Pathology of breast cancer

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INTRODUCTION

Most breast malignancies arise from epithelial elements and are categorized as carcinomas. Breast carcinomas are a diverse group of lesions that differ in microscopic appearance and biologic behavior, although these disorders are often discussed as a single disease.

The in situ carcinomas of the breast are either ductal (also known as intraductal carcinoma) or lobular. This distinction is primarily based upon the growth pattern and cytologic features of the lesions, rather than their anatomic location within the mammary ductal-lobular system.

The invasive breast carcinomas consist of several histologic subtypes; the estimated percentages are from a contemporary population-based series of 135,157 women with breast cancer reported to the Surveillance, Epidemiology, and End Results (SEER) database of the National Cancer Institute between 1992 and 2001 [1]:

- Infiltrating ductal – 76 percent
- Invasive lobular – 8 percent
- Ductal/lobular – 7 percent
- Mucinous (colloid) – 2.4 percent
- Tubular – 1.5 percent
- Medullary – 1.2 percent
- Papillary – 1 percent

Other subtypes, including metaplastic breast cancer and invasive micropapillary breast cancer, all account for less than 5 percent of cases [2].

This topic will review the histology of ductal carcinoma in situ and invasive breast carcinoma. The pathologies of atypical hyperplasia, lobular carcinoma in situ, and other subtypes of breast cancer are discussed separately.

- (See "Atypia and lobular carcinoma in situ: High-risk lesions of the breast".)
- (See "Breast sarcoma: Epidemiology, risk factors, clinical presentation, diagnosis, and staging".)
- (See "Paget disease of the breast (PDB)".)
- (See "Phyllodes tumors of the breast".)
- (See "Prognostic and predictive factors in early, non-metastatic breast cancer".)

DUCTAL CARCINOMA IN SITU

The term ductal carcinoma in situ (DCIS) encompasses a heterogeneous group of lesions that differ in their clinical presentation, histologic appearance, and biologic potential. DCIS is characterized by proliferation of presumably malignant epithelial cells within the mammary ductal system, with no evidence of invasion into the surrounding stroma on routine light microscopic examination [3]. Ductal carcinoma in situ differs from lobular carcinoma in situ with regard to radiologic features, morphology, biologic behavior, and anatomic distribution in the breast (table 1). Lobular carcinoma in situ is discussed in detail elsewhere. (See "Atypia and lobular carcinoma in situ: High-risk lesions of the breast".)

Classification schemes that divide DCIS histologically into a variety of subtypes emphasize architectural features or growth pattern of the neoplastic cells, cytologic features, and cell necrosis, both singly and in combination. The traditional method for classifying DCIS lesions is primarily based upon the growth pattern (architectural features) of the tumor and recognizes five major types [4-7]:

- The comedo type is characterized by prominent necrosis in the center of the involved spaces. The necrotic material frequently becomes calcified; the calcifications may be detected mammographically, characteristically as linear, branching ("casting") calcifications. The tumor cells are large and show nuclear pleomorphism; mitotic activity may be prominent (picture 1). The comedo type is more often associated with invasion [8,9], and the degree of comedo necrosis in patients with DCIS appears to be a strong predictor for the risk of ipsilateral breast recurrence after treatment [10].

- The cribriform type is characterized by the formation of back to back glands without intervening stroma. The cells comprising this subtype are typically small to medium sized and have relatively uniform hyperchromatic nuclei. Mitoses are infrequent, and necrosis is limited to single cells or small cell clusters (picture 2).

- The micropapillary type features small tufts of cells that are oriented perpendicular to the basement membrane of the involved spaces and project into the lumina. The apical region of these small papillations is frequently broader than the base, imparting a club-shaped appearance. The micropapillae lack fibrovascular cores. The cells comprising this type of DCIS are usually small to medium in size, and the nuclei show diffuse hyperchromasia; mitoses are infrequent (picture 3).

- The papillary type shows intraluminal projections of tumor cells that, in contrast to the micropapillary variant, demonstrate fibrovascular cores and thereby constitute true papillations. A variant of papillary DCIS, intracystic papillary carcinoma, is characterized by tumor cells that are primarily or exclusively present in a single cystically dilated space [11].

- The solid type is not as well defined as the other subtypes. It features tumor cells that fill and distend the involved spaces and lack significant necrosis, fenestrations, or papillations. The tumor cells may be large, medium, or small.

Less common variants of DCIS include the "clinging" carcinoma [4], intraductal signet ring cell carcinoma [12], and cystic hypersecretory duct carcinoma [13,14]. Similar to the comedo type, these variants may show calcifications that can be detected mammographically. However, the mammographic appearance of these microcalcifications is less distinctive than the pattern seen in comedo lesions and can resemble a number of benign processes.

A number of authors have proposed alternative classification systems for DCIS (table 2) [15-18]. Although they use different terminology, all are primarily based upon nuclear grade and/or the presence or absence of necrosis, and have in common the recognition of three main categories of DCIS (ie, high, intermediate, and low grade).

- High-grade lesions typically exhibit aneuploidy, lack estrogen and progesterone receptors, and have a high proliferative rate, overexpression of the human epidermal growth factor receptor 2 (*HER2*) oncogene, mutations of the tumor protein p53 tumor suppressor gene (*p53*) with accumulation of its protein product, and angiogenesis in the surrounding stroma.

