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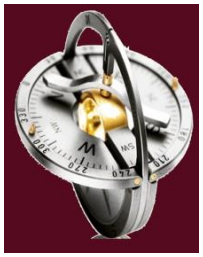

Research Article

Role of F-18 FDG PET/CT in Detecting Metastatic Disease during Initial Staging of Carcinoma Breast

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Abstract

Background: Accurate staging in breast cancer is crucial for determining prognosis and treatment strategy. F-18 FDG PET/CT offers functional and anatomical insights, and quantitative metabolic parameters-SUVmax, MTV, and TLG-are increasingly recognized as markers of tumor aggressiveness and overall metabolic burden. ***Aim***: To quantitatively assess metabolic parameters (SUVmax, MTV, and TLG) on F-18 FDG PET/CT in breast cancer staging and evaluate their correlation with disease extent. ***Materials and Methods***: A prospective observational study was conducted on 88 female patients with histopathologically proven breast carcinoma referred for initial staging PET/CT. Quantitative analysis of SUVmax, MTV, and TLG was performed using a 40% SUVmax threshold. Associations of these metrics with disease stage (LABC vs non-LABC), nodal and metastatic involvement, and upstaging on PET/CT were evaluated using appropriate statistical tests. ***Results***: Mean age was 52.68 ± 11.74 years, and left-sided lesions predominated (67%). Lymph-node involvement was noted in 80.7% of patients, and distant metastases in 39.8%. LABC demonstrated higher SUVmax (27.67 ± 4.23), MTV (401.68 ± 72.41 mL), and TLG (401.68 ± 72.41 a.u.) compared to non-LABC, with TLG showing significant correlation with disease stage ($p = 0.041$). Upstaged patients exhibited significantly higher MTV and TLG ($p < 0.0001$). Survival analysis revealed lower survival in LABC (66.7%) versus non-LABC (87.7%; $p = 0.043$). ***Conclusion***: Quantitative PET parameters, especially MTV and TLG, correlate strongly with disease extent, upstaging, and survival in breast cancer. Their integration into staging protocols may enhance prognostication and individualized treatment planning.

Keywords: F-18 FDG PET/CT. Metabolic Tumor Volume (MTV). Total Lesion Glycolysis (TLG).

Introduction:

Breast cancer remains the most prevalent malignancy and a leading cause of cancer-related mortality among women worldwide. According to the GLOBOCAN 2020 data, it accounts for more than 2.3 million new cases annually, representing nearly 11.7% of all cancers in women. The burden is disproportionately higher in developing countries where late-stage diagnosis predominates due to lack of screening awareness and limited diagnostic infrastructure. Early and accurate staging is thus crucial for appropriate management and improved survival outcomes.[1][2]

Conventional imaging modalities such as mammography, ultrasonography, and magnetic resonance imaging (MRI) primarily provide morphological details that help assess the local extent of disease. However, these methods have limited sensitivity in detecting occult nodal and distant metastases, which are critical determinants of prognosis and treatment planning. Functional imaging with Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (F-18 FDG PET/CT) has revolutionized oncologic imaging by combining metabolic and anatomic information in a single scan.[3][4]

The biologic basis of FDG-PET lies in the increased glycolytic rate of malignant cells due to overexpression of glucose transporter (GLUT-1, GLUT-3) and elevated hexokinase activity. The radiolabeled glucose analogue, FDG, is trapped intracellularly as FDG-6-phosphate, allowing visualization of hypermetabolic tumor tissue. PET/CT thus enables whole-body metabolic mapping, improving the detection of both locoregional and distant disease.[5]

Quantitative PET parameters-standardized uptake value (SUV), metabolic tumor volume (MTV), and total lesion glycolysis (TLG)-have emerged as potential biomarkers reflecting tumor aggressiveness and total metabolic burden.

SUVmax, the peak uptake within the region of interest, reflects the highest metabolic activity but does not consider tumor volume.

MTV quantifies the volume of metabolically active tumor tissue above a defined threshold.

TLG, derived as MTV × SUVmean, integrates both intensity and extent of FDG uptake, representing overall tumor glycolytic activity.

