

Breast Imaging of Pregnant and Lactating Women
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Ayyappan AP, Kulkarni S, Crystal P. Pregnancy-associated breast cancer: spectrum of imaging appearances. <i>Br J Radiol.</i> 2010;83(990):529-534.	Review/Other-Dx	N/A	To illustrate imaging findings of pregnancy-associated breast cancer (PABC) and provide an approach for the evaluation of pregnant and lactating women with palpable abnormalities.	No results stated in abstract.	4
2. McCready J, Arendt LM, Glover E, et al. Pregnancy-associated breast cancers are driven by differences in adipose stromal cells present during lactation. <i>Breast Cancer Res.</i> 2014;16(1):R2.	Experimental-Dx	N/A	To study mammary stromal remodeling during development to examine its role in pregnancy-associated breast cancers (PABCs).	Adipose stromal cell (ASCs) present during lactation (ASC-Ls), but not during other mammary developmental stages, promote the growth of carcinoma cells and angiogenesis. ASCs-Ls are distinguished by their elevated expression of cellular retinoic acid binding protein-1 (crabp1), which regulates their ability to retain lipid. Human breast carcinoma-associated fibroblasts (CAFs) exhibit traits of ASC-Ls and express crabp1. Inhibition of crabp1 in CAFs or in ASC-Ls abolished their tumor-promoting activity and also restored their ability to accumulate lipid.	3
3. Newman J. Breastfeeding and radiologic procedures. <i>Can Fam Physician.</i> 2007;53(4):630-631.	Review/Other-Dx	N/A	To determine if not breastfeeding for 24 to 48 hours after magnetic resonance imaging scan is based on scientific evidence.	No abstract available.	4
4. Ulery M, Carter L, McFarlin BL, Giurgescu C. Pregnancy-associated breast cancer: significance of early detection. <i>J Midwifery Womens Health.</i> 2009;54(5):357-363.	Review/Other-Dx	15 research studies/1570 women	To determine the significance of early detection of Pregnancy-associated breast cancer (PABC) and to alert health care providers to include PABC in the differential diagnosis when evaluating a breast mass in the perinatal period.	In the reviewed studies, breast cancer was diagnosed with greater frequency in the postpartum period than during any trimester in pregnancy. Delay in diagnosis is complicated by axillary lymph node metastasis, high-grade tumors at diagnosis, and poor outcomes. Early detection is a significant predictor of improved outcomes.	4

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5. Bure LA, Azoulay L, Benjamin A, Abenhaim HA. Pregnancy-associated breast cancer: a review for the obstetrical care provider. J Obstet Gynaecol Can. 2011;33(4):330-337.	Review/Other-Dx	N/A	To focus on the presentation of pregnancy-associated breast cancer, to provide current information on the trends in incidence and pathology of breast cancer in pregnancy, and to describe variables associated with the worst prognosis observed in this group.	The incidence of breast cancer in pregnancy and the postpartum period ranges from 2.3 to 40 cases per 100 000 women. Over 90% of patients with breast cancer in pregnancy or during lactation present with a palpable mass, and most often (84%) these are self-reported by patients. Less frequently, breast cancer will present as breast erythema, breast swelling, bloody nipple discharge, or local or distant metastasis. The histology of tumours appears to be similar in women who are pregnant or recently delivered and in age-matched women who are not pregnant. However, the stage of disease at diagnosis is more advanced in women who are pregnant or recently delivered and consequently incurs a worst prognosis, likely due to a delay in diagnosis.	4

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6. Helewa M, Levesque P, Provencher D, Lea RH, Rosolowich V, Shapiro HM. Breast cancer, pregnancy, and breastfeeding. J Obstet Gynaecol Can. 2002;24(2):164-180; quiz 181-164.	Review/Other-Dx	N/A	To provide Canadian physicians up-to-date, accurate information and recommendations regarding: i) impact of pregnancy and lactation on risk of breast cancer; ii) prognosis of breast cancer diagnosed during pregnancy and lactation; iii) risk of recurrence of breast cancer with the occurrence of subsequent pregnancies; iv) feasibility of breastfeeding and its impact on the prognosis of women with breast cancer.	Women should be counselled regarding their risk for breast cancer and be informed that: 1. There is good evidence that there is a transient increase in risk of breast cancer in the first three to four years after delivery of a singleton baby (II-2B). Subsequently, their lifetime risk seems lower than that of women who remain nulliparous (II-2B). 2. There is good evidence that the risk for premenopausal breast cancer is reduced with lactation (II-2A). This protective effect seems to be best for women who had extended periods of breastfeeding during their lifetime (II-2B). Women with familial risks could potentially benefit most from breastfeeding (II-2C). Since breast milk is the ideal nutrient for the newborn, and since breastfeeding is a modifiable risk factor, all women should be encouraged to breastfeed their children (II-2A). 3. All women should be encouraged to practice breast self-examination in pregnancy and during lactation (II-2B). Clinicians should screen all pregnant patients for breast cancer with thorough breast examination early in pregnancy (III-B). The clinician is advised to examine the breast in the postpartum period if the woman is not breastfeeding. The obstetrician is advised to examine the breast at any time in the postpartum period if the woman presents with breast symptoms (III-B). 4. Physicians should be encouraged to use ultrasonography, mammography, needle aspiration, or breast biopsies to assess suspicious breast masses in pregnancy and during lactation, in the same timely fashion as for non-pregnant or non-lactating women (II-2A). Interruption of lactation during investigation is not necessary, nor is it recommended unless	4

