

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Choueiri TK, Dreicer R, Paciorek A, Carroll PR, Konety B. A model that predicts the probability of positive imaging in prostate cancer cases with biochemical failure after initial definitive local therapy. J Urol. 2008;179(3):906-910; discussion 910.	Observational-Dx	292 patients	To identify clinical parameters that were predictive of positive imaging studies.	We identified 292 patients (66% radical prostatectomy and 34% radiation therapy) who had recurrence and had available imaging data, and 31 (11%) patients had a positive imaging study. On multivariate analysis age, imaging type, trigger prostate specific antigen and prostate specific antigen doubling time were significantly associated with imaging results. A multivariate model including age (younger than 60 vs 60 to 69 vs 70 years or older), primary imaging type (bone scan vs computerized tomography vs magnetic resonance imaging), trigger prostate specific antigen (5 or less vs more than 5 ng/ml) and prostate specific antigen doubling time (less than 10 vs 10 or more months) had a concordance index of 84% in predicting positive imaging.	3
2. Han M, Partin AW, Pound CR, Epstein JI, Walsh PC. Long-term biochemical disease-free and cancer-specific survival following anatomic radical retropubic prostatectomy. The 15-year Johns Hopkins experience. Urol Clin North Am. 2001;28(3):555-565.	Observational-Tx	2,404 men	To provide long-term outcome of patients with clinically localized cancer who underwent RRP between 1982 and 1999.	The overall actuarial 5-, 10-, and 15-year recurrence-free survival rates for these men were 84%, 74%, and 66%, respectively. As demonstrated in the authors' previous reports, the actuarial likelihood of a postoperative recurrence increased with advancing clinical stage, Gleason-score, preoperative PSA level, and pathologic stage. Subdivision of men with Gleason 7 tumors resulted in better stratification. There was a similar actuarial likelihood of postoperative recurrence for men with Gleason 4 + 3 and Gleason score 8 to 10 disease. The actuarial rate of recurrence of tumor for men with Gleason 3 + 4 disease was statistically different from the rate for men with Gleason score 6 or Gleason 4 + 3 disease.	2

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3. Teeter AE, Presti JC, Jr., Aronson WJ, et al. Do nomograms designed to predict biochemical recurrence (BCR) do a better job of predicting more clinically relevant prostate cancer outcomes than BCR? A report from the SEARCH database group. Urology. 2013;82(1):53-58.	Observational-Dx	1778 patients	To examine the ability of various postoperative nomograms to predict prostate cancer-specific mortality (PCSM) and to validate that they could predict aggressive biochemical recurrence (BCR). Prostate-specific antigen (PSA), grade, and stage are the classic triad used to predict BCR after radical prostatectomy (RP). Multiple nomograms use these to predict risk of BCR. A previous study showed that several nomograms could predict aggressive BCR (prostate-specific antigen doubling time [PSADT] <9 months) more accurately than BCR. However, it remains unknown if they can predict more definitive endpoints, such as PCSM.	We found that each nomogram could predict aggressive BCR and PCSM in a statistically significant manner and that they all predicted PCSM more accurately than they predicted BCR (ie, with higher c-index values).	3

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4. Hamdy FC, Donovan JL, Lane JA, et al. 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer. <i>N Engl J Med</i> . 2016;375(15):1415-1424.	Experimental-Tx	1643	To compare active monitoring, radical prostatectomy, and external-beam radiotherapy for the treatment of clinically localized prostate cancer.	There were 17 prostate-cancer-specific deaths overall: 8 in the active-monitoring group (1.5 deaths per 1000 person-years; 95% confidence interval [CI], 0.7 to 3.0), 5 in the surgery group (0.9 per 1000 person-years; 95% CI, 0.4 to 2.2), and 4 in the radiotherapy group (0.7 per 1000 person-years; 95% CI, 0.3 to 2.0); the difference among the groups was not significant (P=0.48 for the overall comparison). In addition, no significant difference was seen among the groups in the number of deaths from any cause (169 deaths overall; P=0.87 for the comparison among the three groups). Metastases developed in more men in the active-monitoring group (33 men; 6.3 events per 1000 person-years; 95% CI, 4.5 to 8.8) than in the surgery group (13 men; 2.4 per 1000 person-years; 95% CI, 1.4 to 4.2) or the radiotherapy group (16 men; 3.0 per 1000 person-years; 95% CI, 1.9 to 4.9) (P=0.004 for the overall comparison). Higher rates of disease progression were seen in the active-monitoring group (112 men; 22.9 events per 1000 person-years; 95% CI, 19.0 to 27.5) than in the surgery group (46 men; 8.9 events per 1000 person-years; 95% CI, 6.7 to 11.9) or the radiotherapy group (46 men; 9.0 events per 1000 person-years; 95% CI, 6.7 to 12.0) (P<0.001 for the overall comparison).	1
5. NCCN Clinical Practice Guidelines in Oncology. Prostate Cancer. Version 3.2016. Available at: https://www.nccn.org/professionals/p_hysician_gls/pdf/prostate.pdf .	Review/Other-Tx	N/A	To provide clinical practice guidelines regarding prostate cancer.	No results stated in abstract.	4
6. Cirillo S, Petracchini M, Scotti L, et al. Endorectal magnetic resonance imaging at 1.5 Tesla to assess local recurrence following radical prostatectomy using T2-weighted and contrast-enhanced imaging. <i>Eur Radiol</i> . 2009;19(3):761-769.	Observational-Dx	72 patients	To evaluate diagnostic performance of endorectal magnetic resonance (eMR) for diagnosing local recurrence of prostate cancer (PC) in patients with previous radical prostatectomy (RP) and to assess whether contrast-enhanced (CE)-eMR improved diagnostic accuracy in comparison to unenhanced study.	Sensitivity, specificity, predictive positive value, negative predictive value and accuracy were 61.4%, 82.1%, 84.4%, 57.5% and 69.4% for unenhanced eMR and 84.1%, 89.3%, 92.5%, 78.1% and 86.1% for CE-eMR. A statistically significant difference was found between accuracy and sensitivity of the two evaluations (chi(2) = 5.33; p = 0.02 and chi(2) = 9.00; p = 0.0027).	3

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7. Khan MA, Partin AW. Management of patients with an increasing prostate-specific antigen after radical prostatectomy. <i>Curr Urol Rep.</i> 2004;5(3):179-187.	Review/Other-Dx	N/A	To discuss the factors associated with a high risk for disease recurrence after radical prostatectomy. Factors indicating whether the increasing serum PSA is caused by local recurrence or metastatic disease and the management options available to address serum PSA recurrence also are discussed.	No results stated in abstract.	4
8. Kitajima K, Murphy RC, Nathan MA, et al. Detection of recurrent prostate cancer after radical prostatectomy: comparison of 11C-choline PET/CT with pelvic multiparametric MR imaging with endorectal coil. <i>J Nucl Med.</i> 2014;55(2):223-232.	Observational-Dx	115 patients	To compare (11)C-choline PET/CT with pelvic multiparametric MR imaging for detection of recurrent prostate carcinoma in patients with suspected recurrence after radical prostatectomy and to identify an optimal imaging method to restage these patients.	The standard of reference (either positive or negative) for the diagnosis of local recurrence and pelvic LN and bone metastases was met in 87, 70, and 95 patients, respectively. Documented local recurrence and pelvic LN and bone metastases was present in 61 of 87 (70.1%), 50 of 70 (71.4%), and 16 of 95 (16.8%) patients, respectively. Patient-based area under the receiver-operating-characteristic curves of multiparametric MR imaging versus PET/CT for the diagnosis of local recurrence and pelvic LN and bone metastases were 0.909 versus 0.761 (P = 0.0079), 0.812 versus 0.952 (P = 0.0064), and 0.927 versus 0.898 (P = 0.69), respectively. Among 61 patients with local recurrence, 32 patients (52.4%) were correctly diagnosed as having local recurrence by both multiparametric MR imaging and PET/CT, 22 (36.1%) were correctly diagnosed by multiparametric MR imaging only, 6 (9.8%) could not be diagnosed by either modality, and 1 (1.6%) was correctly diagnosed by PET/CT only. The patient-based sensitivity, specificity, and accuracy of multiparametric MR imaging for diagnosing local recurrence were 88.5% (54/61), 84.6% (22/26), and 87.4% (76/87) whereas those of PET/CT for detecting body LN or bone metastases were 92.3% (72/78), 100% (18/18), and 93.8% (90/96), respectively.	3

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9. Sobol I, Zaid HB, Haloi R, et al. Contemporary Mapping of Post-Prostatectomy Prostate Cancer Relapse with C-11 Choline PET and Multiparametric MRI. J Urol. 2016.	Review/Other-Dx	202 patients	To identify sites and patterns of cancer recurrence in patients with post-prostatectomy biochemical relapse using 11C-choline positron emission tomography/computerized tomography and endorectal coil multiparametric magnetic resonance imaging.	Median prostate specific antigen at positive scan was 2.3 ng/ml (IQR 1.4-5.5) with a median time from prostate specific antigen relapse to lesion visualization of 15 months (IQR 4.8-34.2). Of these 202 men 68 (33%) exhibited local only, 45 (22%) local plus metastatic and 89 (45%) metastatic only relapse. Pelvic node only relapse was observed in 39 (19%) men. Median prostate specific antigen at positive imaging for patients with local only, metastatic only and local plus metastatic relapse was 2.3, 2.7 and 2.2 ng/ml (p=0.46), with a median interval from biochemical recurrence to positive scan of 33.5, 7.0 and 15.0 months, respectively (p <0.001). On multivariable analysis time from biochemical recurrence to positive imaging was independently associated with local only recurrence (OR 1.10 for every 6-month increase, p=0.012).	4
10. Linder BJ, Kawashima A, Woodrum DA, et al. Early localization of recurrent prostate cancer after prostatectomy by endorectal coil magnetic resonance imaging. Can J Urol. 2014;21(3):7283-7289.	Observational-Dx	187 patients	To evaluate the ability of endorectal coil (e-coil) magnetic resonance imaging (MRI) to identify early prostatic fossa recurrence after radical prostatectomy.	Local recurrence was identified in 132 patients, with 124 (94%) detected on e-coil MRI. The median PSA was 0.59 ng/mL (range < 0.1-13.1), and median lesion size on MRI was 1 cm. The sensitivity of MRI was 91%, with a specificity of 45%. The positive predictive value was 85%, with a negative predictive value of 60%. For patients with a PSA < 0.4 ng/mL the sensitivity of e-coil MRI was 86%. When a lesion was identified on MRI, the positive biopsy rate was 65% and lesion size was a significant predictor of positive biopsies. The positive biopsy rates were 51%, 74%, and 88% when the lesion was < 1 cm, 1 cm-2 cm, or > 2 cm, respectively (p = 0.0006).	3
11. Koo PJ, David Crawford E. (1)(8)F-NaF PET/CT and (1)(1)C-Choline PET/CT for the initial detection of metastatic disease in prostate cancer: overview and potential utilization. Oncology (Williston Park). 2014;28(12):1057-1062, 1064-1055.	Review/Other-Dx	N/A	To briefly review (1)(8)F-sodium fluoride (NaF) and radiolabeled cholines and provide potential utilization strategies based on available data.	No results stated in abstract.	4

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12. Freitas JE, Gilvydas R, Ferry JD, Gonzalez JA. The clinical utility of prostate-specific antigen and bone scintigraphy in prostate cancer follow-up. J Nucl Med. 1991;32(7):1387-1390.	Observational-Dx	107 patients	To assess the value of serum prostate-specific antigen (PSA) in prostate cancer follow-up.	Of 107 bone scans, 16 demonstrated metastatic bone disease. A PSA value of less than or equal to 8 ng/ml excluded bone metastases with a predictive value of a negative test of 98.5%. Without radiographic correlation, abnormal bone scans rarely represented metastases if the PSA value was less than or equal to 8 ng/ml.	3
13. Miller PD, Eardley I, Kirby RS. Prostate specific antigen and bone scan correlation in the staging and monitoring of patients with prostatic cancer. Br J Urol. 1992;70(3):295-298.	Observational-Dx	146 patients	To ascertain the ability of PSA to predict the presence of bony metastases at the time of original diagnosis of prostate cancer and their development during follow-up of these patients.	The ability of serum prostate specific antigen (PSA) to predict bone metastases at initial presentation was determined in 146 patients, and in 66 patients during a 3-year period; 14.7% of patients with bone metastases at presentation had a PSA value less than 20 ng/ml. All patients who subsequently developed bone metastases had a PSA greater than 20 ng/ml and the rise in PSA often antedated the detection of bone metastases.	3
14. Terris MK, Klonecke AS, McDougall IR, Stamey TA. Utilization of bone scans in conjunction with prostate-specific antigen levels in the surveillance for recurrence of adenocarcinoma after radical prostatectomy. J Nucl Med. 1991;32(9):1713-1717.	Observational-Dx	118 patients	The utility of serial bone scans in combination with PSA levels is evaluated in patients who were treated by radical prostatectomy and who, at the time of surgery, had no evidence of metastatic disease.	Of the 118 patients, 75.4% had no abnormality on either test (mean follow-up 32.4 mo), 9.3% demonstrated a detectable or rising PSA level with negative bone scan (mean follow-up 35 mo), and 8.5% exhibited a detectable and or rising PSA level and positive bone scan (mean follow-up 30.7 mo). Follow-up bone scans were read as either positive or indeterminate with undetectable PSA levels in 6.8% of patients (mean follow-up 27.3 mo).	3

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15. Evangelista L, Zattoni F, Karnes RJ, Novara G, Lowe V. Radiolabeled choline PET/CT before salvage lymphadenectomy dissection: a systematic review and meta-analysis. Nucl Med Commun. 2016;37(12):1223-1231.	Meta-analysis	18 studies and 750 patients	To provide a systematic review of recently published reports and carry out a meta-analysis on the use of radiolabeled choline PET/computed tomography (CT) as a guide for salvage lymph node dissection (sLND) in prostate cancer patients with biochemical recurrence after primary treatments.	A patient-based, a lesion-based, and a site-based analysis was carried out in nine, four, and five studies, respectively. The pooled sensitivities were 85.3% [95% confidence interval (CI): 78.5-90.3%], 56.2% (95% CI: 41.6-69.7%), 75.3% (95% CI: 56.6-87.7%), and 63.7% (95% CI: 41-81.6%), respectively, for patient-based, lesion-based, pelvic site-based, and retroperitoneal site-based analysis. The pooled positive predictive values (PPVs) were 75% (95% CI: 68-80.9%), 85.8% (95% CI: 66.8-94.8%), 81.2% (95% CI: 70.1-88.9%), and 75.2% (95% CI: 58.7-86.7%), respectively, in the same analyses. High heterogeneities among the studies were found for sensitivities and PPVs ranging between 61.7-93.3% and 60.6-94.5%, respectively. Radiolabeled choline PET/CT has only a moderate sensitivity for the detection of metastatic lymph nodes in patients who are candidates for sLND, although the pooled PPVs ranged between 75 and 85.8% for all type of subanalyses.	M
16. Evangelista L, Briganti A, Fanti S, et al. New Clinical Indications for (18)F/(11)C-choline, New Tracers for Positron Emission Tomography and a Promising Hybrid Device for Prostate Cancer Staging: A Systematic Review of the Literature. Eur Urol. 2016;70(1):161-175.	Review/Other-Dx	N/A	To summarise the last evidences in clinical practice for the assessment of prostate cancer, by using nuclear medicine modalities, like positron emission tomography/computed tomography and positron emission tomography/magnetic resonance imaging.	In the restaging phase, the detection rate of choline PET varies between 4% and 97%, mainly depending on the site of recurrence and prostate-specific antigen levels. Both 68gallium (68Ga)-prostate specific membrane antigen and 18F-fluciclovine are shown to be more accurate in the detection of recurrent disease as compared with radiolabelled choline PET/CT. Particularly, Ga68-PSMA has a detection rate of 50% and 68%, respectively for prostate-specific antigen levels < 0.5ng/ml and 0.5-2ng/ml. Moreover, 68Ga- PSMA PET/magnetic resonance imaging demonstrated a particularly higher accuracy in detecting PCa than PET/CT.	4