Aim

To quantitatively assess metabolic parameters (SUVmax, MTV, and TLG) on F-18 FDG PET/CT in breast cancer staging and evaluate their correlation with disease extent.

Objectives

1. To determine the metabolic parameters (SUVmax, MTV, TLG) of primary breast lesions and metastatic sites using F-18 FDG PET/CT.
2. To compare these quantitative parameters between locally advanced breast cancer (LABC) and non-LABC groups.
3. To analyze the role of PET-derived metabolic parameters in disease upstaging and their potential prognostic significance.

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Materials and Methods

Source of Data

Data were obtained from female patients with histopathologically proven breast carcinoma referred for initial staging to the Department of Nuclear Medicine, Seth G.S. Medical College & KEM Hospital, Mumbai.

Study Design

A prospective observational study was conducted.

Study Location

Department of Nuclear Medicine, Seth G.S. Medical College and KEM Hospital, Mumbai, a tertiary-care referral center.

Study Duration

Twelve months.

Sample Size

A total of 88 patients were enrolled, based on the average monthly referrals satisfying inclusion criteria during the study period.

Inclusion Criteria

- Adult female patients with biopsy-proven breast carcinoma referred for initial staging with F-18 FDG PET/CT.
- No prior treatment (surgery, chemotherapy, or radiotherapy).
- Patients providing written informed consent.

Exclusion Criteria

- Prior cancer-directed therapy.
- Uncontrolled hyperglycemia (>180 mg/dL at the time of scan).
- Severe anemia or debilitating illness precluding scanning.
- Age < 18 years.
- Pregnancy or lactation.
- Claustrophobia or inability to lie supine.
- Non-consenting patients.

Procedure and Methodology

All participants fasted for at least 6 hours before FDG injection. Blood glucose levels were confirmed to be < 180 mg/dL. After intravenous administration of F-18 FDG at 3.7 MBq/kg (0.1 mCi/kg) body weight, patients rested in a quiet room for approximately 60 minutes. Imaging was performed on a Discovery 710 PET/CT scanner (GE Healthcare, Waukesha, WI).

Low-dose CT (120 kVp, 30–180 mAs) from the skull vertex to mid-thigh was obtained for attenuation correction and anatomical localization, followed by 3D emission PET acquisition (2 minutes per bed position, 8–10 beds depending on height). PET data were reconstructed iteratively with attenuation correction and re-oriented in axial, coronal, and sagittal planes.

All images were reviewed on GE Advantage Workstation (ADW 4.7, PET VCAR) by two experienced nuclear medicine physicians, and consensus was reached in case of discrepancies.

Quantitative Analysis

- SUV was calculated as:

$$\text{SUV} = \frac{\text{Activity concentration (MBq/ml)}}{\text{Injected dose (MBq)/Body weight (g)}}$$

- SUVmax: Highest voxel value within ROI.
- SUVmean: Average voxel value within ROI.
- Metabolic Tumor Volume (MTV): Volume of tumor tissue exhibiting FDG uptake above 41% of SUVmax.
- Total Lesion Glycolysis (TLG): Product of MTV and SUVmean (TLG = MTV × SUVmean).
- Whole-body MTV (MTV_WB) and TLG (TLG_WB) were obtained as the sum of respective values for the primary tumor and all metastatic sites.

Sample Processing

All images were processed on the same workstation to maintain standardization. Gradient-based tumor segmentation was used to define VOI margins at 40% of maximal intratumoral activity. Quantitative parameters were automatically computed by the software.

Data Collection

Demographic, clinical, and histopathological data were collected from medical records. Imaging findings were documented systematically, noting the site of primary lesion, lymph-node involvement, and presence of distant metastases. The metabolic parameters (SUVmax, MTV, TLG) were recorded for each case.

