

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. <i>CA Cancer J Clin.</i> 2016;66(1):7-30.	Review/Other-Tx	N/A	To estimate the numbers of new cancer cases and deaths that will occur in the United States in the current year and compile the most recent data on cancer incidence, mortality, and survival. Incidence data were collected by the National Cancer Institute (Surveillance, Epidemiology, and End Results [SEER] Program), the Centers for Disease Control and Prevention (National Program of Cancer Registries), and the North American Association of Central Cancer Registries.	In 2016, 1,685,210 new cancer cases and 595,690 cancer deaths are projected to occur in the United States. Overall cancer incidence trends (13 oldest SEER registries) are stable in women, but declining by 3.1% per year in men (from 2009-2012), much of which is because of recent rapid declines in prostate cancer diagnoses. The cancer death rate has dropped by 23% since 1991, translating to more than 1.7 million deaths averted through 2012. Despite this progress, death rates are increasing for cancers of the liver, pancreas, and uterine corpus, and cancer is now the leading cause of death in 21 states, primarily due to exceptionally large reductions in death from heart disease. Among children and adolescents (aged birth-19 years), brain cancer has surpassed leukemia as the leading cause of cancer death because of the dramatic therapeutic advances against leukemia. Accelerating progress against cancer requires both increased national investment in cancer research and the application of existing cancer control knowledge across all segments of the population.	4

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2. Ma I, Dueck A, Gray R, et al. Clinical and self breast examination remain important in the era of modern screening. <i>Ann Surg Oncol.</i> 2012;19(5):1484-1490.	Observational-Dx	782 patients	To review the methods of detecting newly diagnosed breast neoplasms at our institution.	We identified 782 patients. Patients aged <50 years were more likely to present with palpable disease ( $P<0.001$ ). Overall, 75% of patients had a mammogram within 24 months. There was a higher incidence of Tis tumors and lower incidence of T1 tumors if patients had mammography performed within 12 months vs 13–24 months ( $P<0.01$ ); tumor size, hormonal status, and lymph node status were comparable between these 2 groups. Patients diagnosed by self-breast examination/clinical-breast examination who had mammography performed within 12 months vs 13–24 months did not differ statistically according to tumor characteristics. In the screened cohort (mammography within 24 months), the majority of patients (64%) were diagnosed by mammography. Cancers detected by self-breast examination/clinical-breast examination were larger tumors (2.4 vs 1.3 cm), higher grade, more frequently ER- (29 vs 16%), triple-negative (21 vs 10%), and lymph node-positive (39 vs 18%; all $P\leq 0.01$ ). There were no statistically significant differences in tumor size, T stage, or hormonal status in patients who had analog vs digital mammography.	3
3. Chiarelli AM, Edwards SA, Sheppard AJ, et al. Favourable prognostic factors of subsequent screen-detected breast cancers among women aged 50-69. <i>Eur J Cancer Prev.</i> 2012;21(6):499-506.	Observational-Dx	1,848 breast cancers diagnosed among women	To examine the benefit of mammography screening on breast cancer mortality.	Women with symptomatic detected [OR=7.48, 95% CI=5.38–10.38] and interval cancers (OR=2.20, 95% CI=1.56–3.10) were more often diagnosed at stage III-IV vs I than women with rescreen-detected cancers. After adjusting for tumor size, women with symptomatic cancers had tumors of higher grade (OR=1.50, 95% CI=1.05–2.15) and mitotic score (OR=1.69, 95% CI=1.15–2.49) and women with interval cancers had tumors of higher mitotic score (OR=1.52, 95% CI=1.01–2.28) compared with women diagnosed at screening.	3

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4. Lehman CD, Lee AY, Lee CI. Imaging management of palpable breast abnormalities. <i>AJR Am J Roentgenol.</i> 2014;203(5):1142-1153.	Review/Other-Dx	48 studies	To discuss the evidence informing current management guidelines for the care of patients with palpable breast abnormalities.	US is a highly effective imaging tool for guiding effective evaluation of women with palpable breast abnormalities and should be used for all women with suspicious findings at clinical breast examination. The exception is cases in which mammography shows a clearly benign correlate or a normal, fatty area of breast tissue in the location of the palpable finding. Breast US should be the primary imaging tool for women with palpable lumps who are pregnant, lactating, or younger than 30 years. For women 40 years old and older, mammography, followed in most cases by US, is recommended. For women 30-39 years old, US or mammography may be performed first at the discretion of the radiologist or referring provider. There is little to no role for breast MRI or other advanced imaging technologies in the routine diagnostic evaluation of palpable breast abnormalities.	4
5. Molino A, Pavarana M, Micciolo R, et al. Comparative study of clinical, pathological and biological characteristics of symptomatic versus asymptomatic breast cancers. <i>Ann Oncol.</i> 2000;11(5):581-586.	Review/Other-Dx	1916 patients	To compare the biological, pathological and clinical characteristics of symptomatic vs asymptomatic breast cancers.	The patients in group A were older, and had larger tumors and a higher percentage of positive nodes than those in group B; they also had significantly higher grade tumors, higher Ki-67 levels, and a higher percentage of estrogen receptor and progesterone receptor negative and c-erbB-2 positive tumors (all of the P-values were significant). A logistic regression analysis adjusted for tumor diameter and age showed a reduction in the significance of each of the considered variables, but all of them remained significantly associated with the modality of diagnosis except estrogen receptor, progesterone receptor and c-erbB-2.	4

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6. Kaiser JS, Helvie MA, Blacklaw RL, Roubidoux MA. Palpable breast thickening: role of mammography and US in cancer detection. <i>Radiology</i> . 2002;223(3):839-844.	Observational-Dx	103 consecutive women (123 breasts)	To determine the frequency of breast carcinoma and ascertain the diagnostic yield of mammography and breast US in the detection of breast carcinoma in women with palpable breast thickening.	6 (5%) of 123 cases had a diagnosis of breast carcinoma; 5 (83%) of the 6 had invasive carcinoma. Mammography was performed in all cases, US in 77 (63%) cases. Mammographic sensitivity for invasive cancer detection was 60% (3/5 cases), specificity was 94% (102/108 cases), and NPV was 97% (102/105 cases). Sensitivity of US alone was 100% (2/2 cases), specificity was 96% (65/68 cases), and NPV was 100% (65/65 cases). The combined NPV of mammography and US was 100%. Patients with prior biopsies at the site of palpable thickening accounted for most false-negative mammograms. Median time to initiate follow-up of patients in whom biopsy was not performed was 14 months. Breast cancer was discovered in 5% of women with palpable breast thickening. Women with negative mammograms and US scans are at low risk for cancer but should be followed up at short-term intervals with clinical examination and imaging if biopsy is not elected by their surgeon or clinician.	3
7. Rosner D, Blair D. What ultrasonography can tell in breast masses that mammography and physical examination cannot. <i>J Surg Oncol</i> . 1985;28(4):308-313.	Observational-Dx	400 patients	Prospective study to examine the capability of US to provide additional information to the physical and mammographic examination for therapeutic decision.	Breast cancers were accurately diagnosed in 73% (88/120) by US and 84% (98/116) by mammography ( $P>0.10$ ). Major limitation of US was in the diagnosis of minimal breast cancer (23%, 5/21) due to its inability to visualize microcalcifications. Study validates the importance of US in the diagnosis and therapeutic decision of cystic and fibrocystic masses but cannot substitute mammography in early detection of breast carcinoma.	3
8. Boyd NF, Sutherland HJ, Fish EB, Hiraki GY, Lickley HL, Maurer VE. Prospective evaluation of physical examination of the breast. <i>Am J Surg</i> . 1981;142(3):331-334.	Observational-Dx	100 patients	Prospective evaluation of physical examination of the breast. Reliability of physical examination was evaluated by determining the extent of agreement among four experienced breast surgeons who examined the same patients.	Diagnostic accuracy of surgeons was very similar, and most disagreements concerned the findings in patients who did not have breast cancer. Breast examination carried out by more than 1 surgeon may reduce the frequency with which biopsy is performed in patients who do not have breast cancer.	3

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9. Dennis MA, Parker SH, Klaus AJ, Stavros AT, Kaske TI, Clark SB. Breast biopsy avoidance: the value of normal mammograms and normal sonograms in the setting of a palpable lump. <i>Radiology</i> . 2001;219(1):186-191.	Observational-Dx	600 lumps in 486 women	To review the authors' experience with patients who presented with breast lumps and had normal mammograms and normal US.	No patient in the nonbiopsy group developed carcinoma at the initial site of concern during a mean mammographic and clinical follow-up period of 43 months, and all biopsy specimens were benign (NPV 100%). Results of this retrospective study suggest that breast biopsy may be avoided in women with palpable abnormalities when both US and mammography depict normal tissue at the lump site.	3
10. Moy L, Slanetz PJ, Moore R, et al. Specificity of mammography and US in the evaluation of a palpable abnormality: retrospective review. <i>Radiology</i> . 2002;225(1):176-181.	Observational-Dx	829 patients	Retrospective study to determine the number of patients who received diagnosis of breast cancer after having an area of clinical concern and combined negative mammographic and US findings.	374/829 women had follow-up information. 233 had negative imaging findings with more than 2 years of follow-up. 6 (2.6%) of 233 had a diagnosis of breast cancer in the area of the palpable abnormality. A negative mammographic and US finding of a palpable abnormality does not exclude breast cancer, but the likelihood of breast cancer is low, approximately 2.6%–2.7%. It may be higher if the breast tissues are dense and lower if they are predominantly fatty.	3
11. Shetty MK, Shah YP. Prospective evaluation of the value of negative sonographic and mammographic findings in patients with palpable abnormalities of the breast. <i>J Ultrasound Med</i> . 2002;21(11):1211-1216; quiz 1217-1219.	Observational-Dx	172 patients; 186 palpable abnormalities	Prospective study to evaluate the value of combined negative US and mammographic findings in patients with palpable breast abnormalities.	12 patients underwent biopsy; benign histologic diagnoses were reported in all 12 (12 [6.9%] of 172). In the remaining 160 patients who were followed, there was no interval development of breast cancer at the site of the palpable abnormality. The NPV of combined negative mammographic and US findings in a patient with a palpable abnormality of the breast was 100%. Findings suggest that in a patient with a palpable abnormality of the breast, the NPV of combined normal US and mammographic findings is very high and is therefore reassuring to the patient.	3