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				<p>nuclear studies are entertained (III-B). 5. Once breast cancer is diagnosed, a multidisciplinary approach should be taken. This includes the obstetrician, surgeons, medical and radiation oncologists, and breast cancer counsellors (II-2A). 6. In early pregnancy, the patient should be counselled regarding the effect of proposed therapy on the fetus and on overall maternal prognosis. Termination of pregnancy should be discussed, but the patient should be counselled that prognosis is not altered by termination of pregnancy. Women should be advised that premature menopause may result from breast cancer treatments, especially if chemotherapy is given to patients who are past the age of 30. (II-2C) 7. Up until now, modified radical mastectomy was the cornerstone of surgical treatment of breast cancer during pregnancy. Adjuvant chemotherapy should be entertained and, if required, administered without delay. The patient should be counselled regarding the effect of chemotherapy on the fetus and/or the future reproductive potential of the patient (II-2B). In the third trimester, the risks and benefits of early delivery versus continuation of pregnancy, and the effect of chemotherapy on the fetus, should be addressed (II-2B). Women undergoing chemotherapy or tamoxifen treatment should not breastfeed (III-B). 8. Women treated for breast cancer and who wish to become pregnant should be counselled that pregnancy is possible and does not seem to be associated with a worse prognosis for their breast cancer (II-3C). However, they should be made aware that the evidence to support such advice is relatively poor. 9. Since most breast cancer recurrences</p>	

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				<p>appear within two to three years after initial diagnosis, patients should be advised to postpone pregnancy for three years (III-C). If a patient has axillary node involvement, the recommendation to defer pregnancy should be extended to five years, but this recommendation is based on opinion only (III-C). Prior to attempting pregnancy, a breast cancer survivor should be referred for a full oncologic evaluation.</p> <p>10. There is no evidence that breastfeeding increases the risk of breast cancer recurring or of a second breast cancer developing, nor that it carries any health risk to the child. Women previously treated for breast cancer, who do not show any evidence of residual tumour, should be encouraged to breastfeed their children (III-B).</p>	
<p>7. Langer A, Mohallem M, Stevens D, Rouzier R, Lerebours F, Chereil P. A single-institution study of 117 pregnancy-associated breast cancers (PABC): Presentation, imaging, clinicopathological data and outcome. <i>Diagn Interv Imaging.</i> 2014;95(4):435-441.</p>	<p>Observational-Dx</p>	<p>113 patients of breast cancer</p>	<p>To describe the main clinical, radiological and histological features, as well as the outcome of pregnancy-associated breast cancer (PABC), with a special emphasis on imaging and diagnostic difficulties.</p>	<p>Mean age at diagnosis was 33.7 years. Most cancers (81.2%) were diagnosed after delivery. Intermediate or high family risk was frequent (27.5%). The most common mode of presentation was a palpable mass (89.7%). Mean time to diagnosis was 5.8 months. Sensitivity for mammography was 80.9% and for ultrasound 77%. Most prognostic factors were unfavourable: frequent lymph node involvement (51.8%), high-grade tumours, hormone receptor negativity (45.9%) and HER2 positivity (38.7%). Treatments generally included surgery (61.7% mastectomies), radiotherapy (96%) and chemotherapy (79.6%). Overall 5-year survival was 81.8%.</p>	<p>3</p>

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8. Reed W, Hannisdal E, Skovlund E, Thoresen S, Lilleng P, Nesland JM. Pregnancy and breast cancer: a population-based study. <i>Virchows Arch.</i> 2003;443(1):44-50.	Review/Other-Dx	173 breast-cancer patients	To evaluate the outcome and possible prognostic factors in a population based series of women with breast cancer during pregnancy and lactation and during pregnancy subsequent to breast cancer.	In the two pregnancy-associated breast-cancer groups, tumours were significantly larger, with more extensive lymph-node involvement. For node-negative tumours the respective 5- and 10-year survival rates were 62% and 50% in the pregnancy group and 60% and 50% in the lactation group. For node-positive tumours, respective 5- and 10-year survival rates were 50% and 34% in the pregnancy group and 50% and 33% in the lactation group. In the subsequent group, overall survival was high in both node-negative and -positive groups, with 5- and 10-year survival rates of 80% and 73% and 86% and 76%, respectively.	4
9. Sabate JM, Clotet M, Torrubia S, et al. Radiologic evaluation of breast disorders related to pregnancy and lactation. [Review] [86 refs]. <i>Radiographics.</i> 27 Suppl 1:S101-24, 2007 Oct.	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
10. Vashi R, Hooley R, Butler R, Geisel J, Philpotts L. Breast imaging of the pregnant and lactating patient: physiologic changes and common benign entities. [Review]. <i>AJR Am J Roentgenol.</i> 200(2):329-36, 2013 Feb.	Review/Other-Dx	N/A	To review key clinical, histologic, and imaging features of expected physiologic changes within the breast and common benign breast disease in the pregnant and lactating patient.	No results stated in abstract.	4

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11. Cordoba O, Llurba E, Saura C, et al. Multidisciplinary approach to breast cancer diagnosed during pregnancy: maternal and neonatal outcomes. <i>Breast</i> . 2013;22(4):515-519.	Review/Ot her-Dx	25 consecutive pregnant women	To assess maternal and neonatal outcome in women diagnosed with breast cancer during pregnancy.	Twelve patients were diagnosed during the second trimester. Breast Imaging Reporting and Data System (BI-RADS) category <3 mammographic lesions were diagnosed in 7 patients. A suspicious area was detected by ultrasound in 20 of 21 women who underwent ultrasound studies. Nineteen patients had positive hormone receptors and 7 overexpressed HER2 (human epidermal growth factor receptor 2). One patient was in stage 0, 8 in stage I, 8 in stage II, 3 in stage III and 5 in stage IV. Four patients decided voluntarily to legally terminate their pregnancies, one had a spontaneous miscarriage and in three patients, pregnancy was interrupted at the end of the third trimester before oncological treatment. Eleven patients were treated with chemotherapy during pregnancy after the second trimester using anthracycline-based regimens. In five patients the pregnancy was ended before 34 weeks of gestation. Nine patients had gestation-related complications, including preterm labor, pneumonia, increase in velocity of the middle cerebral artery, oligohydramnios, preeclampsia, extreme prematurity, intrauterine growth restriction, dyspnea, spontaneous miscarriage and chemotherapy-related granulocytopenia. Betamethasone to stimulate fetal lung maturation was used in 6 patients.	4
12. Canoy JM, Mitchell GS, Unold D, Miller V. A radiologic review of common breast disorders in pregnancy and the perinatal period. [Review]. <i>Semin Ultrasound CT MR</i> . 33(1):78-85, 2012 Feb.	Review/Ot her-Dx	N/A	To review the common breast disorders in pregnancy and the perinatal period.	No results stated in abstract.	4

