Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Dialani V, Chadashvili T, Slanetz PJ. Role of imaging in neoadjuvant therapy for breast cancer. *Ann Surg Oncol.* 2015;22(5):1416-1424.	Review/Other-Dx	N/A	To review the role of imaging before and after neoadjuvant therapy and discuss the advantages and limitations of currently available modalities, including mammography, US, MRI, and nuclear imaging.	No results stated in abstract.	4
2. Khan A, Sabel MS, Nees A, et al. Comprehensive axillary evaluation in neoadjuvant chemotherapy patients with ultrasonography and sentinel lymph node biopsy. *Ann Surg Oncol.* 2005;12(9):697-704.	Observational-Dx	91 patients	To report the accuracy of comprehensive pre-neoadjuvant NAC and post-neoadjuvant NAC axillary staging via US imaging, FNA biopsy, and SLNB.	Axillary staging was pathologically negative by pre-NAC SLNB in 53 cases (58%); these patients had no further axillary surgery. In 38 cases (42%), axillary metastases were confirmed at presentation by either US-guided FNA or SLNB. These 38 patients underwent completion axillary lymph node dissection after delivery of NAC. Follow-up lymphatic mapping was attempted in 33 of these cases, and the SLN was identified in 32 (identification rate, 97%). One third of these cases were completely node negative on axillary lymph node dissection. Residual metastatic disease was identified in 22 cases, and the SLN was falsely negative in 1 (4.5%).	3
3. Andrade WP, Lima EN, Osorio CA, et al. Can FDG-PET/CT predict early response to neoadjuvant chemotherapy in breast cancer? *Eur J Surg Oncol.* 2013;39(12):1358-1363.	Experimental-Dx	40 patients	To correlate the relative change in the SUV of FDG-PET/CT with pathologic response after NAC.	The mean age was 41.9 years. Median primary tumor size was 6 cm. pCR was obtained in 12 (30%) patients. The tumor baseline mean SUVmax, and after second cycle were: 8.97 (SD.4.3) and 4.07 (SD.3.2), respectively. The relative change (DeltaSUV) after the second course of NAC was significantly higher for patients with pCR (-81.58%) when compared to the non-pCR patients (-40.18%) (P=0.001). The optimal DeltaSUV threshold that discriminates between pCR and non-pCR was -71.8% (83.3% sensitivity; 78.5% specificity). Moreover, the optimal DeltaSUV threshold to discriminate between NAC responders and nonresponders was -59.1% (68% sensitivity; 75.0% specificity).	1

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4. National Cancer Institute. Imaging Response Criteria. Response Evaluation Criteria in Solid Tumors (RECIST). Available at: http://imaging.cancer.gov/clinicaltrials/imaging/. Accessed March 1, 2017.	Review/Other-Dx	N/A	To describe a standard approach to solid tumor measurement and definitions for objective assessment of change in tumor size for use in adult and pediatric cancer clinical trials.	No results stated in abstract.	4
5. Cocconi G, Di Blasio B, Alberti G, Bisagni G, Botti E, Peracchia G. Problems in evaluating response of primary breast cancer to systemic therapy. *Breast Cancer Res Treat.* 1984;4(4):309-313.	Observational-Dx	49 patients	Response to therapy was evaluated after 4 cycles of CMF or CMF plus tamoxifen in 49 patients with LABC entering a prospective randomized trial.	In 35 patients response was evaluated by both physical examination and mammography. In some cases there was disagreement between physical examination and mammography in quantifying the magnitude of response. In 8/35 (22.9%), the overall response was overestimated by physical examination vs mammography, while in 3/35 (8.6%) the reverse was true. Taking into consideration different criteria in attributing the overall response, ie, selecting physical examination only, mammography only, or the most favorable or the least favorable response between the 2 methods of assessment, the objective remission rates were 65.7%, 54.3%, 71.4% and 45.7%, respectively.	3

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6. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. *Radiology.* 2004;233(3):830-849.	Observational-Dx	111 consecutive women	To prospectively assess the diagnostic accuracy of mammography, clinical examination, US, and MRI in the preoperative imaging of breast cancer.	Mammographic sensitivity was highest for IDC in 89/110 (81%) cases vs 10/29 (34%) cases of ILC (*P*=.001) and 21/38 (55%) cases of DCIS (*P*=.01). US showed higher sensitivity than did mammography for IDC, depicting 104/110 (94%) cases, and for ILC, depicting 25/29 (86%) cases (*P*=.01 for each). US showed higher sensitivity for invasive cancer than DCIS (18/38 [47%], *P*=.001). MRI showed higher sensitivity than did mammography for all tumor types (*P*=.01) and higher sensitivity than did US for DCIS (*P*=.001), depicting 105/110 (95%) cases of IDC, 28/29 (96%) cases of ILC, and 34/38 (89%) cases of DCIS. In anticipation of conservation or no surgery after mammography and clinical examination in 96 breasts, additional tumor (which altered surgical approach) was present in 30. Additional tumor was depicted in 17/96 (18%) breasts at US and in 29/96 (30%) at MRI, though extent was now overestimated in 12/96 (12%) at US and 20/96 (21%) at MRI. After combined mammography, clinical examination, and US, MRI depicted additional tumor in another 12/96 (12%) breasts and led to overestimation of extent in another 6 (6%); US showed no detection benefit after MRI. Bilateral cancer was present in 10/111 (9%) patients; contralateral tumor was depicted mammographically in 6 and with both US and MRI in an additional 3. 1 contralateral cancer was demonstrated only clinically. In non-fatty breasts, US and MRI were more sensitive than mammography for invasive cancer, but both overestimated tumor extent. US showed no detection benefit after MRI. Combined mammography, clinical examination, and MRI were more sensitive than any other individual test or combination of tests.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
7. Bosch AM, Kessels AG, Beets GL, et al. Preoperative estimation of the pathological breast tumour size by physical examination, mammography and ultrasound: a prospective study on 105 invasive tumours. *Eur J Radiol.* 2003;48(3):285-292.	Observational-Dx	96 women	To determine the most accurate clinical method (physical examination, mammography or US) to predict the histological invasive tumor size preoperatively.	The correlation coefficient between US and pathological size (r=0.68) was significantly better than the correlations between physical examination and pathological size (r=0.42) and mammographic and pathological size (r=0.44). Physical examination overestimates and US underestimates breast tumor classification. The most accurate prediction formula was: Pathological tumor size (mm) equals sonographic tumor size (mm)+3 mm.	2
8. Hieken TJ, Harrison J, Herreros J, Velasco JM. Correlating sonography, mammography, and pathology in the assessment of breast cancer size. *Am J Surg.* 2001;182(4):351-354.	Observational-Dx	146 patients	To compare the ability of mammography and US to measure breast cancer size.	In 69% of cases, US was better than or equivalent to mammography in determining tumor size. Both underestimated tumor size; mean (median) underestimation was 3.8 +/- 0.7 mm (1.7 mm) by US and 3.5 +/- 0.9 mm (2 mm) by mammogram. Maximal tumor dimension was accurate within 5 mm in 65% of cases by mammography and 75% of cases by US. For mammographically determined size (vs pathologic size) correlation, r, was 0.4 and for US it was 0.63 and improved for only T1 and T2 tumors.	2
9. Kald BA, Boiesen P, Ronnow K, Jonsson PE, Bisgaard T. Preoperative assessment of small tumours in women with breast cancer. *Scand J Surg.* 2005;94(1):15-20.	Observational-Dx	131 patients	To compare findings from preoperative mammography and US with histopathological tumor size in patients treated with breast-conserving surgery.	The study included 131 patients (median age was 59 years) with grade I, II, and III cancers in 47, 71 and in 13 patients, respectively. The medium histological tumor size was 14 mm, range 4–45 mm. A wide 95% CI between histopathological tumor size and preoperative mammography (SD 4.8 mm) and US (SD 4.8 mm) was found. The combination of mammography and US did not improve the results (SD 4.3 mm). Preoperative mammography tended to overestimate the tumor size compared with histological tumor size whereas preoperative US tended to underestimate the tumor size.	3

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10. Madjar H, Ladner HA, Sauerbrei W, Oberstein A, Prompeler H, Pfleiderer A. Preoperative staging of breast cancer by palpation, mammography and high-resolution ultrasound. *Ultrasound Obstet Gynecol.* 1993;3(3):185-190.	Observational-Dx	100 patients	To compare the ability of mammography and US to measure breast cancer size.	Using a high-resolution real-time system, 98 tumors were visible. It was possible to detect not only early tumors under 1 cm in diameter, but also intraductal tumor components. This contributed greatly to the accuracy of the diagnosis. The sonographic measurement of tumor size demonstrated a correlation coefficient of 0.91 and was thus superior to mammography (0.79) and palpation (0.77). Measurement of the total tumor spread, including 39 multicentric lesions, showed an overestimation of 5% for the mammographic measurements and an overestimation of 4% for the sonographic measurements. Tumor extension was underestimated in 33% of the mammograms but in only 3% using US examination.	3
11. Haas BM, Kalra V, Geisel J, Raghu M, Durand M, Philpotts LE. Comparison of tomosynthesis plus digital mammography and digital mammography alone for breast cancer screening. *Radiology.* 2013;269(3):694-700.	Observational-Dx	13,158 patients	To compare screening recall rates and CDRs of tomosynthesis plus conventional DM to those of conventional DM alone.	A total of 13,158 patients presented for screening mammography; 6100 received tomosynthesis. The overall recall rate was 8.4% for patients in the tomosynthesis group and 12.0% for those in the conventional mammography group ($P<.01$). The addition of tomosynthesis reduced recall rates for all breast density and patient age groups, with significant differences ($P<.05$) found for scattered fibroglandular, heterogeneously dense, and extremely dense breasts and for patients younger than 40 years, those aged 40–49 years, those aged 50–59 years, and those aged 60–69 years. These findings persisted when multivariate logistic regression was used to control for differences in age, breast density, and elevated risk of breast cancer. The cancer detection rate was 5.7 per 1000 in patients receiving tomosynthesis vs 5.2 per 1000 in patients receiving conventional mammography alone ($P=.70$).	3

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12. McCarthy AM, Kontos D, Synnestvedt M, et al. Screening outcomes following implementation of digital breast tomosynthesis in a general-population screening program. *J Natl Cancer Inst.* 2014;106(11).	Observational-Dx	15,571 women screened with DBT and 10,728 screened with DM alone	To report the impact on screening outcomes for DBT screening implemented in an entire clinic population.	DBT screening showed a statistically significant reduction in recalls compared to DM alone. For the entire population, there were 16 fewer recalls (8.8% vs 10.4%, *P*<.001, adjusted odds ratio = 0.80, 95% CI = 0.74 to 0.88, *P*<.001) and 0.9 additional cancers detected per 1000 screened with DBT compared to DM alone. There was a statistically significant increase in PPV1 (6.2% vs 4.4%, *P*=.047). In women younger than age 50 years screened with DBT, there were 17 fewer recalls (12.3% vs 14.0%, *P*=.02) and 3.6 additional cancer detected per 1000 screened (5.7 vs 2.2 per 1000, *P*=.02).	3
13. Mun HS, Kim HH, Shin HJ, et al. Assessment of extent of breast cancer: comparison between digital breast tomosynthesis and full-field digital mammography. *Clin Radiol.* 2013;68(12):1254-1259.	Observational-Dx	173 lesions in 169 patients	To compare the accuracy of DBT and FFDM in preoperative assessment of local extent of breast cancer.	The dataset included 173 malignant breast lesions (mean size 23.8 mm, 43% of lesions were ≤2 cm in size) in 169 patients, two-thirds of which had heterogeneously or extremely dense breasts. Overall, the percentage of lesions mis-sized at DBT was significantly lower than at FFDM (19% vs 29%, *P*=0.003). There was significantly less mis-sizing at DBT in both heterogeneously dense breasts (11.1% difference between DBT and FFDM, *P*=0.016) and extremely dense breasts (15.8% difference, *P*=0.024). DBT also had significantly less mis-sizing than FFDM in the subgroup of lesions that were ≤2 cm in size (14.7% difference, *P*=0.005).	2
14. Lang K, Andersson I, Zackrisson S. Breast cancer detection in digital breast tomosynthesis and digital mammography-a side-by-side review of discrepant cases. *Br J Radiol.* 2014;87(1040):20140080.	Observational-Dx	26 discrepant cases resulting from 24 females with 25 cancer lesions in 24 breasts	To analyze discrepant breast cancer detection in DBT and DM.	The proportion of lesion periphery in fatty tissue was statistically significantly larger, and there were significantly more spiculated masses in DBT compared with DM in the DBT only group (*P*=0.018; *P*=0.015). The main reasons for missing a lesion were poor lesion visibility when using DM and interpretative error when using DBT.	3

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15. Durand MA, Haas BM, Yao X, et al. Early clinical experience with digital breast tomosynthesis for screening mammography. *Radiology*. 2015;274(1):85-92.	Observational-Dx	17,955 screening mammograms	To examine recall rates from screening mammography and the mammographic findings that caused recall in women who underwent DBT with conventional mammography 2D with 3D imaging and in women who underwent conventional mammography alone.	This study included 17, 955 screening mammograms; of the total, there were 8591 (47.8%) 2D + 3D screening examinations and 9364 (52.2%) 2D examinations. The recall rate was 7.8% (671/8592) for 2D + 3D and 12.3% (1154/9364) for 2D (P<.0001); the rate of recall was 36.6% lower in the 2D + 3D group than in the 2D group. Recall rates for the 2D + 3D group were significantly lower for patients with asymmetries, (2D + 3D vs 2D, 3.1% [267 of 8591] vs 7.4% [689 of 9364], respectively; P<.0001) and calcifications (2D + 3D vs 2D, 2.4% [205/8591] vs 3.2% [297/9364], respectively; P=.0014). For patients with masses and architectural distortion, the difference in recall rates was not significant (masses: 2D + 3D vs 2D, 2.5% [215/8591] vs 2.5% [237/9364], respectively; P=.90; architectural distortion: 2D + 3D vs 2D, 0.68% [58/8591] vs 0.69% [65/9364]; P=.88). Cancer detection was highest in the 2D + 3D group at 5.9 cancers per 1000 examinations, with 5.7 cancers per 1000 examinations in the concurrent 2D group, and 4.4 cancers per 1000 examinations in the historic control.	3
16. Brandt KR, Craig DA, Hoskins TL, et al. Can digital breast tomosynthesis replace conventional diagnostic mammography views for screening recalls without calcifications? A comparison study in a simulated clinical setting. *AJR Am J Roentgenol.* 2013;200(2):291-298.	Observational-Dx	146 women	To evaluate DBT as an alternative to conventional diagnostic mammography in the workup of noncalcified findings recalled from screening mammography in a simulated clinical setting that incorporated comparison mammograms and breast US results.	Agreement between DBT and diagnostic mammography BI-RADS categories was excellent for readers 1 and 2 (kappa = 0.91 and kappa = 0.84) and good for reader 3 (kappa = 0.68). For readers 1, 2, and 3, sensitivity and specificity of DBT for breast abnormalities were 100%, 100%, and 88% and 94%, 93%, and 89%, respectively. The clinical workup averaged 3 diagnostic views per abnormality and US was requested in 49% of the cases. DBT was adequate mammographic evaluation for 93%–99% of the findings and US was requested in 33%–55% of the cases.	2