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12. Soo MS, Rosen EL, Baker JA, Vo TT, Boyd BA. Negative predictive value of sonography with mammography in patients with palpable breast lesions. <i>AJR Am J Roentgenol.</i> 2001;177(5):1167-1170.	Observational-Dx	420 patients; 455 palpable breast lesions	Retrospective study of palpable breast lesions in patients examined with mammography and US to determine NPV.	The NPV of US and mammography in the setting of a palpable lesion was 99.8%. Only 1 clinically suspicious lesion, an invasive lobular carcinoma, had negative imaging examinations. The mean imaging follow-up time for the study was 25 months. NPV of US and mammography is high, and together these imaging modalities can be reassuring if follow-up is planned when the physical exam is not highly suspicious. Biopsy should not be delayed if the physical exam is suspicious.	4
13. Ciatto S, Houssami N. Breast imaging and needle biopsy in women with clinically evident breast cancer: does combined imaging change overall diagnostic sensitivity? <i>Breast.</i> 2007;16(4):382-386.	Observational-Dx	1,000 women with clinically evident (clinically presenting and/or clinically palpable) breast cancer	To quantify the incremental gain in sensitivity for the diagnosis of palpable breast cancer, using single vs combined imaging, where needle biopsy is mandatory clinical practice in the diagnostic pathway.	Sensitivity–true positive rate for cancer detection–of different test combinations (with the number of cases missed in 1,000 subjects given in parentheses) is: mammography and US 97.9% (21); mammography with needle biopsy 99.5% (5); US with needle biopsy 99.5% (5); combined imaging with needle biopsy 99.6% (4). Using only 1 imaging test (irrespective of whether that is mammography or US) in combination with needle biopsy provides the same sensitivity, with an incremental gain in sensitivity of 0.1% where combined imaging is included into the diagnostic pathway. This is largely due to needle biopsy identifying most cancers missed on single imaging thus negating the effect of additional imaging on overall sensitivity.	3

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14. Murphy IG, Dillon MF, Doherty AO, et al. Analysis of patients with false negative mammography and symptomatic breast carcinoma. <i>J Surg Oncol.</i> 2007;96(6):457-463.	Observational-Dx	124 patients had false-negative preoperative mammograms and 1,241 patients had abnormal preoperative mammograms	To analyze the characteristics of symptomatic patients with false-negative mammograms.	Following retrospective review, 42% of false-negative mammograms were re-categorized as suspicious. The most commonly misinterpreted lesion was architectural distortion/asymmetrical density. Adjuvant US, where performed (n=27), raised the level of suspicion in 93% of cases. Patients with false-negative mammograms were more likely to be younger ( $P<0.0001$ ), present with nipple discharge ( $P=0.002$ ) and have smaller tumors ( $P<0.0001$ ). Their tumors were more frequently located outside the upper outer quadrant ( $P=0.002$ ). False-negative mammography led to a delay in diagnosis of >2 months in 12 patients. Symptomatic patients with false-negative mammograms often demonstrate definite abnormalities on imaging, the most common of which is architectural distortion/asymmetrical density. Those at particular risk were younger patients, those with nipple discharge, and patients with lesions located outside the upper outer quadrant.	4

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<p>15. Shetty MK, Shah YP, Sharman RS. Prospective evaluation of the value of combined mammographic and sonographic assessment in patients with palpable abnormalities of the breast. <i>J Ultrasound Med.</i> 2003;22(3):263-268; quiz 269-270.</p>	<p>Observational-Dx</p>	<p>411 consecutive cases of palpable abnormalities of the breast</p>	<p>To evaluate the role of combined mammographic and US imaging in patients with palpable abnormalities of the breast.</p>	<p>165 (40.1%) of 411 palpable abnormalities had a benign assessment; 97 (58.7%) of the 165 benign lesions were visible on both mammography and US; 66 (40%) of 165 benign lesions were mammographically occult and identified at US evaluation. In 60 (14.6%) of the 411 cases, imaging evaluation resulted in a suspicious assessment; 49 (81.7%) of the 60 lesions categorized as suspicious underwent biopsy; 14 (28.5%) of 49 lesions were histologically proved to be carcinoma. 19 (31.6%) of the 60 lesions categorized as suspicious were mammographically occult and identified only on US; 14 (73.7%) of these 19 lesions underwent biopsy; 12 (63.1%) of 19 were benign, and 2 (10.5%) were malignant. 186 (45.2%) of the 411 palpable abnormalities had negative imaging assessment findings; 12 patients with negative imaging findings underwent biopsy, and all had benign findings. The sensitivity (14/14) and NPV (186/186) for a combined mammographic and US assessment were 100%; the specificity was 80.1% (186/232). Cancer was diagnosed in 14 (3.4%) of 411 women who underwent combined imaging for palpable abnormalities of the breast. Combined mammographic and US assessment was shown to be very helpful in identifying benign as well as malignant lesions causing palpable abnormalities of the breast.</p>	<p>3</p>



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16. Noroozian M, Hadjiiski L, Rahnama-Moghadam S, et al. Digital breast tomosynthesis is comparable to mammographic spot views for mass characterization. <i>Radiology</i> . 2012;262(1):61-68.	Observational-Dx	67 women	To determine if DBT performs comparably to mammographic spot views in characterizing breast masses as benign or malignant.	Mean mass visibility ratings were slightly better with DBT (range, 3.2–4.4) than with mammographic spot views (range, 3.8–4.8) for all 4 readers, with 1 reader’s improvement achieving statistical significance ( $P=.001$ ). The A(z) ranged 0.89–0.93 for DBT and 0.88–0.93 for mammographic spot views ( $P\geq.23$ ). The A(z)((0.90)) ranged 0.36–0.52 for DBT and 0.25–0.40 for mammographic spot views ( $P\geq.20$ ). The readers characterized 7 additional malignant masses as BI-RADS 4 or 5 with DBT than with mammographic spot views, at a cost of five false-positive biopsy recommendations, with a mean of 1.8 true-positive (range, 0–3) and 1.3 false-positive (range, -1 to 4) assessments per reader.	2
17. Skaane P, Gullien R, Bjorndal H, et al. Digital breast tomosynthesis (DBT): initial experience in a clinical setting. <i>Acta Radiol</i> . 2012;53(5):524-529.	Observational-Dx	129 women	To compare digital mammography and DBT in a side-by-side feature analysis for cancer conspicuity, and to assess whether there is a potential additional value of DBT to standard state-of-the-art conventional imaging workup with respect to detection of additional malignancies.	State-of-the-art conventional imaging resulted in needle biopsy of 45 breasts, of which 20 lesions were benign and a total of 25 cancers were diagnosed. The remaining 84 women were dismissed with a normal/definitely benign finding and without indication for needle biopsy. The subsequent DBT interpretation found suspicious findings in 4 of these 84 women, and these 4 women had to be called back for repeated workup with knowledge of the tomosynthesis findings. These delayed workups resulted in 2 cancers (increasing the cancer detection by 8%) and 2 false-positive findings. The side-by-side feature analysis showed higher conspicuity scores for tomosynthesis compared to conventional 2D for cancers presenting as spiculated masses and distortions.	2

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18. Zuley ML, Guo B, Catullo VJ, et al. Comparison of two-dimensional synthesized mammograms versus original digital mammograms alone and in combination with tomosynthesis images. <i>Radiology</i> . 2014;271(3):664-671.	Observational-Dx	123 patients	To assess interpretation performance and radiation dose when 2D synthesized mammography images vs standard FFDM images are used alone or in combination with DBT images.	Probability of malignancy-based mean AUCs for synthesized mammography and FFDM images alone was 0.894 and 0.889, respectively (difference, -0.005; 95% CI: -0.062, 0.054; $P=.85$ ). Mean AUC for synthesized mammography with tomosynthesis and FFDM with tomosynthesis was 0.916 and 0.939, respectively (difference, 0.023; 95% CI: -0.011, 0.057; $P=.19$ ). In terms of the reader-specific AUCs, 5 readers performed better with synthesized mammography alone vs FFDM alone, and all 8 readers performed better with combined FFDM and tomosynthesis (absolute differences from 0.003 to 0.052). Similar results were obtained by using a nonparametric analysis of forced BI-RADS ratings.	3
19. Bansal GJ, Young P. Digital breast tomosynthesis within a symptomatic "one-stop breast clinic" for characterization of subtle findings. <i>Br J Radiol</i> . 2015;88(1053):20140855.	Observational-Dx	103 symptomatic patients	To evaluate the diagnostic accuracy of combination 2D and DBT, 3D by comparing the combination with 2D imaging in a symptomatic setting.	M3 lesions were reduced from 91 (85.8%) to 18 (16.9%) with the combination imaging. The mean AUC +/- 95% CI for 2D images alone was 0.721 (0.662–0.905) and for combined 2D and 3D images was 0.901 (0.765–1.00). The difference in AUCs between the 2 modalities was 0.180.	2
20. 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. <i>AJR Am J Roentgenol</i> . 2013;200(1):226-231.	Observational-Dx	144 women	To compare the diagnostic value of one-view DBT vs two-view full-field digital mammography alone and 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 full-field digital mammography ( $P<0.001$ ) and were equal to those of the combined reading in both women admitted for diagnostic workup and women recalled from screening. The sensitivity and NPVs of DBT were superior to those of full-field digital mammography 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 full-field digital mammography.	3

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21. 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. <i>AJR Am J Roentgenol.</i> 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
22. Bernardi D, Ciatto S, Pellegrini M, et al. Application of breast tomosynthesis in screening: incremental effect on mammography acquisition and reading time. <i>Br J Radiol.</i> 2012;85(1020):e1174-1178.	Observational-Dx	10 cancers and 90 negative controls	To supplement the paucity of information available on logistical aspects of the application of 3D mammography in breast screening.	Average acquisition time (measured from start of first-view breast positioning to compression release at completion of last view) for 7 radiographers, based on 20 screening examinations, was longer for 2D+3D (4 min 3 s; range 3 min 53 s–4 min 18 s) than 2D mammography (3 min 13 s; range 3 min 0 s–3 min 26 s; $P<0.01$ ). Average radiologists' reading time per screening examination (3 radiologists reading case-mix of 100 screens: 10 cancers, 90 controls) was longer for 2D+3D (77 s; range 60–90 s) than for 2D mammography (33 s; range 25–46 s; $P<0.01$ ). 2D+3D screen-reading was associated with detection of more cancers and with substantially fewer recalls than 2D mammography alone.	2

