

Breast Cancer Classification

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Contents:

Classification of Breast Cancer :

- Non-invasive vs Invasive
- Breast Cancer subtypes
- Locally advanced breast cancer
- Disease progression

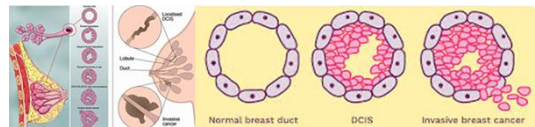
cTNM	Neo-adjv	Sentinel Node	BCT	Mastectomy
DCIS	No	When possible invasive component > 4cm < 55 years Solid component on mammogram DCIS grade II and III	Excision possible with good cosmetic result Multifocal lesion Multifocal within 5 cm DCIS < 4 cm	Good cosmetic result not possible Multicentric DCIS > 4 cm
Localized Cancer Tumor < 5 cm and < 4 axil nodes	Sometimes to make a BCT possible in large tumors	Always unless US-guided fine needle aspiration is positive	Excision possible with good cosmetic result Multifocal lesion Multifocal within 5 cm Invasive Ca < 5 cm	Good cosmetic result not possible with BCT Multicentric Invasive Ca > 5 cm
Loco- regionally Advanced Tumor > 5 cm or > 4 axil nodes	Yes to make surgery possible	No unreliable	Usually mastectomy is performed Sometimes BCT is possible.	

- Breast cancer is a heterogenous disease. Multiple different entities exist (defined by subtype and grade) which display a spectrum of histological and biological features.
- Subtype specific management strategies are thus devised appropriate to patient lifestyle and wishes, genetic profile, comorbidities.
- Multimodality sequential therapy with different elements comprising combinations of surgery, systemic chemotherapy, immunotherapy, loco-regional radiotherapy and endocrine therapy. We advise patients to complete the full treatment journey accessing all advised therapy modalities.

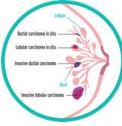
Non-invasive vs Invasive

Definition of Ductal Carcinoma in Situ (DCIS):

- Proliferation of abnormal cells (cancerous cells) but confined within the breast ductal system. Can spread along ducts incl skip lesions.
- Undergoes series of molecular changes to become invasive.
- Risk of and time to progression depends on various genetic and molecular factors as well as subtype differentiation.



Definition and incidence (of DCIS):

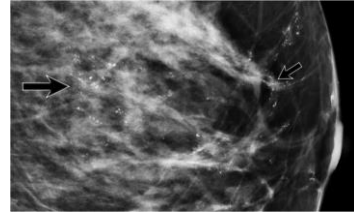


- Proliferation of abnormal cells confined within the mammary ductal system
- Heterogenous group of lesions with different malignant potential
- Pre-invasive

- **Non-obligate precursor of Invasive Ductal Carcinoma**
- **If untreated, 10 – 28% leads to invasive disease**

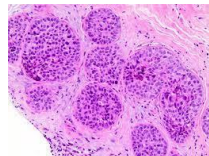
- Screening leads to earlier detection – incidental finding
- DCIS accounts for 20 – 25% of newly Dx'd breast ca

MMG image showing microcalcifications



Precursor lesions (non-invasive):

- DCIS
- 5 subtypes based on histo growth pattern:
1. Comedo
 2. Cribriform
 3. Micropapillary
 4. Papillary
 5. Solid



Classified into 3 grades: LG, IG, HG

- *Classic LCIS* – behaves like DCIS.
- (Note that LCIS is not considered pre-invasive, rather is assoc with a higher risk of breast cancer in either breast.)

In situ breast carcinoma pathology report

- Nuclear grade
- high grade
 - intermediate grade
 - low grade
- Lesion size
- Pathological type/architecture
- comedo, solid, cribriform, micropapillary
- Margin status
- margins involved with tumour, or
 - margins clear of tumour cells (measure clearance in mm)
- Associated microcalcification
- present or not
- Presence of necrosis
- present or not (presence is a poor prognostic feature)
- Hormone receptors
- can be tested (not routinely recommended)
 - the role of hormonal agents such as tamoxifen remains unclear in this setting

Treatment strategies in DCIS:

- Aim of treatment:
 1. Prevent progression to invasive ca
 2. Prevent invasive recurrences that are assoc with increased risk of breast ca mortality (about 1/2 recurrences are invasive)
 - Surgery: BCT
 - RT (shared decision making)
 - ET
- (RT decreases local recurrence risk by 50% after BCS.
Has no impact on overall survival.)