- Low-grade lesions are typically diploid, estrogen- and progesterone receptor-positive, have a low proliferative rate, and rarely (if ever) show abnormalities of the *HER2/neu* or *p53*

oncogenes.

- Lesions categorized histologically as intermediate grade are also intermediate between the high-grade and low-grade lesions with regard to the frequency of alterations in these biological markers.

These classification systems appear to correlate with biologic prognostic markers and predict groups of patients who are likely to have a recurrence of cancer following breast conservation therapy [15,18-30]. (See "Breast ductal carcinoma in situ: Epidemiology, clinical manifestations, and diagnosis".)

In 1997, a consensus conference was convened in an attempt to reach agreement on the classification of DCIS [31]. Although the panel did not endorse any single classification system, they recommended that certain features be routinely documented in the pathology report for DCIS lesions, including nuclear grade, the presence of necrosis, cell polarization, and architectural pattern(s).

INFILTRATING DUCTAL CARCINOMA

Infiltrating ductal carcinoma is the most common type of invasive breast cancer, accounting for 70 to 80 percent of invasive lesions. It is also termed infiltrating carcinoma of no special type or infiltrating carcinoma not otherwise specified (NOS).

On gross pathologic evaluation, these lesions are typically hard, gray-white, gritty masses that invade the surrounding tissue in a haphazard fashion to create the characteristic irregular, stellate shape. They are characterized microscopically by cords and nests of tumor cells with varying amounts of gland formation, and cytologic features that range from bland to highly malignant. The malignant cells induce a fibrous response as they infiltrate the breast parenchyma, and this reaction is, in large part, responsible for the clinically and grossly palpable mass, the radiologic density, and solid sonographic characteristics of typical invasive carcinomas.

Infiltrating ductal carcinomas are divided into three grades based upon a combination of architectural and cytologic features, usually assessed utilizing a scoring system based on three parameters [32]:

- Well-differentiated (grade 1) – Well-differentiated tumors have cells that infiltrate the stroma as solid nests of glands. The nuclei are relatively uniform with little or no evidence of mitotic activity (picture 4).

- Moderately differentiated (grade 2) – Moderately differentiated tumors have cells that infiltrate as solid nests with some glandular differentiation. There is some nuclear pleomorphism and a moderate mitotic rate (picture 5).

- Poorly differentiated (grade 3) – Poorly differentiated tumors are composed of solid nests of neoplastic cells without evidence of gland formation. There is marked nuclear atypia and considerable mitotic activity (picture 6).

A variable amount of associated ductal carcinoma in situ (DCIS) is present in most cases; the extent of DCIS but not lobular carcinoma in situ (LCIS) is an important prognostic factor in patients treated with breast conserving therapy in whom the surgical goal is complete excision of both intraductal and invasive carcinoma [33].

INFILTRATING LOBULAR CARCINOMA

Infiltrating lobular carcinomas are the second most common type of invasive breast cancer, accounting for about 5 to 10 percent of invasive lesions.

Incidence rates of lobular cancer are rising faster than the rates of ductal carcinoma in the United States, and postmenopausal hormone therapy may be more strongly related to lobular cancer risk than to ductal cancer risk. (See "Menopausal hormone therapy and the risk of breast cancer", section on 'Prognosis and tumor characteristics' and "Factors that modify breast cancer risk in women".)

Some infiltrating lobular carcinomas have a macroscopic appearance identical to that of infiltrating ductal cancers. However, in many cases no mass lesion is grossly evident, and the excised breast tissue may have a normal or only slightly firm consistency. Thus, the microscopic size of invasive lobular carcinoma may be significantly greater than that measured grossly. Some pathologists have used lack of immunohistochemical staining for E-cadherin to distinguish invasive lobular carcinoma from invasive duct carcinoma. While it appears to be a reasonably accurate test, it is for the most part unnecessary in practice.

These tumors are characterized microscopically by small cells that insidiously infiltrate the mammary stroma and adipose tissue individually and in a single file pattern, often growing in a target-like configuration around normal breast ducts, frequently inducing only minimal fibrous reaction (picture 7). Associated lobular carcinoma in situ (LCIS) is present in approximately two-thirds of cases; however, ductal carcinoma in situ (DCIS) may also accompany invasive lobular carcinoma.

In addition to their different histologic appearance and mammographic characteristics, there are distinct prognostic and biologic differences between infiltrating lobular and ductal cancers:

- Infiltrating lobular carcinomas have a higher frequency of bilaterality and multicentricity than infiltrating ductal carcinomas [34,35]. Nevertheless, a number of studies have shown that intraductal and infiltrating lobular carcinomas are fairly equivalent in terms of outcomes with breast conserving therapy, according to stage [36-38].

- Infiltrating lobular carcinomas arise in older women and are larger and better differentiated tumors [34,39]. As a rule, invasive lobular carcinomas are estrogen receptor (ER)-positive, with variant lesions showing occasional variable expression.

- While older series report a similar prognosis for infiltrating lobular cancers and invasive ductal lesions, subsequent reports suggest that outcomes (at least in the short-term) may be more favorable for lobular cancers and improving over time [40,41]. However, variants of infiltrating lobular carcinoma exist, some of which have a poorer prognosis [34].

- As a group, invasive lobular carcinomas tend to metastasize later than invasive duct carcinomas and spread to unusual locations such as the peritoneum, meninges, and gastrointestinal tract [42].