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23. Dang PA, Freer PE, Humphrey KL, Halpern EF, Rafferty EA. Addition of tomosynthesis to conventional digital mammography: effect on image interpretation time of screening examinations. <i>Radiology</i> . 2014;270(1):49-56.	Observational-Dx	3665 examinations (1502 combined and 2163 DM)	To determine the effect of implementing a screening tomosynthesis program on real-world clinical performance by quantifying differences between interpretation times for conventional screening mammography and combined tomosynthesis and mammography for multiple participating radiologists with a wide range of experience in a large academic center.	The mean number of studies interpreted in hour was 23.8 +/- 0.55 (SD) (range, 14.4–40.4) for combined tomosynthesis and mammography and 34.0 +/- 0.55 (range, 20.4–54.3) for DM alone. A mean of 10.2 fewer studies were interpreted per hour during combined tomosynthesis and mammography compared with DM sessions ( $P<.0001$ ). The mean interpretation time was 2.8 minutes +/- 0.9 (range, 1.5–4.2 minutes) for combined tomosynthesis and mammography and 1.9 minutes +/- 0.6 (range, 1.1–3.0) for DM; interpretation time with combined tomosynthesis and mammography was 0.9 minute longer (47% longer) compared with DM alone ( $P<.0001$ ). With the increase in years of breast imaging experience, the overall additional time required to read images from combined tomosynthesis and mammography examinations decreased ( $R(2) = 0.52, P=.03$ ).	2
24. Skaane P, Bandos AI, Eben EB, et al. Two-view digital breast tomosynthesis screening with synthetically reconstructed projection images: comparison with digital breast tomosynthesis with full-field digital mammographic images. <i>Radiology</i> . 2014;271(3):655-663.	Experimental-Dx	24,901 examinations	To compare the performance of 2 versions of reconstructed 2D images in combination with DBT vs the performance of standard FFDM plus DBT.	CDRs were 8.0, 7.4, 7.8, and 7.7 per 1000 screening examinations for FFDM plus DBT in period 1, initial reconstructed 2D images plus DBT in period 1, FFDM plus DBT in period 2, and current reconstructed 2D images plus DBT in period 2, respectively. False-positive scores were 5.3%, 4.6%, 4.6%, and 4.5%, respectively. Corresponding reader-adjusted paired comparisons of false-positive scores revealed significant differences for period 1 ( $P=.012$ ) but not for period 2 (ratio = 0.99; 95% CI: 0.88, 1.11; $P=.85$ ).	1

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25. Bennett IC, Freitas R, Jr., Fentiman IS. Diagnosis of breast cancer in young women. <i>Aust N Z J Surg.</i> 1991;61(4):284-289.	Observational-Dx	227 patients; 235 biopsies performed	Retrospective analysis to determine if breast cancer is more difficult to diagnose in the 30–40 year old age group.	235 biopsies were performed in 227 patients, of which 199 were benign (85%) and 36 were malignant (15%), giving a malignant to benign biopsy ratio of 1:5.5. 36 cancers were diagnosed in 35 patients. Among these young women with breast cancer, the average duration of symptoms was 26 weeks, the mean clinical cancer diameter was 3.3 cm and only a small proportion (28%) of women had early (stage I) disease. There were 4 women with breast cancer (11%), in whom the diagnosis of malignancy was unsuspected preoperatively. Mammography in these younger women appears to have a more limited role, with a sensitivity of only 76%. These findings indicate that the diagnosis of breast cancer in younger women is often more difficult than in older age groups and that the presentation and detection of such cancers is often delayed. Younger women need to be educated in relation to seeking early medical review of breast lumps and clinicians need to be aware of the limitations of mammography in such cases.	4
26. Ciatto S, Bravetti P, Bonardi R, Rosselli del Turco M. The role of mammography in women under 30. 1990;80(5):676-678.	Observational-Dx	305 patients	To determine the appropriate use of mammography in younger women with a solid palpable mass.	Mammography missed 5/18 cancers (28%) and is not recommended in women under 30 except for preoperative cases with a strong suspicion of cancer.	3
27. Feig SA. Breast masses. Mammographic and sonographic evaluation. <i>Radiol Clin North Am.</i> 1992;30(1):67-92.	Review/Other-Dx	N/A	Review role of mammography and US in the evaluation of breast masses.	Characteristics that may allow a benign diagnosis for a circumscribed mass include the presence of fat and certain calcification patterns on the mammogram and features of a simple cyst on the US. For palpable breast masses, selection of mammography or US as the primary imaging modality will depend on patient's age and risk factors.	4
28. Harris VJ, Jackson VP. Indications for breast imaging in women under age 35 years. <i>Radiology.</i> 1989;172(2):445-448.	Observational-Dx	625 patients	Correlated patient histories with mammographic and/or US findings and biopsy or follow-up results for patients to determine appropriate indications for breast imaging in younger women.	Important indications: palpable mass and suspected abscess. Imaging helpful in 4/15 suspected abscesses. In patients with palpable masses, 6 cancers were found. No other significant indications. Women with low yield indications should be followed clinically and not referred for imaging.	3

\* See Last Page for Key

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29. Williams SM, Kaplan PA, Petersen JC, Lieberman RP. Mammography in women under age 30: is there clinical benefit? <i>Radiology</i> . 1986;161(1):49-51.	Observational-Dx	76 patients; 2 observers	Retrospective study to determine the utility of mammography in women less than 30 years of age referred for mammography.	55% had a palpable mass. In this group, no mass seen by mammography in 74%. But 14% had a definite lesion found by other means. No cancers were found. US may be best initial approach with mammography reserved for preoperative cases.	4
30. Checka CM, Chun JE, Schnabel FR, Lee J, Toth H. The relationship of mammographic density and age: implications for breast cancer screening. <i>AJR Am J Roentgenol</i> . 2012;198(3):W292-295.	Review/Other-Dx	7,007 screening mammograms	To examine the relationship between age and breast density, particularly focusing on postmenopausal women.	A total of 7,007 screening mammograms were performed. The median age of our cohort was 57 years. Within each subgroup categorized by decade of age, there was a normal distribution among the categories of breast density. There was a significant inverse relationship between age and breast density ( $P < 0.001$ ). 74% of patients between 40 and 49 years old had dense breasts. This percentage decreased to 57% of women in their 50s. However, 44% of women in their 60s and 36% of women in their 70s had dense breasts as characterized on their screening mammograms.	4
31. Carney PA, Miglioretti DL, Yankaskas BC, et al. Individual and combined effects of age, breast density, and hormone replacement therapy use on the accuracy of screening mammography. <i>Ann Intern Med</i> . 2003;138(3):168-175.	Observational-Dx	329,495 women	To determine how breast density, age, and use of hormone replacement therapy individually and in combination affect the accuracy of screening mammography.	Adjusted sensitivity ranged from 62.9% in women with extremely dense breasts to 87.0% in women with almost entirely fatty breasts; adjusted sensitivity increased with age from 68.6% in women 40 to 44 years of age to 83.3% in women 80 to 89 years of age. Adjusted specificity increased from 89.1% in women with extremely dense breasts to 96.9% in women with almost entirely fatty breasts. In women who did not use hormone replacement therapy, adjusted specificity increased from 91.4% in women 40 to 44 years of age to 94.4% in women 80 to 89 years of age. In women who used hormone replacement therapy, adjusted specificity was about 91.7% for all ages.	3

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
32. Durfee SM, Selland DL, Smith DN, Lester SC, Kaelin CM, Meyer JE. Sonographic Evaluation of Clinically Palpable Breast Cancers Invisible on Mammography. <i>Breast J.</i> 2000;6(4):247-251.	Observational-Dx	298 women	To determine the utility of US in the evaluation of palpable breast cancers invisible on mammography.	During the study period 298 women presented with a palpable breast cancer for imaging at our institution. Of these, 38 cancers (12.8%) were not seen on mammography. In 32 patients where no mammographic abnormality was found, US was able to detect a mass corresponding to the area of clinical concern. Histologic tumor types included 30 invasive ductal carcinomas, 5 ductal carcinomas in situ, and 3 invasive lobular carcinomas. Mammographic density was mild with scattered fibroglandular densities in 2 (5%), heterogeneously dense in 12 (32%), and extremely dense in 24 (63%). 31 masses (97%) were hypoechoic and 1 (3%) was echogenic. Lesion margins were irregular in 23 (72%), lobulated in 5 (16%), and well-circumscribed in 4 (12%). In this group of patients the combination of mammography and US of the mass demonstrated 99% of the palpable cancers	3
33. American College of Radiology. ACR Practice Parameter for the Performance of Stereotactic-Guided Breast Interventional Procedures. Available at: <a href="http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/Stereotactically_Guided_Breast.pdf">http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/Stereotactically_Guided_Breast.pdf</a> .	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	No results stated in abstract.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Liew PL, Liu TJ, Hsieh MC, et al. Rapid staining and immediate interpretation of fine-needle aspiration cytology for palpable breast lesions: diagnostic accuracy, mammographic, ultrasonographic and histopathologic correlations. <i>Acta Cytol.</i> 2011;55(1):30-37.	Observational-Dx	408 FNAC specimens from 400 patients	To investigate the role and turnaround time of rapid staining and immediate interpretation of FNAC for women with palpable breast lesions.	Of the 408 specimens, 243 (59.6%) were interpreted as benign, 37 (9.0%) atypical, 22 (5.4%) suspicious, 68 (16.7%) malignant, and 38 (9.3%) unsatisfactory. 132/408 (32.4%) had subsequent surgical procedures; the sensitivity, specificity, PPV, NPV, and accuracy were 88.5%, 100%, 100%, 81.9% and 92.4%, respectively. The average turnaround time was 8.6 min. Mammographic results were available in 242 (59.3%) cases, with 112 (46.3%) undergoing surgical excision. In correlation with mammography and surgical pathology, the false-positive rate, false-negative rate, sensitivity, specificity and accuracy were 1.9%, 10.5%, 98.1%, 89.5% and 95.8%, respectively. Rapid FNAC interpretation is a useful, effective diagnostic method for palpable breast lesions in the healthcare environment.	3
35. Rosa M, Mohammadi A, Masood S. The value of fine needle aspiration biopsy in the diagnosis and prognostic assessment of palpable breast lesions. <i>Diagn Cytopathol.</i> 2012;40(1):26-34.	Observational-Dx	1,583 cases; malignant diagnosis in 357 cases	To assess the diagnostic accuracy of FNAB in palpable breast lesions, the authors reviewed their experience during an 8-year-period and compared FNAB results with follow-up surgical specimens.	139 cases were classified as atypical/suspicious, 135 cases had insufficient cells for establishing a diagnosis, and 952 were categorized as negative. A total of 408 follow-up surgical specimens were available for comparison with cytologic results. There were 19 false-negative, and no false-positive results were found. The majority of false-negative results were secondary to sampling errors. In 93% of the malignant cases, there was enough material obtained in cytological specimens to perform prognostic/predictive factors studies. The data proves that FNAB is a reliable method for the initial evaluation and diagnosis of palpable masses of the breast. In addition, it also has the ability of providing necessary prognostic/predictive information, particularly for patients that may undergo neoadjuvant therapy.	4



