ROLE OF PET/CT SCAN IN THE ASSESSMENT OF PRIMARY AND LOCO REGIONAL RECURRENT BREAST CANCER

Thesis

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List of Abbreviations

Abb.	Full term
ACS	American Cancer Society
BGO	Bismuth germinate
BPA	Bisphenol A
CC	Cranial-caudal
ceCT	Contrast-enhanced CT
CT	Computed tomography
DCIS	Ductal carcinoma in situ
FDG PET	^{18}F-fluoro-2-deoxy-d-glucose positron emission tomography
FNA	Fine-needle aspiration
GLUT	Glucose transporters
GSO	Gadolinium silicate
HRT	Hormone replacement therapy
IBC	Inflammatory breast cancer
ITCs	Isolated tumor cell clusters
LCIS	Lobular carcinoma in situ
LM	Latero-medial
LNs	Lymph nodes
LSO	Lutetium oxyorthosilicate
ML	Medio-lateral
MLO	Medio-lateral-oblique
MM	Mammography
MR	Magnetic resonance
MRI	Magnetic resonance imaging
NOS	Not otherwise specified
NST	No special type
PET	Positron emission tomography
PET/CT	Positron emission tomography/computed tomography

List of Abbreviations Cont...

Abb.	Full term
RT-PCR	Reverse transcriptase/polymerase chain reaction
SLNB	Sentinel lymph node biopsy
SUV	Standardized Uptake Value
SUV_{max}	Maximum standardized uptake value
TLR	Tumor-to-liver-ratio
TNBC	Triple-negative breast cancer
TNM	Tumor-nodes-metastasis
US	Ultrasonography

INTRODUCTION

Breast cancer is the most common type of cancer and the second leading cause of cancer-related death among women. It affects more than 1 million women worldwide. The number of cases worldwide has significantly increased; this could be attributed to modern lifestyle ***(Abdulrahman and Rhman, 2012; Taghipour et al., 2016).***

Despite the increasing incidence of breast cancer in recent decades, mortality rates are decreasing because of earlier diagnosis and new treatment strategies that incorporate the molecular impact of breast cancer ***(Ekmekcioglu et al., 2013).***

Outcomes for breast cancer vary depending on the cancer type, extent of disease, and patient's age. However it is still with poorer prognosis in developing countries when compared to developed countries. Approximately 30% of patients relapse within 15 years after initial treatment ***(Ferlay et al., 2012).***

Early diagnosis and accurate follow-up of these patients are important for efficient patient management. In addition; early diagnosis of recurrent breast cancer is important for planning future therapeutic strategies which, if initiated without delay, aim either to cure or to prolong disease-free survival and to improve the quality of life of patients with cancer ***(Israel and Kuten, 2007).***

Predicting the prognosis of breast cancer is very important for determining the direction of treatment; the conventional prognostic factors include histological type, tumor nuclear grade, tumor size, and preoperative tumor-nodes-metastasis (TNM) staging, hormone receptor and immunohistochemical molecular markers in the specimens ***(Choi et al., 2012).***

Although the identification of these prognostic factors has led to better responses and improved overall survival, continued research is required to add to the repertoire of reliable prognostic factors ***(Ekmekcioglu et al., 2013).***

Standard imaging techniques of breast cancer diagnosis include X-ray mammography (MM), ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI). Nuclear medicine techniques are also playing an increasing role in diagnosing and staging of breast cancer. In the past only bone scintigraphy was used for follow-up of women with breast cancer to detect bone metastases at an early stage. Other non-radiological methods of diagnosis included clinical and physical examination, Laboratory investigations of tumor markers and confirmatory histopathological examination ***(Lind et al., 2004).***

Several studies and systematic reviews were carried out to evaluate and compare the accuracy of the different

radiographic methods in detection of primary and recurrent breast cancer. ***(Groheux et al., 2013)***

In 1990,s; ^{18}F-fluoro-2-deoxy-d-glucose positron emission tomography (^{18}F-FDG PET) was introduced in clinical oncology. It has been shown to be an effective and accurate imaging technique for a variety of tasks in breast cancer diagnosis, lymph node assessment, staging and restaging of recurrent and metastatic disease and treatment response monitoring ***(Czernin et al., 2002).***

^{18}F-FDG PET is an effective whole-body imaging technique; its diagnostic value is based on the detection of metabolic changes preceding structural findings. However, ^{18}F-FDG PET is said to be of limited value in the characterization of primary breast lesions owing to its moderate sensitivity compared to other diagnostic modalities such as MRI. On the other hand, the number of involved lymph nodes and the presence or absence of micro metastatic disease was claimed to be not sufficiently determined by ^{18}F-FDG PET alone ***(Heinisch et al., 2003).***

A new promising modality for the early yet accurate detection of relapsing cancer breast is the ^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography/ computed tomography scan (^{18}F-FDG PET/CT). CT is considered one of the primary methods of investigation in oncology because of its low cost, widespread availability and providing high-resolution

anatomic details but may underestimate the actual tumor burden by overlooking small tumor clusters especially in areas of distorted anatomy after treatment. ^{18}F-FDG PET/CT provides fused images that demonstrate the complementary roles of functional and anatomic assessments in the diagnosis of cancer recurrence through the precise localization of suspected ^{18}F-FDG foci and their characterization as malignant or benign ***(Israel and Kuten, 2007).***

