

Management of Breast Symptoms



**National Guideline
for Primary Care Doctors
& Family Physicians**



Chapter 1

Introduction

1.1. Global and Sri Lankan situation of breast cancer

Breast cancer is the commonest cancer among women all over the world and it is the commonest cancer among women in Sri Lanka as well. It accounted for 27% of all newly diagnosed cancers among females in Sri Lanka in 2010 (**Figure 1.1**) there is an increasing incidence of breast cancer over the past 25 years. (**Figure 1.2**)

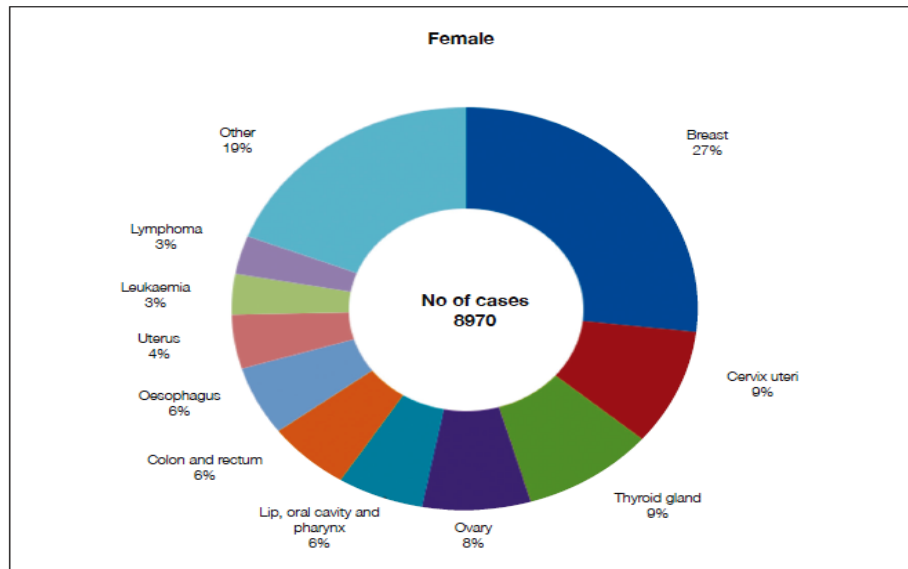


Figure 1.1 – Newly diagnosed cancers among Sri Lankan Females in 2009

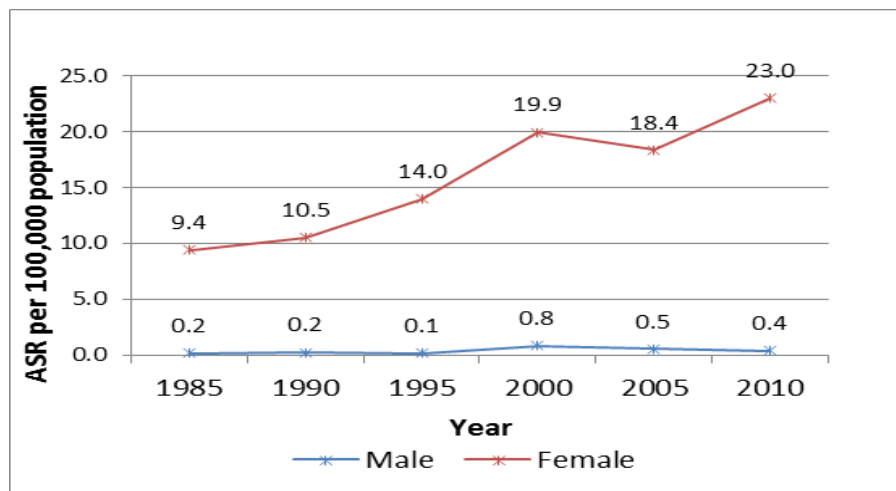


Figure 1.2 – Cancer incidence among females and males in Sri Lanka over 1985 -2010

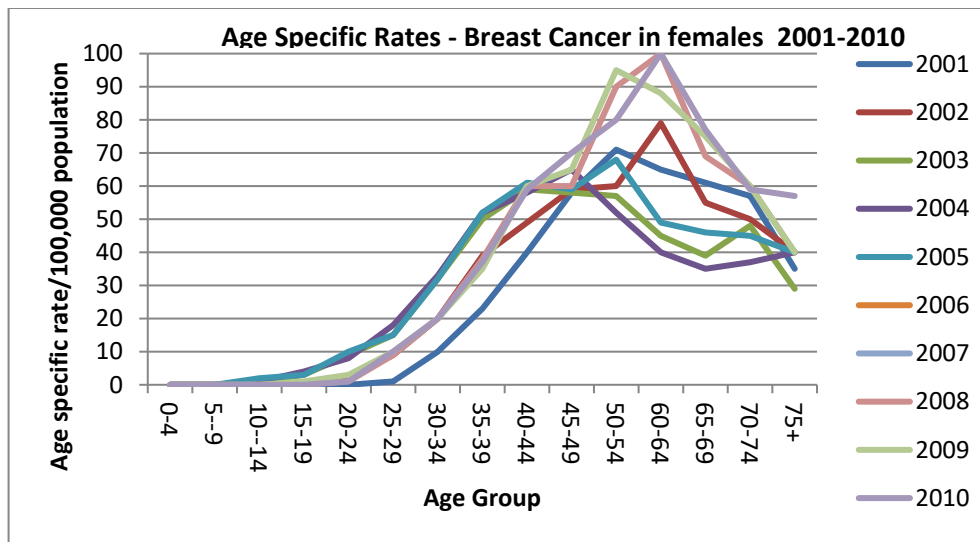


Figure 1.3 – Incidence of Breast cancer in Sri Lankan women by age

1.2. Risk factors

The specific cause of breast cancer is unknown. Most of the risk factors (approximately 90%) are mainly environmental and life-style related; while the rest (5% to 10%) are genetic.

- **Gender:** Breast cancer is the most common cancer in women in Sri Lanka. Approximately 1 in 40 women is expected to develop breast cancer during her life span (1) Females have a 100 times higher risk of getting breast cancer than males (Female: male = 100:1)
- **Age:** 70 % of all breast cancer patients reported in 2010 were in the age group of 40 -70 with peak age range of 45- 65 years (1)
- **Heredity:**
 - a. Family history – having one first degree relative with breast cancer is associated with excess incidence of breast cancer of 5.5% and if two first-degree relatives affected, the risk is increased up to 13.3%. The increase in risk is greater when the relative was affected at a younger age (2)
 - b. Known mutations - in a population-based series of breast cancer cases it has shown that approximately 1 -2% of all women with breast cancer have BRCA 1 or BRCA 2 mutations (3)

Men and women can pass on these hereditary cancer risks to their children and transmission is autosomal dominant so each child has a 50/50 chance of inheriting these gene mutations. Therefore, it is important to assess history of cancer on both maternal and paternal side of the family.

- **Biopsy proven atypical hyperplasia or Lobular carcinoma in situ:** The risk of breast cancer will increase by at least four fold in women with biopsy proven atypical hyperplasia or Lobular carcinoma in situ. This risk will persist for at least 25 years (4)
- **Chest wall radiation:** Women with a history of chest wall radiation for treatment of another cancer have up to 10 fold-increased risk of breast cancer. The risk varies with the age of the woman when she had radiation therapy and the risk is highest if the woman had radiation before menarche. (5)

- **Breast density:** Dense breast means presence of more glandular tissue compared to the fat in the breast. Breast density is a mammographic finding and cannot be reliably defined by a physical exam. Usually younger women are more likely to have dense breasts than older women. However there are outliers at both ends of the age spectrum. Women with extremely dense breasts have about two fold increased risk compared to women with breasts of average density. (6)
- **Hormonal influences:**
 - a. Menarche and Menopause: Women with earlier age of menarche and/or later age of menopause have an increased risk of breast cancer, mediated in part by the increased number of menstrual cycles and the longer lifetime exposure to estrogen and progesterone.
 - b. Reproductive History: Nulliparity also increases a woman's risk of breast cancer and every live birth reduces the relative risk by about 7%. Women 30 years or older at the time of their first live birth have a higher risk of breast cancer than women having their first child at a younger age. The risk is about 20% higher than for women whose first birth was at age 25 to 29, but is about 25% lower than nulliparous women (7).
 - c. Breastfeeding: Reduced lifetime exposure to estrogen and progesterone may also explain the protective effect conferred by increasing duration of breastfeeding. The relative risk of breast cancer decreases by about 4% for every 12 months of breastfeeding (8)
 - d. Hormone Replacement Therapy: Among women who use combination estrogen-progesterone hormone replacement therapy (HRT), the risk of breast cancer increases with the length of use. After five years of using combined HRT, the risk of breast cancer increases by about 15%, and the risk return to baseline within about two years of stopping HRT. Estrogen therapy alone increases breast cancer risk as well, but the increased risk is lower than for combined therapy (9,10)
- **Obesity** - Risk of postmenopausal breast cancer is increased with the obesity (11). It also negatively affects the prognosis of early stage breast cancer (12)
- **Life style :**
 - a. Physical activity: Compared to the least active women breast cancer risk is reduced by 25% among women who are physically active (13).
 - b. Alcohol consumption: regular consumption of as little as one drink per day increases the risk of breast cancer by 4% (14)
 - c. Smoking: association between active smoking and breast cancer is consistent with causality. In addition, the association between second hand smoke and breast cancer among younger, primarily premenopausal women who have never smoked is consistent with causality. (15)