There is an association between mutations in the cadherin (*CDH1*) gene and invasive lobular breast cancers. Lobular breast cancers have been observed to occur in 20 to 54 percent of women from families with hereditary diffuse gastric cancer who carry germline mutations in the *CDH1* gene. However, germline *CDH1* mutations can also be cosegregated with invasive lobular breast cancer in the absence of diffuse gastric cancer, suggesting that gastric cancer is not an obligatory hallmark of families with *CDH1* mutations. (See "Hereditary diffuse gastric cancer".)

One study reported that pathogenic variants in *ATM*, *BRCA2*, *CHEK2*, and *PALB2* (in addition to *CDH1*) are also associated with an increased risk of ILC, whereas *BRCA1* pathogenic variants are not [43]. Furthermore, more than half contain alterations in one of three key genes of the phosphatidylinositol 3-kinase pathway, *PIK3CA*, *PTEN*, and *AKT1* [44], and approximately 50 percent of sporadic lobular breast cancers contain E-cadherin mutations [45,46]. (See "Overview of hereditary breast and ovarian cancer syndromes".)

OTHER HISTOLOGIC TYPES

A number of other histologic types account for the remaining invasive breast cancers. These include tubular carcinoma, mucinous carcinoma, medullary carcinoma, invasive micropapillary

carcinoma, metaplastic carcinoma, adenoid cystic carcinoma, secretory carcinoma, and others. Tumors of other histologies arising in the breast (lymphomas, sarcomas, phyllodes tumors) are discussed elsewhere. (See "Breast sarcoma: Epidemiology, risk factors, clinical presentation, diagnosis, and staging" and "Overview of the pathobiology of the non-Hodgkin lymphomas", section on 'Introduction'.)

Special clinical presentations of breast carcinomas, including Paget disease and inflammatory carcinoma, are discussed elsewhere. (See "Paget disease of the breast (PDB)" and "Inflammatory breast cancer: Pathology and molecular pathogenesis".)

Tubular carcinoma — Tubular carcinomas were relatively infrequent in the pre-mammography era, accounting for 2 percent or less of invasive breast cancers. However, in some series of mammographically screened populations the incidence is higher, accounting for 10 to 20 percent of invasive cancers.

Tubular carcinoma is characterized by the presence of well-formed tubular or glandular structures infiltrating the stroma (picture 8).

- The tubules tend to be elongated, and many have pointed ends
- The cells composing the tubules are cuboidal to columnar and often have apical cytoplasmic protrusions or "snouts"
- The tumor cells are cytologically low grade
- Associated ductal carcinoma in situ (DCIS), typically of the low-grade type, is present in about three-quarters of the cases

These lesions have a relatively favorable prognosis compared with infiltrating ductal carcinomas; the natural history is favorable, and metastases are rare [1,40,47-49].

Mucinous (colloid) carcinoma — Mucinous carcinomas account for between 1 and 2 percent of invasive breast cancers and appear to be more common in older patients. These lesions usually have a soft gelatinous appearance on gross examination, and they tend to be well circumscribed. Mucinous carcinomas are characterized microscopically by nests of tumor cells dispersed in large pools of extracellular mucus; the cells tend to have uniform, low-grade nuclei (picture 9). Similar to tubular carcinomas, these lesions also represent a prognostically favorable variant of invasive breast carcinoma [1,40,48,50].

Medullary carcinoma — Medullary carcinomas account for anywhere from 1 to 10 percent of invasive breast cancers. However, there is considerable interobserver variability in the diagnosis

of this type of breast cancer which is, at least in part, dependent upon the classification system employed [51-53].

Medullary carcinomas are well circumscribed on macroscopic examination and are often soft and tan-brown with areas of hemorrhage or necrosis. Circumscription of the lesion is also evident microscopically. The tumor cells are poorly differentiated (high-grade), grow in a syncytial pattern, and have an intense associated lymphoplasmacytic infiltrate (picture 10), and this tumor is actually quite rare when strict diagnostic criteria are followed.

Medullary and medullary-like carcinomas occur more frequently in younger patients than other types of breast cancer. They are also more frequent in women who inherit mutations of the breast cancer susceptibility 1 (*BRCA1*) gene (10 percent of breast cancers are medullary in this population, as compared with <1 percent of non-*BRCA1*-related breast cancers). However, the majority of breast cancers in patients with *BRCA1* gene mutations (90 percent) are not medullary [54].

The prognosis for pure medullary carcinomas appears to be somewhat more favorable than that of infiltrating ductal carcinomas, despite their aggressive histologic appearance [1,40,48,55,56]. For example, in a retrospective review of 12,409 patients with breast cancer, patients with medullary cancer (n = 127) had a significantly higher overall 14-year disease-free survival rate compared with patients with invasive ductal cancer (n = 8096) (76 versus 64 percent; hazard ratio [HR] 0.52, p = 0.0005) [56]. In addition, patients with medullary cancer also had a significantly higher overall survival rate (66 versus 57 percent; HR 0.75, p = 0.03).

Tubulolobular carcinoma — Tubulolobular carcinoma is an often unrecognized breast cancer variant that, as the name implies, has hybrid histologic characteristics of tubular and invasive lobular carcinoma with the same cells comprising well-formed glands contiguous with single-file infiltration of stroma. While immunohistochemical studies imply a ductal phenotype [57], from a radiologic and clinical point of view, the tumor is more akin to invasive lobular carcinoma in that its imaging characteristics are identical to lobular breast cancer, and there is the same tendency to multifocality and multicentricity. In terms of staging, however, the tumors behave more like invasive moderately differentiated ductal carcinoma in that they have the same likelihood of nodal metastases when matched by size. Often these tumors are misclassified as invasive carcinoma with mixed ductal and lobular features.

