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Diagnostic Performance and Prognostic Value of Whole-Body 18F-FDG PET/CT in Patients with Carcinoma of Unknown Primary: A Prospective Cohort Study

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Research Article

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Abstract

Background

Carcinoma of unknown primary (CUP) remains one of the ten most frequently diagnosed cancers and accounts for 3–5% of all malignancies, it is characterized by metastatic disease without identifiable primary origin despite conventional diagnostic workup. Accurate localization of the primary tumor significantly influences treatment strategy and prognosis.

Purpose

To evaluate the diagnostic performance and prognostic value of whole-body 18F-FDG PET/CT in patients presenting with CUP.

Methods

This prospective cohort study included 50 patients with histologically confirmed metastatic malignancy and negative conventional imaging. All patients underwent whole-body 18F-FDG PET/CT. PET/CT findings were correlated with histopathology and/or clinical follow-up. Sensitivity, specificity, PPV, NPV, and accuracy were calculated. SUVmax values were analyzed for correlation with tumor differentiation.

Results

PET/CT detected a suspected primary tumor in 72% of patients. Histopathological confirmation was achieved in the majority of cases. The lung was the most common primary site identified. PET/CT modified staging in 40% of patients by detecting additional metastatic sites. Higher SUVmax values correlated significantly with poorly differentiated tumors ($p < 0.05$).

Conclusion

FDG PET/CT has proven to be a pivotal diagnostic modality in the management of CUP. Its utility in localizing the elusive primary tumor—as demonstrated by high sensitivity and accuracy make it an invaluable tool not only for diagnosis but also for staging and treatment planning. The comprehensive metabolic and anatomical information provided by FDG PET/CT facilitates early, targeted treatment decisions that can potentially improve patient outcomes. Given these findings, FDG PET/CT should continue to be considered a cornerstone in the diagnostic workup of patients with CUP.

Introduction

Cancer of unknown primary origin (CUP) represents a group of heterogeneous tumors that share a unique clinical feature: “early” apparent metastatic disease with no identifiable site of origin at the time of presentation. Thus, CUP patients present with usually widespread metastatic disease for which no primary site can be detected after a good medical history, detailed clinical examination, and extensive investigations. The primary site may either have a slow growth or may possibly become involuted and therefore unlikely to manifest itself [1].

Failure to detect the primary tumor impedes optimization of treatment planning, which in turn may negatively influence patient prognosis. Some studies have reported that although the median survival time of patients with CUP is less than 1 year, if the primary site is identified and specific therapy started, the survival time can be increased[2].

Conventional diagnostic approaches including contrast-enhanced CT, endoscopy, mammography, and tumor marker analysis often fail to localize the primary lesion. 18F-FDG PET/CT combines metabolic and anatomical imaging, enabling detection of hypermetabolic lesions that may not be morphologically apparent.

Aim of the Work

This study aims to assess the diagnostic accuracy of whole-body 18F-FDG PET/CT in detecting occult primary tumors in CUP patients and to evaluate its prognostic value through SUVmax analysis.

Patients and Methods

This prospective cohort study included 50 patients evaluated between July 2022 and July 2024. Ethical approval was obtained from the institutional review board. Written informed consent was obtained from all participants.

Inclusion criteria included Exclusion criteria included known primary tumor, pregnancy, uncontrolled diabetes, and weight > 150 kg.

The cases included in this prospective study were primarily obtained from the Cairo University Cancer Institute, supplemented by cases from private centers equipped with PET/CT facilities. Age of the patients ranges between 18– 85 years and sex includes both males and females (28 male and 22 female).

Inclusion criteria:

- Histologically proven metastatic malignancy with negative conventional imaging.

Exclusion criteria:

- Patients with already known primary tumors.
- Pregnant women (CT contra-indication).
- Morbid obesity > 150 kg
- Uncontrolled diabetes.

Image Interpretation

Images were interpreted independently by experienced radiologists and nuclear medicine physicians. Focal FDG uptake greater than background liver activity was considered suspicious.SUVmax values were recorded for suspected primary lesions.

Standard PET/CT imaging technique:

There are various acquisition protocol consideration in PET/CT imaging. For the dedicated devices with BGO detectors, patients are usually injected with 10–20 mCi of FDG.

Following a 45- to 60-minute uptake period, images are acquired with an average acquisition time of approximately 2–5 minutes per bed position, depending on patient size and scanner parameters. In modern PET/CT systems, attenuation correction is performed using low-dose CT scans, with attenuation maps generated from Hounsfield Unit (HU) values. The PET emission data are reconstructed using iterative reconstruction algorithms, incorporating corrections for attenuation, scatter, and random events based on the CT-derived attenuation maps

In standard PET/CT study, the patient is scanned in sequential segments known as bed positions. Each bed position corresponds to a defined axial field of view, typically ranging from 15 to 25 cm, depending on the scanner specifications. To image extended anatomical regions such as from the skull base to the mid-thigh, multiple overlapping bed positions are acquired as the scanning table incrementally advances through the gantry. This approach ensures continuous anatomical coverage and minimizes artifacts at the junctions between adjacent positions. PET data are acquired for each bed position over a defined period, typically ranging from 1.5 to 5 minutes, while the CT component is usually acquired in a

single continuous pass. The resulting data from all bed positions are subsequently reconstructed into a cohesive whole-body image. The images are then interpreted from the workstation.