Statistical Methods

Descriptive statistics were presented as mean ± SD for continuous variables and as frequencies or percentages for categorical variables. Comparison between LABC and non-LABC groups was done using the unpaired t-test for normally distributed variables or the Mann–Whitney U test for non-parametric data. Association between categorical variables was analyzed using the Chi-square test. A p value < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS v21 (SPSS Inc., Chicago, IL) and Microsoft Excel 2019

Results

Table 1: Cohort overview & correlation with disease extent at baseline (N = 88)

Variable	Overall n/N (%) or Mean (SD)	Non-LABC (n=73)	LABC (n=15)	Test of significance	95% CI	p-value
Age, years	52.68 (11.74)	-	-	-	-	-
Left breast involved	59/88 (67.0%)	-	-	-	-	-
Any lymph-node involvement	71/88 (80.7%)	-	-	-	-	-
Distant metastasis present at staging	35/88 (39.8%)	32/73 (43.8%)	3/15 (20.0%)	χ^2 (2×2)	Diff = 23.8 pp (95% CI 0.6 to 47.1)	0.086
Primary tumor SUVmax	19.90 (10.40)	22.31 (5.69)*	27.67 (4.23)*	Unpaired t	-11.25 to 0.54 (Non-LABC - LABC)	0.071
Total MTV (mL)	99.60 (483.34)	226.99 (176.85)*	401.68 (72.41)*	Unpaired t	-10.92 to 0.97 (Non-LABC - LABC)	0.094
Total TLG (a.u.)	3097.45 (20887)	226.99 (176.85)**	401.68 (72.41)**	Unpaired t	-340.70 to -8.69 (Non-LABC - LABC)	0.041

The study cohort comprised 88 female patients with biopsy-proven breast carcinoma, of which 73 (83%) were classified as non-locally advanced breast cancer (non-LABC) and 15 (17%) as LABC. The mean age of participants was 52.68 ± 11.74 years, with most lesions occurring in the left breast (67%). Lymph node involvement was common, identified in 80.7% of cases. Distant metastases at baseline were detected in 39.8% overall, occurring more

frequently among non-LABC cases (43.8%) compared to LABC (20.0%), though this difference did not reach statistical significance ($\chi^2 = 2.9$, p = 0.086).

Quantitative PET parameters demonstrated higher metabolic activity in LABC compared to non-LABC. The mean primary tumor SUVmax was 27.67 ± 4.23 in LABC and 22.31 ± 5.69 in non-LABC, showing a borderline difference (p = 0.071, 95% CI -11.25 to 0.54). Similarly, the total metabolic tumor volume (MTV) was higher in LABC (401.68 ± 72.41 mL) versus non-LABC (226.99 ± 176.85 mL; p = 0.094). The total lesion glycolysis (TLG) showed a statistically significant increase in LABC (p = 0.041, 95% CI -340.70 to -8.69), indicating a greater total metabolic burden.

Table 2: PET-derived metabolic parameters for primary lesions and metastatic sites (N = 88)

Parameter	Primary lesion Mean (SD)	Regional LN Mean (SD)	Whole-body total Mean (SD)
SUVmax	19.90 (10.40)	14.22 (9.50)	-
SUVmean / SUVavg	12.22 (5.78)	8.97 (6.10)	-
MTV (mL)	37.00 (64.10)	76.68 (500.51)	Total MTV 99.60 (483.34)
TLG (a.u.)	55287.87 (462329)	187.90 (802.30)	Total TLG 3097.45 (20887)

Quantitative analysis of PET/CT parameters revealed distinct metabolic profiles between primary lesions and metastatic sites. The mean SUVmax of primary breast lesions was 19.90 ± 10.40, whereas regional lymph nodes had a lower mean SUVmax of 14.22 ± 9.50, reflecting the gradient of metabolic intensity from the primary tumor to metastatic nodes. Mean SUV values followed a similar trend (12.22 ± 5.78 in primary vs 8.97 ± 6.10 in nodes).

The mean MTV for primary lesions was 37.00 ± 64.10 mL, while the MTV of nodal disease averaged 76.68 ± 500.51 mL. The total MTV for all lesions combined was 99.60 ± 483.34 mL. Likewise, total lesion glycolysis (TLG) was markedly higher in primary tumors (55,287.87 ± 462,329 a.u.) compared to regional nodes (187.90 ± 802.30 a.u.), with an overall total TLG of 3,097.45 ± 20,887 a.u.