Micropapillary carcinoma — Invasive micropapillary carcinoma is a particularly aggressive form of cancer that has a proclivity for lymph node metastasis even when small in size [58].

Metaplastic carcinoma — Metaplastic carcinoma is a well circumscribed tumor that consists of various combinations of poorly differentiated ductal adenocarcinoma, mesenchymal

(sarcomatous), and other epithelial (eg, squamous cell) components [59,60].

Whether these tumors have a worse prognosis than ordinary invasive ductal cancers is unclear. Some studies suggest that tumors in which the squamous cell component predominates (more than 90 percent of the malignant cells are of squamous type) are more aggressive and frequently treatment-refractory when compared with other infiltrating ductal cancers [61,62]. However, because metaplastic breast cancer was not officially recognized as a distinct pathologic diagnosis until 2000, knowledge about treatment patterns and outcomes is limited.

The characteristics of 892 metaplastic breast cancers reported to the National Cancer Database between 2001 and 2003 were compared with those of 255,164 typical infiltrating ductal carcinomas [60]. In contrast to patients with infiltrating ductal cancers, the following significant differences were noted in the group with metaplastic tumors:

- Fewer T1 tumors (30 versus 65 percent)
- More node-negative tumors (78 versus 66 percent)
- More poorly differentiated or undifferentiated tumors (68 versus 39 percent)
- Fewer estrogen receptor-positive tumors (11 versus 74 percent)

Treatment outcomes were not reported. Despite the perception of a worse prognosis, all metaplastic breast cancers are treated similarly to other invasive breast cancers [63-65].

Adenoid cystic carcinoma — The rare adenoid cystic carcinoma of the breast has a distinctive histologic pattern that is morphologically identical to adenoid cystic carcinoma found in the salivary glands (and other sites) (see "Salivary gland tumors: Epidemiology, diagnosis, evaluation, and staging"). This tumor tends to be associated with a favorable prognosis, even when tumor size is large; the reported incidence of axillary metastases in most series is less than 5 percent [66,67].

Histologic grading based upon the percentage of solid areas (as is used for salivary gland tumors) has been suggested as being prognostically useful [68], although others disagree [67]. At least two series in which outcomes were not as favorable as in most reports were predominated by patients with higher-grade tumors (ie, the solid variant) [69,70].

Secretory carcinoma — Secretory carcinoma is an extremely rare tumor, which is also identical to its salivary gland counterpart (mammary-analogue secretory carcinoma). Having first been described in children, it was initially termed juvenile secretory carcinoma [71]; however, most cases have been reported in adults [72,73]. Still, it is the likely diagnosis for a breast carcinoma in the pediatric population, and, interestingly, it has no sex predilection in this age group.

Despite being triple negative (as is adenoid cystic carcinoma above), it is an indolent tumor whose prognosis is excellent [73], as metastasis is extremely rare [74]. The lesion is not only histologically identical to its analog in salivary gland, but it also shares the same molecular alteration-a chromosomal translocation t(12;15)(p13;q25), which results in a gene fusion *ETS* variant 6 and neurotrophin receptor tyrosine kinase 3 (*ETV6-NTRK3*) [75,76]. This molecular change is of interest due to the development and approval of tropomyosin receptor kinase (TRK) inhibitors, which, to date, have been largely utilized in nonmammary tumors [77]. (See "TRK fusion-positive cancers and TRK inhibitor therapy".)

Apocrine carcinoma — Apocrine carcinoma is an uncommon variant composed of cells that contain large amounts of eosinophilic granular cytoplasm with large, often pleomorphic nuclei that contain prominent large nucleoli. Apocrine carcinomas have a rather distinct immunohistochemical pattern in that they are negative for both estrogen and progesterone receptor proteins, that approximately 50 percent of cases are positive for HER2/neu overexpression, and that the majority are positive for epidermal growth factor receptor (EGFR) and androgen receptor protein, the latter raising the possible utility of antiandrogen therapy [78-80].

SUMMARY

- **Definition** – Ductal carcinoma in situ (DCIS) is characterized by a proliferation of abnormal cells confined within the mammary ductal system. (See 'Ductal carcinoma in situ' above.)
  - DCIS is commonly classified according to architectural and cytologic features and cell necrosis as low and intermediate grade (papillary, cribriform, and solid) and high grade (comedo).
  - DCIS represents a precursor to invasive breast cancer.
- **Histologic types** – The invasive breast carcinomas consist of several histologic subtypes.
  - Infiltrating ductal carcinoma is the most common type of invasive breast cancer, accounting for 70 to 80 percent of invasive cancers. (See 'Infiltrating ductal carcinoma' above.)
  - Infiltrating lobular carcinoma is the second most common invasive breast cancer, accounting for 5 to 10 percent of invasive cancers. (See 'Infiltrating lobular carcinoma' above.)

- As compared with infiltrating ductal carcinomas, infiltrating lobular carcinomas tend to be multicentric and/or bilateral, more differentiated, hormone receptor-positive, arise in older women, metastasize later, and spread to unusual locations, such as the meninges, peritoneum, or gastrointestinal tract. (See 'Infiltrating lobular carcinoma' above.)