- **Negligible radiation risk** – the risk of mammogram induced cancer is generally considered to be negligible because of the very low doses of radiation and the relative insensitivity of the mature breast to ionizing radiation (16,17)

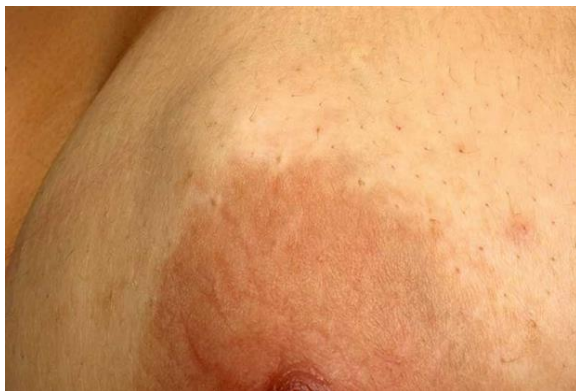
Modifiable lifestyle factors such as body weight, physical activity, alcohol consumption, and smoking should be addressed in the context of an overall wellness strategy.

Chapter 2

2.1 Possible clinical presentations at the primary care level and when to refer

Palpable mass in the breast

A palpable mass is a discrete lesion that can be readily identified during a physical examination and is the commonest form of presentation.



All women with breast lumps should be referred to a surgical unit or Breast clinic

If a woman complains of a lump do not ignore it even you cannot detect it by physical examination

Asymmetric thickening or nodularity



Should be referred to a surgical clinic or breast clinic

Usually this finding is ill defined and often vague on physical breast examination

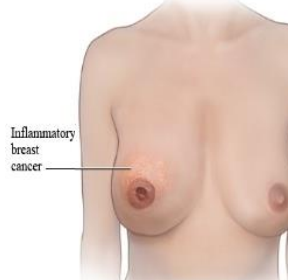
Thickening: whether the thickening is a new or previous finding

Asymmetry: whether it appears to be representative of normal asymmetry

Breast pain (Mastalgia): Cardiac pain and chest wall pain should be clearly differentiated from the history.

Mastalgia (especially unilateral non-cyclical should be referred to a surgical clinic

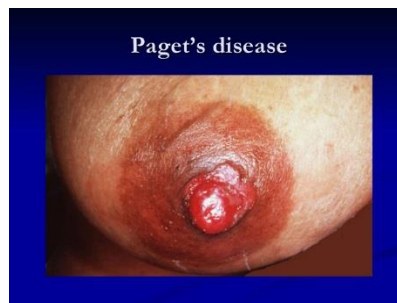
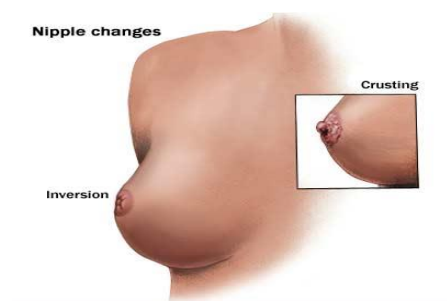
Skin Changes:



Any kind of unusual skin change in the breast including the nipple and areolar may represent serious disease and needs evaluation. Should be referred to a surgical clinic or breast clinic

Inflammatory breast cancer (IBC) should be considered when dermal oedema (Peau d'orange) and breast erythema are present. IBC is a rare form of aggressive breast cancer

Nipple Changes



Nipple excoriation, scaling and eczema should increase clinical suspicion of Paget's disease. Paget's disease of the breast is a rare manifestation of breast cancer characterized by neoplastic cells in the epidermis of the nipple areolar complex. They most commonly present with eczema of the areolar, bleeding, ulceration and itching of the nipple.

Single duct discharge,
unilateral of any
colour should be
referred to a surgical

Nipple discharge other than breast milk



Rare presentation of breast cancer

Nipple discharge without palpable mass – In benign breast cancer disease, nipple discharge is a common symptom that may occur unrelated to breast pathology. However, it can rarely be seen in cancer. Non spontaneous discharge from multiple breast ducts in a non-lactating woman can occur during pregnancy, following breast stimulation, women with certain thyroid conditions and in those taking certain medications (e.g. estrogen, oral contraceptives, opiates, and particular anti-hypertensive agents)

Suspicion of underlying pathology is raised when nipple discharge is persistent and reproducible on examination, spontaneous, unilateral from a single duct with fluid of any consistency and colour.

Axillary mass



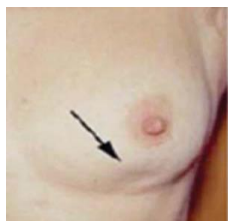
An axillary mass should be referred
to a surgical clinic

Other complaints

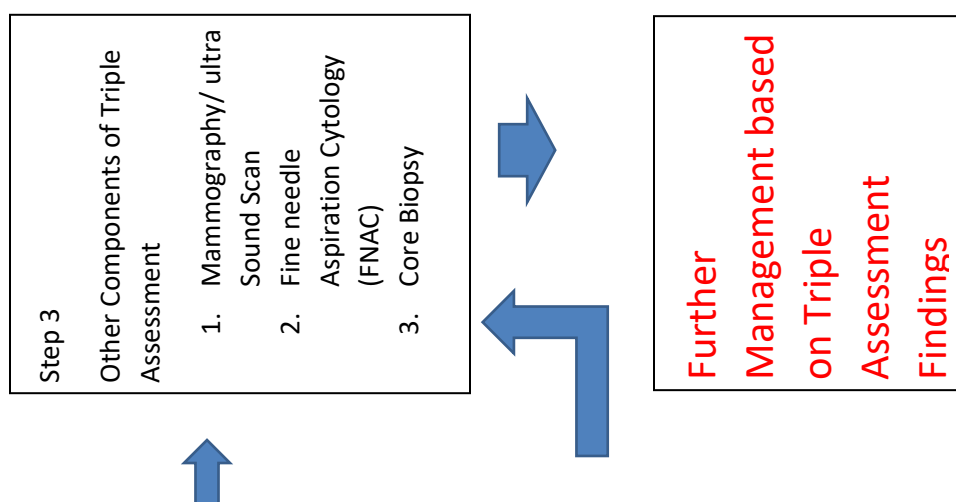


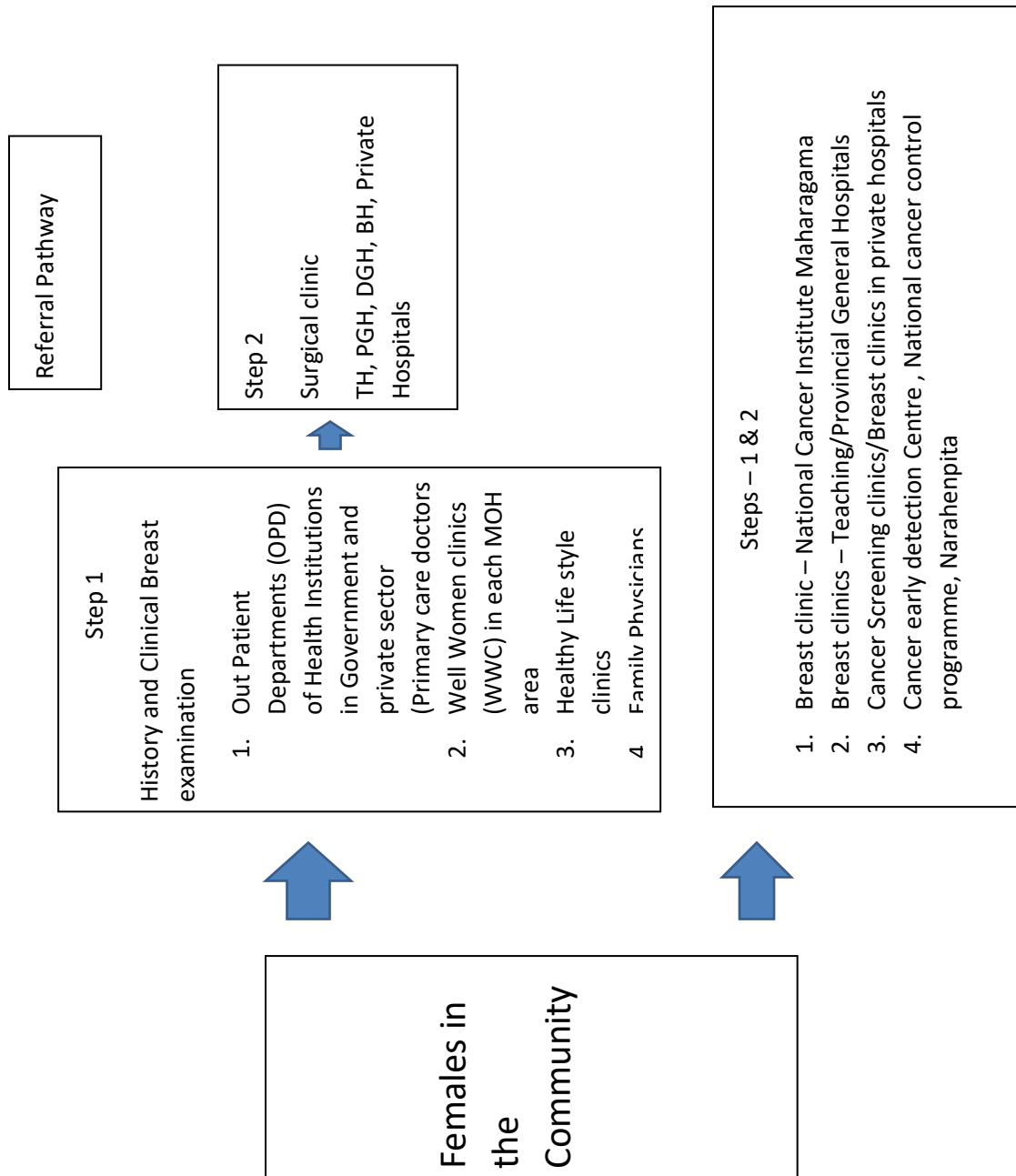


All other complains including changing the contour of the breast, nipple inversion, mastitis, sinuses etc. should be referred to a surgical unit



