

Characterization and Incidence of Non-Physiologic Uptake Of 18f-Fdg In Nonmalignant Lesions on Fdg Pet/Ct

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ABSTRACT

Background: Integrated positron emission tomography/computed tomography (PET/CT) using 18F-fluorodeoxyglucose (FDG) is widely used in oncologic imaging because of its ability to detect increased glucose metabolism in malignant tissue. FDG uptake, however, is not specific to malignancy: infection, inflammation, granulomatous disease, trauma, benign neoplasms and post-therapy change can all show increased tracer accumulation. These benign causes of FDG avidity constitute an important diagnostic challenge and may lead to false-positive interpretation if not recognised.

Aim: To assess the incidence and imaging characteristics of non-physiologic FDG uptake in non-malignant lesions on PET/CT, and to evaluate the role of integrated PET/CT in distinguishing benign from malignant lesions.

Materials and Methods: This hospital-based retrospective observational study with a prospective follow-up component was conducted in the Departments of Radio-Diagnosis and Imaging, Sree Balaji Medical College and Hospital, and Nuclear Medicine, Dr. Rela Institute and Medical Centre, Chennai, over 18 months from July 2024 to January 2026, after Institutional Ethics Committee approval. Approximately 650 PET/CT examinations were reviewed; lesions showing increased FDG uptake clinically suspected to be benign or indeterminate were selected, and 267 patients satisfying the eligibility criteria formed the final study population. All studies used a Siemens Biograph Horizon scanner and a standard institutional protocol. Lesions were assessed for anatomical location, CT morphology, uptake pattern and maximum standardised uptake value (SUVmax). PET-only interpretation was performed independently and then compared with integrated PET/CT interpretation, the final diagnosis being established by histopathology, cytology, laboratory investigation, imaging follow-up or clinical correlation. Data were analysed using IBM SPSS Statistics version 29, with $p < 0.05$ considered significant.

Results: Of 267 patients, 43.82% were aged 61–80 years and the sex distribution was almost equal (50.19% male). Before PET/CT, 63.46% of lesions were classified as indeterminate. On final evaluation 147 lesions (55.06%) were malignant and 120 (44.94%) were non-malignant. Among non-malignant lesions, infective (29.17%), benign tumour (25.0%) and inflammatory (24.17%) aetiologies predominated, infective and inflammatory causes together accounting for 53.33%. Soft tissue (29.21%), lung (15.73%) and lymph nodes (12.73%) were the commonest sites overall, whereas lymph nodes (18.33%) and lung (15.0%) were the commonest sites of non-malignant uptake. Mean SUVmax was 10.93 in malignant and 6.11 in non-malignant lesions, with 37.83% of all lesions falling in the 5–10 range, indicating substantial overlap; infective lesions showed the highest benign mean SUVmax (8.35). PET alone yielded 73 false-positive results (sensitivity 91.84%, specificity 39.17%), whereas integrated PET/CT yielded only 4 (sensitivity 97.28%, 95% CI 93.8–99.1%; specificity 96.67%, 95% CI 91.7–98.9%). Histopathology was the commonest method of diagnostic confirmation (50.19%).

Conclusion: A considerable proportion of FDG-avid lesions detected on PET/CT are attributable to benign aetiologies rather than malignancy, and intensity of uptake alone cannot reliably separate the two. Recognition of benign patterns of FDG uptake, together with careful correlation with CT morphology and clinical information, is essential to avoid false-positive interpretation. Integrated PET/CT substantially improves specificity while maintaining high sensitivity and

plays a crucial role in differentiating benign from malignant lesions, thereby facilitating appropriate patient management.

Keywords: 18F-FDG PET/CT; Non-physiologic FDG uptake; Benign FDG-avid lesions; Standardized Uptake Value (SUV); Infection and inflammation; PET/CT diagnostic accuracy.

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INTRODUCTION

Positron emission tomography (PET) is a functional imaging modality that permits assessment of physiological and biochemical processes within the human body. Unlike computed tomography (CT) and magnetic resonance imaging (MRI), which principally demonstrate structural anatomy, PET provides information on cellular metabolism. Fluorine-18 fluorodeoxyglucose (18F-FDG), a glucose analogue, is taken up by cells through glucose transporter proteins, predominantly GLUT-1 and GLUT-3, and phosphorylated by hexokinase to FDG-6-phosphate. Unlike glucose-6-phosphate, FDG-6-phosphate is not further metabolised in the glycolytic pathway and becomes trapped intracellularly, leading to preferential accumulation in tissues with elevated metabolic activity^{1,2}.

Malignant tumours demonstrate increased glucose metabolism — the Warburg effect — in which glycolysis is preferentially used for energy production even under aerobic conditions, an alteration associated with upregulation of glucose transporters and increased hexokinase activity. FDG PET is therefore widely employed in oncology for tumour detection, staging, restaging, assessment of therapeutic response and identification of recurrence³⁻⁵.

