with PSA levels between 10 and 20 micrograms/L, and 24/112 (21%) with PSA levels above 20 micrograms/L. Although the risk of a positive bone scan increased with increasing PSA levels, PSA is a poor positive predictor of positive bone scans. The risk of a positive bone scan was 8% (5/64 patients) when PSA was between 20 and 50 micrograms/L, and increased to 40% (19/48 patients) for PSA levels &gt;50 micrograms/L. In contrast, serum PSA levels below 10 micrograms/L are strong negative predictors of positive bone scans, with no positive scans in 290 patients with PSA levels &lt;10 micrograms/L. Although the risk of a positive bone scan increased with increasing stage and grade, tumor stage and grade were poor negative predictors of positive bone scans. Up to 4% of patients with clinically confined or well-differentiated to moderately differentiated tumors had positive scans. Scans were positive in 12% of poorly differentiated tumors, but all these patients had PSA levels above 10 micrograms/L.</td>
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<td>90. Hirobe M, Takahashi A, Hisasue S, et al. Bone scanning--who needs it among patients with newly diagnosed prostate cancer? <em>Jpn J Clin Oncol</em>. 2007;37(10):788-792.</td>
<td>Observational-Dx</td>
<td>366 patients</td>
<td>Evaluated the relationship between serum PSA and clinical variables to eliminate bone scanning in patients with PCa having a low probability of bone metastasis.</td>
<td>Bone metastasis was found in 28 (7.7%) of 366 patients. 14 patients had skeletal symptoms related to bone metastasis. The risk for bone metastases increased considerably with increases of PSA level, clinical T stage and GS. The metastasis was not found in 161 patients with serum PSA concentration of 10 ng/mL or lower. In 95 patients with the concentration between 10 and 20 ng/mL only 2 had the metastasis. These 2 patients had T2 disease and GSs of 7 or greater. In 204 patients with clinical stage T1 disease, 1 (0.5%) had the metastasis. In 117 patients with GSs of 6 or less, the metastasis was found in 2 (1.7%).</td>
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**Prostate Cancer—Pretreatment Detection, Surveillance, and Staging**

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<td>91. Lee IH, Roberts R, Shah RB, Wojno KJ, Wei JT, Sandler HM. Perineural invasion is a marker for pathologically advanced disease in localized prostate cancer. <em>Int J Radiat Oncol Biol Phys.</em> 2007;68(4):1059-1064.</td>
<td>Observational-Dx</td>
<td>1550 patients</td>
<td>To determine if perineural invasion should be included in addition to PSA, biopsy GS, and clinical T-stage for risk-stratification of patients with localized PCa.</td>
<td>For the overall population, perineural invasion was associated with a significantly increased frequency of upgrading and of pathologic T3 disease. After stratification, perineural invasion was still associated with significantly increased odds of pathologic T3 disease within each risk group. In particular, for low-risk patients, there was a markedly increased risk of EPE (23% vs 7%), comparable to that of intermediate-risk patients. Among high-risk patients, perineural invasion was associated with an increased risk of SVI and LN involvement. Furthermore, over 80% of high-risk patients with perineural invasion were noted to have an indication for postoperative radiation.</td>
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<td>92. Pettus JA, Masterson TA, Abel EJ, Middleton RG, Stephenson RA. Risk stratification for positive lymph nodes in prostate cancer. <em>J Endourol.</em> 2008;22(5):1021-1025.</td>
<td>Observational-Dx</td>
<td>760 patients</td>
<td>To evaluate the risk of positive LNs using preoperative clinical parameters.</td>
<td>A total of 760 patients with 43 (5.7%) patients with node-positive disease were available for analysis. Risk classification was significantly associated with positive nodes ($P&lt;0.001$), even after controlling for year of surgery and age. The AUC was 0.77 (95% CI: 0.69, 0.83). Omitting pelvic LN dissection in the low-risk group would have spared 368 (49.2%) of the entire cohort with a false-negative rate of 5/369 (1.3%) for the low-risk group, and 5/760 (0.7%) for the entire cohort. Sensitivity was 88.4%, and NPV was 98.7%.</td>
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<td>93. Rhoden EL, Torres O, Ramos GZ, Lemos RR, Souto CA. Value of prostate specific antigen in predicting the existence of bone metastasis in scintigraphy. <em>Int Braz J Urol.</em> 2003;29(2):121-125; discussion 126.</td>
<td>Observational-Dx</td>
<td>214 patients</td>
<td>To evaluate the ability of serum concentration of PSA between 2 cutting points to predict the existence of bone metastasis confirmed by bone scintigraphy in man with PCA.</td>
<td>From the 214 patients, 35 (16.3 x 0025;) presented positive scintigraphic examinations for the presence of bone metastasis. No patient presented bone metastasis in scintigraphy if having PSA &lt;10 ng/mL, and in only 1 patient (0.46 x 0025;) with bone metastasis PSA concentration was &lt;20 ng/mL. Therefore, when the cutting point adopted for PSA serum concentration was 10 ng/mL, a NPV for bone metastasis was 100 x 0025; with sensitivity rates of 100%. Nevertheless, the PPV and the specificity of the method were, respectively, 24.5 x 0025; and 39.7 x 0025;. When the cutting point of PSA serum concentration was 20 ng/mL, an increment was observed in rates of PPV and specificity (41.5 x 0025; and 73.2 x 0025;), respectively, without substantial changes in NPV (99.2 x 0025;) and sensitivity (97.1 x 0025;) of the method.</td>
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### Evidence Table Key