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17. Gennaro G, Hendrick RE, Toledano A, et al. Combination of one-view digital breast tomosynthesis with one-view digital mammography versus standard two-view digital mammography: per lesion analysis. *Eur Radiol.* 2013;23(8):2087-2094.	Observational-Dx	463 breasts of 250 patients	To evaluate the clinical value of combining one-view mammography (cranio-caudal) with the complementary view tomosynthesis (mediolateral-oblique) in comparison to standard two-view mammography in terms of both lesion detection and characterization.	The 463 cases (breasts) reviewed included 258 with 1 to 3 lesions each, and 205 with no lesions. The 258 cases with lesions included 77 cancers in 68 breasts and 271 benign lesions to give a total of 348 proven lesions. The combination, DBT (mediolateral-oblique)+ two-view mammography (cranio-caudal), was superior to two-view mammography (cranio-caudal + mediolateral-oblique) in both lesion detection and lesion characterization overall and for benign lesions. DBT (mediolateral-oblique)+ two-view mammography (cranio-caudal) was noninferior to two-view mammography for malignant lesions.	2
18. Waldherr C, Cerny P, Altermatt HJ, et al. Value of one-view breast tomosynthesis versus two-view mammography in diagnostic workup of women with clinical signs and symptoms and in women recalled from screening. *AJR Am J Roentgenol.* 2013;200(1):226-231.	Observational-Dx	144 women	To compare the diagnostic value of one-view DBT vs two-view FFDM alone, vs a combined reading of both modalities.	86 of the 144 patients were found to have breast cancer. The BI-RADS categories for one-view DBT were significantly better than those for two-view FFDM ($P<0.001$) and were equal to those of the combined reading in both women admitted for diagnostic workup and women recalled from screening. The sensitivity and negative predictive values of DBT were superior to those of FFDM in fatty and dense breasts overall and in women admitted for diagnostic workup and in women recalled from screening. Only 11% of DBT examinations required additional imaging, compared with 23% of FFDMs.	3

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19. Yang TL, Liang HL, Chou CP, Huang JS, Pan HB. The adjunctive digital breast tomosynthesis in diagnosis of breast cancer. *Biomed Res Int.* 2013;2013:597253.	Observational-Dx	59 breasts of 57 patients	To compare the diagnostic performance of DBT and DM for breast cancers.	A total of 59 breast cancers were reviewed, including 17 (28.8%) mass lesions, 12 (20.3%) focal asymmetry/density, 6 (10.2%) architecture distortion, 23 (39.0%) calcifications, and 1 (1.7%) intracystic tumor. Combo DBT was perceived to be more informative in 58.8% mass lesions, 83.3% density, 94.4% architecture distortion, and only 11.6% calcifications. As to the forced BIRADS score, 84.4% BIRADS 0 on DM was upgraded to BIRADS 4 or 5 on DBT, whereas only 27.3% BIRADS 4A on DM was upgraded on DBT, as BIRADS 4A lesions were mostly calcifications. A significant *P* value (<0.001) between the BIRADS category and index lesions was noted.	3
20. Hylton NM, Blume JD, Bernreuter WK, et al. Locally advanced breast cancer: MR imaging for prediction of response to neoadjuvant chemotherapy--results from ACRIN 6657/I-SPY TRIAL. *Radiology.* 2012;263(3):663-672.	Experimental-Dx	216 women	To compare MRI findings and clinical assessment for prediction of pathologic response to NAC in patients with stage II or III breast cancer.	Data in 216 women (age range, 26–68 years) with 2 or more imaging time points were analyzed. For prediction of both pCR and RCB, MRI size measurements were superior to clinical examination at all time points, with tumor volume change showing the greatest relative benefit at the second MRI examination. AUC differences between MRI volume and clinical size predictors at the early, mid-, and posttreatment time points, respectively, were 0.14, 0.09, and 0.02 for prediction of pCR and 0.09, 0.07, and 0.05 for prediction of RCB. In multivariate analysis, the AUC for predicting pCR at the second imaging examination increased from 0.70 for volume alone to 0.73 when all 4 predictor variables were used. Additional predictive value was gained with adjustments for age and race.	1
21. Schott AF, Roubidoux MA, Helvie MA, et al. Clinical and radiologic assessments to predict breast cancer pathologic complete response to neoadjuvant chemotherapy. *Breast Cancer Res Treat.* 2005;92(3):231-238.	Observational-Dx	43 patients	To prospectively compare the ability of clinical examination, mammography, vascularity-sensitive US, and MRI to determine pCR in breast cancer patients undergoing NAC.	41 of 43 enrolled patients had a determination of pathologic response, and 4 patients had a pCR to this chemotherapy (9.8%). The accuracy of physical examination, mammography, US, and MRI in determining pCR was 75%, 89%, 82%, and 89%, respectively.	2

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22. Cox C, Holloway CM, Shaheta A, Nofech-Mozes S, Wright FC. What is the burden of axillary disease after neoadjuvant therapy in women with locally advanced breast cancer? *Curr Oncol.* 2013;20(2):111-117.	Observational-Tx	116 patients (115 women and 1 man)	To describe the extent of nodal metastases after neoadjuvant therapy in patients with LABC.	Of the 116 patients identified, 115 were female (median age: 48.5). Before neoadjuvant therapy, 26 patients were clinically and radiologically node-negative; of those 26, 14 were histologically negative on final pathology. After serial sectioning and immunohistochemistry, 9/26 (35%) were node-negative. Of the 90 patients who had clinical or radiologic evidence of lymph node metastases before neoadjuvant therapy, 23 (26%) had no evidence of lymph node metastases on hematoxylin and eosin staining. After serial sectioning and immunohistochemistry, 19 (21%) had no further axillary lymph node metastases. Overall, 76% of patients had pathology evidence of lymph node metastases after neoadjuvant therapy.	2
23. Aarsvold JN, Alazraki NP. Update on detection of sentinel lymph nodes in patients with breast cancer. *Semin Nucl Med.* 2005;35(2):116-128.	Review/Other-Dx	N/A	To review the present state and roles of nuclear medicine protocols used in breast cancer SLNB procedures with emphasis on discussion of recent results, unresolved issues, and future considerations.	No results stated in abstract.	4
24. Alvarado R, Yi M, Le-Petross H, et al. The role for sentinel lymph node dissection after neoadjuvant chemotherapy in patients who present with node-positive breast cancer. *Ann Surg Oncol.* 2012;19(10):3177-3184.	Observational-Dx	150 patients	To evaluate SLN dissection in node-positive patients and to determine whether postchemotherapy US could select patients for this technique.	Median age was 52 years. Median tumor size at presentation was 2 cm. The SLN was identified in 93% (139/150). In 111 patients in whom a SLN was identified and axillary lymph node dissection performed, 15 patients had a false-negative SLN (20.8%). In the 52 patients with normalized nodes on US, the false-negative rate decreased to 16.1%. Multivariate analysis revealed smaller initial tumor size and fewer SLNs removed (<2) were associated with a false-negative SLN. There were 63 (42%) patients with a pCR in the nodes. Of those with normalized nodes on US, 38 (51%) of 75 had a pCR. Only 25 (33%) of 75 with persistent suspicious/malignant-appearing nodes had a pCR (P=0.047).	3

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25. Hieken TJ, Boughey JC, Jones KN, Shah SS, Glazebrook KN. Imaging response and residual metastatic axillary lymph node disease after neoadjuvant chemotherapy for primary breast cancer. *Ann Surg Oncol.* 2013;20(10):3199-3204.	Observational-Dx	272 patients	To evaluate post-NAC axillary imaging and surgical pathology to understand how imaging might direct axillary surgery.	Pre-NAC axillary staging classified patients as axillary US negative/no FNA (n = 61), FNA/LN negative (n = 42), and FNA/LN positive (n = 169). Post-NAC axillary imaging included axillary US (n = 146), MRI (n = 139), and PET/CT (n = 38). At operation, 128/272 patients (47%) were LN positive: 23.3% (24/103) of cN0 and 61.5% (104/169) of cN1-axillary US/FNA-positive patients at presentation. Of the 65 cN1-ypN0 patients, 58.1% (25/43) had an imaging CR by US, 58.6% (17/29) by MRI, and 84.6% (11/13) by PET/CT. The sensitivity of post-NAC axillary imaging in detecting persistent LN metastases for cN1-axillary US /FNA-positive patients was 69.8% for US, 61.0% for MRI, and 63.2% for PET/CT.	3
26. Boughey JC, Suman VJ, Mittendorf EA, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. *JAMA.* 2013;310(14):1455-1461.	Observational-Dx	756 women	To determine the false-negative rate for SLN surgery following chemotherapy in women initially presenting with biopsy-proven cN1 breast cancer.	756 women were enrolled in the study. Of 663 evaluable patients with cN1 disease, 649 underwent chemotherapy followed by both SLN surgery and ALND. An SLN could not be identified in 46 patients (7.1%). Only 1 SLN was excised in 78 patients (12.0%). Of the remaining 525 patients with 2 or more SLNs removed, no cancer was identified in the axillary lymph nodes of 215 patients, yielding a pathological complete nodal response of 41.0% (95% CI, 36.7%–45.3%). In 39 patients, cancer was not identified in the SLNs but was found in lymph nodes obtained with ALND, resulting in a false-negative rate of 12.6% (90% Bayesian credible interval, 9.85%–16.05%).	3

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27. Heusinger K, Lohberg C, Lux MP, et al. Assessment of breast cancer tumor size depends on method, histopathology and tumor size itself*. *Breast Cancer Res Treat.* 2005;94(1):17-23.	Observational-Dx	503 patients	Aim of our study was (a) to determine the accuracy of all diagnostic methods matched to each other, (b) to find subgroups with higher and lower accuracy depending on histopathological features (tumor type, grading, hormonal receptor status, HER2/neu-status, large tumors vs small tumors, proliferation assessed by MIB-1 and age) and (c) to ascertain the value of axillary US in our collective.	Mammography correlated best with pT (r = 0.752). Mammography (mean = 2.17 cm) overestimated tumors in size (mean (pT) = 2.04 cm) rather than US (mean (breast) = 1.86 cm) and clinical examination (mean (cT) = 1.70 cm). pT of invasive ductal breast could be estimated significantly better than pT of invasive lobular BC. Smaller tumors were better to assess than larger ones. Tumors with a grading G1 were easier to estimate than tumors with G2/3. Best predictor of a pT >2 cm was the mammography with an AUC of 0.876. The combination of all 3 modalities by linear regression performed even better with an AUC of 0.906.	3
28. Tardivon AA, Ollivier L, El Khoury C, Thibault F. Monitoring therapeutic efficacy in breast carcinomas. *Eur Radiol.* 2006;16(11):2549-2558.	Review/Other-Dx	N/A	To discuss the role and the performance of the different imaging modalities (mammography, US, MRI and FDG-PET imaging) for evaluating pathologic response early after the initiation of NAC.	MRI and FDG/PET imaging are very promising for predicting the response early after the initiation of NAC.	4
29. Shoma A, Moutamed A, Ameen M, Abdelwahab A. Ultrasound for accurate measurement of invasive breast cancer tumor size. *Breast J.* 2006;12(3):252-256.	Observational-Dx	162 patients	To compare clinical evaluation, mammography, and breast US for evaluating breast tumor size.	Measurements were compared to the pathologic tumor size of the surgical specimen. Both mammographic and US measurements tend to underestimate tumor size, while clinical assessment tends to overestimate it. US was significantly more accurate in determining tumor size. The maximal tumor diameter measured was within 2 mm of the pathologic tumor size in 45.2% of cases measured by breast US, 28.2% of cases measured by mammography, and 14.5% of cases measured clinically.	3

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30. Boonjunwetwat D, Prueksadee J, Sampatanukul P, Chatamra K. Does color Doppler ultrasound vascularity predict the response to neoadjuvant chemotherapy in breast cancer? *J Med Assoc Thai.* 2005;88(10):1367-1372.	Observational-Dx	69 breast cancer patients	To assess the proportions of response to NAC of breast cancer according to color Doppler US vascularity patterns.	The overall response rate in 70 breast cancers was 20%. 29 lesions (41%) showed hypervascularity and 41 lesions (59%) revealed hypovascularity. There were 5 vascularity patterns and each pattern had the proportion of responders as follows; 33.3% for hypovascularity with single-vessel feeding into the tumor, 25% for hypovascularity with single-vessel feeding at periphery of the tumor, 25% for no vascular feeding to the tumor, 16.7% for hypervascularity with vascular feeding at the periphery of the tumor and 13% for hypervascularity with vascular feeding into the tumor. The highest percentage of responsive group was the pattern of hypovascularity with single-vessel feeding into the tumor (33.3%).	4
31. Lobbes MB, Prevos R, Smidt M, et al. The role of magnetic resonance imaging in assessing residual disease and pathologic complete response in breast cancer patients receiving neoadjuvant chemotherapy: a systematic review. *Insights Imaging.* 2013;4(2):163-175.	Review/Other-Dx	35 studies	To assess the role of MRI in evaluating residual disease extent and the ability to detect pCR after NAC for invasive breast cancer.	A total of 35 eligible studies were selected. Correlation coefficients of residual tumor size assessed by MRI and pathology were good, with a median value of 0.698. Reported sensitivity, specificity, PPV and NPV for predicting pCR with MRI ranged from 25% to 100%, 50%–97%, 47%–73% and 71%–100%, respectively. Both overestimation and underestimation were observed. MRI proved more accurate in determining residual disease than physical examination, mammography and US. Diagnostic accuracy of MRI after NAC could be influenced by treatment regimen and breast cancer subtype.	4
32. Giess CS, Yeh ED, Raza S, Birdwell RL. Background parenchymal enhancement at breast MR imaging: normal patterns, diagnostic challenges, and potential for false-positive and false-negative interpretation. *Radiographics.* 2014;34(1):234-247.	Review/Other-Dx	N/A	To describe the influences on background parenchymal enhancement, illustrate typical and unusual patterns of background parenchymal enhancement, and discuss the potential for false-positive and false-negative interpretations due to background parenchymal enhancement at screening and diagnostic MRI.	Radiologists can improve their interpretive accuracy by increasing their understanding of various background parenchymal enhancement patterns, influences on background parenchymal enhancement, and the potential effects of background parenchymal enhancement on MRI interpretation.	4

Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Houssami N, Ciatto S, Macaskill P, et al. Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: systematic review and meta-analysis in detection of multifocal and multicentric cancer. *J Clin Oncol.* 2008;26(19):3248-3258.	Review/Other-Dx	19 studies	Systematic review and meta-analysis of the accuracy of MRI in detection of multifocal and/or multicentric cancer not identified on conventional imaging.	Results data studies showed MRI detects additional disease in 16% of women with breast cancer (n=2,610). MRI incremental accuracy differed according to the reference standard (*P*=.016) decreasing from 99% to 86% as the quality of the reference standard increased. Summary PPV was 66% (95% CI, 52%–77%) and true-positive: false positive ratio was 1.91 (95% CI, 1.09-3.34). Conversion from wide local excision to mastectomy was 8.1% (95% CI, 5.9-11.3), from wide local excision to more extensive surgery was 11.3% in multifocal/multicentric disease (95% CI, 6.8–18.3). Due to MRI-detected lesions (in women who did not have additional malignancy on histology) conversion from wide local excision to mastectomy was 1.1% (95% CI, 0.3–3.6) and from wide local excision to more extensive surgery was 5.5% (95% CI, 3.1–9.5).	4
34. Bahri S, Chen JH, Mehta RS, et al. Residual breast cancer diagnosed by MRI in patients receiving neoadjuvant chemotherapy with and without bevacizumab. *Ann Surg Oncol.* 2009;16(6):1619-1628.	Observational-Dx	36 patients	To investigate the impact of antiangiogenic therapy with bevacizumab on pathological response and the diagnostic performance of MRI in breast cancer patients.	pCR rates and residual disease (nodular and scattered cell) patterns were comparable between the 2 groups. The diagnostic accuracy rate of MRI (true positive and true negative) was 13/17 (76%) for patients with bevacizumab, and 14/20 (70%) for patients without bevacizumab. The size measured on MRI was accurate for mass lesions that shrank down to nodules, showing <0.7 cm discrepancy from pathological size. For residual disease presenting as scattered cells within a large fibrotic region, MRI could not predict them correctly, resulting in a high false-negative rate and a large size discrepancy.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Marinovich ML, Houssami N, Macaskill P, et al. Meta-analysis of magnetic resonance imaging in detecting residual breast cancer after neoadjuvant therapy. *J Natl Cancer Inst.* 2013;105(5):321-333.	Meta-analysis	44 studies including 2050 patients	To examine MRI accuracy in detecting residual tumor, investigate variables potentially affecting MRI performance, and compare MRI with other tests.	44 studies (2050 patients) were included. The overall AUC of MRI was 0.88. Accuracy was lower for "standard" pCR definitions (referent category) than "less clearly described" (relative diagnostic OR = 2.41, 95% CI = 1.11 to 5.23) or "near-pCR" definitions (relative diagnostic OR = 2.60, 95% CI = 0.73 to 9.24; *P*=.03.) Corresponding AUCs were 0.83, 0.90, and 0.91. Specificity was higher when negative MRI was defined as contrast enhancement less than or equal to normal tissue (0.83, 95% CI = 0.64 to 0.93) vs no enhancement (0.54, 95% CI = 0.39 to 0.69; *P*=.02), with comparable sensitivity (0.83, 95% CI = 0.69 to 0.91; vs 0.87, 95% CI = 0.80 to 0.92; *P*=.45). MRI had higher accuracy than mammography (*P*=.02); there was only weak evidence that MRI had higher accuracy than clinical examination (*P*=.10). No difference in MRI and US accuracy was found (*P*=.15).	M
36. Yeh E, Slanetz P, Kopans DB, et al. Prospective comparison of mammography, sonography, and MRI in patients undergoing neoadjuvant chemotherapy for palpable breast cancer. *AJR Am J Roentgenol.* 2005;184(3):868-877.	Observational-Dx	31 patients	Prospective study to determine the relative accuracy of mammography, US, and MRI in predicting residual tumor after NAC for breast cancer as compared with the gold standards of physical examination and pathology.	Agreement rates about the degree of response were 32%, 48%, and 55%, respectively, for mammography, US, and MRI compared with clinical evaluation and did not differ statistically. Agreement about the rate of response as measured by clinical examination, mammography, US, and MRI compared with the gold standard (pathology) was 19%, 26%, 35%, and 71%, respectively. MRI agreed with the gold standard significantly more often (*P*<0.002 for all 3 paired comparisons with MRI).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Kazama T, Nakamura S, Doi O, Suzuki K, Hirose M, Ito H. Prospective evaluation of pectoralis muscle invasion of breast cancer by MR imaging. *Breast Cancer.* 2005;12(4):312-316.	Experimental-Dx	33 breasts	To evaluate the usefulness of breast MRI for the detection of tumor invasion of the pectoralis muscle in breast cancer patients.	In 33 breasts, disruption of the fat plane between tumor and muscle was noted. 7 of 33 cases showed muscle enhancement contiguous to enhanced tumors. Pathology reports indicated that 5 of 7 of the tumors involved muscle invasion. Of the 2 false positive cases, 1 showed muscle enhancement because of a previous biopsy, and the other was incorrectly interpreted as showing muscle enhancement. Of the 26 breasts which did not demonstrate muscle enhancement, none were found at surgery to have tumor involvement.	2
38. Lehman CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. *N Engl J Med.* 2007;356(13):1295-1303.	Experimental-Dx	969 women	To determine whether MRI could improve on clinical breast examination and mammography in detecting contralateral breast cancer soon after the initial diagnosis of unilateral breast cancer.	MRI detected clinically and mammographically occult breast cancer in the contralateral breast in 30/969 women who were enrolled in the study (3.1%). The sensitivity of MRI in the contralateral breast was 91%, and the specificity was 88%. The NPV of MRI was 99%. A biopsy was performed on the basis of a positive MRI finding in 121/969 women (12.5%), 30 of whom had specimens that were positive for cancer (24.8%); 18 of the 30 specimens were positive for invasive cancer. The mean diameter of the invasive tumors detected was 10.9 mm. The additional number of cancers detected was not influenced by breast density, menopausal status, or the histologic features of the primary tumor.	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Mitchell D, Hruska CB, Boughey JC, et al. 99mTc-sestamibi using a direct conversion molecular breast imaging system to assess tumor response to neoadjuvant chemotherapy in women with locally advanced breast cancer. *Clin Nucl Med.* 2013;38(12):949-956.	Experimental-Dx	19 patients	To determine the ability of breast imaging with 99mTc-sestamibi and a direct conversion-molecular breast imaging system to predict early response to NAC.	19 patients completed imaging and proceeded to surgical resection after NAC. Mean reduction in T/B ratio from baseline to 3 to 5 weeks for patients classified as RCB-0 (no residual disease), RCB-1 and RCB-2 combined, and RCB-3 (extensive residual disease) was 56% (SD, 0.20), 28% (SD, 0.20), and 4% (SD, 0.15), respectively. The reduction in the RCB-0 group was significantly greater than in RCB-1/2 (P=0.036) and RCB-3 (P=0.001) groups. The AUC for determining the presence or absence of residual disease was 0.88. Using a threshold of 50% reduction in T/B ratio at 3 to 5 weeks, molecular breast imaging predicted presence of residual disease at surgery with a diagnostic accuracy of 89.5% (95% CI, 0.64%–0.99%), sensitivity of 92.3% (95% CI, 0.74%–0.99%), and specificity of 83.3% (95% CI, 0.44%–0.99%). The reduction in tumor size at 3 to 5 weeks was not statistically different between RCB groups.	2
40. McDermott GM, Welch A, Staff RT, et al. Monitoring primary breast cancer throughout chemotherapy using FDG-PET. *Breast Cancer Res Treat.* 2007;102(1):75-84.	Observational-Dx	96 patients	To determine whether there is an optimal method for defining tumor volume and an optimal imaging time for predicting pathologic chemotherapy response.	Only tumors with an initial tumor to background ratio of greater than 5 showed a difference between response categories. In terms of response discrimination, there was no statistically significant advantage of any of the methods used for image quantification or any of the time points. The best discrimination was measured for mean SUV at the midpoint of therapy, which identified 77% of low responding tumors whilst correctly identifying 100% of high responding tumors and had an ROC area of 0.93.	2

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Schwarz-Dose J, Untch M, Tiling R, et al. Monitoring primary systemic therapy of large and locally advanced breast cancer by using sequential positron emission tomography imaging with [18F]fluorodeoxyglucose. *J Clin Oncol.* 2009;27(4):535-541.	Experimental-Dx	104 patients	To evaluate FDG-PET for prediction of histopathologic response early during primary systemic therapy of large or LABC.	17 (16%) of 104 patients were histopathologic responders and 87 were (84%) nonresponders. All patients for whom baseline SUV was <3.0 (n = 24) did not achieve a histopathologic response. SUV decreased by 51% +/- 18% after the first cycle of chemotherapy in histopathologic responders (n = 15), compared with 37% +/- 21% in nonresponders (n = 54; *P*=.01). A threshold of 45% decrease in SUV correctly identified 11/15 responders, and histopathologic nonresponders were identified with a NPV of 90%. Similar results were found after the second cycle when using a threshold of 55% relative decrease in SUV.	2
42. Kalinyak JE, Berg WA, Schilling K, Madsen KS, Narayanan D, Tartar M. Breast cancer detection using high-resolution breast PET compared to whole-body PET or PET/CT. *Eur J Nucl Med Mol Imaging.* 2014;41(2):260-275.	Observational-Dx	178 women	To compare the performance characteristics of PEM with those of whole-body PET and PET/CT in women with newly diagnosed breast cancer.	The mean age of the women was 59 +/- 12 years (median 60 years, range 26–89 years), with a mean invasive index tumor size of 1.6 +/- 0.8 cm (median 1.5 cm, range 0.5–4.0 cm). PEM detected more index tumors (61/66, 92%) than whole-body PET (37/66, 56%; *P*<0.001) or PET/CT (95/109, 87% vs 104/109, 95% for PEM; *P*<0.029). Sensitivity for the detection of additional ipsilateral malignancies was also greater with PEM (7/15, 47%) than with whole-body PET (1/15, 6.7%; *P*=0.014) or PET/CT (3/23, 13% vs 13/23, 57% for PEM; *P*=0.003). Index tumor detection decreased with decreasing invasive tumor size for both whole-body PET (*P*=0.002) and PET/CT (*P*<0.001); PEM was not significantly affected (*P*=0.20). FDG uptake, quantified in terms of maximum PEM uptake value, was lowest in D (median 1.5, range 0.7–3.0) and ILC (median 1.5, range 0.7–3.4), and highest in grade III IDC (median 3.1, range 1.4–12.9).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Berg WA, Madsen KS, Schilling K, et al. Breast cancer: comparative effectiveness of positron emission mammography and MR imaging in presurgical planning for the ipsilateral breast. *Radiology.* 2011;258(1):59-72.	Experimental-Dx	380 women	To determine the performance of PEM, as compared with MRI, including the effect on surgical management, in ipsilateral breasts with cancer.	388 women (median age, 58 years; age range, 26–93 years; median estimated tumor size, 1.5 cm) completed the study. Additional cancers were found in 82 (21%) women (82 ipsilateral breasts; median tumor size, 0.7 cm). 28 (34%) of the 82 breasts were identified with both PEM and MRI; 21 (26%) breasts, with MRI only; 14 (17%) breasts, with PEM only; and 7 (8.5%) breasts, with mammography and US. 12 (15%) cases of additional cancer were missed at all imaging examinations. Integration of PEM and MRI increased cancer detection to 61 (74%) of 82 breasts vs 49 (60%) of 82 breasts identified with MRI alone (P<.001). Of 306 breasts without additional cancer, 279 (91.2%) were correctly assessed with PEM compared with 264 (86.3%) that were correctly assessed with MRI (P=.03). The PPV of biopsy prompted by PEM findings (47 [66%] of 71 cases) was higher than that of biopsy prompted by MR findings (61 [53%] of 116 cases) (P=.016). Of 116 additional cancers, 61 (53%) were depicted by MRI and 47 (41%) were depicted by PEM (P=.043). 56 (14%) of the 388 women required mastectomy: 40 (71%) of these women were identified with MRI, and 20 (36%) were identified with PEM (P<.001). 11 (2.8%) women underwent unnecessary mastectomy, which was prompted by only MR findings in 5 women, by only PEM findings in 1, and by PEM and MR findings in 5. 33 (8.5%) women required wider excision: 24 (73%) of these women were identified with MRI, and 22 (67%) were identified with PEM.	1

Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Chagpar AB, Middleton LP, Sahin AA, et al. Accuracy of physical examination, ultrasonography, and mammography in predicting residual pathologic tumor size in patients treated with neoadjuvant chemotherapy. *Ann Surg.* 2006;243(2):257-264.	Observational-Dx	189 patients	To assess the accuracy of physical examination, US, and mammography in predicting residual size of breast tumors following NAC.	Size estimates by physical examination, US, and mammography were only moderately correlated with residual pathologic tumor size after NAC (correlation coefficients: 0.42, 0.42, and 0.41, respectively), with an accuracy of +/-1 cm in 66% of patients by physical examination, 75% by US, and 70% by mammography. Kappa values (0.24–0.35) indicated poor agreement between clinical and pathologic measurements.	3
45. Huber S, Medl M, Vesely M, Czembirek H, Zuna I, Delorme S. Ultrasonographic tissue characterization in monitoring tumor response to neoadjuvant chemotherapy in locally advanced breast cancer (work in progress). *J Ultrasound Med.* 2000;19(10):677-686.	Review/Other-Dx	6 patients	To evaluate the effects of NAC on tumor architecture by using a statistical pattern recognition technique demonstrated in 6 patients with LABC.	Characteristic trends of defined quantitative texture parameters (mean gradient, mean gray value, contrast from the co-occurrence matrix) corresponded to visually depictable changes of the B-mode image and underlying histopathologic changes.	4
46. Huber S, Wagner M, Zuna I, Medl M, Czembirek H, Delorme S. Locally advanced breast carcinoma: evaluation of mammography in the prediction of residual disease after induction chemotherapy. *Anticancer Res.* 2000;20(1B):553-558.	Observational-Dx	44 patients	To assess the mammographic features of LABC treated with NAC and to evaluate morphological criteria that determine the value of mammography in therapy monitoring.	Delineation of the tumor proved to be the most significant criterion. In 34 tumors more than 50% of the lesion was defined; these showed a high correlation between the mammographically determined tumor diameter and that determined on histopathological examination (r = 0.77). Less than 50% of the mass was definable in 14 tumors; here the correlation between mammographically and histopathologically determined tumor diameter was low (r = -0.19).	4
47. Helvie MA, Joynt LK, Cody RL, Pierce LJ, Adler DD, Merajver SD. Locally advanced breast carcinoma: accuracy of mammography versus clinical examination in the prediction of residual disease after chemotherapy. *Radiology.* 1996;198(2):327-332.	Observational-Dx	56 women	To determine the mammographic features of LABC treated with NAC and to evaluate the accuracy of mammography in the prediction of residual carcinoma.	54 (96%) of 56 women had a complete (n = 34 [61%]) or partial (n = 20 [36%]) clinical response. 13 (23%) of 56 women had no residual tumor. Sensitivity of mammography in the prediction of residual carcinoma was greater than that of clinical examination (79% vs 49%), but specificity was lower (77% vs 92%). In 24 women with inflammatory carcinoma, sensitivity of mammography was 78% while that of clinical examination was 39%; specificity was equal (83%).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Adrada BE, Huo L, Lane DL, Arribas EM, Resetkova E, Yang W. Histopathologic correlation of residual mammographic microcalcifications after neoadjuvant chemotherapy for locally advanced breast cancer. *Ann Surg Oncol.* 2015;22(4):1111-1117.	Observational-Dx	106 patients	To determine the histopathologic correlation at surgery of residual mammographic calcifications in patients after NAC for LABC.	Of 494 patients who met the inclusion criteria, 106 demonstrated microcalcifications on pre-, post-chemotherapy, or both sets of mammograms and were included in this study. Of 106 women, 31 (29%) had IDC and 60 (57%) had both IDC and DCIS. Microcalcifications decreased or remained stable in 76 (72%) patients after completion of NAC. Correlation of microcalcifications with histopathology after NAC showed that 43 (40.6%) patients had tumors associated with benign pathology. Of 32 patients with pCR, calcifications were associated with DCIS in 9 (9%) and benign findings in 21 (22%). The proportion of residual malignant calcifications was higher in estrogen receptor(+) vs estrogen receptor(–) patients after NAC.	3
49. Weiss A, Lee KC, Romero Y, et al. Calcifications on mammogram do not correlate with tumor size after neoadjuvant chemotherapy. *Ann Surg Oncol.* 2014;21(10):3310-3316.	Review/Other-Dx	136 patients	To examine the correlation between the extent of calcification on mammography and actual tumor size after NAC as well as MRI for comparison.	There were 136 patients total. Average age was 51 years. 53 patients had calcifications on imaging (calc+); 83 did not (calc-). In the calc- group, extent of disease measured by mammogram and MRI correlated moderately well with pathological tumor size (0.46 and 0.48, *P*=not significant). In the calc+ group, MRI was more likely to correlate with pathology than mammogram (0.55 vs -0.12, *P*=0.01). 25 calc+ patients had increased calcification after NAC; 6 of these had complete pathologic response. MRI correlated better with tumor size on pathology in patients with anti-HER2neu-based regimens than in patients with cytotoxic chemotherapy-alone regimens (0.88 vs 0.4, *P*=0.0001). MRI also is more accurate at predicting pathological tumor size in patients with triple negative disease (*P*=0.002).	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Ollivier L, Balu-Maestro C, Leclere J. Imaging in evaluation of response to neoadjuvant breast cancer treatment. *Cancer Imaging.* 2005;5:27-31.	Review/Other-Dx	N/A	To compare the value of the different conventional and functional imaging techniques for determining response to NAC in breast cancer treatment.	Physical examination and conventional imaging techniques still have an important place in the evaluation of breast cancer treated by NAC. At this time, this morphologic evaluation is the only 1 recognized by the international criteria. The new functional and metabolic imaging modalities, particularly MRI and PET scan, can approach the nature of residual tumor, allow early detection of bad responders and depict multifocal tumors and metastases. The use of these techniques can change the planning of therapy.	4
51. Roubidoux MA, LeCarpentier GL, Fowlkes JB, et al. Sonographic evaluation of early-stage breast cancers that undergo neoadjuvant chemotherapy. *J Ultrasound Med.* 2005;24(7):885-895.	Experimental-Dx	34 women	To evaluate low-stage breast cancers treated with NAC using whole-volume US and color Doppler imaging.	3 (11.3%) of 34 patients had a complete histologic response. After chemotherapy, correlation was r = 0.716 between final histologic and sonographic sizes. Compared with histologic residual tumors, US had 4 false-negative results, 3 false-positive results, and 27 true-positive results (sensitivity, 87%), with no false-negative results among a subgroup of tumors of 7 mm and larger (sensitivity, 100%). The 3 cases with false-positive results were histologic fibrosis or biopsy changes. Mean speed-weighted density was 0.015 before and 0.0082 after chemotherapy (P=.03). After chemotherapy, vascularity was less common within (P=.06) or adjacent to (P=.009) masses or in tumor sites (P=.05). Pre-chemotherapy variables of gray scale characteristics and vascularity were compared with final histologic size, and all had P>.20.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Croshaw R, Shapiro-Wright H, Svensson E, Erb K, Julian T. Accuracy of clinical examination, digital mammogram, ultrasound, and MRI in determining postneoadjuvant pathologic tumor response in operable breast cancer patients. *Ann Surg Oncol.* 2011;18(11):3160-3163.	Observational-Dx	61 patients	To determine the accuracy, PPV, and NPV of clinical examination and breast imaging techniques in determining pCR in patients with LABC after neoadjuvant therapy.	62 tumors in 61 patients with a mean age of 56 (range 34–87) years were evaluated. Overall accuracy ranged from 54% (clinical breast examination) to 80% (breast US). All modalities had a PPV >75% for identifying the presence of residual disease. The PPV of each modality was generally higher in the younger patients. The NPV of all methods was <50%. The accuracy and NPV were compromised even further in younger patients. The combination of our own data with data available from the literature revealed MRI to be superior with regard to accuracy and PPV, but the NPV of MRIs remained poor at 65%.	3
53. Keune JD, Jeffe DB, Schootman M, Hoffman A, Gillanders WE, Aft RL. Accuracy of ultrasonography and mammography in predicting pathologic response after neoadjuvant chemotherapy for breast cancer. *Am J Surg.* 2010;199(4):477-484.	Observational-Dx	192 patients	To assess the ability of mammography and US to predict residual tumor size following NAC.	192 patients with 196 primary breast cancers were studied. Of 104 tumors evaluated by both imaging modalities, US was able to size 91.3%, and mammography was able to size only 51.9% (chi(2)P<.001). US also was more accurate than mammography in estimating residual tumor size (62/104 [59.6%] vs 33/104 [31.7%], P<.001). There was little difference in the ability of mammography and US to predict pCR (ROC, 0.741 vs 0.784).	3
54. Evans A, Armstrong S, Whelehan P, et al. Can shear-wave elastography predict response to neoadjuvant chemotherapy in women with invasive breast cancer? *Br J Cancer.* 2013;109(11):2798-2802.	Observational-Dx	40 patients	To ascertain whether tissue stiffness in breast cancers, as assessed by shear-wave elastography before treatment, is associated with response.	Statistically significant correlations were shown between stiffness and RCB scores and between stiffness and percentage tumor cellularity. The correlation between stiffness and percentage cellularity was strongest (correlation coefficient 0.35 (P<0.0001) compared with correlation coefficient 0.23 (P=0.004) for the RCB score). The results of a general linear model show that cellularity and RCB score maintain independent relationships with stiffness. By multiple linear regression, only cellularity maintained a significant relationship with stiffness.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Hayashi M, Yamamoto Y, Ibusuki M, et al. Evaluation of tumor stiffness by elastography is predictive for pathologic complete response to neoadjuvant chemotherapy in patients with breast cancer. *Ann Surg Oncol.* 2012;19(9):3042-3049.	Observational-Dx	55 patients	To evaluate if tumor stiffness by elastography has the potential to provide additional information useful in predicting the response to chemotherapy in clinical setting.	The mean elastography scores were significant lower for the clinical and pCR groups than for the others. When we categorized patients into 2 groups according to tumor stiffness, 26 patients were assigned to the low elastography group (soft, scores from 1 to 3) and 29 patients were assigned to the high elastography group (hard, score 4 and 5). The low elastography group had significantly higher clinical complete response and pCR rates than the high elastography group (clinical complete response, low elastography group 38% vs high elastography group 10%, P=0.024; pCR, low elastography group 50% vs high elastography group 14%, P=0.003, respectively). Furthermore, multivariate analysis indicated that estrogen receptor, HER2, and low elastography (odds ratio 13.04, 95% CI 1.19-458.28, P=0.035) were independent predictive factors of pCR.	3
56. Cao X, Xue J, Zhao B. Potential application value of contrast-enhanced ultrasound in neoadjuvant chemotherapy of breast cancer. *Ultrasound Med Biol.* 2012;38(12):2065-2071.	Observational-Dx	31 patients	To investigate the value of contrast-enhanced US in evaluating the response of breast cancer to NAC.	All patients were evaluated by both conventional US and contrast-enhanced US. The tumor sizes measured by contrast-enhanced US were larger and more accurately imaged than those evaluated by US. Necrosis at the tumor center could be detected by contrast-enhanced US, which showed a local blood perfusion defect in 26 cases (83.9%) before NAC and 27 cases (87.1%) after NAC, whereas US did not show liquefaction in any patient. The contrast-enhanced US time-intensity curve displayed quantitatively the tumors' blood-perfusion changes; after NAC, blood perfusion reduced, enhancement intensity decreased, time to peak increased, peak intensity reduced, and the wash-in slope reduced (P<0.05).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Belli P, Costantini M, Malaspina C, Magistrelli A, LaTorre G, Bonomo L. MRI accuracy in residual disease evaluation in breast cancer patients treated with neoadjuvant chemotherapy. *Clin Radiol.* 2006;61(11):946-953.	Observational-Dx	45 women	To assess the accuracy of MRI in evaluating residual disease after NAC in patients with large breast cancers.	The sensitivity, specificity and accuracy of MRI in detecting residual disease was 90.5%, 100%, and 91.3%, respectively. The mean of largest diameters measured at histology and at MRI were 26 and 28.2mm, respectively. The tumor size correlation coefficient between MRI and pathology measurements was very high: r(2)=0.9657 (P<0.0001). The interclass correlation coefficient between preoperative imaging measurements and pathological measurements of residual disease was 0.944 (95% CI: 0.906–0.982).	2
58. Hollingsworth AB, Stough RG, O'Dell CA, Brekke CE. Breast magnetic resonance imaging for preoperative locoregional staging. *Am J Surg.* 2008;196(3):389-397.	Observational-Dx	603 patients	To correlate histology and breast MRI findings.	Reoperation for positive margins after lumpectomy occurred in 8.8% of patients. Multicentricity was identified by MRI alone in 7.7% of patients, whereas 3.7% were found to have contralateral cancer by MRI. The sensitivity of MRI was 93% in detecting multicentric disease and 88% for contralateral disease, whereas sensitivity for conventional imaging was 46% and 19%, respectively. Unsuspected disease was identified by MRI equally for IDC and DCIS histology, whereas multicentricity was found more frequently with ILC.	3
59. Yuan Y, Chen XS, Liu SY, Shen KW. Accuracy of MRI in prediction of pathologic complete remission in breast cancer after preoperative therapy: a meta-analysis. *AJR Am J Roentgenol.* 2010;195(1):260-268.	Meta-analysis	25 studies	To determine the ability of MRI to predict pCR in patients with breast cancer after preoperative therapy.	25 studies were included in this meta-analysis. Pooled weighted estimates of sensitivity and specificity were 0.63 (range, 0.56–0.70) and 0.91 (range, 90.89–0.92), respectively. Heterogeneity between studies was highly influenced by the pCR rate, with a regression coefficient of -6.160 (P=0.020). Subgroup analysis showed that the specificity of MRI in studies with a pCR rate of ≥20% was lower than that in studies with a pCR rate of <20% (P=0.0003).	M

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
60. Semiglazov V. RECIST for Response (Clinical and Imaging) in Neoadjuvant Clinical Trials in Operable Breast Cancer. *J Natl Cancer Inst Monogr.* 2015;2015(51):21-23.	Review/Other-Dx	N/A	To review the RECIST criteria for response in neoadjuvant clinical trials in operable breast cancer.	MRI is superior to physical examination, US, and mammography in response evaluation during neoadjuvant systemic therapy. The accuracy of breast MRI to predict pCR has a moderate sensitivity, but high specificity. The accuracy of anatomic imaging to assess residual disease and predict pCR depended on anatomic radiographic imaging cancer subtypes. Response monitoring using breast is accurate in triple-negative or HER2-positive tumors. It was inaccurate in estrogen receptor-positive/HER2-negative subtype. Another approach currently under investigation is dynamic contrast-enhanced MRI and diffusion weighted-imaging, FDG-PET, FDG-PET/CT.	4
61. Straver ME, Loo CE, Rutgers EJ, et al. MRI-model to guide the surgical treatment in breast cancer patients after neoadjuvant chemotherapy. *Ann Surg.* 2010;251(4):701-707.	Observational-Dx	208 patients	To establish an MRI-based interpretation model to facilitate the selection of breast-conserving surgery after NAC.	The accuracy of MRI to detect residual disease was 76% (158/208). The PPV and NPV of MRI were 90% (130/144) and 44% (28/64), respectively. In 35 patients (17%), MRI underestimated the tumor size by >20 mm and in 27 patients (13%) this would have led to incorrect indication of breast-conserving surgery. The features most predictive of indicating feasibility of breast-conserving surgery in tumors <30 mm on preoperative MRI were the largest diameter at the baseline MRI, the reduction in diameter and the tumor subtype based on hormone-, and HER2- (AUC: 0.78).	3
62. Vriens BE, de Vries B, Lobbes MB, et al. Ultrasound is at least as good as magnetic resonance imaging in predicting tumour size post-neoadjuvant chemotherapy in breast cancer. *Eur J Cancer.* 2016;52:67-76.	Observational-Dx	182 patients	To evaluate the accuracy of clinical imaging of the primary breast tumor post-NAC related to the post-neoadjuvant histological tumor size (gold standard) and whether this varies with breast cancer subtype.	MRI estimated residual tumor size with <10-mm discordance in 54% of patients, overestimated size in 28% and underestimated size in 18% of patients. With US, this was 63%, 20% and 17%, respectively. The NPV in hormone receptor-positive tumors for both MRI and US was low, 26% and 33%, respectively. The median deviation in clinical tumor size as percentage of pathological tumour was 63% (P25=26, P75=100) and 49% (P25=22, P75=100) for MRI and US, respectively (P=0.06).	3

Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
63. Hylton N. MR imaging for the prediction of breast cancer response to neoadjuvant chemotherapy. *Radiology.* 2013;266(1):367.	Review/Other-Dx	N/A	Response to comments regarding the results of the American College of Radiology Imaging Network (ACRIN) 6657/Investigation of Serial Studies to Predict Your Therapeutic Response with Imaging and Molecular Analysis (I-SPY TRIAL) breast cancer trial.	No results stated in abstract.	4
64. Akazawa K, Tamaki Y, Taguchi T, et al. Preoperative evaluation of residual tumor extent by three-dimensional magnetic resonance imaging in breast cancer patients treated with neoadjuvant chemotherapy. *Breast J.* 2006;12(2):130-137.	Observational-Dx	38 patients	To evaluate the usefulness of 3D MRI for the preoperative assessment of residual tumor extent in breast cancer patients treated with NAC.	The tumor size determined by calipers, US, and 3D MRI after NAC was compared with that determined by pathologic examination. The tumor size determined by 3D MRI showed a strong correlation with that determined by pathologic examination (r = 0.896). Moderate, but significant correlations were found between measurements obtained with calipers and pathology (r = 0.554), and between US and pathology (r = 0.484). The response rates to NAC were estimated at 84.2% with calipers, 58.0% with US, and 44.7% with 3D MRI. Calipers and US thus tended to overestimate the response to NAC compared to 3D MRI (P<0.001 and 0.240, respectively).	2
65. Loo CE, Teertstra HJ, Rodenhuis S, et al. Dynamic contrast-enhanced MRI for prediction of breast cancer response to neoadjuvant chemotherapy: initial results. *AJR Am J Roentgenol.* 2008;191(5):1331-1338.	Observational-Dx	54 patients	To establish changes in contrast-enhanced MRI of breast cancer during NAC that is indicative of pathology outcome.	Change in largest diameter of late enhancement during chemotherapy was the single most predictive MRI characteristic for tumor response in multivariate analysis (A(z) [AUC] = 0.73, P<0.00001). Insufficient (<25%) decrease in largest diameter of late enhancement during chemotherapy was most indicative of residual tumor at final pathology. Using this criterion, the fraction of unfavorable responders indicated by MRI was 41% (22/54). Approximately half (44%, 14/32) of the patients who showed favorable response at MRI achieved complete remission at pathology. Conversely, 95% (21/22) of patients who showed unfavorable response at MRI had residual tumor at pathology.	3

Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
66. Cheung YC, Chen SC, Hsieh IC, et al. Multidetector computed tomography assessment on tumor size and nodal status in patients with locally advanced breast cancer before and after neoadjuvant chemotherapy. *Eur J Surg Oncol.* 2006;32(10):1186-1190.	Observational-Dx	28 patients	To evaluate the utility of multidetector CT in assessing tumor size and nodal status in patients with advanced breast cancers before and after the NAC.	The multidetector CT measurements documented complete response in 3, partial response in 18, nonresponse in 8, and progressed in 1. The mean tumor diameters on pathology and post-chemotherapy multidetector CT were 3.6cm (SD = +/-2.9cm) and 3.1cm (SD = +/-2.6cm), respectively. The Pearson correlation coefficient was 0.76 (P<0.001). The sensitivity, specificity, PPV, NPV and accuracy of multidetector CT in diagnosing the axillary lymph node metastases after preoperative NAC were counted, respectively, to 72%, 40%, 85.7%, 22.2% and 66.7%. All the 5 downstaged axillary nodal statuses from node-positive to node-negative on multidetector CT had micrometastases.	2
67. Danishad KK, Sharma U, Sah RG, Seenu V, Parshad R, Jagannathan NR. Assessment of therapeutic response of locally advanced breast cancer (LABC) patients undergoing neoadjuvant chemotherapy (NACT) monitored using sequential magnetic resonance spectroscopic imaging (MRSI). *NMR Biomed.* 2010;23(3):233-241.	Observational-Dx	30 patients	To (a) investigate, the systematic changes in the SNR of tCho resonance (ChoSNR) using MRSI and the anatomical parameter (volume) of the tumor in LABC patients, and (b) determine the potential clinical utility of these parameters in the assessment of tumor response during the various stages of NACT.	Sequential data of 25 patients were retrospectively analyzed by classifying them as clinical responders and nonresponders. In 14 responders, the pre-therapy ChoSNR was 7.8 +/- 5.1. In 10/14 responders, no choline was observed after III NACT while in the remaining 4 patients the ChoSNR was reduced to 3.6 +/- 1.1 (P<0.05). Nonresponders showed no statistically significant change in ChoSNR. After III NACT, the tumor volume reduced by 84.0 +/- 14.8% in responders. Using ROC analysis, cut-off values of 53% for ChoSNR and 47.5% for volume were obtained to differentiate responders from nonresponders. The sensitivity to detect responders from nonresponders using ChoSNR was 85.7% with 91% specificity while 100% sensitivity was observed for volume but with reduced specificity of 73%.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Delille JP, Slanetz PJ, Yeh ED, Halpern EF, Kopans DB, Garrido L. Invasive ductal breast carcinoma response to neoadjuvant chemotherapy: noninvasive monitoring with functional MR imaging pilot study. *Radiology.* 2003;228(1):63-69.	Observational-Dx	14 women	To investigate if the extraction flow product (EFP), as determined on dynamic contrast material-enhanced MRI, could be a potential marker of tumor response to NAC in patients with LABC.	Extraction flow product-mean after NAC in partial responders and nonresponders was 33 mL x 100 g-1 x min-1 +/- 9.8 and 54.2 mL x 100 g-1 x min-1 +/- 10.3, respectively (*P*<.005). Extraction flow product-mean decreased after NAC in the responders and nonresponders by 37% +/- 30 and -5% +/- 35, respectively (*P*>.05). An increase in extraction flow product-mean values was observed only in nonresponders who received taxanes. For regimens without taxanes, extraction flow product-mean decreased regardless of the morphologic response. Extraction flow product-mean decreased for all the responders by 77% +/- 33 and increased for all the nonresponders by 45% +/- 68 (*P*<.02).	3
69. Marinovich ML, Sardanelli F, Ciatto S, et al. Early prediction of pathologic response to neoadjuvant therapy in breast cancer: systematic review of the accuracy of MRI. *Breast.* 2012;21(5):669-677.	Review/Other-Dx	13 studies	To examine the evidence on MRI's accuracy in early prediction of pathologic response, including comparisons with alternative assessment methods.	Thresholds for identifying response varied across studies. Definitions of response included pCR, near-pCR, and residual tumor with evidence of NAC effect (range of response 0%–58%). Heterogeneity across MRI parameters and the outcome definition precluded statistical meta-analysis. Based on descriptive presentation of the data, sensitivity/specificity pairs for prediction of pathologic response were highest in studies measuring reductions in Ktrans (near-pCR), early contrast uptake (pCR, but not near-pCR) and tumor volume (pCR or near-pCR), at high thresholds (typically >50%); lower sensitivity/specificity pairs were evident in studies measuring reductions in uni- or bi-dimensional tumor size.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
70. Padhani AR, Hayes C, Assersohn L, et al. Prediction of clinicopathologic response of breast cancer to primary chemotherapy at contrast-enhanced MR imaging: initial clinical results. *Radiology.* 2006;239(2):361-374.	Experimental-Dx	21 women	To prospectively document changes in contrast agent kinetics in patients with primary breast cancer treated with systemic chemotherapy after 1 or 2 cycles and to determine whether kinetic measures can be used to predict final clinicopathologic response.	After the first cycle of treatment, 12/14 clinical responders showed decreases in tumor size, and 6 of 7 nonresponders showed increases or no change in tumor size (P<.001). Transfer constant changes did not differ between responders and nonresponders for either clinical or pathologic assessments. After 2 cycles of treatment, there were tumor size increases in 5 of 6 nonresponders compared with decreases in 8 of 9 responders (P<.001). Reductions in transfer constant range were also observed in responders for both clinical and pathologic assessments (P=.008 and .02, respectively). No other kinetic parameter change predicted response. Size and transfer constant range were equally accurate for predicting the absence of pathologic response after 2 cycles of treatment (sensitivity, specificity, and AUC were 100%, 90%, and 0.93, respectively, for size and 100%, 75%, and 0.94, respectively, for transfer constant range).	2
71. Abramson RG, Li X, Hoyt TL, et al. Early assessment of breast cancer response to neoadjuvant chemotherapy by semi-quantitative analysis of high-temporal resolution DCE-MRI: preliminary results. *Magn Reson Imaging.* 2013;31(9):1457-1464.	Experimental-Dx	21 patients	To evaluate whether semi-quantitative analysis of high temporal resolution dynamic contrast-enhanced MRI acquired early in treatment can predict the response of LABC to NAC.	All 21 patients completed NAC followed by surgery, with 9 patients achieving a pCR. No pretreatment imaging parameters were predictive of pCR. However, change after cycle 1 of NAC in percentage of voxels demonstrating washout kinetics with a 100% enhancement filter discriminated patients with an eventual pCR with an AUC of 0.77. Changes in other parameters, including lesion size, did not predict pCR.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
72. Belli P, Costantini M, Ierardi C, et al. Diffusion-weighted imaging in evaluating the response to neoadjuvant breast cancer treatment. *Breast J.* 2011;17(6):610-619.	Observational-Dx	51 women	To investigate the role of diffusion imaging in the evaluation of response to neoadjuvant breast cancer treatment by correlating ADC value changes with pathological response.	51 women (mean age 48.41 years) were included in this study. Morphological MRI (RECIST classification) well evaluated the responder status after chemotherapy (TRG class; AUC 0.865). Mean pretreatment ADC values obtained with the 2 different methods of region of interest placement were 1.11 and 1.02 x 10(-3) mm(2) /seconds. Mean post-treatment ADC values were 1.40 and 1.35 x 10(-3) mm(2) /seconds, respectively. A significant inverse correlation between mean ADC increase and Mandard's classifications was observed for both the methods of ADC measurements. Diagnostic performance analysis revealed that the single region of interest method has a superior diagnostic accuracy compared with the multiple region of interest method (accuracy: 82% vs 74%).	3
73. Fangberget A, Nilsen LB, Hole KH, et al. Neoadjuvant chemotherapy in breast cancer-response evaluation and prediction of response to treatment using dynamic contrast-enhanced and diffusion-weighted MR imaging. *Eur Radiol.* 2011;21(6):1188-1199.	Observational-Dx	31 patients	To explore the predictive value of MRI parameters and tumor characteristics before NAC and to compare changes in tumor size and tumor ADC during treatment, between patients who achieved pCR and those who did not.	Before NAC, HER2 overexpression was the single significant predictor of pCR (P=0.006). At Tp1 ADC, tumor size and changes in tumor size were all significantly different in the pCR and non-pCR groups. Using 1.42 x 10(-3) mm(2)/s as the cut-off value for ADC, pCR was predicted with sensitivity and specificity of 88% and 80%, respectively. Using a cut-off value of 83% for tumor volume reduction, sensitivity and specificity for pCR were 91% and 80%.	2
74. Iwasa H, Kubota K, Hamada N, Nogami M, Nishioka A. Early prediction of response to neoadjuvant chemotherapy in patients with breast cancer using diffusion-weighted imaging and gray-scale ultrasonography. *Oncol Rep.* 2014;31(4):1555-1560.	Observational-Dx	24 female patients	To evaluate the utility of the pretreatment ADC, which is calculated from DWI, the change in ADC after first administration of NAC, and the change in tumor greatest diameter on US in the early prediction of the tumor response to NAC.	Pearson's correlation test showed a significant correlation between% ADC and the response rate (r=0.597, P=0.016); none of the other 3 independent variables were correlated with the response rate. Therefore, only% ADC was evaluated by ROC analysis. The AUC of% ADC to differentiate between responders and nonresponders on ROC analysis was 0.90 [95% CI, 0.760–1.040]. Breast cancer lesions with high% ADC values responded to NACT, while those with low% ADC values did not.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
75. Sharma U, Danishad KK, Seenu V, Jagannathan NR. Longitudinal study of the assessment by MRI and diffusion-weighted imaging of tumor response in patients with locally advanced breast cancer undergoing neoadjuvant chemotherapy. *NMR Biomed.* 2009;22(1):104-113.	Experimental-Dx	56 patients with LABC, 10 patients with benign tumors, and 15 controls	To evaluate tumor response according to various MR parameters, such as ADC, volume and longest diameter, during the course of various cycles of NAC in a large cohort of patients with LABC.	Mean ADC before treatment of malignant breast tissue was significantly lower than that of controls, disease-free contralateral tissue of the patients, and benign lesions, and gradually increased during the course of NAC. Analysis of the percentage change in ADC, volume and diameter after each cycle of NAC between clinical responders and nonresponders showed that the change in ADC after the first cycle was statistically significant compared with volume and diameter, indicating its potential in assessing early response. After the third cycle, the sensitivity for differentiating responders from nonresponders was 89% for volume and diameter and 68% for ADC, and the respective specificities were 50%, 70% and 100%. A sensitivity of 84% (specificity of 60% with an accuracy of 76%) was achieved when all 3 variables were taken together to predict the response. A cut-off value of ADC was also calculated using ROC analysis to discriminate between normal, benign and malignant breast tissue. Similarly, a cut-off value for ADC, volume and diameter was obtained after the second and third cycles of NAC to predict tumor response.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Shin HJ, Baek HM, Ahn JH, et al. Prediction of pathologic response to neoadjuvant chemotherapy in patients with breast cancer using diffusion-weighted imaging and MRS. *NMR Biomed.* 2012;25(12):1349-1359.	Observational-Dx	90 patients	To determine whether tumor size, MRSI parameters and ADC measurements could be applied to predict pCR after NAC.	After NAC, 30 patients (33%) showed pCR and 60 (67%) showed non-pCR. At pretreatment, ADC was the only significant parameter in differentiating between pCR and non-pCR [(0.83 +/- 0.05) x 10(-)(3) vs (0.97 +/- 0.14) x 10(-)(3) mm(2)/s] (P=0.014). Post-treatment measurements after completion of NAC and changes in tumor size (both P<0.001), MRSI parameters (P=0.027 and P=0.020 for absolute tCho integral, P=0.036 and P=0.023 for normalized tCho integral, and P=0.032 and P=0.061 for tCho SNR) and ADC (P=0.003 and P<0.001) were significantly different between the pCR and non-pCR groups, except for changes in tCho SNR. In ROC analysis, theAUCs of 0.63–0.73 were obtained for tumor size and MRSI parameters. AUCs for pre- and post-treatment ADC and changes in ADC were 0.75, 0.80 and 0.96, respectively. The optimal cut-off of the percentage change in ADC for predicting pCR was 40.7%, yielding 100% sensitivity and 91% specificity.	3
77. Park SH, Moon WK, Cho N, et al. Diffusion-weighted MR imaging: pretreatment prediction of response to neoadjuvant chemotherapy in patients with breast cancer. *Radiology.* 2010;257(1):56-63.	Observational-Dx	53 patients	To evaluate the potential of DWI MRI with an ADC map in the prediction of response to NAC in patients with breast cancer.	After chemotherapy, 36 (68%) patients were classified as responders, and 17 (32%) were classified as nonresponders. Pretreatment mean ADC ([1.036 +/- 0.015] x 10(-3) mm(2)/sec [standard error]) of responders was significantly lower than that of nonresponders ([1.299 +/- 0.079] x 10(-3) mm(2)/sec) (P=.004). Furthermore, mean percentage ADC increase of responders (47.9% +/- 4.8) was higher than that of nonresponders (18.1% +/- 4.5) (P<.001). The best pretreatment ADC cutoff with which to differentiate between responders and nonresponders was 1.17 x 10(-3) mm(2)/sec, which yielded a sensitivity of 94% (95% CI: 81%, 99%) and a specificity of 71% (95% CI: 44%, 90%).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
78. Hahn SY, Ko EY, Han BK, Shin JH, Ko ES. Role of diffusion-weighted imaging as an adjunct to contrast-enhanced breast MRI in evaluating residual breast cancer following neoadjuvant chemotherapy. *Eur J Radiol.* 2014;83(2):283-288.	Observational-Dx	78 patients	To investigate whether the addition of DWI to dynamic contrast-enhanced MRI improves diagnostic performance in predicting pathologic response and residual breast cancer size following NAC.	Of the 78 patients, 59 (75.6%) had residual cancer. For detection of residual cancer, dynamic contrast-enhanced MRI plus DWI had higher specificity (80.0%), accuracy (91.0%), and PPV (93.2%) than dynamic contrast-enhanced MRI or DWI alone (P=0.004, P=0.007, and P=0.034, respectively). The interclass correlation coefficient values for residual cancer size between MRI and histopathology were 0.891 for dynamic contrast-enhanced MRI plus DWI, 0.792 for dynamic contrast-enhanced MRI, and 0.773 for DWI. ADC values showed no significant differences between residual cancer and chemotherapeutic changes (P=0.130).	2
79. Chen JH, Bahri S, Mehta RS, et al. Impact of factors affecting the residual tumor size diagnosed by MRI following neoadjuvant chemotherapy in comparison to pathology. *J Surg Oncol.* 2014;109(2):158-167.	Observational-Dx	98 patients	To investigate accuracy of MRI for measuring residual tumor size in breast cancer patients receiving NAC.	The mean (+/-SD) of the absolute difference between MRI and pathological residual tumor size was 1.0 +/- 2.0 cm (range, 0–14 cm). Univariate regression analysis showed tumor type, morphology, hormone receptor status, HER2 status, and MRI scanner (1.5 T or 3.0 T) were significantly associated with MRI-pathology size discrepancy (all P<0.05). Multivariate regression analyses demonstrated that only tumor type, tumor morphology, and biomarker status considering both hormone receptor and HER2 were independent predictors (P=0.0014, 0.0032, and 0.0286, respectively).	2
80. De Los Santos JF, Cantor A, Amos KD, et al. Magnetic resonance imaging as a predictor of pathologic response in patients treated with neoadjuvant systemic treatment for operable breast cancer. Translational Breast Cancer Research Consortium trial 017. *Cancer.* 2013;119(10):1776-1783.	Observational-Dx	746 women	To estimate the accuracy of preoperative MRI in predicting a pCR in the breast.	For the total group, the radiographic complete response and pCR rates were 182/746 patients (24%) and 179/746 patients (24%), respectively, and the highest pCR rate was observed for the triple-negative subtype (57/155 patients; 37%) and the HER2-positive subtype (38/101 patients; 38%). The overall accuracy of MRI for predicting pCR was 74%. The variables sensitivity, NPV, PPV, and accuracy differed significantly among tumor subtypes, and the greatest NPV was observed in the triple-negative (60%) and HER2-positive (62%) subtypes.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
81. Londero V, Bazzocchi M, Del Frate C, et al. Locally advanced breast cancer: comparison of mammography, sonography and MR imaging in evaluation of residual disease in women receiving neoadjuvant chemotherapy. *Eur Radiol.* 2004;14(8):1371-1379.	Experimental-Dx	15 patients	The purpose of this study was to evaluate the diagnostic accuracy of different imaging methods (mammography, breast US and breast MRI) in the assessment of neoplastic residual tissue and the ability of each imaging method in the evaluation of the real extent of the disease after NAC in patients affected by LABC.	MRI identified 2/15 (13.3.%) clinically complete response, 9/15 (60%) partial response, 3/15 (20%) stable disease and 1/15 (6.7%) progressive disease. Mammography identified 1/15 (6.7%) clinically complete response, 8/15 (53.3%) partial response and 4/15 (27%) stable disease, and was not able to evaluate the disease in 2/15 (13%) cases. US presented the same results as MRI. Therefore, MRI and US compared to mammography correctly identified residual disease in 100% vs 86%. MRI resulted in 2 false-negative results because of the presence of microfoci of DCIS and ILC. MRI was superior to mammography in cases of multifocal or multicentric disease (83 vs 33%). US performed after MRI improves the accuracy in evaluation of uncertain foci of multifocal disease seen on MR images with an increase of diagnostic accuracy from 73% to 84.5%.	2
82. Mann RM. The effectiveness of MR imaging in the assessment of invasive lobular carcinoma of the breast. *Magn Reson Imaging Clin N Am.* 2010;18(2):259-276, ix.	Review/Other-Dx	N/A	To determine the effectiveness of MRI in the assessment of ILC of the breast	No results stated in abstract.	4
83. McGuire KP, Toro-Burguete J, Dang H, et al. MRI staging after neoadjuvant chemotherapy for breast cancer: does tumor biology affect accuracy? *Ann Surg Oncol.* 2011;18(11):3149-3154.	Observational-Dx	203 patients	To determine the difference between tumor size as estimated by postchemotherapy MRI vs final surgical pathology, and to determine if the accuracy of MRI varies with tumor subtype.	203/592 patients undergoing surgery after NAC for breast cancer had MRI staging pre- and post-chemotherapy. All patients had intact tumors prior to the initiation of chemotherapy. Average tumor size by MRI was 4.0 cm pre-chemotherapy and 1.2 cm post-chemotherapy. The average pathologic tumor size was 1.7 cm (range 0–13 cm). The difference between MRI and pathologic tumor size was greatest in luminal (1.1 cm) and least in triple-negative and HER2-positive tumors (<0.1 cm) (P=0.015). MRI was a good discriminator for pCR [AUC 0.777]. Its predictive value for pCR was much greater in triple-negative and estrogen receptor-/HER2-positive than in luminal tumors (73.6% vs 27.3%)	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
84. Michishita S, Kim SJ, Shimazu K, et al. Prediction of pathological complete response to neoadjuvant chemotherapy by magnetic resonance imaging in breast cancer patients. *Breast.* 2015;24(2):159-165.	Observational-Dx	229 patients	To evaluate whether the baseline breast MRI findings would be useful for the prediction for pCR by breast cancer patients to NAC.	Before chemotherapy, breast MRI studies were performed. Breast tumors were dichotomized into round + oval and irregular types based on MRI morphology. The round + oval tumors showed a significantly higher pCR rate than the irregular tumors (42.0% vs 17.3%; $P<0.001$). In addition, PAM50 analysis revealed that basal and HER2-enriched tumors were significantly more prevalent among round + oval than irregular type tumors ($P=0.015$).	3
85. Richard R, Thomassin I, Chapellier M, et al. Diffusion-weighted MRI in pretreatment prediction of response to neoadjuvant chemotherapy in patients with breast cancer. *Eur Radiol.* 2013;23(9):2420-2431.	Observational-Dx	118 women	To evaluate the accuracy of the ADC provided by DWI in predicting the response to NAC at baseline in patients according to their breast tumor phenotypes.	After surgery, the pathologist recognized 24 complete responders and 94 non-complete responders. No difference was identified between the pretreatment ADCs of the complete responders and non-complete responder's patients. There were differences in pretreatment ADCs among the luminal A (1.001 +/- 0.143 x 10(-3) mm(2)/s), luminal B (0.983 +/- 0.150 x 10(-3) mm(2)/s), HER2-enriched (1.132 +/- 0.216 x 10(-3) mm(2)/s), and triple-negative (1.168 +/- 0.245 x 10(-3) mm(2)/s; $P=0.0003$) tumor subtypes. In triple-negative tumors, the pretreatment ADC was higher in non-complete responders (1.060 +/- 0.143 x 10(-3) mm(2)/s) than in complete responders patients (1.227 +/- 0.271 x 10(-3) mm(2)/s; $P=0.047$).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
86. Schelfout K, Van Goethem M, Kersschot E, et al. Preoperative breast MRI in patients with invasive lobular breast cancer. *Eur Radiol.* 2004;14(7):1209-1216.	Observational-Dx	26 women	To compare findings on preoperative MRI with mammography and US in 26 patients with ILC, using results from histopathological examination as gold standard.	Most ILC presented on MRI as a single spiculated/irregular, inhomogeneous mass (pattern 1, n=12) or as a dominant lesion surrounded by multiple small enhancing foci (pattern 2, n=8). Multiple small enhancing foci with interconnecting enhancing strands (pattern 3) and an architectural distortion (pattern 4) were both described in 3 cases. There was 1 case of a focal area of inhomogeneous enhancement (pattern 5) and 1 normal MR examination (pattern 6). Unifocal and multifocal lesions were identified on MRI in 4 patients with normal conventional imaging. In 9 women, multiple additional lesions or more extensive multiquadrant disease were correctly identified only on MRI.	3
87. Yeh ED, Slanetz PJ, Edmister WB, Talele A, Monticciolo D, Kopans DB. Invasive lobular carcinoma: spectrum of enhancement and morphology on magnetic resonance imaging. *Breast J.* 2003;9(1):13-18.	Review/Other-Dx	19 patients	To determine if there are specific morphologic and enhancement features that favor the diagnosis of ILC by retrospectively reviewing 19 patients with pathologically confirmed ILC and preoperative MRI.	For the 15 cases of ILC that had echoplanar data, analysis showed peak extraction flow ranging between 25 and 120, and the majority showed extraction flows in the 30s. A substantial portion of 2 tumors enhanced in a similar fashion to normal breast tissue, with extraction flows in the low 20s. Morphologically MRI showed a focal mass in 8 cases, regional enhancement in 5, segmental enhancement in 1, segmental enhancement with multiple small nodules in 1, a mixture of a focal mass and regional enhancement in 1, diffuse enhancement in 1, multiple small nodules in 1, and bilateral disease in 1. Of the focal masses, 7 were irregular in shape and 1 was round; 6 had ill-defined margins and 2 had spiculated margins. All 8 enhanced heterogeneously. 4 cases had multifocal disease and 1 case had unsuspected contralateral disease discovered only on MRI.	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
88. Ko ES, Han H, Han BK, et al. Prognostic Significance of a Complete Response on Breast MRI in Patients Who Received Neoadjuvant Chemotherapy According to the Molecular Subtype. *Korean J Radiol.* 2015;16(5):986-995.	Observational-Dx	174 patients	To evaluate the relationship between response categories assessed by MRI or pathology and survival outcomes, and to determine whether there are prognostic differences among molecular subtypes.	There were 41 recurrences (9 locoregional and 32 distant recurrences). There were statistically significant differences in recurrence outcomes between patients who achieved a radiologic or a pCR and patients who did not achieve a radiologic or a pCR (recurrence hazard ratio, 11.02; *P*=0.018 and recurrence hazard ratio, 3.93; *P*=0.022, respectively). Kaplan-Meier curves for recurrence-free survival showed that triple-negative breast cancer was the only subtype that showed significantly better outcomes in patients who achieved a CR compared to patients who did not achieve a CR by both radiologic and pathologic assessments (*P*=0.004 and 0.001, respectively). A multivariate analysis found that patients who achieved a rCR and a pCR did not display significantly different recurrence outcomes (recurrence hazard ratio, 2.02; *P*=0.505 and recurrence hazard ratio, 1.12; *P*=0.869, respectively).	2
89. Ko ES, Han BK, Kim RB, et al. Analysis of factors that influence the accuracy of magnetic resonance imaging for predicting response after neoadjuvant chemotherapy in locally advanced breast cancer. *Ann Surg Oncol.* 2013;20(8):2562-2568.	Observational-Dx	166 patients	To evaluate the accuracy of breast MRI to predict residual lesion size after NAC and to determine the factors that influence the accuracy of response prediction.	Of the 166 women, 40 achieved pCR. The overall sensitivity, specificity, and accuracy for diagnosing invasive residual disease by using MRI were 96%, 65%, and 89%, respectively. The Pearson's correlation coefficient between the tumor sizes measured using MRI and pathology was 0.749 (*P*<0.001). The size discrepancy was significantly greater in patients with estrogen receptor-positive cancer (*P*=0.037), in cancers with low nuclear grade (*P*=0.007), and in cancers shown as diffuse non-mass-like enhancement on MRI (*P*=0.001).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
90. Kim HJ, Im YH, Han BK, et al. Accuracy of MRI for estimating residual tumor size after neoadjuvant chemotherapy in locally advanced breast cancer: relation to response patterns on MRI. *Acta Oncol.* 2007;46(7):996-1003.	Observational-Dx	50 patients	To evaluate the accuracy of MRI for estimating residual tumor size after NAC in patients with LABC and assessed whether the tumor pattern on MRI after chemotherapy influenced the accuracy of the MRI measurement of the residual tumor size.	The correlation coefficient between the residual tumor sizes determined by MRI and by pathology was 0.645. The MRI measurement agreed with the pathologically determined size in 36 patients (72%) and disagreed in 14 patients 928%), overestimating the size in 13 (26%) and underestimating the size in 1 (2%). Disagreement appeared to be more frequent in the cases showing a nest or rim pattern than in those exhibiting a shrinkage pattern, although this was not statistically significant (P=0.119).	2
91. Chen JH, Feig B, Agrawal G, et al. MRI evaluation of pathologically complete response and residual tumors in breast cancer after neoadjuvant chemotherapy. *Cancer.* 2008;112(1):17-26.	Experimental-Dx	51 patients	To investigate the role of MRI in evaluation of pathologically complete response and residual tumors in patients who were receiving NAC for both positive and negative HER2 breast cancer.	Complete clinical response as seen through MRI, including clinically complete response and probable clinically complete response, was identified in 35 (35/51, 69%) patients. MRI correctly diagnosed pCR in 26 (26/35, 74%) patients, including 18/19 (95%) patients in the HER2-positive group and 8/16 (50%) patients in the HER2-negative group (P<.005). The accuracy of MRI in identifying pCR varied according to the chemotherapy agent that was administered. MRI was more accurate in identifying pCR in patients who were receiving trastuzumab and less accurate in patients receiving bevacizumab. The high false-negative rate found in HER2-negative patients was associated with residual disease that presented as scattered cells or small foci. In cases with residual bulk tumor, the lesion size, determined by MRI, correlated highly with that found in histopathological measurements (r = 0.93).	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
92. Denis F, Desbiez-Bourcier AV, Chapiron C, Arbion F, Body G, Brunereau L. Contrast enhanced magnetic resonance imaging underestimates residual disease following neoadjuvant docetaxel based chemotherapy for breast cancer. *Eur J Surg Oncol.* 2004;30(10):1069-1076.	Experimental-Dx	40 patients	To compare the ability of MRI to measure residual breast cancer in patients treated with different NAC regimen.	MRI over/underestimation of the spread of residual tumor was never superior to 15mm in 5-fluoro-uracyl-epirubicin-cyclophosphamide group, whereas it appeared in 11/28 (39%, 30%–48%–95% CI) patients in docetaxel-based group (P=0.017). Tumor shrinkage led to single nodular residual lesions in 5-fluoro-uracyl-epirubicin-cyclophosphamide group, whereas vast numerous microscopic nests were observed in docetaxel group in pathology.	2
93. Wahner-Roedler DL, Boughey JC, Hruska CB, et al. The use of molecular breast imaging to assess response in women undergoing neoadjuvant therapy for breast cancer: a pilot study. *Clin Nucl Med.* 2012;37(4):344-350.	Experimental-Dx	20 patients	To report our findings from a prospective pilot study evaluating the accuracy of molecular breast imaging in assessing tumor response to NAC for breast cancer.	3 patients in whom post-NAC molecular breast imaging could not be performed because of scheduling problems were excluded from analysis. 18 cancers were diagnosed in 17 patients. A correlation coefficient of r = 0.681 (P=0.002) was found between molecular breast imaging and residual tumor size. The average tumor-to-background ratio on molecular breast imaging decreased from a pretreatment value of 3.0 to a posttreatment value of 1.4. The relative decrease in tumor-to-background ratio did not appear to be predictive of response.	2
94. Dunnwald LK, Gralow JR, Ellis GK, et al. Residual tumor uptake of [99mTc]-sestamibi after neoadjuvant chemotherapy for locally advanced breast carcinoma predicts survival. *Cancer.* 2005;103(4):680-688.	Observational-Dx	62 patients	To test whether 99mTc-sestamibi uptake post NAC predicts survival.	Patients with high uptake on the last observed 99mTc-sestamibi scan (ie, the L:N ratio was greater than the median value) had poorer disease-free survival and overall survival (P<0.01 and P=0.01, respectively). Residual 99mTc-sestamibi uptake retained independent prognostic significance in preliminary multivariate analysis that included other established prognostic markers.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
95. Lee HS, Ko BS, Ahn SH, et al. Diagnostic performance of breast-specific gamma imaging in the assessment of residual tumor after neoadjuvant chemotherapy in breast cancer patients. *Breast Cancer Res Treat.* 2014;145(1):91-100.	Observational-Dx	122 patients	To evaluate the diagnostic performance of breast-specific gamma imaging in the assessment of residual tumor after NAC in breast cancer patients.	The sensitivity and specificity of breast-specific gamma imaging for residual tumor detection in 122 enrolled patients were 74.0% and 72.2%, respectively, and were comparable to those of MRI (81.7% and 72.2%; $P>0.100$). The residual tumor size was significantly underestimated by breast-specific gamma imaging in the luminal subtype ($P=0.008$) and by MRI in the luminal ($P<0.001$) and HER2 subtypes ($P=0.032$), with a significantly lesser degree of underestimation by breast-specific gamma imaging than MRI in both subtypes. In the triple-negative subtype, both breast-specific gamma imaging and MRI generated accurate tumor size measurements. The residual cellularity of triple-negative tumors was significantly higher than that of the non-triple-negative tumors ($P=0.017$). The diagnostic performance of breast-specific gamma imaging in the assessment of residual tumor is comparable to that of MRI in breast cancer patients.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
96. Bassa P, Kim EE, Inoue T, et al. Evaluation of preoperative chemotherapy using PET with fluorine-18-fluorodeoxyglucose in breast cancer. *J Nucl Med.* 1996;37(6):931-938.	Observational-Dx	16 patients	To investigate the value of FDG-PET for preoperative chemotherapy response in patients with LABC.	Sensitivity for detection of pathologically proven primary lesions was 100%, 62.5% and 87.5% with FDG-PET, mammography and US, respectively; and sensitivity for detection of initial nodal involvement was 77%, 70% and 87.5%, respectively. Sensitivity for detection of residual primary tumor was 75%, 71.4% and 87.5%, respectively; and sensitivity for detection of residual nodal involvement was 41.6%, 71.4% and 66.6%, respectively. The mean SUV of primary lesions was 9.4 (range 2.0–20.7, n = 16), with only 2 lesions showing an SUV below 3. Clinical improvement of primary lesions was seen in all patients; improvement with smaller size and less FDG uptake was visible as early as the second study in 11 patients (69%). Mean SUV values obtained at the second and third studies decreased significantly from those obtained in the first study. In 4 patients, the disease recurred after breast surgery with high SUV values. The mammograms and sonograms obtained before surgery showed a decrease in the diameter of 6 and 12 primary lesions of the 13 and 14 patients examined, respectively.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
97. Duch J, Fuster D, Munoz M, et al. PET/CT with [18F] fluorodeoxyglucose in the assessment of metabolic response to neoadjuvant chemotherapy in locally advanced breast cancer. *Q J Nucl Med Mol Imaging.* 2012;56(3):291-298.	Experimental-Dx	50 patients	To prospectively evaluate FDG-PET/CT in the assessment of metabolic response to NAC and correlation with tumor cellularity in LABC.	Baseline mean tumor size was 4.4+/-1.6 cm. 38 patients were considered responders and 12 nonresponders. According to Miller & Payne scale, 10 patients had good prognosis (grades 4-5) and 40 patients had bad prognosis (grades 1-3). All patients with grade 5 Miller & Payne had no significant postchemotherapy FDG uptake. Patients with bad prognosis had lower SUVmax variation than patients with good prognosis (60.7% vs 80.5%, P=0.0016). SUVmax was lower in nonresponders than in partial responders according to RECIST criteria (38.9% vs 67.6%, P<0.001), and was also lower in partial responders than complete responders (67.6% vs 85.4%, P=0.005). A cut-off SUVmax value of 52% differentiates responders from nonresponders with a sensitivity of 86% and a specificity of 90%. Probability densities of the SUVmax (%) for stable disease (<45), partial (>45 to <82) and complete response (>82) showed an overall accuracy of 78% (Weighted Kappa=0.74).	2
98. Cheng X, Li Y, Liu B, Xu Z, Bao L, Wang J. 18F-FDG PET/CT and PET for evaluation of pathological response to neoadjuvant chemotherapy in breast cancer: a meta-analysis. *Acta Radiol.* 2012;53(6):615-627.	Meta-analysis	17 studies including 781 subjects	To determinate the diagnostic performance of FDG-PET/CT and FDG-PET for evaluating response to NAC in patients with breast cancer.	17 studies (a total of 781 subjects) met the inclusion criteria. The pooled sensitivity was 0.840 (95% CI, 0.796–0.878). The pooled specificity was 0.713 (95% CI, 0.667–0.756). For FDG-PET/CT (10 studies included), the pooled sensitivity was 0.847 (95% CI, 0.793–0.892), the pooled specificity was 0.661 (95% CI, 0.598–0.720). The pooled likelihood ratio, negative likelihood ratio, and diagnostic odds ratio were 2.835 (95% CI, 1.640–4.900), 0.221 (95% CI, 0.160–0.305), and 17.628 (95% CI, 7.431–41.818). The AUC was 0.8934. For FDG-PET (7 studies included), the pooled sensitivity and specificity were 0.826 (95% CI, 0.741–0.892) and 0.789 (95% CI, 0.719–0.849). The pooled likelihood ratio (+) , likelihood ratio (-), and diagnostic odds ratio were 3.601 (95% CI, 2.601–4.986), 0.242 (95% CI, 0.157–0.374), and 13.641 (95% CI, 7.433–25.030). The AUC was 0.8764.	M