- Other less common invasive breast carcinoma histologies include tubular, mucinous, and medullary carcinomas. (See 'Other histologic types' above.)

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Topic 783 Version 22.0

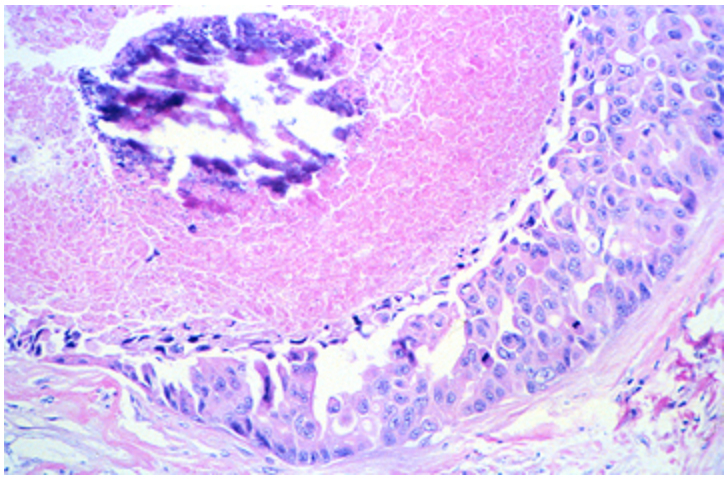
GRAPHICS

Comparative features of ductal carcinoma in situ (DCIS) and lobular carcinoma in situ (LCIS)

	DCIS	LCIS
Presentation	Incidental finding, mammographic abnormality, occasionally palpable, unifocal	Incidental finding, often multifocal
Predominant location	Ducts	Lobules
Cell size	Medium or large	Small
Pattern	Comedo, cribriform, micropapillary, papillary, solid	Solid
Calcifications	Yes or no	Usually no
Risk of subsequent invasive cancer	Higher	Lower
Location of subsequent invasive cancer	Ipsilateral	Ipsilateral or contraleteral

Graphic 72750 Version 1.0

Comedo ductal carcinoma in situ

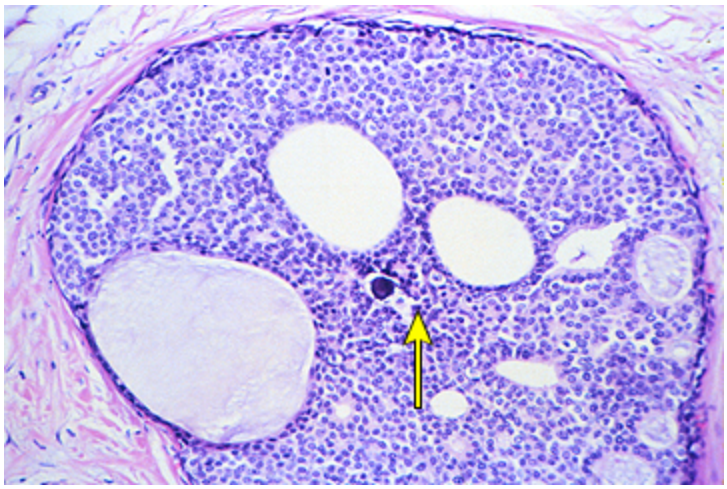


Light microscopic specimen of comedo ductal carcinoma in situ shows a large central area of necrosis that is focally calcified. The nuclei are poorly differentiated (high grade).

Courtesy of Stuart Schnitt, MD.

Graphic 77048 Version 2.0

Cribriform ductal carcinoma in situ

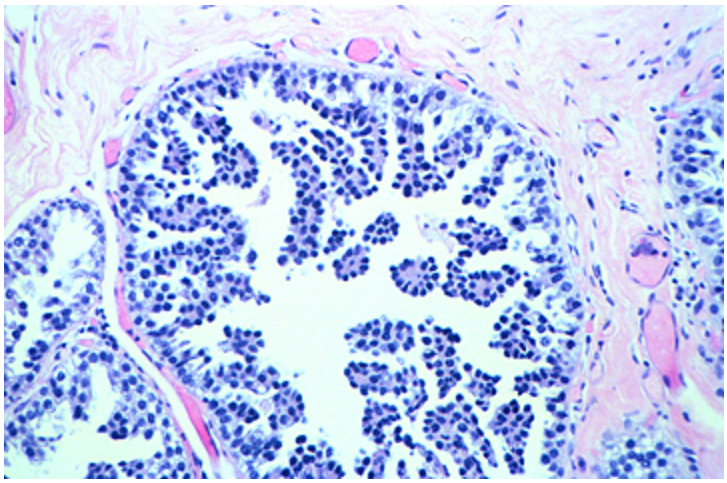


Light micrograph of a lesion from the breast of a woman with cribriform ductal carcinoma in situ shows a back to back glandular growth pattern. The nuclei are well differentiated (low grade). A small calcification is noted near the center of the involved space (arrow).

Courtesy of Stuart Schnitt, MD.

Graphic 71553 Version 3.0

Micropapillary ductal carcinoma in situ



Light micrograph of a specimen from the breast of a women with micropapillary ductal carcinoma in situ . The tumor cells form tufts which project into the lumen of the involved space. The nuclei are well differentiated (low grade).

Courtesy of Stuart Schnitt, MD.