Despite its high sensitivity, FDG PET is limited by relatively poor anatomical localisation, a drawback largely addressed by hybrid PET/CT, which combines functional and structural information in a single examination. The CT component enables accurate localisation and morphological assessment, and multiple studies have shown that PET/CT enhances diagnostic accuracy compared with PET alone by decreasing false-positive results⁶⁻⁸. PET/CT is consequently regarded as a standard imaging modality in oncologic practice.

Increased FDG uptake is, however, not specific to malignant cells and is observed in a broad range of benign conditions. Activated inflammatory cells, including neutrophils, macrophages and lymphocytes, show increased glucose metabolism owing to upregulation of glucose transporters and glycolytic enzymes; infectious and inflammatory processes therefore frequently demonstrate significant FDG uptake that closely resembles malignant lesions⁹⁻¹¹. Granulomatous diseases, particularly tuberculosis and sarcoidosis, are of special significance because activated macrophages and lymphocytes within granulomas may produce intense uptake. In tuberculosis-endemic regions this overlap

creates a substantial diagnostic challenge, and tuberculous lesions may mimic metastatic disease^{12,13}.

Physiological FDG uptake is a further consideration in interpretation. Normal tracer distribution is seen in metabolically active organs such as the brain, myocardium, liver, gastrointestinal tract and urinary system. Brown adipose tissue shows uptake through non-shivering thermogenesis mediated by sympathetic stimulation, while skeletal muscle uptake may follow recent physical activity or insulin-mediated glucose utilisation¹⁴⁻¹⁷. Iatrogenic and post-therapeutic factors also contribute: surgery, chemotherapy and radiotherapy may produce inflammatory change persisting for weeks to months, and foreign materials such as prosthetic implants, surgical sutures and indwelling devices may show uptake because of chronic inflammatory or granulomatous responses¹⁸. Several benign neoplasms, including schwannomas, adenomas, fibrous tumours and certain benign bone and soft tissue lesions, may likewise exhibit uptake overlapping with that of malignant lesions¹⁹.

The standardised uptake value (SUV) is commonly used as a semi-quantitative measure of uptake, SUVmax representing the maximum voxel value within a lesion^{20,21}. Although malignant lesions typically show higher SUV values, overlap with benign conditions is substantial: inflammatory and granulomatous processes may show elevated values, whereas certain low-grade malignancies exhibit low uptake. Dual time-point imaging, metabolic tumour volume and total lesion glycolysis have been investigated to improve specificity, but the limitation of overlapping metabolic activity persists²².

The consequences of misinterpreting benign uptake are significant: false-positive results may lead to unnecessary invasive procedures, incorrect staging, patient anxiety and higher costs, while failure to recognise benign patterns may cause overestimation of disease burden. The present study was therefore performed to assess the incidence and characteristics of non-physiologic FDG uptake in benign lesions on PET/CT and to compare PET-only with integrated PET/CT interpretation.

MATERIALS AND METHODS

The present work was designed as a hospital-based retrospective observational study with a prospective follow-up component, conducted in the Department of Radio-Diagnosis and Imaging, Sree Balaji Medical College and Hospital, Chromepet, Chennai, and the

Department of Nuclear Medicine, Dr. Rela Institute and Medical Centre, Chromepet, Chennai. The study was carried out over 18 months, from July 2024 to January 2026. The study population comprised patients referred for FDG PET/CT to the Department of Nuclear Medicine during that period.

Patients undergoing FDG PET/CT for assessment of known or suspected malignancy, in whom lesions demonstrated increased FDG uptake that was indeterminate or suspected to be benign, and for whom histopathological confirmation, imaging follow-up or clinical correlation was available, were included. Patients lost to follow-up, lesions with confirmed malignancy at the time of inclusion, and cases with inadequate clinical or imaging data were excluded. Non-probability purposive sampling was used. The sample size was calculated as 267 using $n = Z^2 \times p \times (1 - p) / E^2$, where $Z = 1.96$ (95% confidence level), $p = 0.5$ (maximum variability) and $E = 0.06$.

All PET/CT examinations were performed on a Siemens Biograph Horizon PET/CT scanner. Patients fasted for at least 4–6 hours before the study and blood glucose was confirmed to be below 200 mg/dL in accordance with standard imaging protocols^{23,24}. 18F-FDG was administered intravenously at a dose of approximately 3.5–5.5 MBq/kg body weight, and imaging was performed after an uptake period of approximately 60 minutes in a resting state. Low-dose CT was obtained for attenuation correction and anatomical localisation, followed by PET acquisition; images were reconstructed using iterative reconstruction algorithms and analysed on dedicated workstations.

Lesions were evaluated on the basis of anatomical location, CT morphology, pattern of FDG uptake (focal or diffuse), intensity of uptake (mild, moderate or marked, graded visually against liver activity) and SUVmax. PET-only interpretation was performed independently and subsequently compared with integrated PET/CT interpretation. The final diagnosis was established using

histopathology, cytology, laboratory investigation, imaging follow-up or clinical correlation.

