HYPERMETABOLIC IMAGES OF DIGESTIVE TRACT IN PET-CT, DIFFERENTIAL DIAGNOSIS

Verónica Gigirey MD (1), Liliana Servente MD(2), Margarita García Fontes MD(3)

(1) Ex assistant (2) Assistant Professor (3) Associate Professor, Hospital de Clínicas, Montevideo, Uruguay.
Radiologist physicians, Uruguayan Center of Molecular Imaging (CUDIM)

Abstract

Positron emission tomography (PET), using 18 F-fluorodeoxyglucose (18 F-FDG) has been successfully implemented for evaluation of malignant tumors, showing high sensitivity in detecting tumors in the digestive tract, but with low specificity due to several physiological and pathological patterns of FDG uptake in the digestive tract. By combining PET and CT (PET-CT) we can localize and characterize the FDG uptake focus. It is necessary to be familiar with uptake patterns in the digestive tract to differentiate between physiological and pathological patterns and within these in order to distinguish between inflammatory and tumoral alterations. To achieve this we set the following goals: 1) To describe and characterize physiological versus pathological uptake of 18F-FDG in the digestive tract in PET-CT studies. 2) To revise findings of PET-CT studies with 18F-FDG carried out in CUDIM(Uruguayan Center of Molecular Imaging) with oncologic patients who present hyper-metabolic lesions in the digestive tract and its pathological correlation. Correlation with CT and combination of PET-CT can sometimes help identify the cause in uptake increase and it is recommended that focuses of higher uptake in the bowel should be evaluated with endoscopy.

Keywords

Gastrointestinal tract, focal lesions, 18 F-FDG, PET-CT, Oncology , Pitfalls
1- Introduction

Combining positron emission tomography (PET) and computed tomography (CT) in a single unit (PET-CT) represents an important milestone in Oncology, Nuclear Medicine and Radiology fields, allowing a highly precise fusion and correlation of morphological images (obtained with CT) and metabolic images (obtained by PET).

Fluor-18-fluorodeoxyglucose (18 F-FDG) PET has been successfully implemented for evaluation of malignant tumors especially in the last decade. Increase in accumulation of radiotracer 18 F-FDG (FDG) in neoplastic tissues is a consequence of an increase in the expression and activity of glucose transport proteins which are the result of a greater anaerobic metabolism of tumoral cells. (1,2). However, uptake of FDG is not specific to neoplastic processes. It accumulates physiologically in several normal organs, including the brain, muscles, salivary glands, myocardium, gastrointestinal apparatus and urinary tract. Furthermore, FDG also accumulates in benign lesions: inflammatory or granulomatous processes. (3,4).

18F-FDG PET-CT is sensitive in the detection of malignant tumors of the intestine, but its specificity is reduced due to several physiological and pathological patterns of FDG uptake in the bowel. It is important to know these physiological variants and the metabolic uptake patterns since they might lead us to false positive diagnosis of malignancy. Any segment of the digestive tract (DT) can uptake FDG in a focal, segmental or diffused way and also with a variable intensity (mild, moderate or intense), which we will define later (section 2.d). The exact etiology of this physiological uptake of the gastrointestinal tract is unknown but it is probably due to multiple factors. Among described causes for such uptake are: metabolic activity of smooth muscle, metabolic activity of mucosa and/or lymphoid tissue associated with mucosa and active excretion of FDG. (4,5). Diffuse uptake of FDG in the DT can be defined as physiological and not related to malignant pathology with high certainty. However a focal and circumscribed area of FDG increase can suggest malignancy. (4,5).

Hybrid PET-CT units provide an anatomical localization of these sites of FDG accumulation (6,7). Several authors have shown that precise localization of hyper-metabolic lesions using PET-CT improve diagnosis efficacy. (7,8).

It is important to also know that there are certain non-hypermetabolic neoplasms such as slow-growth lesions, which have a great mucous component and tumors with signet-ring cells, which may not be very avid for FDG; therefore their analysis should be cautious.
Other tumors such as low-grade neuroendocrine, lymphomas and carcinoids may not show significant metabolic activity. Extensive superficial lesions, such as those with central necrosis can have a low FDG uptake. (9,10).

FDG PET-CT has shown to be very sensitive in detecting primary neoplasia, however its specificity is lower due to physiological uptake and the abovementioned inflammatory causes. The main use of PET-CT using FDG is in the staging and re-staging of patients with colon cancer, due to detection of regional lymphatic ganglia and distant metastasis.

Focal nodular uptake and multi-focal nodular uptake are predictive of pathological findings that can include malignancy. It is necessary to perform a colonoscopy for a correct evaluation of these cases. (13). A pattern of diffuse uptake, regardless of its grade is predictive of normal results in colonoscopy, whereas a segmental and intense pattern can indicate an inflammatory condition. It has been observed that dysplastic adenomas and hyper-plastic polyps may present a pattern of focal or multi-focal uptake; therefore FDG may be useful in the detection of pre-malignant entities in the colon (14).

Figure 1. 73 years old male. PET-CT for evaluation of solitary pulmonary nodule (SPN). A) PET coronal image: focal uptake in the inferior mediastinum middle line B-C) CT axial plane and sagittal reconstruction: with out obvious lesions D-E) Axial and sagittal fusion: Increase in physiological focal uptake in esophagus gastric union.
In this work we revised studies in which we found focal uptake of FDG at the level of the digestive tract in patients with known tumoral pathology of the digestive sphere and in those in which it was a finding. In this last case, monitoring was carried out to determine if they were malignant or premalignant lesions or another etiology.