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17. Graziani T, Ceci F, Castellucci P, et al. (11)C-Choline PET/CT for restaging prostate cancer. Results from 4,426 scans in a single-centre patient series. Eur J Nucl Med Mol Imaging. 2016;43(11):1971-1979.	Observational-Dx	3,203 patients	To evaluate (11)C-choline PET/CT as a diagnostic tool for restaging prostate cancer (PCa), in a large, homogeneous and clinically relevant population of patients with biochemical recurrence (BCR) of PCa after primary therapy. The secondary aim was to assess the best timing for performing (11)C-choline PET/CT during BCR.	Overall, 52.8 % of the (11)C-choline PET/CT scans (2,337/4,426) and 54.8 % of the patients (1,755/3,203) were positive. In 29.4 % of the scans, at least one distant finding was observed. The mean and median PSA values were, respectively, 4.9 and 2.1 ng/mL at the time of the scan (range 0.2 - 50 ng/mL). In our series, 995 scans were performed in patients with PSA levels between 1 and 2 ng/mL. In this subpopulation the positivity rate in the 995 scans was 44.7 %, with an incidence of distant findings of 19.2 % and an incidence of oligometastatic disease (one to three lesions) of 37.7 %. The absolute PSA value at the time of the scan and ongoing androgen deprivation therapy were associated with an increased probability of a positive (11)C-choline PET/CT scan ($p < 0.0001$). In the ROC analysis, a PSA value of 1.16 ng/mL was the optimal cut-off value. In patients with a PSA value < 1.16 ng/mL, 26.8 % of 1,426 (11)C-choline PET/CT scans were positive, with oligometastatic disease in 84.7 % of positive scans.	3
18. Kane CJ, Amling CL, Johnstone PA, et al. Limited value of bone scintigraphy and computed tomography in assessing biochemical failure after radical prostatectomy. Urology. 2003;61(3):607-611.	Observational-Dx	132 patients	To define the utility of bone scan and computed tomography (CT) in the evaluation of patients with biochemical recurrence after radical prostatectomy.	One hundred thirty-two patients with biochemical recurrence and a bone scan or CT scan were identified. Of the 127 bone scans, 12 (9.4%) were positive. The patients with true-positive bone scans had an average PSA at the time of the bone scan of 61.3 +/- 71.2 ng/mL (range 1.3 to 123). Their PSA velocities, calculated from the PSA levels determined immediately before the radiographic studies, averaged 22.1 +/- 24.7 ng/mL/mo (range 0.14 to 60.0). Only 2 patients with a positive bone scan had a PSA velocity of less than 0.5 ng/mL/mo. Of the 86 CT scans, 12 (14.0%) were positive. On logistic regression analysis, PSA and PSA velocity predicted the bone scan result ($P < 0.001$ each) and PSA velocity predicted the CT scan result ($P = 0.047$).	3

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19. Cher ML, Bianco FJ, Jr., Lam JS, et al. Limited role of radionuclide bone scintigraphy in patients with prostate specific antigen elevations after radical prostatectomy. J Urol. 1998;160(4):1387-1391.	Observational-Dx	93 patients	To evaluate more systematically the role of radionuclide bone scintigraphy as a screening test for metastatic disease in patients with increasing serum PSA after radical prostatectomy.	In univariate analysis tPSA (p = 0.003), slope 1 (p = 0.005) and slope 2 (p = 0.004) were useful in predicting the bone scintigram result but pathological stage, Gleason score, preoperative PSA and time to recurrence were not. In multivariate analysis the single most useful parameter in predicting the bone scintigram result was tPSA (p = 0.01). Based on a logistic regression model the probability of a positive bone scintigram was less than 5% until tPSA increased to 40 to 45 ng/ml.	3
20. American Urological Association Education and Research, Inc. PSA testing for the pretreatment staging and posttreatment management of prostate cancer: 2013 Revision of 2009 Best Practice Statement. 2013; Available at: https://www.auanet.org/common/pdf/education/clinical-guidance/Prostate-Specific-Antigen.pdf .	Review/Other-Dx	N/A	Guideline that addresses the use of PSA testing for the pre-treatment staging and post-treatment management of prostate cancer.	No results stated in abstract.	4
21. Thompson IM, Valicenti RK, Albertsen P, et al. Adjuvant and salvage radiotherapy after prostatectomy: AUA/ASTRO Guideline. J Urol. 2013;190(2):441-449.	Review/Other-Tx	N/A	Guideline to provide a clinical framework for the use of RT after RP as adjuvant or salvage therapy.	Guideline statements are provided for patient counseling, the use of RT in the adjuvant and salvage contexts, defining biochemical recurrence, and conducting a re-staging evaluation.	4
22. Loeb S, Makarov DV, Schaeffer EM, Humphreys EB, Walsh PC. Prostate specific antigen at the initial diagnosis of metastasis to bone in patients after radical prostatectomy. J Urol. 2010;184(1):157-161.	Review/Other-Dx	193 patients	To examine the prostate specific antigen distribution at bone scan conversion by time from radical prostatectomy to metastasis.	Median prostate specific antigen was 31.9 ng/ml at the initial diagnosis of metastatic disease. Bone scan conversion occurred at a prostate specific antigen of less than 10, 10 to 100 and greater than 100 ng/ml in 50 (25.9%), 98 (50.8%) and 45 (23.3%) men, respectively. Lower prostate specific antigen at diagnosis, higher prostatectomy Gleason scores and shorter time to metastasis were associated with lower prostate specific antigen at bone metastasis, whereas prostate specific antigen at metastasis was not significantly associated with other clinicopathological features.	4

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23. Wondergem M, van der Zant FM, van der Ploeg T, Knol RJ. A literature review of 18F-fluoride PET/CT and 18F-choline or 11C-choline PET/CT for detection of bone metastases in patients with prostate cancer. Nucl Med Commun. 2013;34(10):935-945.	Meta-analysis	13 studies	To present a review of the contemporary literature on the performance of F-fluoride and C-choline or F-choline and to reconsider the arguments based on which the present European and US guidelines are founded.	On a lesion basis, we found a sensitivity and specificity of 84.0 and 97.7% for C-choline and F-choline and 88.6 and 90.7% for F-fluoride, respectively. On a patient basis, the sensitivity and specificity were 85.2 and 96.5% for C-choline and F-choline and 86.9 and 79.9% for F-fluoride, respectively. No significant differences were found between the sensitivity and specificity of C-choline or F-choline and F-fluoride. There was large inconsistency in the reported sensitivity (range 39-100%) and specificity (range 57-80%) for Tc-BS.	M
24. Fortuin AS, Deserno WM, Meijer HJ, et al. Value of PET/CT and MR lymphography in treatment of prostate cancer patients with lymph node metastases. International journal of radiation oncology, biology, physics. 2012;84(3):712-718.	Observational-Dx	29 patients	To determine the clinical value of two novel molecular imaging techniques: (11)C-choline positron emission tomography (PET)/computed tomography (CT) and ferumoxtran-10 enhanced magnetic resonance imaging (magnetic resonance lymphography [MRL]) for lymph node (LN) treatment in prostate cancer (PCa) patients.	Of the 738 LNs visible on MRL, 151 were positive in 23 of 29 patients. Of the 132 LNs visible on PET/CT, 34 were positive in 13 of 29 patients. MRL detected significantly more positive LNs ($p < 0.001$) in more patients than PET/CT ($p = 0.002$). The mean diameter of the detected suspicious LNs on MRL was significantly smaller than those detected by PET/CT, 4.9 mm and 8.4 mm, respectively ($p < 0.0001$). In 14 (61%) of 23 patients, suspicious LNs were found outside the clinical target volume with MRL and in 4 (31%) of 13 patients with PET/CT.	2
25. Hricak H, Schoder H, Pucar D, et al. Advances in imaging in the postoperative patient with a rising prostate-specific antigen level. Semin Oncol. 2003;30(5):616-634.	Review/Other-Dx	N/A	To explore the imaging evaluation of recurrent/persistent/metastatic prostate cancer, each modality— transrectal ultrasonography (TRUS), magnetic resonance imaging (MRI), computed tomography (CT), radionuclide bone scan, and positron emission tomography (PET)— has advantages, disadvantages, and specific indications.	No results provided in abstract.	4
26. Beresford MJ, Gillatt D, Benson RJ, Ajithkumar T. A systematic review of the role of imaging before salvage radiotherapy for post-prostatectomy biochemical recurrence. Clin Oncol (R Coll Radiol). 2010;22(1):46-55.	Review/Other-Dx	N/A	To review current and investigational imaging techniques, including bone scan, computed tomography, magnetic resonance imaging, positron emission tomography and Prostatecint, assessing their utility in the situation of biochemical recurrence after radical prostatectomy.	No results stated in abstract.	4

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27. Rouviere O, Vitry T, Lyonnet D. Imaging of prostate cancer local recurrences: why and how? Eur Radiol. 2010;20(5):1254-1266.	Review/Other-Dx	N/A	To discuss recent advances in imaging.	Local recurrences after RP are treated by radiotherapy, those after radiotherapy by RP, cryotherapy, brachytherapy or HIFU ablation. Recurrences after cryotherapy or HIFU ablation can be treated by a second session or radiotherapy. Recurrences after brachytherapy are difficult to treat. In patients with BF, MRI can detect local recurrences, whatever the initial treatment was. Dynamic contrast-enhanced MRI seems particularly accurate. The role of spectroscopy remains controversial. Ultrasound-based techniques are less accurate, but this may change with the advent of ultrasonic contrast media.	4
28. Casciani E, Poletini E, Carmenini E, et al. Endorectal and dynamic contrast-enhanced MRI for detection of local recurrence after radical prostatectomy. AJR Am J Roentgenol. 2008;190(5):1187-1192.	Observational-Dx	46 patients	To evaluate the sensitivity and specificity of endorectal MRI combined with dynamic contrast-enhanced MRI to detect local recurrence after radical prostatectomy.	Overall data of 46 (25 recurred, 21 nonrecurred) out of 51 evaluated patients were analyzed. All recurrences showed signal enhancement after gadolinium administration and, in particular, 22 of 24 patients (91%) showed rapid and early signal enhancement. The overall sensitivity and specificity of MR dynamic imaging was higher compared with MRI alone (88%, [95% CI] 69-98% and 100%, 84-100% compared with 48%, 28-69% and 52%, 30-74%). MRI combined with dynamic imaging allowed better identification of recurrences compared with MRI alone (McNemar test: chi-square(1) = 16.67; p = < 0.0001).	2

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29. Sciarra A, Panebianco V, Salciccia S, et al. Role of dynamic contrast-enhanced magnetic resonance (MR) imaging and proton MR spectroscopic imaging in the detection of local recurrence after radical prostatectomy for prostate cancer. <i>Eur Urol.</i> 2008;54(3):589-600.	Observational-Dx	70 patients with high risk of local recurrence and 10 patients with no suspicion of recurrence or progression (control).	To assess the accuracy of 1H-MRSI and DCE-MRI in the depiction of local prostate cancer recurrence in patients with biochemical progression after RP.	In group A, 1H-MRSI analysis alone showed a sensitivity of 84% and a specificity of 88%; the DCE-MRI analysis alone, a sensitivity of 71% and a specificity of 94%; combined 1H-MRSI-DCE-MRI, a sensitivity of 87% and specificity of 94%. AUC for 1H-MRSI, DCEMR, and combined 1HMRSI/DCE-MRI were 0.942, 0.93,1 and 0.964, respectively. In group B, 1H-MRSI alone showed a sensitivity of 71% and a specificity of 83%; DCE-MRI, a sensitivity of 79% and a specificity of 100%; combined 1H-MRSI and DCE-MRI, a sensitivity of 86% and a specificity of 100%. AUC for each of these groups were 0.81, 0.923, and 0.94, respectively.	1
30. Sella T, Schwartz LH, Swindle PW, et al. Suspected local recurrence after radical prostatectomy: endorectal coil MR imaging. <i>Radiology.</i> 2004;231(2):379-385.	Observational-Dx	82 patients	To evaluate endorectal coil magnetic resonance (MR) imaging in the depiction of local recurrence after radical prostatectomy.	Thirty-four of 82 patients did not meet inclusion criteria. Forty-one of 48 remaining patients had clinically documented local recurrence, which MR imaging depicted in 39 of 41 (95%) patients. Seven of 48 patients had no evidence of local or distant metastases, and none had positive MR imaging findings. Sensitivity of MR imaging was 95%, and specificity was 100%. Local recurrences were perianastomotic in 12 (29%) patients and retrovesical in 17 (40%), within retained seminal vesicles in nine (22%), and at anterior or lateral surgical margins in four (9%). All local recurrences were hyperintense to adjacent pelvic muscles on T2-weighted MR images. The mean diameter of tumors was 1.4 cm (range, 0.8-4.5 cm). PSA levels at MR imaging in patients with clinically proved recurrences ranged from undetectable to 10 ng/mL (mean, 2.18 ng/mL).	3

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31. Panebianco V, Barchetti F, Sciarra A, et al. Prostate cancer recurrence after radical prostatectomy: the role of 3-T diffusion imaging in multi-parametric magnetic resonance imaging. <i>Eur Radiol.</i> 2013;23(6):1745-1752.	Observational-Dx	242 patients	To validate the role of 3-T diffusion-weighted imaging (DWI) in the detection of local prostate cancer recurrence after radical prostatectomy (RP).	In group A combined T2-weighted and DCE-MRI (T2+DCE) shows 98 % sensitivity, 94 % specificity and 93 % accuracy in identifying local recurrence; combined T2-weighted and DWI with a b value of 3,000 s/mm(2) (T2+DW3) displays 97 % sensitivity, 95 % specificity and 92 % accuracy, while with a b value of 1,000 s/mm(2) (T2+DW1) affords 93 % sensitivity, 89 % specificity and 88 % accuracy. In group B T2+DCE shows 100 % sensitivity, 97 % specificity and 91 % accuracy in detecting local cancer recurrence; T2+DW3 displays 98 % sensitivity, 96 % specificity and 89 % accuracy; T2+DW1 has 94 % sensitivity, 92 % specificity and 86 % accuracy.	2
32. Harisinghani MG, Barentsz J, Hahn PF, et al. Noninvasive detection of clinically occult lymph-node metastases in prostate cancer. <i>N Engl J Med.</i> 2003;348(25):2491-2499.	Observational-Dx	80 patients	We investigated whether highly lymphotropic superparamagnetic nanoparticles, which gain access to lymph nodes by means of interstitial-lymphatic fluid transport, could be used in conjunction with high-resolution magnetic resonance imaging (MRI) to reveal small nodal metastases.	Of the 334 lymph nodes that underwent resection or biopsy, 63 (18.9 percent) from 33 patients (41 percent) had histopathologically detected metastases. Of these 63 nodes, 45 (71.4 percent) did not fulfill the usual imaging criteria for malignancy. MRI with lymphotropic superparamagnetic nanoparticles correctly identified all patients with nodal metastases, and a node-by-node analysis had a significantly higher sensitivity than conventional MRI (90.5 percent vs. 35.4 percent, $P < 0.001$) or nomograms.	1
33. Daldrup-Link HE, Franzius C, Link TM, et al. Whole-body MR imaging for detection of bone metastases in children and young adults: comparison with skeletal scintigraphy and FDG PET. <i>AJR Am J Roentgenol.</i> 2001;177(1):229-236.	Observational-Dx	Thirty-nine children and young adults who were 2--19 years old.	To compare the diagnostic accuracy of whole-body MR imaging, skeletal scintigraphy, and 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET) for the detection of bone metastases in children.	Twenty-one patients exhibited 51 bone metastases. Sensitivities for the detection of bone metastases were 90% for FDG PET, 82% for whole-body MR imaging, and 71% for skeletal scintigraphy; these data were significantly different ($p < 0.05$). False-negative lesions were different for the three imaging modalities, mainly depending on lesion location. Most false-positive lesions were diagnosed using FDG PET.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Goudarzi B, Kishimoto R, Komatsu S, et al. Detection of bone metastases using diffusion weighted magnetic resonance imaging: comparison with (11)C-methionine PET and bone scintigraphy. Magn Reson Imaging. 2010;28(3):372-379.	Observational-Dx	29 patients	To evaluate the ability of diffusion-weighted imaging (DWI) to detect bone metastasis by comparing the results obtained using this modality with those obtained using (11)C-methionine (MET) positron emission tomography (PET) and bone scintigraphy.	Among the 19 patients who were diagnosed using DWI and PET, the PET identified 39 bone metastases, while the DWI identified 60 metastases out of 69 metastases revealed with conventional magnetic resonance imaging (MRI). Among the 15 patients who were diagnosed using DWI and bone scintigraphy, the bone scintigraphy identified 18 bone metastases, while the DWI identified 72 metastases out of 78 metastases revealed with conventional MRI. The overall bone metastasis detection rates were 56.5% for PET, 23.1% for bone scintigraphy and 92.3% for DWI.	3
35. Gutzeit A, Doert A, Froehlich JM, et al. Comparison of diffusion-weighted whole body MRI and skeletal scintigraphy for the detection of bone metastases in patients with prostate or breast carcinoma. Skeletal Radiol. 2010;39(4):333-343.	Observational-Dx	36 patients	To prospectively compare the diagnostic accuracy of diffusion-weighted whole body imaging with background whole body signal suppression (DWIBS) with skeletal scintigraphy for the diagnosis and differentiation of skeletal lesions in patients suffering from prostate or breast cancer.	Overall, 45 circumscribed bone metastases and 107 benign lesions were found. DWIBS performed significantly better in detecting malignant skeletal lesions in patients with more than 10 lesions (sensitivity: 0.97/0.91) compared to skeletal scintigraphy (sensitivity: 0.48/0.42). No statistical difference could be found between DWIBS (0.58/0.33) and skeletal scintigraphy (0.67/0.58) in the sensitivity values for malignant skeletal lesions in patients with less than 5 lesions. For benign lesions, scintigraphy scored best with a sensitivity of 0.93/0.87 compared to 0.20/0.13 for DWIBS. Interobserver agreement with Cohen's kappa coefficient was calculated as 0.784 in the case of scintigraphy and 0.663 for DWIBS.	2
36. Turner JW, Hawes DR, Williams RD. Magnetic resonance imaging for detection of prostate cancer metastatic to bone. J Urol. 1993;149(6):1482-1484.	Observational-Dx	18 patients	To use magnetic resonance imaging in patients with known prostate cancer to resolve conflicting evidence of metastases found on bone scans, plain films and serum enzyme determinations.	Of 8 bone scans interpreted as positive MRI was read as negative for metastatic disease in 2. Of 5 negative bone scans 1 MRI study was interpreted as positive. All 5 equivocal bone scans demonstrated no osseous lesions on MRI. In addition, in 6 patients with evidence of bone metastases the serial MRI scans following hormonal therapy demonstrated radiographic and clinical improvement.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Roy C, Foudi F, Charton J, et al. Comparative sensitivities of functional MRI sequences in detection of local recurrence of prostate carcinoma after radical prostatectomy or external-beam radiotherapy. AJR Am J Roentgenol. 2013;200(4):W361-368.	Observational-Dx	83 patients	To determine the respective accuracies of three types of functional MRI sequences-diffusion-weighted imaging (DWI), dynamic contrast-enhanced (DCE) MRI, and 3D (1)H-MR spectroscopy (MRS)-in the depiction of local prostate cancer recurrence after two different initial therapy options.	All patients presented with a local relapse. Sensitivity with T2-weighted MRI and 3D (1)H-MRS sequences was 57% and 53%, respectively, for group A and 71% and 78%, respectively, for group B. DCE-MRI alone showed a sensitivity of 100% and 96%, respectively, for groups A and B. DWI alone had a higher sensitivity for group B (96%) than for group A (71%). The combination of T2-weighted imaging plus DWI plus DCE-MRI provided a sensitivity as high as 100% in group B.	2