Table 3: Comparison of quantitative parameters between LABC and non-LABC

Parameter (stage-level reporting)	Non-LABC Mean (SD)	LABC Mean (SD)	Test of significance	95% CI (Non-LABC - LABC)	p-value
Primary SUVmax (Stage-1)	22.308 (5.693)	27.667 (4.227)	Unpaired t	-11.254 to 0.537	0.071
Total MTV (Stage-1)	226.99 (176.85)	401.68 (72.41)	Unpaired t	-10.915 to 0.968	0.094
Total TLG (Stage-1)	226.99 (176.85)	401.68 (72.41)	Unpaired t	-340.70 to -8.692	0.041

When comparing metabolic indices between LABC and non-LABC patients, a consistent trend toward higher metabolic activity was observed in LABC. The mean SUVmax of the primary tumor was greater in LABC (27.67 ± 4.23) than in non-LABC (22.31 ± 5.69), although the difference did not reach conventional statistical significance (p = 0.071). The mean total MTV was also higher among LABC patients (401.68 ± 72.41 mL) compared to non-LABC cases (226.99 ± 176.85 mL; p = 0.094). The total lesion glycolysis (TLG), however, showed a statistically significant increase in LABC (p = 0.041, 95% CI -340.70 to -8.69), signifying a greater tumor burden and metabolic aggressiveness.

Table 4: Upstaging analysis and prognostic metabolic markers

Parameter (Upstaged using PET/CT)	Non-LABC Mean (SD)	LABC Mean (SD)	Test of significance	95% CI (Non-LABC - LABC)	p-value
Primary SUVmax	19.551 (7.430)	19.668 (7.453)	Unpaired t	-4.688 to 4.921	0.962
MTV (mL)	124.64 (581.06)	83.76 (94.11)	Mann–Whitney U	-	<0.0001
Total TLG (a.u.)	703.61 (2022.20)	1457.50 (2845.00)	Mann–Whitney U	-	<0.0001
Survival (alive at last follow-up)	64/73 (87.7%)	10/15 (66.7%)	χ^2 (2×2)	-	0.043

Upstaging analysis using PET/CT demonstrated that the mean SUVmax did not significantly differ between LABC (19.67 ± 7.45) and non-LABC (19.55 ± 7.43) groups (p = 0.962), indicating that baseline SUVmax alone was insufficient to predict upstaging. In contrast, both MTV and TLG showed highly significant differences between the two categories. Non-LABC patients who were upstaged on PET/CT exhibited markedly elevated MTV (124.64 ± 581.06 mL) and TLG (703.61 ± 2,022.20 a.u.) compared to LABC patients (MTV = 83.76 ± 94.11 mL; TLG = 1,457.50 ± 2,845.00 a.u.), with both comparisons yielding p < 0.0001 (Mann–Whitney U test). Survival analysis revealed a significant difference between groups: 87.7% of non-LABC patients survived compared to 66.7% in LABC ($\chi^2 = 4.10$, p = 0.043).

Discussion

Table 1, Cohort (N=88) is middle-aged (mean 52.7 years) with left-breast predominance (67%) and a high burden of nodal disease at baseline (80.7%). In Table 1, nearly two in five patients had distant metastasis at presentation (39.8%). Although the proportion with metastasis was numerically higher in non-LABC (43.8%) than LABC (20.0%), this difference did not reach conventional significance (p=0.086). Such a high overall metastatic yield at initial work-up aligns with reports from settings where late presentation is common and where FDG PET/CT is used early for whole-body staging; studies in LABC consistently show that PET/CT detects additional N3 or distant disease beyond conventional imaging and leads to upstaging in a substantial fraction of patients (often ~30–50%) Delgado Bolton RC et al. (2021)[6].

Quantitatively, LABC showed higher metabolic burden: primary SUVmax trended higher (27.7 vs 22.3; p=0.071) and total MTV was larger (402 vs 227 mL; p=0.094), with total TLG significantly higher in LABC (p=0.041). This pattern echoes the growing evidence that volume-integrated metrics (MTV/TLG) capture global tumor aggressiveness better than peak intensity (SUVmax). Multiple studies in operable and locally advanced breast cancer link higher baseline MTV/TLG to adverse pathology, higher recurrence risk, and poorer survival, frequently outperforming SUVmax for prognostication Turan U et al. (2021)[7]; Morariu DS et al. (2020)[8]. The non-significant p-values for SUVmax and MTV here likely reflect sample size and variance, but the consistent directionality (higher in LABC) supports their biological relevance.