Graphic 58302 Version 2.0

Proposed classification systems for ductal carcinoma in situ

Lagios*	Van Nuys•	EuropeanΔ
Low grade	Non-high grade without necrosis	Well differentiated
Intermediate grade	Non-high grade with necrosis	Intermediately differentiated
High grade	High grade	Poorly differentiated

** Adapted from Lagios MD, Margolin FR, Westdahl PR, Rose MR. Cancer 1989; 63:618.*

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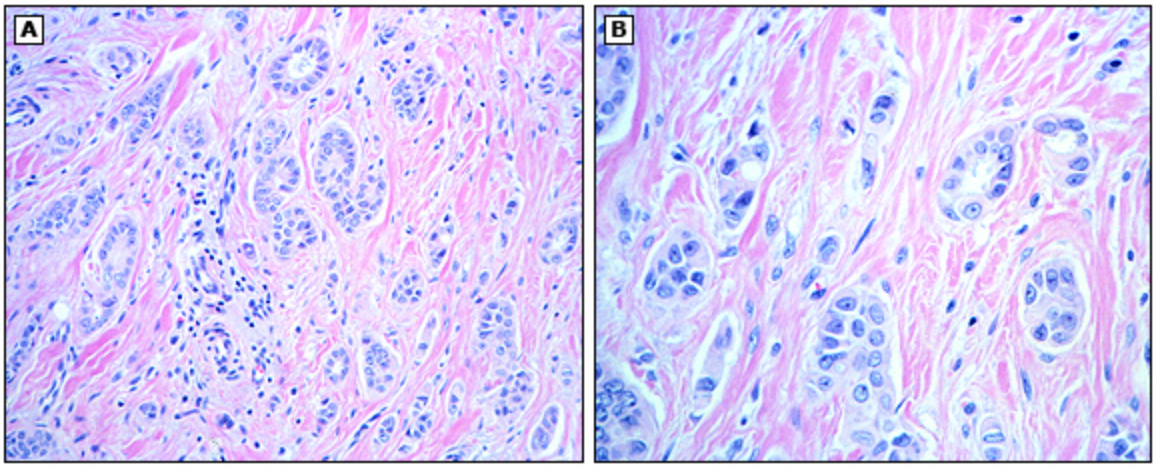
Grade I infiltrating ductal carcinoma of the breast



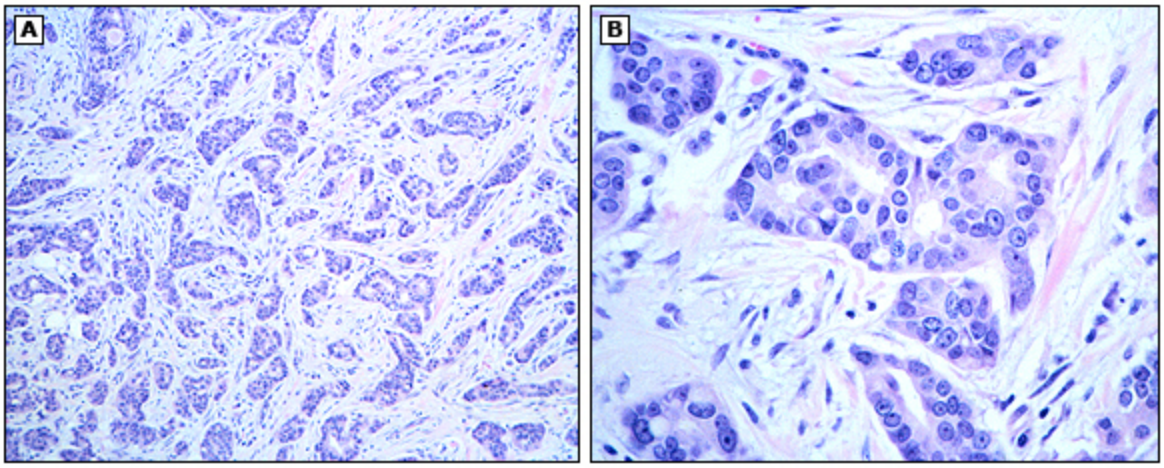
(Panel A) Low-power view of a well-differentiated infiltrating ductal carcinoma shows tumor cells that infiltrate the stroma as solid nests and glands.

(Panel B) High-power view demonstrates relatively uniform nuclei with no evidence of mitotic activity.

Courtesy of Stuart Schnitt, MD.

Graphic 76328 Version 5.0

Grade II infiltrating carcinoma of the breast



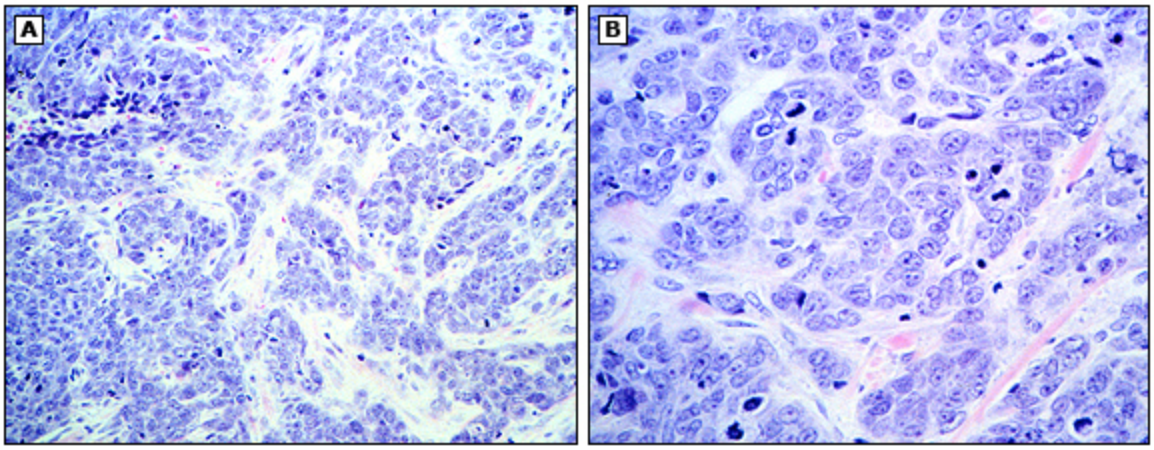
(Panel A) Low power view of a moderately differentiated breast carcinoma shows tumor cells infiltrating as solid nests with some glandular differentiation.

