

World Journal of *Radiology*

World J Radiol 2017 July 28; 9(7): 295-320



MINIREVIEWS

- 295 Interventional radiology treatment for pulmonary embolism
De Gregorio MA, Guirola JA, Lahuerta C, Serrano C, Figueredo AL, Kuo WT

ORIGINAL ARTICLE**Retrospective Study**

- 304 Incidental extravascular findings in computed tomographic angiography for planning or monitoring endovascular aortic aneurysm repair: Smoker patients, increased lung cancer prevalence?
Mazzei MA, Guerrini S, Gentili F, Galzerano G, Setacci F, Benevento D, Mazzei FG, Volterrani L, Setacci C

SYSTEMATIC REVIEWS

- 312 Preoperative [18]fluorodeoxyglucose-positron emission tomography/computed tomography in early stage breast cancer: Rates of distant metastases
Vinh-Hung V, Everaert H, Farid K, Djassemi N, Baudin-Veronique J, Bougas S, Michailovich Y, Joachim-Contaret C, Cécilia-Joseph E, Verschraegen C, Nguyen NP

ABOUT COVER

Editorial Board Member of *World Journal of Radiology*, Ozgur Oztekin, MD, Associate Professor, Radiology Department, Tepecik Research and Education Hospital, 35540 Izmir, Turkey

AIM AND SCOPE

World Journal of Radiology (*World J Radiol*, *WJR*, online ISSN 1949-8470, DOI: 10.4329) is a peer-reviewed open access academic journal that aims to guide clinical practice and improve diagnostic and therapeutic skills of clinicians.

WJR covers topics concerning diagnostic radiology, radiation oncology, radiologic physics, neuroradiology, nuclear radiology, pediatric radiology, vascular/interventional radiology, medical imaging achieved by various modalities and related methods analysis. The current columns of *WJR* include editorial, frontier, diagnostic advances, therapeutics advances, field of vision, mini-reviews, review, topic highlight, medical ethics, original articles, case report, clinical case conference (clinicopathological conference), and autobiography.

We encourage authors to submit their manuscripts to *WJR*. We will give priority to manuscripts that are supported by major national and international foundations and those that are of great basic and clinical significance.

INDEXING/ABSTRACTING

World Journal of Radiology is now indexed in PubMed, PubMed Central, and Emerging Sources Citation Index (Web of Science).

FLYLEAF

I-III Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Ya-Jing Lu*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Fang-Fang Ji*
Proofing Editorial Office Director: *Jin-Lai Wang*

NAME OF JOURNAL
World Journal of Radiology

ISSN
 ISSN 1949-8470 (online)

LAUNCH DATE
 January 31, 2009

FREQUENCY
 Monthly

EDITORS-IN-CHIEF
Kai U Juergens, MD, Associate Professor, MRT und PET/CT, Nuklearmedizin Bremen Mitte, ZEMODI - Zentrum für morphologische und molekulare Diagnostik, Bremen 28177, Germany

Edwin JR van Beek, MD, PhD, Professor, Clinical Research Imaging Centre and Department of Medical Radiology, University of Edinburgh, Edinburgh EH16 4TJ, United Kingdom

Thomas J Vogl, MD, Professor, Reader in Health Technology Assessment, Department of Diagnostic and Interventional Radiology, Johann Wolfgang Goethe University of Frankfurt, Frankfurt 60590,

Germany

EDITORIAL BOARD MEMBERS
 All editorial board members resources online at <http://www.wjnet.com/1949-8470/editorialboard.htm>

EDITORIAL OFFICE
 Xiu-Xia Song, Director
World Journal of Radiology
 Baishideng Publishing Group Inc
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: editorialoffice@wjnet.com
 Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLISHER
 Baishideng Publishing Group Inc
 7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
 Telephone: +1-925-2238242
 Fax: +1-925-2238243
 E-mail: bpgoffice@wjnet.com
 Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjnet.com>

PUBLICATION DATE
 July 28, 2017

COPYRIGHT
 © 2017 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
 All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
<http://www.wjnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.f6publishing.com>

Preoperative [18]fluorodeoxyglucose-positron emission tomography/computed tomography in early stage breast cancer: Rates of distant metastases

Vincent Vinh-Hung, Hendrik Everaert, Karim Farid, Navid Djassemi, Jacqueline Baudin-Veronique, Stefanos Bougas, Yuriy Michailovich, Clarisse Joachim-Contaret, Elsa Cécilia-Joseph, Claire Verschraegen, Nam P Nguyen

Vincent Vinh-Hung, Stefanos Bougas, Department of Radiation Oncology, University Hospital of Martinique, Fort-de-France 97200, Martinique

Hendrik Everaert, Department of Nuclear Medicine, Universitair Ziekenhuis Brussel, Brussels 1090, Belgium

Karim Farid, Department of Nuclear Medicine, University Hospital of Martinique, Fort-de-France 97200, Martinique

Navid Djassemi, Ross University School of Medicine, Miramar, FL 33027, United States

Jacqueline Baudin-Veronique, Cancer Research Department, University Hospital of Martinique, Fort-de-France 97200, Martinique

Yuriy Michailovich, Cancer Control Department, National Cancer Institute, Kyiv 03022, Ukraine

Clarisse Joachim-Contaret, Cancer Registry of the Martinique, Fort-de-France 97200, Martinique

Elsa Cécilia-Joseph, Biostatistics, Sciences Department, Schoelcher Campus of the University of the French West Indies, 97233 Schoelcher, Martinique

Claire Verschraegen, Department of Medical Oncology, Ohio State University Comprehensive Cancer Center, Columbus, OH 43210, United States

Nam P Nguyen, Department of Radiation Oncology, Howard University, Washington, DC 20060, United States

Author contributions: Vinh-Hung V and Nguyen NP conceptualized and designed the review; Nguyen NP carried out the analysis and drafted the initial manuscript; Cécilia-Joseph E reviewed the statistics; Vinh-Hung V, Everaert H, Farid K, Djassemi N, Baudin-Veronique J, Bougas S, Michailovich Y, Joachim-Contaret C, Cécilia-Joseph E and Verschraegen C contributed to the literature search, interpretation of the data, and critical revisions; all

authors reviewed and approved the final manuscript as submitted.

Conflict-of-interest statement: The authors declare no conflicts of interests for this article.

Data sharing statement: No additional data are available.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Correspondence to: Vincent Vinh-Hung, MD, PhD, Chair, Department of Radiation Oncology, University Hospital of Martinique, Bld Pasteur, Fort-de-France 97200, Martinique. vincent.vinh-hung@chu-martinique.fr
Telephone: +596-696-542019

Received: March 28, 2017

Peer-review started: March 29, 2017

First decision: April 18, 2017

Revised: May 20, 2017

Accepted: June 19, 2017

Article in press: June 20, 2017

Published online: July 28, 2017

Abstract

AIM

To investigate rates of distant metastases (DM) detected with [18]fluorodeoxyglucose-positron emission

tomography/computed tomography (¹⁸FDG-PET/CT) in early stage invasive breast cancer.

