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Advances in Breast MRI in the setting of Ductal Carcinoma in situ

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Abstract

Ductal carcinoma in situ (DCIS) of the breast is a pre-invasive breast malignancy with controversial clinical relevance and management. These lesions have increased in incidence with breast cancer screening programs and are associated with increasingly recognized clinical issues of overdiagnosis and overtreatment. This article discusses the imaging presentation of these lesions with emphasis on advances in breast MRI and its role in the management of DCIS.

Keywords

Breast cancer screening; overdiagnosis; overtreatment; precision diagnostics; individualized therapy

Introduction

Ductal carcinoma in situ (DCIS) is a pre-invasive breast cancer that is often diagnosed as a result of abnormal screening mammography. With the widespread implementation of screening programs in the United States, the rate of DCIS diagnoses has increased from 2.4 to 27.7 per 100,000 women between 1981–2001^{1–3}. Despite DCIS lacking the potential to metastasize, it currently is treated aggressively, with nearly all patients undergoing either breast conserving surgery with radiation or mastectomy, often with adjuvant hormonal therapy. This treatment approach is due the heterogeneous biological behavior DCIS exhibits, which cannot be predicted accurately with current pathological and clinical markers. Although detection of DCIS was once thought to be the key to invasive breast cancer detection, current oncology opinions have shifted to implicate DCIS as the main driver of breast cancer overdiagnosis and overtreatment^{4,5}. This article reviews the

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presentation and epidemiology of DCIS, its multimodality imaging features, current management, and opportunities for advanced imaging in guiding DCIS management.

DCIS Presentations and Epidemiology

In the late 1970s and early 1980s, before widespread implementation of mammographic screening, the incidence of DCIS in the United States was reported to be 2.4 per 100,000 women³, comprising only 2.1% of all breast malignancies⁶. A recent study performed on an unscreened population in Cape Town, South Africa, reported a similarly low percentage of pure DCIS (1.1%) among all detected breast cancers⁷. In unscreened populations, DCIS most often presents as a palpable concern, followed by nipple discharge, and Paget's disease of the nipple⁸.

In contrast, the incidence of DCIS has now risen to 27.7 per 100,000³, representing 21% of all diagnosed breast malignancies⁹. Once often detected clinically, DCIS is now more commonly detected on routine mammographic screening⁸. It is important to note, however, that the number of invasive breast cancers detected by implementation of screening mammography still far outweighs the number of detected pure DCIS⁹. Furthermore, the proportion of high grade DCIS, which is thought to have a higher upgrade rate on surgical excision and a shorter average time to progression to invasive disease if left untreated, has, in fact, increased since implementation of mammographic screening⁸.

DCIS detected today is rare before the age of 35, and incidence peaks in the 7th-8th decade of life. Most screen detected DCIS are small (<15 mm). Risk factors for developing DCIS--similar to those for invasive breast cancer--include dense breasts, nulliparity, personal history of atypical ductal or lobular hyperplasia, family history, and BRCA 1 and 2 genetic mutations. Increased body mass index and use of hormone replacement therapy are also suggested as possible but indefinite risk factors^{2,9}.

DCIS Pathologic Descriptions and Risk Stratification Tools

In the prevailing theory of breast cancer pathogenesis, DCIS represents the most biologically aggressive lesion in a spectrum of intraductal proliferations¹⁰ and is a non-obligate precursor to invasive breast cancer. Traditional pathologic classification of DCIS describes DCIS features as one of five architectural patterns (Figure 1)¹¹; however, this descriptive classification has not been found to provide prognostic information useful for guiding management. Subsequently, various histopathological classification systems have been developed based on nuclear grade, presence of necrosis, and cellular dedifferentiation, which have been found to correlate with clinical outcomes such as risk of ipsilateral breast recurrence after treatment better than traditional methods¹². One commonly used system is the Van Nuys Pathologic Classification (VNPC, Figure 2), which combines nuclear grade and comedonecrosis to aid in determining the risk of a DCIS lesion to progress to invasive disease and recur in the ipsilateral breast after treatment^{13,14}. However, in most cases, these pathologic assessments still do not provide enough prognostic value to be relied upon for treatment decision-making, even when combined with other clinical features such as lesion size and surgical margins (e.g. Van Nuys Prognostic Index and Memorial Sloan Kettering Cancer Center DCIS Nomogram)¹⁵⁻¹⁸.

Several newer pathology markers^{13,19} and a tissue-based multigene assay have been developed and may aid in determining risk of DCIS recurrence (Table 1)^{20,21}. In particular, a 12 gene assay, *Oncotype DX-DCIS*, has been developed to quantify the 10-year risk of local recurrence after therapy. This scoring system has been proposed to help identify DCIS at low risk of recurrence, which may not require radiation therapy²¹. However, its high cost (~\$4,000) and lack of validation in a broad spectrum of DCIS lesion size and pathologic features have limited its use in clinical practice to date. Fortunately, the use of this tool in conjunction with breast MRI is being evaluated further in an ongoing clinical trial (Eastern Cooperative Oncology Group (ECOG)-American College of Radiology Imaging Network (ACRIN) trial E4112)²².