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13. Joshi S, Dialani V, Marotti J, Mehta TS, Slanetz PJ. Breast disease in the pregnant and lactating patient: radiological-pathological correlation. <i>Insights Imaging</i> . 2013;4(5):527-538.	Review/Other-Dx	N/A	To review the imaging challenges of the breast during pregnancy and lactation.	No results stated in abstract.	4
14. Ramsay DT, Kent JC, Hartmann RA, Hartmann PE. Anatomy of the lactating human breast redefined with ultrasound imaging. <i>J Anat</i> . 2005;206(6):525-534.	Observational-Dx	21 Caucasian women	To use ultrasound imaging to re-investigate the anatomy of the lactating breast.	Milk ducts appeared as hypoechoic tubular structures with echogenic walls that often contained echoes. Ducts were easily compressed and did not display typical sinuses. All ducts branched within the areolar radius, the first branch occurring 8.0 ± 5.5 mm from the nipple. Duct diameter was 1.9 ± 0.6 mm, 2.0 ± 90.7 mm and the number of main ducts was 9.6 ± 2.9 , 9.2 ± 2.9 , for left and right breast, respectively. Milk ducts are superficial, easily compressible and echoes within the duct represent fat globules in breastmilk. The low number and size of the ducts, the rapid branching under the areola and the absence of sinuses suggest that ducts transport breastmilk, rather than store it. The distribution of adipose and glandular tissue showed wide variation between women but not between breasts within women. The proportion of glandular and fat tissue and the number and size of ducts were not related to milk production.	2
15. Vashi R, Hooley R, Butler R, Geisel J, Philpotts L. Breast imaging of the pregnant and lactating patient: imaging modalities and pregnancy-associated breast cancer. [Review]. <i>AJR. American Journal of Roentgenology</i> . 200(2):321-8, 2013 Feb.	Review/Other-Dx	N/A	To review key clinical, histologic, and imaging features of expected physiologic changes within the breast and common benign breast disease in the pregnant and lactating patient.	No results stated in abstract.	4

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16. Barnes DM, Newman LA. Pregnancy-associated breast cancer: a literature review. <i>Surg Clin North Am.</i> 2007;87(2):417-430, x.	Review/Other-Dx	N/A	To highlight patient care in women with breast cancer during pregnancy, where aggressive care must be modified to ensure fetal protection.	No results stated in abstract.	4
17. Hartman EK, Eslick GD. The prognosis of women diagnosed with breast cancer before, during and after pregnancy: a meta-analysis. <i>Breast Cancer Res Treat.</i> 2016;160(2):347-360.	Meta-analysis	41 studies comprising of 4929 cases and a total of 65,970 individuals	To examine the prognosis for women who become pregnant before, during and after a diagnosis of breast cancer. Also to analyze the various subgroups within pregnancy-associated breast cancer (PABC) such as pregnancy and postpartum cases, as well as on time periods postpartum.	41 studies met our inclusion criteria (cases = 4929; controls = 61,041) for pregnancy occurring during or before breast cancer diagnosis. There was an overall increased risk of death amongst patients compared to non-pregnant controls [HR 1.57; 95 % CI 1.35-1.82]. Subgroup analysis indicated poor survival outcomes for those diagnosed either during pregnancy or postpartum (PABC) [HR 1.46; 95 % CI 1.17-1.82] as well as those diagnosed during pregnancy alone [HR 1.47; 95 % CI 1.04-2.08]. Those diagnosed postpartum had the poorest overall survival [HR 1.79; 95 % CI 1.39-2.29]. Similarly, patients with PABC had decreased DFS compared to controls [HR 1.51; 95 % CI 1.22-1.88]. Those diagnosed postpartum were the most at risk of disease progression or relapse [HR 1.86; 95 % CI 1.17-2.93]. 19 studies met our inclusion criteria (cases = 1829; controls = 21,907) for pregnancy following breast cancer diagnosis. Such women had a significantly reduced risk of death compared to those who did not become pregnant [pHR 0.63; 95 % CI 0.51-0.79]. A subgroup analysis to account for the "healthy mother effect" generated similar results [pHR 0.65; 95 % CI 0.52-0.81].	Good

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18. Madaras L, Kovacs KA, Szasz AM, et al. Clinicopathological features and prognosis of pregnancy associated breast cancer - a matched case control study. <i>Pathol Oncol Res.</i> 2014;20(3):581-590.	Observational-Dx	31 pregnant woman with breast cancer	To investigate differences in clinicopathological features, immunophenotype, treatment and outcome of pregnancy associated breast cancer (PABC) and matched control, non-PABC cases.	Thirty-one breast cancer cases were pregnancy related. Clinical management data did not differ in cases and controls. Histopathology of disease at presentation was not significantly different, but nottingham prognostic index (NPI), assessed the pregnancy associated breast cancer (PABC) group as having poor, whereas controls as having intermediate prognosis. Associated in situ lesion was more often high grade Extensive Intraductal Carcinoma Component (EIC) in PABC. Triple negative and Luminal B prol tumors predominated in PABC. Disease-free and overall survival was inferior compared to controls. PABC patients with LuminalB prol and Triple negative tumors had inferior outcomes. On multivariate analysis inferior prognosis of PABC was associated with pregnancy.	3