METHODS

We searched the English language literature databases of PubMed, EMBASE, ISI Web of Knowledge, Web of Science and Google Scholar, for publications on DM detected in patients who had ¹⁸FDG-PET/CT scans as part of the staging for early stages of breast cancer (stage I and II), prior to or immediately following surgery. Reports published between 2011 and 2017 were considered. The systematic review was conducted according to the PRISMA guidelines.

RESULTS

Among the 18 total studies included in the analysis, the risk of DM ranged from 0% to 8.3% and 0% to 12.9% for stage I and II invasive breast cancer, respectively. Among the patients with clinical stage II, the rate of occult metastases diagnosed by ¹⁸FDG-PET/CT was 7.2% (range, 0%-19.6%) for stage II A and 15.8% (range, 0%-40.8%) for stage II B. In young patients (< 40-year-old), ¹⁸FDG-PET/CT demonstrated a higher prevalence of DM at the time of diagnosis for those with aggressive histology (*i.e.*, triple-negative receptors and poorly differentiated grade).

CONCLUSION

Young patients with poorly differentiated tumors and stage II B triple-negative breast cancer may benefit from ¹⁸FDG-PET/CT at initial staging to detect occult DM prior to surgery.

Key words: Breast cancer; Early stage; Staging workup; Distant metastases; [18]fluorodeoxyglucose-positron emission tomography/computed tomography scan

© **The Author(s) 2017.** Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: This systematic review identifies groups of patients with early stage breast cancer who might benefit most from [18]fluorodeoxyglucose-positron emission tomography/computed tomography (commonly known as ¹⁸FDG-PET/CT) scan at initial staging, prior to surgery.

Vinh-Hung V, Everaert H, Farid K, Djassemi N, Baudin-Veronique J, Bougas S, Michailovich Y, Joachim-Contaret C, Cécilia-Joseph E, Verschraegen C, Nguyen NP. Preoperative [18]fluorodeoxyglucose-positron emission tomography/computed tomography in early stage breast cancer: Rates of distant metastases. *World J Radiol* 2017; 9(7): 312-320 Available from: URL: <http://www.wjgnet.com/1949-8470/full/v9/i7/312.htm> DOI: <http://dx.doi.org/10.4329/wjr.v9.i7.312>

INTRODUCTION

Breast cancer is the most common cancer in women

worldwide^[1]. Mortality of breast cancer has declined notably in the United States, with death rates in 2012 decreasing 36% from peak rates as a result of improvements in early detection and treatment^[2]. Yet, there remains considerable heterogeneity in the outcomes of early stage breast cancer^[3]. The rate of death at 7 year due to stage I breast cancer was 2.1% in women aged 40 years or younger (as compared to 1.6% in women aged over 50) and was 3.8% in women with negative estrogen receptor status (as compared to 1.1% in those with positive estrogen receptor status)^[3].

There is a large consensus that imaging should be limited to patients with apparent advanced disease or clinical suspicion of metastases^[4-7]. Accordingly, staging scans are seldom performed^[6,8]. The question arises, then, as to whether the excess mortality observed in "early stage" patients^[3] is due to unfavorable biological factors or instead to the initial misclassification as "early stage". We hypothesize that some clinically early stage breast cancer patients could benefit from a formal staging workup.

[18]fluorodeoxyglucose-positron emission tomography (¹⁸FDG-PET) scan is a valuable, well established tool for diagnostic staging in numerous cancer sites^[9-12], as well as for locally advanced breast cancer to detect distant metastases (DM)^[13-15]. Even though PET imaging is more sensitive for detection of loco-regional spread and metastatic disease in breast cancer compared to computed tomography (CT) scan alone, its high cost precludes the routine use of PET scan in clinical practice. Thus, a review of the literature is necessary for future guidelines about the benefit of PET scan in early stage breast cancer.

Standard-of-care for early stage breast cancer is surgery, either alone or followed by adjuvant radiotherapy and/or systemic therapy, depending on the pathologic stage and the type of surgery to be performed. The presence or absence of axillary lymph node metastases in patients with clinically non-palpable lymph nodes is routinely assessed through sentinel lymph node sampling or axillary lymph node dissection. Alternatively, PET scan could be most helpful in assessing the presence of DM in early stage breast cancer, which would preclude first-line surgery^[16]. The prevalence of occult DM diagnosed by PET scan in patients with early stage breast cancer has not been analyzed and was the topic of this literature review. In particular, we sought to identify subsets of early stage breast cancer patients who might benefit most from PET scan, prior to surgery.

MATERIALS AND METHODS

Literature search strategy

Electronic searches were performed in the following databases: PubMed, EMBASE, ISI Web of Knowledge (Web of Science), and Google Scholar. The following terms were explored and used in each database search: "Breast cancer", "surgery", "PET scan", "distant

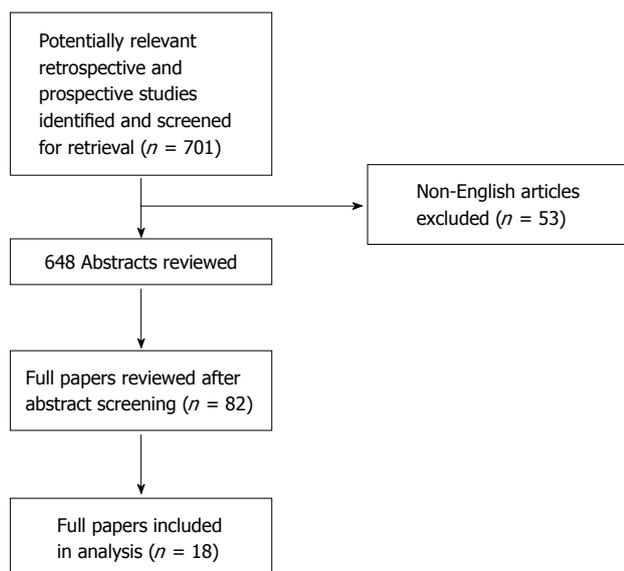


Figure 1 PRISMA flow diagram of the included studies.

metastases”, and “stage I (T1N0M0) and II (T0-2N1M0, T3N0M0)”. All relevant articles were accessed in full-text. The reference lists of relevant papers were then searched for additional publications.

Selection criteria

Eligible studies over the past 6 year (2011-2017) in the present review included those in which patients had ¹⁸F-DG-PET/CT scan as part of their workup prior to or immediately after surgery for histologically-proven breast cancer, regardless of age or sex, and in which the rates of DM were reported by ¹⁸F-DG-PET/CT scan. All patients had clinical stage I or stage II breast cancer. Only studies reported in English were considered. Duplicated studies were excluded.