(Panel B) High power view demonstrates some nuclear pleomorphism in the tumor cells.

Courtesy of Stuart Schnitt, MD.

Graphic 55284 Version 3.0

Grade III infiltrating ductal carcinoma of the breast



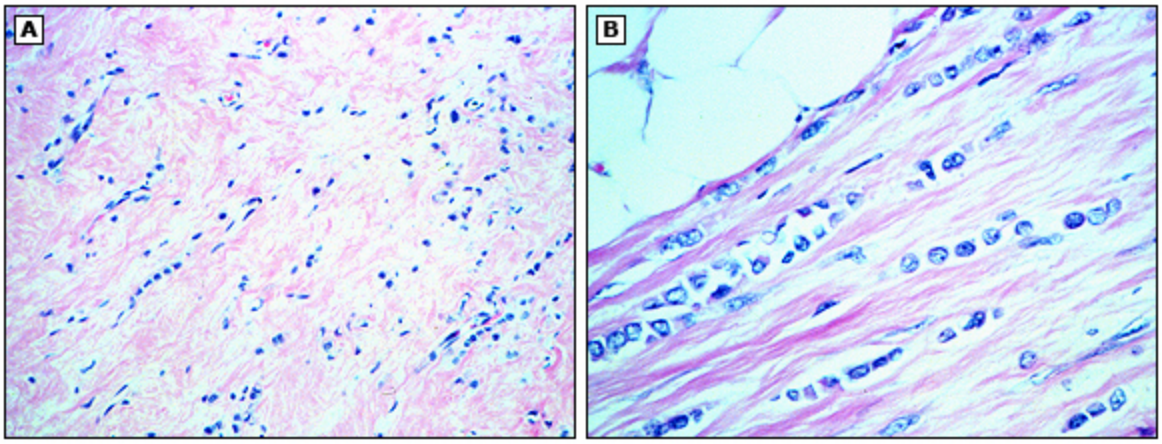
(Panel A) Low-power view of a poorly differentiated breast carcinoma shows that the tumor is composed of solid nests of neoplastic cells without evidence of gland formation.

(Panel B) The high-power view demonstrates marked nuclear atypia in the tumor cells with considerable mitotic activity.

Courtesy of Stuart Schnitt, MD.

Graphic 67082 Version 5.0

Infiltrating lobular carcinoma of the breast



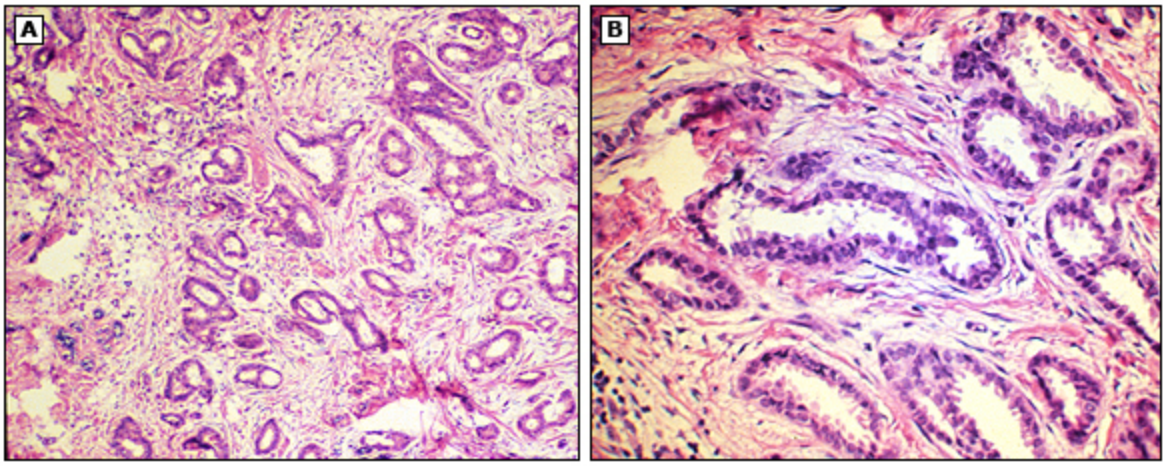
(Panel A) Low-power view of an infiltrating lobular breast carcinoma shows small tumor cells that infiltrate the stroma singly and in a single-file pattern.

(Panel B) High-power view demonstrates that the tumor cells are relatively small and uniform in appearance.

Courtesy of Stuart Schnitt, MD.