Presence of any of the above clinical features do not always indicate the presence of a breast cancer





2.2 Diagnosis at the tertiary care level

- ❖ Diagnosis of a breast cancer is made at the tertiary care level
- ❖ It is diagnosed by the Triple assessment
- ❖ Triple Assessment refers to three diagnostic components
- ❖ Medical history and clinical breast examination
- ❖ Imaging - Mammography and or Ultrasound scan

- ❖ Non excision biopsy
- ❖ Cytology (FNAC) and or core biopsy is not available or if lump is too small for core biopsy

The sensitivity of the triple assessment is greater compared to any of the individual component alone.

The triple assessment is positive, if any component is indeterminate, suspicious or malignant, and they will need further follow up at a specialist center.

2.3 Recommendations for patients presenting with symptoms

- Presenting complaint and all the risk factors identified should be documented
- Any breast lump should be considered as a cancer until proven otherwise. Special attention should be paid for pregnant women and lactating women when they complain of or you detect any abnormality
- Attention should be paid to benign conditions such as nipple discharge and mastalgia as they could precede the symptoms of cancer

- If a specialized breast clinic is available in the area, women with any breast symptom can be referred directly to those clinics. (The breast clinic is a dedicated clinic for breast problems. Breast clinic is conducted by a team led by a Consultant surgeon or a Consultant oncosurgeon. Medical and nursing staff are specially trained in providing services for breast problems. Patients attending breast clinics have the opportunity for timely access to radiological and pathological laboratory services for triple assessment.
- No surgery should be done on the breast unless supervised or authorized by a consultant surgeon/ consultant oncosurgeon
- Women over the age of 50 years should be discouraged to be on Hormone Replacement Therapy (HRT) unless with severe postmenopausal symptoms (WHO recommendation)
- Women on HRT with a family history of breast cancer should be referred for surgical or oncological opinion at least once in two years. If HRT has to be started for severe postmenopausal symptoms, it should not be continued for more than two years without opinion of the oncologist. These women should be given special attention for early detection of breast cancer. Preferably they should undergo a screening mammography.
- Any male with breast symptoms should be referred to a surgical clinic

If any abnormality is detected during clinical breast examination, suggesting a breast pathology it does not indicate that she is having a cancer. Diagnosis should be confirmed by conducting other components of triple assessment at the next level of care. So need to communicate in a proper way without unnecessarily frightening the client but persuading her to attend for further evaluation.

Chapter 3

3.1 Early detection of Breast Cancer

Importance of early detection of breast cancer

- Less aggressive treatments
- Wide range of treatment options
- Better outcome

Methods of early detection of breast cancer (Breast Screening)

Breast screening is performed in women without any signs or symptoms of breast cancer. So that disease can be detected as early as possible.

The components and timing of breast screening evaluation depend on the woman's risk level.

Components of breast cancer screening include:

3.1.1 Breast awareness

3.1.2 Clinical breast examination and risk assessment

3.1.3 Screening mammography, ultrasonography and in selected cases screening breast MRI

3.1.1 **Breast awareness** (familiarity with the breasts)/ Breast self-examination) - (Annexure 1)

Women should be familiar with their breasts and encouraged to report changes; periodic breast self-examination (BSE) may facilitate breast self-awareness

3.1.2 **Clinical Breast examination**

Clinical breast examination is used as a method of early detection of breast lesions as well as a component in triple assessment in diagnosing breast cancer. A detailed history and thorough clinical examination provide important information on which, further investigations would be based.

Clinical history

- Relevant history includes the details of breast symptoms

Breast Lump	• Site – Constant or changing
	• Duration – when and how it was noticed
	• Any new changes since first notice
	• Relationship to menstrual cycles or exogenous hormones
	• Associated symptoms
Breast Pain	• Site – Constant or changing/ Unilateral or bilateral
	• Cyclical or noncyclical

	• Duration – how long and characteristics of pain
	• Any recent change such as intensity, frequency, site of pain
	• Relationship to menstrual cycles or exogenous hormones
	• Associated symptoms
Nipple discharge or change any other nipple changes	• Duration – when and how first noted (Spontaneous or not)
	• Any changes since first notice
	• Bilateral or unilateral
	• From single duct or multi duct

- Previous history of any pathological condition in either breast:
- Previous breast investigations:

Most recent imaging if available (Screening or diagnostic) date and results

Biopsy results – FNAC/Histology/Lumpectomy

- Risk factors – History should be taken on the risk factors (please refer page 2 & 3)

Steps of clinical breast examination (CBE)

CBE should be done in a covered room with good light. A female chaperone should be there if the examiner is a male.

Before starting the examination, it is necessary to explain the procedure to the woman

Inspection

The breast should be inspected in each of the following sitting positions and supine positions.

1. Arms relaxed at her sides
2. Arms raised over her head
3. Hands placed on the hips and pushing inward (contraction of the Pectoralis Major muscle)

The breasts should be inspected from the front and from each side.

Pay particular attention to:

- Breast size, contour, shape, symmetry
- Skin changes such as erythema, dimpling, tethering or puckering, Peau d' orange, eczematous skin changes, visible lumps

- Nipple – position, height, any inversion, retraction, erythema, eczema, nodules ulceration and discharge



Step 1 – Arms by the side



Step 2 – Arms over the head



Step 3 – Hands on hip and
Leaning forward

Palpation

The ability to identify breast cancers by palpation is influenced by the characteristics of the tumour, surrounding breast tissue, the position of the lesion in the breast, proper positioning of the client, and thoroughness of the search, the area covered and use of a consistent pattern of search.

During the process of palpation, the client should feel comfortable and one needs to ask about it.

Step 4 – Positioning the female for palpation

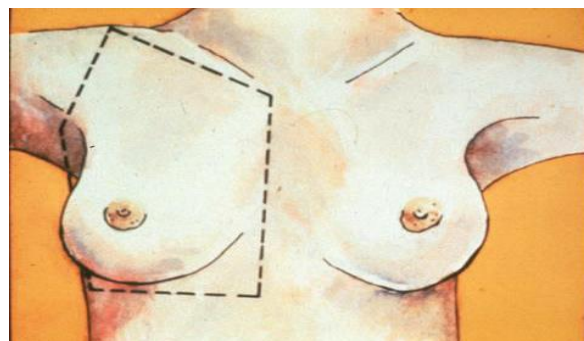
For the palpation of the breasts, the woman should be placed in the supine position. Place both arms under head, which will facilitate palpation of outer quadrant of a large breast.

Use both hands to stabilize breast position.

Step 5 – Identifying the perimeter of the breast

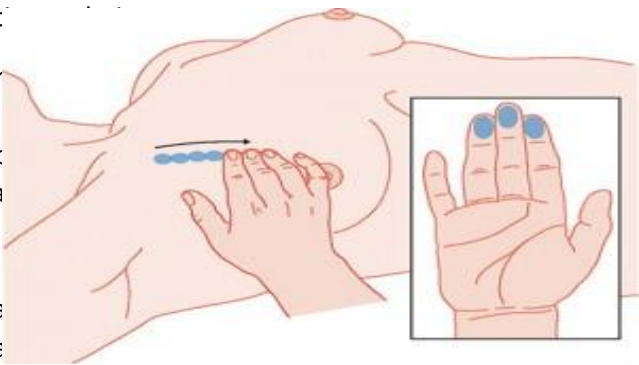
Perimeter of breast should be noted during Clinical breast examination

Anatomically, breast tissue extends superiorly from the second rib or clavicle, medially to the lateral border of the sternum, inferiorly to the sixth rib and laterally to the Latissimus Dorsi muscle.



Step 6 – Palpation

The examiner should use the pads of the middle, ring, and middle fingers to palpate the breast. The fingers should be pressed together to form a tripod shape. The examiner should use a systematic pattern to palpate the breast, starting from the outer edge and moving towards the nipple. The examiner should palpate the breast in a systematic pattern, starting from the outer edge and moving towards the nipple. The examiner should palpate the breast in a systematic pattern, starting from the outer edge and moving towards the nipple.