**Post-treatment Follow-up of Prostate Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>38. Wu LM, Xu JR, Gu HY, et al. Role of magnetic resonance imaging in the detection of local prostate cancer recurrence after external beam radiotherapy and radical prostatectomy. Clin Oncol (R Coll Radiol). 2013;25(4):252-264.</p>	<p>Meta-analysis</p>	<p>14 studies including 683 patients.</p>	<p>To carry out a meta-analysis to assess the effectiveness of magnetic resonance imaging (MRI) during the follow-up of patients with prostate cancer after undergoing external beam radiotherapy (EBRT) or radical prostatectomy.</p>	<p>Fourteen of 768 initially identified studies were included in the meta-analysis. Seven studies examining patient after radical prostatectomy had a pooled sensitivity and specificity on the patient level of 82% (95% confidence interval 78-86%) and 87% (95% confidence interval 81-92%), respectively. In the subgroup analysis, compared with T2-weighted imaging (T2WI), dynamic contrast-enhanced (DCE) MRI showed higher pooled sensitivity (85%, 95% confidence interval 78-90%) and specificity (95%, 95% confidence interval 88-99%). DCE MRI combined with magnetic resonance spectroscopic imaging (1H-MRSI) had the highest pooled sensitivity (92%, 95% confidence interval 83-97%). Nine studies examining men after EBRT had a pooled sensitivity and specificity on the patient level of 82% (95% confidence interval 75-88%) and 74% (95% confidence interval 64-82%), respectively. Compared with T2WI, DCE MRI showed higher pooled sensitivity (90%, 95% confidence interval 77-97%) and specificity (81%, 95% confidence interval 64-93%). DCE combined with 1H-MRSI had the highest pooled specificity (90%, 95% confidence interval 56-100%). The pooled sensitivity and specificity on sextant analysis was 58% (95% confidence interval 53-64%) and 85% (95% confidence interval 82-88%), respectively. DCE MRI showed the highest pooled sensitivity: 71% (95% confidence interval 60-80%).</p>	<p>M</p>

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Deliveliotis C, Manousakas T, Chrisofos M, Skolarikos A, Delis A, Dimopoulos C. Diagnostic efficacy of transrectal ultrasound-guided biopsy of the prostatic fossa in patients with rising PSA following radical prostatectomy. World J Urol. 2007;25(3):309-313.	Observational-Dx	30 patients	To evaluate the diagnostic efficacy of transrectal ultrasound (TRUS)-guided biopsy of the prostatic fossa in men with biochemical relapse following radical retropubic prostatectomy (RP).	Twelve patients (40%) were found with local recurrence. Sensitivities of TRUS and DRE were 75 and 50%, while specificities were 83 and 100%, respectively. Local recurrence was detected in 25% of the patients with PSA \leq 1 ng/ml, and higher PSA levels were correlated with an increased positive biopsy rate. All patients with positive DRE had positive biopsy and positive TRUS as well. When both TRUS and DRE were positive it was more likely for the patient to have positive biopsy than when both TRUS and DRE were negative.	2
40. Drudi FM, Giovagnorio F, Carbone A, et al. Transrectal colour Doppler contrast sonography in the diagnosis of local recurrence after radical prostatectomy--comparison with MRI. Ultraschall Med. 2006;27(2):146-151.	Observational-Dx	18 patients	To assess the usefulness of colour power-Doppler transrectal sonography before/after contrast agent in the detection of local recurrence in patients with rising prostate-specific antigen values after radical prostatectomy and to compare with magnetic resonance imaging .	Baseline and contrast-enhanced transrectal colour power-Doppler sonography and contrast-enhanced magnetic resonance imaging identified recurrent disease in 6, 10 and 10 patients, respectively. Biopsy confirmed recurrence in 10 patients, but was positive also in 2 additional patients who were negative at contrast-enhanced transrectal colour power-Doppler sonography and contrast-enhanced magnetic resonance imaging. The remaining 6 patients were negative also at diagnostic imaging and biopsy after 30 days. Grey-scale transrectal sonography values were: sensitivity 91.7 %, specificity 66 %, PPV 91.6 %, NPV 40 %. Baseline colour power-Doppler transrectal sonography values were: sensitivity 38.5 %, specificity 85 %, diagnostic accuracy 50 %, PPV 83.3 %, NPV 33.3 %. Contrast enhanced colour power-Doppler transrectal sonography and magnetic resonance imaging values were: sensitivity 76.9 %, specificity 100 %, diagnostic accuracy 83.3 %, PPV 100 %, NPV 62.5 %.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Sudakoff GS, Smith R, Vogelzang NJ, Steinberg G, Brendler CB. Color Doppler imaging and transrectal sonography of the prostatic fossa after radical prostatectomy: early experience. AJR Am J Roentgenol. 1996;167(4):883-888.	Observational-Dx	23 patients and 7 controls.	To determine if the addition of color Doppler imaging (CDI) during transrectal sonography can improve the detection of residual or recurrent prostatic cancer after radical prostatectomy.	Fourteen of 23 patients (61%) had positive transrectal sonography or transrectal sonography and CDI-directed biopsies. Transrectal sonography alone detected grayscale abnormalities in 11 of 23 patients (48%), of whom 10 (43%) had positive transrectal sonography-directed biopsies. CDI during transrectal sonography showed hypervascularity in 12 of 23 patients (52%). Biopsies of these hypervascular regions were positive in all 12 patients (100%). Hypervascularity was detected in 10 of 11 (91%) gray-scale abnormalities initially detected with transrectal sonography alone. CDI during transrectal sonography detected two patients with hypervascular areas without associated gray-scale findings. Both patients had positive biopsies of their hypervascular sites. Transrectal sonography had a sensitivity and specificity of 71% and 89%, respectively, with positive and negative predictive values of 91% and 67%, respectively. CDI during transrectal sonography had a sensitivity and specificity of 86% and 100%, respectively, with positive and negative predictive values of 100% and 82%, respectively.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Tamsel S, Killi R, Apaydin E, Hekimgil M, Demirpolat G. The potential value of power Doppler ultrasound imaging compared with grey-scale ultrasound findings in the diagnosis of local recurrence after radical prostatectomy. Clin Radiol. 2006;61(4):325-330; discussion 323-324.	Observational-Dx	18 patients	To determine the value of power Doppler ultrasound (PDUS) imaging during transrectal ultrasonography (TRUS) in detecting local recurrence after radical retropubic prostatectomy (RRP).	Fifteen of the 18 patients (83%) had positive biopsies for local recurrent tumour at histological examination. TRUS alone detected grey-scale abnormalities in 15 of 18 patients (83%), of whom 14 (77%) had positive TRUS-guided biopsies. PDUS during TRUS showed hypervascularity in 14 of 18 patients (77%). Biopsies of these hypervascular regions were positive in all patients (100%). The sensitivity and specificity of TRUS alone in detecting recurrent tumour were 93 and 67%, respectively, with a positive predictive value (PPV) of 93% and a negative predictive value (NPV) of 67%. TRUS combined with PDUS had a sensitivity and specificity of 93 and 100%, respectively, with a PPV and a NPV of 100 and 75%, respectively.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Evangelista L, Zattoni F, Guttilla A, Saladini G, Colletti PM, Rubello D. Choline PET or PET/CT and biochemical relapse of prostate cancer: a systematic review and meta-analysis. Clin Nucl Med. 2013;38(5):305-314.	Meta-analysis	19 studies including 1555 patients	To evaluate the diagnostic performance of 18F-choline and 11C-choline PET or PET/CT in detection of locoregional or distant metastases in PCa.	From the years 2000 to 2012, we found 53 complete articles that critically evaluated the role of choline PET in restaging patients with PCa recurrence. The meta-analysis was carried out and dealt with 19 selected studies (12 studies for all sites of disease, 3 for lymph node metastases, and 4 for local recurrence), with a total of 1555 patients. The meta-analysis provided a pooled sensitivity of 85.6% (95% CI: 82.9%-88.1%) and pooled specificity of 92.6% (95% CI: 90.1%-94.6%) for all sites of disease (prostatic fossa, lymph nodes, and bone), a pooled sensitivity of 75.4% (95% CI: 66.9%-82.6%) and pooled specificity of 82% (95% CI: 68.6%-91.4%) for prostatic fossa recurrence, and a pooled sensitivity of 100% (95% CI: 90.5%-100%) and pooled specificity of 81.8% (95% CI: 48.2%-97.7%) for lymph node metastases. The heterogeneity ranged between 0.00% and 88.6%. The diagnostic odds ratios were 62.123 (95% CI: 24.783-155.72), 5.869 (95% CI: 1.818-18.946), and 138.57 (95% CI: 11.27-1703.8), respectively, for all sites of disease, local recurrence, and lymph node disease.	M

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Umbehrl MH, Muntener M, Hany T, Sulser T, Bachmann LM. The role of 11C-choline and 18F-fluorocholine positron emission tomography (PET) and PET/CT in prostate cancer: a systematic review and meta-analysis. Eur Urol. 2013;64(1):106-117.	Meta-analysis	10 studies	To systematically review and conduct a meta-analysis of the available evidence of PET and PET/CT using 11C-choline and 18F-fluorocholine as tracers in imaging PCa patients in staging and restaging settings.	In staging patients with proven but untreated PCa, the results of the meta-analysis on a per-patient basis (10 studies, n = 637) showed pooled sensitivity, specificity, and diagnostic odds ratio (DOR) of 84% (95% confidence interval [CI], 68-93%), 79% (95% CI, 53-93%), and 20.4 (95% CI, 9.9-42.0), respectively. The positive and negative likelihood ratios were 4.02 (95% CI, 1.73-9.31) and 0.20 (95% CI, 0.11-0.37), respectively. On a per-lesion basis (11 studies, n = 5117), these values were 66% (95% CI, 56-75%), 92% (95% CI, 78-97%), and 22.7 (95% CI, 8.9-58.0), respectively, for pooled sensitivity, specificity, and DOR; and 8.29 (95% CI, 3.05-22.54) and 0.36 (95% CI, 0.29-0.46), respectively, for positive and negative likelihood ratios. In restaging patients with biochemical failure after local treatment with curative intent, the meta-analysis results on a per-patient basis (12 studies, n = 1055) showed pooled sensitivity, specificity, and DOR of 85% (95% CI, 79-89%), 88% (95% CI, 73-95%), and 41.4 (95% CI, 19.7-86.8), respectively; the positive and negative likelihood ratios were 7.06 (95% CI, 3.06-16.27) and 0.17 (95% CI, 0.13-0.22), respectively.	M