Imaging Features of DCIS

Currently, greater than 90% of DCIS lesions are detected on imaging alone through screening mammography and screening breast MRI. Ultrasound generally has been considered less effective for DCIS detection because of its low sensitivity for identification of microcalcifications²³, and is generally better suited for characterization of invasive breast cancer^{24–27}.

Mammography—The most common mammographic imaging presentation of DCIS is that of microcalcifications, which can be seen in approximately 50–75% of cases²⁸. When DCIS does present mammographically as a mass without associated calcifications, such lesions are more likely to be lower grade¹. Fine-linear and pleomorphic calcifications in a linear or segmental distribution without an associated mass account for the most classic presentation of DCIS on mammography; however, many DCIS lesions present as more equivocal calcifications and can overlap with the appearance of nonmalignant pathologies such as sclerosing adenosis, fibroadenomatoid change, and atypical ductal hyperplasia, the latter of which is a high-risk lesion closely resembling low grade DCIS on pathology. Various morphologies of calcifications that reflect DCIS are illustrated in Figure 3. In general, the mammographic appearance of calcifications has not proven to be reliably useful for determining DCIS biological behavior or treatment outcomes. One exception is the correlation of fine-linear or fine-linear branching calcifications with DCIS exhibiting comedonecrosis and high nuclear grade (Figure 4) on pathologic assessment; such lesions are associated with higher risk of DCIS recurrence after surgery²⁹.

Ultrasound—The primary use of ultrasound in the setting of calcified DCIS is to further assess for a mass, which may indicate the presence of an associated invasive component. Ultrasound may also be used to guide biopsy, as ultrasound guided biopsy is often less costly, more readily available, and does not necessitate ionizing radiation. Features that increase the likelihood of sonographic visibility includes mammographic size greater than 10 mm, high density of calcifications and segmental distribution³⁰. While some advocate for targeted ultrasound to be performed regularly to further evaluate pure suspicious mammographic calcifications³¹, this practice is not uniform across institutions.

Ultrasound plays a more prominent role for a minority of non-calcified DCIS. Mammographic appearances of non-calcified DCIS range from mass, asymmetry, to

mammographically occult, and non-calcified DCIS are also more likely to present symptomatically³². In these settings, sonographic visibility is suggested to be as high as 88%³³. The most common sonographic appearance of DCIS is mass (44 – 72%), with a wide range of shapes and margins, followed by microcalcifications, ductal changes, and architectural distortion (Figure 5)^{31,33–35}. Similar to trends seen in mammography, DCIS appearing as masses on ultrasound have been associated with low-intermediate grade³⁴, whereas those appearing as microcalcifications on ultrasound have been associated with high grade^{33–35}.

MRI—Breast MRI was initially considered to be relatively poor for DCIS evaluation, with high false-negative rates due to its inability to identify microcalcifications³⁶. However, as MRI techniques shifted from an emphasis on high temporal resolution to high spatial resolution, morphologic features such as non-mass enhancement that commonly represent DCIS on MRI were recognized³⁷. Multiple studies have since shown the superiority of MRI over mammography for DCIS detection (sensitivity 92% versus 56% respectively) and determination of DCIS extent of disease^{38,39}. Interestingly, MRI also identifies a greater fraction of high nuclear grade lesions when compared to mammography⁴⁰, and one study has identified an imaging model utilizing dynamic contrast enhanced (DCE) and diffusion weighted imaging (DWI) features that may identify high nuclear grade DCIS lesions in vivo⁴¹.

DCIS most commonly presents on breast MRI as segmental or linear non-mass enhancement (NME) with clumped internal enhancement morphology, accounting for 60–80% of DCIS lesions visible on MRI^{42–44}. However, NME is not specific for DCIS, as benign proliferative pathology (including fibrocystic changes and pseudoangiomatous stromal hyperplasia), invasive breast cancer (both ductal and lobular phenotypes), and even normal tissue (asymmetric physiologic background parenchymal enhancement) can present as suspicious NME. Less common presentations of DCIS on MRI include enhancing masses (14–34%) and foci of enhancement (1–12%) (Figure 6)^{42–44}. The enhancement characteristics of DCIS and invasive carcinomas are based on tumor angiogenesis, with abnormal periductal or stromal vascularity, which may be due to disruption in the myoepithelial cells (which secrete angiogenesis inhibitors) that line the duct^{1,45}.

On DCE MRI, DCIS lesions exhibit variable kinetic enhancement features. On initial phase, DCIS lesions most commonly exhibit fast (pre-contrast to initial post-contrast signal increase 100%) initial phase enhancement (49–68% of cases), but can also demonstrate medium (50 to 99% signal increase), slow (<50% signal increase), or even no initial phase enhancement (approximately 5–10% of cases). On delayed-phase images, the typical kinetic profile suggestive of malignancy (“washout”, which is defined as signal intensity decrease 10%) is seen in the minority of cases (28–44%)^{1,42}.

DCIS Staging and Management

Historically, all breast malignancies, including DCIS, were surgically treated with radical mastectomy, a procedure which included removal of the entire breast, the pectoral fascia, and axillary content⁴⁶. The landmark randomized controlled trial by Fisher et al⁴⁶, which

demonstrated no difference in 5-year survival and recurrence rates between breast malignancies treated with radical mastectomy versus breast conservation therapy, significantly alter the surgical standard of care. Non-invasive carcinoma comprised 1.4% of this study. Subsequently, observational studies focused only on DCIS have also found no survival benefits of mastectomy over breast conservation therapy^{47,48}.