There are three typical patterns used to palpate the breast:

- Circular technique
- Vertical strip technique
- Radial spoke technique



Circles



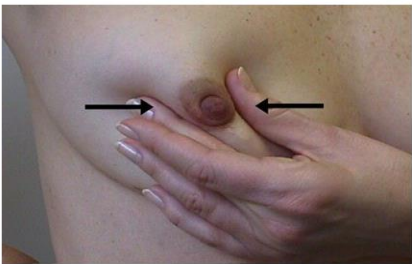
Wedges



Lines

Note that the circular method does not always cover the entire perimeter of the breast unless a conscious effort is made to do so.

The woman should be asked to squeeze the areolar region of the nipple to see whether there is any nipple discharge. Nipple discharge that occurs only with nipple or breast stimulation is a normal physiological function.



Step 7 - Palpation of Regional Lymph Nodes

The regional lymph nodes (Supra-clavicular, Infra-clavicular and axillary nodes) should be palpated while the woman is in the sitting position. These lymph nodes include the supraclavicular, infra-clavicular and axillary nodes.



Palpation of axillary lymph nodes



Palpation of supra and infra clavicular lymph nodes

3.1.3 Mammography / Ultra sound scan/ MRI scan

These investigations are used in breast cancer screening as well as a component of triple assessment in diagnosing breast cancer.

Mammogramme

A mammography is a low-dose x-ray of the breast. It is used for screening and diagnosis of breast cancer. Mammography is the investigation of choice for screening of early breast cancer when the lumps are not palpable by the patient or the doctor. However, although relatively fast and accurate, it is a highly- technological test that requires highly-trained personnel and elaborate equipment. Sensitivity of mammography increases with age. Before the age of 40 years, mammography is not usually recommended for screening. This is because younger women tend to have denser breasts which reduce the sensitivity of mammography. Therefore risk of radiation tends to outweigh the benefits of screening mammography below the age of 40 years.

Ultrasound

There is insufficient evidence to support the use of ultrasound for routine screening. Ultrasound should not be used as a stand-alone screening test. It is generally used when further evaluating a mammographically detected anomaly in breast screening. Ultrasound scan may also have a role as an adjunct to mammography in screening women with dense breasts, as determined by a radiologist.

Magnetic Resonance Imaging (MRI)

MRI is a non-radiation incurring imaging modality with high sensitivity for detecting breast cancer.

It is however, relatively less specific and more costly and is not readily available.

MRI is recognized as a screening tool, either stand alone or as an adjunct to mammography, for screening of women at high risk of breast cancer.

3.2 Recommended screening protocol

- Breast self-examination should be conducted once a month by all women starting from 20 years of age.
- Clinical breast examinations (CBE) are recommended every 3 years for all women from the age of 20 to 40. For women aged 40 or over, CBE is recommended annually.
- In women whose relatives developed breast or ovarian cancer under the aged of 40 years, annual clinical breast examination should be started 5 years before the index case.
- Breast self-examination should be taught and reinforced at every consultation.
- Screening mammography is offered once in 2-3 years for women age 50 – 69 years, if they request it. (Can be adopted only when adequate mammography facilities are available throughout the country)

3.3 Women requiring more intensive screening

- Women with one or two first degree relatives with invasive breast cancer
- Women with a breast biopsy showing atypical hyperplasia or lobular carcinoma in situ
- Women with a history of chest wall radiation (e.g. mantle radiation for treatment of Hodgkin's lymphoma) at age 30 or younger
- Women with known mutations (e.g. BRCA 1 BRCA 2)

Annexure 1

Breast Self-Examination

Health education on breast self-examination

Breast self-examination is the Inspection and palpation of the breast by the woman herself. The role of the primary health care physician is to provide necessary information regarding this to women and to make them competent in breast self-examination.

Information that should be provided to the woman

• Need for breast self-examination

If breast cancer is detected early, it gives the best outcome. A practice of breast self-examination on monthly basis is very important for early detection of breast cancers.

Frequency of carrying out the breast self-examination

This should be carried out once a month by all women over the age of 20.

- **Date for conduction of breast self-examination**

This should be conducted on a fixed date every month. It is better to conduct this, one week after the start of menstruation. If she is not menstruating, a fixed date in every month should be used.

- **Place and postures to conduct Breast Self-Examination**

A woman can use any place that suites her. It can be conducted in a lying down, sitting or a standing position or while bathing.

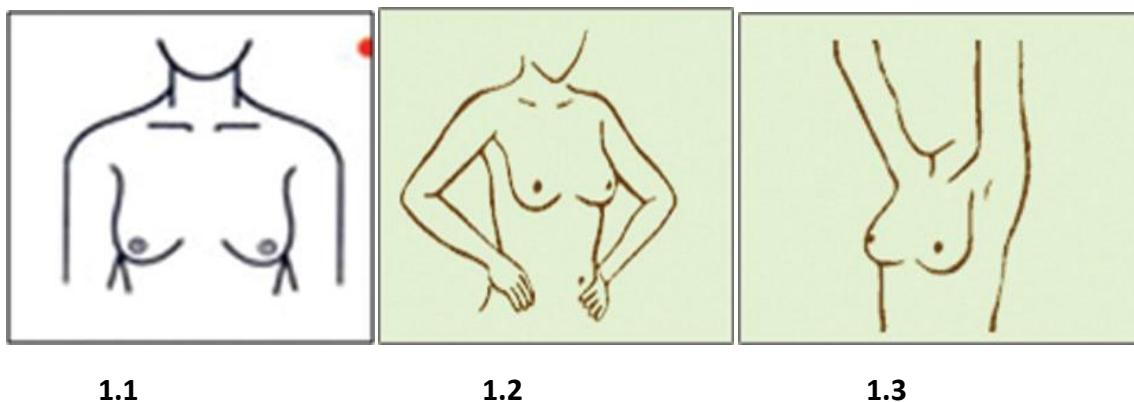
Instructions to be given to the woman on steps of Breast Self-Examination

Breast self-examination has two components:

1. Inspection
2. Palpation

Inspection

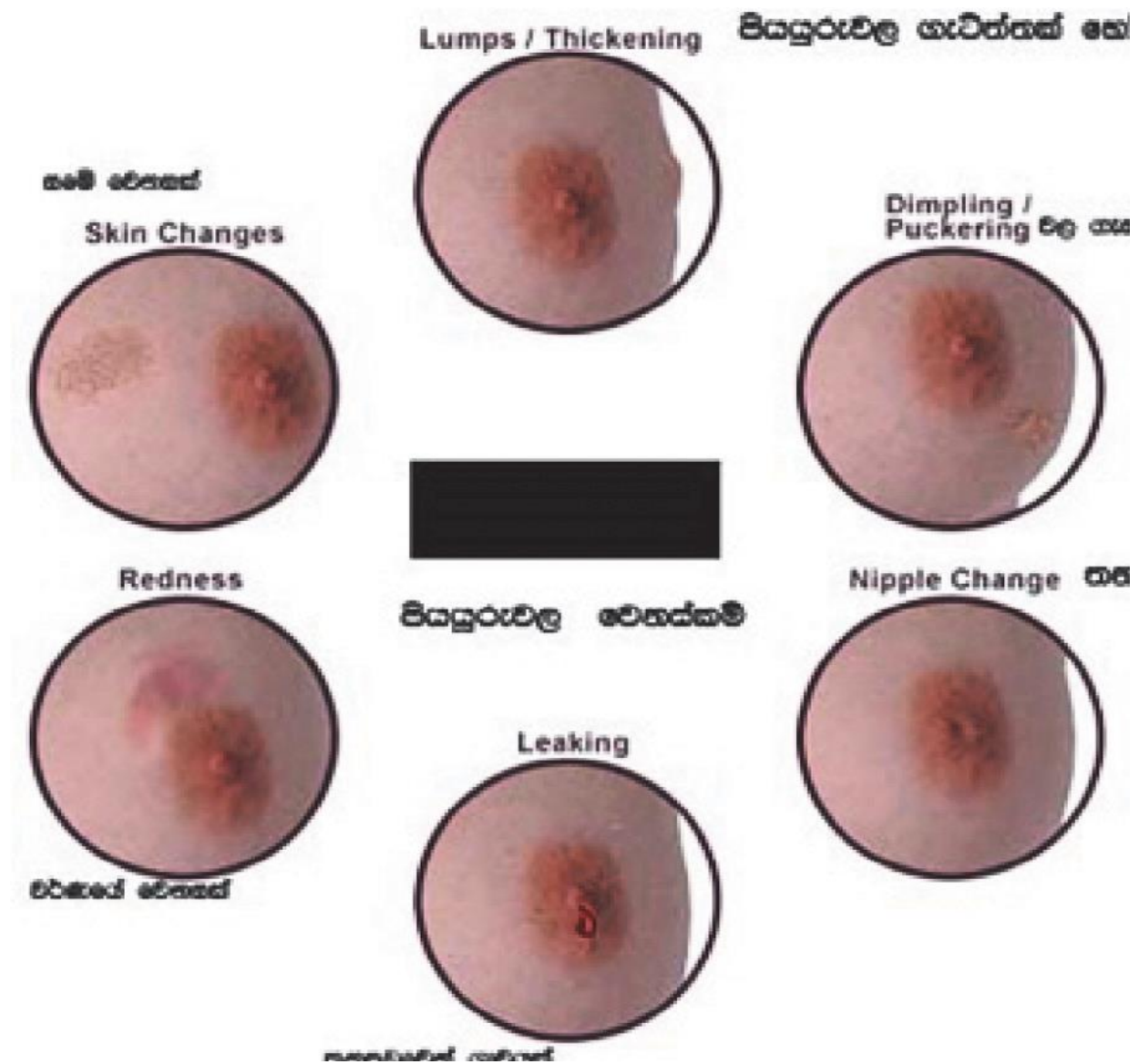
Picture 1



Stand in front of the mirror exposing the chest up to the waist. Observe the breasts for the following changes while keeping the arms in positions shown in picture 1 (1. arms hanging by the side, 2. hands pressed on the waist, 3. arms lifted above the head)