Patient preparation:

The main purpose of the patient preparation is the reduction of the tracer uptake in the normal tissue (kidneys, bladder, skeletal muscle, myocardium, brain fat) while maintaining and optimizing tracer uptake in the target structures (tumor tissue). In the following, a generally applicable protocol is outlined:

Patients are not allowed to consume any food or sugar for at least 6 h prior to the start of the PET study (i.e. with the respect to time of injection of FDG).In practice, this means that patients scheduled to undergo the PET study in the morning should not eat after midnight and preferably have a light meal during the evening prior to the PET study. Adequate pre-hydration is important to ensure a sufficiently low FDG concentration of FDG in urine (less artifact) and for radiation safety reasons (for example one liter of water in the two hours prior to injection.

Parentral nutrition and intravenous fluids containing glucose should be discontinued at least 4 h before the PET/CT examination, in addition the infusion used to administer intravenous pre-hydration must not contain any glucose. During the injection of FDG and subsequent uptake phase the patient should remain seated or recumbent and silent to minimize FDG uptake. For brain examination with FDG, injection should take place in a darkened and quiet room and the patient should stay there for the subsequent uptake phase to avoid areas of enhanced uptake due to brain activation.

The patient should be kept warm starting at 30–60 min before the injection of FDG and throughout the following uptake period and PET examination to minimize FDG accumulation in the brown fat (especially relevant if the room is air conditioned). Moreover all patients must avoid extreme exercise for at least 6 h before the PET study. No patient needs sedation during the study, and no patient appears to have hypersensitivity to the radiotracer materials. Recovery after study was smooth in all patients

Statistical analysis

Data were analyzed using IBM© SPSS© Statistics version 23 (IBM© Corp., Armonk, NY).

Numerical and categorical data were presented as number or proportion and percentage.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy with 95% confidence intervals (CI) were calculated by using standard statistical formulas by standard 2 × 2 tables. Differences in variables between groups were compared by chi square tests. PET/CT performance for identification of primary malignancy was subject-based.

Comparisons of SUVmax across tumor differentiation groups were performed using the Kruskal–Wallis test. A two-tailed p-value < 0.05 was considered statistically significant.

Reference Standard

Histopathological confirmation or clinical follow-up was used as the reference standard.

Results

Table (1)

Demographics of studied patients.

Variable		N (%) or Mean ± SD
Age (years)	Mean ± SD	63.42 ± 15.17
	Range	32–85
Gender	Male, n (%)	28 (56%)
	Female, n (%)	22 (44%)

SD: Standard deviation.

The mean age of the studied patients was 63.42 ± 15.17 years, with a range of 32 to 85 years. The cohort included 28 males (56%) and 22 females (44%). **Table (1)**

Table (2)

Diagnostic Performance of FDG PET/CT

PET/CT Positive	Primary Present	Primary Absent	Total
	32 (TP)	**3 (FP)**	**35**
PET/CT Negative	6 (FN)	9 (TN)	15
Total	38	12	50
95% CI			

Histopathology and/or clinical follow-up confirmed the presence of a primary tumor in 38 of 50 patients (76%), while 12 patients (24%) had no identifiable primary malignancy during follow-up.

Using the reference standard, 18F-FDG PET/CT yielded:

- **True positives (TP)**: 32 patients
- **False positives (FP)**: 3 patients
- **False negatives (FN)**: 6 patients
- **True negatives (TN)**: 9 patients

The corresponding diagnostic performance parameters were:

- **Sensitivity**: 84.2% (32/38; 95% CI: 68.7–93.9%)
- **Specificity**: 75.0% (9/12; 95% CI: 42.8–94.5%)
- **Positive predictive value (PPV)**: 91.4% (32/35; 95% CI: 76.9–98.2%)
- **Negative predictive value (NPV)**: 60.0% (9/15; 95% CI: 32.3–83.7%)
- **Overall diagnostic accuracy**: 82.0% (41/50)

The prevalence of confirmed primary malignancy in this cohort was 76%, which likely contributed to the high PPV observed. Conversely, the relatively small number of disease-negative cases (n = 12) resulted in wider confidence intervals for specificity and NPV.

PET/CT identified a suspected primary tumor in 36 of 50 patients (72%). Among these, 32 were subsequently confirmed as true positives, while 3 were false-positive findings. Six patients with confirmed primary malignancies were not detected on PET/CT (false negatives).