Today, the most common surgical treatment for DCIS is breast conservation therapy⁹. Treatment via unilateral mastectomy, although still indicated in cases such as multicentric disease, extensive diffuse disease, or positive margins after multiple surgical resections⁴⁹, is less common, followed by bilateral mastectomy. Interestingly, despite a very low risk of contralateral breast malignancy in setting of DCIS in the general population⁵⁰, the rate of bilateral mastectomy in treatment of DCIS has notably increased over the past two decades^{51,52}, and is mostly attributed to patients younger than 40 years old⁹. The National Comprehensive Cancer Network (NCCN) generally does not recommend axillary dissection in treatment of pure DCIS, except on rare occasions where surgical treatment is in an anatomic location that may limit possible future sentinel lymph node biopsy⁴⁹.

Radiation and hormone therapy is also often considered in treatment of DCIS. Randomized control trials comparing lumpectomy with or without radiation therapy have demonstrated decreased recurrence in the former group². Despite lack of evidence for significant reduction in mortality, the NCCN has uniform consensus based upon high-level evidence that combination of lumpectomy and radiation therapy is the appropriate treatment of choice. Similarly, hormone therapy is also recommended due to reduction of disease recurrence⁴⁹.

Despite the comprehensive treatment outlined above, it is estimated that over half of DCIS lesions will never impact a woman's health if left untreated and the prevailing DCIS treatment is aggressive due to a lack of ability to stratify DCIS risk^{53,54}. Because the great majority (>90%) of DCIS lesions present in asymptomatic women, questions have been raised regarding the value of early breast cancer detection in the form of DCIS through screening mammography⁴. These controversies are often described with terms such as "overdiagnosis," which implies radiologists and imaging tests are to blame for identifying the DCIS, and "overtreatment," which transfers responsibility for the DCIS conundrum to the treating physician. In reality and as outlined by the National Institutes of Health⁵⁵, all parties involved in breast cancer diagnosis and care must work together to find pathologic, clinical, and imaging markers that can help differentiate more aggressive forms of DCIS from those that can safely be followed. Accordingly, future research on DCIS imaging should center on how advanced imaging can improve determination of appropriate treatments and whether MRI features can serve as unique biomarkers of DCIS risk.

Opportunities for MRI to Improve DCIS Treatment

Emerging research poses the benefit of MRI in many time points of DCIS care. In the diagnostic stage, MRI may be able to predict malignant potential of mammographic calcifications, possibly reducing number of unnecessary needle biopsies. Once DCIS is diagnosed, MRI is superior to mammography in delineating extent of disease, which may lead to more precise surgical treatment and avoidance of radiation therapy. Even after

surgical treatment, MRI may be able to guide long term care by predicting pathological aggressiveness and risk of recurrence.

MRI to Guide Biopsy of Mammographic Calcifications—While DCIS most often presents as microcalcifications, this finding can represent a wide range of benign to malignant pathologies. Currently, the American of Radiology Breast Imaging Reporting and Data System (BI-RADS) recommends biopsy for histological evaluation for all microcalcifications with greater than 2% risk of malignancy as deemed by interpreting radiologist. With this recommendation, the positive predictive value of microcalcifications is cited to be less than 30%⁵⁶. Therefore, there is great interest in exploring other imaging modalities, including MRI, to improve the positive predictive value of microcalcifications and reduce number of unnecessary biopsies.

Numerous studies have been performed to explore MRI's role in predicting malignant potential of microcalcifications with differing results. A recently published meta-analysis pooling a total of 1843 cases of BI-RADS category 3, 4, and 5 microcalcifications attempts to consolidate and generalize this body of research⁵⁷. Similar to a previous meta-analysis⁵⁸, while MRI performance was found to be too heterogenous among BI-RADS category 3 lesions to be of benefit, not cost-effective among BI-RADS category 5 lesions, for which the prevalence of malignancy was found to be 94%, MRI may be useful to guiding management of BI-RADS category 4 lesions. MRI sensitivity and specificity of BI-RADS category 4 microcalcifications were 92% and 82% respectively, with a negative likelihood ratio of 0.099. This result suggests that microcalcifications mammographically interpreted as BI-RADS category 4 with a negative MRI may be downgraded to BI-RADS category 3, which would decrease the number of needle biopsies recommended.

Additionally, the study found that among the 106 MRI false negative cases for all lesions, only 7 were invasive carcinoma, resulting in a negative predictive value for invasive carcinoma of 99%. This result suggests that MRI may be able exclude the risk of pathological upgrade even prior to performing a biopsy, which would aid in surgical planning.