Kind of clinical features to be checked in inspection and palpation

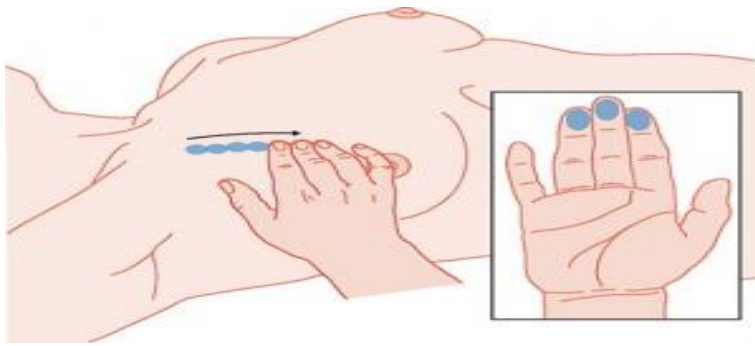
- ❖ Skin changes of the breast
- ❖ Color changes of the breast
- ❖ Change in shape of the breast
- ❖ Orange peel / Peau d'orange appearance of breast
- ❖ Ulceration on the breast
- ❖ Late occurrence of breast asymmetry (usually both breasts are not of equal size. Therefore, a long standing breast asymmetry is not a sign of a cancer)
- ❖ Nipple change/discharge other than breast milk (Having inverted nipples from birth is not a sign of a cancer)
- ❖ Breast lump or thickening of the breast skin
- ❖ Lumps in the arm pit or around the neck



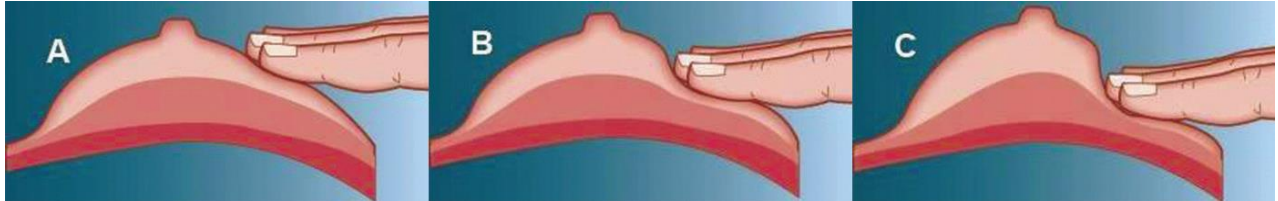
Palpation

Picture 2: Palpate the breast using fingers for any increase in thickness or lump. Use the palmar surfaces of the fingers (flat surface of the three middle fingers). This can be conducted in a sitting/lying down/standing or bathing position

On examining right breast, lift the right upper arm and palpate the right breast using the left hand). While examining the left breast lift the left upper arm and palpate the left breast using the right hand



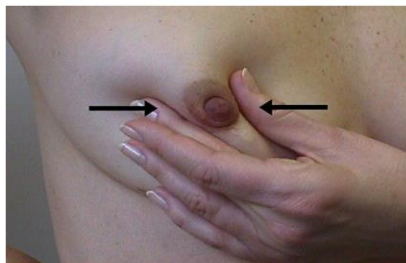
Picture 2.1: Continue palpating the breast in a clockwise direction from outside of the breast towards the nipple.



Picture 2.2: Start with applying 'minimal' pressure as indicated (to feel the area just beneath the skin) and then gradually increase the pressure (to feel the tissue deeper within)



Picture 2.3: Then examine the arm pit



Picture 2.4: Find out whether there is a nipple discharge using thumb and first finger to squeeze the areola.

Use the same technique to examine the other breast.



Picture 2.5: If Breast Self-Examination is conducted in a lying down position, follow the following procedure. For the right breast examination, keep the right palm beneath the head and palpate the breast using the left hand.

For the examination of the left breast, keep the left palm under the head and examine with the right hand.

What to do after breast self-examination?

If any abnormality is detected during breast self-examination, it is necessary to consult a doctor. It is important to note that all the changes in the breast are not cancers.

National recommendation for breast self-examination:
All women should practice breast self-examination once a month from 20 years of age.

Annexure II

Management of Breast Cancer at tertiary care level

Dr. Kanishka De Silva
Consultant Onco-surgeon
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1. Diagnosis

The diagnosis is based on clinical, radiological and pathological examinations. Clinical examination includes bimanual palpation of the breasts and loco-regional lymph nodes. Radiological examinations include bilateral mammography and ultrasound of the breasts (and regional lymph

nodes depending on local expertise). Magnetic resonance imaging (MRI) of the breast is not needed as a routine procedure, but may be considered in cases involving diagnostic challenges arising, for example, because of dense breast tissue especially in young women or where multiple tumour foci are suspected, in particular with lobular breast cancer. Pathological diagnosis should be based on core needle biopsy obtained by manual, or preferably by ultrasound or stereotactic, guidance. A core needle biopsy (or, if that is not possible, at least a fine needle aspiration indicating carcinoma) must be obtained before any surgical operation. If preoperative chemotherapy is anticipated, a core needle biopsy is preferred. Final pathological diagnosis should be made according to the World Health Organization (WHO) classification and the tumour–node–metastases (TNM) staging system analysing all tissue removed.

2. Staging and risk assessment

Patient-related staging assessment includes complete personal medical history, family history relating to breast/ovarian and other cancers, physical examination, full blood count, liver and renal function tests, alkaline phosphatase and calcium. Assessing the menopausal status is imperative [if in doubt by measuring serum Oestradiol and follicle-stimulating hormone (FSH) levels].

Preoperative disease-related staging includes clinical TNM staging, pathological examination of the core needle biopsy with a pathologist's report on histological type and grade, needle cytology of axillary nodes if involvement is suspected clinically or on ultrasound, and determination of Oestrogen receptor (ER), progesterone receptor (PgR) and HER2 receptor status. Alternatively, these biological markers can be assessed on the definitive surgical specimen if primary systemic therapy is not planned.

If preoperative (neoadjuvant) systemic therapy is planned, additional investigations such as chest X-ray, abdominal ultrasound or CT scan and bone scintigraphy should be considered to exclude metastatic disease. These investigations are also recommended for patients with clinically positive axillary nodes, large tumours (e.g. >5 cm) or clinical signs, symptoms or laboratory values indicating the presence of metastases, even if preoperative systemic treatment is not planned.

The postoperative pathological assessment of the surgical specimen should be made according to the pTNM system to include: number, location and maximum diameter of tumours removed, the total number of removed and number of positive lymph nodes, and the extent of metastases in the lymph nodes. The report should also include histological type and grade of the tumour, evaluation of the resection margins including the location and minimum distance of the margin, vascular and lympho-vascular invasion; immune-histochemical evaluation of ER, PgR and HER2 receptor expression.

3. Treatment by disease stage

Multidisciplinary treatment planning involving at least a breast surgeon, radiologist, pathologist, and medical and radiation oncologists should be used.

3.1 Surgery:

About two-thirds of newly diagnosed cancers are amenable to breast conservation (wide local excision and radiotherapy), but in the remaining third mastectomy is still recommended because of larger tumour size, or tumour multifocality / multicentricity, and prior radiation to the chest wall or breast.

3.1.1 Breast conservation surgery (BCS):

For patients undergoing wide local excision, greater emphasis is now placed on achieving acceptable cosmesis. Newer volume displacement techniques using adjacent breast tissues, have allowed surgeons to get a wider clearance maintaining an acceptable cosmesis. Newer oncoplastic procedures such as therapeutic mammoplasty (breast reduction at the same time as wide local tumour excision) can achieve better cosmetic outcomes in patients with large breasts. Postoperative radiotherapy is strongly recommended after BCS.

3.1.2 Mastectomy:

European treatment guidelines recommend that breast reconstruction should be available to those women-requiring mastectomies. Immediate reconstruction in some women can make the prospect of losing a breast easier to accept, but not all women will be suitable for immediate reconstruction. When post-mastectomy radiation therapy is anticipated, some women will be advised against immediate reconstruction as there is a possibility of flap sinkage with radiation. Skin-sparing and nipple sparing mastectomy allows the skin envelope to be conserved for use in the breast reconstruction.