**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
36. Garg S, Mohan H, Bal A, Attri AK, Kochhar S. A comparative analysis of core needle biopsy and fine-needle aspiration cytology in the evaluation of palpable and mammographically detected suspicious breast lesions. <i>Diagn Cytopathol.</i> 2007;35(11):681-689.	Observational-Dx	50 patients	To compare value of needle core biopsy and FNAC in the evaluation of palpable and mammographically detected suspicious breast lesions.	Sensitivity and specificity of mammography for malignant diagnosis was 84.37% and 83.33%, respectively. Sensitivity and specificity of FNAC for malignant diagnosis was 78.15% and 94.44%, respectively, and of needle core biopsy was 96.5% and 100%, respectively. Needle core biopsy is superior to FNAC in the diagnosis of breast lesions in terms of sensitivity, specificity, correct histological categorization of the lesions and tumor grading.	3
37. Homesh NA, Issa MA, El-Sofiani HA. The diagnostic accuracy of fine needle aspiration cytology versus core needle biopsy for palpable breast lump(s). <i>Saudi Med J.</i> 2005;26(1):42-46.	Experimental-Dx	296 patients	Prospective randomized controlled clinical trial to compare the accuracy of FNAC and core needle biopsy in patients with palpable breast masses.	FNAC had sensitivity of 66.66%, specificity of 81.8% accuracy of 75.7%, PPV of 100% and NPV of 90%. Core needle breast biopsy had sensitivity of 92.3%, specificity of 94.8%, and accuracy of 93.4%, PPV of 100% and NPV 100%. Core needle biopsy is more accurate than FNAC. Both procedures are simple, easy, safe, cheap and reliable, but core needle biopsy is more accurate than the FNAC.	3
38. Pisano ED, Fajardo LL, Caudry DJ, et al. Fine-needle aspiration biopsy of nonpalpable breast lesions in a multicenter clinical trial: results from the radiologic diagnostic oncology group V. <i>Radiology.</i> 2001;219(3):785-792.	Experimental-Dx	442 patients	Multicenter study to determine the diagnostic accuracy of US and stereotactically guided FNAB in the diagnosis of nonpalpable breast lesions.	Sensitivity and specificity of FNAB were 85%–88% and 55.6%–90.5%, respectively; accuracy ranged from 62.2%–89.2%. Diagnostic accuracy of FNAB was significantly better for detection of masses than for detection of calcifications (67.3% vs 53.8%, $P=.006$ ) and with US guidance than with stereotactic guidance (77.2% vs 58.9%; $P=.002$ ). FNAB of nonpalpable breast lesions has limited value given the high insufficient sample rate and greater diagnostic accuracy of other interventions, including core-needle biopsy and needle-localized open surgical biopsy.	3

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Liberman L, Ernberg LA, Heerdt A, et al. Palpable breast masses: is there a role for percutaneous imaging-guided core biopsy? <i>AJR Am J Roentgenol.</i> 2000;175(3):779-787.	Observational-Dx	107 women; 115 palpable masses	Review findings to evaluate percutaneous imaging-guided core biopsy in assessment of selected palpable breast masses.	Percutaneous image-guided core biopsy spared additional diagnostic tissue sampling in 74% of selected women. Imaging-guided core biopsy is useful in evaluating palpable breast masses that are small, deep, mobile, vaguely palpable, or multiple. In this study, percutaneous imaging-guided core biopsy spared additional diagnostic tissue sampling in 74% women with palpable breast masses.	3
40. Giess CS, Smeglin LZ, Meyer JE, Ritner JA, Birdwell RL. Risk of malignancy in palpable solid breast masses considered probably benign or low suspicion: implications for management. <i>J Ultrasound Med.</i> 2012;31(12):1943-1949.	Observational-Dx	381 patients	To determine whether solid palpable breast masses with benign sonographic features have <2% incidence of malignancy, allowing management by surveillance instead of biopsy.	The study population included 440 lesions in 381 patients (mean age, 31.0 years; range, 15–68 years). A total of 161 lesions were prospectively classified as BI-RADS 3 and 279 as BI-RADS 4A. A total of 295 lesions (67%) had biopsy within 4.5 months of presentation, with 3 invasive malignancies; 145/440 lesions (33%) underwent surveillance. 41 lesions were considered benign for the following reasons: stability for at least 24 months (n = 28), benign tissue diagnosis during surveillance (n = 5), and decrease/resolution during follow-up (n = 8). The malignancy rate in lesions with adequate follow-up or biopsy was 3 of 336 (0.9%). All 3 malignancies occurred in women older than 40 years.	3
41. Ha R, Kim H, Mango V, Wynn R, Comstock C. Ultrasonographic features and clinical implications of benign palpable breast lesions in young women. <i>Ultrasonography.</i> 2015;34(1):66-70.	Observational-Dx	68 patients	To describe the breast US features and to investigate whether performing a core biopsy is warranted in young women having palpable solid breast masses.	All 76 palpable solid masses yielded benign pathology. On the US, the shape of the mass was described by radiologists 1 and 2 as oval or round (63.2% and 71.1%), margin as circumscribed (68.4% and 77.6%) and orientation as parallel (85.5% and 90.8%); the frequency of using all 3 benign descriptors was 61.8% and 68.5%, respectively. Suspicious descriptors were used less frequently by radiologists 1 and 2 including irregular shape (9.2% and 13.1%), noncircumscribed margin (31.6% and 22.4%) and nonparallel orientation (14.5% and 9.2%); the frequency of using all 3 suspicious descriptors was 9.2% and 11.8%, respectively.	3

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
42. Loving VA, DeMartini WB, Eby PR, Gutierrez RL, Peacock S, Lehman CD. Targeted ultrasound in women younger than 30 years with focal breast signs or symptoms: outcomes analyses and management implications. <i>AJR Am J Roentgenol.</i> 2010;195(6):1472-1477.	Observational-Dx	830 patients	To assess the accuracy of targeted breast US in women younger than 30 years presenting with focal breast signs or symptoms.	Among 830 study patients, lesions were assessed as BI-RADS category 1 or 2 in 526 (63.4%), BI-RADS category 3 in 140 (16.9%), BI-RADS category 4 in 163 (19.6%), and BI-RADS category 5 in 1 (0.1%) patient. 3 malignancies were detected, for a cancer yield of 0.4%. No BI-RADS category 3 lesions, 2 BI-RADS category 4 lesions, and the single BI-RADS category 5 lesion were malignant. US sensitivity was 100%, specificity was 80.5%, NPV was 100%, PPV2 was 1.8%, and PPV3 was 1.9%.	3
43. Patterson SK, Neal CH, Jeffries DO, et al. Outcomes of solid palpable masses assessed as BI-RADS 3 or 4A: a retrospective review. <i>Breast Cancer Res Treat.</i> 2014;147(2):311-316.	Review/Other-Dx	487 women	To evaluate the outcomes and cancer rate in solid palpable masses with benign features assessed as BI-RADS 3 or 4A.	There were 197 BI-RADS 3 and 376 BI-RADS 4A masses. The overall cancer rate was 1.6 % (9/573). All cancers were BI-RADS 4A (cancer rate 2.4%, 9/376). Smaller mean size and younger age at presentation in BI-RADS 3 women was found compared to BI-RADS 4A ( $P<0.0001$ ). There was a significant increase in cancer rate across age quartiles ( $P=0.03124$ ). The cancer rate is very low in solid palpable masses with benign features.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. Raza S, Chikarmane SA, Neilsen SS, Zorn LM, Birdwell RL. BI-RADS 3, 4, and 5 lesions: value of US in management--follow-up and outcome. <i>Radiology</i> . 2008;248(3):773-781.	Observational-Dx	767 patients with 926 masses (476 palpable, 450 nonpalpable)	To evaluate the use, final outcome, and positive biopsy rate of American College of Radiology Ultrasonographic (US) Breast Imaging Reporting and Data System (BI-RADS) categories 3, 4, and 5 recommended for breast masses.	In BI-RADS 3 masses (n=356), imaging follow-up of 252 masses documented stability for 6–24 months. Aspiration of 24 masses revealed cysts. Biopsy in 80 masses revealed 3 malignancies, all of which were diagnosed within 6 months of the index examination, were <1 cm, and were node negative (NPV 99.2%). In BI-RADS 4 masses (n=524), aspiration results indicated 35 cysts; biopsy in 455 revealed 85 malignancies (PPV 16.2%). Imaging follow-up only in 34 revealed no cancers 2 and more years later. Among BI-RADS 5 masses (n=46), 43 were malignant and 3 benign (PPV 93.4%). Inconsistent use of BI-RADS category 3 occurred in 14.0% of cases when biopsy was recommended. Although biopsy was performed in almost equal numbers of palpable and nonpalpable masses, only 11% of palpable BI-RADS 3 and 4 masses were malignant, as compared with 22% of nonpalpable masses. Strict adherence to lexicon characteristics of probably benign lesions should improve specificity.	3
45. Smith GE, Burrows P. Ultrasound diagnosis of fibroadenoma - is biopsy always necessary? <i>Clin Radiol</i> . 2008;63(5):511-515; discussion 516-517.	Observational-Dx	447 patients	To retrospectively review US characteristics of fibroadenoma and the necessity to biopsy all fibroadenomas in patients under 25 years.	357/447 patients had US diagnosis of fibroadenoma. This was histologically proven in 281 (78.8%) cases. In 75 (21.5%) of these patients, the final histology was either another benign pathology or normal. Most patients in the 25 years and under age group have benign breast pathology, most commonly fibroadenoma. US is a reliable technique to diagnose fibroadenoma.	3

