# Semiquantitative Analysis of Maximum Standardized Uptake Values of Regional Lymph Nodes in Inflammatory Breast Cancer:

## *Is There a Reliable Threshold for Differentiating Benign from Malignant?*

Selin Carkaci, MD, Beatriz E. Adrada, MD, Eric Rohren, MD, Wei Wei, MS, Mohammad A. Quraishi, MD, Osama Mawlawi, PhD, Thomas A. Buchholz, MD, Wei Yang, MD

**Rationale and Objectives:** The aim of this study was to determine an optimum standardized uptake value (SUV) threshold for identifying regional nodal metastasis on $^{18}$F–fluorodeoxyglucose (FDG) positron emission tomographic (PET)/computed tomographic (CT) studies of patients with inflammatory breast cancer.

**Materials and Methods:** A database search was performed of patients newly diagnosed with inflammatory breast cancer who underwent $^{18}$F-FDG PET/CT imaging at the time of diagnosis at a single institution between January 1, 2001, and September 30, 2009. Three radiologists blinded to the histopathology of the regional lymph nodes retrospectively analyzed all $^{18}$F-FDG PET/CT images by measuring the maximum SUV (SUVmax) in visually abnormal nodes. The accuracy of $^{18}$F-FDG PET/CT image interpretation was correlated with histopathology when available. Receiver-operating characteristic curve analysis was performed to assess the diagnostic performance of PET/CT imaging. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated using three different SUV cutoff values (2.0, 2.5, and 3.0).

**Results:** A total of 888 regional nodal basins, including bilateral axillary, infraclavicular, internal mammary, and supraclavicular lymph nodes, were evaluated in 111 patients (mean age, 56 years). Of the 888 nodal basins, 625 (70%) were negative and 263 (30%) were positive for metastasis. Malignant lymph nodes had significantly higher SUVmax than benign lymph nodes ($P < .0001$). An SUVmax of 2.0 showed the highest overall sensitivity (89%) and specificity (99%) for the diagnosis of malignant disease.

**Conclusions:** SUVmax of regional lymph nodes on $^{18}$F-FDG PET/CT imaging may help differentiate benign and malignant lymph nodes in patients with inflammatory breast cancer. An SUV cutoff of 2 provided the best accuracy in identifying regional nodal metastasis in this patient population.

**Key Words:** Inflammatory breast cancer; lymph node metastasis; SUV; threshold; PET CT.



Inflammatory breast cancer (IBC) is an aggressive disease that accounts for 1% to 5% of all breast cancers. It is a clinicopathologic entity characterized by changes in the breast such as erythema, edema involving more than two thirds of the breast, peau d'orange, enlargement, warmth, tenderness, and induration on palpation (1). In general, compared to women with noninflammatory breast cancer, women with IBC present at a younger age, are more likely to have metastatic disease at diagnosis, and have shorter overall survival (2). The mean 5-year overall survival rate of patients with IBC who have undergone current multidisciplinary therapy is between 20% and 40% (2).

The most significant prognostic factor for women with IBC is axillary lymph node involvement. Patients with axillary lymph node metastasis have shorter disease-free and overall survival than patients with node-negative disease (3,4). Accurate preoperative staging of patients with IBC is vital, because the standard of care for these patients is neoadjuvant therapy prior to mastectomy and surgical removal of the lymph nodes, after which histopathologic information about the number of involved axillary lymph nodes and the actual size of the primary tumor is no longer available.

**Acad Radiol 2012;** 19:535–541

From the Department of Diagnostic Radiology, Unit 1350, (S.C., B.E.A., M.A.Q., W.Y.), the Department of Nuclear Medicine (E.R.), the Department of Biostatistics (W.W.), the Department of Imaging Physics (O.M.), and the Department of Radiation Oncology Treatment (T.A.B.), The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd, Houston, TX 77030. Received October 27, 2011; accepted January 3, 2012. **Address correspondence to:** S.C. e-mail: selincarkaci@msn.com


doi:10.1016/j.acra.2012.01.001

Detecting disease in nodal basins beyond the axilla also has implications for locoregional radiotherapy (5) and has prognostic significance. Assessing breast cancer metastasis to regional nodal sites outside the axilla, particularly in the internal mammary, mediastinal, and supraclavicular basins, is more challenging, because these nodal regions are not routinely sampled given their relative inaccessibility. Anatomically based imaging modalities, such as computed tomographic (CT) imaging, ultrasonography, and magnetic resonance imaging, use the size and morphologic features of lymph nodes to determine tumor involvement. These techniques are limited in their ability to detect metastases in normal-sized lymph nodes.

