INTRODUCTION

Breast cancer is a malignancy arising either from the breast epithelium (Carcinoma) or breast stroma (Sarcoma). Epithelial malignancy is the most common cause of cancer in women accounting for one third of female cancers. It also affects the male breast though incidence is lower. 10% of breast cancers can be linked directly to germ line mutations. Due to improved treatment and early detection, mortality rate from breast cancer has substantially reduced.

NORMAL RANGE

<30.0 U/mL

SUBTYPES OF BREAST CANCER

There are 5 subtypes of breast cancer based on gene expression profiling.

Luminal A:
- Expresses Cytokeratins 8 & 18
- Highest levels of Estrogen receptor (ER) expression
- Low grade tumors
- Most likely to respond to endocrine therapy
- Less responsive to chemotherapy
- Good prognosis

Luminal B:
- Origin from luminal epithelium
- Gene expression pattern different from Luminal A
- Bad prognosis

Normal breast like:
- Gene expression resembles non-malignant normal breast epithelium
- Bad prognosis

HER2 amplified:
- Amplification of HER2 gene on chromosome 17q
- Poor prognosis
- Clinical outcome improving due to availability of drugs like Herceptin

Basal:
- ER, PR & HER2 negative tumors (Triple negative)
High grade tumors
Express Cytokeratins 5/6 & 17, p63, EGFR & Vimentin
Usually BRCA mutation detected

**CLINICAL USE**
- An aid in the management of Breast cancer patients. It is useful in monitoring therapy and progression in Metastatic Breast cancer patients. A significant increase in levels must be at least 25% that correlates with disease progression in 90% of the patients. A decrease of at least 25% in levels correlates with regression of the disease in 78% of patients
- Predict recurrence in patients with stage II / III Breast carcinoma

<table>
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<tr>
<th>DISEASE</th>
<th>PERCENTAGE POSITIVITY OF CA 15.3</th>
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<td>Primary Breast Cancer</td>
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<td>Metastatic Breast Cancer</td>
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<td>Pancreatic Cancer</td>
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**INTERPRETATION**
Increased Levels
- Approximately 80% metastatic breast cancer
- Pancreas / Lung / Ovary / Colorectal / Liver cancers with low specificity

**HIGH RISK FACTORS FOR BREAST CANCER**
- Increased age
- Female gender
- Race
- Pre-existing benign breast disease
- Family history of breast / ovarian cancer
- Exposure to radiation
- Environmental factors
- Increased calorie intake
- Moderate alcohol intake
- Long term Hormone Replacement Therapy (HRT)
Algorithm Of Breast Mass Palpation

Premenopausal Patient

Questionable Mass “thickening”

Reexamine follicular phase menstrual cycle

Mass gone

Routine Screening

Dominant Mass

Mass persists

Aspiration

Solid Mass

Suspicious

Mammogram

“Benign”

Management by “triple diagnosis” or Biopsy

Postmenopausal Patient (With dominant Mass)

Cyst

Routine Screening

Biopsy

“Benign”

Management by “triple diagnosis” or Biopsy
LABORATORY DIAGNOSIS

The diagnosis of breast cancer is made by –

- Mammography / Ultrasound
- Biopsy & histologic evaluation
- Fine Needle Aspiration Cytology (FNAC)
- Immunohistochemistry for Estrogen receptor (ER), Progesterone receptor (PR) & HER2
- BRCA1 & BRCA2 screening in patients with family history of breast cancer

LIMITATIONS

- This test is not recommended to screen Breast cancer in the general population. However it has been observed that increased levels may occur 9 months before clinical evidence of disease.
- False negative / positive results are observed in patients receiving mouse monoclonal antibodies for diagnosis or therapy.
- Patients with confirmed Breast cancer may show normal pre-treatment CA 15.3 levels. Hence this assay, regardless of level, should not be interpreted as absolute evidence for the presence or absence of malignant disease. The assay value should be used in conjunction with findings from clinical evaluation and other diagnostic procedures.