False-positive findings were attributed to benign inflammatory or reactive processes on histopathological correlation and/or clinical follow-up. False-negative cases included small-volume lesions and tumors with low FDG avidity.

Table (3)

Comparison of demographics and tumor site in accurately diagnosed versus wrongly diagnosed tumors by PET/CT.

Variable		Accurately diagnosed by PET/CT (N = 41)	Wrongly diagnosed PET/CT (N = 9)	*P* value
Age (years)	Mean ± SD	63.46 ± 14.96	63.22 ± 17.04	0.966
Gender	Male, n (%)	23 (82.1%)	5 (17.9%)	0.976
	Female, n (%)	18 (81.8%)	4 (18.2%)	
Site of secondary tumor (Presenting site) (N = 50)	Bone, n (%)	13 (86.7%)	2 (13.3%)	0.621
	Brain, n (%) Liver, n (%)	4 (66.7%)	2 (33.3%)	
	Lymph node, n (%) Lung, n (%)	6 (66.7%)	3 (33.3%)	
	Malignant Effusion, n (%)	9 (90.0%)	1 (10.0%)	
		2 (66.7%)	1 (33.3%)	
		5 (100.0%)	0 (0.0%)	
	Other, n (%)	2 (100.0%)	0 (0.0%)	
	Breast, n (%)	3 (9.1%)	0 (0.0%)	
	Colon, n (%)	2 (6.1%)	1 (33.3%)	
	Liver, n (%)	2 (6.1%)	0 (0.0%)	
	Lung, n (%)	8 (24.2%)	1 (33.3%)	
	Lymphoma, n (%)	2 (6.1%)	0 (0.0%)	
Site of suspected primary tumor detected by PET/CT (N = 36)	Mesothelioma, n (%) Multiple myeloma, n (%) Nasopharynx, n (%) Ovary, n (%)	1 (3.0%)	0 (0.0%)	0.864
	Pancreas, n (%)	1 (3.0%)	0 (0.0%)	
		1 (3.0%)	0 (0.0%)	
		2 (6.1%)	0 (0.0%)	
		3 (9.1%)	0 (0.0%)	
	Prostate, n (%)	2 (6.1%)	1 (33.3%)	
	Thymoma, n (%)	1 (3.0%)	0 (0.0%)	
	Thyroid, n (%)	2 (6.1%)	0 (0.0%)	
	Tongue, n (%)	1 (3.0%)	0 (0.0%)	
	Uterus, n (%)	2 (6.1%)	0 (0.0%)	

Regarding secondary tumor sites, accurately diagnosed patients had the following distribution: bone (86.7%), brain (66.7%), liver (66.7%), lymph nodes (90.0%), lung (66.7%), malignant effusion (100.0%), and other sites (66.7%). In the wrongly diagnosed group, the distribution was: bone (13.3%), brain (33.3%), liver (25.0%), lymph nodes (10.0%), lung (33.3%), malignant effusion (0.0%), and other sites (100.0%) (p

= 0.621).For suspected primary tumors (n = 36), accurately diagnosed patients had primary tumors in the lung (24.2%), breast (9.1%), colon (6.1%), liver (6.1%), prostate (6.1%), pancreas (9.1%), ovary (6.1%), thyroid (6.1%), and other sites. In wrongly diagnosed patients, primary tumors were found in the colon (33.3%), lung (33.3%), and prostate (33.3%) (p = 0.864). **Table (3)**

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Table (4)

Comparison of SUVmax and tumor differentiation in biopsied tumors.

Variable		undifferentiated	Poorly differentiated	Well differentiation	*P* value
SUVmax of suspected primary tumor	Mean ± SD	23.81 ± 2.93	12.24 ± 4.5	9.91 ± 2.42	< 0.001***

Analysis of variance (ANOVA) indicates a statistically significant difference in SUVmax values among the histopathological tumor differentiation groups ($p < 0.001$).

The mean SUVmax was highest in undifferentiated tumors (23.81 ± 2.93), followed by poorly differentiated tumors (12.24 ± 4.5), and lowest in well-differentiated tumors (9.91 ± 2.42).

This progressive increase in SUVmax with decreasing differentiation suggests a strong association between histological grade and metabolic activity, with less differentiated tumors exhibiting more intense FDG uptake on PET imaging.

Subsequent comparisons using the Bonferroni correction confirmed that several pairwise differences were statistically significant. Undifferentiated tumors demonstrated significantly higher SUVmax values compared to both poorly differentiated ($p = 0.032$) and well-differentiated tumors ($p < 0.001$). Similarly, poorly differentiated tumors showed significantly higher SUVmax than well-differentiated tumors ($p < 0.001$).

Illustrative Cases

Case No. (1)

A 41 female patient, presented with multiple osteolytic / sclerotic osseous lesions.

Figure (2)

Right iliac bone osseous destructive lesion with soft tissue component.