MRI to Guide Surgical Approach—Once a DCIS diagnosis has been made, mammography is known to underestimate the full extent on final pathology since it typically detects only calcified portions of the in situ cancer. Dillon and colleagues demonstrated that mammography considerably underestimates DCIS size (imaging-to-pathology size discrepancy of more than 1 cm) in 40% of patients who ultimately have positive surgical margins compared to 14% of women who have uninvolved margins⁵⁹. Despite the known higher sensitivity of MRI for DCIS detection⁶⁰ and higher accuracy for evaluation of extent of disease^{19,61}, the routine use of MRI for newly diagnosed DCIS remains controversial due to a lack of evidence to support treatment outcomes and potential adverse effects including unnecessary mastectomies⁶². Most of the prior studies assessing the value of MRI to assess DCIS extent of disease were performed at 1.5 tesla, and two recent studies have found that the use of higher field strength MRI (3 tesla) can provide an even more accurate assessment of pathological extent of disease when compared to 1.5 tesla technique⁶³ and mammography⁶⁴. However, it remains unclear to date whether this improved ability to

delineate extent of disease prior to surgery will lead to better long term outcomes, such as decreased rates of local recurrence. It is conceivable that in the context of current management approaches that overtreat the majority of patients diagnosed with DCIS, the already very low local recurrence rates will not be lowered through the use of MRI. Conversely, it is possible that such treatment approaches, such as requiring radiation therapy for nearly all patients with DCIS who undergo breast conserving therapy, were effective in the setting of less advanced imaging techniques and that through advanced imaging such as MRI, appropriate patient populations who can avoid radiation therapy can be identified. An ongoing multi-center trial (4112 trial) is designed to assess this very question: can MRI in conjunction with an advanced a 12 gene assay (Oncotype DX-DCIS)²¹ safely allow low risk patients to avoid radiation therapy and thereby decrease overtreatment?²² It is this role in precision diagnostics and tailored, individualized therapies that MRI could provide the most benefit in DCIS diagnosis and treatment.

MRI to Stratify DCIS Biological Risk—Compared to mammography and ultrasound, MRI has greater potential to reflect the biologic features of breast pathology, such as vascularity and permeability, cell membrane integrity, and cellularity. Through the use of DCE techniques, radiologists can measure the differential enhancement of DCIS lesions relative to normal breast tissue, theoretically assessing the rates at which the abnormal vessels that support DCIS lesions growth both deposit nutrients into a tumor and remove cell cycle byproducts. This can be achieved semi-quantitatively by measuring basic kinetic enhancement curves (e.g. slow, medium, or fast initial phase and persistent, plateau, or washout delayed phase) or quantitatively for high temporal resolution acquisitions (e.g. K^{trans} , k_{ep} , and v_e)⁶⁵. The use of DWI in breast imaging can provide complementary biological information by indirectly measuring cellular density and membrane integrity⁶⁶. DWI utilizes motion-sensitizing gradients during MR image acquisition to probe local water diffusion characteristics, and the level by which water diffusion is restricted can be quantified by measuring apparent diffusion coefficients (ADCs)⁶⁷. It has been hypothesized that since most breast malignancies have high cellular density and intact cell membranes, many malignancies demonstrate reduced water diffusivity when compared to normal tissue or benign pathologies.

Using these parameters, several prior studies have identified promising MRI features that can capture DCIS biology, and, in general, have found that, small, focal areas of enhancement that exhibit high contrast-to-noise ratios (CNR) with corresponding high standard ADC values on DWI are more likely to reflect lower grade DCIS^{19,68,69}. A recent study at 3 tesla has demonstrated that low risk DCIS (as defined by the VNPC) tends to exhibit lower normalized ADC values and higher CNR on DWI⁷⁰. In a pilot study using a mouse model of DCIS, Jansen et al showed a trend of lower K^{trans} values in DCIS lesions when compared to invasive tumors⁷¹. Jansen and colleagues also evaluated 12 DCIS lesions in humans using high temporal resolution DCE MRI and found that solid forms of DCIS exhibit unique early contrast features when compared to cribriform subtypes⁷². Finally, Li et al found that K^{trans} and ADC can accurately discriminate between DCIS and invasive cancer, and that they correlated with markers of proliferation (Ki-67) and angiogenesis (CD105)⁷³.

More recently, two retrospective studies have demonstrated that MRI imaging features of both the DCIS lesion and surrounding normal tissue may be able to directly predict treatment outcomes of DCIS. In a study examining 15 DCIS cases that recurred after treatment, Kim et al found that higher amounts of background parenchymal enhancement (BPE) surrounding DCIS lesions correlated with recurrence risk⁷⁴, suggesting that MRI features of normal tissue have potential to predict which patients are most likely to develop recurrent breast malignancies. Another study of 11 women with DCIS that experienced ipsilateral recurrences matched to 11 women who did not recur but had similar clinical, pathologic, and treatment features found that MRI features of higher DCIS lesion signal enhancement ratio, larger DCIS lesion functional tumor volume, and greater ipsilateral whole breast BPE were associated with women who recurred. These two studies also provide increasing validation of BPE as a possible imaging marker of general breast cancer risk and tumorigenesis, building on work by both King et al and Dontchos et al^{75,76}.

Conclusion

The diagnosis rate of DCIS has been steadily rising over the past decade due to improved imaging techniques such as digital mammography and breast MRI. While this has allowed breast imagers to identify breast cancer at its earliest possible stage, this also has created concerns of exposing women to aggressive therapies for a pre-invasive process that may not impact a woman's life if left undetected. Through this challenge, there is a unique opportunity for radiologists to address these concerns through advanced imaging, therefore, guiding more personalized treatments by confirming disease extent and measuring biology of DCIS lesions in vivo.