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Mitchell CR, Lowe VJ, Rangel LJ, Hung JC, Kwon ED, Karnes RJ. Operational characteristics of (11)c-choline positron emission tomography/computerized tomography for prostate cancer with biochemical recurrence after initial treatment. J Urol. 2013;189(4):1308-1313.	Observational-Dx	176 patients	To examine the performance of (11)C-choline positron emission tomography/computerized tomography for its ability to delineate prostate cancer distribution and extent after initial therapy.	Using patient based analysis (11)C-choline positron emission tomography yielded a sensitivity, specificity, positive predictive value and negative predictive value of 93%, 76%, 91% and 81%, respectively. Of the 176 positron emission tomography/computerized tomography scans performed 56 (32%) were deemed clinically useful as defined by the ability to identify lesions not delineated using conventional imaging, thereby prompting changes in clinical management. The optimal prostate specific antigen for lesion detection was 2.0 ng/ml. On multivariate analysis prostate specific antigen at positron emission tomography (HR 1.37, p = 0.04) and clinical stage at initial diagnosis of prostate cancer (HR 5.19, p = 0.0035) were significant predictors of positive (11)C-choline positron emission tomography/computerized tomography.	3
46. Fuccio C, Castellucci P, Schiavina R, et al. Role of 11C-choline PET/CT in the re-staging of prostate cancer patients with biochemical relapse and negative results at bone scintigraphy. Eur J Radiol. 2012;81(8):e893-896.	Observational-Dx	123 patients	To evaluate the utility of (11)C-choline PET/CT in prostate cancer (PC) patients who have demonstrated a biochemical recurrence and a negative bone scintigraphy (BS).	(11)C-choline PET/CT was positive in 42/123 patients (34.1%). (11)C-choline PET/CT detected lesions in: bone (10 patients), lymph nodes (20 patients), bone and lymph nodes (7 patients), bone and lung (1 patient), lymph nodes and lung (1 patient), local relapse (3 patients). Overall, (11)C-choline PET/CT showed a total of 30 unknown bone lesions in 18/123 (14.6%) patients.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Breeuwsma AJ, Rybalov M, Leliveld AM, Pruijm J, de Jong IJ. Correlation of [11C]choline PET-CT with time to treatment and disease-specific survival in men with recurrent prostate cancer after radical prostatectomy. Q J Nucl Med Mol Imaging. 2012;56(5):440-446.	Observational-Dx	64 patients	To correlate PET/CT data with clinical data, PSA kinetics and disease specific and overall survival.	The 64 patients had median PSA of 1.4 ng/mL. Median follow-up period of patients was 50 (6-124) months. Ten patients died during the course of follow-up of which 5 due to metastasized disease. No significant differences were seen in age, time to recurrence, total PSA at recurrence and PET-CT results. Patients with abnormal PET had higher PSAvel (median 3.09 ng/mL/yr versus 10.17, P=0.002) and shorter PSADT (med 4.83 months vs. 0.53, P=0.016). Median time to treatment was significantly lower in the PET-CT negative group. Age of patients at death from the whole group did not differ from the age of death in an age matched group. Disease specific survival was significantly higher in the PET-CT negative group (P=0.05).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Castellucci P, Fuccio C, Nanni C, et al. Influence of trigger PSA and PSA kinetics on 11C-Choline PET/CT detection rate in patients with biochemical relapse after radical prostatectomy. J Nucl Med. 2009;50(9):1394-1400.	Observational-Dx	106 patients	To investigate the effect of total prostate-specific antigen (PSA) at the time of (11)C-choline PET/CT (trigger PSA), PSA velocity (PSAvel), and PSA doubling time (PSAdt) on (11)C-choline PET/CT detection rate in patients treated with radical prostatectomy for prostate cancer, who showed biochemical failure during follow-up.	(11)C-choline PET/CT detected disease relapse in 74 of 190 patients (38.9%). The detection rate of (11)C-choline PET/CT was 19%, 25%, 41%, and 67% in the 4 subgroups- PSA ≤ 1 ng/mL (51 patients), 1 < PSA ≤ 2 ng/mL (39 patients), 2 < PSA ≤ 5 ng/mL (51 patients), and PSA > 5 ng/mL (49 patients)-respectively. Trigger PSA values were statistically different between PET-positive patients (median PSA, 4.0 ng/mL) and PET-negative patients (median PSA, 1.4 ng/mL) (P = 0.0001). Receiver-operating-characteristic analysis showed an optimal cutoff point for trigger PSA of 2.43 ng/mL (area under the curve, 0.76). In 106 patients, PSAdt and PSAvel values were statistically different between patients with PET-positive and -negative scan findings (P = 0.04 and P = 0.03). The (11)C-choline PET/CT detection rate was 12%, 34%, 42%, and 70%, respectively, in patients with PSAvel < 1 ng/mL/y (33 patients), 1 < PSAvel ≤ 2 ng/mL/y (26 patients), 2 < PSAvel ≤ 5 ng/mL/y (19 patients), and PSAvel > 5 ng/mL/y (28 patients). The (11)C-choline PET/CT detection rate was 20%, 40%, 48%, and 60%, respectively, in patients with PSAdt > 6 mo (45 patients), 4 < PSAdt ≤ 6 mo (20 patients), 2 < PSAdt ≤ 4 mo (31 patients), and PSAdt ≤ 2 mo (10 patients). There was no statistical difference between PET-positive and -negative scan detection rates according to the Gleason score, pT and N status, patient age, or duration between surgery and biochemical relapse. Trigger PSA and PSAvel were found to be independent predictive factors for a PET-positive result (P = 0.002; P = 0.04) and PSAdt was found to be an independent factor only in patients with trigger PSA less than 2 ng/mL (P = 0.05) using multivariate analysis.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Giovacchini G, Picchio M, Coradeschi E, et al. Predictive factors of [(11)C]choline PET/CT in patients with biochemical failure after radical prostatectomy. <i>Eur J Nucl Med Mol Imaging</i> . 2010;37(2):301-309.	Observational-Dx	358 patients	To identify clinical and pathological factors predictive of positive [11C]choline PET/CT findings in prostate cancer patients with biochemical failure after radical prostatectomy.	The mean PSA level was 3.77 +/- 6.94 ng/ml (range 0.23-45 ng/ml; median 1.27 ng/ml). PET/CT was positive for recurrence in 161 of 358 patients (45%). On an anatomical region basis, [(11)C]choline pathological uptake was observed in lymph nodes (107/161 patients, 66%), prostatectomy bed (55/161 patients, 34%), and in the skeleton (46/161 patients, 29%). PET/CT findings were validated using histological criteria (46/358, 13%), and follow-up clinical and imaging criteria (312/358, 87%). Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were, respectively, 85%, 93%, 91%, 87%, and 89%. In multivariate analysis, high PSA levels, advanced pathological stage, previous biochemical failure and older age were significantly ($P < 0.05$) associated with an increased risk of positive PET/CT findings. The percentage of positive scans was 19% in those with a PSA level between 0.2 and 1 ng/ml, 46% in those with a PSA level between 1 and 3 ng/ml, and 82% in those with a PSA level higher than 3 ng/ml. ROC analysis showed that PET/CT-positive and PET/CT-negative patients could be best distinguished using a PSA cut-off value of 1.4 ng/ml.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Giovacchini G, Picchio M, Scattoni V, et al. PSA doubling time for prediction of [(11)C]choline PET/CT findings in prostate cancer patients with biochemical failure after radical prostatectomy. <i>Eur J Nucl Med Mol Imaging</i> . 2010;37(6):1106-1116.	Observational-Dx	170 patients	To compare PSA levels and PSA doubling time (PSADT) to predict [(11)C]choline PET/CT findings.	The median PSA was 1.25 ng/ml (range: 0.23-48.6 ng/ml), and the median PSADT was 7.0 months (range: 0.97-45.3 months). [(11)C]choline PET/CT was positive in 75 of 170 patients (44%). PET/CT findings were validated using histological criteria (11%) and clinical and imaging criteria (89%). The overall accuracy of [(11)C]choline PET/CT was 88%. Multivariate logistic regression showed that high PSA and short PSADT were significant ($p < 0.05$) predictors of positive [(11)C]choline PET/CT [PSA: odds ratio (OR) = 1.43; 95% confidence interval (CI): 1.15-1.78; PSADT: OR = 1.12; 95% CI: 1.04-1.21]. The percentage of patients with positive [(11)C]choline PET/CT was 27% for PSADT >6 months, 61% for PSADT between 3 and 6 months and 81% for PSADT <3 months. The percentage of patients who displayed pathological [(11)C]choline uptake in the skeleton significantly increased ($p < 0.05$) from 3% for PSADT >6 months to 52% for PSADT <3 months. Conversely, patients who displayed pathological [(11)C]choline uptake in the prostatectomy bed were 0% for PSADT <3 months and 17% for PSADT >6 months ($p < 0.05$). A nomogram based on age, PSA, PSADT, time to trigger PSA, Gleason score, pathological stage and androgen deprivation therapy demonstrated bootstrap-corrected predictive accuracy of 81%.	3
51. Krause BJ, Souvatzoglou M, Tuncel M, et al. The detection rate of [(11)C]choline-PET/CT depends on the serum PSA-value in patients with biochemical recurrence of prostate cancer. <i>Eur J Nucl Med Mol Imaging</i> . 2008;35(1):18-23.	Observational-Dx	63 patients	To assess the relationship between the detection rate of [(11)C]Choline-PET/CT and the serum PSA-level in patients with a biochemical recurrence of prostate cancer with the view towards localisation of recurrent disease.	Of the 63 patients, 35 (56%) showed a pathological [(11)C]Choline uptake. The detection rate of [(11)C]Choline-PET/CT showed a relationship with the serum PSA-level: The detection rate was 36% for a PSA-value <1 ng/ml, 43% for a PSA-value 1-<2 ng/ml, 62% for a PSA-value 2-<3 ng/ml and 73% for a PSA-value >or=3 ng/ml. Anti-androgen therapy did not show a significant effect on the detection rate of [(11)C]Choline-PET/CT ($p = 0.374$).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Kwee SA, Coel MN, Lim J. Detection of recurrent prostate cancer with 18F-fluorocholine PET/CT in relation to PSA level at the time of imaging. <i>Ann Nucl Med.</i> 2012;26(6):501-507.	Observational-Dx	50 patients	To evaluate fluorine-18 fluorocholine (FCH) PET/CT for the detection of recurrent prostate cancer in relation to prostate-specific antigen (PSA) level.	Findings consistent with recurrent prostate cancer were noted on FCH PET/CT in 31/50 (62%) patients, with positive findings in 17/18 (94%), and 11/13 (85%), 2/7 (29%), and 1/12 (8%) patients with PSA >4, >2-4, >0.5-2, and ≤0.5 ng/mL, respectively. These findings were indicative of local/regional recurrence in 23 cases and systemic recurrence in 8 cases, with only a single route of recurrence (i.e., either hematogenous, lymphatic, or intraprostatic) in 84% of PET scans with positive findings. Abnormal tumor activity was detected in 88% of patients with a PSA level of 1.1 ng/mL or higher, and in only 6% of patients with a PSA level below this threshold value.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Odewole OA, Tade FI, Nieh PT, et al. Recurrent prostate cancer detection with anti-3-[(18)F]FACBC PET/CT: comparison with CT. Eur J Nucl Med Mol Imaging. 2016;43(10):1773-1783.	Observational-Dx	53 patients	To compare the diagnostic performance of the synthetic amino acid analogue PET radiotracer anti-3-[(18)F]FACBC (fluciclovine) with that of CT in the detection of recurrent prostate carcinoma.	Of 53 fluciclovine PET/CT and 53 CT examinations, 41 (77.4 %) and 10 (18.9 %), respectively, had positive findings for recurrent disease. Positivity rates were higher with fluciclovine PET/CT than with CT at all prostate-specific antigen (PSA) levels, PSA doubling times and original Gleason scores. In the prostate/bed, fluciclovine PET/CT was true-positive in 31 and CT was true-positive in 4 of 51 patients who met the reference standard. In extraprostatic regions, fluciclovine PET/CT was true-positive in 12 and CT was true-positive in 3 of 41 patients who met the reference standard. Of the 43 index lesions used to prove positivity, 42 (97.7 %) had histological proof. In 51 patients with sufficient follow-up to calculate diagnostic performance in the prostate/bed, fluciclovine PET/CT demonstrated a sensitivity of 88.6 %, a specificity of 56.3 %, an accuracy of 78.4 %, a positive predictive value (PPV) of 81.6 %, and a negative predictive value (NPV) of 69.2 %; the respective values for CT were 11.4 %, 87.5 %, 35.3 %, 66.7 % and 31.1 %. In 41 patients with sufficient follow-up to calculate diagnostic performance in extraprostatic regions, fluciclovine PET/CT demonstrated a sensitivity of 46.2 %, a specificity of 100 %, an accuracy of 65.9 %, a PPV of 100 %, and an NPV of 51.7 %; the respective values for CT were 11.5 %, 100 %, 43.9 %, 100 % and 39.5 %.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
54. Nanni C, Schiavina R, Boschi S, et al. Comparison of 18F-FACBC and 11C-choline PET/CT in patients with radically treated prostate cancer and biochemical relapse: preliminary results. Eur J Nucl Med Mol Imaging. 2013;40 Suppl 1:S11-17.	Observational-Dx	15 patients	To assess the rate of detection rate of recurrent prostate cancer by PET/CT using anti-3-(18)F-FACBC, a new synthetic amino acid, in comparison to that using (11)C-choline as part of an ongoing prospective single-centre study.	No adverse reactions to anti-3-(18)F-FACBC PET/CT were noted. On a patient basis, (11)C-choline PET/CT was positive in 3 patients and negative in 12 (detection rate 20%), and anti-3-(18)F-FACBC PET/CT was positive in 6 patients and negative in 9 (detection rate 40%). On a lesion basis, (11)C-choline detected 6 lesions (4 bone, 1 lymph node, 1 local relapse), and anti-3-(18)F-FACBC detected 11 lesions (5 bone, 5 lymph node, 1 local relapse). All (11)C-choline-positive lesions were also identified by anti-3-(18)F-FACBC PET/CT. The TBR of anti-3-(18)F-FACBC was greater than that of (11)C-choline in 8/11 lesions, as were image quality and contrast.	3
55. Nanni C, Schiavina R, Brunocilla E, et al. 18F-Fluciclovine PET/CT for the Detection of Prostate Cancer Relapse: A Comparison to 11C-Choline PET/CT. Clin Nucl Med. 2015;40(8):e386-391.	Observational-Dx	50 patients	To compare the detection rate of (18)F-FACBC and (11)C-choline in patients presenting a biochemical relapse.	On a patient-based analysis, (18)F-fluciclovine detection turned out to be significantly superior to (11)C-choline ($P < 0.000001$). This result was also true on lesion, lymph node, bone lesion, and local relapse analysis ($P < 0.0001$ in all the cases). There was no significant difference in terms of target to background of positive lesions between (11)C-choline and (18)F-fluciclovine. When the patients were divided into groups with different PSA levels, (18)F-fluciclovine had a superior detection rate for low, intermediate, and high PSA levels.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
56. Nanni C, Zanoni L, Pultrone C, et al. (18)F-FACBC (anti1-amino-3-(18)F-fluorocyclobutane-1-carboxylic acid) versus (11)C-choline PET/CT in prostate cancer relapse: results of a prospective trial. Eur J Nucl Med Mol Imaging. 2016;43(9):1601-1610.	Observational-Dx	89 patients	To compare the accuracy of (18)F-FACBC and (11)C-choline PET/CT in patients radically treated for prostate cancer presenting with biochemical relapse.	In 51 patients the results were negative and in 25 patients positive with both the tracers, in eight patients the results were positive with (18)F-FACBC but negative with (11)C-choline, and in five patients the results were positive with (11)C-choline but negative with (18)F-FACBC. Overall in 49 patients the results were false-negative (FN), in two true-negative, in 24 true-positive (TP) and in none false-positive (FP) with both tracers. In terms of discordances between the tracers: (1) in one patient, the result was FN with (11)C-choline but FP with (18)F-FACBC (lymph node), (2) in seven, FN with (11)C-choline but TP with (18)F-FACBC (lymph node in five, bone in one, local relapse in one), (3) in one, FP with (11)C-choline (lymph node) but TP with (18)F-FACBC (local relapse), (4) in two, FP with (11)C-choline (lymph nodes in one, local relapse in one) but FN with (18)F-FACBC, and (5) in three, TP with (11)C-choline (lymph nodes in two, bone in one) but FN with (18)F-FACBC. With (11)C-choline and (18)F-FACBC, sensitivities were 32 % and 37 %, specificities 40 % and 67 %, accuracies 32 % and 38 %, PPVs 90 % and 97 %, and NPVs 3 % and 4 %, respectively. Categorizing patients by PSA level (<1 ng/ml 28 patients, 1 - <2 ng/ml 28 patients, 2 - <3 ng/ml 11 patients, >=3 ng/ml 22 patients), the number (percent) of patients with TP findings were generally higher with (18)F-FACBC than with (11)C-choline: six patients (21 %) and four patients (14 %), eight patients (29 %) and eight patients (29 %), five patients (45 %) and four patients (36 %), and 13 patients (59 %) and 11 patients (50 %), respectively.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Ren J, Yuan L, Wen G, Yang J. The value of anti-1-amino-3-18F-fluorocyclobutane-1-carboxylic acid PET/CT in the diagnosis of recurrent prostate carcinoma: a meta-analysis. <i>Acta Radiol.</i> 2016;57(4):487-493.	Meta-analysis	6 studies	To systematically review and perform a meta-analysis of published data regarding the performance of 18F-FACBC PET/CT in the diagnosis of recurrent prostate carcinoma.	Six studies comprising 251 patients, suspicious of prostate carcinoma recurrence, were included in this meta-analysis. 18F-FACBC PET/CT had an 87% pooled sensitivity, 66% pooled specificity, 0.93 the area under the receiver-operating characteristic curve on a per patient-based analysis in detecting prostate carcinoma recurrence.	M
58. Bach-Gansmo T, Nanni C, Nieh PT, et al. Multisite Experience of the Safety, Detection Rate and Diagnostic Performance of Fluciclovine (18F) Positron Emission Tomography/Computerized Tomography Imaging in the Staging of Biochemically Recurrent Prostate Cancer. <i>J Urol.</i> 2017;197(3 Pt 1):676-683.	Observational-Dx	596 patients	To describe a multisite experience of the efficacy and safety of the positron emission tomography/computerized tomography agent fluciclovine (18F) after biochemical recurrence.	The subject level fluciclovine (18F) positron emission tomography/computer tomography detection rate was 67.7% (403 of 595 scans). Positive findings were detected in the prostate/bed and pelvic lymph node regions in 38.7% (232 of 599) and 32.6% of scans (194 of 596), respectively. Metastatic involvement outside the pelvis was detected in 26.2% of scans (155 of 591). The subject level detection rate in patients in the lowest quartile for baseline prostate specific antigen (0.79 ng/ml or less) was 41.4% (53 of 128). Of these patients 13 had involvement in the prostate/bed only, 16 had pelvic lymph node involvement without distant disease and 24 had distant metastases. The positive predictive value of fluciclovine (18F) positron emission tomography/computerized tomography scanning for all sampled lesions was 62.2%, and it was 92.3% and 71.8% for extraprostatic and prostate/bed involvement, respectively. Fluciclovine (18F) was well tolerated and the safety profile was not altered following repeat administration.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Afshar-Oromieh A, Zechmann CM, Malcher A, et al. Comparison of PET imaging with a (68)Ga-labelled PSMA ligand and (18)F-choline-based PET/CT for the diagnosis of recurrent prostate cancer. <i>Eur J Nucl Med Mol Imaging</i> . 2014;41(1):11-20.	Observational-Dx	37 patients	To compare such a novel tracer with standard choline-based PET/CT.	A total of 78 lesions characteristic for PC were detected in 32 patients using (68)Ga-PSMA PET/CT and 56 lesions were detected in 26 patients using choline PET/CT. The higher detection rate in (68)Ga-PSMA PET/CT was statistically significant (p=0.04). In five patients no lesion was found with both methods. All lesions detected by (18)F-fluoromethylcholine PET/CT were also seen by (68)Ga-PSMA PET/CT. In (68)Ga-PSMA PET/CT SUVmax was clearly (>10 %) higher in 62 of 78 lesions (79.1 %) and the tumour to background ratio was clearly (>10 %) higher in 74 of 78 lesions (94.9 %) when compared to (18)F-fluoromethylcholine PET/CT.	3
60. Schwenck J, Rempp H, Reischl G, et al. Comparison of 68Ga-labelled PSMA-11 and 11C-choline in the detection of prostate cancer metastases by PET/CT. <i>Eur J Nucl Med Mol Imaging</i> . 2017;44(1):92-101.	Observational-Dx	123 patients	To compare the PSMA ligand 68Ga-PSMA-11 with 11C-choline in patients with primary and recurrent prostate cancer.	In 67 patients with biochemical relapse, we detected 458 lymph nodes suspicious for metastasis. PET using 68Ga-PSMA-11 showed a significantly higher uptake and detection rate than 11C-choline PET. Also 68Ga-PSMA-11 PET identified significantly more patients with suspicious lymph nodes as well as affected lymph nodes regions especially at low PSA levels. Bone lesions suspicious for prostate cancer metastasis were revealed in 36 patients' biochemical relapse. Significantly more bone lesions were detected by 68Ga-PSMA-11, but only 3 patients had only PSMA-positive bone lesions. Nevertheless, we detected also 29 suspicious lymph nodes and 8 bone lesions, which were only positive as per 11C-choline PET. These findings led to crucial differences in the TNM classification and the identification of oligometastatic patients. In the patients who underwent initial staging, all primary tumors showed uptake of both tracers. Although significantly more suspicious lymph nodes and bone lesions were identified, only 2 patients presented with bone lesions only detected by 68Ga-PSMA-11 PET.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Eiber M, Maurer T, Souvatzoglou M, et al. Evaluation of Hybrid (6)(8)Ga-PSMA Ligand PET/CT in 248 Patients with Biochemical Recurrence After Radical Prostatectomy. J Nucl Med. 2015;56(5):668-674.	Observational-Dx	248 patients	To describe the detection rate as a function of the absolute PSA level and PSA kinetics and the evaluation of the diagnostic performance, compared with primary histologic differentiation and antihormonal treatment.	Two hundred twenty-two (89.5%) patients showed pathologic findings in (68)Ga-PSMA ligand PET/CT. The detection rates were 96.8%, 93.0%, 72.7%, and 57.9% for PSA levels of ≥ 2 , 1 to < 2 , 0.5 to < 1 , and 0.2 to < 0.5 ng/mL, respectively. Whereas detection rates increased with a higher PSA velocity (81.8%, 82.4%, 92.1%, and 100% in < 1 , 1 to < 2 , 2 to < 5 , and ≥ 5 ng/mL/y, respectively), no significant association could be found for PSA doubling time (82.7%, 96.2%, and 90.7% in > 6 , 4-6, and < 4 mo, respectively). (68)Ga-PSMA ligand PET (as compared with CT) exclusively provided pathologic findings in 81 (32.7%) patients. In 61 (24.6%) patients, it exclusively identified additional involved regions. In higher Gleason score (≤ 7 vs. ≥ 8), detection efficacy was significantly increased ($P = 0.0190$). No significant difference in detection efficacy was present regarding antiandrogen therapy ($P = 0.0783$).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
62. Albrecht S, Buchegger F, Soloviev D, et al. (11)C-acetate PET in the early evaluation of prostate cancer recurrence. Eur J Nucl Med Mol Imaging. 2007;34(2):185-196.	Observational-Dx	32 patients	To investigate the diagnostic potential of (11)C-acetate PET in the early detection of prostate cancer recurrence. A second aim was the evaluation of early and late PET in this context.	Group A: Taking a SUV(max)> or =2 as the cut-off, PET showed local recurrences in 14/17 patients and two equivocal results. Distant disease was observed in six patients and an equivocal result was obtained in one. Endorectal MRI was positive in 12/12 patients. Biopsy confirmed local recurrence in six of six (100%) patients. PET was positive in five of the six patients with biopsy-proven recurrences, the result in the remaining patient being equivocal. Group B: Among the 15 patients, visual interpretation was positive for local recurrences in five patients and equivocal in four. One obturator lymph node was positive. Endorectal MRI was positive in 11/15 patients and equivocal in two. Positional correlation of positive/equivocal results on PET and endorectal MRI was observed in seven of nine patients. PSA decreased significantly after salvage radiotherapy in 8/14 patients, providing strong evidence for local recurrence. PET of the eight patients responding to RT was positive in three and equivocal in two.	3
63. Oyama N, Miller TR, Dehdashti F, et al. 11C-acetate PET imaging of prostate cancer: detection of recurrent disease at PSA relapse. J Nucl Med. 2003;44(4):549-555.	Experimental-Dx	46 patients	To confirm the findings of the initial reports, that showed a high sensitivity of AC PET for prostate cancer lesions, in a larger number of patients with recurrent prostate cancer after attempted curative therapy.	Twenty-seven of 46 AC PET studies (59%) had positive findings, whereas only 8 (18)F-FDG PET studies had positive findings (17%). Limiting the analysis to patients with findings confirmed by CT, bone scintigraphy, or biopsy or considered highly likely to represent tumor, 14 (30%) had disease identified by AC PET, whereas only 4 (9%) had disease identified by (18)F-FDG PET. CT was performed on 22 patients and had positive findings in 3 (14%). Thirteen of 22 patients (59%) with serum PSA > 3 ng/mL had positive AC PET findings, whereas only 1 of 24 patients (4%) with serum PSA levels < or = 3 ng/mL had positive findings.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
64. Cimitan M, Bortolus R, Morassut S, et al. [18F]fluorocholine PET/CT imaging for the detection of recurrent prostate cancer at PSA relapse: experience in 100 consecutive patients. <i>Eur J Nucl Med Mol Imaging</i> . 2006;33(12):1387-1398.	Observational-Dx	100 patients	To evaluate the potential of PET/CT and [(18)F]fluoromethylcholine (FCH) in the assessment of suspected recurrence of prostate cancer after treatment.	Of the 100 patients, 54 (PSA 0.22-511.79 ng/ml) showed positive FCH PET/CT scans. Thirty-seven patients had bone and/or abdominal lymph node uptake, while 17 showed pelvic activity. Malignant disease was confirmed in all but one. Delayed SUV(max) of bone metastases was significantly higher ($p < 0.0001$ by paired t test) than that measured at < 15 min, whereas no differences were observed between early and delayed SUVs of malignant lymph nodes or pelvic disease. Forty-six patients (PSA 0.12-14.3 ng/ml) showed negative FCH PET/CT scans. Of the negative PET/CT scans, 89% were obtained in patients with serum PSA < 4 ng/ml and 87% in patients with a Gleason score < 8 . In none of these cases could recurrent tumour be proven clinically during a follow-up of 6 months.	3
65. Heinisch M, Dirisamer A, Loidl W, et al. Positron emission tomography/computed tomography with F-18-fluorocholine for restaging of prostate cancer patients: meaningful at PSA < 5 ng/ml? <i>Mol Imaging Biol</i> . 2006;8(1):43-48.	Observational-Dx	34 patients	To determine whether this is true also for PET/CT using F-18-fluorocholine (FCH PET/CT) or whether it is possible to obtain true positive results by FCH PET/CT even at lower PSA levels.	Median PSA in FCH positive patients was 6.1 ng/ml (mean PSA 17.1 ng/ml), median PSA in FCH negative patients was 2.3 ng/ml (mean PSA 3.4 ng/ml), respectively ($p < 0.05$). In eight of 17 examinations (47%) with PSA < 5 ng/ml, at least one FCH-positive focus was detected. So far the findings could be confirmed by correlating imaging methods (CT and/or MR), biopsy/histology and the course of the disease, respectively, in seven of the eight FCH-positive cases with PSA < 5 ng/ml, so that a true positive FCH PET/CT finding was obtained all in all in seven of 17 (41%) examinations with PSA < 5 ng/ml. In four of these seven FCH PET-positive patients with PSA < 5 ng/ml, adjuvant hormonal therapy was administered at the time of the examination or prior to the examination.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Husarik DB, Miralbell R, Dubs M, et al. Evaluation of [(18)F]-choline PET/CT for staging and restaging of prostate cancer. <i>Eur J Nucl Med Mol Imaging</i> . 2008;35(2):253-263.	Observational-Dx	111 patients	To evaluate the accuracy of [(18)F]-choline (FCH) positron emission tomography/computed tomography (PET/CT) for staging and restaging of prostate cancer.	FCH PET/CT scans at initial staging correctly showed no metastases in 36/38 patients undergoing radical surgery, as confirmed by PSA levels <0.1 microg/l 6 months postoperatively. Lymphadenectomy was performed in 24 of these patients, revealing four false FCH-negative lymph nodes (LN). In one patient, only lymphadenectomy was performed since a FCH-positive LN was confirmed by histology. Four patients showed FCH-positive bone metastases, as proven by bone scan. FCH PET/CT scans at restaging correctly revealed local recurrence in 36 patients. No pathological FCH uptake was observed in 11 patients with biochemical recurrence. Twenty-three patients showed FCH-positive LN. Twenty LN were surgically removed in seven patients. Histopathology verified metastases in all LN, but revealed two additional metastatic, FCH-negative LN. Seventeen patients showed FCH-positive bone metastases, as proven by bone scan or MRI. Sensitivity to detect recurrent disease was 86%.	3
67. Afshar-Oromieh A, Babich JW, Kratochwil C, et al. The Rise of PSMA Ligands for Diagnosis and Therapy of Prostate Cancer. <i>J Nucl Med</i> . 2016;57(Suppl 3):79S-89S.	Review/Other-Dx	N/A	To discuss highlights of the development and clinical application of PSMA ligands.	No results stated in abstract.	4
68. Rowe SP, Drzezga A, Neumaier B, et al. Prostate-Specific Membrane Antigen-Targeted Radiohalogenated PET and Therapeutic Agents for Prostate Cancer. <i>J Nucl Med</i> . 2016;57(Suppl 3):90S-96S.	Review/Other-Dx	N/A	To review the available literature on the preclinical and clinical development of radiohalogenated small-molecule inhibitors of PSMA, with particular emphasis on 18F-labeled agents applicable to PET	No results stated in abstract.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. Schuster DM, Votaw JR, Nieh PT, et al. Initial experience with the radiotracer anti-1-amino-3-18F-fluorocyclobutane-1-carboxylic acid with PET/CT in prostate carcinoma. J Nucl Med. 2007;48(1):56-63.	Observational-Dx	15 patients	To examine anti-(18)F-FACBC uptake in patients with newly diagnosed and recurrent prostate carcinoma.	In the 8 patients with newly diagnosed prostate carcinoma who underwent dynamic scanning, visual analysis correctly identified the presence or absence of focal neoplastic involvement in 40 of 48 prostate sextants. Pelvic nodal status correlated with anti-(18)F-FACBC findings in 7 of 9 patients and was indeterminate in 2 of 9. In all 4 patients in whom there was proven recurrence, visual analysis was successful in identifying disease (1 prostate bed, 3 extraprostatic). In 3 of these patients, (111)In-capromab-pendetide had no significant uptake at nodal and skeletal foci. Malignant lymph node uptake in both the staging and restaging patients was significantly higher than benign nodal uptake. Though uptake faded with time, in all 6 patients with either lymph node metastases or recurrent prostate bed carcinoma, there was intense persistent uptake at 65 min.	2
70. Schoder H, Herrmann K, Gonen M, et al. 2-[18F]fluoro-2-deoxyglucose positron emission tomography for the detection of disease in patients with prostate-specific antigen relapse after radical prostatectomy. Clin Cancer Res. 2005;11(13):4761-4769.	Observational-Dx	91 patients	To assess the potential clinical role of FDG-PET using optimal image reconstruction in a large group of patients with PSA relapse.	PET was true positive in 28 of 91 (31%) patients, showing isolated disease in the prostate bed (n = 3) or metastatic disease with (n = 2) or without (n = 23) simultaneous disease in the prostate bed. In detail, PET identified lesions in the prostate bed (n = 5, all true positives), bones (n = 22; 20 true positives, 2 false positives), lymph nodes (n = 7; 6 true positives, 1 likely false positive), and one liver metastasis. Mean PSA was higher in PET-positive than in PET-negative patients (9.5 +/- 2.2 versus 2.1 +/- 3.3 ng/mL). PSA of 2.4 ng/mL and PSA velocity of 1.3 ng/mL/y provided the best tradeoff between sensitivity (80%; 71%) and specificity (73%; 77%) of PET in a receiver operating curve analysis. Combination with other clinical parameters in a multivariate analysis did not improve disease prediction. There were only two patients in whom other imaging studies showed isolated local recurrence or metastatic disease.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Shreve PD, Grossman HB, Gross MD, Wahl RL. Metastatic prostate cancer: initial findings of PET with 2-deoxy-2-[F-18]fluoro-D-glucose. <i>Radiology</i> . 1996;199(3):751-756.	Observational-Dx	34 patients	To evaluate the accuracy of positron emission tomography (PET) with 2-deoxy-2-[fluorine-18] fluoro-D-glucose (FDG) in the detection of osseous and soft-tissue metastases of prostate cancer.	In 202 untreated osseous metastases in 22 patients, the sensitivity of FDG PET was 65% (131 of 202 metastases), with a positive predictive value of 98% (131 of 133 positive findings). The estimated standardized uptake value in metastases was 2.1-5.7. Soft-tissue metastases to the lymph nodes or liver were identified, but evaluation of pelvic lymph node metastases was severely limited because of bladder tracer activity.	3
72. Ghanem N, Uhl M, Brink I, et al. Diagnostic value of MRI in comparison to scintigraphy, PET, MS-CT and PET/CT for the detection of metastases of bone. <i>Eur J Radiol</i> . 2005; 55(1):41-55.	Review/Other-Dx	N/A	To compare the diagnostic value of MRI with scintigraphy, PET, multislice CT and PET/CT for the detection of bone metastases.	FDG-PET and 18F-fluoride-PET as well as the side by side PET/CT image fusion and the two in one PET/CT examinations appears to be slightly less sensitive to whole-body MRI in detection of osteal metastases.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>73. Elgamal AA, Troychak MJ, Murphy GP. ProstaScint scan may enhance identification of prostate cancer recurrences after prostatectomy, radiation, or hormone therapy: analysis of 136 scans of 100 patients. <i>Prostate</i>. 1998;37(4):261-269.</p>	<p>Observational-Dx</p>	<p>100 patients including 136 ProstaScint scans.</p>	<p>To evaluate the ability of the ProstaScint (Cytogen Corp., Princeton, NJ) scan to identify soft tissue recurrence of prostate cancer in patients who failed primary treatment, and we monitored their responses to a secondary treatment.</p>	<p>Overall, no adverse reactions were related to any of the radioactive antibody infusions. The average age was 69 years (range, 48-89 years), serum PSA was 55.9 ng/ml (range, 0-2,185 ng/ml), and serum PSMA was 0.32 (relative intensity levels range, 0.04-0.55). The initial therapies given were radical prostatectomy (55 scans), prostate radiation (74 scans), and/or hormonal therapy (77 scans). Twelve patients exhibited a negative scan. Local recurrence alone was identified in 58 scans (42.6%). Lymph node metastases were identified in 66 scans (48.5%). Of these, 21 had regional metastases alone, and 45 had distant lymph node metastases. Ten scans showed skip lymph node metastases without regional failure. PSA significantly correlated with negative, pelvic, and extrapelvic scan findings ($P < \text{or} = 0.02$). PSMA correlated best with pelvic recurrence and extrapelvic metastases in prostatectomized patients. Thirty-four patients had repeated scans for monitoring treatment response. Of these patients, 19 (56%) showed progression on the second scan, consistent with persistent increase in PSA and PSMA levels in all but 2 patients. Another 11 patients showed no change, and 4 patients showed partial remission, suggesting a response to the salvage treatment. All 20 positive prostate biopsies and 4 of the 7 positive lymph node biopsies correlated with ProstaScint findings, whereas 4 of the 6 patients with a negative biopsy had negative scans (i.e., 89% sensitivity and 67% specificity). Bone metastases were identified in 42 bone scans; 45% of these showed no lymph node metastasis on ProstaScint. In another 24 patients (57%), bone metastases were detected on ProstaScint examinations.</p>	<p>3</p>