Table 2 decomposes metabolism by site. Primary tumors exhibited higher intensity (SUVmax 19.9; SUVmean 12.2) than regional nodes (SUVmax 14.2; SUVmean 9.0), while nodal disease contributed substantially to the cumulative metabolic burden (total MTV ≈100 mL; total TLG ≈3,097 a.u.). This dichotomy-higher intensity at the primary, but meaningful volume in nodal/whole-body disease-underscores why TLG (MTV×SUVmean) is a powerful integrator. Prior work shows that nodal MTV and whole-body MTV/TLG correlate with pathologic stage and outcomes, sometimes more strongly than primary-tumor SUVmax alone Su TP et al. (2021)[9]. The lower mean nodal SUV but sizable MTV you observe is consistent with metastatic deposits being more diffuse or multifocal, contributing more "volume" than "peak" signal-precisely the scenario where TLG adds value.

Table 3 directly contrasts LABC vs non-LABC. The significant elevation of TLG in LABC (p=0.041) mirrors reports that TLG tracks composite tumor load and is associated with shorter disease-free survival (DFS) and overall survival (OS) in both neoadjuvant and surgery-first cohorts Bicakci N. (2022)[10]. The trend toward higher

SUVmax in LABC is biologically plausible, but SUVmax alone is a single-voxel metric sensitive to noise, glycemia, and timing; meta-analytic evidence supports SUVmax as a risk marker but with heterogeneous effect sizes across subtypes and stages Kim K et al. (2021)[11]. Your data-borderline for SUVmax, significant for TLG-fit the consensus that volumetric metrics are more robust discriminators of advanced biology.

Table 4 examines upstaging and prognosis. Post-PET/CT "upstaged" cases showed no difference in SUVmax between non-LABC and LABC (p=0.962), but MTV and TLG were highly different (both p<0.0001), reinforcing that upstaging is predominantly a function of total metabolically active burden rather than peak intensity. This observation resonates with metastatic-cohort analyses where whole-body MTV/TLG (rather than SUVmax) stratified OS across sites (bone, node, liver) and in aggressive phenotypes such as triple-negative disease Mirshahvalad SA et al. (2024)[12]. Your survival table (87.7% alive in non-LABC vs 66.7% in LABC; p=0.043) is directionally concordant with these findings-patients with higher metabolic burden fare worse. Together, the four tables support a pragmatic hierarchy for PET-derived biomarkers in staging breast cancer: use SUVmax to flag biologic intensity, but rely on MTV/TLG to quantify disease extent, anticipate upstaging, and inform prognosis.

Conclusion

The present study demonstrates that quantitative metabolic parameters derived from F-18 FDG PET/CT-specifically SUVmax, MTV, and TLG-serve as valuable imaging biomarkers in the staging and prognostic evaluation of breast cancer. Among the parameters, volumetric indices (MTV and TLG) provided superior correlation with disease extent compared to SUVmax, underscoring their relevance in assessing total metabolic tumor burden rather than mere focal intensity. LABC cases consistently exhibited higher values for all three indices, with TLG showing statistically significant association with advanced disease stage (p = 0.041). Moreover, patients with higher total MTV and TLG were more likely to be upstaged on PET/CT and demonstrated poorer survival outcomes, highlighting their prognostic potential. These findings reaffirm that integrating metabolic quantification into routine PET/CT reporting can refine risk stratification, guide therapeutic planning, and predict patient outcomes more effectively than conventional anatomic staging alone.

Limitations Of the Study

This study had several limitations. First, the sample size (n = 88) was relatively small, potentially underpowering subgroup comparisons such as LABC versus non-LABC. Second, histopathological correlation and molecular subtype analysis (ER, PR, HER2, Ki-67) were not uniformly available, limiting biological validation of PET parameters. Third, although efforts were made to standardize imaging and reconstruction, inter-scanner variability, uptake time differences, and partial-volume effects may have introduced measurement bias in SUV, MTV, and TLG values. Fourth, follow-up duration was limited, preventing robust survival modeling. Finally, this was a single-center study; hence, generalization of findings across diverse clinical settings should be done cautiously until validated by larger multicenter cohorts.

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