References:

1. Yamada T, Mori N, Watanabe M, et al. Radiologic-pathologic correlation of ductal carcinoma in situ. *Radiographics*. 2010;30(5):1183–1198. [PubMed: 20833844]
2. Allegra CJ, Aberle DR, Ganschow P, et al. National Institutes of Health State-of-the-Science Conference Statement: Diagnosis and Management of Ductal Carcinoma In Situ September 22–24, 2009. *Journal of the National Cancer Institute*. 2010;102(3):161–169. [PubMed: 20071686]
3. Sumner WE 3rd, Koniaris LG, Snell SE, et al. Results of 23,810 cases of ductal carcinoma-in-situ. *Annals of surgical oncology*. 2007;14(5):1638–1643. [PubMed: 17245612]
4. Esserman L, Yau C. Rethinking the Standard for Ductal Carcinoma In Situ Treatment. *JAMA oncology*. 2015.
5. Solin LJ. Selecting individualized treatment for patients with ductal carcinoma in situ of the breast: the search continues. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2012;30(6):577–579. [PubMed: 22253465]
6. Rosner D, Bedwani RN, Vana J, Baker HW, Murphy GP. Noninvasive breast carcinoma: results of a national survey by the American College of Surgeons. *Ann Surg*. 1980;192(2):139–147. [PubMed: 6250497]
7. Mutebi M, Simonds H. Breast ductal carcinoma in situ in an unscreened population: presentation, diagnosis and management at a single tertiary centre. *S Afr J Surg*. 2017;55(1):4–9.
8. Pandya S, Mackarem G, Lee AKC, et al. Ductal Carcinoma In Situ: The Impact of Screening on Clinical Presentation and Pathologic Features. *Breast J*. 1998; 4(3):146–151.
9. Ward EM, DeSantis CE, Lin CC, et al. Cancer statistics: Breast cancer in situ. *CA Cancer J Clin*. 2015;65(6):481–495. [PubMed: 26431342]

10. Cichon MA, Degnim AC, Visscher DW, Radisky DC. Microenvironmental influences that drive progression from benign breast disease to invasive breast cancer. *Journal of mammary gland biology and neoplasia*. 2010;15(4):389–397. [PubMed: 21161341]
11. Kumar V, Abul K. Abbas, Nelson Fausto, Stanley L. Robbins, and Ramzi S. Cotran Robbins and Cotran Pathologic Basis of Disease. Philadelphia: Elsevier Saunders; 2005:1139–1140.
12. Evans A, Pinder S, Wilson R, et al. Ductal carcinoma in situ of the breast: correlation between mammographic and pathologic findings. *AJR American journal of roentgenology*. 1994;162(6):1307–1311. [PubMed: 8191988]
13. Kerlikowske K, Molinaro A, Cha I, et al. Characteristics associated with recurrence among women with ductal carcinoma in situ treated by lumpectomy. *J Natl Cancer Inst*. 2003;95(22):1692–1702. [PubMed: 14625260]
14. Silverstein MJ, Poller DN, Waisman JR, et al. Prognostic classification of breast ductal carcinoma-in-situ. *Lancet*. 1995;345(8958):1154–1157. [PubMed: 7723550]
15. Kelley L, Silverstein M, Guerra L. Analyzing the risk of recurrence after mastectomy for DCIS: a new use for the USC/Van Nuys Prognostic Index. *Annals of surgical oncology*. 2011;18(2):459–462. [PubMed: 20859695]
16. MacAusland SG, Hepel JT, Chong FK, et al. An attempt to independently verify the utility of the Van Nuys Prognostic Index for ductal carcinoma in situ. *Cancer*. 2007;110(12):2648–2653. [PubMed: 17960606]
17. Rudloff U, Jacks LM, Goldberg JJ, et al. Nomogram for predicting the risk of local recurrence after breast-conserving surgery for ductal carcinoma in situ. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2010;28(23):3762–3769. [PubMed: 20625132]
18. Yi M, Meric-Bernstam F, Kuerer HM, et al. Evaluation of a breast cancer nomogram for predicting risk of ipsilateral breast tumor recurrences in patients with ductal carcinoma in situ after local excision. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2012;30(6):600–607. [PubMed: 22253459]
19. Esserman LJ, Kumar AS, Herrera AF, et al. Magnetic resonance imaging captures the biology of ductal carcinoma in situ. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2006;24(28):4603–4610. [PubMed: 17008702]
20. Kerlikowske K, Molinaro AM, Gauthier ML, et al. Biomarker expression and risk of subsequent tumors after initial ductal carcinoma in situ diagnosis. *J Natl Cancer Inst*. 102(9):627–637. [PubMed: 20427430]
21. Solin LJ, Gray R, Baehner FL, et al. A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast. *J Natl Cancer Inst*. 2013;105(10):701–710. [PubMed: 23641039]
22. Lehman CD, Gatsonis C, Synder BS, et al. Impact of magnetic resonance imaging on conversion from wide local excision to mastectomy in patients with ductal carcinoma in situ: First results from the ECOG-ACRIN 4112 prospective study. Poster presented at: San Antonio Breast Cancer Symposium; December 6–10, 2016; San Antonio, TX.
23. Bassett LW, Kimme-Smith C. Breast sonography. *AJR American journal of roentgenology*. 1991;156(3):449–455. [PubMed: 1899737]
24. Kaplan SS. Clinical utility of bilateral whole-breast US in the evaluation of women with dense breast tissue. *Radiology*. 2001;221(3):641–649. [PubMed: 11719658]
25. Kolb TM, Lichy J, Newhouse JH. Comparison of the performance of screening mammography, physical examination, and breast US and evaluation of factors that influence them: an analysis of 27,825 patient evaluations. *Radiology*. 2002;225(1):165–175. [PubMed: 12355001]
26. Berg WA, Blume JD, Cormack JB, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *Jama*. 2008;299(18):2151–2163. [PubMed: 18477782]
27. Weigert J, Steenbergen S. The connecticut experiment: the role of ultrasound in the screening of women with dense breasts. *The breast journal*. 2012;18(6):517–522. [PubMed: 23009208]