In contrast, some studies have underestimated the role and accuracy of ^{18}F-FDG PET/CT techniques in diagnosing primary or recurrent breast malignancy when compared with other conventional modalities as sonomammography and MRI ***(Lim et al., 2007; Groheux et al., 2013).***

^{18}F-FDG PET/CT is a functional modality that indirectly represents the biological characteristics of cancer, but there are few studies exploring the association between it and the prognostic factors of breast cancer such as tumor size, tumor type, grade, hormonal receptor status and immunohistochemical molecular markers ***(Nakajo et al., 2010).*** Hence, our study attempts to evaluate this mutual association by comparing the results of ^{18}F-FDG PET/CT images of the biopsy proven malignant breast lesions and some of these prognostic factors.

AIM OF THE WORK

- To study the accuracy of ^{18}F-fluoro-2-deoxy-D-glucose positron emission tomography/ computed tomography scan (^{18}F-FDG PET/CT) in diagnosis of primary and loco regional recurrent breast cancer compared with histopathological results.
- To investigate the prognostic value of ^{18}F-FDG PET/CT in breast cancer by calculating the maximum standardized uptake value (SUV_{max}) of the biopsy proven malignant breast cancer and correlating the results with some of the prognostic parameters of breast cancer via a prospective study conducted on breast cancer patients presented to Ain Shams University hospitals.

REVIEW OF LITERATURE

Breast carcinoma is the most common cancer in women with an incidence highest in the 40–55 age range ***(Ekmekcioglu et al., 2013).***

Despite major progress in surgical treatment, radiotherapy, and adjuvant chemotherapy protocols, breast cancer's incidence is still on the rise. The survival of patients suffering from breast cancer is strikingly different according to local recurrence and distant metastases being the two most important prognostic factors which can change the intention of therapy from curative to palliative. Thus, it became critical to detect these prognostic factors in the follow-up of women with breast cancer ***(Pan et al., 2010).***

The diagnosis of breast cancer is based on clinical examination combined with radiological imaging and is confirmed by histopathological assessment ***(Lind et al., 2004).***

Chapter 1

BREAST ANATOMY

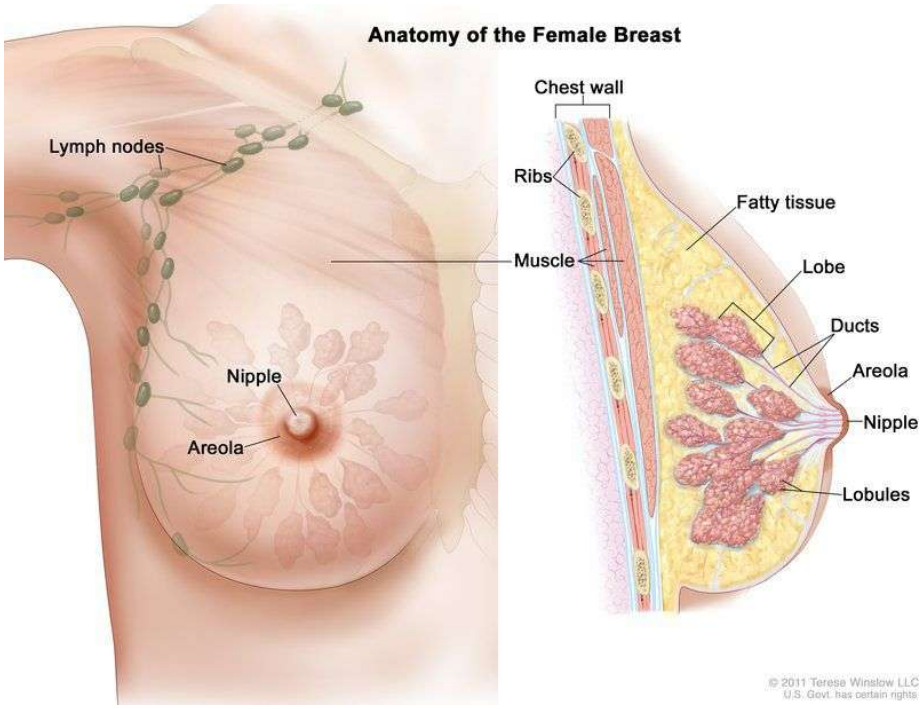

Figure (1): Longitudinal cut section of breast layers ***(Habib et al., 2017).***

The Female breast is composed of skin, subcutaneous tissue, breast glandular and ductal tissue. The breast has an anatomic boundaries from the level of the second or third rib superiorly to the inframammary fold at the sixth rib inferiorly, and from the lateral border of the sternum medially to the midaxillary line laterally ***(Sonali and Richard, 2011).***

Pectoralis major muscle nearly underlies two thirds of the breast, and remainder of the breast contacts with the