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19. Myers KS, Green LA, Lebron L, Morris EA. Imaging Appearance and Clinical Impact of Preoperative Breast MRI in Pregnancy-Associated Breast Cancer. <i>AJR Am J Roentgenol.</i> 2017;209(3):W177-W183.	Observational-Dx	53 women	To describe the imaging features of pregnancy-associated breast cancer (PABC) on breast MRI and to consider the impact of preoperative MRI on patient management.	Of the 53 women, nine (17%) presented during pregnancy and 44 (83%) presented during the first year postpartum. The sensitivity of MRI was 98% (52/53). Among the 53 patients, the most common findings of PABC on MRI included a solitary mass (29 patients [55%]), nonmass enhancement (12 patients [23%]), and multiple masses (eight patients [15%]). For 12 patients (23%), MRI showed a pathologically proven larger tumor size or greater extent of disease than did mammography or ultrasound, with an additional eight patients (15%) having findings suspicious for greater extent of disease but having unavailable pathologic data. Breast MRI changed surgical management for 15 patients (28%), with four patients (8%) requiring a larger lumpectomy, seven (13%) no longer being considered candidates for lumpectomy, two (4%) having contralateral disease, and two (4%) having unsuspected metastasis.	2
20. Doyle S, Messiou C, Rutherford JM, Dineen RA. Cancer presenting during pregnancy: radiological perspectives. <i>Clin Radiol.</i> 2009;64(9):857-871.	Review/Other-Dx	N/A	To review the outlines of the general principles and approach to imaging the pregnant patient with suspected malignancy, following which there is a more detailed discussion of the effects of pregnancy on tumour biology and presentation of specific tumours.	No results stated in abstract.	4
21. Janni W, Rack B, Gerber B, et al. Pregnancy-associated breast cancer -- special features in diagnosis and treatment. <i>Onkologie.</i> 2006;29(3):107-112.	Review/Other-Dx	N/A	To summarize the special features of the diagnosis and primary therapy of pregnancy-associated breast cancer with particular consideration of cytostatic therapy.	No results in abstract.	4

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22. Kalogerakos K, Sofoudis C, Tzonis P, Koutsouradis P, Katsoulis G. Breast cancer and pregnancy; overview of international bibliography. [Review]. Journal of B.U.On.. 18(2):308-13, 2013 Apr-Jun.	Review/Other-Dx	N/A	No abstract available.	No abstract available.	4
23. Psyrris A, Burtneess B. Pregnancy-associated breast cancer. Cancer J. 2005;11(2):83-95.	Review/Other-Dx	100 articles.	To review the pathophysiology, clinical presentation, and diagnostic and therapeutic approach to the pregnant breast cancer patient. In addition, the impact of pregnancy on subsequent breast cancer development in high-risk groups, such as BRCA1 and BRCA2 mutation carriers and patients with a prior history of breast cancer, is discussed.	A thorough breast examination at the first antenatal visit, before the physiologic changes in breast parenchyma obscure a possible mass, is essential. The work-up of masses detected during pregnancy should not be postponed until after delivery. Delays in diagnosis may contribute to the higher proportion of patients with advanced stage at presentation. The prognosis of the pregnant breast cancer patient is similar to her stage-matched nonpregnant counterparts in most series. Radiation therapy is contraindicated during pregnancy; this limits breast conservation to cases presenting during the third trimester. Some chemotherapies can be administered during the second and third trimesters. Therapeutic abortion is not necessary, although women with high-risk disease may find this preferable. Women with a history of breast cancer should be reassured that subsequent pregnancy is not known to increase the risk of recurrence. Women with a history of BRCA1/2 mutations should not be advised that early pregnancy decreases their breast cancer risk.	4

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24. Taylor D, Lazberger J, Ives A, Wylie E, Saunders C. Reducing delay in the diagnosis of pregnancy-associated breast cancer: how imaging can help us. <i>J Med Imaging Radiat Oncol.</i> 2011;55(1):33-42.	Review/Ot her-Dx	22 pregnant/L actating women with breast cancer	To review 22 cases of breast cancer detected during pregnancy and lactation as part of a population-based cohort.	The commonest presenting symptom was a lump. Diagnosis by percutaneous biopsy was made correctly in 21 of 23 lesions. Lesions were predominantly invasive ductal carcinoma (91%). One third had extensive associated ductal carcinoma in situ (DCIS). Ultrasound (US) was abnormal in all symptomatic patients. The most common sonographic finding was a solitary hypoechoic mass with irregular margins. 'Expanded stroma' with prominent ducts and architectural distortion was noted in three cases; all had extensive high-grade DCIS. In three women, bilateral breast US detected cancer in the asymptomatic breast. Mammography (performed in 86% of women) was abnormal in 74%, despite the presence of dense breast tissue in 47%. Widespread calcifications were visible in 26%, with detection of asymptomatic contra-lateral disease in one patient. MRI was performed in six patients. Background parenchymal enhancement did not impair lesion detection; however, overestimation of lesion size can occur.	4
25. Yang WT. Staging of breast cancer with ultrasound. <i>Semin Ultrasound CT MR.</i> 2011;32(4):331-341.	Review/Ot her-Dx	N/A	To evaluate the staging of breast cancer using ultrasound.	No results stated in abstract.	4

