



Round : ..Major surgery.....

Group no : B8.....

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Breast cancer

INTRO:

It's the most common type of cancer in females, and among the three most important cancers worldwide.

It can be classified according to histology, immuno-histochemistry and molecular characteristics.

☆ We screen for breast cancer because it has all the factors that favours early discovery. It's common, slowly growing, early detection with benefits, the pathogenesis is known and there's a high benefit of screening in comparison to its harmful effects.

RISK FACTORS:

Risk factors can be classified into 3 important categories:

1. Family related: previous history of breast/ovarian cancers, genetic predisposition (BRCA 1 & BRCA 2), familial syndromes, ethnicity..
2. Breast related: female lactation and pregnancy, early menarche or late menopause, previous breast surgeries and implants, chest radiation, breast diseases, dense breasts..
3. Systemic diseases related: thyroid function, liver cirrhosis, alcohol consumption, smoking history, hormonal imbalance (reproductive history/hormonal therapy)

☆ The most important risk factor in females is pre-menopausal cancers in the first degree relatives. History of ovarian cancers are linked to BRCA 1/2 mutations which are autosomal dominant.

☆ In males, the most important risk factor is BRCA2 and klinefelter syndrome.

ASSESSMENT:

First we start by taking a thorough history, and do a physical examination. Then we can start with imaging studies like chest ultrasound, chest MRI or a mammogram. Indications depend on different factors. For example, when we have low suspicion for malignancy, absence of physical and historical findings we can start with an ultrasound.

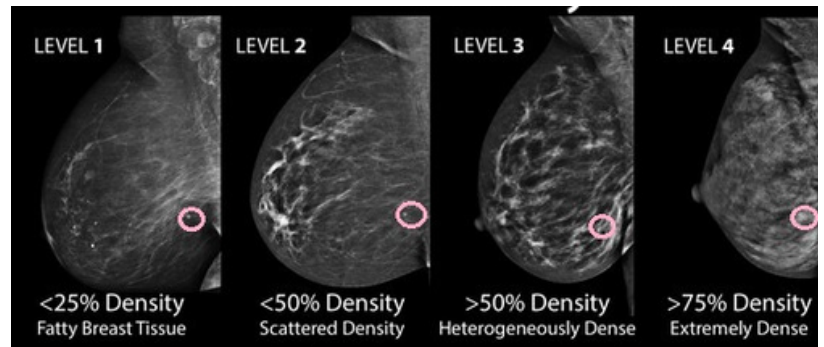
- If the patient is an elderly patient, had positive findings on ultrasound images, is symptomatic or is very likely to have a breast cancer we can choose a more accurate imaging modality according to the age.

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SCREENING:

If the patient is less than 40, mammogram is of a little importance and its accuracy is near 60% so we prefer MRI. If the patient is older than 40, order a mammogram. We can reduce the age to 35 if the patient is symptomatic.

Breast density can be categorised into 4 classes. Mammogram accuracy for class A is near 95%, and for class D it's nearly 42%.



☆ We have two types of mammogram images, screening mammogram images and diagnostic mammogram images. The normal views we use in a regular screening mammogram included two: mediolateral oblique (MLO) and craniocaudal (CC) view.

The difference between a diagnostic or a screening one is that the diagnostic mammogram includes magnification and a focused image with extra planes involving the suspicious area, which is also known as Mag-view/Mag-spot. It is used to distinguish between the presence of a true lesion and an overlap of tissues, as well to better show the borders of an abnormality or questionable area or a little cluster of faint microcalcifications in a dense area. An example of an indication for a diagnostic mammogram include the presence of a pleomorphic (non-ductal) lesion.

BI-RADS:

It stands for “breast imaging-reporting and data system.” It’s a system that radiologists use to describe results from breast imaging tests like ultrasound, mammography and MRI. They also use it to help determine next steps after an imaging test. It ranges between 0 - 6.

According to the score we choose the next step to take. As the following table shows:

	Category	Management	Likelihood of cancer
0	Need additional imaging or prior examinations	Recall for additional imaging and/or await prior examinations	n/a
1	Negative	Routine screening	Essentially 0%
2	Benign	Routine screening	Essentially 0%
3	Probably Benign	Short interval-follow-up (6 month) or continued	>0 % but ≤ 2%
4	Suspicious	Tissue diagnosis	4a. low suspicion for malignancy (>2% to ≤ 10%) 4b. moderate suspicion for malignancy (>10% to ≤ 50%) 4c. high suspicion for malignancy (>50% to <95%)
5	Highly suggestive of malignancy	Tissue diagnosis	≥95%
6	Known biopsy-proven	Surgical excision when clinical appropriate	n/a

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BI-RADS:

According to BI-RADS, we could give B-SCORE to each finding and according to that we decide what we are going to do next.