Data extraction and critical appraisal

Prevalence of DM was extracted from each study and correlated to the disease stage. The influence of age, histology (e.g., lobular vs ductal), tumor grade (e.g., well differentiated vs poorly differentiated), and receptor status on the rate of DM (if reported) was also analyzed using descriptive summaries.

RESULTS

Number of reports analyzed

Figure 1 summarizes the search strategy. A total of 701 reports published between 2011 and 2017 were considered. Out of the 82 full papers that were assessed according to their potential for consisting of information relevant to the review, 18 were found to match the selection criteria and were selected for study inclusion. ¹⁸F-DG-PET/CT scanning had been performed in addition to the clinical staging with or without conventional imaging in those 18 studies, either through a retrospective review or within a prospective protocol.

As none of the studies was randomized, bias could not be excluded. Publications reviewing patients with early stage invasive breast cancer were included.

Prevalence of DM diagnosed by ¹⁸F-DG-PET/CT scan according to patient characteristics

Clinical stage: The rates of DM ranged from 0% to 30%^[17-34] for the entire group of reported patients. However, only 9 of the studies correlated DM rates detected by ¹⁸F-DG-PET/CT with the clinical stage^[17,22-24,27,29,31,32,34]. The rate of DM was lowest among studies of patients with invasive lobular cancer compared to studies that had included a mixture of other histologies, such as invasive ductal carcinoma^[18] (Tables 1 and 2).

Overall, the rate of DM for presumed stage I was low for all cancer types but non-negligible, ranging from 0% to 8.3%^[22,27,29,31,32,34]. Among the 9 studies that reported the rate of DM in patients with stage II breast cancer separately, the prevalence ranged from 0% to 12.4%^[17,22,24,27,29,31,32,34]. Patients with large tumors and/or axillary lymph node metastases appeared to be at increased risk of DM; specifically, the rate of DM was 7.2% (range, 0%-19.6%) and 15.8% (range, 0%-40.8%) for stage II A and stage II B, respectively^[17,22,24,27,31,32,34].

Tumor size: Among studies that included a significant proportion of patients with large tumors (T2 and/or T3), the DM rate was higher and ranged from 8% to 8.4%^[18,19], as compared to the range of 1.5% to 4.8% in studies including patients with smaller tumors^[21,23,28]. However, since those latter studies also included a small proportion of patients with stage III disease and did not analyze the metastatic rate in relation to the clinical stage, the correlation between tumor size and DM rate remains unclear.

Nodal status: Patients who presented with N1 disease also presented with a higher risk of having DM. The rate of DM was 6% and 20% for N0 and N1 disease, respectively^[31].

Receptor status: Among the 232 patients with triple-negative breast cancer, the DM rate was 0% and 10.9% for clinical stage I and stage II diseases, respectively, but there was no comparison performed with receptor-positive cases^[32]. Other studies did not report the rates of DM according to receptor status.

Age: Two studies reported the influence of age on DM rate^[27,33]. In the first study, among 134 young patients (< 40-year-old), the DM rate was 5% and 10.9% for clinical stage I and stage II, respectively^[27]. In the second study, among 214 stage I-III patients, the DM rates did not differ significantly between the age groups of < 40-year-old and ≥ 40-year-old^[33]. However, the DM rates in the younger age group were 8% in stage I, 9% in stage II A and 17% in stage II B, equating to 2x's

Table 1 Prevalence of distant metastases in patients with invasive breast cancer who had [¹⁸F]fluorodeoxyglucose-positron emission tomography scan as part of the workup before or immediately after surgery

Ref.	Subjects, n	Stage	Age, median	Histology	Tumor grade	Tumor receptors	Distant metastases	2 nd primaries
Groheux <i>et al</i> ^[17]	131	II: 84 III: 47 T1: 2 T2: 71 T3: 58 N0: 50 N1: 59 N2: 18	NS	IDC: 114 ILC: 8 Other: 9	1: 9 2: 5 3: 53 NS: 4	ER+: 82 HER2+: 30	5.90% (II)	1% (II)
Bernsdorf <i>et al</i> ^[18]	103	T2 or higher	55 (24-81)	IDC: 83 ILC: 14 Other: 6	1: 11 2: 54 3: 37 NS: 1	ER+: 74 HER2+: 22 TN: 13	8%	1.90%
Choi <i>et al</i> ^[19]	154	I: 69 II: 51 III: 21 IV: 13 T1: 89 T2: 51 T3: 14	52 (30-81)	IDC: 141 ILC: 4 Other: 9	NS: 154	NS	8.40%	NS
Garami <i>et al</i> ^[20]	115	T1: 56 T2: 48 NS: 11 N0: 57 N+: 46 NS: 12	55.7	IDC: 92 ILC: 11 Other: 12	1: 16 2: 50 3: 48 NS: 1	ER+: 89 ER-: 26	6.90%	2.60%
Groves <i>et al</i> ^[21]	70	T1: 34 T2: 30 N1: 24	61	IDC: 45 ILC: 10 Other: 5	1: 02 2: 33 3: 25	ER+: 64 HER2+: 15	2.80%	NS
Gunalp <i>et al</i> ^[22]	141	I: 19 II: 100 III: 14	47 (28-78)	NS	2 + 3: 141	NS	5% (I) 30% (II)	NS
Pritchard <i>et al</i> ^[23]	325	T1: 207 T2: 110 T3: 8 N0: 325	56 (28-83)	IDC: 290 ILC: 35	1: 68 2: 158 3: 92	NS	1.50%	NS
Cochet <i>et al</i> ^[24]	142	II: 79 III: 46 IV: 17 T2 or Higher	51 (25-85)	IDC: 128 ILC: 11 Other: 3	1+2: 81 3: 56 NS: 3	ER+/HER2-: 63 HER2+: 33 TN: 31	7.5% (II)	NS
Jeong <i>et al</i> ^[25]	178	N0: 178 T1: 108 T2: 64 T3: 6	54.9 (33-82)	IDC: 145 ILC: 11 DCIS: 12 Other: 10	NS	NS	0%	2.80%
Koolen <i>et al</i> ^[26]	62	I: 35 II: 25 III: 2 T1: 62	59.8 (26-75)	IDC: 58 ILC: 1 Other: 3	1: 21 2: 29 3: 09 NS: 3	ER+/HER2-: 48 TN: 7 HER2+: 7	16%	3%
Riedl <i>et al</i> ^[27]	134	I: 20 II: 91 III: 19	36.2 (22-39)	IDC: 124 ILC: 1 Other: 9	1: 01 2: 23 3: 110	ER+/HER2-: 75 HER2+: 26	5% (I) 10.9% (II)	4%
Zhang <i>et al</i> ^[28]	164	T1: 127 T2: 35 T3: 2 N0: 123 N1: 29 N2: 9 N3: 3	45 (21-70)	IDL: 150 ILC: 14	1: 23 2-3: 141	ER+: 140 HER2+: 18	4.80%	NS
Hogan <i>et al</i> ^[29]	146	I: 8 II: 50 III: 88	57 (34-92)	ILC: 146	NS	ER+/HER2-: 132 HER2+: 8 TN: 5	0% (I) 4% (II)	NS
Krammer <i>et al</i> ^[30]	101	II: 75 III: 15 IV: 11 T1: 7	54	IDC: 80 ILC: 15 Other: 9	1: 05 2: 48 3: 45 NS: 6	ER+: 67 HER2+: 56	15.80%	NS