Prognostics: Rates of Local Recurrence

- 1. **BCS + Whole Breast RT**: 9 - 20%
- 2. **BCS alone**: 23 - 35%
- 3. **Mastectomy +/- SLNB +/- recon**: 1 - 2%
- About 1/2 recurrences are invasive cancers
- Individualized treatment decisions: predict who will benefit from RT after BCS based on individual risk profile i.e. tumour genetics
- Traditional clinicopathological features assoc with local recurrence
- Van Nuys Prognostic Index (not validated): Young age, tumour size, tumour grade, margin width, comedonecrosis
- **DCISionRT** – Biosignature that evaluates recurrence risk
- High risk situations (necrosis, close margin <2mm, larger size >1cm)
- RT standard of care for most post BCS. Consider omission if advanced age, extensive comorbidities, small focus of LG disease.
- ET: 75% of DCIS expresses ER / PR.

Young women with DCIS:

- Incidence DCIS in young women (20 – 39yr) increased 4-fold from 1975 to 2015
- Young age (<40/<50 yrs) = poor prognostic factor
- Higher 10-yr breast tumour recurrence risk for women Dxd <40 (11.2 – 31%) vs 3 – 9% for those Dxd >40
- Young age assoc with higher breast ca mortality rate

Benign proliferative breast lesions

Benign proliferative breast lesions with atypia:

- ADH – Atypical Ductal Hyperplasia
- ALH – Atypical Lobular Hyperplasia
- LCIS – Lobular Carcinoma In Situ

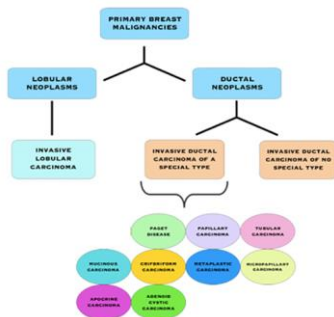
Classified as high risk lesions due to association with increased risk for breast cancer. Cancer may develop in either breast and not necessarily at the site of the atypia.

Lobular Carcinoma in Situ - LCIS

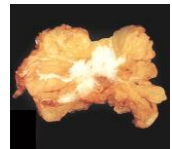
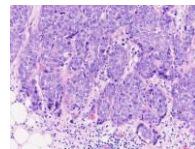
- Increased risk of future breast carcinoma in either breast (either IDC or ILC)
- ~ 12 % increased risk
- Assoc with diagnostic difficulty: extent of lesion may be underestimated on core biopsy. Excision biopsy may yield invasive ca (either IDC or ILC).
- Lesions confirmed as LCIS on excision biopsy require close surveillance of both breasts for future invasive carcinoma.

Invasive carcinoma – histo subtypes

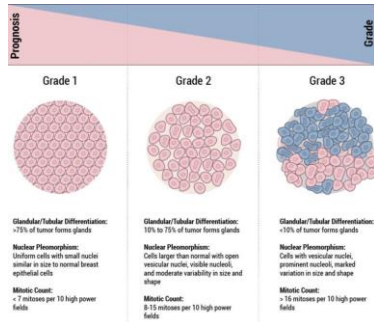
- Arise from epithelial elements - Inner lining epithelium of the ducts or lobules.
 - Malignant cells invade stroma.
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- Invasive ductal carcinoma of no special type (70 - 80%). IDC NST
 - Invasive lobular carcinoma (5 – 10%). ILC
 - Mucinous (colloid), Tubular, Medullary, Papillary, Metaplastic, Invasive micropapillary
 - Tumours of other histologies: lymphomas, sarcomas, phyllodes.



Invasive
Ductal Ca
- IDC NST

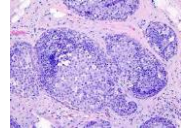


- Irregular, stellate infiltrating growth pattern.
- Microscopically, cords and nests of tumour cells are seen invading surrounding tissue. Eventually presents as a palpable mass, radiologic density.
- Gr 1, 2, 3 dependant on the degree of differentiation and mitotic activity. (Tubule formation, nuclear pleomorphism, mitotic count.)
- There may be an associated DCIS component.