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
74. Kahn D, Williams RD, Manyak MJ, et al. 111Indium-capromab pendetide in the evaluation of patients with residual or recurrent prostate cancer after radical prostatectomy. The ProstaScint Study Group. J Urol. 1998;159(6):2041-2046; discussion 2046-2047.	Experimental-Dx	183 patients	To evaluate the role of immunoscintigraphy with the radiolabeled monoclonal antibody, 111indium ((111In)-capromab pendetide, to differentiate between local and distant recurrence in patients with prostate cancer in whom the only evidence of disease after radical prostatectomy is a detectable prostate specific antigen (PSA) level.	Immunoscintigraphy revealed disease in 108 of 181 patients (60%) with interpretable scans. The antibody was localized most frequently to the prostatic fossa (34% of the cases), abdominal lymph nodes (23%) and pelvic lymph nodes (22%). Of the 181 men the scan localized the antibody outside the prostatic fossa in 42%. Half of the positive localizations in the fossa were confirmed by biopsy.	1
75. Thomas CT, Bradshaw PT, Pollock BH, et al. Indium-111-capromab pendetide radioimmunoscintigraphy and prognosis for durable biochemical response to salvage radiation therapy in men after failed prostatectomy. J Clin Oncol. 2003;21(9):1715-1721.	Observational-Dx	30 patients	To evaluate the prognostic significance of indium-111 (111In)-capromab pendetide imaging for patients with prostate cancer who underwent salvage radiotherapy (RT) for recurrent disease after prostatectomy.	Using an American Society of Therapeutic Radiation and Oncology definition of PSA failure, in men with a positive scan in at least one location (n = 14), the cumulative 2-year PSA control after salvage RT was 0.38 +/- 0.13 (+/- SE) compared with 0.31 +/- 0.13 for men with a normal antibody scan in and outside the prostate fossa (n = 15; proportional hazard ratio [PHR] = 1.32; 95% confidence interval [CI], 0.52 to 3.36). For men with a positive antibody scan limited to the prostate fossa (n = 9), PSA control at 2 years was 0.13 +/- 0.12 (PHR 1.77; 95% CI, 0.65 to 4.85). The 2-year probability of PSA control after salvage RT for men with positive scan results outside the prostate bed irrespective of In-mab findings in the prostate fossa (n = 5) was 0.60 +/- 0.22 (PHR 0.81; 95% CI, 0.17 to 3.78).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Wilkinson S, Chodak G. The role of 111indium-capromab pentetide imaging for assessing biochemical failure after radical prostatectomy. J Urol. 2004;172(1):133-136.	Observational-Dx	42 patients	To evaluate the role of the indium-capromab pentetide scan, otherwise known as the ProstaScint (Cytogen Corp., Princeton, New Jersey) scan, in this setting.	Median prostate specific antigen (PSA) immediately prior to ProstaScint imaging was 1.2 ng/ml (range 0.2 to 4.8). Abnormal accumulation on the ProstaScint scan was detected in 36 patients (85.7%). Of the 16 patients undergoing salvage radiation therapy 15 had uptake isolated to the prostatic fossa on ProstaScint imaging. Ten of these 15 patients (66.7%) achieved undetectable PSA after radiation therapy, while 5 (33.3%) had little or no response. Using American Society for Therapeutic Radiology and Oncology criteria 3 of 10 responders had relapse after an average of 9 months. The remaining 7 patients remained biochemically free of disease at last followup.	3
77. Liauw SL, Weichselbaum RR, Zagaja GP, Jani AB. Salvage radiotherapy after postprostatectomy biochemical failure: does pretreatment radioimmunoscinigraphy help select patients with locally confined disease? Int J Radiat Oncol Biol Phys. 2008;71(5):1316-1321.	Observational-Dx	82 patients	To retrospectively review the biochemical outcomes for salvage RT patients treated with or without pre-RT RIS and to describe the effect of RIS on outcome compared with other established clinical and pathologic factors.	Patients with a pre-RT RIS scan had a lower preoperative PSA level (p = 0.0240) and shorter follow-up (p = 0.0221) than those without RIS. With a median follow-up of 44 months, the biochemical control rate was 56% at 3 years and 48% at 5 years. Margin status was the only factor associated with biochemical control on univariate (p = 0.0055) and multivariate (p = 0.0044) analysis. Patients who had prostate bed-only uptake on RIS (n = 38) did not have improved outcomes, with biochemical control rates of 51% at 3 years and 40% at 5 years.	3