Nursal <i>et al</i> ^[31]	419	T2: 69	51.5	IDC: 305 ILC: 29 Other: 85	NS	NS	2.9% (I) 12.4% (II)	NS
		T3: 4						
		T4: 5						
		I : 104 II : 315 T1: 127 T2: 270 T3: 20						
Ulaner <i>et al</i> ^[32]	232	I : 23	51 (25-93)	IDC: 217 ILC: 2	2: 8 3: 217 NS: 7	TN: 232	0% (I) 10% (II)	NS
		II : 169						
		III: 40						
Lebon <i>et al</i> ^[33]	214	I : 24	45.2	IDC: 181 ILC: 10 Other: 23	1: 13 2: 68 3: 133	HR+/HER2-: 89 HER2+: 61 TN: 63 NS: 1	8.3% (I) 12.9% (II)	NS
		II : 124						
		III: 66						
Ulaner <i>et al</i> ^[34]	483	I : 36	52.7 (23.6-89.5)	IDC: 414 ILC: 41 Other: 28	1: 5 2: 55 3: 400 NS: 23	ER+: 402 HER2+: 245 TN: 0	2.8% (I) 9.7% (II) 24.1% (III)	1.40%
		II : 331						
		III: 116						

DCIS: Ductal carcinoma *in situ*; ER: Estrogen receptor; ¹⁸FDG-PET: [18]fluorodeoxyglucose-positron emission tomography; HER2: Human epidermal growth factor receptor 2; IDC: Invasive ductal carcinoma; ILC: Invasive lobular carcinoma; NS: Not specified; PR: Progesterone receptor; TN: Triple-negative.

Table 2 Prevalence of occult distant metastases in clinical stage II patients who had [18]fluorodeoxyglucose-positron emission tomography scan as part of a staging workup before or immediately after surgery

Ref.	Subjects, n	Age, median	Distant metastases rate		
			II A	II B	All
Groheux <i>et al</i> ^[17]	84	NS	2.80% (1/36)	8.30% (4/48)	5.95%
Gunalp <i>et al</i> ^[22]	100	51	19.60% (10/51)	40.80% (20/49)	30%
Cochet <i>et al</i> ^[24]	142	51	9.10% (2/22)	7.00% (4/57)	7.60%
Jeong <i>et al</i> ^[25]	70	54.9	0% (0/64)	0% (0/6)	0%
Riedl <i>et al</i> ^[27]	91	36.2	5% (2/44)	17% (8/47)	10.90%
Nursal <i>et al</i> ^[31]	315	51.5	9.50% (19/199)	17.20% (20/116)	12.40%
Ulaner <i>et al</i> ^[32]	169	51	5% (4/82)	15% (13/87)	9.50%
Lebon <i>et al</i> ^[33]	124	45.2	11% (7/64)	15% (9/60)	12.90%
Ulaner <i>et al</i> ^[34]	483	52.7	4.20% (6/143)	13.80% (26/188)	9.70%
All	1578	47.8	7.20% (0%-19.6%)	15.80% (0%-40.8%)	11.40% (0%-12.9%)

¹⁸FDG-PET: [18]fluorodeoxyglucose-positron emission tomography; NS: Not specified.

higher than those found in the first study.

Histologic grade: Histologic grade of the tumor may also be associated with increased risk of developing DM. Among 141 patients with moderate to poorly differentiated invasive breast cancers, the rate of DM was 30% for stage II patients^[22]. However, correlation between tumor histologic grade and DM risk was not investigated in other studies^[17-21,23,24,26-33].

DISCUSSION

This article reviews the role of ¹⁸FDG-PET/CT scan in the detection of DM in patients with early stages (*i.e.*, I and II) of invasive breast cancer. The findings might represent important information applicable to discussions with patients about the utility of the scan. In contrast to stage III breast cancer, the role of ¹⁸FDG-PET/CT scan in identifying patients with clinical stages I and II who are at high risk of DM is

controversial. Even though ¹⁸FDG-PET/CT scan may also be capable of identifying a second primary cancer, its main role in patients with breast cancer is the detection of DM, which could preclude upfront surgery^[16]. Furthermore, the detection of DM could be of critical importance for the correct classification of patients and in the evaluation of treatment outcomes.

As the risk of DM is low in “early stage” asymptomatic breast cancer patients, an expensive imaging study, such as with the ¹⁸FDG-PET/CT scan, is not justified for the staging workup of all patients^[6,35]. However, breast cancer is a heterogeneous disease, with some subgroups of patients at risk of developing DM even at the early stage. Subgroups of breast cancer patients with worse outcome include younger patients^[36] and patients that have tumors with a more aggressive biological profile^[37]. Rare histologic subtypes, such as metaplastic carcinoma of breast and invasive micropapillary carcinoma, are also more frequently associated with poor prognosis because of the high

rate of axillary lymph node involvement and DM^[38,39]. Genomic classification of risk, such as the oncoType DX and Perou's studies, also identified the risk of distant recurrence^[40-42]. Thus, those patients at high risk of systemic spread may benefit from early diagnosis of DM, for which chemotherapy may be initiated in a timely manner and unnecessary surgery may be avoided. The benefit of ¹⁸FDG-PET scan may outweigh its cost in those circumstances.

In patients with clinical stage I breast cancer, regardless of age, tumor grade or aggressive histology, the risk of DM as diagnosed by ¹⁸FDG-PET scan ranged from 0% to 8.3%^[22,27,29,31-34]. This low, though not negligible, metastatic rate has been corroborated in studies with a high proportion of patients with T1 and N0 disease^[21,23]. Even though the number of patients with stage I disease in those studies was small, preliminary evidence suggested that ¹⁸FDG-PET scan may not be cost effective for clinical stage I patients.

In patients with clinical stage II breast cancer, the prevalence of occult DM detected through ¹⁸FDG-PET scan ranged from 0% to 12.4%^[17,22,24,27,29,31,32,34]. As stage II breast cancer patients also comprise a heterogeneous group, the risk of DM is higher for patients with stage II B disease (T3N0M0, T2N1M0) than for those with stage II A (T1N1M0, T2N0M0) disease. Discounting the one study that included only 6 patients with stage II B disease^[25], the risk of unsuspected DM diagnosed by ¹⁸FDG-PET scan ranged from 2.8% to 19.6% for stage II A and 9.1% to 40% for stage II B, respectively^[17,22,27,31,32,34] (Table 2).