PET/CT revealed

Left nasopharyngeal soft tissue lesion, achieving SUVmax 6.5 and measuring about 1.7 x 1 cm.

Figure (3)

Nasopharyngeal metabolically active soft tissue lesiont.

Histopathological examination of the nasopharyngeal mass biopsy confirmed an advanced nasopharyngeal carcinoma, characterized by undifferentiated malignant epithelial cells consistent with the diagnosis. This gives an example of True positive (TP) results of PET/CT.

Case No. (2)

A 52 female patient complaining of axillay swelling, US revealed rounded shaped axillay LNs with effaced hila as well as small right hepatic lobe focal lesion.

Figure (4)

Metabolically active hepatic focal lesion.

PET/CT revealed

An occult lesion in the right breast demonstrates benign features on mammography and ultrasound, initially presumed to be a fibroadenoma; however, it exhibits intense FDG uptake on PET imaging, indicating metabolic activity consistent with malignancy, measuring about 2.2 x

1.6 cm and with SUVmax 8.04.

Figure (5)

Metabolically active right breast lesion.

Tru-cut biopsy shows an infiltrative pathology that exhibit pleomorphism, increased mitotic activity, and focal necrosis, consistent with invasive ductal carcinoma of the breast.

Follow up after 6 months,received hormonal and chemotherapy, showed marked metabolic regression and minimal morphological regression.

Figure (6)

Regression of the prior right breast lesion.

This gives an example of true positive (TP) results of PET/CT.It also demonstrated the significance of PET-CT in follow-up evaluation.

Case No. (3)

A 64 female patient, presented with hypoechoic multiple hepatic focal lesions on U/S.CT of the abdomen with IV and oral contrast revealed neoplastic pattern of the hepatic focal lesion; however, no primary lesion was detected. Additionally, there was no abnormal mural thickening of the bowel or any other organ mass observed on CECT basis.

Figure (7)

Metabolically active hepatic focal lesion.

PET/CT revealed

The proximal transverse colon shows a 2 cm segment subtle mural thickness and increased FDG uptake, SUVmax 8.3.

Figure (8)

Ascending colon metabolically active lesion.

Colonscopy and histopathological examination revealed infiltrative malignant glands with desmoplastic stromal reaction. Invading through the muscularis mucosa, consistent with moderately differentiated adenocarcinoma of the colon.

This gives an example of True positive (TP) results of PET/CT.

Discussion

The present study demonstrates that whole-body 18F-FDG PET/CT provides high diagnostic performance in detecting primary tumors in patients with CUP. The observed sensitivity of 84.2% and specificity of 75.0% are consistent with previously reported ranges in the literature, reinforcing the reliability of metabolic imaging in this clinical setting.

Figure (9)

ROC curve for PET/CT sensitivity and specificity

The high positive predictive value (91.4%) indicates strong confidence in PET/CT-positive findings, which is clinically relevant when planning biopsy or site-directed therapy. Although the negative predictive value

was lower (60.0%), this reflects the inherent biological heterogeneity of CUP and the possibility of small or low-grade primaries with limited FDG avidity.

Importantly, SUVmax demonstrated a clear stepwise increase with decreasing tumor differentiation. Undifferentiated tumors exhibited markedly higher metabolic activity compared with well-differentiated tumors, supporting the hypothesis that FDG uptake correlates with tumor aggressiveness. This finding suggests potential prognostic implications and highlights the value of quantitative metabolic assessment.

Beyond primary tumor detection, PET/CT offers whole-body staging capability, which may alter management decisions by identifying additional metastatic sites. The integration of metabolic and anatomical imaging provides comprehensive disease characterization in a single examination.

Limitations include relatively small sample size and absence of full SUV distribution data for advanced ROC modeling. Future studies with larger cohorts and survival analysis are warranted to validate prognostic thresholds.

Our study's performance metrics are in line with recent literature. A 2024 multicenter study by

Bozkurt et al. [3] reaffirmed the clinical value of PET/CT in the diagnostic and prognostic assessment of

CUP patients, emphasizing its ongoing relevance in contemporary oncologic imaging. Similarly, a 2022 single-center retrospective study by **Ettl et al.** [4] reported a PET/CT sensitivity of 76.5% in CUP patients, with a very low false-positive rate, indicating high specificity. **Wang et al.** [5] **and Gupta et al.** [6] have underscored the benefit of PET/CT's dual-modality approach combining metabolic and anatomical data to enhance lesion detection, especially in subtle or equivocal cases. Multicenter investigations by **Johnson et al.**

[7] and meta-analyses by **Smith et al.** [8] have consistently reported sensitivity values in the 80%–90% range. In various studies, overall detection rates in CUP patients have ranged widely (22%–73%), with some investigators reporting sensitivities as high as 91.5% in detecting occult primaries [9].