- **B0**: insufficient tissue.
- **B1**: negative, no findings.
- **B2**: benign, we have finding but they're benign.
- **B3**: high risk lesion (suspicious)
- **B4**: pre-malignant. It needs management of cancer.
- **B5**: malignant, needs management of cancer.

☆ B3 lesions include: Radial scar, Intraductal papilloma, Atypical ductile hyperplasia, and LCIS (high risk of bilateral cancers but its not pre-malignant).

DCIS, pre-malignant lesion.

- Following that, we use this to determine the next step. For B3 lesions, the recommendations point to short-interval follow up, once every 6months. But this could lead to mass upgrading. So it's better if the patient has family history or is symptomatic to take biopsy.

BI-RADS CATEGORIES	
BI-RADS 0 (incomplete):	Recommend additional imaging -- mammogram or targeted ultrasound
BI-RADS 1 (negative):	Routine breast MR screening if cumulative lifetime risk $\geq 20\%$
BI-RADS 2 (benign):	Routine breast MR screening if cumulative lifetime risk $\geq 20\%$
BI-RADS 3 (probably benign):	Short-interval (6-month) follow-up
BI-RADS 4 (suspicious):	Tissue diagnosis
BI-RADS 5 (highly suggestive of malignancy):	Tissue diagnosis
BI-RADS 6 (known biopsy-proven malignancy):	Surgical excision when clinically appropriate

If we have discordance between BI-RADS and the B-score we rely more on imaging modalities as they give wider and full overview unlike FNA which could give false data.

Upgrading could be either:

1. Report (b3 lesions resection and referred to histopathology upgrading it to B4)
2. Mass (B3 lesions followed up for 6months, then on the next imaging the lesion has upgraded to B4 lesions on imaging)

ULTRASOUND:

We visualize the lesion focusing on 4 important features: shapes, echogenesity, orientation, and echostic shadow.

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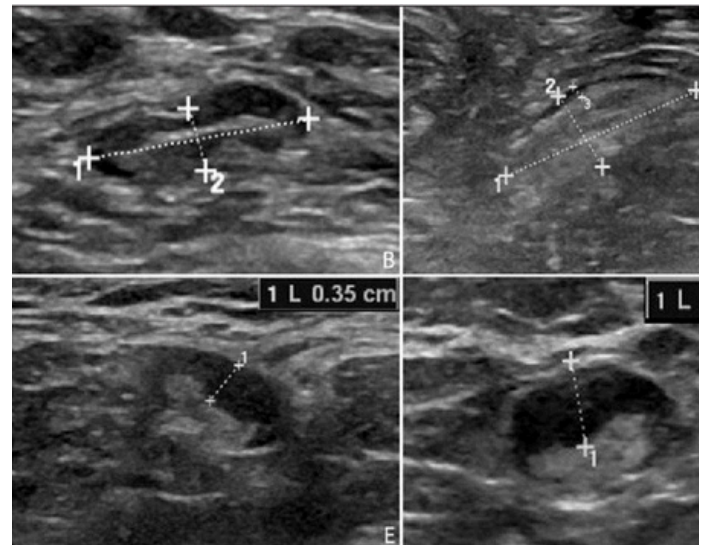
ULTRASOUND:

1. Shape: irregular then it's suspicious.
2. Echogenesity: Anechoic for fluids and air, hypoechoic which is the most suspicious, isoechoic which's also somewhat suspicious and hyperechoic.
3. The presence of echostic shadowing.
4. Orientation: If it was parallel to chest wall, or non- parallel to chest wall which is suspicious.

☆ When assessing parallelism we compare it to the extent of the chest wall, then measure the longest diameter before assessing it.

For lymph nodes on ultrasound:

- if the size is more than 1 cm then it's suspicious.
- if the thickness of the cortex is more than 3 mm then it is suspicious (appears black on ultrasound)
- if the hilum is lost, with thinning then it's suspicious And if the hilum is displaced, then it is the most suspicious.
- Normal cortex appears like eyebrow.