**Post-treatment Follow-up of Prostate Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
78. Nagda SN, Mohideen N, Lo SS, et al. Long-term follow-up of 111In-capromab pendetide (ProstaScint) scan as pretreatment assessment in patients who undergo salvage radiotherapy for rising prostate-specific antigen after radical prostatectomy for prostate cancer. <i>Int J Radiat Oncol Biol Phys.</i> 2007;67(3):834-840.	Observational-Dx	58 patients	To evaluate the long-term failure patterns in patients who underwent an (111)In-capromab pendetide (ProstaScint) scan as part of their pretreatment assessment for a rising prostate-specific antigen (PSA) level after prostatectomy and subsequently received local radiotherapy (RT) to the prostate bed.	Of the 58 patients, 20 had biochemical failure (post-RT PSA level >0.2 ng/mL or a rise to greater than the nadir PSA), including 6 patients with positive uptake outside the bed (positive elsewhere). The 4-year biochemical relapse-free survival (bRFS) rates for patients with negative (53%), positive in the prostate bed alone (45%), or positive elsewhere (74%) scan findings did not differ significantly (p = 0.51). The positive predictive value of the capromab pendetide scan in detecting disease outside the bed was 27%. The capromab pendetide scan status had no effect on bRFS. Those with a pre-RT PSA level of <1 ng/mL had improved bRFS (p = 0.003).	3
79. Nudell DM, Wefer AE, Hricak H, Carroll PR. Imaging for recurrent prostate cancer. <i>Radiol Clin North Am.</i> 2000;38(1):213-229.	Review/Other-Dx	N/A	To examine the imaging modalities currently available to assist in detection and localization of both local and distant recurrent prostate cancer following definitive treatment with either RP, RT, or cryosurgical ablation of the prostate.	Multiple imaging modalities are available to evaluate recurrent prostate cancer following primary treatment with RP, RT, or cryosurgery. These tests must be used in close conjunction with clinical parameters, such as the characteristics of the tumor itself (grade, stage) as well as specific PSA characteristics that can help predict the sites of probable recurrence. As more treatments become available for recurrent prostate cancer, it will be necessary to monitor disease response with many of the imaging modalities discussed in this article.	4
80. Roach M, 3rd, Hanks G, Thames H, Jr., et al. Defining biochemical failure following radiotherapy with or without hormonal therapy in men with clinically localized prostate cancer: recommendations of the RTOG-ASTRO Phoenix Consensus Conference. <i>Int J Radiat Oncol Biol Phys.</i> 2006;65(4):965-974.	Review/Other-Tx	N/A	Consensus statement to revise the 1996 definition of biochemical failure after EBRT.	Concluded that 1) biochemical failure defined by a rise by 2 ng/mL or more above the nadir PSA after EBRT with or without hormonal therapy; and 2) the date of failure be determined “at call” (not backdated). They recommended that investigators be allowed to use the ASTRO Consensus Definition after EBRT alone (no hormonal therapy) with strict adherence to guidelines as to “adequate follow-up.” The reported date of control should be listed as 2 years short of the median follow-up.	4

**Post-treatment Follow-up of Prostate Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
81. Nguyen PL, D'Amico AV, Lee AK, Suh WW. Patient selection, cancer control, and complications after salvage local therapy for postradiation prostate-specific antigen failure: a systematic review of the literature. <i>Cancer</i> . 2007;110(7):1417-1428.	Review/Other-Tx	N/A	To describe the selection criteria for men who are most likely to benefit from a salvage local therapy, and we summarize the published literature on the oncologic outcome and toxicity of the currently available treatment approaches.	No results stated in abstract.	4
82. Caloglu M, Ciezki J. Prostate-specific antigen bounce after prostate brachytherapy: review of a confusing phenomenon. <i>Urology</i> . 2009;74(6):1183-1190.	Review/Other-Tx	N/A	A review of 19 articles summarized to delineate the facts of (PSA) level fluctuation and increase.	Although several patient and treatment related factors were assessed by studies, only age remained as the most consistent predictor.	4
83. Vicini FA, Vargas C, Abner A, Kestin L, Horwitz E, Martinez A. Limitations in the use of serum prostate specific antigen levels to monitor patients after treatment for prostate cancer. <i>J Urol</i> . 2005;173(5):1456-1462.	Review/Other-Dx	16 articles	To help clarify the benefits and/or hazards associated with monitoring serum prostate specific antigen (PSA) after treatment with surgery or radiation therapy (RT) for nonmetastatic prostate cancer.	Although a lower PSA nadir after treatment with RT has been associated with cancer cure, 5% to 25% of patients ultimately have failure (beyond 5 years) even with the most optimal biochemical response. The most appropriate BF definitions to use after treatment for prostate cancer with RT remains controversial due to substantial differences in their accuracy, sensitivity, specificity and positive predictive value for clinical outcome. No pattern of PSA kinetics after treatment has conclusively been associated with a specific recurrence site. Biochemical failure definitions in patients treated with RT appear to provide a 6 to 18 month lead time to clinical failure but there are only limited published data to suggest that early intervention of any type (androgen deprivation, RT, surgery, etc) impacts survival.	4

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
84. Cotter SE, Chen MH, Moul JW, et al. Salvage radiation in men after prostate-specific antigen failure and the risk of death. <i>Cancer</i> . 2011;117(17):3925-3932.	Observational-Tx	519 patients	To assess whether salvage RT was associated with a decreased risk of all-cause mortality for men with either a rapid or protracted PSA rise after RP adjusting for known prostate cancer prognostic factors, cardiac comorbidity, and age at the time of PSA failure.	After a median follow-up of 11.3 years after PSA failure, 195 men died. Salvage RT was associated with a significant reduction in all-cause mortality for men with either a PSA DT of < 6 months (adjusted hazard ratio [AHR], 0.53; P = .02) or a PSA DT of >= 6 months (AHR, 0.52; P = .003). In a subset of patients with comorbidity data at the time of PSA failure, salvage RT remained associated with a significant reduction in all-cause mortality for both men with a PSA DT of < 6 months (AHR, 0.35; P = .042) or a PSA DT of >= 6 months (AHR, 0.60; P = .04).	2
85. Catalona WJ, Smith DS. 5-year tumor recurrence rates after anatomical radical retropubic prostatectomy for prostate cancer. <i>J Urol</i> . 1994;152(5 Pt 2):1837-1842.	Observational-Tx	925 patients	To evaluate cancer control with this operation (radical retropubic prostatectomy with its nerve sparing option) by determining the 5-year tumor recurrence rates using detectable serum prostate specific antigen levels as a criterion for tumor recurrence in a series of 925 consecutive men with clinical stage T1 or T2 prostate cancer.	Overall, the 5-year probability of nonprogression was 78% (95% confidence limits 74 to 82%). The 5-year nonprogression rate was higher in patients whose tumors were not palpable (90% for impalpable tumors detected through transurethral resection of the prostate, 97% for impalpable prostate specific antigen detected tumors and 74% for palpable tumors). Nonprogression correlated with pathological tumor stage (91% for organ confined disease, 74% for positive margins or microscopic capsular perforation, 32% for seminal vesical invasion and virtually nil for lymph node metastases) and tumor grade (89% for well, 78% for moderately and 51% for poorly differentiated tumors).	2
86. Epstein JI, Pizov G, Walsh PC. Correlation of pathologic findings with progression after radical retropubic prostatectomy. <i>Cancer</i> . 1993;71(11):3582-3593.	Observational-Tx	507 patients	To evaluate the effect of positive margins, Gleason grade, and capsular penetration on progression after RP. Authors followed men with totally embedded RRP specimens performed for clinical Stages A and B prostate cancer.	Positive margins and Gleason sum strongly correlated with progression in a multivariate analysis. Approximately 50% of patients with positive margins experienced disease progression during 5 years of follow-up. The most common single sites of positive margins were distal (22%), posterior (17%), and posterolateral (14%); 22% of positive margins were extensive. RP provided excellent local control, with only 8% of patients exhibiting local recurrence. 61% of men with progression had an elevated serum PSA level as their only manifestation of progression.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
87. Kupelian PA, Katcher J, Levin HS, Klein EA. Stage T1-2 prostate cancer: a multivariate analysis of factors affecting biochemical and clinical failures after radical prostatectomy. <i>Int J Radiat Oncol Biol Phys.</i> 1997;37(5):1043-1052.	Observational-Tx	423 patients	Review stage T1-2 prostate cancer treated with RP to understand the impact of PSA on pathologic findings, outcome, and salvage treatment.	5-year clinical RFS rate was 84%. At 5 years, the local control and distant failure rates were 92% and 91%, respectively. Pretreatment PSA is the most potent clinical factor independently predicting biochemical relapse.	2
88. Lowe BA, Lieberman SF. Disease recurrence and progression in untreated pathologic stage T3 prostate cancer: selecting the patient for adjuvant therapy. <i>J Urol.</i> 1997;158(4):1452-1456.	Observational-Dx	156 patients	To improve understanding of the natural history of T3 prostate cancer and to identify clinical parameters useful in patient selection for adjuvant therapy.	After a median of 45 months, PSA recurrence was seen in 29.4% of pT3a (10/34), 30% of pT3b (24/80), 27.3% of pT3c (6/22), and 80% of pT3N+ (16/20 cases). Local or distant progression was seen in 2.9% of pT3a (1), 6.2% of pT3b (5), 9.1% of pT3c (2), and 55% of pT3N+ (11 cases). Recurrence and progression correlated with the number of surgical margins involved by tumor, pathological Gleason score and baseline pre-prostatectomy PSA levels. PSA recurrence was seen in 20.8% (10/48) patients with 1 surgical margin involved, 40.9% (9/22) with 2 margins involved and 50% (5/10) with 3 or more margins involved. PSA recurrence was 20.3% (14/69) with Gleason scores of less than 7, 33.9% (19/56) with a score of 7 and 74.2% (23/31) with scores of greater than 7. Pre-prostatectomy PSA levels less than 10 ng./ml. were associated with a PSA recurrence of 17.3% (14/81) and 45.4% (25/55), with levels greater than 10 ng./ml. Selecting patients for high or low risk based upon the results of these parameters allowed accurate prediction of PSA recurrence; 8.5% (4/47) for low risk patients and 44.8% (30/67) for high risk. Tumor progression was seen in no low risk patient and in 9% (6) with high risk. The difference between the 2 risk groups was highly significant (p <0.0001).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
89. Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. JAMA. 1999;281(17):1591-1597.	Observational-Tx	1997 patients	Retrospective review of a large surgical series to characterize the time course of disease progression in men with biochemical recurrence after RP.	Metastasis-free survival for all the men was 82% at 15 years after surgery. Of the 1997 men, 315 (15%) developed biochemical PSA level elevation. The median actuarial time to metastases was 8 years from the time of PSA level elevation. In survival analysis, time to biochemical progression (P<.001), Gleason score (P<.001), and PSA doubling time (PSADT) (P<.001) were predictive of the probability and time to the development of metastatic disease. Once men developed metastatic disease, the median actuarial time to death was 5 years. The time interval from surgery to the appearance of metastatic disease was predictive of time until death (P<.02).	2
90. Swindle P, Eastham JA, Ohori M, et al. Do margins matter? The prognostic significance of positive surgical margins in radical prostatectomy specimens. J Urol. 2005;174(3):903-907.	Observational-Tx	1,389 consecutive patients	To evaluate the prognostic significance of positive surgical margins using multiple methods of analysis accounting for patients who received adjuvant therapy.	Overall 179 patients (12.9%) had a positive surgical margin, including 6.8% of 847 patients with pT2 and 23% of 522 patients with pT3 disease. A positive surgical margin was a significant predictor of cancer recurrence when analyzed using methods 1, 3, 4 and 5 (P=0.005, P=0.014, P=0.0005, P=0.002, respectively). However, it was not a predictor of recurrence using method 2 in which adjuvant therapy was ignored (P=0.283). Using method 5 multivariate analysis demonstrated that a positive surgical margin (P=0.002) was an independent predictor of 10-year progression-free probability along with Gleason score (P=0.0005), extracapsular extension (P=0.0005), SVI (P<0.0005), positive lymph nodes (P<0.0005) and preoperative serum prostate specific antigen (P<0.0001). Using method 5 the 10-year progression-free probability was 58% +/- 12% and 81% +/- 3% for patients with and without a positive surgical margin, respectively (P<0.00005). The RR of recurrence in men with a positive surgical margin using method 5 was 1.52 (95% CI, 1.06–2.16).	2

* See Last Page for Key

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
91. Zietman AL, Edelstein RA, Coen JJ, Babayan RK, Krane RJ. Radical prostatectomy for adenocarcinoma of the prostate: the influence of preoperative and pathologic findings on biochemical disease-free outcome. <i>Urology</i> . 1994;43(6):828-833.	Observational-Tx	62 patients	Retrospective study to evaluate the outcome for a cohort of men undergoing RRP alone as primary treatment for clinical T1-2 prostate adenocarcinoma.	Strongest preoperative predictors of pT3 disease were the biopsy Gleason grade and the initial serum PSA value. Actuarial analysis showed the overall likelihood of remaining free from detectable PSA at 4 years to be 43% (75% for those with organ-confined disease and 27% for those who were pT3).	2
92. Martino P, Scattoni V, Galosi AB, et al. Role of imaging and biopsy to assess local recurrence after definitive treatment for prostate carcinoma (surgery, radiotherapy, cryotherapy, HIFU). <i>World J Urol</i> . 2011;29(5):595-605.	Review/Other-Dx	N/A	To define the site of recurrent disease early after definitive treatment for a localized prostate cancer.	Despite the fact that diagnosis of a local recurrence is based on PSA values and kinetics, imaging by means of different techniques may be a prerequisite for effective disease management. Unfortunately, prostate cancer local recurrences are very difficult to detect by TRUS and conventional imaging that have shown limited accuracy at least at early stages. On the contrary, functional and molecular imaging such as dynamic contrast-enhanced MRI (DCE-MRI), and diffusion-weighted imaging (DWI), offers the possibility of imaging molecular or cellular processes of individual tumors. Recently, PET/CT, using 11C-choline, 18F-fluorocholine or 11C-acetate has been successfully proposed in detecting local recurrences as well as distant metastases. Nevertheless, in controversial cases, it is necessary to perform a biopsy of the prostatic fossa or a biopsy of the prostate to assess the presence of a local recurrence under guidance of MRI or TRUS findings.	4