28. Barreau B, de Mascarel I, Feuga C, et al. Mammography of ductal carcinoma in situ of the breast: review of 909 cases with radiographic-pathologic correlations. *European journal of radiology*. 2005;54(1):55–61. [PubMed: 15797293]
29. Holmberg L, Wong YN, Tabar L, et al. Mammography casting-type calcification and risk of local recurrence in DCIS: analyses from a randomised study. *British journal of cancer*. 2013;108(4):812–819. [PubMed: 23370209]
30. Soo MS, Baker JA, Rosen EL. Sonographic detection and sonographically guided biopsy of breast microcalcifications. *AJR American journal of roentgenology*. 2003;180(4):941–948. [PubMed: 12646433]
31. Wang LC, Sullivan M, Du H, Feldman MI, Mendelson EB. US Appearance of Ductal Carcinoma in Situ. *RadioGraphics*. 2013;33(1):213–228. [PubMed: 23322838]
32. Ikeda DM, Andersson I. Ductal carcinoma in situ: atypical mammographic appearances. *Radiology*. 1989;172(3):661–666. [PubMed: 2549563]
33. Lee MH, Ko EY, Han BK, Shin JH, Ko ES, Hahn SY. Sonographic findings of pure ductal carcinoma in situ. *Journal of clinical ultrasound : JCU*. 2013;41(8):465–471. [PubMed: 23949917]
34. Park JS, Park YM, Kim EK, et al. Sonographic findings of high-grade and non-high-grade ductal carcinoma in situ of the breast. *Journal of ultrasound in medicine : official journal of the American Institute of Ultrasound in Medicine*. 2010;29(12):1687–1697. [PubMed: 21098839]
35. Yang WT, Tse GM. Sonographic, mammographic, and histopathologic correlation of symptomatic ductal carcinoma in situ. *AJR American journal of roentgenology*. 2004;182(1):101–110. [PubMed: 14684521]
36. Boetes C, Strijk SP, Holland R, Barentsz JO, Van Der Sluis RF, Ruijs JH. False-negative MR imaging of malignant breast tumors. *European radiology*. 1997;7(8):1231–1234. [PubMed: 9377507]
37. Lehman CD. Magnetic resonance imaging in the evaluation of ductal carcinoma in situ. *Journal of the National Cancer Institute Monographs*. 2010;2010(41):150–151. [PubMed: 20956821]
38. Lehman CD, Gatsonis C, Kuhl CK, et al. MRI evaluation of the contralateral breast in women with recently diagnosed breast cancer. *The New England journal of medicine*. 2007;356(13):1295–1303. [PubMed: 17392300]
39. Berg WA, Gutierrez L, NessAiver MS, et al. Diagnostic accuracy of mammography, clinical examination, US, and MR imaging in preoperative assessment of breast cancer. *Radiology*. 2004;233(3):830–849. [PubMed: 15486214]
40. Kuhl CK, Schrading S, Bieling HB, et al. MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. *The Lancet*. 2007;370(9586):485–492.
41. Rahbar H, Partridge SC, Demartini WB, et al. In vivo assessment of ductal carcinoma in situ grade: a model incorporating dynamic contrast-enhanced and diffusion-weighted breast MR imaging parameters. *Radiology*. 2012;263(2):374–382. [PubMed: 22517955]
42. Jansen SA, Newstead GM, Abe H, Shimauchi A, Schmidt RA, Karczmar GS. Pure ductal carcinoma in situ: kinetic and morphologic MR characteristics compared with mammographic appearance and nuclear grade. *Radiology*. 2007;245(3):684–691. [PubMed: 18024450]
43. Rosen EL, Smith-Foley SA, DeMartini WB, Eby PR, Peacock S, Lehman CD. BI-RADS MRI enhancement characteristics of ductal carcinoma in situ. *The breast journal*. 2007;13(6):545–550. [PubMed: 17983393]
44. Menell JH, Morris EA, Dershaw DD, Abramson AF, Brogi E, Liberman L. Determination of the presence and extent of pure ductal carcinoma in situ by mammography and magnetic resonance imaging. *The breast journal*. 2005;11(6):382–390. [PubMed: 16297080]
45. Buadu LD, Murakami J, Murayama S, et al. Breast lesions: correlation of contrast medium enhancement patterns on MR images with histopathologic findings and tumor angiogenesis. *Radiology*. 1996;200(3):639–649. [PubMed: 8756909]
46. Fisher B, Bauer M, Margolese R, et al. Five-year results of a randomized clinical trial comparing total mastectomy and segmental mastectomy with or without radiation in the treatment of breast cancer. *The New England journal of medicine*. 1985;312(11):665–673. [PubMed: 3883167]

