QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF BREAST CANCER
(2nd Edition)

MINISTRY OF HEALTH MALAYSIA

ACADEMY OF MEDICINE MALAYSIA
KEY MESSAGES

- Breast cancer is the commonest cancer in all ethnic groups and in all age groups in females from the age of 15 years onwards. The overall Age-Standardised Incidence Rate (ASR) was 39.3 per 100,000 populations in 2006 in Malaysia.

- Of the cases diagnosed in 2003, 33.6% were women between 40 and 49 years of age.

- All Chinese women had the highest incidence with an ASR of 46.4 per 100,000 population.

- Triple assessment which consists of clinical assessment, imaging (ultrasound and/or mammography) and pathology (cytology and/or histology) is an established method for the diagnosis of breast cancer.

- The American Joint Committee on Cancer (AJCC) Cancer Staging Manual (7th Edition) has been used for staging of cancers in these guidelines.

- Surgery is the mainstay of treatment for early breast cancer and consists of either breast conserving surgery (BCS) or mastectomy, and assessment of axillary lymph node.

- Breast cancer is recognised as a systemic condition even in early stage of the disease, with a significant risk of distant micro-metastases. As a result, adjuvant chemotherapy has an established role in eradicating these micro-metastases, thus improving survival.

- The diagnosis of breast cancer is undeniably distressing. In addition to the normal reactions to such a diagnosis, many women experience elevated levels of distress as the illness progresses.

- Palliative care aims to maximise the quality of life in the time remaining for the patient with breast cancer.

This Quick Reference provides key messages and a summary of the main recommendations in the Clinical Practice Guidelines (CPG) Management of Breast Cancer (2nd Edition) November 2010.

Detail of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:

- Ministry of Health Malaysia : http://www.moh.gov.my
- Academy of Medicine Malaysia : http://www.acadmed.org.my
**STRATIFICATION OF RISK FACTORS**

<table>
<thead>
<tr>
<th>Low Risk</th>
<th>Moderate Risk</th>
<th>High Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Alcohol consumption</td>
<td>• Increasing age from 40 years old</td>
<td>• Personal history of invasive breast cancer</td>
</tr>
</tbody>
</table>
| • Reproductive factors:  
  o Increasing age at first full term pregnancy > 30 year  
  o Hormone replacement therapy  
  o Oral contraceptive pill usage | • Reproductive factors:  
  o Early menarche (< 12 year old)  
  o Late menopause (> 55 year old)  
  o Nulliparity | • Lobular Carcinoma In Situ (LCIS) and Ductal Carcinoma In Situ (DCIS) |
| • Obesity | • Benign breast disease with proliferation without atypia | • Benign breast disease with atypical hyperplasia |
| | • Dense breast | • Ionising radiation from treatment of breast cancer, Hodgkin’s disease, etc. |
| | | • Carrier of BRCA1 and 2 genetic mutation |
| | | • Significant family history i.e. 1st degree family with breast cancer |

**SCREENING**

Mammography may be performed biennially in women from 50 – 74 years of age

Breast cancer screening using mammography in low & intermediate risk women aged 40 – 49 years old should not be offered routinely

Women aged 40 – 49 years should not be denied mammography screening if they desire to do so

BSE is recommended for raising awareness among women at risk rather than as a screening method

**CRITERIA FOR EARLY REFERRAL**

- Age > 40 years old women presenting with a breast lump
- Lump > 3 cm in diameter at any age
- Clinical signs of malignancy
PATHOLOGY REPORTING

An adequate pathology report for breast cancer must have the following minimum parameters:

- Location (side and quadrant), maximum diameter, multifocality
- Tumour type (histology)
- Histological grade
- Lymph node involvement and total number of nodes examined
- Resection margins
- Lymphovascular invasion
- Non-neoplastic breast changes
- Hormone receptor status [estrogen-receptor/progesterone receptor (ER/PR)]
- HER-2 assessment

CONTRAINDICATIONS OF BREAST CONSERVING SURGERY (BCS)

- The ratio of the size of the tumour to the size of the breast and location of the tumour would not result in acceptable cosmesis
- Presence of multifocal/multicentric disease clinically or radiologically
- Conditions where local radiotherapy is contraindicated (such as previous radiotherapy at the site, connective tissue disease and pregnancy)

SENTINEL LYMPH NODE BIOPSY (SLNB)

SLNB should not be carried out in women with clinically involved nodes. The safety and efficacy of the procedure for breast cancer > 3 cm or multifocal disease has yet to be demonstrated in randomised controlled trials

SLNB may be offered to the following:

- Unifocal tumour of ≤ 3 cm
- Clinically non-palpable axillary nodes

SLNB should only be performed by surgeons trained and experienced in the technique

Dual technique with isotope and blue dye in performing the SLNB is preferred
SYSTEMIC THERAPY

Adjuvant chemotherapy should be considered in all patients with early breast cancer

Adjuvant chemotherapy should be offered to all women with any of the following risk factors especially in pre-menopausal women:

- One or more positive axillary lymph nodes
- ER and PR negative disease
- HER2 3+ disease
- Tumour size > 2 cm
- Grade 3 disease

ENDOCRINE THERAPY

Tamoxifen should be offered to all women with ER positive invasive early breast cancer

RADIOThERAPY

Adjuvant radiotherapy should be offered to the following post-mastectomy patients with:

- ≥ 4 lymph nodes
- Positive margin

Adjuvant radiotherapy can be offered to the following post-mastectomy patients with:

- 1 - 3 lymph nodes
- Node negative disease with high risk of recurrence with two or more risk factors such as presence of lymphovascular invasion, tumours > 2 cm, grade 3 tumours, close resection margin (< 2 mm) and premenopausal status
- T3 and T4 tumours

All patients with post-BCS should be offered adjuvant radiotherapy for both invasive breast cancer and DCIS

PSYCHOLOGY SUPPORT

Women diagnosed with breast cancer should be screened for emotional distress

Validated self-assessment psychological tests such as Hospital Anxiety and Depression Scale (HADS), administered by a trained personnel may be used to screen for emotional distress at the time of diagnosis

All patients with breast cancer should be assigned to a breast care nurse who will support them throughout the diagnosis, treatment and follow up
### FOLLOW UP

Regular follow up should be scheduled as follows:

- three monthly for the first year
- then six-monthly for five years
- then an annual review thereafter

Annual mammography should be offered to all patients with early breast cancer who has undergone treatment to detect recurrence or contra-lateral new breast cancer

### LIFESTYLE MODIFICATION

Diet high in fibre and low in fat together with physical activity should be advised in women after diagnosis of breast cancer

### FAMILIAL BREAST CANCER

Women whose family history is associated with an increased risk for deleterious mutations in BRCA1, BRCA2 or TP53 genes should be referred for genetic counselling and evaluation for genetic testing. This includes individuals with affected blood relatives with any one of the following family history patterns:

- 3 or more individuals with breast or ovarian cancer at any age
- 2 or more individuals with breast cancer, 1 of whom was diagnosed at ≤ 50 years old
- 1 individual with breast cancer diagnosed at ≤ 40 years old
- 1 individual with both breast and ovarian cancer at any age
- 1 individual with bilateral breast cancer at any age
- 1 individual with male breast cancer
- 2 or more individuals with ovarian cancer at any age
- Family history of breast cancer in combination with other BRCA-related cancers such as pancreas, prostate and oesophageal cancers
- Family history of early onset breast cancer in combination with other TP53-related cancers such as sarcomas and multiple cases of childhood cancers
ALGORITHM FOR TREATMENT OF OPERABLE BREAST CANCER

**OPERABLE BREAST CANCER**

- **Surgery**
  - Breast Conserving Surgery\(^1\), axillary surgery
  - Mastectomy Axillary surgery ± Reconstruction

**Risk Stratification**

<table>
<thead>
<tr>
<th>Low risk</th>
<th>Intermediate risk</th>
<th>High risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0 and all of the following criteria:</td>
<td>pN0 and at least 1 further criteria:</td>
<td>pN+ (N(_1)-3) and HER2 over-expression or pN+ (N (\geq) 4)</td>
</tr>
<tr>
<td>Age</td>
<td>size of tumour &gt; 2 cm</td>
<td></td>
</tr>
<tr>
<td>Tumour histology (lymphovascular invasion, grade, extensive in-situ component and tumour type such as lobular carcinoma)</td>
<td>Grade 2/3</td>
<td></td>
</tr>
<tr>
<td>Which margin is approximated by tumour (smaller margins may be acceptable for deep and superficial margins)</td>
<td>vessel invasion present</td>
<td></td>
</tr>
<tr>
<td>Extent of cancer approaching the margin</td>
<td>HER2 over-expression</td>
<td></td>
</tr>
<tr>
<td>(\geq 35) years old</td>
<td>age &lt; 35 years old</td>
<td></td>
</tr>
<tr>
<td></td>
<td>or pN+(N1-3) and HER2-negative</td>
<td></td>
</tr>
</tbody>
</table>

**Indication for adjuvant radiotherapy**

- 4 or more lymph nodes
- Positive margin
- \(\pm 1-3\) lymph nodes
- \(\pm\) Node negative disease with high risk of recurrence with 2 or more risk factors such as:
  - presence of lymphovascular invasion, tumours greater than 2 cm, grade 3 tumours, close resection margin (< 2 mm) and premenopausal status

\(^1\) If the surgical margin is \(\geq 2\) mm, several factors should be considered in determining whether re-excision is required. These includes:

- Age
- Tumour histology (lymphovascular invasion, grade, extensive in-situ component and tumour type such as lobular carcinoma)
- Which margin is approximated by tumour (smaller margins may be acceptable for deep and superficial margins)
- Extent of cancer approaching the margin

\(^2\) Risk Stratification

- Low risk
- Intermediate/ high risk\(^2\)
- Low risk
- Intermediate/ high risk\(^2\)

\(^3\) Indication for adjuvant radiotherapy
ALGORITHM FOR TREATMENT OF LOCALLY ADVANCED BREAST CANCER

LOCALLY ADVANCED BREAST CANCER

Operable

Inoperable

Mastectomy & axillary surgery

Neo-adjuvant Chemotherapy

Chemotherapy ± Herceptin

Operable

Inoperable

Chemotherapy ± Herceptin

Breast Conserving Surgery

Mastectomy & surgery

Operable

Inoperable

Radiotherapy ± Hormone Therapy

Radiotherapy ± Hormone Therapy

Surgery

Individualised Treatment Palliative Care

Radiotherapy ± Hormone Therapy

CLINICAL PRACTICE GUIDELINES SECRETARIAT
Health Technology Assessment Section, Medical Development Division
Ministry of Health Malaysia, 4th Floor, Block E1, Parcel E, 62590 Putrajaya
Tel: 603 8883 1246, e-mail: htamalaysia@moh.gov.my