Graphic 54150 Version 4.0

Tubular carcinoma of the breast



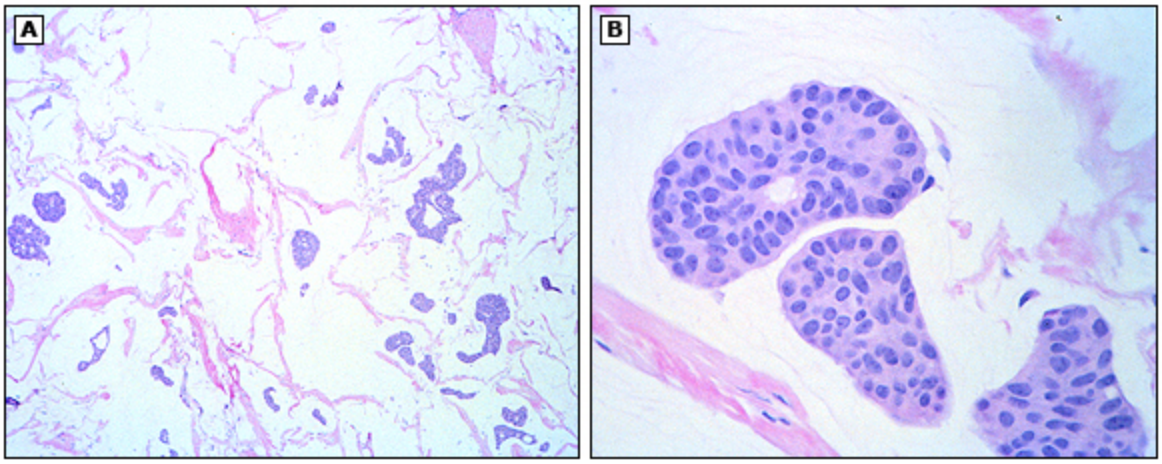
(Panel A) Low-power view of a tubular breast carcinoma shows that the tumor is composed of well-formed glands or tubules that invade the mammary stroma.

(Panel B) High-power view demonstrates that the tubules are composed of columnar cells with relatively uniform nuclei. Many of the cells show "snouts" of eosinophilic cytoplasm at their lumenal ends.

Courtesy of Stuart Schnitt, MD.

Graphic 50273 Version 4.0

Mucinous carcinoma of the breast



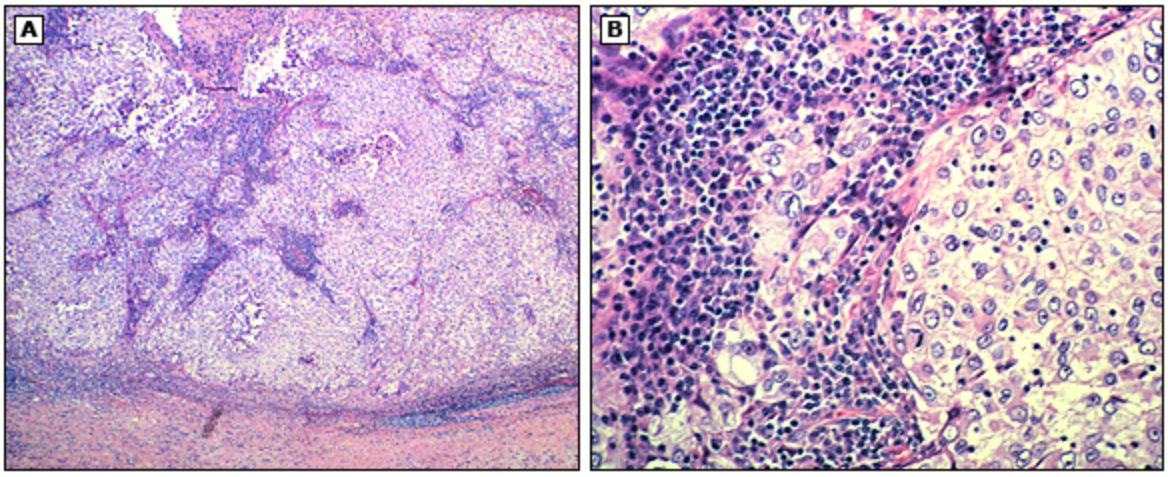
(Panel A) Low power view of a mucinous breast carcinomashows small nests of tumor cells dispersed in large pools of extracellular mucous.

(Panel B) High power view demonstrates that the nests are composed of cells with relatively uniform, low grade nuclei.

Courtesy of Stuart Schnitt, MD.

Graphic 79319 Version 3.0

Medullary carcinoma of the breast



(Panel A) Low power view of a medullary breast carcinoma shows that the tumor has a well circumscribed border.

(Panel B) High power view demonstrates that the tumor cells grow in a syncytial pattern and have marked nuclear atypia. A prominent lymphoplasmacytic infiltrate is also present.

Courtesy of Stuart Schnitt, MD.

Graphic 59804 Version 3.0

Contributor Disclosures

Ira J Bleiweiss, MD No relevant financial relationship(s) with ineligible companies to disclose. **Anees B Chagpar, MD, MSc, MA, MPH, MBA, FACS, FRCS(C)** Consultant/Advisory Boards: Guardant Health [Breast cancer]; Merck [Breast cancer]; Novartis [Breast cancer]; Protean BioDiagnostics [Breast cancer]; Sanofi-Aventis [Breast cancer]. Speaker's Bureau: Merck [Breast cancer]. All of the relevant financial relationships listed have been mitigated. **Sadhna R Vora, MD** No relevant financial relationship(s) with ineligible companies to disclose.

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