3.1.3 Advances in axillary staging:

Regional lymph node status remains the strongest predictor of long-term prognosis in primary breast cancer. Sentinel lymph node biopsy (SLNB) rather than full nodal clearance is now accepted as the safe procedure of care for axillary staging in early breast cancer, unless axillary node involvement is suspected clinically or on ultrasound.

SLNB delivers less morbidity in terms of shoulder stiffness and arm swelling, and allows for reduced hospital stay.

The presence of macrometastatic spread in the sentinel node traditionally mandates conventional axillary lymph node clearance. Axillary clearance is associated with lymphedema affecting the upper limb in 3–5% of women following surgery alone, but the incidence of lymphedema rises significantly to 40% when axillary clearance is combined with radiotherapy to the axilla. Women who have undergone axillary clearance are advised to avoid cannulation, venesection and blood pressure monitoring in the ipsilateral arm, and to start antibiotic treatment promptly for potentially infected wounds on the ipsilateral arm. Once established, lymphedema should be treated by trained therapists using a combination of compression bandaging, manual lymphatic drainage and graduated compression garments.

3.1.4 Surgery for in situ malignancy (intraepithelial neoplasia):

Ductal carcinoma in situ (DCIS, ductal intraepithelial neoplasia) may be treated with BCS providing clear resection margins can be achieved (margins <1 mm are considered inadequate). Adjuvant breast irradiation after BCS decreases the risk of local recurrence but has no effect on survival. Total mastectomy with clear margins in DCIS is curative, and radiation therapy is not recommended. Axillary node evaluation with SLNB is not required with in situ malignancy but may be reasonable in the context of large tumours requiring mastectomy or tumours in the tail of the breast. Lobular neoplasia (formerly called lobular carcinoma in situ, LCIS), unlike DCIS, is considered a non-obligate precursor to invasive cancer and is best regarded as a risk factor for future development of invasive cancer in both breasts. The pleomorphic variant of lobular neoplasia may behave similarly to DCIS and should be treated accordingly.

3.1.5 Risk-reducing mastectomy:

Risk-reducing surgery with prophylactic bilateral mastectomy and reconstruction (with or without oophorectomy) may be an option for women at very high risk, such as those with previous chest wall irradiation for lymphoma or carrying the BRCA1 or BRCA2 gene mutations. The lifetime risk of breast cancer in a BRCA1 carrier is 80–85%, with a 60% chance that the cancer will be bilateral. The risk for both subsequent breast cancer incidence and mortality is reduced by 90–95%, but surgery cannot guarantee prevention of developing breast cancer in the future. In addition, mutations in BRCA 1 and BRCA 2 account for around 15% of ovarian cancers overall. Careful genetic assessment and psychological counselling is mandatory before undertaking such surgery.

3.1.6 Surgery after primary systemic therapy

Down-sizing of a large unifocal primary tumour with neoadjuvant therapy will allow BCS to be undertaken in some patients who would at presentation have otherwise required mastectomy. With multifocal disease, or where the primary tumour size reduction is more limited, mastectomy will still be required. Breast MRI is the most accurate modality for assessing the extent of residual disease following neoadjuvant treatment.

3.2 Radiation therapy:

3.2.1 Invasive carcinoma:

3.2.1.1 Radiation therapy after BCS: Whole breast radiotherapy

Postoperative radiotherapy is strongly recommended after BCS. Whole breast radiotherapy reduces the risk of local recurrence by two-thirds and an additional boost gives a further 50% risk reduction. Furthermore, radiotherapy has a beneficial effect on survival. In patients >70 years of age who have endocrine-responsive invasive breast cancer with maximum stage pT1N0 and clear margins, it may be possible to omit radiation therapy without compromising survival.³⁹

3.2.1.2 Accelerated partial breast irradiation (PBI) only

PBI is an attractive approach to shorten the overall treatment time substantially. PBI is considered an acceptable treatment option in patients at least 50 years old with unicentric, unifocal node-negative non-lobular breast cancer up to 3 cm in size without the presence of an extensive intraductal component and lymphovascular invasion, and with negative margins of at least 2 mm.

3.2.1.3 Radiation after mastectomy

Post mastectomy radiotherapy (PMRT) is always recommended for patients with four or more positive axillary nodes, and indicated for patients with T3–T4 tumours independent of the nodal status. PMRT may also be considered in patients with 1–3 positive axillary lymph nodes in the presence of additional risk factors, such as young age, vessel invasion and low number of examined axillary lymph nodes.

3.2.2 Non-invasive carcinoma (intraepithelial neoplasia)

Adjuvant whole breast irradiation after BCS of DCIS decreases the risk of local recurrence but has no effect on survival. The decrease in risk of local recurrence by radiotherapy is evident in all subtypes of DCIS.

However, in some patients with low-risk DCIS (tumour size <10 mm, low/intermediate nuclear grade, adequate surgical margins), the risk of local recurrence following excision only is so low that omitting radiation may be an option. In ER-positive DCIS, Tamoxifen may be considered following

BCS (with or without adjuvant radiation). Total mastectomy with clear margins in DCIS is curative, and radiation therapy is not recommended. In this group of patients, Tamoxifen may also be considered to decrease the risk of contralateral breast cancer. Lobular neoplasia (formerly called LCIS) is a risk factor for future development of invasive cancer in both breasts; radiotherapy is not warranted, perhaps with an exception for the pleomorphic subtype.

3.3 Systemic therapy

3.3.1 Adjuvant systemic therapy

ER and HER2 status are the most relevant predictive factors for the choice of treatment modality. Tumours with any detectable expression of ER and/or PgR by IHC are considered hormone-receptor positive. Tumours with no detectable expression of ER and PgR are considered hormone receptor negative or endocrine non-responsive. Features indicative of uncertainty of endocrine responsiveness include low levels of steroid hormone receptor immune-reactivity, lack of PgR, poor differentiation, high proliferation markers, HER2 overexpression and high gene expression score results. In the absence of all these features, tumours are considered highly endocrine responsive.

Patients with tumours of different degrees of endocrine responsiveness may receive endocrine treatment alone, or a combination of chemotherapy and endocrine therapy. Patients with tumours of uncertain endocrine responsiveness are usually treated with a combination of endocrine therapy and chemotherapy.

Patients with endocrine-non-responsive tumours benefit from chemotherapy and should not receive endocrine therapy. In addition to endocrine therapy and chemotherapy, patients with tumours indicative of HER2 overexpression or amplification should be considered for adjuvant treatment with Trastuzumab and chemotherapy.

3.3.2 Endocrine therapy

Patients with tumours considered of high or uncertain responsiveness should be treated with endocrine therapy.

3.3.3 Chemotherapy

Adjuvant chemotherapy is recommended for patients with tumours of uncertain or absent endocrine responsiveness and for patients with HER2-overexpressing or amplified tumours. If both chemotherapy and endocrine therapy are indicated, chemotherapy should be started first followed by endocrine therapy.

3.3.4 Systemic adjuvant therapy for ductal intraepithelial neoplasia (DCIS)

Tamoxifen reduces the risk of invasive and non-invasive recurrences after breast-conserving resection of ER-positive DCIS but has no impact on survival.

3.3.5 Primary (neoadjuvant) systemic therapy

Primary systemic therapy is indicated for locally advanced breast cancer (stages IIIA–B) including inflammatory breast cancer and for large operable tumours for reducing tumour size in order possibly to perform BCS. Prior to primary systemic therapy, a core needle biopsy and complete pathological assessment (i.e. histological type, grade, ER, PgR and HER2 status) is essential. In addition, full clinical staging to rule out gross metastatic disease is recommended.

3.2 Follow-up: ASCO GUIDELINE UPDATE

Breast Cancer Follow-Up and Management after Primary Treatment: American Society of Clinical Oncology Clinical Practice Guideline Update

Key Recommendations

- Regular history, physical examination, and mammography are recommended
- Examinations should be performed every 3 to 6 months for the first 3 years, every 6 to 12 months for years 4 and 5, and annually thereafter
- For women who have undergone breast-conserving surgery, a post-treatment mammogram should be obtained 1 year after the initial mammogram and at least 6

months after completion of radiation therapy (whichever the longest); thereafter, unless otherwise indicated, a yearly mammographic evaluation should be performed

- Use of CBCs, chemistry panels, bone scans, chest radio-graphs, liver ultrasounds, computed tomography scans, magnetic resonance imaging, or tumour markers (carcino-embryonic antigen, CA 15-3, and CA 27.29) is not recommended for routine breast cancer follow-up in an otherwise asymptomatic patient with no specific findings on clinical examination.

Annexure III

Psychological Considerations in the Management of Breast Symptoms

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For a vast majority, the possibility of a diagnosis of cancer is a very real fear. In considering the emotional upheaval that this challenging disease arouses, it is essential that doctors take the utmost interest in uplifting the psychological status of their patients who present with 'suspicious' breast symptoms and/or a diagnosis of breast cancer. This section gives you some psychological aspects that we recommend you consider in the management of breast symptoms.