Studies reported in the literature indicate that $^{18}$F–fluorodeoxyglucose (FDG) positron emission tomographic (PET)/CT imaging has high specificity (84%–100%) for diagnosing axillary nodal metastasis in patients with breast cancer (6–14). Visual assessment (6,9,10,12) and semiquantitative analysis with standardized uptake value (SUV) cutoffs that ranged between 1.8 and 2.5 (7–9,14) were used to differentiate benign from malignant lymph nodes. However, to our knowledge, no data have been published on definitive SUV cutoffs for regional nodal metastasis in patients with IBC. If validated, a reliable SUV cutoff could prove useful for the noninvasive assessment of lymph nodes throughout the body, and maximum (SUVmax) might have prognostic significance.

In this study, our primary aim was to document the SUVmax of regional lymph nodes (including nodes in the axillary, infraclavicular, supraclavicular, and internal mammary regions) that were identified on the $^{18}$F-FDG PET/CT studies of patients with IBC at diagnosis and to determine an optimum SUV threshold for identifying nodal metastasis. The SUVmax of lymph nodes was also correlated with the sizes of lymph nodes, SUVmax of the breast, and histopathologic and biologic features of the tumor.

## MATERIALS AND METHODS

### Patients

A database search was performed to identify patients at one institution who were either newly diagnosed with IBC between January 1, 2001, and September 30, 2009, or diagnosed with recurrent IBC during the same time period after being in remission for ≥1 year and had $^{18}$F-FDG PET/CT data available for review. Patients who had undergone neoadjuvant chemotherapy or surgery prior to $^{18}$F-FDG PET/CT imaging were excluded. A retrospective review of patient records was performed to document patient demographics (age, height, weight, body mass index); tumor type and grade; estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) status; and clinical, imaging, and histopathologic findings when available. The institutional review board waived informed consent and approved the retrospective review, which was compliant with the Health Insurance Portability and Accountability Act (15).

### Imaging and Review

Fluorine-18-FDG PET/CT imaging was performed using a Discovery ST camera (GE Healthcare, Milwaukee, WI) in combination with the CT component of an eight-slice LightSpeed scanner (GE Healthcare). Patients were positioned supine in the PET/CT device, with their arms raised, and had fasted for ≥6 hours before the $^{18}$F-FDG injection. A normal fasting blood glucose level of <150 mg/dL was a standard requirement for imaging in all patients. An intravenous injection of 555 to 629 MBq (15–17 mCi) of $^{18}$F-FDG was administered in the arm or central venous catheter on the side opposite the cancer, and two-dimensional emission scans were acquired at 3 minutes per field of view 70 ± 10 minutes after the $^{18}$F-FDG injection. PET images were reconstructed using standard vendor-provided reconstruction algorithms. Non-contrast-enhanced CT images were acquired in helical mode (speed, 13.5 mm/rotation) from the base of the skull to the midthigh during suspended midexpiration at a 3.75-mm slice thickness, a tube voltage of 120 kVp, a tube current–time product of 300 mAs, and a 0.5-second rotation.

The CT, PET, and coregistered $^{18}$F-FDG PET/CT images were retrospectively reviewed jointly in all standard planes with maximum-intensity whole-body coronal projection images on an Advantage Workstation (GE Healthcare) by three radiologists, who had details on the patients' clinical histories but did not know the results of the lymph node biopsies, other imaging studies, and clinical follow-up. Interpretation was based on both semiquantitative and qualitative interpretation (visual comparison of signal intensity between lymph nodes and other physiologic structures such as background soft tissue) and agreement among the three readers. The readers visually assessed the ipsilateral and contralateral axillary, infraclavicular, supraclavicular, internal mammary basins of each patient and had a region of interest positioned on the lymph nodes with measurement of the SUVmax and the short-axis diameter.

### Interpretation of $^{18}$F-FDG PET/CT Findings

Patients with multiple sites of ipsilateral nodal involvement were subjected to biopsy of a single (the highest) nodal station instead of biopsy of multiple nodal regions to confirm metastases. The accuracy of $^{18}$F-FDG PET/CT image interpretation was assessed by histopathologic analysis (fine-needle aspiration and/or axillary dissection) if available, concurrent or subsequent imaging findings (contrast-enhanced CT imaging, contrast-enhanced magnetic resonance imaging, ultrasonography, or follow-up PET/CT imaging), or clinical follow-up. Results were considered true-negatives when $^{18}$F-FDG PET/CT imaging correctly classified a histologically benign lymph node or when $^{18}$F-FDG PET/CT imaging indicated that a lymph node was benign and no evidence of disease was documented during clinical or imaging follow-up (mean, 24 months; range, 6–48 months). Results were considered false-negatives when $^{18}$F-FDG