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26. Ahn BY, Kim HH, Moon WK, et al. Pregnancy- and lactation-associated breast cancer: mammographic and sonographic findings. <i>J Ultrasound Med.</i> 2003;22(5):491-497; quiz 498-499.	Observational-Dx	22 consecutive breast cancer patients	To evaluate the mammographic and sonographic findings of pregnancy-associated breast cancer.	Mammography revealed positive findings in 13 (86.7%) of 15 patients, even though all 15 patients had dense breasts. Mammographic findings included masses (n = 5), masses with calcifications (n = 2), calcifications with axillary lymphadenopathy (n = 2), a mass with axillary lymphadenopathy (n = 1), calcifications alone (n = 1), asymmetric density alone (n = 1), and diffuse skin and trabecular thickening alone (n = 1). Sonographic findings were positive and showed masses for all 19 patients (100%). The common sonographic findings of masses were irregular shapes (n = 15), irregular margins (n = 16), parallel orientation (n = 11), complex echo patterns (n = 14, including marked cystic [anechoic] components [n = 4]), and posterior acoustic enhancement (n = 12). Surrounding tissue effects could be seen in 5 patients, including ductal changes (n = 2), Cooper ligament thickening (n = 1), edema (n = 3), and skin thickening (n = 3). Calcifications within or outside a mass (n = 7) and axillary lymphadenopathy (n = 8) were also detected.	3
27. Liberman L, Giess CS, Dershaw DD, Deutch BM, Petrek JA. Imaging of pregnancy-associated breast cancer. <i>Radiology.</i> 1994;191(1):245-248.	Observational-Dx	85 pregnant women with breast cancer.	To assess the use of mammography in diagnosis of pregnancy-associated breast cancer (PABC).	Mammographic findings were present in 18 of 23 cases (78%), including mass (n = 13) (nine cases with calcification), suspicious calcifications (n = 4), and diffusely increased parenchymal density (n = 1). Breast sonography revealed focal solid mass in six of six cases. Axillary lymph node metastases occurred in 15 of 23 cases (65%). Although symptoms occurred before or during pregnancy in 12 cases (52%), pregnancy-associated breast cancer (PABC) was diagnosed after pregnancy in 19 cases (83%).	3

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28. Robbins J, Jeffries D, Roubidoux M, Helvie M. Accuracy of diagnostic mammography and breast ultrasound during pregnancy and lactation.[Erratum appears in AJR Am J Roentgenol. 2011 May;196(5):1237]. AJR Am J Roentgenol. 196(3):716-22, 2011 Mar.	Observational-Dx	155 pregnant, lactating, and postpartum women	To determine the accuracy of mammography and sonography 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, four were malignant and 36 were benign. Mammograms were dense or heterogeneously dense in 88% of patients. All four malignancies were BI-RADS category 4 or 5 according to both mammography and ultrasound. For the 85 lesions evaluated with mammography, there was 100% sensitivity, 93% specificity, 40% positive predictive value, and 100% negative predictive value. For the 122 lesions evaluated with sonography, there was 100% sensitivity, 86% specificity, 19% positive predictive value, and 100% negative predictive value	3
29. Faridi MM, Dewan P, Batra P. Rusty pipe syndrome: counselling a key intervention. Breastfeed Rev. 2013;21(3):27-30.	Review/Other-Dx	2 women.	To describe two mothers who presented with rusty pipe syndrome between March 2012 and May 2012, along with a review of literature and management of this condition by proper counselling, enabling mothers to successfully breastfeed.	No results stated in abstract.	4
30. Silva JR, Carvalho R, Maia C, Osorio M, Barbosa M. Rusty pipe syndrome, a cause of bloody nipple discharge: case report. Breastfeed Med. 2014;9(8):411-412.	Review/Other-Dx	1 women.	To present a case of rusty pipe syndrome and discuss the implications.	No results stated in abstract.	4

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31. Lafreniere R. Bloody nipple discharge during pregnancy: a rationale for conservative treatment. J Surg Oncol. 1990;43(4):228-230.	Review/Other-Dx	5 women.	To recommend a conservative treatment for the cases of bloody nipple discharge during pregnancy and to illustrate the pathophysiology associated with this disease process.	In all instances, the discharge appeared late during the second trimester or during the third trimester of pregnancy. It was unilateral and spontaneous and arose from multiple ducts, and it was associated with an increase in breast size and always with the larger breast of the two. The discharge cytologic study done on all cases was negative for neoplastic cells and the discharges resolved spontaneously within 2 months of onset. Postpartum follow-up ranging from 6 months to 3 years has revealed no evidence of neoplastic changes thus far. Mammograms ordered before these patients were referred were not helpful due to the increase in density of the breast tissue secondary to the pregnancy.	4
32. Lee SJ, Trikha S, Moy L, et al. ACR Appropriateness Criteria(R) Evaluation of Nipple Discharge. J Am Coll Radiol. 2017;14(5S):S138-S153.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for evaluation of nipple discharge	No results stated in abstract.	4
33. American College of Radiology. Manual on Contrast Media. Available at: https://www.acr.org/Clinical-Resources/Contrast-Manual .	Review/Other-Dx	N/A	Guidance document on contrast media to assist radiologists in recognizing and managing risks associated with the use of contrast media.	N/A	4