All statistical analyses were performed using IBM SPSS Statistics version 29. Continuous variables were expressed as mean $\pm$ standard deviation or median with range as appropriate, and categorical variables as frequencies and percentages. Lesions were categorised by uptake intensity, pattern and aetiology. Sensitivity and specificity of PET alone and of integrated PET/CT were calculated using histopathology, imaging follow-up or clinical correlation as the reference standard, and the McNemar test was used to compare paired proportions, as both modalities were applied to the same lesions; $p < 0.05$ was considered significant. Subgroup analyses were performed by presence of known malignancy, inflammatory conditions and organ system. Overlap between benign and malignant SUV ranges was evaluated descriptively, and no fixed SUV cut-off was applied as a sole discriminator.

The research was conducted within the ethical framework of the Declaration of Helsinki and the ICMR Ethical Guidelines for Biomedical and Health Research involving Human Participants (2017), with approval from the Institutional Ethics Committee of Sree Balaji Medical College and Hospital, Chennai. Participation was voluntary and written informed consent was obtained from every participant. FDG PET/CT is non-invasive and no additional invasive intervention was performed solely for study purposes; histopathological and immunohistochemical investigations were undertaken only where medically indicated. All data were anonymised, stored securely and accessed only by the principal investigator.

RESULTS

Approximately 650 PET/CT studies were reviewed during the study period. Lesions clinically categorised as benign or indeterminate on the basis of clinical suspicion and previous imaging were selected, and 267 patients met the inclusion criteria and were included in the final analysis.

Table 1: Age and Sex Distribution of the Study Population (n = 267)

Variable	Frequency	Percentage (%)
Age group (years)		
≤20	19	7.12
21–30	9	3.37
31–40	22	8.24
41–50	47	17.60
51–60	52	19.48
61–70	58	21.72
71–80	59	22.10
>80	1	0.37
Sex	Frequency	Percentage (%)
Male	134	50.19
Female	133	49.81

Finding: The study population showed a predominance of elderly patients, the highest proportions being in the 71–80 year (22.10%) and 61–70 year (21.72%) groups; 43.82% of all patients were aged between 61 and 80

years. Younger age groups constituted a relatively smaller proportion. The proportion of male and female patients was nearly equal, indicating a balanced representation of both sexes within the cohort.

Table 2: Clinical Classification of Lesions Prior to PET/CT and Final Lesion Category (n = 267)

Category	Frequency	Percentage (%)
Clinical status before PET/CT		
Indeterminate	165	63.46
Benign	95	36.54
Final lesion category		
Malignant	147	55.06
Non-malignant	120	44.94
Total	267	100

Finding: The majority of lesions were classified as indeterminate before PET/CT on the basis of clinical suspicion or previous imaging, highlighting the role of PET/CT as a problem-solving modality. On final

evaluation, malignant lesions constituted the larger proportion (55.06%), but a substantial 44.94% of FDG-avid lesions proved to be non-malignant.

Table 3: Aetiological Distribution of Non-Malignant FDG Uptake (n = 120)

Aetiology	Frequency	Percentage (%)
Infective	35	29.17
Benign tumour	30	25.00
Inflammatory	29	24.17
Iatrogenic	8	6.67
Trauma	7	5.83
Reactive / post-therapy	6	5.00
Ischaemic	3	2.50
Artefact	2	1.67
Total	120	100

Finding: Infective lesions were the commonest cause of non-malignant FDG uptake (29.17%), followed by benign tumours (25.00%) and inflammatory lesions (24.17%).

Infective and inflammatory aetiologies together accounted for 53.33% of all non-malignant FDG-avid lesions.

Table 4: Site-wise Distribution of All FDG-Avid Lesions (n = 267)

Site	Number of cases	Percentage (%)
Soft tissue	78	29.21
Lung	42	15.73
Lymph nodes	34	12.73
Bone	29	10.86
Liver	23	8.61
Gastrointestinal tract	22	8.24
Hepatobiliary system	10	3.75
Breast	10	3.75
Genitourinary system	8	3.00
Thyroid	7	2.62
Adrenal	4	1.50
Total	267	100

Finding: Soft tissue lesions constituted the largest proportion of FDG-avid lesions (29.21%), followed by lung (15.73%) and lymph nodes (12.73%). Bone, liver

and the gastrointestinal tract were also commonly involved.

Table 5: Organ-wise Distribution of Non-Malignant FDG-Avid Lesions (n = 120)

Organ / system	Number of cases	Percentage (%)
Lymph nodes	22	18.33
Lung	18	15.00
Liver	14	11.67
Bone	12	10.00
Gastrointestinal tract	11	9.17
Soft tissue	10	8.33
Hepatobiliary system (incl. spleen)	9	7.50
Genitourinary system	7	5.83
Thyroid	6	5.00
Breast	6	5.00
Adrenal	5	4.17
Total	120	100

Finding: Among non-malignant lesions, lymph nodes (18.33%) and lung (15.00%) were the most commonly involved sites, followed by liver (11.67%) and bone (10.00%). Gastrointestinal tract and soft tissue

involvement were also notable, while the hepatobiliary system, genitourinary system, thyroid, breast and adrenal glands contributed smaller proportions.