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>46. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. <i>Radiology</i>. 2004;233(3):830-849.</p>	<p>Observational-Dx</p>	<p>111 consecutive women</p>	<p>To prospectively assess the diagnostic accuracy of mammography, clinical examination, US, and MRI in the preoperative imaging of breast cancer.</p>	<p>Mammographic sensitivity was highest for invasive ductal carcinoma in 89/110 (81%) cases vs 10 of 29 (34%) cases of invasive lobular carcinoma (<math>P=.001</math>) and 21/38 (55%) cases of DCIS (<math>P=.01</math>). US showed higher sensitivity than did mammography for invasive ductal carcinoma, depicting 104/110 (94%) cases, and for invasive lobular carcinoma, depicting 25/29 (86%) cases (<math>P=.01</math> for each). US showed higher sensitivity for invasive cancer than DCIS (18/38 [47%], <math>P=.001</math>). MR showed higher sensitivity than did mammography for all tumor types (<math>P=.01</math>) and higher sensitivity than did US for DCIS (<math>P=.001</math>), depicting 105/110 (95%) cases of invasive ductal carcinoma, 28/29 (96%) cases of invasive lobular carcinoma, and 34/38 (89%) cases of DCIS. In anticipation of conservation or no surgery after mammography and clinical examination in 96 breasts, additional tumor was present in 30. Additional tumor was depicted in 17/96 (18%) breasts at US and in 29/96 (30%) at MR, though extent was now overestimated in 12/96 (12%) at US and 20/96 (21%) at MRI. After combined mammography, clinical examination, and US, MR 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 MR in an additional 3. 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.</p>	<p>3</p>

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Spick C, Szolar DH, Preidler KW, Tillich M, Reittner P, Baltzer PA. Breast MRI used as a problem-solving tool reliably excludes malignancy. <i>Eur J Radiol.</i> 2015;84(1):61-64.	Observational-Dx	111 patients	To evaluate the diagnostic performance of breast MRI if used as a problem-solving tool in BI-RADS 0 cases.	111 patients with BI-RADS 0 conventional imaging findings revealed 30 (27%) mammographic masses, 57 (51.4%) mammographic architectural distortions, 5 (4.5%) mammographic microcalcifications, 17 (15.3%) US-only findings, and 2 palpable findings without imaging correlates. There were 15 true-positive, 85 true-negative, 11 false-positive, and zero false-negative breast MRI findings, resulting in a sensitivity, specificity, PPV, and NPV of 100% (15/15), 88.5% (85/96), 57.7% (15/26), and 100% (85/85), respectively. Breast density and reasons for referral had no significant influence on the diagnostic performance of breast MRI ( $P>0.05$ ).	3
48. Olsen ML, Morton MJ, Stan DL, Pruthi S. Is there a role for magnetic resonance imaging in diagnosing palpable breast masses when mammogram and ultrasound are negative? <i>J Womens Health (Larchmt).</i> 2012;21(11):1149-1154.	Observational-Dx	77 studies	To examine the use and utility of breast MRI in evaluating palpable breast masses with negative diagnostic mammogram and US studies.	77 studies were included, comprising 1.3% of all breast MRI studies performed at our institution during the study period (2005-2011). 22 patients underwent biopsy, and 55 were followed clinically without biopsy. Approximately half (27/55) of the patients without biopsy were lost to follow-up after negative MRI, and the rest had no evidence of cancer on imaging or clinical examination at 1 year. Of the 22 patients who underwent biopsy, 2 were diagnosed with cancer, both with positive MRI studies. Sensitivity of MRI when compared to tissue diagnosis was 100%, and specificity was 70%. PPV and NPV were 25% and 100%, respectively.	3

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
49. Yau EJ, Gutierrez RL, DeMartini WB, Eby PR, Peacock S, Lehman CD. The utility of breast MRI as a problem-solving tool. <i>Breast J.</i> 2011;17(3):273-280.	Observational-Dx	3,001 consecutive breast MR examinations	Records of breast MR examinations were reviewed to identify all those performed for the clinical indication of problem solving. Details of clinical presentation, mammography and US findings, follow-up recommendations, and pathology outcomes were recorded.	36 biopsies were performed based on MRI findings and 14 cancers were diagnosed. Biopsy was indicated for 11/14 (79%) cancers based on suspicious mammographic or US findings identified prior to MRI. 1 incidental cancer was detected by MRI alone in a patient at high risk for breast cancer, and 2 cancers were detected in patients with suspicious nipple discharge and negative mammogram and US. A single false-negative MRI occurred in a patient whose evaluation for a palpable lump prompted biopsy. Problem-solving breast MRI rarely identifies otherwise occult cancer and can be falsely negative in patients with suspicious findings on mammogram and US. Until the benefits and risks of problem-solving MRI are clarified, it should be used judiciously.	3
50. Leung JW. MR imaging in the evaluation of equivocal clinical and imaging findings of the breast. <i>Magn Reson Imaging Clin N Am.</i> 2010;18(2):295-308, ix-x.	Review/Other-Dx	N/A	To examine the clinical scenarios and imaging findings in which MRI is contributory to patient management after conventional workup with equivocal results.	No results stated in abstract.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
<p>51. Berg WA, Weinberg IN, Narayanan D, et al. High-resolution fluorodeoxyglucose positron emission tomography with compression ("positron emission mammography") is highly accurate in depicting primary breast cancer. <i>Breast J.</i> 2006;12(4):309-323.</p>	<p>Observational-Dx</p>	<p>92 lesions in 77 women</p>	<p>To prospectively assess the diagnostic performance of a high-resolution PET scanner using mild breast compression (PEM).</p>	<p>Of 48 cancers, 16 (33%) were clinically evident; 11 (23%) were DCIS, and 37 (77%) were invasive (30 ductal, 4 lobular, and 3 mixed; median size 21 mm). PEM depicted 10/11 (91%) DCIS and 33/37 (89%) invasive cancers. PEM was positive in 1 of 2 T1a tumors, 4 of 6 T1b tumors, 7 of 7 T1c tumors, and 4 of 4 cases where tumor size was not available (eg, no surgical follow-up). PEM sensitivity for detecting cancer was 90%, specificity 86%, PPV 88%, NPV 88%, accuracy 88%, and AUC 0.918. In 3 patients, cancer foci were identified only on PEM, significantly changing patient management. Excluding 8 diabetic subjects and 8 subjects whose lesions were characterized as clearly benign with conventional imaging, PEM sensitivity was 91%, specificity 93%, PPV 95%, NPV 88%, accuracy 92%, and Az 0.949 when interpreted with mammographic and clinical findings. FDG-PEM has high diagnostic accuracy for breast lesions, including DCIS.</p>	<p>2</p>



**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. 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. <i>Radiology</i> . 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

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. Surti S. Radionuclide methods and instrumentation for breast cancer detection and diagnosis. <i>Semin Nucl Med.</i> 2013;43(4):271-280.	Review/Other-Dx	N/A	To describe some of the dedicated imaging systems (PEM and BSGI) that have been developed both commercially and in research laboratories for radionuclide imaging of breast cancer.	Clinical studies with dedicated PEM scanners show improved sensitivity to detecting cancer in patients when using PEM in conjunction with additional imaging modalities, such as MRI or mammography or both, as well as improved disease staging that can have an effect on surgical planning. High-resolution BSGI systems are more widely available commercially and several clinical studies have shown very high sensitivity and specificity in detecting cancer in high-risk patients.	4
54. Samson DJ, Flamm CR, Pisano ED, Aronson N. Should FDG PET be used to decide whether a patient with an abnormal mammogram or breast finding at physical examination should undergo biopsy? <i>Acad Radiol.</i> 2002;9(7):773-783.	Meta-analysis	13 studies	To assess the performance of FDG-PET in the differential diagnosis of benign from malignant lesions among patients with abnormal mammograms or a palpable breast mass and to examine the effects of PET findings on patient care and health outcomes.	A point on the summary receiver operating characteristic curve was selected that reflected average performance, with an estimated sensitivity of 89% and a specificity of 80%. When the prevalence of malignancy is 50%, 40% of all patients would benefit by avoiding the harm of a biopsy with negative biopsy results. The risk of a false-negative result, leading to delayed diagnosis and treatment, is 5.5%. The NPV is 87.9%; thus, the false-negative risk is 12.1%. For a patient with a negative PET scan, a 12% chance of missed or delayed diagnosis of breast cancer is probably too high to make it worth the 88% chance of avoiding biopsy of a benign lesion.	M

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
55. Mathieu I, Mazy S, Willemart B, Destine M, Mazy G, Lonneux M. Inconclusive triple diagnosis in breast cancer imaging: is there a place for scintimammography? <i>J Nucl Med.</i> 2005;46(10):1574-1581.	Observational-Dx	104 patients; 118 procedures	Retrospective study to evaluate impact of SM in patients with doubtful or discordant triple diagnosis — that is mammography, US, and FNAC.	Breast cancer was proven in 69 cases. SM-SPECT had a sensitivity of 88.4% and a specificity of 67%. 11 cancers were detected by SPECT, although planar images were negative. SM-SPECT was more sensitive in patients scanned at initial presentation (95%) than in those with suspected recurrence (81%). SM-SPECT correctly evaluated multicentricity or bilaterally in 8/11 patients and resulted in an increased tumor size in 8 patients. Overall, SM-SPECT modified the patient management in 58/118 cases (49%): SM made the diagnosis of cancer in 30 cases with doubtful or discordant triple diagnosis and ruled out malignancy in 28 cases. SM-SPECT had a sensitivity of 88.4% and a specificity of 67%. Overall, SM-SPECT modified patient management in 58/118 cases (49%).	3
56. Yutani K, Shiba E, Kusuoka H, et al. Comparison of FDG-PET with MIBI-SPECT in the detection of breast cancer and axillary lymph node metastasis. <i>J Comput Assist Tomogr.</i> 2000;24(2):274-280.	Observational-Dx	40 patients	Compare FDG-PET to Tc-99m MIBI-SPECT for breast cancer diagnosis and axillary lymph node metastasis in the same patients.	38 patients had breast cancer, and the remaining 2 had benign breast lesions. The sensitivities of FDG-PET and MIBI-SPECT were 78.9% and 76.3% for breast cancer and 50.0% and 37.5% for axillary lymph node metastasis, respectively. MIBI-SPECT is comparable with FDG-PET in detecting breast cancer. Neither FDG-PET nor MIBI-SPECT is sufficiently sensitive to rule out axillary lymph node metastasis.	2