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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
34. Espinosa LA, Daniel BL, Vidarsson L, Zakhour M, Ikeda DM, Herfkens RJ. The lactating breast: contrast-enhanced MR imaging of normal tissue and cancer. <i>Radiology</i> . 2005;237(2):429-436.	Observational-Dx	7 lactating women	To retrospectively describe the magnetic resonance (MR) imaging characteristics of normal breast tissue and breast cancer in the setting of lactation.	Magnetic Resonance (MR) findings of normal breast tissue in the seven women included increased glandular density in six women, high T2-weighted signal intensity in six, dilated central ducts in seven, and rapid initial glandular contrast enhancement in seven. MR findings of invasive ductal carcinoma in five women, compared with findings of the normal glandular tissue, included lower T2-weighted signal intensity in five women, more avid and rapid contrast enhancement in five, and early contrast enhancement washout in four. One minute after contrast agent injection, tumor signal intensity increased significantly more than normal lactating tissue signal intensity (153% vs 60% from baseline, $P = .016$). The median two-compartment model K(21) exchange rate in the tumors, 0.078 sec ⁻¹ , was significantly faster than the K(21) exchange rate in normal tissue, 0.011 sec ⁻¹ ($P = .03$).	3
35. Talele AC, Slanetz PJ, Edmister WB, Yeh ED, Kopans DB. The lactating breast: MRI findings and literature review. <i>Breast J</i> . 2003;9(3):237-240.	Review/Other-Dx	N/A	To report the MRI appearance of the lactating breast and address potential difficulties that may be encountered in this clinical situation.	No results stated in abstract.	4
36. Moy L, Heller SL, Bailey L, et al. ACR Appropriateness Criteria(R) Palpable Breast Masses. <i>J Am Coll Radiol</i> . 2017;14(5S):S203-S224.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for palpable breast masses.	No results stated in abstract.	4
37. Mainiero MB, Moy L, Baron P, et al. ACR Appropriateness Criteria(R) Breast Cancer Screening. <i>J Am Coll Radiol</i> . 2017;14(11S):S383-S390.	Review/Other-Dx	N/A	Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for breast cancer screening.	No results stated in abstract.	4

**Breast Imaging of Pregnant and Lactating Women
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
38. Obenauer S, Dammert S. Palpable masses in breast during lactation. Clin Imaging. 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
39. Brem RF, Tabar L, Duffy SW, et al. Assessing improvement in detection of breast cancer with three-dimensional automated breast US in women with dense breast tissue: the SomoInsight Study. Radiology. 2015;274(3):663-673.	Observational-Dx	112 women	To determine improvement in breast cancer detection by using supplemental three-dimensional (3D) automated breast (AB) ultrasonography (US) with screening mammography versus screening mammography alone in asymptomatic women with dense breasts.	Breast cancer was diagnosed at screening in 112 women: 82 with screening mammography and an additional 30 with AB US. Addition of AB US to screening mammography yielded an additional 1.9 detected cancers per 1000 women screened (95% confidence interval [CI]: 1.2, 2.7; P < .001). Of cancers detected with screening mammography, 62.2% (51 of 82) were invasive versus 93.3% (28 of 30) of additional cancers detected with AB US (P = .001). Of the 82 cancers detected with either screening mammography alone or the combined read, 17 were detected with screening mammography alone. Of these, 64.7% (11 of 17) were ductal carcinoma in situ versus 6.7% (two of 30) of cancers detected with AB US alone. Sensitivity for the combined read increased by 26.7% (95% CI: 18.3%, 35.1%); the increase in the recall rate per 1000 women screened was 284.9 (95% CI: 278.0, 292.2; P < .001).	3

Breast Imaging of Pregnant and Lactating Women
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
40. Giuliano V, Giuliano C. Improved breast cancer detection in asymptomatic women using 3D-automated breast ultrasound in mammographically dense breasts. Clin Imaging. 2013;37(3):480-486.	Observational-Dx	3418 women	to demonstrate that ABUS increases the detection of non-palpable breast cancers in mammographically dense breasts when used as an adjunct diagnostic modality in asymptomatic women	Automated breast ultrasound (ABUS) was performed in 3418 asymptomatic women with mammographically dense breasts. The addition of ABUS to mammography in women with greater than 50% breast density resulted in the detection of 12.3 per 1,000 breast cancers, compared to 4.6 per 1,000 by mammography alone. The mean tumor size was 14.3 mm and overall attributable risk of breast cancer was 19.92 (95% confidence level, 16.75 - 23.61) in our screened population. These preliminary results may justify the cost-benefit of implementing the judicious use of ABUS in conjunction with mammography in the dense breast screening population.	2
41. Boivin G, de Korvin B, Marion J, Duvauferrier R. Is a breast MRI possible and indicated in case of suspicion of breast cancer during lactation? Diagn Interv Imaging. 2012;93(11):823-827.	Review/Other-Dx	N/A	To determine the answers for the following two questions: the safety of the injection of gadolinium during breastfeeding; the value of a breast MRI in the nursing mother if breast cancer is suspected.	No results stated in abstract.	4
42. Kubik-Huch RA, Gottstein-Aalame NM, Frenzel T, et al. Gadopentetate dimeglumine excretion into human breast milk during lactation. Radiology. 2000;216(2):555-558.	Experimental-Dx	20 lactating women	To analyze the amount of gadopentetate dimeglumine excreted into human breast milk following intravenous injection of a clinical dose.	The cumulative amount of gadolinium excreted in human breast milk during 24 hours was 0.57 micromol +/- 0.71 (SD; range, 0.05-3.0 micromol). The excreted dose was thus less than 0.04% of the administered intravenous dose (range, 0.001%-0.04%; mean, 0.009% +/- 0.010) for all cases.	3
43. Tremblay E, Therasse E, Thomassin-Naggara I, Trop I. Quality initiatives: guidelines for use of medical imaging during pregnancy and lactation. Radiographics. 2012;32(3):897-911.	Review/Other-Dx	N/A	To perform a comprehensive review of the radiology literature regarding potential risks to the fetus or infant related to maternal exposure to radiation, high magnetic fields, or iodinated or gadolinium-based contrast agents at imaging performed during pregnancy or lactation.	No results listed in abstract.	4