Table 6: SUVmax of Lesions — Mean Values, Distribution by Range and Mean Values Across Non-Malignant Aetiologies

Parameter	Value
Mean SUVmax, non-malignant lesions	6.11
Mean SUVmax, malignant lesions	10.93
SUVmax range <5, n (%)	72 (26.97)
SUVmax range 5–10, n (%)	101 (37.83)
SUVmax range 10–15, n (%)	70 (26.22)
SUVmax range 15–20, n (%)	17 (6.37)
SUVmax range >20, n (%)	7 (2.62)
Mean SUVmax, infective	8.35
Mean SUVmax, artefact	6.20
Mean SUVmax, benign tumour	5.79
Mean SUVmax, iatrogenic	5.30
Mean SUVmax, reactive / post-therapy	5.05
Mean SUVmax, inflammatory	4.82
Mean SUVmax, trauma	4.34
Mean SUVmax, ischaemic	3.80

Finding: Malignant lesions demonstrated a higher mean SUVmax (10.93) than non-malignant lesions (6.11), although overlap between the two groups was evident. Most lesions showed moderate uptake, the largest proportion (37.83%) falling within the SUVmax range of 5–10 g/mL, while very high values were uncommon.

Among non-malignant aetiologies, infective lesions exhibited the highest mean SUVmax (8.35), followed by artefact and benign tumours, whereas inflammatory, traumatic and ischaemic lesions showed relatively lower values.

Table 7: PET Versus PET/CT Interpretation (n = 267)

Category	PET	PET/CT
True positive	135	143
True negative	47	116
False positive	73	4
False negative	12	4

Finding: PET-only interpretation produced 73 false-positive results, whereas integrated PET/CT reduced these

to 4, with a parallel increase in true negatives from 47 to 116 and a fall in false negatives from 12 to 4.

Table 8: Diagnostic Performance of PET and PET/CT, and Methods of Diagnostic Confirmation

Parameter	Value
PET sensitivity (%)	91.84
PET specificity (%)	39.17
PET/CT sensitivity (%)	97.28 (95% CI: 93.8–99.1)
PET/CT specificity (%)	96.67 (95% CI: 91.7–98.9)
Histopathology, n (%)	134 (50.19)
Clinical / other, n (%)	71 (26.59)
Laboratory, n (%)	27 (10.11)
Imaging follow-up, n (%)	19 (7.12)
FNAC / cytology, n (%)	16 (5.99)

Finding: PET alone achieved a sensitivity of 91.84% but a specificity of only 39.17%. Integrated PET/CT achieved a sensitivity of 97.28% and a specificity of 96.67%, representing a marked improvement in specificity while maintaining high sensitivity. Histopathological examination was the commonest method of confirming the final diagnosis (50.19%), followed by clinical correlation, laboratory investigation, imaging follow-up and cytology.

DISCUSSION

The present study assessed lesions demonstrating increased FDG uptake on PET/CT that were considered benign or indeterminate on prior imaging or clinical evaluation, and compared the diagnostic performance of PET alone with that of integrated PET/CT. Of approximately 650 examinations reviewed, 267 patients satisfied the predefined criteria and were analysed.

Most patients were in the sixth to eighth decades of life, an expected observation since PET/CT is performed principally in individuals with suspected or known malignancy, and since infections, chronic inflammatory

conditions and degenerative disorders are also commoner in the elderly. The nearly equal sex distribution reflects the wide range of conditions assessed by whole-body PET/CT, which is performed for diverse indications rather than for a single organ system⁵.

A substantial proportion of lesions were classified as indeterminate before PET/CT, emphasising its role as a problem-solving modality. Conventional CT and MRI provide anatomical information but cannot consistently distinguish benign from malignant lesions, whereas PET provides functional information related to tissue metabolism. Increased glycolytic activity is not, however, specific to malignant cells, and integration of metabolic information from PET with anatomical detail from CT is therefore central to accurate interpretation^{30,31}.

Assessment of anatomical distribution showed that soft tissue, lung and lymph nodes were the commonest sites of FDG-avid lesions overall, while lymph nodes, lung and liver predominated among non-malignant lesions. This distribution accords with the known patterns of both malignant and inflammatory disease. The lungs represent one of the most frequent sites of uptake, reflecting the high prevalence of pulmonary infection, inflammatory lung disorders and primary lung malignancy; pneumonia, tuberculosis, granulomatous disease and organising pneumonia may all show significant uptake and mimic malignancy. Meta-analytic data on solitary pulmonary nodules have similarly reported high sensitivity but only moderate specificity for FDG PET/CT, the reduced specificity being largely attributable to granulomatous and infectious disease prevalent in certain geographic regions^{27,28}. Lymph nodes commonly show increased uptake due to reactive hyperplasia, infectious lymphadenitis and inflammatory conditions, making differentiation from metastatic disease challenging, and benign hepatic lesions such as abscesses, inflammatory pseudotumours and focal infections may likewise exhibit increased metabolic activity.