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
99. Choi JH, Lim HI, Lee SK, et al. The role of PET CT to evaluate the response to neoadjuvant chemotherapy in advanced breast cancer: comparison with ultrasonography and magnetic resonance imaging. *J Surg Oncol.* 2010;102(5):392-397.	Observational-Dx	41 patients	To estimate the predictive role of PET/CT and other imaging modalities (US, MRI) through NAC.	7 patients (17.1%) showed pCR. As a result of comparison of the image index, all image indexes of MRI were predictive for pCR ($P<0.05$). In contrast, only delta and response rate of US, response rate of PET CT were significant. The AUC of delta and response rate in MRI were higher (0.91, 0.90) than US (0.83, 0.80) and PET CT (0.62, 0.72). The MRI is superior to the US or PET/CT.	3
100. Gebhart G, Gamez C, Holmes E, et al. 18F-FDG PET/CT for early prediction of response to neoadjuvant lapatinib, trastuzumab, and their combination in HER2-positive breast cancer: results from Neo-ALTTO. *J Nucl Med.* 2013;54(11):1862-1868.	Experimental-Dx	86 patients	To explore whether FDG-PET imaging would capture a higher rate of metabolic response with the dual HER2 blockade as opposed to single blockade.	77 of the 86 enrolled patients presented an evaluable baseline FDG-PET/CT scan; of these, 68 and 66 were evaluable at weeks 2 and 6, respectively. Metabolic responses in the primary tumors were evident after 2 weeks of targeted therapy and correlated highly with metabolic responses at week 6 (R(2) = 0.81). The pCRs were associated with greater SUVmax reductions at both time points. Mean SUVmax reductions for pCR and non-pCR, respectively, were 54.3% vs 32.8% at week 2 ($P=0.02$) and 61.5% vs 34.1% at week 6 ($P=0.02$). FDG-PET/CT metabolic response rates at weeks 2 and 6 were 71.6% and 60%, respectively using European Organization for Research and Treatment of Cancer criteria; pCR rates were twice as high for FDG-PET/CT responders than nonresponders (week 2: 42% vs 21%, $P=0.12$; week 6: 44% vs 19%, $P=0.05$).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
101. Groheux D, Giacchetti S, Hatt M, et al. HER2-overexpressing breast cancer: FDG uptake after two cycles of chemotherapy predicts the outcome of neoadjuvant treatment. *Br J Cancer.* 2013;109(5):1157-1164.	Observational-Dx	30 women	To investigate the ability of interim PET regarding early prediction of pathology outcomes.	30 women were prospectively included and 60 PET/CT examination performed. At baseline, 22 patients had PET+ axilla and in 9 of them FDG uptake was higher than in the primary tumor. At surgery, 14 patients (47%) showed residual tumor (non-pCR), whereas 16 (53%) reached pCR. Best prediction was obtained when considering the absolute residual SUVmax value at PET(2) (AUC=0.91) vs 0.67 for SUVmax at PET(1) and 0.86 for DeltaSUVmax. The risk of non-pCR was 92.3% in patients with any site of residual uptake >3 at PET(2), no matter whether in breast or axilla, vs 11.8% in patients with uptake ≤3 (P=0.0001). The sensitivity, specificity, PPV, NPV and overall accuracy of this cutoff were, respectively: 85.7%, 93.8%, 92.3%, 88.2% and 90%.	2
102. Humbert O, Cochet A, Riedinger JM, et al. HER2-positive breast cancer: (1)(8)F-FDG PET for early prediction of response to trastuzumab plus taxane-based neoadjuvant chemotherapy. *Eur J Nucl Med Mol Imaging.* 2014;41(8):1525-1533.	Observational-Dx	57 patients	To investigate the value of FDG-PET/CT to predict a pCR after NAC in women with HER2-positive breast cancer.	In univariate analysis, negative hormonal receptor status (P=0.04), high tumor grade (P=0.03), and low tumor PET(2). SUVmax (P=0.001) were predictive of pCR. Tumor DeltaSUVmax correlated with pCR (P=0.03), provided that tumors with low metabolic activity at baseline were excluded. Delta Total Lesion Glycolysis did not correlate with pCR. In multivariate analysis, tumor PET(2).SUVmax <2.1 was the best independent predictive factor (odds ratio =14.3; P=0.004) with both NPV and PPV of 76%. Although the metabolic features of the primary tumor did not depend on hormonal receptor status, both the baseline metabolism and early response of axillary nodes were higher if estrogen receptors were not expressed (P=0.01 and P=0.03, respectively).	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
103. Groheux D, Hindie E, Giacchetti S, et al. Triple-negative breast cancer: early assessment with 18F-FDG PET/CT during neoadjuvant chemotherapy identifies patients who are unlikely to achieve a pathologic complete response and are at a high risk of early relapse. *J Nucl Med.* 2012;53(2):249-254.	Observational-Dx	20 patients	To investigate whether early changes in FDG tumor uptake during NAC can predict outcomes.	At surgery, 6 patients had a pCR, whereas 14 had residual tumor. 4 patients showed early relapse (in the 2 y after surgery). There were 11 metabolic responders and 9 nonresponders using a 42% decrease in SUVmax as a cutoff. In nonresponding patients, the risk of residual tumor at surgery was 100% (vs 45% in responders; P=0.014), and the risk of early relapse was 44% (vs 0%; P=0.024).	3
104. Avril N, Rose CA, Schelling M, et al. Breast imaging with positron emission tomography and fluorine-18 fluorodeoxyglucose: use and limitations. *J Clin Oncol.* 2000;18(20):3495-3502.	Experimental-Dx	144 patients	To evaluate the diagnostic value of FDG-PET for the diagnosis of primary breast cancer.	Breast carcinomas were identified with an overall sensitivity of 64.4% conventional image reading and 80.3% sensitive image reading. The increase in sensitivity (sensitive image reading) resulted in a noticeable decrease in specificity, from 94.3% conventional image reading to 75.5% sensitive image reading. At stage pT1, only 30 (68.2%) of 44 breast carcinomas were detected, compared with 57 (91.9%) of 62 at stage pT2. A higher percentage of ILCs were false-negative (65.2%) compared with IDCs (23.7%). Nevertheless, positive PET scans provided a high PPV (96.6%) for breast cancer.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
105. Groheux D, Majdoub M, Sanna A, et al. Early Metabolic Response to Neoadjuvant Treatment: FDG PET/CT Criteria according to Breast Cancer Subtype. *Radiology.* 2015;277(2):358-371.	Observational-Dx	169 patients	To investigate parameters based on FDG-PET imaging that is best correlated with pCR in HER2-positive cancer and triple-negative breast cancer and with partial or complete response in estrogen-positive/HER2-negative breast cancer.	Included were 169 consecutive patients (mean age, 50 years). pCR was more frequent in HER2-positive tumors (16/33 patients [48.5%]) and triple-negative breast cancers (20/54 patients [37%]) than in estrogen-positive/HER2-negative tumors (4/82 [4.9%]) (P<.001). Among patients with estrogen-positive/HER2-negative cancers, 33 patients had partial response. In triple-negative breast cancer, best association with pCR was obtained with change in SUVmax (AUC, 0.86) or change in total lesion glycolysis (AUC, 0.88). In HER2-positive phenotype, absolute SUVmax (or SUV(peak)) values at PET imaging after 2 cycles of chemotherapy (AUC for each cycle, 0.93) were better correlated with pCR than change in SUVmax (AUC, 0.78; P=.11) or change in total lesion glycolysis (AUC, 0.62; P=.005). Regarding estrogen-positive/HER2-negative cancers, change in SUVmax or change in total lesion glycolysis (AUC, 0.75) were parameters best correlated with partial or complete response. Baseline SUVmax was higher in lymph nodes than in primary tumor in 31 patients. Findings were similar considering the site with highest FDG uptake.	3
106. Henry-Tillman R, Glover-Collins K, Preston M, et al. The SAVE review: sonographic analysis versus excision for axillary staging in breast cancer. *J Am Coll Surg.* 2015;220(4):560-567.	Observational-Dx	95 patients	To compare the cost-effectiveness of axillary US-guided core needle biopsy with SLNB when evaluating the status of the axilla in operable invasive breast cancer.	The cohort of 95 patients was divided into 2 groups: clinically positive (32%) and clinically negative (68%) axilla. In the clinically positive group, 83% had a suspicious axillary US, of which 90% were positive. In the clinically negative group, axillary US was suspicious in 70%, with a positive biopsy in 59%. The sensitivity and specificity of axillary US-core needle biopsy were 90% (95% CI, 84.8% to 98.8%) and 100% (95% CI, 27% to 59.1%), respectively. Cost estimates comparing axillary US-core needle biopsy with SLNB demonstrated a cost saving of $236,517 in the clinically positive axilla and $248,490 in the clinically negative axilla, for a total cost savings of $485,007.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
107. Bedrosian I, Bedi D, Kuerer HM, et al. Impact of clinicopathological factors on sensitivity of axillary ultrasonography in the detection of axillary nodal metastases in patients with breast cancer. *Ann Surg Oncol.* 2003;10(9):1025-1030.	Observational-Dx	208 patients	To identify factors influencing the sensitivity of US for detection of nodal metastasis.	Of 208 patients, axillary US was negative in 180 (86%) and suspicious or indeterminate in 28 (14%). FNA was performed in 22 patients whose findings were indeterminate or suspicious, and 3 were positive for malignancy. Final pathological examinations revealed positive nodes in 53 patients: 39 (22%) of 180 with negative US findings and 14 (50%) of 28 with indeterminate or suspicious US findings (*P*=.001). Excisional biopsy was more common for patients with indeterminate or suspicious findings on preoperative US (*P*=.038). There were no significant differences in tumor size, histological features, size of nodal metastasis, or number of positive nodes between patients whose US findings were negative and those whose findings were indeterminate or suspicious.	3
108. Dellaportas D, Koureas A, Contis J, et al. Contrast-Enhanced Color Doppler Ultrasonography for Preoperative Evaluation of Sentinel Lymph Node in Breast Cancer Patients. *Breast Care (Basel).* 2015;10(5):331-335.	Observational-Dx	50 patients	To evaluate the usefulness of contrast-enhanced US in preoperative detection of malignant SLNs.	Contrast-enhanced US scan identified a negative SLN in the axilla of 27 patients and final histopathology was negative for 30 cases in total, so NPV was calculated as 90% and PPV was 75%. Overall sensitivity was 83.33% and specificity was 84.38%. Moreover, the ability of contrast-enhanced US to differentiate between SLN status was only statistically significantly correlated with the actual final histopathological report (*P*<0.001), while successful US prediction was not correlated with any factor.	3
109. Moorman AM, Bourez RL, de Leeuw DM, Kouwenhoven EA. Pre-operative Ultrasonographic Evaluation of Axillary Lymph Nodes in Breast Cancer Patients: For Which Group Still of Additional Value and in Which Group Cause for Special Attention? *Ultrasound Med Biol.* 2015;41(11):2842-2848.	Observational-Dx	1124 patients	To evaluate the diagnostic accuracy of axillary US and fine-needle aspiration cytology in a large cohort of breast cancer patients.	The sensitivity and specificity of US and fine-needle aspiration cytology in our cohort of 1124 patients were 42.2% and 97.1%, respectively. As the number of axillary nodes increased, sensitivity increased. The percentage of false-negative US results was 18.9%; patients in this subgroup were significantly younger, had larger tumors, more often had lymph vascular invasion and were more likely to have estrogen receptor-positive tumors.	3