Psychological aspects when motivating women to do regular Breast Self-Examinations (BSE)

- We are aware that a majority of Sri Lankan women are not informed of the need for regular BSE. Hence, it is the duty of her doctor to inform her of this necessity.
- In notifying a woman of this necessity, it is important that the doctor gives her clear information (i) about what a cancer is, (ii) what breast cancer is, (iii) that the prognosis is good if cancer is detected early, (iv) the need for regular BSE, (v) what indicators to look out for when doing so, (vi) how to do the BSE, and (vi) the need to immediately inform the doctor if any suspicious indicators are detected, respectively.
- When giving the above information, be focused and serious but do not evoke fear as the latter may actually prevent the woman from doing the BSE. You have to balance your approach.

Psychological aspects when motivating women to do regular clinical breast examinations (CBE)

- Being a traditional culture, many Sri Lankan women would feel uncomfortable when having to do a CBE. This is so even when done by a female doctor.
- Hence, the doctor should be careful when introducing the need for a CBE. Give the woman clear information on the necessity to do this and inform her that a female doctor. This latter aspect would do it may make her comfortable with the idea.
- When introducing the need for a CBS, be focused and serious but do not evoke undue fear as the latter may actually prevent the woman in getting the CBE done.
- When doing the CBE, keep your facial expression and body posture friendly, relaxed and neutral. Even if anything suspicious is detected, do not show any worry. This point is essential. Do not in any way indicate to the woman that you are worried about the findings as this may affect her psychological health and make her worried prematurely and possibly unnecessarily. But also, do not seem casual if you indeed detect anything suspicious as this may not motivate her to go onto do further investigations. You have to keep your attitude in balance.

Psychological aspects when referring the woman for further investigations

- The manner in which you do the referral for further investigations, after finding anything suspicious at the CBE, should be done delicately. You should not raise undue worry in the woman. Nor should you appear casual, as if the referral is a routine one, as the woman may interpret this as nothing to worry about her condition.
- Communicate to the woman in a clear, focused and gentle manner that you need her to do some further investigations. You could inform her that it is part of the routine care process, but you must also be firm when you say so as some women may not go on to do the further investigations.

- Inform the woman clearly, where she needs to go to in order to do these routine investigations and give her an appointment for her to come back to you once these investigations are done.

This latter aspect is intended to bind the woman to come back to you. This means that there is a higher chance that she will do these investigations.

Psychological aspects if a diagnosis of cancer is made

- If the woman comes to you with a diagnosis of a malignancy, she may then already know the process she needs to follow in her course of treatment. Or, you may need to inform her of this.
- There will be an enormous amount of emotional disturbance in the woman at this stage. This is normal and is to be expected. She may consider her life be in shatters now. As her doctor, you need to give her kind hearing ear when she expresses her feelings about her unexpected condition. Of course, this may take a considerable amount of your time. However, it is essential that you devote your time to this process, nevertheless. For, we know that talking about ones fears and worries, particularly with a trustworthy and knowledgeable doctor is very therapeutic.
- If you feel that you are not inclined to talking with the woman about her diagnosis, try to develop empathy. One of the best ways to develop empathy is to consider if you were the one with the diagnosis and if so how you may be feeling at that moment.
- When talking to the patient, encourage and give her hope for the future. Cite examples of those whom you know who had gone on towards 'recovery'.
- In the event that the prognosis is not that good, it is important not to inculcate undue hope but also not to make the patient despair. In this situation, a listening ear by the doctor is a must and maybe the only solace the woman may have.
- At all cost, avoid developing guilt in the woman. Do not tell her what she should have done (e.g. that she should have done the CBE much earlier on in life) that could have minimized her diagnosis. Blaming and developing guilt does not help anyone and especially not a woman with a breast cancer.

Kindness and compassion are essential requisites in a doctor. A doctor so endowed would be a pillar of strength to a patient. This is particularly so when it comes to the domain of cancer. Your approach to the patient would make a vast difference in her life. By being kind and compassionate towards the patient, it is not only she who would benefit, so will you. By being kind and compassionate towards those whom you serve will uplift you and make your life more meaningful, the goal that all of us human beings strive for.

Annex IV Hereditary Breast Cancer

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Breast cancer is the commonest cancer among Sri Lankan women, accounting for approximately 27% of all female cancers. Although all cancers are genetic, only some are hereditary. Five to ten percent of breast cancers have a strong hereditary component due to highly penetrant germ-line mutations in autosomal dominant cancer predisposition genes (CPGs), while 15–25% are familial

due to a combination of multiple moderate-low penetrant genes and shared environmental/lifestyle risk factors.

Hereditary breast cancers occur in individuals with germ line variants in various CPGs such as

- High-penetrance genes: *BRCA1*, *BRCA2*, *TP53*, *PTEN*, *STK11*, *CDH1*, *APC*, *MLH1*, *MSH2*
- Moderate-penetrance genes: *ATM*, *CHEK2*, *PALB2*, *BRIP1*
- Low-penetrance genes: *BARD1*, *CDKN2A*, *RAD51*, *RAD51C*, *RAD51D*, *XRCC2*, *NBN*, *FANCA*, *FANCC*, *FANCCM*

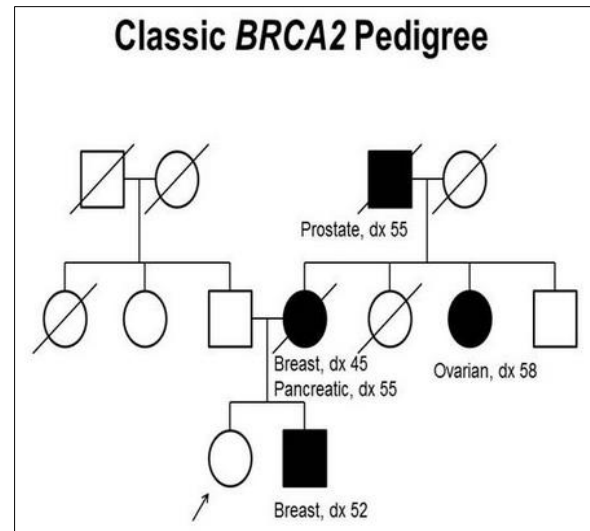
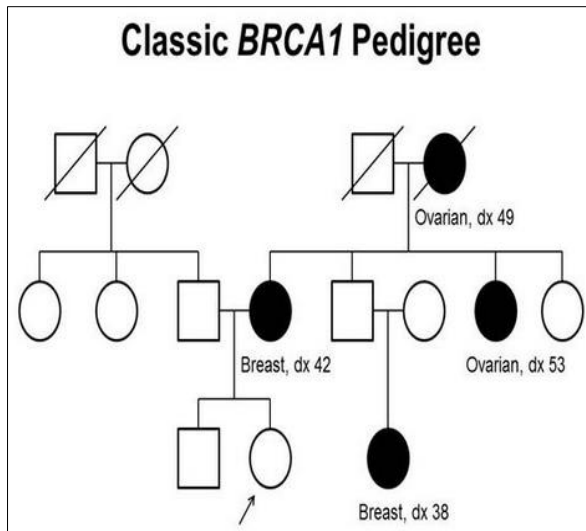
Genetically determined breast cancer syndromes

- Hereditary breast and ovarian cancer syndrome (HBOC) - *BRCA1* and *BRCA2* genes [OMIM 604370, 612555]
- Cowden syndrome (Multiple Hamartoma syndrome) - *PTEN* gene [OMIM 158350]
- Li-Fraumeni syndrome - *TP53* gene [OMIM 151623]
- Peutz-Jegher's syndrome - *STK11* gene [OMIM 175200]
- Lobular breast cancer and hereditary diffuse gastric cancer - *CDH1* gene [OMIM 137215]

OMIM – Online Mendelian Inheritance in Man: http://www.ncbi.nlm.nih.gov/omim Gene Reviews – <i>BRCA1</i> and <i>BRCA2</i> Hereditary Breast and Ovarian Cancer: http://www.ncbi.nlm.nih.gov/books/NBK1247/
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Identifying hereditary breast cancer

The key to identifying individuals who are at risk for a hereditary predisposition to breast cancer lies in obtaining and analyzing a complete and accurate three-generation family history (pedigree). Pedigrees should include detailed medical history of the person seeking consultation (who may or may not be a person affected with breast cancer at the time of consultation), as well as their first-, second- and third-degree maternal and paternal relatives (i.e. children, parents, siblings, grandparents, aunts, uncles, nephews, nieces and first cousins). The pedigree should document the type and primary site of cancer, laterality, age at diagnosis and the current age or, if deceased, the age at death for each affected individual as well as information about other family members. Confirmation of cancer diagnosis through review of medical records, pathology reports or death certificates of family members will be useful in families where the verbal history appear to be unreliable.



When to refer patients for a genetic consultation?