Among the benign lesions identified, infective and inflammatory conditions constituted the commonest causes of elevated FDG uptake, together accounting for more than half of non-malignant uptake in this cohort. This is consistent with published literature. Metser and Even-Sapir reported that inflammatory processes are among the most frequent causes of benign FDG uptake, observing that approximately 73.3% of benign FDG-avid lesions in their series were inflammatory in origin, and demonstrated that more than half of benign lesions exhibited moderate to marked uptake¹². Activated inflammatory cells show elevated glucose metabolism due to upregulation of glucose transporters and enhanced hexokinase activity, so that inflammatory lesions may demonstrate uptake comparable to or greater than that of malignant tumours^{26,32,33}. FDG PET/CT has correspondingly been shown to be highly sensitive in

detecting occult inflammatory foci in fever of unknown origin, although specificity estimates remain variable in the absence of standardised diagnostic criteria²⁵. Post-therapy change is a further important cause: surgery, radiotherapy and chemotherapy induce inflammatory change that may persist for weeks to months, and awareness of these patterns is essential to avoid misinterpreting post-treatment inflammation as recurrent malignancy³⁵. Comparable pitfalls have been described in head and neck imaging, where physiological and post-treatment uptake frequently simulates disease³⁴.

Quantitative assessment showed higher mean SUVmax in malignant than in non-malignant lesions, in keeping with the increased glycolytic activity, GLUT-1 overexpression and enhanced hexokinase activity characteristic of malignant cells. Nevertheless, considerable overlap was observed, several benign conditions — particularly infections — demonstrating moderate to high uptake, with infective lesions showing the highest mean SUVmax among benign aetiologies. This overlap underscores the limitation of relying solely on SUVmax for lesion characterisation, a limitation also emphasised in musculoskeletal imaging, where benign lesions such as osteomyelitis, fractures and certain benign neoplasms may exhibit uptake comparable to malignant tumours¹⁹, and in gastrointestinal imaging, where inflammatory conditions may yield false-positive results²⁹. SUV measurements should therefore be interpreted alongside CT morphology and clinical context rather than in isolation²¹.

The comparison of PET-only with integrated PET/CT interpretation demonstrated a marked improvement in diagnostic specificity when CT information was incorporated, specificity rising from 39.17% to 96.67% while sensitivity also improved from 91.84% to 97.28%.

Histopathology, the gold standard in many oncologic and inflammatory conditions, was the commonest method of confirmation, and this relatively high rate strengthens the reliability of the present findings. Obtaining tissue is not always feasible or ethically justified when imaging features strongly favour a benign aetiology; in such cases imaging follow-up and clinical correlation provide important information on lesion behaviour over time, lesions that remain stable or regress being more likely to represent benign processes.

These findings have direct implications for reporting practice. Increased FDG uptake is not specific to malignancy, and careful correlation of PET findings with CT morphology and clinical history is essential to avoid false-positive interpretation — particularly in regions where infectious diseases such as tuberculosis are prevalent, where the likelihood of benign uptake is high. A multidisciplinary approach involving radiologists, nuclear medicine physicians, oncologists and treating clinicians further enhances diagnostic accuracy.