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
93. Cooperberg MR, Broering JM, Carroll PR. Time trends and local variation in primary treatment of localized prostate cancer. J Clin Oncol. 2010;28(7):1117-1123.	Review/Other-Tx	11,892 men at 36 sites	To determine trends over time in treatment of cancers at varying levels of progression risk, and to characterize and quantify variation in primary treatment at the level of the clinical practice site.	Among 11,892 men analyzed, 6.8% elected surveillance, 49.9% prostatectomy, 11.6% external-beam radiation, 13.3% brachytherapy, 4.0% cryoablation, and 14.4% androgen deprivation monotherapy. Prostate cancer risk drives treatment selection, but the data suggest both overtreatment of low-risk disease and undertreatment of high-risk disease. The former trend appears to be improving over time, while the latter is worsening. Treatment varies with age, comorbidity, and socioeconomic status. However, treatment patterns vary markedly across clinical sites, and this variation is not explained by case-mix variability or known patient factors. Practice site explains a proportion of this variation ranging from 13% for androgen deprivation monotherapy to 74% for cryoablation.	4
94. Tamada T, Sone T, Jo Y, et al. Locally recurrent prostate cancer after high-dose-rate brachytherapy: the value of diffusion-weighted imaging, dynamic contrast-enhanced MRI, and T2-weighted imaging in localizing tumors. AJR Am J Roentgenol. 2011;197(2):408-414.	Observational-Dx	16 patients	To retrospectively evaluate the utility of prostate MRI for detecting locally recurrent prostate cancer after high-dose-rate (HDR) brachytherapy.	Biopsy revealed locally recurrent prostate cancer in 22 (17 in PZ and five in TZ) of 128 regions (17.2%). The sensitivity, specificity, and accuracy of each MRI method in the detection of recurrent tumor were 27%, 99%, and 87%, respectively, for T2-weighted imaging; 50%, 98%, and 90%, respectively, for DCE-MRI; and 68%, 95%, and 91%, respectively, for DWI. The sensitivity of DWI in detecting recurrent tumor was significantly higher than that of T2-weighted imaging ($p = 0.004$). Multiparametric MRI achieved the highest sensitivity (77%) but with slightly decreased specificity (92%).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
95. Coakley FV, Teh HS, Qayyum A, et al. Endorectal MR imaging and MR spectroscopic imaging for locally recurrent prostate cancer after external beam radiation therapy: preliminary experience. <i>Radiology</i> . 2004;233(2):441-448.	Observational-Dx	21 patients	To evaluate endorectal magnetic resonance (MR) imaging and MR spectroscopic imaging for the depiction of locally recurrent prostate cancer after external beam radiation therapy.	Biopsy demonstrated locally recurrent prostate cancer in nine hemiprostates in six patients. The area under the receiver operating characteristic curve for the detection of locally recurrent cancer with MR imaging was 0.49 and 0.51 for readers 1 and 2, respectively. By using the number of suspicious voxels to define different diagnostic thresholds, the area under the receiver operating characteristic curve for MR spectroscopic imaging was significantly ($P < .005$) higher, at 0.81. In particular, the presence of three or more suspicious voxels in a hemiprostate showed a sensitivity and specificity of 89% and 82%, respectively, for the diagnosis of local recurrence. Seven hemiprostates demonstrated complete metabolic atrophy at spectroscopic imaging and only postirradiation atrophy at biopsy.	2
96. Pucar D, Shukla-Dave A, Hricak H, et al. Prostate cancer: correlation of MR imaging and MR spectroscopy with pathologic findings after radiation therapy-initial experience. <i>Radiology</i> . 2005;236(2):545-553.	Observational-Dx	9 patients	To prospectively evaluate magnetic resonance (MR) imaging and MR spectroscopy for depiction of local prostate cancer recurrence after external-beam radiation therapy, with step-section pathologic findings as the standard of reference.	MR imaging and MR spectroscopy showed estimated sensitivities of 68% and 77%, respectively, while sensitivities of biopsy and digital rectal examination were 48% and 16%, respectively. MR spectroscopy appears to be less specific (78%) than the other three tests, each of which had a specificity higher than 90%. MR spectroscopic feature analysis showed that a metabolically altered benign gland could be falsely identified as tumor by using MR spectroscopic criteria; further analysis of MR spectroscopic features did not lead to improved MR spectroscopic criteria for recurrent tumor.	3
97. Westphalen AC, Coakley FV, Roach M, 3rd, McCulloch CE, Kurhanewicz J. Locally recurrent prostate cancer after external beam radiation therapy: diagnostic performance of 1.5-T endorectal MR imaging and MR spectroscopic imaging for detection. <i>Radiology</i> . 2010;256(2):485-492.	Observational-Dx	64 patients	To determine if performing MRSI, compared with performing T2-weighted MRI alone, improves the detection of locally recurrent prostate cancer after definitive EBRT.	Recurrent prostate cancer was identified at biopsy in 37 (58%) of the 64 men. Recurrence was unilateral in 28 patients and bilateral in 9 (total of 46 affected prostate sides). A(Z) analysis revealed that use of combined T2-weighted MRI and MRSI ($A(Z) = 0.79$), as compared with T2-weighted MRI alone ($A(Z) = 0.67$), significantly improved the detection of local recurrence ($P = .001$).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
98. Haider MA, Chung P, Sweet J, et al. Dynamic contrast-enhanced magnetic resonance imaging for localization of recurrent prostate cancer after external beam radiotherapy. <i>Int J Radiat Oncol Biol Phys</i> . 2008;70(2):425-430.	Observational-Dx	33 patients	To compare the performance of T2W imaging and DCE-MRI of the prostate gland in the localization of recurrent prostate cancer in patients with biochemical failure after EBRT.	On a sextant basis, DCE-MRI had significantly better sensitivity (72% [21/29] vs 38% [11/29]), PPV (46% [21/46] vs 24% [11/45]) and NPV (95% [144/152] vs 88% [135/153]) than T2W. Specificities were high for both DCE-MRI and T2W (85% [144/169] vs 80% [135/169]). There was a linear relationship between tumor diameters on DCE-MRI and the percentage of cancer tissue in the corresponding biopsy core ($r = 0.9$, $P < 0.001$), with a slope of 1.2. DCE-MRI performs better than T2W in the detection and localization of prostate cancer in the peripheral zone after EBRT. This may be helpful in the planning of salvage therapy.	2
99. Kim CK, Park BK, Park W, Kim SS. Prostate MR imaging at 3T using a phased-arrayed coil in predicting locally recurrent prostate cancer after radiation therapy: preliminary experience. <i>Abdom Imaging</i> . 2010;35(2):246-252.	Observational-Dx	24 patients	To retrospectively assess the diagnostic performance of diffusion-weighted imaging (DWI) and dynamic contrast-enhanced imaging (DCEI) at 3T in predicting locally recurrent prostate cancer after radiation therapy.	The sensitivity and specificity for recurrent cancer detection were significantly higher for DWI (49% and 93%), DCEI (49% and 92%), and combined DCEI and DWI (59% and 91%) than for T2WI (27% and 80%) ($P < 0.008$). However, no statistical difference among DCEI, DWI, and combined DCEI and DWI was seen ($P > 0.05$). The accuracy in each of DWI (82%), DCEI (81%), and combined DCEI and DWI (83%) was greater than that for T2WI (67%) ($P < 0.001$). However, no statistical difference among DWI, DCEI and combined DCEI and DWI was found ($P > 0.05$).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
100. Rouviere O, Valette O, Grivolat S, et al. Recurrent prostate cancer after external beam radiotherapy: value of contrast-enhanced dynamic MRI in localizing intraprostatic tumor--correlation with biopsy findings. <i>Urology</i> . 2004;63(5):922-927.	Observational-Dx	22 patients	To assess the accuracy and interobserver variability of T2W and DCE-MRI in predicting the results of transrectal biopsy in patients with suspected recurrent prostate cancer after EBRT.	Biopsy cores were obtained in 147 prostate sectors. Of these, 63 were positive for cancer in 19 patients. On the T2W images, the 3 readers interpreted as positive for cancer 15, 15, and 13 of the 19 patients showing cancer at biopsy. They interpreted as negative 3, 0, and 1 of the 3 patients showing no cancer at biopsy. On DCE-MRI, the 3 readers correctly classified all the patients as positive or negative for cancer. The T2W and DCE-MRI findings were concordant with biopsy results in, respectively, 81 to 95 and 107 to 117 prostate sectors (P<0.001 and P<0.01 for readers 1 and 2 and was nonsignificant for reader 3). The interobserver agreement was better for DCE-MRI (kappa = 0.63 to 0.70) than for the T2W images (kappa = 0.18 to 0.39). The MRI-calculated tumor volumes and the mean biopsy core invasion rates were significantly correlated on the DCE-MRI for all readers. They correlated significantly on T2W images only for 1 reader. DCE-MRI depicts the intraprostatic distribution of recurrent cancer after EBRT more accurately and with less interobserver variability than T2W MRI.	2
101. Kim CK, Park BK, Lee HM. Prediction of locally recurrent prostate cancer after radiation therapy: incremental value of 3T diffusion-weighted MRI. <i>J Magn Reson Imaging</i> . 2009;29(2):391-397.	Observational-Dx	36 patients	To prospectively evaluate the incremental value of DWI with apparent diffusion coefficient maps in addition to T2W imaging for predicting locally recurrent prostate cancer in patients with biochemical failure after RT.	Of 216 sectors, 65 prostate sectors (30%) were positive for cancer in 18 patients. For predicting recurrent cancer, combined T2W and DWI showed a greater sensitivity compared to T2W (P<0.001). A significantly greater AUC was determined for combined T2W and DWI (AUC = 0.879, P<0.01) as compared to T2W (AUC = 0.612). Mean apparent diffusion coefficient values between recurrent cancer and benign tissue showed a statistically significant difference (P<0.01).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
102. Pucar D, Hricak H, Shukla-Dave A, et al. Clinically significant prostate cancer local recurrence after radiation therapy occurs at the site of primary tumor: magnetic resonance imaging and step-section pathology evidence. <i>Int J Radiat Oncol Biol Phys.</i> 2007;69(1):62-69.	Observational-Dx	9 patients	To determine whether prostate cancer local recurrence after radiation therapy (RT) occurs at the site of primary tumor by retrospectively comparing the tumor location on pre-RT and post-RT magnetic resonance imaging (MRI) and using step-section pathology after salvage radical prostatectomy (SRP) as the reference standard.	All nine significant tumor foci (one in each patient; volume range, 0.22-8.63 cm ³) were detected both on pre-RT and post-RT MRI and displayed strikingly similar appearances on pre-RT and post-RT MRI and step-section pathology. Two clinically insignificant tumor foci (<=0.06 cm ³) were not detected on imaging. The ratios between tumor volumes on pathology and on post-RT MRI ranged from 0.52 to 2.80.	3
103. Crook J, Robertson S, Collin G, Zaleski V, Esche B. Clinical relevance of trans-rectal ultrasound, biopsy, and serum prostate-specific antigen following external beam radiotherapy for carcinoma of the prostate. <i>Int J Radiat Oncol Biol Phys.</i> 1993;27(1):31-37.	Observational-Dx	100 patients	To correlate the results of routine transrectal ultrasound-guided prostate biopsies with the usual clinical parameters of digital rectal examination, prostate specific antigen and ultrasound in the follow-up of one hundred patients treated with radical radiotherapy for prostate cancer.	Negative biopsies were obtained at 12 months (range 9-15) in only 52%. Of 31 patients with a positive first biopsy who have had a second or third examination, 21 converted to negative at 16-29 months (median: 19) (stage T1b: 3, T2a: 6, T2b: 8, T3: 4). All 21 patients had maintained a normal or decreasing prostate specific antigen (PSA). At last review, negative biopsies had been obtained in 74% patients: 79% (15/19) of T1b, 71% (17/24) of T2a, 72%, (26/36) of T2b, and 76% (16/21) of T3/4. No patient with a negative biopsy has had a local recurrence. Transrectal ultrasound alone (sens: 49%, spec: 57%) was no better than rectal exam (sens: 73%, spec: 66%) in predicting a positive post radiotherapy biopsy. Metastatic disease developed in seven patients, 12% (3/26) of those with a positive biopsy and 5% (4/74) of those with a negative biopsy (p < 0.01). All seven presented first with a rising PSA.	3
104. D'Amico AV, Crook J, Beard CJ, DeWeese TL, Hurwitz M, Kaplan I. "Radiation therapy for prostate cancer". In: Walsh PC, Retik AB, eds. <i>Campbell's Urology.</i> 8th ed. Philadelphia, PA: WB Saunders; 2002:3147-3170.	Review/Other-Dx	N/A	Book chapter	N/A	4

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
105. Crook J, Malone S, Perry G, Bahadur Y, Robertson S, Abdoell M. Postradiotherapy prostate biopsies: what do they really mean? Results for 498 patients. Int J Radiat Oncol Biol Phys. 2000;48(2):355-367.	Observational-Tx	498 men	To determine the time course for histologic tumor resolution, and to correlate biopsy results with PSA and clinical outcome.	Median follow-up is 54 months (range 13-131). 175 patients (34%) had prior hormonal therapy for a median of 5 months (range 1-60). Clinical stage distribution was T1b: 46; T1c: 50; T2a: 115; T2b/c: 170; T3: 108; T4: 11; Tx: 1. Distribution by Gleason score was: 28% Gleason score 2-4; 42%: 5-6; 18%: 7; and 12%: 8-10. Seventy-one men have died, 26 of prostate cancer and 45 of other causes. Actuarial failure-free survival by T stage at 5 years is T1b: 78%; T1c: 76%; T2a: 60%; T2b/c: 55%; T3: 30%; and T4: 0%. Actuarial freedom from local failure at 5 years is T1b: 83%; T1c: 88%; T2a: 72%; T2b/c: 66%; T3: 58%; and T4: 0%. The proportion of indeterminate biopsies decreases with time, being 33% for biopsy 1, 24% for biopsy 2, 18% for biopsy 3, and 7% for biopsy 4. Thirty percent of indeterminate biopsies resolved to NED status, regardless of the degree of RT effect, 18% progressed to local failure, and 34% remained as biopsy failures with indeterminate status within the time frame of this report. Positive staining for proliferation markers was associated with both subsequent local failure and also any type of failure. In multivariate analysis, only PSA nadir (p = 0.0002) and biopsy status at 24-36 months (p = 0.0005) were independent predictors of outcome.	1

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
106. Parker WP, Davis BJ, Park SS, et al. Identification of Site-specific Recurrence Following Primary Radiation Therapy for Prostate Cancer Using C-11 Choline Positron Emission Tomography/Computed Tomography: A Nomogram for Predicting Extrapelvic Disease. Eur Urol. 2017;71(3):340-348.	Observational-Dx	161 patients	To describe the anatomic patterns and clinical features associated with CaP recurrence following RT identified on advanced imaging.	Recurrence site was identified in 161 (87%) patients, with 95 (59%) sites histologically confirmed. Factors associated with the detection of recurrence included the difference between PSA nadir and PSA at CholPET (odds ratio: 1.30, p<0.01) and National Comprehensive Cancer Network high-risk classification (odds ratio: 10.83, p=0.03). One hundred (54.3%) patients recurred in the pelvic soft tissue only, while 61 (33%) had extrapelvic recurrence. Of 21 patients who underwent CholPET prior to meeting the Phoenix criteria of biochemical failure, 15 (71%) had recurrence identified on CholPET with 11 localized to the pelvis. On multivariable analysis, the difference between PSA nadir and PSA at CholPET, time from RT, and National Comprehensive Cancer Network risk group were predictive of recurrence outside of the pelvis, and a nomogram was generated with a c-index of 0.79.	3

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
107. Parker WP, Evans JD, Stish BJ, et al. Patterns of Recurrence After Postprostatectomy Fossa Radiation Therapy Identified by C-11 Choline Positron Emission Tomography/Computed Tomography. International journal of radiation oncology, biology, physics. 2017;97(3):526-535.	Observational-Dx	41 patients	To evaluate C-11 choline positron emission tomography/computed tomography (CholPET) in staging and determining patterns of recurrence in prostate cancer patients with rising prostate-specific antigen levels after prostatectomy radiation therapy (RT).	Forty-one patients were identified with 121 sites of recurrence (median 2 sites; interquartile range [IQR], 1-4). The median prostate-specific antigen level at CholPET was 3.1 (IQR, 1.9-5.6) ng/mL. Median interval from RT to biochemical failure was 24 (IQR, 10-46) months, with recurrence identified on CholPET at a median of 15 (IQR, 7-28) months from biochemical failure. Histologic confirmation of recurrence was obtained in 20 patients (49%), with the remainder confirmed by treatment response. Five patients (12%) had IF recurrences, 10 patients (24%) had EOF recurrences (median dose 10 Gy; IQR, 5-30 Gy), and 36 patients (88%) had OOF recurrences. Ten patients had combination failures: 6 (15%) EOF/OOF and 4 (10%) IF/OOF. Fifty-seven recurrences (47%) were pelvic nodal sites inferior to the L5-S1 interspace, of which 52 (43%) were within a pelvic RT field. Eighty-one recurrences (67%) were nodal and inferior to the aortic bifurcation.	3

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
108. Kairemo K, Rasulo N, Partanen K, Joensuu T. Preliminary clinical experience of trans-1-Amino-3-(18)F-fluorocyclobutanecarboxylic Acid (anti-(18)F-FACBC) PET/CT imaging in prostate cancer patients. Biomed Res Int. 2014;2014:305182.	Observational-Dx	26 patients	To assess the role of [(18)F]-FACBC-PET/CT in the prostatic cancer staging.	On 16 [(18)F]-FACBC (53.3%) scans, 58 metabolically active lesions were found. 12 (20.7%) lesions corresponding to the local relapse were found in prostate/prostate bed and seminal vesicles, 9 (15.5%) lesions were located in regional lymph nodes, 10 (17.2%) were located in distal lymph nodes, and 26 (44.8%) metabolically active lesions were found in the skeleton. In one case, focal uptake was found in the brain, confirmed further on MRI as meningioma. The mean S-PSA level in patients with positive [(18)F]-FACBC findings was 9.5 +/- 16.9 mu g/L (0.54-69 mu g/L) and in patients with negative [(18)F]-FACBC findings was 1.96 +/- 1.87 mu g/L (0.11-5.9 mu g/L), but the difference was not statistically significant. However, the PSA doubling time (PDT) in patients with positive findings was significantly shorter than PDT in patients with negative findings: 3.25 +/- 2.09 months (0.3-6 months) versus 31.2 +/- 22.02 months (8-84 months), P < 0.0001. There was a strong positive correlation between PSA value and number of metabolically active lesions (R = 0.74) and a negative correlation between PDT and number of metabolically active lesions (R = -0.56). There was a weak negative correlation between PDT and SUVmax (R = -0.30).	3
109. Risk M, Corman JM. The role of immunotherapy in prostate cancer: an overview of current approaches in development. Risk, M. 2009;11(1):16-27.	Review/Other-Dx	N/A	To outline some of the recent advances in immunotherapy strategies for prostate malignancy.	Ongoing clinical trials provide promise for the introduction of immunotherapy into the armamentarium against prostate cancer, but the precise role for immunotherapy remains to be determined. Combinations of immunotherapies may be needed to improve the response rates and the duration of response.	4