Patients with stage II B have larger tumors than those with stage II A. As tumor size has been reported to be correlated with an increased risk of DM, this may be one of the reasons underlying the higher rate of DM at diagnosis^[43]. Other studies have corroborated the increased prevalence of DM diagnosed with ¹⁸FDG-PET scan for patients with large tumors compared to those with smaller tumors^[18-21,23,28]. It is likely that other factors, like axillary lymph node metastases and tumor biology, may also lead to a high rate of DM at diagnosis^[22,24,27,29,31].

Patients with triple-negative breast cancer frequently have a worse prognosis than their counterparts who harbor other subtypes because of the high rate of DM^[44]. A 10% rate of unsuspected DM was seen on ¹⁸FDG-PET scan compared to conventional imaging for patients with clinical stage II breast cancer^[32]. However, even among those triple-negative breast cancer patients, the rate of DM remained low for stage II A disease. Specifically, the DM rate was 5% and 15% for stage II A and II B triple-negative breast cancers, respectively.

Another prognostic factor that has been reported in the literature is the patient age at diagnosis. Young patients (< 40-year-old) may have a more aggressive tumor biology that translates to a lower survival rate compared to older patients^[36]. Among young patients with breast cancer, those with stage II B disease had

a 17% rate of DM compared to 5% for stage II A. The incidence of DM in patients with clinical stage II A with moderate to poorly differentiated grade carcinoma climbs to 19.6% after ¹⁸FDG-PET scanning^[22]. Tumor biology needs to be taken into account beyond the conventional TNM staging. In patients with invasive micropapillary carcinoma, for example, a high rate of DM detected by ¹⁸FDG-PET scan before surgery has been reported. Among 16 patients with invasive micropapillary carcinoma who underwent ¹⁸FDG-PET scan when the tumor was diagnosed, axillary lymph node metastases and DM were observed in 12 (75% of cases)^[45].

To date, this is the first study looking at the impact of ¹⁸FDG-PET on the management of invasive micropapillary carcinoma, a rare tumor with a high rate of axillary lymph node invasion and DM, even in the case of a relatively small tumor. Moreover, no study has been performed yet to investigate the role of ¹⁸FDG-PET scan for the diagnosis of occult DM in patients who had surgery for metaplastic carcinoma of the breast, another rare tumor with a poor survival rate associated with a high propensity to metastasize to distant sites.

Our study was restricted by the limited availability of the data correlating clinical stages and biology with the risk of DM diagnosed with ¹⁸FDG-PET/CT scan in patients with early stage breast cancer. Ki-67 is a known prognostic marker^[46] but was not reported in any of the recent and largest studies^[31-34]. Most studies were retrospective. The classification of patients into stages was usually done after the ¹⁸FDG-PET/CT image acquisition, which might have affected the selection of patients. Some studies included the more advanced stages, stage III and IV, and a few studies included post-operative patients. Many issues of importance are relevant for breast cancer, notably the emerging role of PET/MRI and its comparison with PET/CT^[47], the use of PET in the monitoring of neoadjuvant therapy^[48], the use for staging and restaging^[49], the standardized uptake values (commonly known as SUVs) and how they relate to lymph node status^[50], the prognostic role of FDG-PET^[51] and the suitability for treatment planning^[52]; all these represent immensely exciting domains of breast cancer research, but would have confused the scope of the present study, namely the rates of DM.

In summary, the current review suggests a need for future prospective studies looking at subgroups of patients who would most likely benefit from PET scan before surgery-stage II B, poorly differentiated tumors, rare tumors with aggressive biology, such as invasive micropapillary carcinoma, and young age. These patients would most likely receive systemic therapy. Detection of DM could help in selecting the optimal sequence of therapies and the monitoring thereof. Incorporating biomarkers such as c-erbB2 and genetic arrays in those studies may further help the clinician to define the risk of DM at diagnosis for patients with early stage breast cancer.

Conclusion

In patients with clinical stage I breast cancer, the systematic use of ¹⁸FDG-PET/CT scan for staging is not cost effective because the yield of ¹⁸FDG-PET/CT-detected DM in clinical stage I is low. In young patients with stage II B triple-negative and/or poorly differentiated breast cancer, ¹⁸FDG-PET/CT scan identifies a substantial rate of DM and should therefore be considered for these patients. Finally, the role of ¹⁸FDG-PET for stage II breast cancer and for rare tumors with aggressive biology needs to be defined in future prospective studies.

ACKNOWLEDGMENTS

The authors would like to express their heartfelt gratitude to Carl Leak, for revising the language of this manuscript, to Jessica Malki, Olga Morgan, Brentwood Oftedal, Yeoshina Pillay and Andrew Westfall of the RUSM Oncology Society, Ross University School of Medicine, Dominica, West Indies for their enthusiastic interest and partaking in the discussion and the writing.

COMMENTS

Background

Staging of cancer is the process of identifying and classifying the extent of the disease. Staging is important to aid the clinician in planning treatment, to inform the patient on prognosis, to evaluate the results of treatment, and to facilitate the exchange of information between treatment centers. Initial staging is based on all evidence acquired before treatment. The evidence arises from physical examination, imaging, pathology, and/or endoscopic or surgical exploration.

Research frontiers

In early breast cancer (small tumor and no symptom), previous diagnostic studies rarely detected metastases. The contentious issue is that the earlier studies were based on the use of conventional imaging with poor detection performance. Metastatic disease might have been missed.

Innovations and breakthroughs

[¹⁸F]fluorodeoxyglucose-positron emission tomography/computed tomography (¹⁸FDG-PET/CT) combines metabolic and anatomic imaging. It requires a dual competence in radiology and in nuclear medicine. Negative reviews of its role in breast cancer confounded it with ¹⁸FDG-PET alone, did not have the joint nuclear-radiologist's expertise to analyze the images, or focused only on the detection of regional lymph node involvement. There has been no pooled evaluation of the rates of distant metastases detected with ¹⁸FDG-PET/CT. This study fills the gap.

Applications

The present review identifies groups of patients with early breast cancer, who are at high risk for distant metastases, notably those with stage II B or aggressive histologies, in whom it might be prudent to reconsider the role of ¹⁸FDG-PET/CT.

Terminology

¹⁸FDG is a radioactively labeled glucose analog. It allows the detection of tissues that have a high glucose uptake, such as tumors with a high metabolic activity. Imaging with ¹⁸FDG, the ¹⁸FDG-PET, shows areas of high activity. The ¹⁸FDG-PET imaging combined with CT imaging shows where the areas of high activity are distributed in the body; N1 disease: Cancer that has spread to regional lymph nodes; Distant metastases: Cancer that has spread beyond the breast and regional lymph nodes to distant organs or distant lymph nodes;

Triple-negative breast cancer: Breast tumor that tested negative for the estrogen receptor, the progesterone receptor, and the human epidermal growth receptor HER2. Triple negative tumors might respond to chemotherapy but will not to receptor targeted treatments.