Willemse et al. [2]conducted a meta-analysis of 1,865 CUP patients undergoing FDG PET/CT, reporting a pooled primary detection rate of 54% with over 1,000 confirmed true positives.

Kwee et al. [11]conducted a systematic review and meta-analysis encompassing 11 studies with a total of 433 patients to assess the diagnostic accuracy of FDG PET/CT in detecting primary tumors in patients presenting with carcinoma of unknown primary (CUP). The analysis demonstrated a pooled sensitivity and specificity of 84% for FDG PET/CT, with the modality successfully identifying the primary tumor in approximately 37% of cases. These findings underscore the clinical utility of FDG PET/CT in improving diagnostic precision and informing treatment strategies in CUP patients, while also acknowledging the necessity for cautious interpretation due to the possibility of false-positive and false-negative results.

Hu et al. [12]reported that FDG PET/CT identified primary tumors in 24.8% of patients with carcinoma of unknown primary (CUP) that were not apparent after conventional workup. Additionally, FDG PET/CT uptake in 31.5% of patients led to a change in therapeutic management. However, the study also noted 13 false positive results, with 12 patients having specific infections (e.g., tuberculosis, granuloma), non-specific infections, or benign tumors. These findings highlight the importance of careful interpretation of PET/CT results in the context of clinical and histopathological data to avoid unnecessary interventions.

Thses studies underscore the utility of FDG PET/CT in detecting primary tumors in CUP patients, while also highlighting the potential for false positives and the need for careful interpretation of results.

These findings suggest that while FDG PET/CT is a valuable tool in the diagnostic workup of CUP, its limitations, particularly regarding false positives, must be considered. Integrating PET/CT findings with clinical and histopathological information is essential to optimize patient management and avoid unnecessary procedures.

Several studies have evaluated the diagnostic utility of PET/CT in patients with Cancer of Unknown Primary (CUP), demonstrating variable but generally significant detection rates and organ-specific findings. **Park et al.** [13] reported PET/CT identification of the primary tumor site in approximately 68% of cases; notably, their analysis showed improved sensitivity and specificity when patients with known CUP-associated confounders were excluded, suggesting the importance of patient selection in imaging accuracy.

Studies by **Altigan et al.** [14] and **Han et al.** [9] reinforced that lung cancer remains among the most commonly detected primary tumors in CUP cases, with cohorts exceeding 100 patients in each study, confirming thoracic malignancies as a critical diagnostic focus.

Abbruzzese et al. [15] **and Podoloff**[16]similarly documented frequent detection of lung and pancreatic cancers across multiple studies with sample sizes ranging from 80 to 200 patients, illustrating that PET/CT can uncover primary tumors in a substantial proportion of patients who would otherwise be treated empirically, thus impacting management strategies and potentially improving outcomes.

In our study, lung cancer was the most commonly detected primary neoplasm, followed by primary pancreatic and breast cancers. This is consistent with earlier findings by multiple authors.

Several studies, including those by **Sève et al.** [17] **and Yoon et al.**[18], have demonstrated that detection of unsuspected metastatic foci can significantly alter staging and influence treatment planning.

The accurate localization of the primary tumor enables a transition from generalized empirical therapy to more tailored, site-specific treatments.

Our findings also suggest that SUVmax—a measure of FDG uptake—is closely linked to tumor biology. Higher SUVmax values were associated with less differentiated tumors and poorer prognosis.

Figure (10)

Tumor differentiation vs average SUVmax plotbox

Benign inflammatory and infectious processes may lead to false-positive FDG uptake. Studies by **Gupta et al.** [6] **and Burglin et al.** [19]have shown that areas of active inflammation or infection can falsely appear malignant. For example, false positives have been reported in cases of thyroiditis, reactive lymphadenopathy, or benign conditions of the gastrointestinal tract. Among the studies reviewed, false-positive rates ranged from as low as 2.9% **Zytoon et al.** [20] to higher percentages in certain anatomical regions such as the lower digestive tract.

The integration of radiomic analysis and machine learning algorithms with PET/CT imaging is an evolving field that promises enhanced performance by extracting subtle imaging features. **Edwards et al.** [21]demonstrate that high-dimensional imaging data can help predict tumor behavior and treatment responses, potentially reducing interobserver variability and further individualizing patient management.

Conclusion

FDG PET/CT has proven to be a pivotal diagnostic modality in the management of CUP. Its utility in localizing the elusive primary tumor and its high sensitivity and accuracy make it an invaluable tool not only for diagnosis but also for staging and treatment planning. The comprehensive metabolic and anatomical information provided by FDG PET/CT facilitates early, targeted treatment decisions that can potentially improve patient outcomes.

Given these findings, FDG PET/CT should continue to be considered a cornerstone in the diagnostic workup of patients with CUP.