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
110. Javid S, Segara D, Lotfi P, Raza S, Golshan M. Can breast MRI predict axillary lymph node metastasis in women undergoing neoadjuvant chemotherapy. *Ann Surg Oncol.* 2010;17(7):1841-1846.	Observational-Dx	74 women	To evaluate the predictive value of breast MRI in detecting axillary lymph node metastases prior to initiation of NAC and in detecting residual lymph node metastases after NAC in women found to be node positive prior to NAC.	74 women completed NAC and underwent surgery. Sensitivity of MRI in detecting axillary node involvement prior to NAC was 64.7% and specificity was 100%, with PPV and NPV of MRI of 100% and 77.8%, respectively. Sensitivity and specificity of MRI to identify residual pathologic axillary lymph node disease following NAC were 85.7% and 89%, respectively, while the PPV and NPV were 92% and 80.9%, respectively	2
111. Garcia Vicente AM, Soriano Castrejon A, Leon Martin A, et al. Early and delayed prediction of axillary lymph node neoadjuvant response by (18)F-FDG PET/CT in patients with locally advanced breast cancer. *Eur J Nucl Med Mol Imaging.* 2014;41(7):1309-1318.	Experimental-Dx	76 patients	To determine the utility of FDG-PET/CT performed in an early and delayed phase during NAC in the prediction of lymph node histopathological response in patients with LABC.	Lymph node pCR was seen in 34 patients. The sensitivity, specificity, and PPV and NPV of PET-2 and PET-3 in establishing the final status of the axilla after chemotherapy were 52%, 45%, 50% and 47%, and 33%, 84%, 67% and 56%, respectively. No significant relationship was observed between metabolic complete response on PET-2 and PET-3 and pCR (P=0.31 and 0.99, respectively). Lymph node metabolism on PET-1 was not able to predict the final histopathological status, whereas basal carcinomas showed a higher rate of pCR (70.6%) than the other groups (P=0.03).	2
112. Wahl RL, Siegel BA, Coleman RE, Gatsonis CG. Prospective multicenter study of axillary nodal staging by positron emission tomography in breast cancer: a report of the staging breast cancer with PET Study Group. *J Clin Oncol.* 2004;22(2):277-285.	Experimental-Dx	360 women	To determine the accuracy of FDG-PET in detecting axillary nodal metastases in women with primary breast cancer.	For detecting axillary nodal metastasis, the mean estimated AUC for the 3 readers was 0.74 (range, 0.70 to 0.76). If at least 1 probably or definitely abnormal axillary focus was considered positive, the mean (and range) sensitivity, specificity, and PPV and NPV for PET were 61% (54% to 67%), 80% (79% to 81%), 62% (60% to 64%), and 79% (76% to 81%), respectively. False-negative axillae on PET had significantly smaller and fewer tumor-positive lymph nodes (2.7) than true-positive axillae (5.1; P<.005). Semiquantitative analysis of axillary FDG uptake showed that a nodal SUV (lean body mass) more than 1.8 had a PPV of 90%, but a sensitivity of only 32%. Finding 2 or more intense foci of tracer uptake in the axilla was highly predictive of axillary metastasis (78% to 83% PPV), albeit insensitive (27%).	1