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. Brem RF, Fishman M, Rapelyea JA. Detection of ductal carcinoma in situ with mammography, breast specific gamma imaging, and magnetic resonance imaging: a comparative study. <i>Acad Radiol.</i> 2007;14(8):945-950.	Observational-Dx	20 women with 22 biopsy-proven DCIS	To evaluate the sensitivity of high-resolution BSGI for the detection of DCIS based on histopathology and to compare the sensitivity of BSGI with mammography and MRI for the detection of DCIS.	Pathologic tumor size of the DCIS ranged from 2 to 21 mm (mean 9.9 mm). Of 22 cases of biopsy-proven DCIS in 20 women, 91% were detected with BSGI, 82% were detected with mammography, and 88% were detected with MRI. BSGI had the highest sensitivity for the detection of DCIS, although this small sample size did not demonstrate a statistically significant difference. 2 cases of DCIS (9%) were diagnosed only after BSGI demonstrated an occult focus of radiotracer uptake in the contralateral breast, previously undetected by mammography. There were 2 false-negative BSGI studies. BSGI has higher sensitivity for the detection of DCIS than mammography or MRI and can reliably detect small, subcentimeter lesions.	3
58. Brem RF, Floerke AC, Rapelyea JA, Teal C, Kelly T, Mathur V. Breast-specific gamma imaging as an adjunct imaging modality for the diagnosis of breast cancer. <i>Radiology.</i> 2008;247(3):651-657.	Observational-Dx	146 women	To retrospectively determine the sensitivity and specificity of BSGI for the detection of breast cancer by using pathologic results as the reference standard.	In 146 patients, 167 lesions underwent biopsy, of which 83 (16 DCIS and 67 invasive cancers) were malignant. Of 84 nonmalignant lesions, 82 were benign and 2 showed atypical histologic results (1 atypical lobular hyperplasia and 1 lobular carcinoma in situ). BSGI helped detect cancer in 80/83 malignant lesions with a sensitivity of 96.4% (95% CI: 92%, 99%) and correctly identified 50/84 nonmalignant lesions as negative for cancer with a specificity of 59.5% (95% CI: 49%, 70%). The PPV for 80/114 malignant lesions with a BSGI examination with findings positive for cancer was 68.8% (95% CI: 60%, 78%) and the NPV for 50/53 nonmalignant lesions was 94.3% (95% CI: 88%, 99%). The smallest invasive cancer and DCIS detected were both 1 mm. BSGI helped detect occult cancer not visualized at mammography or US in 6 patients. BSGI has high sensitivity (96.4%) and moderate specificity (59.5%) helping detect breast cancers.	3

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Rhodes DJ, Hruska CB, Phillips SW, Whaley DH, O'Connor MK. Dedicated dual-head gamma imaging for breast cancer screening in women with mammographically dense breasts. <i>Radiology</i> . 2011;258(1):106-118.	Observational-Dx	936 patients	To compare performance characteristics of dedicated dual-head gamma imaging and mammography in screening women with mammographically dense breasts.	Of 936 participants, 11 had cancer (1 with mammography only, 7 with gamma imaging only, 2 with both combined, and 1 with neither). Diagnostic yield was 3.2 per 1000 (95% CI: 1.1, 9.3) for mammography, 9.6 per 1000 (95% CI: 5.1, 18.2) for gamma imaging, and 10.7 per 1000 (95% CI: 5.8, 19.6) for both ( $P=.016$ vs mammography alone). 1 participant had a second ipsilateral cancer detected with gamma imaging only. Prevalent screening gamma imaging demonstrated equivalent specificity relative to incident screening mammography (93% [861/925] vs 91% [840/925], $P=.069$ ). Of 8 cancers detected with gamma imaging only, 6 (75%) were invasive (median size, 1.1 cm; range, 0.4–5.1 cm); all were node negative. The ratio of the number of patients with breast cancer per number of screening examinations with abnormal findings was 3% (3/88) for mammography and 12% (9/73) for gamma imaging ( $P=.01$ ). The number of breast cancers diagnosed per number of biopsies performed was 18% (3/17) for mammography and 28% (10/36) for gamma imaging ( $P=.36$ ).	2
60. Liu L, Song Y, Gao S, et al. (99mTc-3PRGD2 scintimammography in palpable and nonpalpable breast lesions. <i>Mol Imaging</i> . 2014;13.	Observational-Dx	94 patients	To explore the diagnostic performance of 99mTc-3(poly-(ethylene glycol),PEG)4-RGD2 (99mTc-3PRGD2) SM in patients with either palpable or nonpalpable breast lesions and compare SM to mammography to assess the possible incremental value of SM in breast cancer detection. We also investigated the alphavbeta3 expression in malignant and benign breast lesions.	Histopathology revealed 46 malignant lesions and 64 benign lesions. The overall sensitivity, specificity, accuracy, PPV, and NPV of SM were 83%, 73%, 77%, 69%, and 85%, respectively. The kappa value between the 2 reviewers was 0.63. The diagnostic values of SM were higher than those of mammography in evaluating overall breast lesions. A sensitivity of 91% was achieved when SM and mammography results were combined with 60% of all false-negative mammography findings classified as true-positive results by SM. Integrin alphavbeta3 expression was positively identified using SM imaging.	2

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
61. Pearson KL, Sickles EA, Frankel SD, Leung JW. Efficacy of step-oblique mammography for confirmation and localization of densities seen on only one standard mammographic view. <i>AJR Am J Roentgenol.</i> 2000;174(3):745-752.	Review/Other-Dx	69 consecutive women	To describe the step-oblique technique and evaluate its efficacy.	Step-oblique mammography differentiated 50 real lesions from 19 summation artifacts. All 50 real lesions, although initially visible on only 1 standard projection, were successfully localized in 3D. Subsequent management resulted in the prompt detection and diagnosis of 7 breast cancers and 21 benign lesions. None of the remaining findings managed by follow-up rather than biopsy have subsequently been found to be malignant. Step-oblique mammography is an effective means of evaluating the mammographic finding visible on multiple images on only one standard projection.	4
62. Harvey JA. Sonography of palpable breast masses. <i>Semin Ultrasound CT MR.</i> 2006;27(4):284-297.	Review/Other-Dx	N/A	Review usefulness of US in the evaluation of palpable breast masses.	US is useful in characterizing palpable masses as well as detecting cancer in women with negative mammograms. The NPV of imaging for cancer in the evaluation of a palpable lump is very high, which may reassure women with low-suspicion palpable findings. Short-term follow-up of a palpable mass with benign features may be feasible, though further study is needed to establish criteria. A suspicious dominant palpable finding should be further evaluated even if imaging is negative.	4
63. American College of Radiology. ACR Practice Parameter for the Performance of a Breast Ultrasound Examination. Available at: <a href="http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/US_Breast.pdf">http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/US_Breast.pdf</a> .	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	No results stated in abstract.	4
64. American College of Radiology. ACR Practice Parameter for the Performance of Ultrasound-Guided Percutaneous Breast Interventional Procedures . Available at: <a href="http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/US_Guided_Breast.pdf">http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/US_Guided_Breast.pdf</a> .	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	No results stated in abstract.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
65. American College of Radiology. ACR Practice Parameter for Performing and Interpreting Magnetic Resonance Imaging (MRI). Available at: <a href="http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/MRI.pdf">http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/MRI.pdf</a> .	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	No results stated in abstract.	4
66. Schradin S, Distelmaier M, Dirrichs T, et al. Digital breast tomosynthesis-guided vacuum-assisted breast biopsy: initial experiences and comparison with prone stereotactic vacuum-assisted biopsy. <i>Radiology</i> . 2015;274(3):654-662.	Observational-Dx	205 patients	To use DBT-guided VAB to sample target lesions identified at FFDM and compare clinical performance with that of prone stereotactic VAB.	Technical success was achieved in 51 of 51 lesions (100%) with DBT VAB vs 154 of 165 lesions (93%) with prone stereotactic VAB. In 1 of 11 lesions in which prone stereotactic VAB failed, DBT VAB was performed successfully. Mean time to complete VAB was 13 minutes +/- 3.7 for DBT VAB vs 29 minutes +/- 10.1 for prone stereotactic VAB ( $P<.0001$ ). Reidentifying and targeting lesions during prone stereotactic VAB took longer than it did during DBT VAB ( $P<.0001$ ). Tissue sampling took about the same time for prone stereotactic VAB and DBT VAB ( $P=.067$ ). Significantly more “low-contrast” (ie, uncalcified) target lesions were biopsied with DBT VAB (13/51 lesions) vs prone stereotactic VAB (9/165 lesions) ( $P<.0002$ ). No major complications were observed with either system. 1 patient who underwent DBT VAB in the sitting position and 1 patient who underwent prone stereotactic VAB developed self-limiting vasovagal reactions.	3