Peer-review

A well-written review article, summarising important information to the field.

REFERENCES

- 1 **Schnitt SJ**, Lakhani SR. Breast Cancer in: World Cancer Report 2014. Lyon, France: International Agency for Research on Cancer, 2014: 362-373
- 2 **Siegel RL**, Miller KD, Jemal A. Cancer statistics, 2016. *CA Cancer J Clin* 2016; **66**: 7-30 [PMID: 26742998 DOI: 10.3322/caac.21332]
- 3 **Iqbal J**, Ginsburg O, Rochon PA, Sun P, Narod SA. Differences in breast cancer stage at diagnosis and cancer-specific survival by race and ethnicity in the United States. *JAMA* 2015; **313**: 165-173 [PMID: 25585328 DOI: 10.1001/jama.2014.17322]
- 4 **Barrett T**, Bowden DJ, Greenberg DC, Brown CH, Wishart GC, Britton PD. Radiological staging in breast cancer: which asymptomatic patients to image and how. *Br J Cancer* 2009; **101**: 1522-1528 [PMID: 19861999 DOI: 10.1038/sj.bjc.6605323]
- 5 **Senkus E**, Kyriakides S, Ohno S, Penault-Llorca F, Poortmans P, Rutgers E, Zackrisson S, Cardoso F. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2015; **26** Suppl 5: v8-30 [PMID: 26314782 DOI: 10.1093/annonc/mdv298]
- 6 **Merrill SA**, Stevens P, Verschraegen C, Wood ME. Utility and Costs of Routine Staging Scans in Early-Stage Breast Cancer. *Am J Hematol Oncol* 2016; **12**: 4
- 7 **Schnipper LE**, Smith TJ, Raghavan D, Blayney DW, Ganz PA, Mulvey TM, Wollins DS. American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. *J Clin Oncol* 2012; **30**: 1715-1724 [PMID: 22493340 DOI: 10.1200/JCO.2012.42.8375]
- 8 **Chand N**, Cutress RI, Oepfen RS, Agrawal A. Staging Investigations in Breast Cancer: Collective Opinion of UK Breast Surgeons. *Int J Breast Cancer* 2013; **2013**: 506172 [PMID: 24349790 DOI: 10.1155/2013/506172]
- 9 **Zhang Y**, Feng B, Zhang GL, Hu M, Fu Z, Zhao F, Zhang XL, Kong L, Yu JM. Value of 18F-FDG PET-CT in surveillance of postoperative colorectal cancer patients with various carcinoembryonic antigen concentrations. *World J Gastroenterol* 2014; **20**: 6608-6614 [PMID: 24914384 DOI: 10.3748/wjg.v20.i21.6608]
- 10 **Tantiwongkosi B**, Yu F, Kanard A, Miller FR. Role of (18)F-FDG PET/CT in pre and post treatment evaluation in head and neck carcinoma. *World J Radiol* 2014; **6**: 177-191 [PMID: 24876922 DOI: 10.4329/wjr.v6.i5.177]
- 11 **Sun L**, Wan Y, Lin Q, Sun YH, Zhao L, Luo ZM, Wu H. Multiple primary malignant tumors of upper gastrointestinal tract: a novel role of 18F-FDG PET/CT. *World J Gastroenterol* 2010; **16**: 3964-3969 [PMID: 20712059 DOI: 10.3748/wjg.v16.i31.3964]
- 12 **Abuodeh Y**, Naghavi AO, Ahmed KA, Venkat PS, Kim Y, Kis B, Choi J, Biebel B, Sweeney J, Anaya DA, Kim R, Malafa M, Frakes JM, Hoffe SE, El-Haddad G. Prognostic value of pre-treatment F-18-FDG PET-CT in patients with hepatocellular carcinoma undergoing radioembolization. *World J Gastroenterol* 2016; **22**: 10406-10414 [PMID: 28058021 DOI: 10.3748/wjg.v22.i47.10406]
- 13 **Groheux D**, Giacchetti S, Delord M, Hindié E, Vercellino L, Cuvier C, Toubert ME, Merlet P, Hennequin C, Espié M. 18F-FDG PET/CT in staging patients with locally advanced or inflammatory breast cancer: comparison to conventional staging. *J Nucl Med* 2013; **54**: 5-11 [PMID: 23213197 DOI: 10.2967/jnumed.112.106864]
- 14 **Champion L**, Lerebours F, Cheral P, Edeline V, Giraudet AL, Wartski M, Bellet D, Alberini JL. 18F-FDG PET/CT imaging versus dynamic contrast-enhanced CT for staging and prognosis of inflammatory breast cancer. *Eur J Nucl Med Mol Imaging* 2013; **40**: 1206-1213 [PMID: 23640467 DOI: 10.1007/s00259-013-2405-z]
- 15 **Liu Y**. Role of FDG PET-CT in evaluation of locoregional nodal