BIOPSY:

We can take a biopsy in two different ways, either through a fine needle aspiration (FNA) or through trucut core biopsy.

A fine needle aspiration (FNA) is when some fluid or cells are removed from a lump through a smaller needle. it could give an idea about the presence of malignant cells or not, but can not tell if the tumor is invasive or in-situ. So we can use FNA to assess whether Axillary lymph nodes are affected or not.

Whereas trucut biopsy can be used to visualize whether the basement membrane has been invaded by the cancer cells or not. So it's more important to stage this cancer.

- ☆ Invasion of the basement membrane is needed for metastasis to occur.
- DCIS does not metastasise to the lymph nodes due to that.

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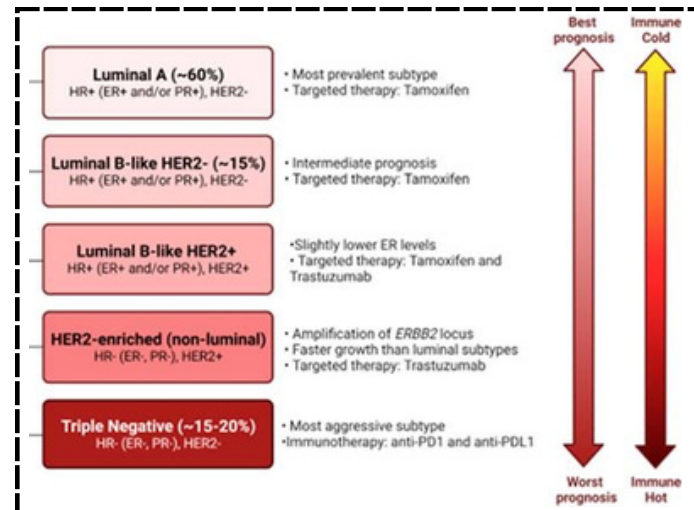
MOLECULAR SUBTYPE:

Molecular subtypes depend on which hormonal receptors are positive/ negative on these tumor cells. Breast cancers can be classified to 4 molecular subtypes, according to Estrogen, progesterone, HER- receptors, or all negative. .

- Luminal A and Luminal B, mostly ER+, slowly growing tumors so it can't be treated with chemotherapy that targets rapidly growing cells. However, it has better prognosis.

☆ complete pathological respond with chemotherapy (5-11%)

- Her-2 enriched and triple negative, complete pathological respond following chemotherapy (70%) so treated first with neu-adjuvant.



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TNM STAGING:

TNM staging contains two division, pathological and clinical.

- clinical: N depends on the staging of the nodes before surgery.
- pathological: N depends on the number of lymph nodes affected after surgical resection. We use it to decide what adjuvant therapy we want to give the patient following surgery.

Easy illustration of clinical staging..

☆ T1 and both NM negative -zero- then stage 1

☆ N1 then stage 2 (mobile NOT fixed) & T3 only WITH N0

☆ N2 then stage 3 (fixed nodes or mammary nodes) & T3 WITH N1,N2,N3 & T4 WITH anything

- ☆ M1 then immediately stage 4 no matter what TN we have.

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TNM STAGING:

- ☆ Regional lymph nodes include: ipsilateral axillary lymph nodes, supraclavicular and infraclavicular lymph nodes.
- ☆ Ipsilateral cervical lymph nodes and contralateral lymph nodes are considered sites for metastases (M1)

Stage 1:

T1N0M0 ; infiltrating tumor, size of 2 cm or less. NO mets or nodes involvement.

Stage 2: A

T1N1M0 ; infiltrating tumor size of 2cm or less, with mobile regional nodes involvement but no mets.

T2N0M0 ; infiltrating tumor size of more than 2 cm and less than 5cm WITHOUT nodes.

Stage 2: B

T2N1M0 ; infiltrating tumor size of more than 2cm and less than 5cm with mobile regional nodes involvement.

T3N1M0 ; infiltrating tumors size of more than 5cm WITHOUT regional nodes involvement.

Stage 3: A

T3N1M0 ; infiltrating tumor size of more than 5cm with mobile regional nodes involvement but no mets.

T (1,2,3)N2M0 ; infiltrating tumor size of any size with FIXED regional nodes but no mets.

Stage 3: B

T4N(0,1)M0 ; infiltrating tumor size of any size but involvement of the chest wall or the skin or inflammatory cancer, or peau d'orange

T(1,2,3)N2M0 ; any size but ipsilateral involvement of internal mammary nodes.