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
67. Viala J, Gignier P, Perret B, et al. Stereotactic vacuum-assisted biopsies on a digital breast 3D-tomosynthesis system. <i>Breast J.</i> 2013;19(1):4-9.	Review/Other-Dx	118 stereotactic VABs	To describe our operating process and to report results of 118 stereotactic VABs performed on a 3D DBT system.	A total of 106 patients had a lesion, 6 had 2 lesions. 61 lesions were clusters of micro-calcifications, 54 were masses and 3 were architectural distortions. Patients were in lateral decubitus position to allow shortest skin-target approach (or sitting). Specific compression paddle, adapted on the system, performed, and graduated, allowing localization in X-Y. Tomosynthesis views define the depth of lesion. Graduated Coaxial localization kit determines the beginning of the biopsy window. Biopsies were performed with an ATEC-Suros, 9 Gauge handpiece. All biopsies, except 1, have reached the lesions. 5 hemorrhages were incurred in the process, but no interruption was needed. 8 breast hematomas, were all spontaneously resolved. 1 was an infection. About 40% of patients had a skin ecchymosis. Processing is fast, easy, and requires lower irradiation dose than with classical stereotactic biopsies. Histology analysis reported 45 benign clusters of micro-calcifications, 16 malignant clusters of micro-calcifications, 24 benign masses, and 33 malignant masses. Of 13 malignant lesions, digital 2D-mammography failed to detect 8 lesions and underestimated the classification of 5 lesions.	4



**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
68. Harvey JA, Nicholson BT, Lorusso AP, Cohen MA, Bovbjerg VE. Short-term follow-up of palpable breast lesions with benign imaging features: evaluation of 375 lesions in 320 women. <i>AJR Am J Roentgenol.</i> 2009;193(6):1723-1730.	Observational-Dx	320 women with 375 masses	To evaluate the feasibility of short-term follow-up of palpable masses that has benign imaging features.	Lesions were evaluated with mammography and US (n=186) or US alone (n=189). Masses were typically identified only with US (n=258, 68.8%); were oval (n=275, 73.3%), of equal density to normal breast tissue on mammograms (n=95 on 117 mammograms, 81.2%), and hypoechoic (n=336 in 372 US examinations, 90.3%); and were prospectively believed to be fibroadenoma (n=304, 81.1%). 85 lesions (22.7%) were biopsied soon after evaluation, and one 1.5 mm DCIS was diagnosed. At follow-up (mean, 2.7 years), 26 lesions (6.9%) had grown. 24/26 lesions were biopsied, and no cancer was diagnosed. The overall cancer prevalence was similar for palpable (0.3%) and nonpalpable (1.6%) masses. The cost of short-term follow-up was less than that of biopsy. Short-term follow-up is a reasonable alternative to biopsy of palpable breast lesions with benign imaging features, particularly for young women with probable fibroadenoma.	3
69. Stavros AT, Thickman D, Rapp CL, Dennis MA, Parker SH, Sisney GA. Solid breast nodules: use of sonography to distinguish between benign and malignant lesions. <i>Radiology.</i> 1995;196(1):123-134.	Observational-Dx	622 women; 750 lesions	Prospective classification of nodules to determine whether US could accurately distinguish benign from malignant lesions and whether this distinction could be definite enough to obviate biopsy.	Benign histologic features were found in 625 (83%) lesions; malignant histologic features, in 125 (17%). Of benign lesions, 424 had been prospectively classified as benign. 2 lesions classified as benign were found to be malignant at biopsy. Thus, the classification scheme had a NPV of 99.5%. Of 125 malignant lesions, 123 were correctly classified as indeterminate or malignant (98.4% sensitivity). US can be used to accurately classify some solid lesions as benign, allowing imaging follow-up rather than biopsy.	2
70. D'Orsi CJ, Sickles EA, Mendelson EB, Morris EA, et al. <i>ACR BI-RADS® Atlas, Breast Imaging Reporting and Data System.</i> 5th ed. Reston, VA: American College of Radiology; 2013.	Review/Other-Dx	N/A	To provide standardized breast imaging findings terminology, report organization, assessment structure and a classification system for mammography, US and MRI of the breast.	No results stated in abstract.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Shin JH, Han BK, Ko EY, Choe YH, Nam SJ. Probably benign breast masses diagnosed by sonography: is there a difference in the cancer rate according to palpability? <i>AJR Am J Roentgenol.</i> 2009;192(4):W187-191.	Observational-Dx	352 women	Retrospective study to determine whether there is a difference in cancer rates between palpable and nonpalpable probably benign breast nodules detected by US.	Among the 374 masses, 86 masses (23%) that were lost to follow-up were excluded. Of the 288 masses with follow-up or excision, the cancer rate was 2.4% (7/288). The cancer rate of the nonpalpable masses was 2.1% (4/194) (95% CI, 0.6%–5.2%), and the cancer rate of the palpable masses was 3.2% (3/94) (95% CI, 0.6%–9.0%), with no statistically significant difference ( $P=0.6864$ ). Of the 7 cancers, 5 were diagnosed by a US guided core biopsy and 2 were diagnosed by surgical excision after a benign biopsy. The 7 US false-negative masses in 7 patients were identified as 3 invasive ductal carcinomas, 2 DCIS, 1 mucinous carcinoma, and 1 papillary carcinoma on the basis of pathology results. There is no statistically significant difference between the cancer rates of palpable and nonpalpable BI-RADS category 3 masses seen on US.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
72. Barr RG, Zhang Z, Cormack JB, Mendelson EB, Berg WA. Probably benign lesions at screening breast US in a population with elevated risk: prevalence and rate of malignancy in the ACRIN 6666 trial. <i>Radiology</i> . 2013;269(3):701-712.	Review/Other-Dx	2662 participants	To prospectively validate predefined breast US BI-RADS category 3 criteria in a multicenter setting in an elevated-risk population.	Of 2662 participants, 519 (19.5%) had 745 BI-RADS category 3 lesions (25.5% of 2916 US lesions other than simple cysts), with a median size of 7 mm (range, 2–135 mm). The number of new BI-RADS category 3 lesions decreased with year 2–3 screening, but the percentage of new BI-RADS category 3 lesions was stable at 26.4% (506/1920 lesions), 23.6% (142/601 lesions), and 24.6% (97/395 lesions), respectively. Of 745 BI-RADS category 3 lesions, 124 (16.6%) were ultimately sampled for biopsy. 6 malignancies (0.8% of BI-RADS category 3 lesions; 95% CI: 0.3%, 1.7%) occurred in 5 (1.0%) of 519 participants: 5 malignancies were invasive (median size, 10 mm; size range, 2–18 mm), and 1 was node positive. When the analysis is limited to lesions with at least 2-year follow-up or biopsy, the malignancy rate among BI-RADS category 3 lesions is 0.9% (95% CI: 0.3%, 2.0%). 3 malignant BI-RADS category 3 lesions were sampled for biopsy because of a suspicious change at follow-up (2 N0 lesions, 1 each at 6- and 12-month follow-up; 1 N1 lesion at 24-month follow-up), 1 was sampled for biopsy because of an upgrade after additional mammography (NX), 1 was found at mastectomy for another cancer (N0), and 1 was found at prophylactic contralateral mastectomy in the same patient (NX).	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
73. Gordon PB, Gagnon FA, Lanzkowsky L. Solid breast masses diagnosed as fibroadenoma at fine-needle aspiration biopsy: acceptable rates of growth at long-term follow-up. <i>Radiology</i> . 2003;229(1):233-238.	Review/Other-Dx	1070 patients	To determine what growth rate is acceptable before recommending histologic diagnosis of solid breast lesions diagnosed as fibroadenoma at FNAB.	There were 567 interval measurements of 179 masses in 173 patients younger than 50 years and 50 measurements of 15 masses in 14 patients 50 years or older at the time of FNAB. The 95th percentile for percentage change in volume per month was approximately 16% for patients younger than 50 years; the 90th percentile was approximately 13% for patients 50 years or older. The 95th percentile mean change in dimension in a 6-month interval for those younger than 50 years was 20%; the 90th percentile change for those 50 years or older was also 20%. All excised masses with slower growth proved benign at histologic examination.	4
74. Andersson I, Ikeda DM, Zackrisson S, et al. Breast tomosynthesis and digital mammography: a comparison of breast cancer visibility and BIRADS classification in a population of cancers with subtle mammographic findings. <i>Eur Radiol</i> . 2008;18(12):2817-2825.	Observational-Dx	36 patients	To compare breast cancer visibility in one-view breast tomosynthesis to cancer visibility in one- or two-view DM.	40 breast cancers were found in 37 breasts. The cancers were rated more visible on breast tomosynthesis compared to one-view and two-view DM in 22 and 11 cases, respectively, ( $P<0.01$ for both comparisons). Comparing one-view DM to one-view breast tomosynthesis, 21 patients were upgraded on BIRADS classification ( $P<0.01$ ). Comparing two-view DM to one-view breast tomosynthesis, 12 patients were upgraded on BIRADS classification ( $P<0.01$ ).	3
75. Lei J, Yang P, Zhang L, Wang Y, Yang K. Diagnostic accuracy of digital breast tomosynthesis versus digital mammography for benign and malignant lesions in breasts: a meta-analysis. <i>Eur Radiol</i> . 2014;24(3):595-602.	Meta-analysis	7 studies involving 2,014 patients and 2,666 breast lesions	To evaluate the diagnostic performance of DBT and DM for benign and malignant lesions in breasts.	A total of 7 studies involving 2,014 patients and 2,666 breast lesions were included. Compared with the gold standard (histological results), the pooled sensitivity and specificity of DBT were 90.0% and 79.0%, and for DM they were 89.0% and 72.0%, respectively. The pooled positive likelihood ratio of DBT and DM was 3.50 and 2.83; the pooled negative likelihood ratio of DBT and DM was 15% and 18%; the pooled diagnostic OR for DBT and DM was 26.04 and 16.24, respectively.	M