CASE ILLUSTRATIONS

Case 1: Post-traumatic FDG Uptake Mimicking Metastasis

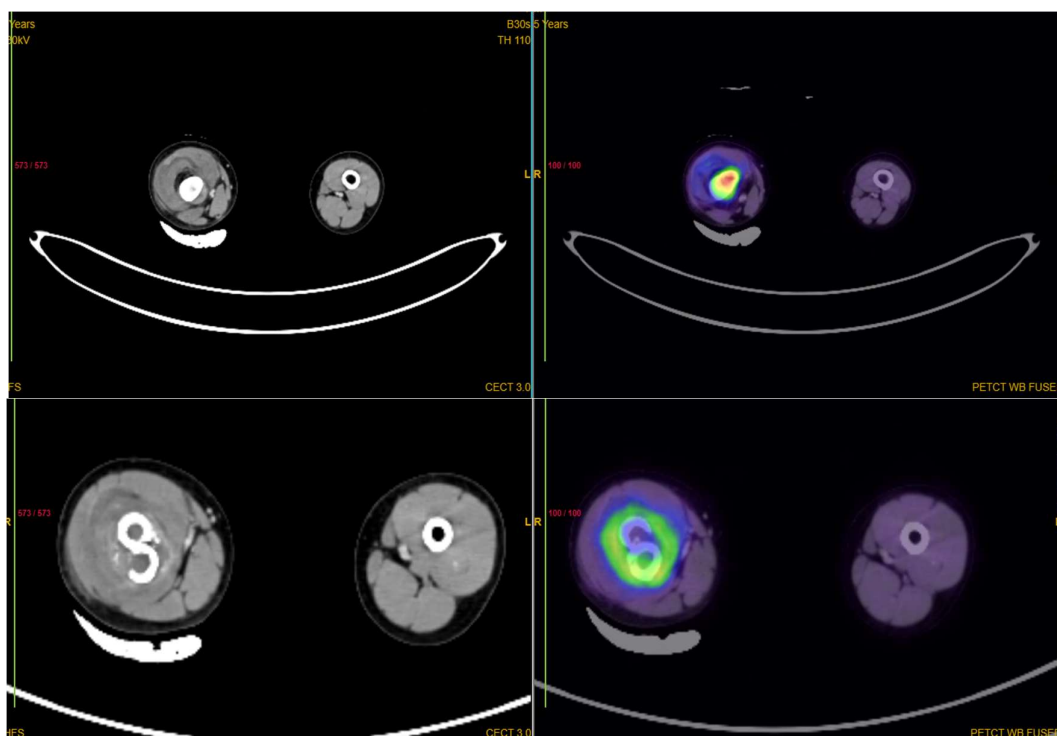


Figure 1: Case 1 – Post-traumatic FDG Uptake - Axial CT, PET, and fused PET/CT images of a 5-year-old male with a history of left adrenal neuroblastoma status post adrenalectomy, presenting after a recent fall. The images demonstrate **focal increased FDG uptake in a long bone**, raising suspicion for skeletal metastasis on PET-alone evaluation. However, corresponding CT images reveal **cortical irregularity and features consistent with fracture**, without aggressive bone destruction.

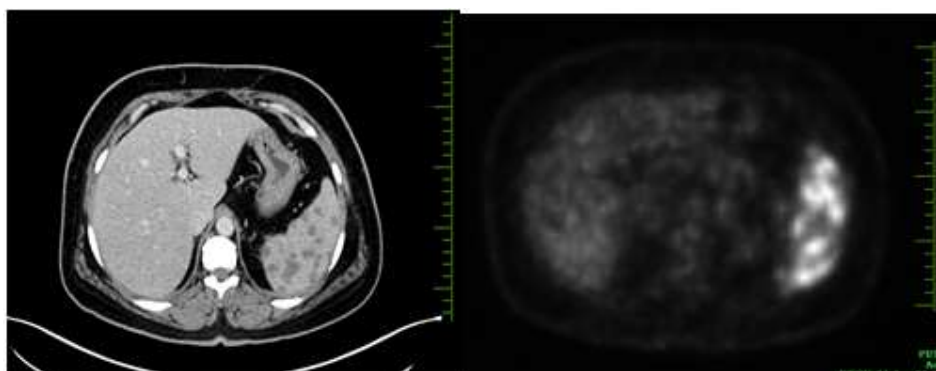
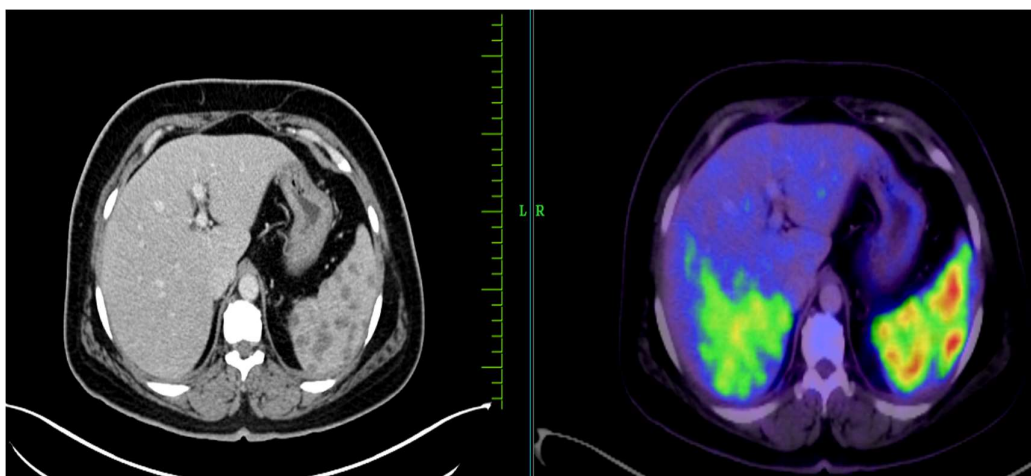


Figure 2: Case 2 – Hepatosplenic FDG Uptake Mimicking Lymphoma, Proven Granulomatous Disease (Hepatosplenic Sarcoidosis)

(A) Axial CT and PET images show **splenomegaly with multiple predominantly subcentimetric coalescent hypodense lesions throughout the spleen** with intense FDG uptake (SUVmax up to ~12.0).



(B) Axial PET and fused PET/CT images demonstrate heterogeneously increased FDG uptake in the liver, predominantly involving segments VI, VII, VIII, and II (SUVmax ~9.7), without corresponding focal structural abnormality on CT.