Breast Imaging of Pregnant and Lactating Women
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
44. NCCN Clinical Practice Guidelines in Oncology. Breast Cancer Screening and Diagnosis. Version 1.2016. 2016; Available at: https://www.nccn.org/professionals/physician_gls/pdf/breast-screening.pdf .	Review/Other-Dx	N/A	To provide screening and diagnosis clinical practice guidelines for breast cancer.	No abstract available.	4
45. Swinford AE, Adler DD, Garver KA. Mammographic appearance of the breasts during pregnancy and lactation: false assumptions. Acad Radiol. 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.	Three of six pregnant women had unchanged breast density compared with baseline studies and had scattered fibroglandular or heterogeneously dense tissue. Of the three without baseline studies, one had extremely dense, one had heterogeneously dense, and one had scattered fibroglandular tissue. All seven lactating women had either heterogeneously dense or extremely dense tissue. The breast tissue in four was unchanged in density and increased in two; no baseline study was available for the remaining patient. Seven studies in five 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
46. Bock K, Hadji P, Ramaswamy A, Schmidt S, Duda VF. Rationale for a diagnostic chain in gestational breast tumor diagnosis. Arch Gynecol Obstet. 2006;273(6):337-345.	Observational-Dx	25 gestational breast tumors patients.	To review the value of imaging (mammography and ultrasonography) and biopsy techniques in order to work out a reliable protocol for evaluating gestational tumors.	Invasive breast cancer was diagnosed in five patients, malignant lymphoma of the skin in one patient. The tumors in the remaining 19 patients proved benign. The overall accuracy was 0.91 for conventional mammography, 0.76 for conventional and panoramic ultrasound and 0.48 for color-coded sonography.	3

**Breast Imaging of Pregnant and Lactating Women
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
47. Son EJ, Oh KK, Kim EK. Pregnancy-associated breast disease: radiologic features and diagnostic dilemmas. <i>Yonsei Med J.</i> 2006;47(1):34-42.	Review/Other-Dx	49 women.	To evaluate the radiological features of pregnancy-associated breast lesions and discuss the difficulties in diagnosis by imaging.	The imaging features of pregnancy-associated breast lesions did not differ from the features of non-pregnancy-associated breast lesions; however, some pregnancy associated benign lesions had suspicious sonographic features.	4
48. Stavros AT. <i>Breast ultrasound.</i> Philadelphia, Pa: Lippincott, Williams & Wilkins; 2004.	Review/Other-Dx	N/A	No abstract available.	No abstract available.	4
49. McGrath SE, Ring A. Chemotherapy for breast cancer in pregnancy: evidence and guidance for oncologists. <i>Ther Adv Med Oncol.</i> 2011;3(2):73-83.	Review/Other-Dx	N/A	To provide guidance for oncologists about chemotherapy for breast cancer in pregnant women.	Management is critically influenced by the stage of pregnancy, especially the first trimester. Anthracycline-based chemotherapy may be administered during the second and third trimesters, with apparently few short-term implications. Limited data shows the taxanes may also be given with few adverse events at these stages. Weekly fractionation regimens may allow closer monitoring of pregnancy with prompt termination of agents, if necessary. Data concerning the long-term risks of systemic anticancer treatment are limited. All stages of patient management should be discussed within a multidisciplinary team and a clear consensus of treatment options communicated to the mother. Delaying chemotherapy until after delivery may be reasonable in some cases, but where the delay is likely to be prolonged, a decision must be made on the basis of risks versus benefits.	4

**Breast Imaging of Pregnant and Lactating Women
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
50. Nye L, Huyck TK, Gradishar WJ. Diagnostic and treatment considerations when newly diagnosed breast cancer coincides with pregnancy: a case report and review of literature. J Natl Compr Canc Netw. 2012;10(2):145-148.	Review/Other-Dx	1 women case.	To report a recent case of a young primigravid woman with a newly appreciated breast mass seen at Northwestern University Feinberg School of Medicine as a means of discussing diagnostic considerations, therapeutic options, and supportive care available to the practitioner when managing a pregnant patient with breast cancer.	No results stated in abstract.	4
51. Yang WT, Dryden MJ, Gwyn K, Whitman GJ, Theriault R. Imaging of breast cancer diagnosed and treated with chemotherapy during pregnancy. Radiology. 2006;239(1):52-60.	Observational-Tx	23 women	To retrospectively assess mammography, high-frequency-transducer ultrasonography (US), and color Doppler US for the initial and subsequent evaluation of breast cancer diagnosed and treated with chemotherapy during pregnancy.	Twenty-three women with 24 cancers that were imaged prior to surgery with mammography (n = 3), US (n = 4), or mammography and US (n = 17) were included in the study. The histologic diagnosis of the primary tumor was invasive ductal cancer in 22 lesions, and the diagnosis was invasive carcinoma in the two other cancers. The median age in this study was 34 years (range, 24-45 years). Of the 20 women who underwent preoperative mammography, findings were positive for malignancy in 18 of 20 (90%) cancers despite dense breast parenchymal patterns (BI-RADS types 3 and 4). 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 of 18 women who underwent US nodal assessment. Of the 12 patients who were evaluated for response to chemotherapy, US demonstrated complete response in two patients, partial response in three, stable findings in one, and progression of disease in six.	3