Referral for genetic counseling and testing for individualized cancer risk assessment should be offered to patients who meet any of the following “hereditary breast cancer” criteria:

- Multiple cases of breast and/or ovarian cancer in the family occurring in two or more close relatives:
 - Two 1st degree, or one 1st and one 2nd degree relative with breast cancer <60 yrs and/or ovarian cancer at any age on the same side of the family.
 - Three or more family members (1st or 2nd degree) with breast or ovarian cancer on the same side of the family, any age.
- Patient or 1st degree relative with breast cancer <40 yrs, with or without family history.
- A family member with bilateral breast cancer.
- A family member with both breast and ovarian cancers.
- A family member with primary cancer in both breasts if one or both cancers diagnosed before age 50 years.
- A family member with male breast cancer.
- A family member with ovarian cancer.
- Diagnosis of a hereditary breast cancer syndrome in a family member.
- A family member with an identified *BRCA1* or *BRCA2* mutation.

(First degree relatives - parents, children, siblings; Second degree relatives - grandparents, grandchildren, aunts/uncles, nephews, nieces, half-siblings; Third-degree relatives - first-cousins, great grandparents, great grandchildren).

Predictive Cancer Genetics Steering Committee (PCGSC). Ontario physicians’ guide to referral of patients with family history of cancer to a familial cancer genetics clinic. Toronto, ON: Ontario Medical Association; 2001. Available at: www.oma.org/pcomm/OMR/nov/01genetics.htm. All recommendations are level 2A evidence-based with uniform PCGSC consensus

Genetic counselling for hereditary breast cancer

Genetic counseling allows individuals an opportunity to learn how heredity contributes to cancer risk, understand their personal risk of developing cancer, understand their options for managing their cancer risk and encourages adoption of risk-reducing behaviors that are appropriate for them. All those undergoing genetic testing should be offered comprehensive pre-test and post-test counseling.

Pre-test counseling is a process that includes discussion of personal risks of cancer based on the family history, the possible outcomes of genetic testing, including benefits, risks, limitations of testing and obtaining informed consent prior to testing.

Post-test counseling is a process in which the genetic test results and their significance are discussed, and medical management is reviewed, including screening and treatment options.

Other matters to be discussed during counseling include: privacy and confidentiality of genetic information; potential insurance, employment and social discrimination; adverse psychological reactions; and sharing test results with relatives.

Although *BRCA1* and *BRCA2* mutations are inherited in an autosomal dominant manner, their expression depends on acquiring a second mutation in the normal *BRCA1* or *BRCA2* gene in somatic cells. Although children of mutation carriers are at 50% risk of inheriting the mutation, the age of onset of their cancer is difficult to predict. It is important therefore to explain the difference between inheriting the mutation and development of the cancer to those seeking genetic counseling to help them understand the meaning of a positive test result and discuss with them the estimated lifetime risk of cancer for *BRCA1* and *BRCA2* mutation carriers given below:

Table 1- Estimated lifetime risk for developing cancer in *BRCA1* and *BRCA2* mutation carriers

Type of Cancer	Lifetime risk of developing cancer	
	<i>BRCA 1</i>	<i>BRCA 2</i>
Breast cancer before the age of 50 years	50%	28%
Breast cancer up to the age of 70 years	50 -85%	50 – 85%
Ovarian cancer up to the age of 70 years	40 – 60%	10 – 20%
Male breast cancer	1.2%	Up to 8.9%%
Prostate cancer	8.6% by age 65	15% by age 65 20% lifetime
Pancreatic cancer	1%-3%	2%-7%
Melanoma (cutaneous & ocular)	No increase	Increased Risk

Daly MD: National Comprehensive Cancer Network (NCCN) Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 2. 2017.

Gene Reviews – *BRCA1* and *BRCA2* Hereditary Breast and Ovarian Cancer:

<http://www.ncbi.nlm.nih.gov/books/NBK1247/>.

All recommendations are level 2A evidence-based with uniform NCCN consensus.

Genetic testing

Advances in molecular genetics have led to the identification of numerous genes associated with inherited susceptibility to cancer. Inherited genetic alterations (germ line mutations) can be identified by testing DNA extracted from blood of any person using Next-Generation Sequencing (NGS) cancer gene panels. Identifying the underlying germ line variants using multi-gene cancer panel testing is valuable in guiding treatment decisions and genetic counseling/screening of at-risk family members.

Cancer panel testing for germ line mutations in CPGs is now available in Sri Lanka. Testing is done on DNA extracted from a 5ml sample of venous blood collected to a green top EDTA tube from the patient. The cancer gene panel test that we offer tests 94 genes associated with inherited predisposition to cancer, including genes associated with both common (e.g. breast, ovarian, uterine, colorectal, prostate, thyroid) and rare cancers. It is performed using the Illumina TruSight Cancer® sequencing kit produced by Illumina, Inc., USA. This kit has been developed by Illumina in collaboration with Professor Nazneen Rahman and team at The Institute of Cancer Research (ICR), London, UK (http://www.illumina.com/products/trusight_cancer.html). It provides a rapid and economical solution to single-gene tests as it can analyze multiple genes simultaneously at a lower cost.

The steps involved in genetic testing:

- Test an affected family member FIRST after providing pre-test counseling and obtaining written informed consent to identify the mutation and confirm it.
- If a mutation is found, then other family members, including those who are not affected, can be tested for that mutation.
- Always provide post-test counseling.

Benefits of cancer gene panel testing:

- Clarify risks of hereditary breast cancer.
- Identify individuals who are at increased risk who could benefit from increased cancer surveillance, or measures to decrease risk.
- Identify individuals who may not be at increased risk.
- Simultaneous analysis of multiple cancer predisposition genes allows rapid diagnosis of specific hereditary breast cancer syndromes.
- Saves money and time than single gene testing for patients suspected of having multiple hereditary cancer syndromes.
- A greater likelihood of identifying a hereditary cause for the cancer(s) in patients and/or their families.
- Reduces false negative results.
- Offers treatment guidance once the mutation is identified.
- Identification of the family mutation allows other at-risk healthy family members to be screened with targeted genetic testing to determine their individual risk status.
- Allows for earlier intervention through targeted individualized cancer screening and prevention programs in individuals who are mutation carriers.
- Assists couples in reproductive decision making.

What are the limitations of cancer gene panel testing?

- The test may miss large structural genetic variations. These are usually very rare.

Who should undergo genetic testing?

Breast cancer, with at least one of the following:

- Diagnosed at age ≤ 45 years
- Diagnosed at age ≤ 50 years with
 - Two breast primaries; or
 - ≥ 1 close relative with breast, pancreatic, or prostate cancer
- Diagnosed at age ≤ 60 years with triple negative breast cancer
- Family history of cancer:
 - ≥ 1 close relative with breast cancer diagnosed at age ≤ 50 years
 - ≥ 1 close relative with ovarian cancer
 - ≥ 2 close relatives with breast, pancreatic or prostate cancer; or male breast cancer relative
- Male breast cancer
- Ovarian cancer
- Pancreatic cancer or prostate cancer with:
 - ≥ 1 close relative with ovarian cancer (any age) or breast cancer (age ≤ 50 years); or
 - ≥ 2 close relatives with breast, pancreatic or prostate cancer
- Unaffected individual (family history only):
 - 1st, 2nd-degree relative meeting any of the above criteria;
 - 3rd-degree relative with breast/ovarian cancer and has ≥ 2 relatives with breast/ovarian cancer

Daly MD: National Comprehensive Cancer Network (NCCN) Guidelines for Genetic/Familial High-Risk Assessment: Breast and Ovarian, Version 2. 2017.

Gene Reviews – *BRCA1* and *BRCA2* Hereditary Breast and Ovarian Cancer:
<http://www.ncbi.nlm.nih.gov/books/NBK1247/>.

All recommendations are level 2A evidence-based with uniform NCCN consensus.

Implications of a positive test result:

- Clinical intervention can improve outcomes e.g. risk reduction mastectomy reduces risk of breast cancer and salpingo-oophorectomy reduces risk of ovarian and breast cancer (in premenopausal women).
- Family members at risk can be offered testing and identified.
- Healthy life styles can be reinforced.

Implications of a negative test result:

- Reassures the individual and their family members.

Management Guidelines

The options described below are available for managing the increased cancer risk in *BRCA1* and *BRCA2* mutation carriers:

For women:

- Breast awareness starting at age 18 years
- Clinical breast exam, every 6-12 months, starting at age 25 years
- Breast screening:
 - age 25-29 years, annual breast MRI screening with contrast, or mammogram
 - age 30-75 years, annual mammogram and MRI with contrast
 - age > 75 years, individual basis
- Consider options of risk-reducing mastectomy and/or salpingo-oophorectomy
- Consider trans-vaginal ultrasound starting at age 30-35 years, or CA-125 screening
- Consider risk reduction agents

For men:

- Breast self-exam, starting at age 35 years
- Clinical breast exam, every 12 months, starting at age 35 years
- Prostate cancer screening, starting at age 45 years

For men/women:

- Pancreatic cancer and melanoma screening, based on family history
- Advise about options for prenatal diagnosis and assisted reproduction

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<http://www.ncbi.nlm.nih.gov/books/NBK1247/>.

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STATEMENT OF INTENT

The main purpose of this guideline is to improve the quality of clinical care provided in the health institutions. This guideline is not intended to be construed (understood) or to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns evolve.

These parameters of practice should be considered recommendations only. Adherence to them will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgment regarding a particular clinical procedure or treatment plan must be made by the doctor in light of the clinical data presented by the patient and diagnostic and treatment options available