Limitations

Several limitations should be acknowledged. The study was retrospective in design, which may introduce selection bias and restricts the ability to determine causal relationships. Although 650 PET/CT examinations were reviewed, only 267 patients met the inclusion criteria, which may limit generalisability. Not all lesions were confirmed histopathologically; in several cases the final diagnosis was based on imaging follow-up or clinical correlation, introducing a degree of diagnostic uncertainty. SUVmax was used as a semi-quantitative parameter and can be influenced by patient preparation, blood glucose levels and acquisition parameters. Finally, as the study was conducted in a single tertiary care centre, the results may not fully represent patterns of benign FDG uptake in other populations or clinical settings.

Future directions

Prospective multicentre studies with larger cohorts are required to further characterise the patterns and causes of non-physiologic FDG uptake. Quantitative PET parameters beyond SUVmax, including metabolic tumour volume and total lesion glycolysis, may add discriminatory value, and the incorporation of artificial intelligence and machine learning into PET/CT interpretation may further improve diagnostic accuracy and reduce false-positive findings.

CONCLUSION

FDG PET/CT, although highly sensitive in detecting metabolically active lesions, has inherent limitations in specificity because of substantial overlap between benign and malignant FDG uptake. In the present study 44.94% of FDG-avid lesions were ultimately found to be benign, with infective and inflammatory conditions the commonest causes, followed by benign tumours, iatrogenic and post-traumatic changes. Many of these lesions demonstrated moderate to marked uptake, closely mimicking malignancy, and mean SUVmax values overlapped considerably between the two groups, confirming that intensity of uptake alone cannot reliably

distinguish benign from malignant disease. Integrated PET/CT demonstrated markedly improved diagnostic performance compared with PET alone, sensitivity increasing from 91.84% to 97.28% and specificity from 39.17% to 96.67%, by enabling accurate anatomical localisation and better morphological characterisation of FDG-avid lesions. Certain benign conditions nonetheless continue to mimic malignancy, necessitating correlation with clinical findings, laboratory parameters and, where required, histopathological confirmation. A systematic and integrated approach combining metabolic, anatomical and clinical information is therefore crucial for accurate diagnosis, for avoiding unnecessary invasive procedures and for optimising patient management.

REFERENCES

1. Alavi A, Gupta N, Alberini JL, Hickeson M, Adam LE, Bhargava P, Zhuang H. Positron emission tomography imaging in nonmalignant thoracic disorders. *Semin Nucl Med.* 2002;32(4):293–321. doi:10.1053/snuc.2002.36812
2. Avril N. Glucose metabolism in cancer: FDG PET imaging and GLUT1 expression. *J Nucl Med.* 2004;45(6):930–932. doi:10.2967/jnumed.104.019877
3. Jadvar H. FDG PET in oncology: basics and clinical applications. *J Nucl Med.* 2016;57(Suppl 1):144S–149S. doi:10.2967/jnumed.115.157859
4. Gambhir SS. Molecular imaging of cancer with positron emission tomography. *Nat Rev Cancer.* 2002;2(9):683–693. doi:10.1038/nrc882
5. Kumar R, Basu S, Torigian D, Anand V, Zhuang H, Alavi A. Role of FDG PET in oncology. *Radiographics.* 2008;28(2):507–531. doi:10.1148/rg.282075027
6. Townsend DW. Combined PET/CT: the historical perspective. *Semin Ultrasound CT MR.* 2008;29(4):232–235. doi:10.1053/j.sult.2008.05.006