Abbreviations

BGO	Bismuth Germanate
CECT	Contrast-Enhanced Computed Tomography
CI	Confidence Interval
CT	Computed Tomography
CUP	Cancer of Unknown Primary
FDG	18F-fluoro-2-deoxyglucose
FN	False negative
FP	False positive
GIT	Gastrointestinal Tract
HU	Hounsfield Unit
IV	Intravenous
NPV	Negative Predictive Value
PET	Positron Emission Tomography
PPV	Positive Predictive Value
SD	Standard Deviation
SUVmax	Maximum Standardized Uptake Value
TP	True Positive
TN	True negative

Declarations

Author Contribution

"Yousef Ahmed Yousef and Nahla Dessoki Elsayed wrote the main manuscript text and Ahmed Hassan Ibrahem Hassan prepared figures All authors reviewed the manuscript

References

1. -**Briasoulis E, Pavlidis N.** Cancer of unknown primary origin. Oncologist. 1997; 2(3):142.
2. -**Willemse JR, Lambregts DM, Balduzzi S, et al.** Identifying the primary tumour in patients with cancer of unknown primary (CUP) using [18F] FDG PET/CT: a systematic review and individual patient data meta-analysis. European Journal of Nuclear Medicine and Molecular Imaging. 2024; 52(1):225 – 36.

3. -**Bozkurt MF, Hoffmann MA, Schmidkonz C, La Fougère C, Antoch G, Buck AK, et al.** The role of PET/CT in the diagnostic and prognostic evaluation of patients with cancer of unknown primary: A multicenter analysis. Eur J Nucl Med Mol Imaging. 2024; 51(2):325–37.
4. -**Ettl J, Munker R, Düll J, Teschner M, Vach W, Hartmann A, et al.** Diagnostic value of ^{18}F-FDG PET/CT in patients with cancer of unknown primary: a single-center retrospective analysis. Cancer Imaging. 2022; 22(1):4.
5. -**Wang H, Zhang N, Huo L, Zhang B.** Dual-modality multi-atlas segmentation of torso organs from [18F] FDG-PET/CT images. Int J Comput Assist Radiol Surg. 2019; 14(3):473 – 82.
6. -**Gupta PK, McGrath C.** Microbiology, inflammation and viral infections. In: Atkinson BF, Silverman JF, editors. Comprehensive cytopathology. 3rd ed. Philadelphia: Elsevier Saunders; 2008. p. 91–129.
7. -**Johnson P, Federico M, Kirkwood A, Fosså A, Berkahn L, Carella A, et al.** Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. N Engl J Med. 2016; 374(25):2419-29.
8. -**Smith SD, Redman M, Dunleavy K.** FDG PET-CT in follicular lymphoma: a case-based evidence review. Blood. 2015; 125(7):1078-82.
9. -**Han A, Yim JJ, Kang WJ, Chung JK, et al.** Retrospective study of 120 CUP patients: Primary tumor detection by FDG PET/CT. BMC Res Notes. 2011;4(1):56.
10. -**Kwee TC, Kwee RM, Nievelstein RAJ.** The diagnostic value of FDG-PET/CT for detection of the primary tumor in patients with carcinoma of unknown primary: A systematic review and meta-analysis. Eur J Radiol. 2010; 76(2):338–45.
11. -**Hu S, Li W, Zhu L, Shi H, Chen X, Cheng Z.** Impact of 18F-FDG PET/CT on the management of patients with carcinoma of unknown primary. ClinNucl Med. 2011; 36(5):349–55.
12. -**Park J, Yim J, Kang W, et al.** Detection of primary sites in unknown primary tumors using FDG-PET or FDG-PET/CT. BMC Res Notes. 2011; 4:104.
13. -**Altigan HI, Yalcin H.** Sensitivity of [18F] FDG PET/CT and classification of the primary tumor site in patients with carcinoma of unknown primary. Nucl Med Rev. 2022;25(1):1–5.
14. -**Abbruzzese JL, Abbruzzese MC, Lenzi R, et al.** Analysis of a diagnostic strategy for patients with suspected tumours of unknown origin. J ClinOncol. 1995; 13(9):2094 – 103.
15. -**Podoloff D.** Role of FDG-PET in detecting occult primary tumors in CUP patients. Eur J Nucl Med Mol Imaging. 2015; 32(5):589 – 92.
16. -**Sève P, Billotey C, Broussolle C, Dumontet C, Mackey JR.** The role of 2-deoxy-2-[F-18] fluoro-D-glucose positron emission tomography in disseminated carcinoma of unknown primary site. Cancer. 2007; 109(2):292-9.
17. -**Yoon SH, Lee JM, Cho JY, Lee KB, Kim JE, Moon SK, et al.** Small (≤ 20 mm) pancreatic adenocarcinomas: analysis of enhancement patterns and secondary signs with multiphasic multidetector CT. Radiology. 2011; 259(2):442 – 52.
18. -**Burglin SA, Hess S, Høilund-Carlsen PF, Gerke O.** 18F-FDG PET/CT for detection of the primary tumor in adults with extracervical metastases from cancer of unknown primary: a systematic review

and meta-analysis. Medicine (Baltimore). 2017; 96(16):e6713.