Invasive Lobular Carcinoma - ILC

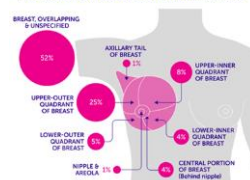
- Often no mass lesion evident
- May be microscopically of greater extent than expected clinically / on imaging.
- Shows lack of E-cadherin staining.
- Associated LCIS present in 2/3 of cases.
- Higher frequency of bilaterality and multicentricity
- Arise in older women
- Often ER +
- Metastasizes later
- Association with CDH1 gene mutations also seen with hereditary diffuse gastric cancer.



Diagnosis and management of invasive breast cancer

- Triple assessment: clinical examination, breast imaging, biopsy.
- Staging for presence of metastases.
- Shared decision making in MDT. Consider subtype (IHC), grade, size of tumour, LN involvement.
- Consider Genetics.
- Multimodal sequential therapy: (NACT), surgery, (Adj chemo), RT, ET.
- Management of the breast – WLE + RT, Mastectomy
- Management of the axilla – SLNB / ALND – prognostication and local control.
- Ongoing surveillance.

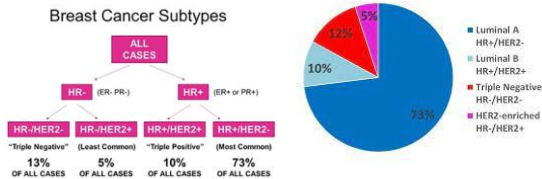
INVASIVE BREAST CANCER CASES: PERCENTAGE DISTRIBUTION BY ANATOMICAL SITE



The invasive breast carcinoma pathology report

Tumour size • Important prognostic factor Histological type • Invasive ductal carcinoma accounts for 80% of breast cancers • Invasive lobular carcinoma accounts for 10-15% of breast cancers • "Special" types: tubular, cribriform, and mucinous carcinomas (particularly good prognosis tumours¹) Biological grade • Papillary, medullary and other uncommon histological types Important prognostic factor • grade 1-3 based on the combination of three pathological features: nuclear grade, tubule formation, and mitotic rate Accompanying DCIS • associated with local recurrence if "extensive" in patients treated for invasive carcinoma by breast-conservative surgery with close or positive margins^{2,3} Lymph node involvement • Important prognostic factor: the number of nodes dissected and the number involved with metastatic carcinoma Margins of resection • involvement of resection margins with invasive carcinoma or DCIS and margin distance from cancer cells • Base factors guide further treatment such as additional surgery or radiotherapy • may also predict risk, local recurrence Lymphovascular invasion (LVI) • evidence of tumour cells invading into vessels • Presence of LVI is a poor prognostic factor Changes in adjacent breast tissue • e.g. DCIS, ADH, ACH, LCIS Hormone and other receptors • predict response to adjuvant treatment • ER (estrogen) and PR (progesterone) receptors • HER2 receptor overexpression is a marker of poor prognosis and also of response of the carcinoma to therapeutic therapy. HER2 positive tumours may respond better to anti-HER2 type chemotherapy and are generally less responsive to endocrine therapy
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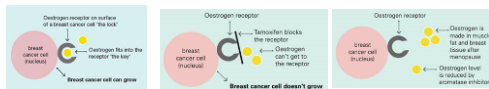
Breast Cancer Subtypes



Breast Cancer Intrinsic Subtypes

Subtype	Molecular markers	Appropriate Systemic Treatment
Luminal A	ER + PR + Her 2 - Ki67 <20%	Endocrine Therapy (consider chemotherapy if high tumour burden)
Luminal B	ER + Her 2 - PR +/low Ki67 >20%	Use tumour-profiling predictive test to determine benefit of chemo eg Oncotype DX, Mammprint. +/ Chemotherapy Endocrine therapy
Luminal B	ER + Her 2 + (Triple +)	Chemotherapy Anti-Her 2 therapy Endocrine Therapy
Her 2 +	ER - PR - Her 2 +	Chemotherapy Anti-Her 2 therapy
Triple -	ER - PR - Her 2 -	Chemotherapy

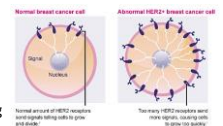
Significance of Immunohistochemistry (IHC)



- ER, PR and Her 2 status determines subtype, informs prognosis and directs management options.
- ER positivity is a predictor for response to Endocrine therapy (Tamoxifen – Selective Estrogen Receptor Modulator / Anastrozole - Aromatase Inhibitor).