47. Meijnen P, Oldenburg HS, Peterse JL, Bartelink H, Rutgers EJ. Clinical outcome after selective treatment of patients diagnosed with ductal carcinoma in situ of the breast. *Annals of surgical oncology*. 2008;15(1):235–243. [PubMed: 17987342]
48. Schouten van der Velden AP, van Vugt R, Van Dijck JA, Leer JW, Wobbes T. Local recurrences after different treatment strategies for ductal carcinoma in situ of the breast: a population-based study in the East Netherlands. *Int J Radiat Oncol Biol Phys*. 2007;69(3):703–710. [PubMed: 17544591]
49. Gradishar WJ, Anderson BO, Balassanian R, et al. Invasive Breast Cancer Version 1.2016, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw*. 2016;14(3):324–354. [PubMed: 26957618]
50. Miller ME, Muhsen S, Olcese C, Patil S, Morrow M, Van Zee KJ. Contralateral Breast Cancer Risk in Women with Ductal Carcinoma In Situ: Is it High Enough to Justify Bilateral Mastectomy? *Annals of surgical oncology*. 2017.
51. Steiner CA, Weiss AJ, Barrett ML, Fingar KR, Davis PH. Trends in Bilateral and Unilateral Mastectomies in Hospital Inpatient and Ambulatory Settings, 2005–2013: Statistical Brief #201. Healthcare Cost and Utilization Project (HCUP) Statistical Briefs. Rockville (MD)2006.
52. Yao K, Stewart AK, Winchester DJ, Winchester DP. Trends in contralateral prophylactic mastectomy for unilateral cancer: a report from the National Cancer Data Base, 1998–2007. *Annals of surgical oncology*. 2010;17(10):2554–2562. [PubMed: 20461470]
53. Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L. Screening for breast cancer: an update for the U.S. Preventive Services Task Force. *Annals of internal medicine*. 2009;151(10):727–737, w237–742. [PubMed: 19920273]
54. Allred DC. Ductal carcinoma in situ: terminology, classification, and natural history. *Journal of the National Cancer Institute Monographs*. 2010;2010(41):134–138. [PubMed: 20956817]
55. Allegra CJ, Aberle DR, Ganschow P, et al. National Institutes of Health State-of-the-Science Conference statement: Diagnosis and Management of Ductal Carcinoma In Situ September 22–24, 2009. *J Natl Cancer Inst*. 2010;102(3):161–169. [PubMed: 20071686]
56. Kettritz U, Rotter K, Schreer I, et al. Stereotactic vacuum-assisted breast biopsy in 2874 patients: a multicenter study. *Cancer*. 2004;100(2):245–251. [PubMed: 14716757]
57. Bennani-Baiti B, Baltzer PA. MR Imaging for Diagnosis of Malignancy in Mammographic Microcalcifications: A Systematic Review and Meta-Analysis. *Radiology*. 2017;283(3):692–701. [PubMed: 27788035]
58. Dorrius MD, Pijnappel RM, Jansen-van der Weide MC, Oudkerk M. Breast magnetic resonance imaging as a problem-solving modality in mammographic BI-RADS 3 lesions. *Cancer Imaging*. 2010;10 Spec no A:S54–58. [PubMed: 20880790]
59. Dillon MF, Mc Dermott EW, O'Doherty A, Quinn CM, Hill AD, O'Higgins N. Factors affecting successful breast conservation for ductal carcinoma in situ. *Annals of surgical oncology*. 2007;14(5):1618–1628. [PubMed: 17443388]
60. Kuhl CK, Schrading S, Bieling HB, et al. MRI for diagnosis of pure ductal carcinoma in situ: a prospective observational study. *Lancet*. 2007;370(9586):485–492. [PubMed: 17693177]
61. Marcotte-Bloch C, Balu-Maestro C, Chamorey E, et al. MRI for the size assessment of pure ductal carcinoma in situ (DCIS): a prospective study of 33 patients. *European journal of radiology*. 2011;77(3):462–467. [PubMed: 19896789]
62. Schmale I, Liu S, Rayhanabad J, Russell CA, Sener SF. Ductal carcinoma in situ (DCIS) of the breast: perspectives on biology and controversies in current management. *Journal of surgical oncology*. 2012;105(2):212–220. [PubMed: 21751217]
63. Rahbar H, DeMartini WB, Lee AY, Partridge SC, Peacock S, Lehman CD. Accuracy of 3 T versus 1.5 T breast MRI for pre-operative assessment of extent of disease in newly diagnosed DCIS. *European journal of radiology*. 2015;84(4):611–616. [PubMed: 25604909]
64. Pickles MD, Gibbs P, Hubbard A, Rahman A, Wieczorek J, Turnbull LW. Comparison of 3.0 T magnetic resonance imaging and X-ray mammography in the measurement of ductal carcinoma in situ: a comparison with histopathology. *European journal of radiology*. 2015;84(4):603–610. [PubMed: 25604907]