**Study Quality Category Definitions**

- **Category 1**  The study is well-designed and accounts for common biases.
- **Category 2**  The study is moderately well-designed and accounts for most common biases.
- **Category 3**  There are important study design limitations.
- **Category 4**  The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  - c) the study is an expert opinion or consensus document.
- **M = Meta-analysis**

### Abbreviations Key

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<tr>
<td>ADC</td>
<td>Apparent diffusion coefficient</td>
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<td>Androgen-deprivation therapy</td>
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<td>AS</td>
<td>Active surveillance</td>
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<td>AUC</td>
<td>Area under the receiver operating characteristic curve</td>
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<td>BCR</td>
<td>Biochemical recurrence</td>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>DCE</td>
<td>Dynamic contrast-enhanced</td>
</tr>
<tr>
<td>DRE</td>
<td>Digital rectal examination</td>
</tr>
<tr>
<td>DWI</td>
<td>Diffusion-weighted imaging</td>
</tr>
<tr>
<td>EBRT</td>
<td>External-beam radiation therapy</td>
</tr>
<tr>
<td>ECE</td>
<td>Extracapsular extension</td>
</tr>
<tr>
<td>EPE</td>
<td>Extraprostatic extension</td>
</tr>
<tr>
<td>FDG-PET</td>
<td>Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography</td>
</tr>
<tr>
<td>GS</td>
<td>Gleason score</td>
</tr>
<tr>
<td>HR</td>
<td>Hazard ratio</td>
</tr>
<tr>
<td>LN</td>
<td>Lymph node</td>
</tr>
<tr>
<td>mpMRI</td>
<td>Multiparametric MRI</td>
</tr>
<tr>
<td>MRF-TB</td>
<td>Magnetic resonance imaging-ultrasound fusion targeted prostate biopsy</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
</tr>
<tr>
<td>MRSI</td>
<td>Magnetic resonance spectroscopic imaging</td>
</tr>
<tr>
<td>NPV</td>
<td>Negative predictive value</td>
</tr>
<tr>
<td>NVB</td>
<td>Neurovascular bundle</td>
</tr>
<tr>
<td>OR</td>
<td>Odds ratio</td>
</tr>
<tr>
<td>OS</td>
<td>Overall survival</td>
</tr>
<tr>
<td>PCa</td>
<td>Prostate cancer</td>
</tr>
<tr>
<td>PPV</td>
<td>Positive predictive value</td>
</tr>
<tr>
<td>PSA</td>
<td>Prostate-specific antigen</td>
</tr>
<tr>
<td>RP</td>
<td>Radical prostatectomy</td>
</tr>
<tr>
<td>RT</td>
<td>Radiation therapy</td>
</tr>
<tr>
<td>SVI</td>
<td>Seminal vesicle invasion</td>
</tr>
<tr>
<td>TRUS</td>
<td>Transrectal ultrasound</td>
</tr>
<tr>
<td>US</td>
<td>Ultrasound</td>
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</tbody>
</table>

**Dx** = Diagnostic

**Tx** = Treatment