7. Fletcher JW, Djulbegovic B, Soares HP, et al. Recommendations on the use of 18F-FDG PET in oncology. *J Nucl Med.* 2008;49(3):480–508. doi:10.2967/jnumed.107.047787
8. Czernin J, Allen-Auerbach M, Schelbert HR. Improvements in cancer staging with PET/CT. *J Nucl Med.* 2007;48(Suppl 1):78S–88S.
9. Culverwell AD, Scarsbrook AF, Chowdhury FU. False-positive uptake on 2-[18F]-FDG PET/CT in oncological imaging. *Clin Radiol.* 2011;66(4):366–382. doi:10.1016/j.crad.2010.12.004
10. Love C, Tomas MB, Tronco GG, Palestro CJ. FDG PET of infection and inflammation. *Radiographics.* 2005;25(5):1357–1368. doi:10.1148/rg.255045122
11. Zhuang H, Alavi A. 18F-FDG PET imaging in infection and inflammation. *Radiol Clin North Am.* 2005;43(1):121–134. doi:10.1016/j.rcl.2004.10.002
12. Metser U, Even-Sapir E. Benign nonphysiologic lesions with increased 18F-FDG uptake on PET/CT: characterization and incidence. *AJR Am J Roentgenol.* 2007;189(5):1203–1210. doi:10.2214/AJR.07.2260
13. Sathekge M, Maes A, Van de Wiele C. FDG PET in tuberculosis. *Clin Nucl Med.* 2012;37(6):e124–e130. doi:10.1097/RLU.0b013e31824d2c1a
14. Engel H, Steinert H, Buck A, Berthold T, Huch Boni RA, von Schulthess GK. Whole-body PET: physiological and artifactual fluorodeoxyglucose accumulations. *J Nucl Med.* 1996;37(3):441–446.
15. Hany TF, Gharehpapagh E, Kamel EM, Buck A, Himms-Hagen J, von Schulthess GK. Brown adipose tissue: a factor to consider in symmetrical tracer uptake. *Eur J Nucl Med Mol Imaging.* 2002;29(10):1393–1398. doi:10.1007/s00259-002-0902-6
16. Yeung HW, Grewal RK, Gonen M, Schöder H, Larson SM. Patterns of FDG uptake in adipose tissue and muscle. *J Nucl Med.* 2003;44(11):1789–1796.
17. Cohade C, Osman M, Pannu HK, Wahl RL. Uptake in supraclavicular area fat ("USA-fat"). *J Nucl Med.* 2003;44(2):170–176.
18. Shreve PD, Anzai Y, Wahl RL. Pitfalls in oncologic FDG PET imaging. *Radiographics.* 1999;19(1):61–77. doi:10.1148/radiographics.19.1.g99ja0761
19. Aoki J, Watanabe H, Shinozaki T, et al. FDG PET/CT evaluation of musculoskeletal tumors: differentiation of benign and malignant lesions. *Ann Nucl Med.* 2008;22(7):603–609. doi:10.1007/s12149-008-0145-5
20. Boellaard R. Standards for PET image acquisition and quantitative data analysis. *J Nucl Med.* 2009;50(Suppl 1):11S–20S. doi:10.2967/jnumed.108.057182
21. Van den Hoff J, Oehme L, Schramm G. The standardized uptake value revisited. *Eur J Nucl Med Mol Imaging.* 2015;42(3):329–339. doi:10.1007/s00259-014-2954-4
22. Cheng G, Torigian DA, Zhuang H, Alavi A. When should we consider dual-time-point FDG PET imaging? *Eur J Nucl Med Mol Imaging.* 2013;40(5):779–787. doi:10.1007/s00259-012-2335-4
23. Delbeke D, Coleman RE, Guiberteau MJ, et al. Procedure guideline for tumor imaging with FDG PET/CT. *J Nucl Med.* 2006;47(5):885–895.
24. Boellaard R, Delgado-Bolton R, Oyen WJG, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging. *Eur J Nucl Med Mol Imaging.* 2015;42(2):328–354. doi:10.1007/s00259-014-2961-x
25. Bharucha T, Rutherford A, Skeoch S, et al. Diagnostic yield of FDG PET/CT in fever of unknown origin: a systematic review. *Clin Radiol.* 2017;72(9):764–771. doi:10.1016/j.crad.2017.05.004
26. Basu S, Alavi A. FDG PET in infection and inflammation: current and emerging clinical applications. *Radiographics.* 2009;29(5):1289–1303. doi:10.1148/rg.295085245
27. Jia Y, Gong W, Zhang Z, et al. Diagnostic value of 18F-FDG PET/CT versus CT for solitary pulmonary nodules: meta-analysis. *J Thorac Dis.* 2019;11(5):2082–2098. doi:10.21037/jtd.2019.05.21
28. Gould MK, Maclean CC, Kuschner WG, Rydzak CE, Owens DK. Accuracy of PET for pulmonary nodules: a meta-analysis. *JAMA.* 2001;285(7):914–924. doi:10.1001/jama.285.7.914
29. Gollub MJ, Grewal RK, Pannu HK. Diagnostic accuracy of 18F-FDG PET/CT for detection of advanced colorectal adenoma. *Clin Radiol.* 2014;69:611–618.
30. Kamel EM, Burger C, Buck A, et al. Impact of CT on PET imaging. *J Nucl Med.* 2002;43(8):1079–1086.
31. Antoch G, Statta J, Nemat AT, et al. Non-small cell lung cancer: PET/CT vs PET. *Radiology.* 2003;229(2):526–533. doi:10.1148/radiol.2292021598
32. Kwee TC, Kwee RM. FDG PET/CT in infection and inflammation: a systematic review. *Eur J Radiol.* 2008;67(2):241–253. doi:10.1016/j.ejrad.2007.07.036
33. Kostakoglu L, Goldsmith SJ. FDG-PET evaluation of infection and inflammation. *Radiol Clin North Am.* 2005;43(1):47–59. doi:10.1016/j.rcl.2004.10.001

34. Purohit BS, Ailianou A, Dulguerov N, Becker CD, Ratib O, Becker M. FDG-PET/CT pitfalls in oncological head and neck imaging. *Insights Imaging*. 2014;5(5):585–602. doi:10.1007/s13244-014-0349-x
35. Israel O, Kuten A. Early detection of cancer recurrence: FDG PET/CT. *Eur J Nucl Med Mol Imaging*. 2007;34(2):193–212. doi:10.1007/s00259-006-0273-1