Common Pitfalls in PET/CT Imaging: A Pictorial Review

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Learning objectives

By the end of this presentation, readers should be able:

- To understand the basis of PET/CT imaging pitfalls and artifacts through a brief review of PET imaging physics and physiology
- To recognize a few frequently encountered pitfalls in PET/CT imaging and help avoid misinterpretation
- To be cognizant of methods for minimizing and correcting common PET/CT artifacts
Background

With the widespread use of Positron Emission Tomography (PET) coupled with Computed Tomography (CT) imaging to guide the treatment of complex oncologic patients, it becomes critical for proper patient care to not only accurately localize the presence or absence of disease but to also recognize potential pitfalls that may lead to study misinterpretation and suboptimal patient management. These include PET/CT misregistration, misinterpretation of physiologic activity, and failure to recognize hypometabolic malignancies.

A basic review of the physics and physiology inherent to PET/CT imaging is helpful in understanding the mechanics behind many potential pitfalls. The radiotracer used in PET imaging, commonly 18F-fluorodeoxyglucose (18F-FDG), serves as a glucose analog. Once injected intravenously, the radiotracer is redistributed to areas of increased metabolic (and hence glucose) demand. Phosphorylation traps the tracer in the cell, but a missing 2'-hydroxyl group prevents further metabolism and effectively traps the radiotracer in the cell.

After allowing for biologic redistribution (typically one hour), PET imaging is performed. Radioactive decay of 18-fluorine into a stable 18-oxygen occurs by positron emission 97% of the time. Emitted positrons quickly undergo positron-electron annihilation events and emit two 511keV photons in opposite directions that are detected by the PET machine. These annihilation events are localized along Lines of Response and pooled into datasets that are ultimately used to reconstruct 3D images of increased 18F (and hence metabolic) activity.

Concurrent CT imaging provides an anatomic correlate to the physiologic data that PET provides. However, there is a short delay between acquisition of these data and errors such as PET/CT misregistration become more likely. Recognizing these technical errors as well as common physiologically hypermetabolic lesions will lead to fewer study misinterpretations and improved patient management.
Findings and procedure details

Although not comprehensive, these examples illustrate a few of the most commonly encountered pitfalls in PET/CT image interpretation. Recognition of these scenarios can help avoid misinterpretation:

**PET/CT Dataset Misregistration**

- Extreme cases of dataset misregistration are often easily recognized, such as head repositioning between PET and CT data acquisition. However, more subtle position misregistration could lead to an erroneously hypermetabolic or hypometabolic focus. For example, Fig 1 demonstrates an erroneously non-FDG-avid lymph node at the uncinate process. Adjacent slices demonstrate misregistered FDG-uptake (Fig 2) that proved to be pancreatic malignancy with locoregional nodal metastatic disease.
- Recognition of the misregistration by close inspection of adjacent misregistered landmarks (such as the liver & spleen or spine) can help prevent this error.
- Manual registration correction can often be performed within PET/CT viewing software. Datasets can be panned in three dimensions, rotated about a user-defined axis, or even scaled to a best-fit.

**Benign Activity: Brown Fat**

- Physiologically, brown fat is rich in mitochondria and serves to produce heat. In typical tissues, oxidative phosphorylation couples the stored energy in glucose to the production of ATP via the electron transport chain. However, in brown fat, the process is decoupled and the stored energy in higher-energy metabolic intermediates is immediately released as heat without generating ATP.
- Being rich in mitochondria, these areas of brown fat are extremely glucose (and 18F-FDG) avid, yielding relatively increased radiotracer activity to the surrounding tissue.
- These areas of brown fat are typically supraclavicular and readily identified by their correlation to fat-density foci on CT data (Fig 3).
- However, with an increased background of brown fat, the detection of truly abnormal FDG-avid foci becomes increasingly difficult. For example, a hypermetabolic right axillary lymph node that corresponded to biopsy-proven lymphoma recurrence could easily be overlooked on a background of increased brown fat activity (Fig 4).
- Brown fat can also appear in atypical locations. As an example, the lipomatous hypertrophy of the interatrial septum can be focally FDG-avid
and mistaken for pathology (Fig 5). Again, correlation with fat-density on CT images will prove its benignity.

- Measures can be taken to reduce brown fat activity on future imaging. These include ensuring patient warmth and premedication with beta-blockers or benzodiazepines.