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
110. Scher HI, Halabi S, Tannock I, et al. Design and end points of clinical trials for patients with progressive prostate cancer and castrate levels of testosterone: recommendations of the Prostate Cancer Clinical Trials Working Group. Scher, H. I. 2008;26(7):1148-1159.	Review/Other-Tx	N/A	To update eligibility and outcome measures in trials that evaluate systemic treatment for patients with progressive prostate cancer and castrate levels of testosterone.	The Prostate Cancer Clinical Trials Working Group (PCWG2) recommends a two-objective paradigm: (1) controlling, relieving, or eliminating disease manifestations that are present when treatment is initiated and (2) preventing or delaying disease manifestations expected to occur. Prostate cancers progressing despite castrate levels of testosterone are considered castration resistant and not hormone refractory. Eligibility is defined using standard disease assessments to authenticate disease progression, prior treatment, distinct clinical subtypes, and predictive models. Outcomes are reported independently for prostate-specific antigen (PSA), imaging, and clinical measures, avoiding grouped categorizations such as complete or partial response. In most trials, early changes in PSA and/or pain are not acted on without other evidence of disease progression, and treatment should be continued for at least 12 weeks to ensure adequate drug exposure. Bone scans are reported as "new lesions" or "no new lesions," changes in soft-tissue disease assessed by RECIST, and pain using validated scales. Defining eligibility for prevent/delay end points requires attention to estimated event frequency and/or random assignment to a control group.	4
111. Lipton A. Implications of bone metastases and the benefits of bone-targeted therapy. Lipton, A. 2010;37 Suppl 2:S15-29.	Review/Other-Dx	N/A	To summarize the clinical data regarding the efficacy and safety of currently available bone-targeted therapies in the treatment of bone metastasis due to breast cancer, prostate cancer, lung cancer, and multiple myeloma bone disease.	No results stated in abstract.	4

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
112. Halabi S, Small EJ, Kantoff PW, et al. Prognostic model for predicting survival in men with hormone-refractory metastatic prostate cancer. Scher, H. I. 2003;21(7):1232-1237.	Review/Other-Dx	1,101 patients	To develop and validate a model that can be used to predict the overall survival probability among metastatic hormone-refractory prostate cancer patients (HRPC).	The final model included the following factors: lactate dehydrogenase, prostate-specific antigen, alkaline phosphatase, Gleason sum, Eastern Cooperative Oncology Group performance status, hemoglobin, and the presence of visceral disease. The area under the ROC curve was 0.68. Patients were classified into one of four risk groups. We observed a good agreement between the observed and predicted survival probabilities for the four risk groups. The observed median survival durations were 7.5 (95% confidence interval [CI], 6.2 to 10.9), 13.4 (95% CI, 9.7 to 26.3), 18.9 (95% CI, 16.2 to 26.3), and 27.2 (95% CI, 21.9 to 42.8) months for the first, second, third, and fourth risk groups, respectively. The corresponding median predicted survival times were 8.8, 13.4, 17.4, and 22.80 for the four risk groups.	4
113. Evangelista L, Bertoldo F, Boccardo F, et al. Diagnostic imaging to detect and evaluate response to therapy in bone metastases from prostate cancer: current modalities and new horizons. Eur J Nucl Med Mol Imaging. 2016;43(8):1546-1562.	Review/Other-Dx	N/A	To provide an overview of current management of advanced PC and discuss the choice of diagnostic modality for the detection of metastatic skeletal lesions in different phases of the disease.	No results stated in abstract.	4
114. American College of Radiology. ACR Appropriateness Criteria®: Suspected Liver Metastases. Available at: https://acsearch.acr.org/docs/69475/Narrative/ .	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for a specific clinical condition.	No results stated in abstracts.	4

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
115. Ceci F, Castellucci P, Graziani T, et al. (11)C-Choline PET/CT in castration-resistant prostate cancer patients treated with docetaxel. Eur J Nucl Med Mol Imaging. 2016;43(1):84-91.	Observational-Dx	61 patients	To investigate the role of (11)C-choline PET/CT for evaluating the response to treatment in patients with metastatic castration-resistant prostate cancer (mCRPC) treated with docetaxel in comparison with PSA response.	Of the 61 patients, 40 (65.5 %) showed PD on PET2, 13 (21.3 %) showed SD, 2 (3.4 %) showed PR, and 6 (9.8 %) showed CR. An increasing PSA trend was seen in 29 patients (47.5 %) and a decreasing PSA trend in 32 patients (52.5 %). A PSA response of ≥ 50 % was seen in 25 patients (41 %). Radiological PD was seen in 23 of the 29 patients (79.3 %) with an increasing PSA trend, in 16 of the 32 patients (50 %) with a decreasing PSA trend, and in 11 of the 25 patients (44 %) with a PSA response of ≥ 50 %. In the multivariate statistical analysis, the presence of more than ten bone lesions detected on PET1 was significantly associated with an increased probability of PD on PET2. No association was observed between PSA level and PD on PET2.	3
116. De Giorgi U, Caroli P, Burgio SL, et al. Early outcome prediction on 18F-fluorocholine PET/CT in metastatic castration-resistant prostate cancer patients treated with abiraterone. Oncotarget. 2014;5(23):12448-12458.	Experimental-Dx	43 patients	To investigate the role of 18F-fluorocholine positron emission tomography/computed tomography (FCH-PET/CT) in the early evaluation of abiraterone and outcome prediction in patients with metastatic castration-resistant prostate cancer (CRPC).	Declines in PSA level of ≥ 50 % were seen in 21 of 43 (49%) patients. Forty-two patients were evaluable for FCH-PET/CT response. FCH-PET/CT bone flare was observed in 4 of 42 (10%) evaluable patients. In univariate analysis, PSA decline and FCH-PET/CT response predicted PFS, while PSA decline and FCH-PET/CT (progression vs non progression) predicted OS. In multivariate analysis, only FCH-PET/CT (progression vs nonprogression) remained significant for PFS and OS (p = 0.022 and p = 0.027, respectively).	1

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
117. De Giorgi U, Caroli P, Scarpi E, et al. (18)F-Fluorocholine PET/CT for early response assessment in patients with metastatic castration-resistant prostate cancer treated with enzalutamide. <i>Eur J Nucl Med Mol Imaging</i> . 2015;42(8):1276-1283.	Observational-Dx	36 patients	To investigate the role of (18)F-methylcholine (FCH) PET/CT in the early evaluation of patients with metastatic castration-resistant prostate cancer (mCRPC) treated with enzalutamide.	At a median follow-up of 24.2 months (range 1.8-27.3 months), 34 patients were evaluable for early FCH PET/CT evaluation of response, and of these 17 showed progressive disease (PD) and 17 had stable disease or a partial response. A decrease in PSA level of more than 50% was observed in 21 patients. Early FCH PET/CT PD predicted radiological PD 3 months in advance of CT in 12 of 18 patients (66%) and was discordant with the decrease in PSA level in 13 patients. In 6 of these, biochemical PD was confirmed in 2 months. In multivariate analysis, only decrease in PSA level and FCH PET/CT were significant predictors of PFS (p = 0.0005 and p = 0.029, respectively), whereas decrease in PSA level alone was predictive of OS (p = 0.007).	3
118. Maines F, Caffo O, Donner D, et al. Serial 18F-choline-PET imaging in patients receiving enzalutamide for metastatic castration-resistant prostate cancer: response assessment and imaging biomarkers. <i>Future Oncol</i> . 2016;12(3):333-342.	Observational-Dx	30 patients	To investigate the role of (18)F-choline (FCH)-PET/CT in patients receiving enzalutamide after docetaxel.	Univariate analysis showed no significant correlation between biochemical and FCH-PET responses. Multivariate analysis showed that only baseline maximum standardized uptake value (SUVmax) significantly correlated with biochemical progression-free survival, radiological progression-free survival and overall survival.	2
119. Okudaira H, Oka S, Ono M, et al. Accumulation of trans-1-amino-3-[(18)F]fluorocyclobutanecarboxylic acid in prostate cancer due to androgen-induced expression of amino acid transporters. <i>Mol Imaging Biol</i> . 2014;16(6):756-764.	Review/Other-Dx	Cell Cultures	To examine the effect of androgen on the expression of amino acid transporters related to anti-[(18)F]FACBC transport and uptake of trans-1-amino-3-fluoro-[1-(14)C]cyclobutanecarboxylic acid (anti-[(14)C]FACBC).	DHT stimulated the expression of amino acid transporters ASCT2, SNAT5, 4F2 heavy chain, and LAT3 in LNCaP but not in DU145 cells. Anti-[(14)C]FACBC uptake was enhanced, in a DHT-dependent manner, in LNCaP cells only.	4
120. Ono M, Oka S, Okudaira H, et al. [(14)C]Fluciclovine (alias anti-[(14)C]FACBC) uptake and ASCT2 expression in castration-resistant prostate cancer cells. <i>Nucl Med Biol</i> . 2015;42(11):887-892.	Review/Other-Dx	Number of cell cultures not specified.	To investigate the uptake mechanisms and feasibility of [18F]fluciclovine for CRPC in the androgen-dependent PCa cell line LNCaP and LNCaP-derivatives LNCaP-SF and LN-REC4.	The contribution of Na(+)-dependent AATs to [(14)C]fluciclovine uptake in all cell lines was 88-98%, and [(14)C]fluciclovine uptake was strongly inhibited by L-glutamine and L-serine, the substrates for Na(+)-dependent alanine-serine-cysteine (system ASC) AATs, in the presence of Na(+). DHT enhanced ASCT2 expression in LNCaP, LN-Pre, and LN-REC4, but not in LNCaP-SF, and the responses of ASCT2 expression to DHT correlated with [(14)C]fluciclovine uptake.	4

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
121. Jadvar H. PET of Glucose Metabolism and Cellular Proliferation in Prostate Cancer. J Nucl Med. 2016;57(Suppl 3):25S-29S.	Review/Other-Dx	N/A	To summarize the experience with the utility and limitations of PET for the imaging examination of glucose metabolism and cellular proliferation in prostate cancer.	Despite the seemingly prevalent notion that 18F-FDG PET may not be useful in prostate cancer, relatively limited evidence suggests that this imaging modality can be useful for the evaluation of the extent of metastatic disease and the assessment of the therapy response and prognosis in men with castration-resistant prostate cancer. Incidental high focal 18F-FDG uptake in the prostate gland, although generally rare, may also indicate occult prostate cancer that may need to be further scrutinized. In general, 18F-FDG PET is not useful for initial staging and is of limited utility in the clinical setting of biochemical failure after prior definitive therapy for primary cancer. Although more experience is needed, it appears that the imaging of cellular proliferation with PET and 3'-deoxy-3'-18F-fluorothymidine or 2'-18F-fluoro-5-methyl-1-beta-d-arabinofuranosyluracil may also allow for targeted biopsy and localization for focal therapy of aggressive prostate tumors as well as assessment of the therapy response to various standard and novel treatment regimens in patients with metastatic disease.	4
122. Liu J, Chen Z, Wang T, et al. Influence of Four Radiotracers in PET/CT on Diagnostic Accuracy for Prostate Cancer: A Bivariate Random-Effects Meta-Analysis. Cell Physiol Biochem. 2016;39(2):467-480.	Meta-analysis	56 studies containing 3,586 patients	To compare the diagnostic accuracy among four PET/CT radiotracers: fluorine-18 fluorodeoxyglucose (18F-FDG), carbon-11 labeled choline (11C-choline), 18-F fluorocholine (18F-FCH) and carbon-11 acetate (11C-acetate).	A total of 56 studies containing 3,586 patients were included in this meta-analysis. Parameter estimates of the overall analysis are as follows: sensitivity, 0.80 (95% CI: 0.74-0.85); specificity, 0.84 (95% CI: 0.77-0.89) and area under roc curve-AUC of SROC, 0.89 (95% CI: 0.86-0.91), indicating a relatively high level of accuracy in diagnosis of PCa. When different radiotracers of PET/CT were compared, 18F-FCH-PET/CT was ranked as the most favorable with the highest value of AUC (AUC = 0.94; 95% CI: 0.92-0.96) whereas 18F-FDG was the least favorable (AUC = 0.73, 95% CI: 0.69-0.77).	M

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
123. Seltzer MA, Barbaric Z, Beldegrun A, et al. Comparison of helical computerized tomography, positron emission tomography and monoclonal antibody scans for evaluation of lymph node metastases in patients with prostate specific antigen relapse after treatment for localized prostate cancer. J Urol. 1999;162(4):1322-1328.	Observational-Dx	45 patients	To compare the detection of metastatic disease by helical computerized tomography (CT), positron emission tomography (PET) with F-18 fluorodeoxyglucose and monoclonal antibody scan with 111 indium capromab pendetide in patients with an elevated prostate specific antigen (PSA) after treatment for localized prostate cancer.	PET and CT were positive for distant disease in 50% of 22 patients with PSA greater than 4, and in 4 and 17%, respectively, of 23 with PSA less than 4 ng./ml. The detection rate for metastatic disease was similar for CT and PET, and higher overall than that for monoclonal antibody scan. Monoclonal antibody scan was true positive in only 1 of 6 patients, while PET was true positive in 6 of 9 with CT guided fine needle aspiration proved metastases.	3
124. Meirelles GS, Schoder H, Ravizzini GC, et al. Prognostic value of baseline [18F] fluorodeoxyglucose positron emission tomography and 99mTc-MDP bone scan in progressing metastatic prostate cancer. Clin Cancer Res. 2010;16(24):6093-6099.	Observational-Dx	43 patients	To compare the diagnostic and prognostic value of [(18F) fluorodeoxyglucose positron emission tomography (FDG-PET) and bone scans (BS) in the assessment of osseous lesions in patients with progressing prostate cancer.	Osseous lesions were detected in 39 patients on BS and 32 on FDG-PET (P = 0.01). Follow-up was available for 105 FDG-positive lesions, and 84 (80%) became positive on subsequent BS. Prognosis correlated inversely with SUV (median survival 14.4 versus 32.8 months if SUVmax > 6.10 versus ≤ 6.10; P = 0.002) and BSI (14.7 versus 28.2 months if BSI > 1.27 versus < 1.27; P = 0.004). Only SUV was an independent factor in multivariate analysis.	3
125. Morris MJ, Akhurst T, Larson SM, et al. Fluorodeoxyglucose positron emission tomography as an outcome measure for castrate metastatic prostate cancer treated with antimicrotubule chemotherapy. Clin Cancer Res. 2005;11(9):3210-3216.	Experimental-Dx	23 patients	To test the hypothesis that serial fluorodeoxyglucose positron emission tomography (FDG-PET) scans can serve as an outcome measure for patients with castrate metastatic prostate cancer treated with antimicrotubule chemotherapy.	Twenty-two PET scans were reviewed and compared with PSA at 4 weeks; 18 PETs were compared at 12 weeks with standard outcome measures. Applying the PSA Working Group Consensus Criteria guideline that a 25% PSA increase constitutes progression to the SUVmaxavg, PET correctly identified the clinical status of 20 of 22 patients (91%) at 4 weeks and 17 of 18 patients at 12 weeks (94%). The accuracy of PET could be further optimized if a >33% increase in PSA and SUVmaxavg were used to define progression.	3

**Post-treatment Follow-up of Prostate Cancer
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
126. Morris MJ, Akhurst T, Osman I, et al. Fluorinated deoxyglucose positron emission tomography imaging in progressive metastatic prostate cancer. <i>Urology</i> . 2002;59(6):913-918.	Observational-Dx	17 patients	To correlate the abnormalities on computed tomography, magnetic resonance imaging, and bone scan with fluorinated deoxyglucose positron emission tomography (FDG-PET) in patients with progressive metastatic prostate cancer, using a lesion-by-lesion analysis, and to preliminarily explore post-treatment changes in standard uptake value (SUV) with changes in prostate-specific antigen (PSA).	One hundred fifty-seven lesions in 17 patients were examined; 134 osseous lesions were evident on PET and/or bone scan, 95 lesions (71%) were evident on both, 31 (23%) were seen only on bone scan, and 8 (6%) were seen only on PET (adjusted McNemar's chi-square = 8.32, P = 0.004). All but one of the lesions seen only on bone scan were "stable" compared with the previous bone scans. All lesions seen only on PET proved to be active disease on subsequent bone scans. Twenty-three soft-tissue lesions were present on CT/MRI or PET, or both; 9 (39%) lesions were evident on both and 14 (61%) were evident only on one imaging modality. In 9 (75%) of 12 cases in which serial PET scans were available, the SUV changed in parallel with the PSA level.	3
127. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: http://www.acr.org/~media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf .	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	N/A	4

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
-

Dx = Diagnostic

Tx = Treatment