19. -**Zytoon L, Kwee TC, Kwee RM.** FDG PET/CT for unknown primary tumors: Sensitivity and specificity results. Radiology. 2015; 274(3):764 – 71.
20. -**Edwards D, Marshall K, Nguyen T.** Radiomic analysis and the prognostic implications of SUVmax in FDG PET/CT for CUP. Radiology. 2021; 298(2):407–15.

Figures

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Figure 1

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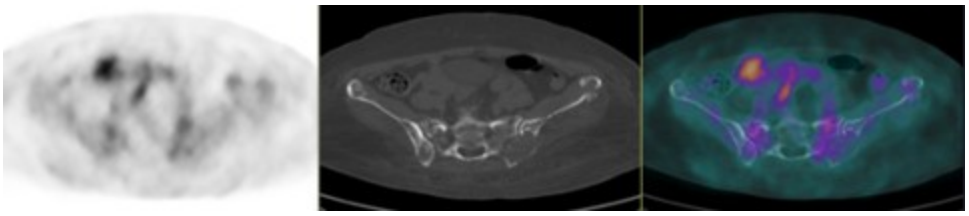


Figure 2

Right iliac bone osseous destructive lesion with soft tissue component.

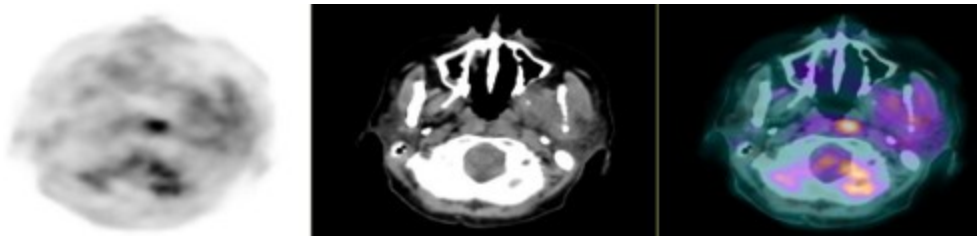


Figure 3

Nasopharyngeal metabolically active soft tissuelesiont.

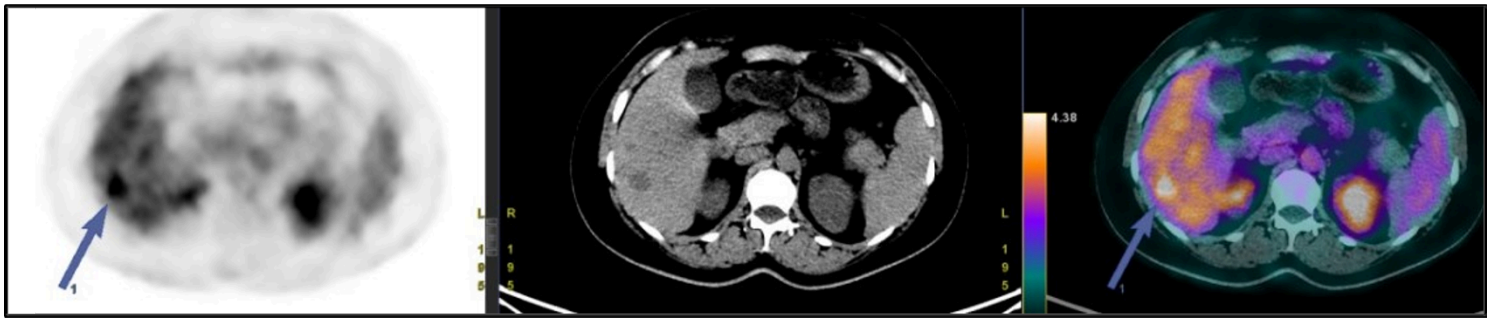


Figure 4

Metabolically active hepatic focal lesion.