Stage 3: C

T(1,2,3)N3M0 ; infiltrating tumor of any size, with involvement of supra/infra and internal lymph nodes

Stage 4:

T (1,2,3,4) N(1,2,3)M1 ; any tumor size, any regional involvement with distance metastases.

T- Tumour	
T1	Tumour $\leq$ 2 cm
T2	Tumour $\geq$ 2 cm but $\geq$ 5 cm
T3	Tumour $\geq$ 5 cm
T4	Tumour of any size with direct extension to chest wall or skin
N- Lymph node	
N0	No cancer in regional node
N1	Regional movable metastasis
N2	Non-movable regional metastases
N3	Cancer in the internal mammary lymph nodes
M- Metastasis	
M0	No distant metastases
M1	Distant metastases

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TREATMENT:

Treatment plan depends on the clinical stage, the molecular subtype as well as the genetic mutation if possible to identify. If not then rely on the subtype as well as the stage. 5 keys of treatment:

1. Surgery
2. Chemotherapy
3. Radiotherapy
4. Hormonal therapy (tamoxifen for any ER+)
5. Immunotherapy (trastuzumab for any Her-2 +)

SURGERY:

- Breast Surgery; either breast-conserving surgery or mastectomy.
- Nodes dissection; either sentinel nodes or axillary clearance.

Breast-conserving surgery (lumpectomy) focuses on removing the tumor while preserving as much normal breast as possible. It's mainly used when the tumor is unicentric, stage 1 or 2, medium/large sized breasts. In case it's contraindicated we can perform a mastectomy.

These contraindications include: a multicentric lesion, advanced/high grade tumor, positive pathological margins, large tumor/breast ratio, diseased opposite breast, prior radiotherapy, collagen or vascular diseases and pregnancy/lactation.

After mastectomy or breast-conserving surgery we need to pay attention to the female's cosmetic worries. Especially after mastectomy or wide- incision which can result in flat chest and deformity respectively. So we need to pay attention to volume replacement and reshaping. If the female has large breasts we rely on reduction and oncoplasty to symmetrize the opposite breast. If she has a small one, then reconstruction is needed whether with implants or skin flaps when possible.

For lymph nodes dissection, what we do is inject a blue dye and/or technetium-labeled sulfur colloid within the tumor lesion, then we remove these primary draining lymph nodes (sentinel) that are gonna catch the dye, and examine it microscopically. If they're not invaded by cancer (negative), it's called sentinel dissection and no further action is needed. If they're invaded with cancer (positive), then we need to remove axillary lymph nodes in what's known as axillary clearance.

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TREATMENT:

Upon surgical excision, we need to provide a safety margin.

- for DCIS 2mm (microcalcifications)
- for invasive carcinoma 1mm

Indications for radiotherapy include the following:

- After breast-conserving surgery and in patients with DCIS.
- Early stages of cancer (stage 1 and 2)
- T3 or tumor size more than 5cm.
- Lymph nodes positive for cancer.
- In cases of a positive tissue margin after surgically removing the tumor.

Chemotherapy is indicated after radiotherapy in all cases to prevent the recurrence, to get rid of wandering tumor cells and to downsize tumors of higher grades and stages pre-OP.

Hormonal (tamoxifen) targets estrogen receptors so given to E+ tumors but it increases the risk for endometrial cancer , DVT and PE

To rule out mets, we order PET-scan for the chest, abdomen and bone scan.

TREATMENT OF EACH STAGE:

Stage 1: treatment is mainly by a surgery (up-front surgery) either mastectomy or breast-conserving surgery depending on the site and the distribution and the size of the breast.

☆ Stage 2: treatment depends on which subtype (luminal A & B are low risk) treated with hormonal therapy and surgery.

- High risk molecular subtypes (HER-2 enriched and triple negative) are treated with chemotherapy as it's highly sensitive to chemo, as well as targeted therapy and surgery.

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☆ Stage 3: regarded as locally advanced cancer. Whatever the subtype, start with neo-adjuvant chemotherapy, which helps in offering safe margins for resection, down-sizes the tumor making it more approachable with surgery. In addition, it gets rid of these circulating tumor cells preventing the progression to stage 4. Then surgery, and post-OP radiotherapy.

☆ Stage 4: (M1) then the patient is in a terminal stage, needs chemotherapy as a palliative therapy, only to improve the quality of life. (mainly in elderly patients)