**Benign Activity: Corpus Luteum & Adrenal Adenoma**

- Although there are many non-malignant lesions that could focally increase FDG-uptake that could easily fill textbooks, the entities generally revolve around the underlying principle of increased activity corresponding to increased glucose uptake.
- These include inflammatory and osteoclast/osteoblast activity from healing bone fractures and physiologic ovarian luteal bodies (Fig 6). Conversely, recognition of a non-FDG-avid lesion can instill confidence of lesion benignity, such as an adrenal adenoma (Fig 7).

**Benign Activity: Medications**

- Diffusely increased GI activity can be seen throughout the colon in diabetic patients taking Metformin (Fig 8). Its presentation is fairly typical but should not be mistaken for inflammatory bowel conditions or malignancy.
- If there is concern for underlying GI malignancy, a repeat evaluation can be performed after withholding Metformin for at least 48 hours.

**Benign Activity: Post-operative Events**

- Surgically placed devices can cause increased FDG uptake due to foreign body reactions that can persist for years after the procedure.
- Inflammation from immediate post-operative states or recently irradiated tissues can simulate and be indistinguishable from malignancies. Correlation with history and prior imaging is critical.
- Left hernia repair plug placed in 2007 still appear focally FDG-avid 7 years after placement in 2014 (Fig 9).
- Marrow reactivation shortly after chemotherapy administration is also common (Fig 10). History and distribution will be useful in distinguishing reactivation from diffuse skeletal pathology. Diffuse and homogenous distribution at sites of red marrow favors reactivation while heterogenous and spotty distribution favors metastatic disease.
- Recognition of implanted devices and prior surgical/radiotherapy treatments is imperative to avoid erroneously diagnosing infection or neoplasm.

"PET Occult" Malignancies
• Although most malignancies are heavily energy-dependent due to their rapid division, a few can be occult on PET/CT. For example, renal cell carcinoma is commonly minimally to mildly FDG-avid with a PET detection sensitivity of 60%.
• Figure 11 demonstrates a large heterogenously-enhancing exophytic left renal mass that falls into Bosniak 4 classification and was proven to represent renal cell carcinoma. However, only mild FDG uptake is noted that is similar to the adjacent normal renal parenchyma (Fig 12).
• Be cognizant of malignant entities that not well-detected by PET imaging such as RCC and utilize other imaging modalities to complement suspicious lesions.
Images for this section:

Fig. 1: Misregistered lymph node at the uncinate process, corresponding to proven metastatic pancreatic disease. No significant FDG uptake on this slice.

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Fig. 2: Misregistered FDG-avid focus corresponding to hypermetabolic lymph node at the uncinate process representing metastatic pancreatic disease.

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Fig. 3: CT and PET images of typical brown fat activity in the supraclavicular region.
Fig. 4: Enlarged FDG-avid right axillary lymph node superimposed on a background of intense brown fat activity. This node was later biopsied and represented lymphoma recurrence.

Fig. 5: Focus of increased FDG uptake at interatrial septum corresponds anatomically to benign lipomatous hypertrophy of the interatrial septum and should not be mistaken for malignancy.
**Fig. 6:** Focally increased moderate FDG uptake in the leftward pelvis corresponds to benign corpus luteum on contract-enhanced CT.

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**Fig. 7:** Left adrenal nodule is of indeterminate density on CT imaging. FDG uptake of the nodule is similar to (or less than) the adjacent liver parenchyma and confers confidence of lesion benignity. This represented an adrenal adenoma.

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Fig. 8: Diffuse FDG uptake throughout the colon in this diabetic patient taking Metformin should not be mistaken for a diffuse inflammatory bowel condition or malignancy.

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Fig. 9: Focal FDG uptake in the left inguinal region corresponds to known hernia repair plug that was placed in 2007. This area remains FDG-avid on 2014 PET/CT study and represents persistent foreign body reaction and should not be mistaken for developing infection or malignancy.

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Fig. 10: 3D MIP image demonstrates diffusely increased FDG uptake in the marrow spaces of the spine, pelvis, and proximal femurs in this patient with marrow reactivation who recently underwent chemotherapy treatment.

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**Fig. 11:** Contrast-enhanced CT image shows a large exophytic left renal mass that represented a mildly-FDG-avid renal cell carcinoma.

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**Fig. 12:** Unenhanced PET/CT images show an exophytic left renal mass that is difficult to distinguish from the adjacent renal parenchyma by attenuation and FDG activity in this patient with renal cell carcinoma.

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Conclusion

Hybrid functional-anatomical PET/CT imaging has become an integral and powerful modality in the management of many oncologic diseases. Therefore, it is critical that the radiologist be cognizant of the potential pitfalls in PET/CT imaging to avoid misinterpretation that would lead to suboptimal patient management.
References