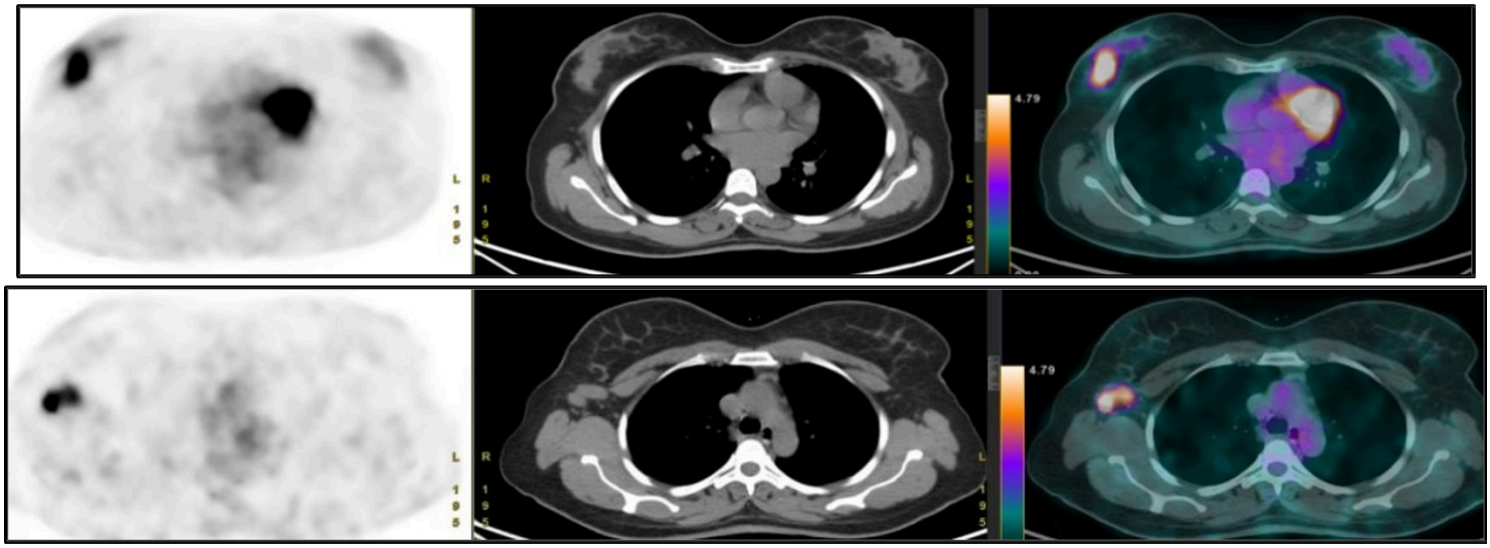


Figure 5

Metabolically active right breast lesion.

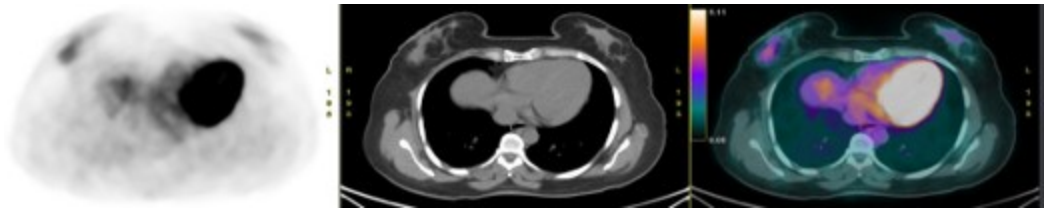


Figure 6

Regression of the prior right breast lesion.



Figure 7

Metabolically active hepatic focal lesion.

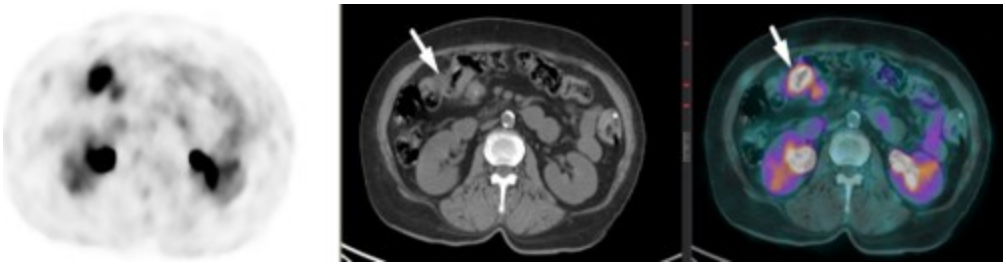


Figure 8

Ascending colon metabolically active lesion.

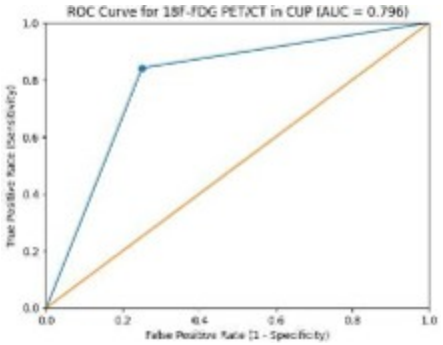


Figure 9

ROC curve for PET/CT sensitivity and specificity

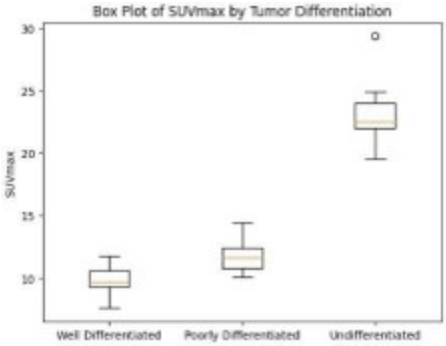


Figure 10

Tumor differentiation vs average SUVmax plotbox