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
113. Koolen BB, Valdes Olmos RA, Elkhuizen PH, et al. Locoregional lymph node involvement on 18F-FDG PET/CT in breast cancer patients scheduled for neoadjuvant chemotherapy. *Breast Cancer Res Treat.* 2012;135(1):231-240.	Observational-Dx	311 patients	To assess the value of FDG-PET/CT for detecting locoregional lymph node metastases in primary breast cancer patients scheduled for NAC.	Sensitivity, specificity, PPV, NPV, and accuracy of FDG-avid nodes for the detection of axillary metastases (score 2 or 3) were 82%, 92%, 98%, 53%, and 84%, respectively. Of 28 patients with questionable axillary FDG uptake (score 1), 23 (82%) were node-positive. Occult lymph node metastases in the internal mammary chain and periclavicular area were detected in 26 (8%) and 32 (10%) patients, respectively, resulting in changed regional radiotherapy planning in 50 (16%) patients. In breast cancer patients scheduled for NAC, PET/CT renders pre-chemotherapy SLNB unnecessary in case of an FDG-avid axillary node, enables axillary response monitoring during or after NAC, and leads to changes in radiotherapy for a substantial number of patients because of detection of occult N3-disease.	2
114. Koolen BB, Valdes Olmos RA, Wesseling J, et al. Early assessment of axillary response with (1)(8)F-FDG PET/CT during neoadjuvant chemotherapy in stage II-III breast cancer: implications for surgical management of the axilla. *Ann Surg Oncol.* 2013;20(7):2227-2235.	Observational-Dx	219 patients	To evaluate the value of FDG-PET/CTs during NAC for axillary response monitoring in stage II-III breast cancer	A total of 32 (40%) patients experienced axillary pCR. The relative decrease in SUVmax was significantly higher in patients with pCR than in those without, both on PET/CT2 (P<0.001) and PET/CT3 (P=0.025). The AUC values for PET/CT2 and PET/CT3 were 0.80 (95% CI, 0.68–0.92) and 0.65 (95% CI, 0.52–0.79), respectively. A relative decrease of ≥60% on PET/CT2 had an excellent specificity (35/37, 95%), a high PPV (12/14, 86%), and a sensitivity of 48%, that is, it accurately identified histologic pCR in 12/25 patients with disease that responded to therapy.	2

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
115. Holwitt DM, Swatske ME, Gillanders WE, et al. Scientific Presentation Award: The combination of axillary ultrasound and ultrasound-guided biopsy is an accurate predictor of axillary stage in clinically node-negative breast cancer patients. *Am J Surg.* 2008;196(4):477-482.	Observational-Dx	256 patients	To determine the accuracy of axillary US and FNAB/needle core biopsy in axillary breast cancer staging.	Axillary US-guided FNAB/needle core biopsy and final pathology were positive in 72/256 patients (28%). In 125/256 cases (49%), the axillary US and final pathology were negative. 2 of 110 patients had a false-positive FNAB (1.8%); both received NAC. 9 patients (8%) had a false-negative FNAB/needle core biopsy; the median size of lymph node metastasis was 3 mm. The sensitivity and specificity of axillary US-guided FNAB/needle core biopsy was 71% and 99%, respectively, with a NPV of 84% and a PPV of 97%.	3
116. Jain A, Haisfield-Wolfe ME, Lange J, et al. The role of ultrasound-guided fine-needle aspiration of axillary nodes in the staging of breast cancer. *Ann Surg Oncol.* 2008;15(2):462-471.	Observational-Dx	68 patients	To evaluate US-guided FNA of normal and abnormal axillary nodes in breast cancer patients.	Of 65 axillae analyzed, 39 (60%) were positive, 4 (6%) were nondiagnostic, and 22 (34%) were negative by US-guided FNA. US-guided FNA had 89% sensitivity, 100% specificity, and 100% PPV in patients with palpable or US suspicious nodes. US-guided FNA sensitivity dropped significantly for nonpalpable, US normal nodes (54%), while specificity and PPV remained 100%. None of the primary tumor features predicted concordance of US-guided FNA and SLN dissection/ axillary lymph node dissection.	3
117. Sauer T, Suciu V. The role of preoperative axillary lymph node fine needle aspiration in locoregional staging of breast cancer. *Ann Pathol.* 2012;32(6):e24-28, 410-414.	Review/Other-Dx	N/A	To review the recent data in the literature regarding the diagnostic accuracy of lymph node FNA in breast cancer staging, and present the experience of the Breast Diagnostic Centre of Oslo University Hospital Ullevaal, Norway, in this context.	No results stated in abstract.	4
118. Iwase H, Yamamoto Y, Kawasoe T, Ibusuki M. Advantage of sentinel lymph node biopsy before neoadjuvant chemotherapy in breast cancer treatment. *Surg Today.* 2009;39(5):374-380.	Review/Other-Dx	N/A	To discuss improvements in SLN mapping, the timing of SLNB in relation to delivery of NAC, and a new decision tree for operable breast cancer involving SLNB and NAC.	To identify the initial cancer stage in patients who will be treated by systemic therapy before surgery, SLNB should be performed prior to systemic treatments, using a well-developed navigating tool, such as single photon emission computed tomography/CT.	4

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EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
119. Rousseau C, Devillers A, Campone M, et al. FDG PET evaluation of early axillary lymph node response to neoadjuvant chemotherapy in stage II and III breast cancer patients. *Eur J Nucl Med Mol Imaging.* 2011;38(6):1029-1036.	Experimental-Dx	52 patients	To assess sequential FDG-PET findings as early predictors of axillary lymph node response to NAC in stage II and III breast cancer patients.	The sensitivity, specificity and accuracy of axillary node staging was higher with PET (75%, 87%, and 80%) than with US (50%, 83%, and 65%), and even more so when PET images were corrected for partial volume effects (86%, 83%, and 84%). While FDG uptake did not vary much in nonresponders, as confirmed by histopathological analysis, it markedly decreased to baseline levels in responders ($P<10(-5)$). 50% of baseline SUV was considered the best cutoff value to distinguish responders from nonresponders. The sensitivity, specificity, NPV and accuracy of FDG-PET after 1 course of chemotherapy were, respectively, 96%, 75%, 95%, and 84%.	2
120. Mamounas EP. Sentinel lymph node biopsy after neoadjuvant systemic therapy. *Surg Clin North Am.* 2003;83(4):931-942.	Review/Other-Dx	N/A	To discuss the feasibility and accuracy of SNLB following NAC.	No results stated in abstract.	4
121. Tennant S, Evans A, Macmillan D, et al. CT staging of loco-regional breast cancer recurrence. A worthwhile practice? *Clin Radiol.* 2009;64(9):885-890.	Review/Other-Dx	63 patients	To assess the usefulness of CT of the chest, abdomen, and pelvis in the detection of metastatic disease in patients presenting with loco-regional recurrence of breast cancer, and to identify subgroups particularly likely to have metastases.	21 patients (32%) had metastases, including bony (n=5, 8%), liver (n=7, 11%), and thoracic disease (n=11, 17%). Patients with recurrence in a conserved breast had lower rates of metastasis on CT than those with other sites of recurrence [3/21 (14%) vs 18/44 (41%), $P=0.03$]. Patients younger than 50 years at primary diagnosis or younger than 60 years at recurrence had statistically significantly higher rates of metastasis than older patients [10/16 (63%) vs 11/48 (23%), $P=0.003$, and 13/23 (57%) vs 8/42 (19%), $P=0.002$, respectively].	4

Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
122. Kumar R, Chauhan A, Zhuang H, Chandra P, Schnall M, Alavi A. Clinicopathologic factors associated with false negative FDG-PET in primary breast cancer. *Breast Cancer Res Treat.* 2006;98(3):267-274.	Observational-Dx	111 patients	To determine the clinicopathologic factors that predict false negative FDG-PET results in patients with primary breast cancer.	Of 116 breast lesions, 85 were malignant and 31 were benign on histopathology. Of the 85 malignant lesions, 41 were true positive and 44 were false negative. Among the 31 benign lesions, 30 were true negative and 1 was false positive. There was significant difference in the tumor size (P=0.003) and tumor grade (P=0.001) in patients with true positive and false negative PET results. Multivariate logistic regression demonstrated that tumor size (≤10 mm) and low tumor grade were independently associated with false negative results. No significant relationship of false negative PET results was found with age, menopausal status, tumor type, c-erbB-2, estrogen and progesterone receptors, SLN or distant metastasis, parenchymal density and multifocality of primary breast tumor.	2
123. Groheux D, Espie M, Giacchetti S, Hindie E. Performance of FDG PET/CT in the clinical management of breast cancer. *Radiology.* 2013;266(2):388-405.	Review/Other-Dx	N/A	To review the role of metabolic imaging with FDG in breast cancer.	FDG-PET/CT is very useful for restaging of cancer in patients with documented breast cancer recurrence or in those who are suspected of having breast cancer recurrence and is more efficient than PET alone and conventional imaging methods. FDG-PET/CT is also efficient to perform the staging of locally advanced and inflammatory breast cancer. It allows detection of extraaxillary lymph nodes and distant metastases. PET/CT also brings valuable information in the staging of clinical stage IIB and primary operable stage IIIA breast carcinoma. In contrast, the spatial resolution of PET (approximately 5–6 mm) is not sufficient to allow the detection of early axillary node involvement and micrometastases. PET/CT cannot replace staging by using the sentinel node procedure. Also, PET is not recommended for the initial assessment of stage I breast cancer. The metabolic information provided by using PET has been shown to be valuable for the early assessment of response to chemotherapy (at the neoadjuvant and metastasis settings), but this indication remains to be validated.	4

Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
124. Groheux D, Giacchetti S, Espie M, et al. The yield of 18F-FDG PET/CT in patients with clinical stage IIA, IIB, or IIIA breast cancer: a prospective study. *J Nucl Med.* 2011;52(10):1526-1534.	Observational-Dx	131 patients	To prospectively evaluate the role of FDG-PET/CT in patients with stage IIA, IIB, or IIIA breast cancer.	Of the 131 examined patients, 36 had clinical stage IIA (34 T2N0 and 2 T1N1), 48 stage IIB (20 T3N0 and 28 T2N1), and 47 stage IIIA (29 T3N1, 9 T2N2, and 9 T3N2). FDG-PET/CT modified staging for 5.6% of stage IIA patients, for 14.6% of stage IIB patients, and for 27.6% of stage IIIA patients. However, within stage IIIA, the yield was specifically high among the 18 patients with N2 disease (56% stage modification). When considering stage IIB and primary operable IIIA (T3N1) together, the yield of FDG-PET/CT was 13% (10/77); extraaxillary regional lymph nodes were detected in 5 and distant metastases in 7 patients. In this series, FDG-PET/CT outperformed bone scanning, with only 1 misclassification vs 8 for bone scanning (P=0.036).	3
125. Groheux D, Giacchetti S, Moretti JL, et al. Correlation of high 18F-FDG uptake to clinical, pathological and biological prognostic factors in breast cancer. *Eur J Nucl Med Mol Imaging.* 2011;38(3):426-435.	Experimental-Dx	132 women	To determine the impact of the main clinicopathological and biological prognostic factors of breast cancer on FDG uptake.	There was no influence of T and N stage on SUV. IDC showed higher SUV than lobular carcinoma. However, the highest uptake was found for metaplastic tumors, representing 5% of patients in this series. Several biological features usually considered as bad prognostic factors were associated with an increase in FDG uptake: the median of SUVmax was 9.7 for grade 3 tumors vs 4.8 for the lower grades (P<0.0001); negativity for estrogen receptors was associated with higher SUV (estrogen receptors+ SUV = 5.5; estrogen receptors- SUV = 7.6; P=0.003); triple-negative tumors (estrogen and progesterone receptor negative, no overexpression of c-erbB-2) had an SUV of 9.2 vs 5.8 for all others (P=0005); p53 mutated tumors also had significantly higher SUV (7.8 vs 5.0; P<0.0001). Overexpression of c-erbB-2 had no effect on the SUV value.	1

Monitoring Response to Neoadjuvant Systemic Therapy for Breast Cancer
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
126. Berriolo-Riedinger A, Touzery C, Riedinger JM, et al. [18F]FDG-PET predicts complete pathological response of breast cancer to neoadjuvant chemotherapy. *Eur J Nucl Med Mol Imaging.* 2007;34(12):1915-1924.	Experimental-Dx	47 women	To evaluate, in breast cancer patients treated by NAC, the predictive value of reduction in FDG uptake with regard to pCR.	The relative decrease in FDG uptake (DeltaSUV) after the first course of NAC was significantly greater in the pCR group than in the non-pCR group (P<0.000066). The 4 FDG uptake indices were all strongly correlated with each other. A decrease in SUV(max-BSA-G) of 85.4% +/- 21.9% was found in pCR patients, vs 22.6% +/- 36.6% in non-pCR patients. DeltaSUV(max-BSA-G) <-60% predicted the pCR with an accuracy of 87% and DeltaSUVs were found to be only factors predictive of the pCR at multivariate analysis. An elevated baseline SUV was associated with high mitotic activity (P<0.0016), tumor grading (P<0.004), high nuclear pleomorphism score (P<0.03) and negative hormonal receptor status (P<0.005).	3
127. Lee JH. Radionuclide methods for breast cancer staging. *Semin Nucl Med.* 2013;43(4):294-298.	Review/Other-Dx	N/A	To discuss radionuclide imaging modalities FDG-PET in locoregional staging.	No results stated in abstract.	4
128. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: http://www.acr.org/~/media/ACR/Documents/AppCriteria/RadiationDoseAssessmentIntro.pdf. Accessed March 1, 2017.	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

Abbreviations Key

ADC = Apparent diffusion coefficient
AUC = Area under the receiver operating characteristic curve
CI = Confidence interval
CT = Computed tomography
DBT = Digital breast tomosynthesis
DCIS = Ductal carcinoma in situ
DM = Digital mammography
DWI = Diffusion-weighted imaging
FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography
FFDM = Full-field digital mammography
FNAB = Fine-needle aspiration biopsy
HER = Human epidermal growth
IDC = Invasive ductal carcinoma
ILC = Invasive lobular carcinoma
LABC = Locally advanced breast cancer
NAC = Neoadjuvant chemotherapy
NPV = Negative predictive value
PPV = Positive predictive value
SUV = Standardized uptake value
SUVmax = maximum standardized uptake value
MRI = Magnetic resonance imaging
MRSI = Magnetic resonance spectroscopic imaging
pCR = Pathologic complete response
PEM = Positron emission mammography
RCB = Residual cancer burden
ROC = Receiver-operator characteristic
SD = Standard deviation
SLN = Sentinel lymph node
SLNB = Sentinel lymph node biopsy
SNR = Signal-to-noise ratio
tCho = total choline-containing compound
US = Ultrasound