Introduction

The breast is the most frequent site of cancer in women (excluding skin cancer) and cause 20% of cancer deaths in women ranking the second to lung cancer in the number of deaths in women ***(American Cancer Society; 2004).***

In Egypt, breast cancer is number one among the female malignancies, and number 10 among the male malignancies ***(Elattar; 2003 and Omar, et al; 2003).*** It is number three ranking after urinary bladder tumors and malignant lymphoma. The relative frequency of breast cancer in relation to total malignancies was 19% ***(Elattar, et al; 2003).***

While the incidence rate for breast cancer rose 24% in U.S.A., the progress in both early detection and treatment of breast cancer has resulted in decreasing mortality rates in most segments of the population during the 1990s. More than 90% of breast cancers are now diagnosed at localized and regional stages. Thus, five-year survival rates are increased from 79% to 97% ***(American Cancer Society; 2004)***.

Internationally there is great variation in incidence and mortality with the highest rates in the Western and developed countries and lowest rates in the Eastern and non-developed countries. Breast cancer is very rare before age 20 and is rarely diagnosed in women younger than age 25. Past that age, the incidence rises steadily to reach a peak around the age of menopause. The rate of increase is lessened after menopause, but older women are still at increasing risk over time ***(McPherson, et al; 2000)***.

Neoplasms may arise in ductal epithelium, lobules, or the stroma. However, the majority of cancers arise in the ducts. Infiltrating or invasive ductal cancer is the most common histologic type of breast

cancer, comprising 70% to 80% of all cases ***(American Joint Committee on Cancer; 2002).***

It is generally accepted that important prognostic factors in breast cancer include the size of the primary breast tumor, the histologic type, the histologic grade, the presence or absence of regional/axillary lymph node metastases (included in the TNM staging system), the presence or absence of distant metastases (included in the TNM staging system), and the presence or absence of estrogen receptors and progesterone receptors. Research for other prognostic factors is ongoing with the goal to predict aggressiveness and response to treatment ***(Judy, et al; 2004).***

Neoplastic cells form only one part of a complex network of cell types that make up a breast tumor. The normal cell types that make up the non-neoplastic components of tumors include fibroblasts, endothelium, and inflammatory cells, such as tumor-associated macrophages (TAMs) which could be detected by CD68 ***(Dabiri, et al; 2004).*** TAMs have the potential to carry out both anti- and protumor activities. In their antitumor role, TAMs can present tumor antigens to cytotoxic T-cells and are capable of being directly cytotoxic to neoplastic cells. Conversely, TAMs are also able to promote tumor growth directly by secreting breast tumor mitogens, such as epidermal growth factor, and indirectly by stimulating tumor angiogenesis and metastasis. Recent studies have indicated that in breast cancers the protumor role of TAMs is dominant ***(Leek and Harris, 2002).***

Metastasis of breast cancer occurs primarily through the lymphatic system, and the extent of lymph node involvement is a key prognostic factor for the disease ***(Skobe, et al, 2001).*** Previous study shows that tumor-associated macrophages (TAMs) are related to lymphatic

metastasis and may play a major role in peritumoral lymphatic neoangiogenesis and lymphatic metastasis ***(Feng, et al; 2004)***

Angiogenesis and the cell proliferation index can predict the prognosis of invasive breast carcinoma. Angiogenesis can be studied by using antibodies against VEGF-R ***(Gasparini, 2000)***, CD34 ***(van de Rijn & Gilks; 2004)***, CD31 ***(Dales, et al; 2004),*** factor VIII antigen. Cellular proliferation may be quantitated using diverse methodologies: mitotic index ***(Kato, et al***; ***2002 and Manders, et al; 2003)***, proliferating cell nuclear antigen (PCNA) ***(Kato, et al; 2003)***, AgNOR or using antibodies against proliferation-associated nuclear antigen Ki67 ***(Cao, 2004)***.

CD34 was initially described as being a useful adjunct in the diagnosis of vascular tumors ***(Traweek, et al; 1991)*** but subsequently was found to be a marker of solitary fibrous tumor ***(van de Rijn, et al; 1994)***. This was followed by a number of publications reporting the presence of CD34 in wide variety of soft tissue tumors ***(Kindblom, et al; 1998, Natkunam, et al; 2000 and van de Rijn & Gilks; 2004).***

CD34 is a heavily glycosylated type-1 transmembrane molecule that can be phosphorylated by a variety of kinases including protein kinase C and tyrosin kinase. Angiogenesis can be evaluated by measuring microvessel density (MVD) that can be assessed by visual quantitification of stained microvessels with anti-CD34 monoclonal antibody which is a specific MVD marker ***(Suda, et al; 1992 and Mineo, et al; 2004).***