- disease for initial staging of breast cancer. *World J Clin Oncol* 2014; **5**: 982-989 [PMID: 25493234 DOI: 10.5306/wjco.v5.i5.982]
- 16 **Badwe R**, Hawaldar R, Nair N, Kaushik R, Parmar V, Siddique S, Budrukkar A, Mitra I, Gupta S. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. *Lancet Oncol* 2015; **16**: 1380-1388 [PMID: 26363985 DOI: 10.1016/S1470-2045(15)00135-7]
 - 17 **Groheux D**, Giacchetti S, Espié M, Vercellino L, Hamy AS, Delord M, Berenger N, Toubert ME, Misset JL, Hindié E. The yield of 18F-FDG PET/CT in patients with clinical stage IIA, IIB, or IIIA breast cancer: a prospective study. *J Nucl Med* 2011; **52**: 1526-1534 [PMID: 21880576 DOI: 10.2967/jnumed.111.093864]
 - 18 **Bernsdorf M**, Berthelsen AK, Wielenga VT, Kroman N, Teilmann D, Binderup T, Tange UB, Andersson M, Kjær A, Loft A, Graff J. Preoperative PET/CT in early-stage breast cancer. *Ann Oncol* 2012; **23**: 2277-2282 [PMID: 22357250 DOI: 10.1093/annonc/mds002]
 - 19 **Choi YJ**, Shin YD, Kang YH, Lee MS, Lee MK, Cho BS, Kang YJ, Park JS. The Effects of Preoperative (18)F-FDG PET/CT in Breast Cancer Patients in Comparison to the Conventional Imaging Study. *J Breast Cancer* 2012; **15**: 441-448 [PMID: 23346174 DOI: 10.4048/jbc.2012.15.4.441]
 - 20 **Garami Z**, Hascsi Z, Varga J, Dinya T, Tanyi M, Garai I, Damjanovich L, Galuska L. The value of 18-FDG PET/CT in early-stage breast cancer compared to traditional diagnostic modalities with an emphasis on changes in disease stage designation and treatment plan. *Eur J Surg Oncol* 2012; **38**: 31-37 [PMID: 21937190 DOI: 10.1016/j.ejso.2011.09.002]
 - 21 **Groves AM**, Shastry M, Ben-Haim S, Kayani I, Malhotra A, Davidson T, Kelleher T, Whittaker D, Meagher M, Holloway B, Warren RM, Ell PJ, Keshtgar MR. Defining the role of PET-CT in staging early breast cancer. *Oncologist* 2012; **17**: 613-619 [PMID: 22539550 DOI: 10.1634/theoncologist.2011-0270]
 - 22 **Gunalp B**, Ince S, Karacalioglu AO, Ayan A, Emer O, Alagoz E. Clinical impact of (18)F-FDG PET/CT on initial staging and therapy planning for breast cancer. *Exp Ther Med* 2012; **4**: 693-698 [PMID: 23170128 DOI: 10.3892/etm.2012.659]
 - 23 **Pritchard KI**, Julian JA, Holloway CM, McCready D, Gulenchyn KY, George R, Hodgson N, Lovrics P, Perera F, Elavathil L, O'Malley FP, Down N, Bodurtha A, Shelley W, Levine MN. Prospective study of 2-[¹⁸F]fluorodeoxyglucose positron emission tomography in the assessment of regional nodal spread of disease in patients with breast cancer: an Ontario clinical oncology group study. *J Clin Oncol* 2012; **30**: 1274-1279 [PMID: 22393089 DOI: 10.1200/JCO.2011.38.1103]
 - 24 **Cochet A**, Dygai-Cochet I, Riedinger JM, Humbert O, Berriolo-Riedinger A, Toubeau M, Guiu S, Coutant C, Coudert B, Fumoleau P, Brunotte F. 18F-FDG PET/CT provides powerful prognostic stratification in the primary staging of large breast cancer when compared with conventional explorations. *Eur J Nucl Med Mol Imaging* 2014; **41**: 428-437 [PMID: 24196916 DOI: 10.1007/s00259-013-2595-4]
 - 25 **Jeong YJ**, Kang DY, Yoon HJ, Son HJ. Additional value of F-18 FDG PET/CT for initial staging in breast cancer with clinically negative axillary nodes. *Breast Cancer Res Treat* 2014; **145**: 137-142 [PMID: 24682676 DOI: 10.1007/s10549-014-2924-8]
 - 26 **Koolen BB**, van der Leij F, Vogel WV, Rutgers EJ, Vrancken Peeters MJ, Elkhuizen PH, Valdés Olmos RA. Accuracy of 18F-FDG PET/CT for primary tumor visualization and staging in T1 breast cancer. *Acta Oncol* 2014; **53**: 50-57 [PMID: 23672678 DOI: 10.3109/0284186X.2013.783714]
 - 27 **Riedl CC**, Slobod E, Jochelson M, Morrow M, Goldman DA, Gonen M, Weber WA, Ulaner GA. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. *J Nucl Med* 2014; **55**: 1578-1583 [PMID: 25214641 DOI: 10.2967/jnumed.114.143297]
 - 28 **Zhang X**, Wu F, Han P. The role of (18)F-FDG PET/CT in the diagnosis of breast cancer and lymph nodes metastases and micrometastases may be limited. *Hell J Nucl Med* 2014; **17**: 177-183 [PMID: 25526754]
 - 29 **Hogan MP**, Goldman DA, Dashevsky B, Riedl CC, Gönen M, Osborne JR, Jochelson M, Hudis C, Morrow M, Ulaner GA. Comparison of 18F-FDG PET/CT for Systemic Staging of Newly Diagnosed Invasive Lobular Carcinoma Versus Invasive Ductal Carcinoma. *J Nucl Med* 2015; **56**: 1674-1680 [PMID: 26294295 DOI: 10.2967/jnumed.115.161455]
 - 30 **Krammer J**, Schnitzer A, Kaiser CG, Buesing KA, Sperk E, Brade J, Wasgindt S, Suetterlin M, Schoenberg SO, Sutton EJ, Wasser K. (18)F-FDG PET/CT for initial staging in breast cancer patients - Is there a relevant impact on treatment planning compared to conventional staging modalities? *Eur Radiol* 2015; **25**: 2460-2469 [PMID: 25680729 DOI: 10.1007/s00330-015-3630-6]
 - 31 **Nursal GN**, Nursal TZ, Aytac HO, Hasbay B, Torun N, Reyhan M, Yapar AF. Is PET/CT Necessary in the Management of Early Breast Cancer? *Clin Nucl Med* 2016; **41**: 362-365 [PMID: 26914560 DOI: 10.1097/RLU.00000000000001165]
 - 32 **Ulaner GA**, Castillo R, Goldman DA, Wills J, Riedl CC, Pinker-Domenig K, Jochelson MS, Gönen M. (18)F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. *Eur J Nucl Med Mol Imaging* 2016; **43**: 1937-1944 [PMID: 27129866 DOI: 10.1007/s00259-016-3402-9]
 - 33 **Lebon V**, Alberini JL, Pierga JY, Diéras V, Jehanno N, Wartski M. Rate of Distant Metastases on 18F-FDG PET/CT at Initial Staging of Breast Cancer: Comparison of Women Younger and Older Than 40 Years. *J Nucl Med* 2017; **58**: 252-257 [PMID: 27587709 DOI: 10.2967/jnumed.116.178749]
 - 34 **Ulaner GA**, Castillo R, Wills J, Gönen M, Goldman DA. (18)F-FDG-PET/CT for systemic staging of patients with newly diagnosed ER-positive and HER2-positive breast cancer. *Eur J Nucl Med Mol Imaging* 2017; Epub ahead of print [PMID: 28456837 DOI: 10.1007/s00259-017-3709-1]
 - 35 **Debald M**, Wolfgarten M, Kreklau P, Abramian A, Kaiser C, Höller T, Leutner C, Keyver-Paik MD, Braun M, Kuhn W. Staging of primary breast cancer is not indicated in asymptomatic patients with early tumor stages. *Oncol Res Treat* 2014; **37**: 400-405 [PMID: 25138300 DOI: 10.1159/000363528]
 - 36 **Ribnikar D**, Ribeiro JM, Pinto D, Sousa B, Pinto AC, Gomes E, Moser EC, Cardoso MJ, Cardoso F. Breast cancer under age 40: a different approach. *Curr Treat Options Oncol* 2015; **16**: 16 [PMID: 25796377 DOI: 10.1007/s11864-015-0334-8]
 - 37 **Braunstein LZ**, Niemierko A, Shenouda MN, Truong L, Sadek BT, Abi Raad R, Wong JS, Punglia RS, Taghian AG, Bellon JR. Outcome following local-regional recurrence in women with early-stage breast cancer: impact of biologic subtype. *Breast J* 2015; **21**: 161-167 [PMID: 25559656 DOI: 10.1111/tbj.12371]
 - 38 **Chen HL**, Ding A. Comparison of invasive micropapillary and triple negative invasive ductal carcinoma of the breast. *Breast* 2015; **24**: 723-731 [PMID: 26392199 DOI: 10.1016/j.breast.2015.09.001]
 - 39 **Lai HW**, Tseng LM, Chang TW, Kuo YL, Hsieh CM, Chen ST, Kuo SJ, Su CC, Chen DR. The prognostic significance of metaplastic carcinoma of the breast (MCB)—a case controlled comparison study with infiltrating ductal carcinoma. *Breast* 2013; **22**: 968-973 [PMID: 23787124 DOI: 10.1016/j.breast.2013.05.010]
 - 40 **Sorlie T**, Perou CM, Tibshirani R, Aas T, Geisler S, Johnsen H, Hastie T, Eisen MB, van de Rijn M, Jeffrey SS, Thorsen T, Quist H, Matese JC, Brown PO, Botstein D, Lønning PE, Børresen-Dale AL. Gene expression patterns of breast carcinomas distinguish tumor subclasses with clinical implications. *Proc Natl Acad Sci USA* 2001; **98**: 10869-10874 [PMID: 11553815 DOI: 10.1073/pnas.191367098]
 - 41 **Reis-Filho JS**, Pusztai L. Gene expression profiling in breast cancer: classification, prognostication, and prediction. *Lancet* 2011; **378**: 1812-1823 [PMID: 22098854 DOI: 10.1016/S0140-6736(11)61539-0]
 - 42 **Cardoso F**, van't Veer LJ, Bogaerts J, Slaets L, Viale G, Delaloge S, Pierga JY, Brain E, Causeret S, DeLorenzi M, Glas AM, Goulinopoulos V, Goulioti T, Knox S, Matos E, Meulemans B, Neijenhuis PA, Nitz U, Passalacqua R, Ravdin P, Rubio IT, Saghathian M, Smilde TJ, Sotiriou C, Stork L, Straehle C, Thomas G, Thompson AM, van der Hoeven JM, Vuylsteke P, Bernards R, Tryfonidis K, Rutgers E, Piccart M. 70-Gene Signature as an Aid to Treatment Decisions in Early-Stage Breast Cancer. *N Engl J Med* 2016; **375**: 717-729 [PMID: 27557300 DOI: 10.1056/NEJMoa1602253]
 - 43 **Fei F**, Messina C, Slaets L, Chakiba C, Cameron D, Bogaerts J, Bonnefoi