Significance of IHC

- HER2 protein in the cancer cells – Human Epidermal Growth Factor Receptor 2.
- Transmembrane protein essential in controlling epithelial cell growth and differentiation.
- Poor prognostic indicator - associated with increased disease recurrence and is a poor prognostic factor for survival.
- Assoc with increased proliferation rates, high histologic and nuclear grade, low ER and PR levels, tendency to metastasize to CNS, relative resistance to endocrine therapy, and increased sensitivity to chemotherapy.
- Expect response to targeted anti-Her 2 therapy – Herceptin (Trastuzumab)-based.



Locally-Advanced Breast Cancer

• Definition:

Stage III disease: T3N1, T4 any N, any T N2, any T N3.

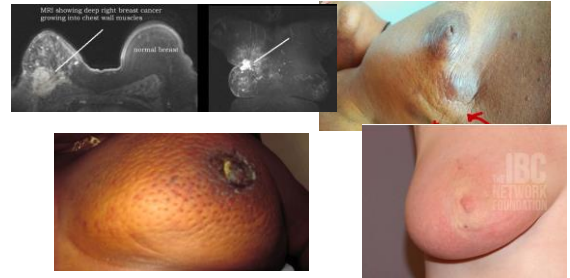
T3: tumours >5cm

T4: tumours with infiltration into the skin / chest wall / inflammatory breast cancer.

cN2 disease: fixed / matted axillary nodes. pN2 4-9 LN

cN3 disease: Ipsilat infraclav / supraclav / int mammary and axillary nodes. pN3 >- 10 LN

What does locally advanced breast cancer look like?



Locally advanced breast cancer



Disease Progression

- Recurrent Breast Cancer
- Metastatic Cancer

What it looks like:

- Local recurrence after breast conservation or mastectomy.
- Incidence post WLE: 6 - 9 %. Majority occur at original lumpectomy site or closely related.
- Post Mx: 1 - 3% chest wall / nodal recurrence 10 yrs out.
- 1/3 will have synchronous distant disease.
- Chest wall recurrence: significant morbidity with potential ulceration, bleeding, pain.
- Regional recurrence to LN basins.

Recurrent Breast Cancer

- Management of local recurrence may entail:
- Local excision vs completion Mx.
- Decision making considers: size of recurrence, location, single vs multicentric, prior RT, pt age and comorbidities, presence of metastatic disease, tumour subtype & prognostic markers, pt preference.
- Wound healing depends on previous RT, pt comorbidities, extent of local recurrence.
- Obtain tissue diagnosis, stage the patient with approp whole body imaging incl imaging of the regional LN basin.

Systemic metastatic disease.

- Always restage in presence of local recurrence.
- Obtain tissue diagnosis.
- Systemic disease may present with LOW, bone pain, night sweats, a cough. Often silently – detected on staging scans.
- Treatment should be approached wholistically, a multi-disciplinary team approach.
- Goals of care clearly discussed with patient and family.
- Multiple systemic agents are available and chosen dependant on the immunohistochemistry and patient's general health. These may include cytotoxic chemotherapy, Endocrine therapy, Immunotherapy, Biologic agents.
- 5 – year survival of metastatic breast cancer patients: 22%.

Conclusion

- Pt symptoms, medical comorbs, performance status, previous exposure to chemotherapy, menopausal status and disease location are considered.
- Location of metastases influence Mx and Px:
- Mets in chest wall, bone, lymph nodes – expect prolonged progression-free survival.
- Hepatic / lymphangitic pulmonary disease – shorter progression-free survival and overall survival.

We discussed:

- Non-invasive vs Invasive
- Breast Cancer subtypes
- Locally advanced breast cancer
- Disease progression
- The diagnostic and management process is a multidisciplinary and collaborative endeavour.
- Breast cancer management represents a rapidly developing field with great strides made in understanding the disease and prognostic indicators as well as in the surgical and systemic management options available.
- Should always include thorough patient education and support.

Are you at high risk of breast cancer?

Do you have any of the following:

- More than 2 family members with breast or ovarian cancer?
- A family member who has had breast cancer before they were 40 years old?
- A male relative who has had breast cancer?

Contact your GP for a referral to the 'Familial High Risk Breast Cancer Clinic' or email FamilialBreastCNC@health.qld.gov.au for more information



Screen 1.1 updated 03/2024