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
76. Gumus H, Gumus M, Mills P, et al. Clinically palpable breast abnormalities with normal imaging: is clinically guided biopsy still required? <i>Clin Radiol</i> . 2012;67(5):437-440.	Observational-Dx	251 patients	To determine the need for a fine-needle or core biopsy in patients with clinically palpable breast abnormalities who have negative mammographic and sonographic findings.	3 (1.2%) of the 251 clinically guided biopsies were reported as malignant; 2 (0.8%) of which were invasive. 46 (18.3%) of the 251 cases were regarded as clinically suspicious or malignant while the remaining 215 examinations were categorized as benign or probably benign. All 3 malignancies were in the clinically suspicious or malignant group.	3
77. Lehman CD, Lee CI, Loving VA, Portillo MS, Peacock S, Demartini WB. Accuracy and value of breast ultrasound for primary imaging evaluation of symptomatic women 30-39 years of age. <i>AJR Am J Roentgenol</i> . 2012;199(5):1169-1177.	Observational-Dx	1,208 cases in 954 patients	To determine the accuracy and value of breast US for primary imaging evaluation of women 30-39 years of age who present with focal breast signs or symptoms.	Outcomes were benign in 1,185/1,208 (98.1%) and malignant in 23/1,208 (1.9%) cases. Sensitivities for US and mammography were 95.7% and 60.9%, respectively. Specificities for US and mammography were 89.2% and 94.4%, respectively. NPV was 99.9% for US and 99.2% for mammography. PPV was 13.2% for US and 18.4% for mammography. Mammography detected 1 additional malignancy in an asymptomatic area in a 32-year-old woman who was subsequently found to have a BRCA2 gene mutation.	3
78. Sabate JM, Clotet M, Torrubia S, et al. Radiologic evaluation of breast disorders related to pregnancy and lactation. <i>Radiographics</i> . 2007;27 Suppl 1:S101-124.	Review/Other-Dx	N/A	Review imaging of breast disorders related to pregnancy and lactation.	US is the most appropriate radiologic method and is useful in the diagnosis and treatment of abscesses. Knowledge of the unique entities that are specifically related to pregnancy and lactation and of their radiologic-pathologic appearances can help the radiologist make the correct diagnosis.	4
79. Obenauer S, Dammert S. Palpable masses in breast during lactation. <i>Clin Imaging</i> . 2007;31(1):1-5.	Observational-Dx	27 patients	To examine the value of various radiological methods in patients with palpable breast masses during the lactation period.	18 US guided biopsies performed revealed 3 cysts, 7 hyperplasias/mastopathia, 3 cases of papilloma, and 2 carcinomas. US should be the method of choice. If possible mammography and MR mammography should be done after lactating period.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
80. Robbins J, Jeffries D, Roubidoux M, Helvie M. Accuracy of diagnostic mammography and breast ultrasound during pregnancy and lactation. <i>AJR Am J Roentgenol.</i> 2011;196(3):716-722.	Observational-Dx	155 pregnant, lactating, and postpartum women	To determine the accuracy of mammography and US in evaluating pregnant, lactating, and postpartum women.	Of 134 lesions, 87 (65%) were in patients who presented during lactation, 34 (25%) who presented during pregnancy, and 13 (10%) who presented postpartum. The presenting symptom for 86 lesions (64%) was a palpable mass. Biopsies were performed for 40 lesions. Of these lesions, 4 were malignant and 36 were benign. Mammograms were dense or heterogeneously dense in 88% of patients. All 4 malignancies were BI-RADS category 4 or 5 according to both mammography and US. For the 85 lesions evaluated with mammography, there was 100% sensitivity, 93% specificity, 40% PPV, and 100% NPV. For the 122 lesions evaluated with US, there was 100% sensitivity, 86% specificity, 19% PPV, and 100% NPV	3
81. Yang WT, Dryden MJ, Gwyn K, Whitman GJ, Theriault R. Imaging of breast cancer diagnosed and treated with chemotherapy during pregnancy. <i>Radiology.</i> 2006;239(1):52-60.	Observational-Dx	23 women with 24 cancers	To retrospectively assess mammography, high-frequency-transducer US, and color Doppler US for the initial and subsequent evaluation of breast cancer diagnosed and treated with chemotherapy during pregnancy.	Findings were positive for malignancy in 18/20 (90%) cancers. A mass in all 21 cancers (100%) was depicted in the 20 women who underwent breast and nodal US. US correctly depicted axillary metastasis in 15/18 women who underwent US nodal assessment. Of 12 patients who were evaluated for response to chemotherapy, US demonstrated complete response in 2 patients, partial response in 3, stable findings in 1, and progression of disease in 6. Breast cancer diagnosed during pregnancy is mammographically evident despite dense parenchymal background. US, when performed, demonstrate all masses and provide information regarding response to neoadjuvant chemotherapy.	4

**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
82. Sechopoulos I, Suryanarayanan S, Vedantham S, D'Orsi CJ, Karellas A. Radiation dose to organs and tissues from mammography: Monte Carlo and phantom study. <i>Radiology</i> . 2008;246(2):434-443.	Review/Other-Dx	N/A	To prospectively determine the radiation dose to the organs of the body during standard bilateral two-view mammography by using Monte Carlo simulations and a phantom.	The organs that received an relative organ dose of 0.10% or higher in at least one view and one spectrum were the contralateral breast, ipsilateral eye and eye lens, heart, ipsilateral lung, and thymus. Among the organs, the maximum relative organ dose was 0.62%. The maximum relative organ dose for the bone surfaces was 2.36% and that for the red bone marrow was 0.56%. The highest relative organ dose measured for the uterus or fetus at the first trimester was less than 10(-5)	4
83. American College of Radiology. ACR-SPR Practice Parameter for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation. Available at: <a href="http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/Pregnant_Patients.pdf">http://www.acr.org/~media/ACR/Documents/PGTS/guidelines/Pregnant_Patients.pdf</a> .	Review/Other-Dx	N/A	Guidance document to promote the safe and effective use of diagnostic and therapeutic radiology by describing specific training, skills and techniques.	No results stated in abstract.	4
84. Swinford AE, Adler DD, Garver KA. Mammographic appearance of the breasts during pregnancy and lactation: false assumptions. <i>Acad Radiol</i> . 1998;5(7):467-472.	Observational-Dx	18 women; 18 controls	Retrospective study to examine the accuracy of the assumption that pregnant and lactating women have dense breasts, thus limiting the usefulness of mammography.	3/6 pregnant women had unchanged breast density compared with baseline studies and had scattered fibroglandular or heterogeneously dense tissue. Of the 3 without baseline studies, 1 had extremely dense, 1 had heterogeneously dense, and 1 had scattered fibroglandular tissue. All 7 lactating women had either heterogeneously dense or extremely dense tissue. The breast tissue in 4 was unchanged in density and increased in 2; no baseline study was available for the remaining patient. 7 studies in 5 women who had discontinued lactation 1 week to 5 months prior to mammography showed no change in density compared with baseline. Pregnant and lactating women do not always have dense breasts, and so mammography can be performed. Mammography can be as useful in these women as it is in other women with breast signs and symptoms.	4

**Palpable Breast Masses**  
**EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
85. Lee WK, Chung J, Cha ES, Lee JE, Kim JH. Digital breast tomosynthesis and breast ultrasound: Additional roles in dense breasts with category 0 at conventional digital mammography. <i>Eur J Radiol.</i> 2016;85(1):291-296.	Observational-Dx	108 patients	To compare the diagnostic performances of DBT and US for the dense breasts with category 0 at conventional digital mammography.	Among 108 lesions, 17 (15.7%) were malignant and 91 (84.3%) were benign. Sensitivity was 100% for both US (17/17) and DBT (17/17) and NPV was also 100% for both US (49/49) and DBT (74/74). Specificity and PPV for US were 53.9% (49/91) and 28.8% (17/59), respectively. Specificity and PPV for DBT were 81.3% (74/91) and 50% (17/34), respectively. DBT showed higher diagnostic accuracy than that of breast US (DBT: 84.3%, 91/108; US: 61.1%, 66/108; $P<0.001$ ). The benign biopsy rate of DBT (50%, 17/34) was lower than that of US (71.2%, 42/59).	2
86. Yue D, Swinson C, Ravichandran D. Triple assessment is not necessary in most young women referred with breast symptoms. <i>Ann R Coll Surg Engl.</i> 2015;97(6):466-468.	Observational-Dx	955 females aged under 25 years	To see whether core biopsy/FNAB could be avoided in young women with benign findings on clinical examination and imaging.	The most common presenting complaint was a lump, followed by pain and nipple discharge. Clinical examination was normal or revealed benign findings in all except 15 patients, in whom it was indeterminate. US was performed in 692 patients (72%) and was normal (n=289) or benign (n=382) in all except 21 patients, in whom it was indeterminate. In 6 patients, both were indeterminate. A total of 317 patients (35%) had triple assessment: FNA in 106, core biopsy in 239 and both in 9 cases. No cancers were diagnosed.	3



**Palpable Breast Masses  
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
87. Osako T, Iwase T, Takahashi K, et al. Diagnostic mammography and ultrasonography for palpable and nonpalpable breast cancer in women aged 30 to 39 years. <i>Breast Cancer</i> . 2007;14(3):255-259.	Observational-Dx	165 patients	To investigate the relationship between the tumor size of breast cancer by palpation and the sensitivity of mammography and US, and which modality can detect nonpalpable breast cancer in women aged 30 to 39 years.	Of 165 patients, 147 patients (89%) showed mammographically dense breasts. Of 165 cancers, 14 (8%) were Tnp, 40 (24%) were T1p, 82 (50%) were T2p, and 29 (18%) were T3p. The sensitivity of mammography was 57% (8/14) for Tnp, 78% (31/40) for T1p, 90% (74/82) for T2p, and 97% (28/29) for T3p. The sensitivity of US was 43% (6/14) for Tnp and 100% for palpable cancers. Of 14 nonpalpable cancers, 4 (29%), 4 (29%), and 2 (14%) could be detected by only mammography, bloody nipple discharge, and US. The sensitivity of mammography depends on the tumor size on palpation in this age range. Mammography fails to detect relatively large palpable cancers. On the other hand, US can detect all palpable cancers. However, the sensitivity of US declines for nonpalpable cancers. For the detection of nonpalpable cancers, mammography, US, and nipple discharge are complementary modalities.	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

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Dx = Diagnostic

Tx = Treatment

## Abbreviations Key

AUC = Area under the receiver operating characteristic curve

BSGI = Breast-specific gamma imaging

CI = Confidence interval

DBT = Digital breast tomosynthesis

DCIS = Ductal carcinoma in situ

FFDM = Full-field digital mammography

FDG-PET = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography

FNAB = Fine-needle aspiration biopsy

FNAC = Fine-needle aspiration cytology

MIBI = Methoxyisobutylisonitrile

MRI = Magnetic resonance imaging

NPV = Negative predictive value

OR = Odds ratio

PEM = Positron emission mammography

PPV = Positive predictive value

SD = Standard deviation

SM = Scintimammography

SPECT = Single-photon emission tomography

US = Ultrasound

VAB = Vacuum-assisted biopsy