- H. Tumour size is the only predictive factor of distant recurrence after pathological complete response to neoadjuvant chemotherapy in patients with large operable or locally advanced breast cancers: a sub-study of EORTC 10994/BIG 1-00 phase III trial. *Eur J Cancer* 2015; **51**: 301-309 [PMID: 25578377 DOI: 10.1016/j.ejca.2014.11.023]
- 44 **Kast K**, Link T, Friedrich K, Petzold A, Niedostatek A, Schoffer O, Werner C, Klug SJ, Werner A, Gatzweiler A, Richter B, Baretton G, Wimberger P. Impact of breast cancer subtypes and patterns of metastasis on outcome. *Breast Cancer Res Treat* 2015; **150**: 621-629 [PMID: 25783184 DOI: 10.1007/s10549-015-3341-3]
- 45 **Yun SU**, Choi BB, Shu KS, Kim SM, Seo YD, Lee JS, Chang ES. Imaging findings of invasive micropapillary carcinoma of the breast. *J Breast Cancer* 2012; **15**: 57-64 [PMID: 22493629 DOI: 10.4048/jbc.2012.15.1.57]
- 46 **de Azambuja E**, Cardoso F, de Castro G, Colozza M, Mano MS, Durbecq V, Sotiriou C, Larsimont D, Piccart-Gebhart MJ, Paesmans M. Ki-67 as prognostic marker in early breast cancer: a meta-analysis of published studies involving 12,155 patients. *Br J Cancer* 2007; **96**: 1504-1513 [PMID: 17453008 DOI: 10.1038/sj.bjc.6603756]
- 47 **Tabouret-Viaud C**, Botsikas D, Delattre BM, Mainta I, Amzalag G, Rager O, Vinh-Hung V, Miralbell R, Ratib O. PET/MR in Breast Cancer. *Semin Nucl Med* 2015; **45**: 304-321 [PMID: 26050658 DOI: 10.1053/j.semnuclmed.2015.03.003]
- 48 **Rousseau C**, Devillers A, Sagan C, Ferrer L, Bridji B, Champion L, Ricaud M, Bourbouloux E, Doutriaux I, Clouet M, Berton-Rigaud D, Bouriel C, Delecroix V, Garin E, Rouquette S, Resche I, Kerbrat P, Chatal JF, Campone M. Monitoring of early response to neoadjuvant chemotherapy in stage II and III breast cancer by [¹⁸F]fluorodeoxyglucose positron emission tomography. *J Clin Oncol* 2006; **24**: 5366-5372 [PMID: 17088570 DOI: 10.1200/JCO.2006.05.7406]
- 49 **Groheux D**, Cochet A, Humbert O, Alberini JL, Hindié E, Mankoff D. ¹⁸F-FDG PET/CT for Staging and Restaging of Breast Cancer. *J Nucl Med* 2016; **57** Suppl 1: 17S-26S [PMID: 26834096 DOI: 10.2967/jnumed.115.157859]
- 50 **Futamura M**, Asano T, Kobayashi K, Morimitsu K, Nawa M, Kanematsu M, Morikawa A, Mori R, Yoshida K. Prediction of macrometastasis in axillary lymph nodes of patients with invasive breast cancer and the utility of the SUV lymph node/tumor ratio using FDG-PET/CT. *World J Surg Oncol* 2015; **13**: 49 [PMID: 25885028 DOI: 10.1186/s12957-014-0424-2]
- 51 **Vinh-Hung V**, Everaert H, Lamote J, Voordeckers M, van Parijs H, Vanhoeij M, Verfaillie G, Fontaine C, Vees H, Ratib O, Vlastos G, De Ridder M. Diagnostic and prognostic correlates of preoperative FDG PET for breast cancer. *Eur J Nucl Med Mol Imaging* 2012; **39**: 1618-1627 [PMID: 22777335 DOI: 10.1007/s00259-012-2181-1]
- 52 **Bral S**, Vinh-Hung V, Everaert H, De Coninck P, Storme G. The use of molecular imaging to evaluate radiation fields in the adjuvant setting of breast cancer: a feasibility study. *Strahlenther Onkol* 2008; **184**: 100-104 [PMID: 18259702 DOI: 10.1007/s00066-008-1769-7]

P- Reviewer: Bilir C, Wang L, Wang SK **S- Editor:** Ji FF
L- Editor: A **E- Editor:** Lu YJ





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