**Breast Imaging of Pregnant and Lactating Women
EVIDENCE TABLE**

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
52. Candelaria RP, Huang ML, Adrada BE, et al. Incremental Cancer Detection of Locoregional Restaging with Diagnostic Mammography Combined with Whole-Breast and Regional Nodal Ultrasound in Women with Newly Diagnosed Breast Cancer. <i>Academic Radiology</i> . 24(2):191-199, 2017 Feb.	Observational-Dx	401 women.	To determine if locoregional restaging with diagnostic mammography and ultrasound (US) of the whole breast and regional nodes performed for quality assurance in women with newly diagnosed breast cancer who were referred to a tertiary care center yields incremental cancer detection.	Final analyses included 401 women. Of the 401 women, 138 (34%) did not have their outside images available for review upon referral. The median age was 54 years (range 21-92); the median tumor size was 2.9 cm (range 0.6-18.0) for women whose disease was upstaged and 2.2 cm (range 0.4-15.0) for women whose disease was not upstaged. Incremental cancer detection rates were 15.5% (62 of 401) in the ipsilateral breast and 3.9% (6 of 154) in the contralateral breast (P < 0.0001). The total upstage rate was 25% (100 of 401). Surgical management changed from segmentectomy to mastectomy in 12% (50 of 401). The re-excision rate after segmentectomy was 19% (35 of 189).	2

Breast Imaging of Pregnant and Lactating Women
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
53. 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.	Observational-Dx	111 consecutive women	To prospectively assess the diagnostic accuracy of mammography, clinical examination, US, and MRI in the preoperative imaging of breast cancer.	Mammographic sensitivity was highest for invasive ductal carcinoma (IDC) in 89 of 110 (81%) cases versus 10 of 29 (34%) cases of invasive lobular carcinoma (ILC) (P .001) and 21 of 38 (55%) cases of DCIS (P .01). US showed higher sensitivity than did mammography for IDC, depicting 104 of 110 (94%) cases, and for ILC, depicting 25 of 29 (86%) cases (P .01 for each). US showed higher sensitivity for invasive cancer than DCIS (18 of 38 [47%], P .001). MR showed higher sensitivity than did mammography for all tumor types (P .01) and higher sensitivity than did US for DCIS (P .001), depicting 105 of 110 (95%) cases of IDC, 28 of 29 (96%) cases of ILC, and 34 of 38 (89%) cases of DCIS. In anticipation of conservation or no surgery after mammography and clinical examination in 96 breasts, additional tumor (which altered surgical approach) was present in 30. Additional tumor was depicted in 17 of 96 (18%) breasts at US and in 29 of 96 (30%) at MR, though extent was now overestimated in 12 of 96 (12%) at US and 20 of 96 (21%) at MR imaging. After combined mammography, clinical examination, and US, MR depicted additional tumor in another 12 of 96 (12%) breasts and led to overestimation of extent in another six (6%); US showed no detection benefit after MR imaging. Bilateral cancer was present in 10 of 111 (9%) patients; contralateral tumor was depicted mammographically in six and with both US and MR in an additional three. One contralateral cancer was demonstrated only clinically. In non-fatty breasts, US and MRI were more sensitive than mammography for invasive cancer, but both overestimated tumor extent. US	3

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				showed no detection benefit after MRI. Combined mammography, clinical examination, and MRI were more sensitive than any other individual test or combination of tests.	
54. Kim J, Han W, Moon HG, et al. Low rates of additional cancer detection by magnetic resonance imaging in newly diagnosed breast cancer patients who undergo preoperative mammography and ultrasonography. <i>J Breast Cancer</i> . 2014;17(2):167-173.	Observational-Dx	1038 women	To evaluate the efficacy of breast magnetic resonance imaging (MRI) for detecting additional malignancies in breast cancer patients newly diagnosed by breast ultrasonography and mammography.	Among the 1,038 cases, 228 additional lesions (22.0%) and 30 additional malignancies (2.9%) were detected by breast MRI. Of these 228 lesions, 109 were suspected to be malignant (Breast Imaging-Reporting and Data System category 4 or 5) on breast MRI and second-look ultrasonography and 30 were pathologically confirmed to be malignant (13.2%). Of these 30 lesions, 21 were ipsilateral to the main lesion and nine were contralateral. Fourteen lesions were in situ carcinomas and 16 were invasive carcinomas. The positive predictive value of breast MRI was 27.5% (30/109). No clinicopathological factors were significantly associated with additional malignant foci.	3
55. American College of Radiology. ACR-SPR Practice Parameter for the Safe and Optimal Performance of Fetal Magnetic Resonance Imaging (MRI). Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/mr-fetal.pdf	Review/Other-Dx	N/A	To promote safe and optimal performance of fetal magnetic resonance imaging (MRI).	N/A	4
56. American College of Radiology. ACR-SPR Practice Parameter for Imaging Pregnant or Potentially Pregnant Adolescents and Women with Ionizing Radiation. Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/pregnant-pts.pdf	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.	N/A	4

**Breast Imaging of Pregnant and Lactating Women
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Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
57. American College of Radiology. ACR-ACOG-AIUM-SRU Practice Parameter for the Performance of Obstetrical Ultrasound. Available at: https://www.acr.org/-/media/ACR/Files/Practice-Parameters/us-ob.pdf	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.	N/A	4
58. Expert Panel on MR Safety, Kanal E, Barkovich AJ, et al. ACR guidance document on MR safe practices: 2013. J Magn Reson Imaging. 37(3):501-30, 2013 Mar.	Review/Other-Dx	N/A	Guidance document on MR safety practices to help guide MR practitioners regarding MR safety issues and provide a basis for them to develop and implement their own MR policies and practices.	N/A	4
59. American College of Radiology. ACR Appropriateness Criteria® Radiation Dose Assessment Introduction. Available at: https://www.acr.org/-/media/ACR/Files/Appropriateness-Criteria/RadiationDoseAssessmentIntro.pdf .	Review/Other-Dx	N/A	Guidance document on exposure of patients to ionizing radiation.	No results stated in abstract.	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.
- Meta-analysis
 - a. *Good quality* – the study design, methods, analysis, and results are valid and the conclusion is supported.
 - b. *Inadequate quality* – the study design, analysis, and results lack the methodological rigor to be considered a good meta-analysis study.

Abbreviations Key

Dx = Diagnostic

Tx = Treatment