65. Jacobs MA. Multiparametric magnetic resonance imaging of breast cancer. *Journal of the American College of Radiology : JACR*. 2009;6(7):523–526. [PubMed: 19560072]
66. Partridge SC, McDonald ES. Diffusion weighted magnetic resonance imaging of the breast: protocol optimization, interpretation, and clinical applications. *Magnetic resonance imaging clinics of North America*. 2013;21(3):601–624. [PubMed: 23928248]
67. Le Bihan D, Breton E, Lallemand D, Grenier P, Cabanis E, Laval-Jeantet M. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Radiology*. 1986;161(2):401–407. [PubMed: 3763909]
68. Iima M, Yano K, Kataoka M, et al. Quantitative Non-Gaussian Diffusion and Intravoxel Incoherent Motion Magnetic Resonance Imaging: Differentiation of Malignant and Benign Breast Lesions. *Investigative radiology*. 2014.
69. Rahbar H, Partridge SC, W.B. D, et al. In vivo assessment of ductal carcinoma in situ grade: a model incorporating dynamic contrast-enhanced and diffusion-weighted Breast MR imaging parameters. *Radiology*. 2012.
70. Rahbar H, Parsian S, Lam DL, et al. Can MRI biomarkers at 3 T identify low-risk ductal carcinoma in situ? *Clin Imaging*. 2016;40(1):125–129. [PubMed: 26365872]
71. Jansen SA, Paunesku T, Fan X, et al. Ductal carcinoma in situ: X-ray fluorescence microscopy and dynamic contrast-enhanced MR imaging reveals gadolinium uptake within neoplastic mammary ducts in a murine model. *Radiology*. 2009;253(2):399–406. [PubMed: 19864527]
72. Jansen SA, Fan X, Medved M, et al. Characterizing early contrast uptake of ductal carcinoma in situ with high temporal resolution dynamic contrast-enhanced MRI of the breast: a pilot study. *Physics in medicine and biology*. 2010;55(19):N473–485. [PubMed: 20858914]
73. Li L, Wang K, Sun X, et al. Parameters of dynamic contrast-enhanced MRI as imaging markers for angiogenesis and proliferation in human breast cancer. *Medical science monitor : international medical journal of experimental and clinical research*. 2015;21:376–382. [PubMed: 25640082]
74. Kim SA, Cho N, Ryu EB, et al. Background parenchymal signal enhancement ratio at preoperative MR imaging: association with subsequent local recurrence in patients with ductal carcinoma in situ after breast conservation surgery. *Radiology*. 2014;270(3):699–707. [PubMed: 24126372]
75. Dontchos BN, Rahbar H, Partridge SC, et al. Are Qualitative Assessments of Background Parenchymal Enhancement, Amount of Fibroglandular Tissue on MR Images, and Mammographic Density Associated with Breast Cancer Risk? *Radiology*. 2015;276(2):371–380. [PubMed: 25965809]
76. King V, Brooks JD, Bernstein JL, Reiner AS, Pike MC, Morris EA. Background parenchymal enhancement at breast MR imaging and breast cancer risk. *Radiology*. 2011;260(1):50–60. [PubMed: 21493794]

Figure. 1 –

Traditional Pathologic Classification of DCIS. This includes 5 types (comedo, solid, cribriform, papillary, and micropapillary) based on architectural pattern.

Figure. 2 –.

Van Nuys Pathologic Classification. This system stratifies DCIS into two major groups – non-high and high nuclear grade, with the non-high grade divided based based on the presense of comedonecrosis. (color image)

Figure 3. Different morphologies of DCIS presenting as calcifications. Group of punctate (a) and group of amorphous (b) calcifications. Biopsy revealed low grade DCIS. Group of coarse heterogeneous (c) and pleomorphic (d) calcifications. Biopsy revealed high grade DCIS.

Figure 4. Segmental fine pleomorphic and fine linear branching calcifications. Biopsy revealed high grade DCIS. Fine linear and fine linear-branching calcifications are often seen in high nuclear grade lesions with comedonecrosis.

Figure 5.

Sonographic appearances of DCIS. Oval, hypoechoic mass with circumscribed margins with no specific posterior acoustic features (a). Biopsy revealed intermediate grade DCIS. Irregular mass with indistinct margins and echogenic foci consistent with calcifications (b). Biopsy revealed DCIS with microinvasion. Dilated ducts with debris and echogenic foci consistent with calcifications in a 39 year old women with suspicious nipple discharge (c). Biopsy revealed high grade DCIS.

Figure 6.

MRI appearances of DCIS. Axial T1-weighted fat-suppressed subtraction image (a) shows segmental non-mass enhancement with clumped internal enhancement. Pathology confirmed extensive high grade DCIS. Axial post-contrast T1 fat suppressed MRI image (b) shows an irregular mass with spiculated margins with a biopsy marker clip within the mass (arrow). Pathology confirmed high grade DCIS. Axial maximum intensity projection (c) shows a focus of enhancement (arrow) in a patient who had a breast MRI for recently diagnosed contralateral breast cancer. This was biopsied under MRI guidance and shown to represent low grade DCIS.

Table 1–

Pathologic Biomarkers for use in improving DCIS risk stratification

Biomarker	Indicator
Ki-67	Proliferation
CD34	Angiogenesis
CD68	Inflammation
ER/PR	Hormone receptor
Her2/neu	Epidermal growth factor receptor
COX-2	Inflammation