**Objectives** of this work are:

1. Describe and characterize physiological versus pathological uptake of 18-F-FDG in the digestive tract in PET-CT studies.
2. Revise findings in 18-F-FDG PET-CT studies performed in CUDIM on oncologic patients who presented hypermetabolic lesions in the digestive tract and its pathological correlation.

### 2- Material and methods.

#### 2.a. Patients: Reports of 18-F-FDG PET-CT total body studies of those patients who attended CUDIM for a period of 4 months (March to June 2011) with different oncologic indications were revised retrospectively. Out of this population (450 patients) metabolically active images of the DT of 32 patients who were referred for staging of tumors of gastrointestinal tract, were analyzed. Patients bearing carcinoid tumors (on whom a study with 68Ga was performed) and those indicated for re-staging were excluded. Furthermore, findings from hypermetabolic lesions informed in 8 patients with other primary tumors were revised and characteristics of these images were analyzed. This selection was not performed randomly. Patients who could be monitored in order to show endoscopic, anatomical-pathological and or developmental correlation were selected.

**Figure 2** - Increased physiological diffused Uptake in the colon. 58 years old male. SPN high surgical risk. A) Coronal PET image: increased diffuse uptake in the colon (arrow), B) CT coronal reconstruction: without solid focal or diffuse lesions, C) Coronal fusion.
2.b. PET-CT Protocol: A hybrid General Electric PET-CT Unit, which acquires PET and multiple detector CT images (64 detectors) of the patients in one session was used. The axes of both systems are mechanically aligned for correct correlation. Images were obtained from the vertex to the superior third of the thigh. To achieve coincidence between CT and PET images, the study was performed with the patient breathing easily. CT data was first acquired within the following parameters: 140 kV and 80 mA; with a 4,75 mm thick sections. Next, PET emission data was acquired in 3D mode during 3 minutes for each field (each 20 cm long). A repetitive reconstruction and an attenuation CT map was used for PET images. The images were analyzed in Advantage work station, analyzing CT, PET image and the fusion of both in axial, coronal and sagittal planes. PET data were also examined in maximum intensity projection (MIP) in the coronal plane.

2.c. Preparation of the patient:
Preparation of the patient includes: 6 hours of fasting, resting the previous day, adequate hydration, decrease in consumption of carbohydrates 24 hours before and to avoid smoking. Glycemia before performing the study must be less than or equal to 150 mg/dl. 18F-FDG 4.07 MBq/kg of weight (10-15 mCi) is administered intravenously an hour before the study, time in which bio-distribution of the drug occurs. After the injection the patient must rest. 1000 ml of iodine contrast diluted at 5% were orally administered before the study in cases of known digestive pathology. Once discarded contraindications for its use, water-soluble iodinated contrast medium was injected (1-2 cc/kg body weight) as long as the patient does not have recent studies or diagnostic doubts. When the study is over patient must be re-hydrated.

2d. Evaluation of PET-CT images: The grade of FDG uptake in the digestive tract was evaluated via a visual analysis of the images comparing with normal uptake of liver (background) considering it mild when it is less that liver uptake and moderate to intense when it is more pronounced. Quantitative analysis was also used by measuring SUV (“standardized uptake value”) which measures radiation activity detected by PET, normalized according to the patient’s weight and the injected dose. It is considered mild uptake if SUV is lower than 2.5, moderate if it is between 2.5 and 4 and intense if SUV is higher than 4. (12).

These studies were revised by a radiologist and a nuclear medicine physician who identified the pattern of FDG uptake: focal, segmental or diffuse and also identified the grade of uptake: mild, moderate or intense. It was correlated with the area of the digestive tract, dividing it in: esophagus, stomach, small intestine, colon (ascending, transverse, descending, sigmoid) and rectum. In cases in which a distension of the lumen was achieved, it was attempted to identify a parietal alteration in the
6 HYPERMETABOLIC IMAGES OF DIGESTIVE TRACT IN PET-CT, DIFFERENTIAL DIAGNOSIS

Figure 3. Gastritis- 62 years old, male. Testicle carcinoma, staging. PET/CT: A-B) PET axial and coronal planes: Moderate diffuse uptake in gastric fundus associated to diffuse parietal thickening (arrows), C-D) CT axial plane and coronal reconstruction: mild parietal thickening in gastric fundus, E-F) Axial and coronal fusion: diffuse gastric fundus uptake is confirmed (arrows).

<table>
<thead>
<tr>
<th>Organ</th>
<th>Grade and uptake pattern</th>
<th>CT Findings</th>
<th>History/Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>Moderate, segmental in third distal</td>
<td>None</td>
<td>GE Reflux Esophagitis</td>
</tr>
<tr>
<td>Stomach</td>
<td>Moderate, J-shaped</td>
<td>Diffuse parietal thickening</td>
<td>Smoker. Bearer of testicular carcinoma Gastritis</td>
</tr>
<tr>
<td>Sigmoid colon</td>
<td>Focal, moderate</td>
<td>Increase in fat density. Sigmoid diverticula</td>
<td>Diverticula/Diverticulitis</td>
</tr>
<tr>
<td>Rectum</td>
<td>Moderate, diffuse</td>
<td>Parietal thickening, increase in fat density</td>
<td>Radiotherapy/Rectitis</td>
</tr>
</tbody>
</table>

Chart 1. Inflammatory diseases.

3- Results

Of a total of 450 patients who attended the center in the mentioned period on whom the PET-CT study with FDG was performed, we analyzed a total of 32 patients who presented an indication of initial staging of their tumoral digestive pathology. We also revised the findings of 8 metabolically active lesions in the digestive tract of patients bearing other tumors. We selected patients whose diagnosis could be confirmed by biopsy, surgery or development control. We proceeded to present two patients who presented FDG uptakes, which we considered physiological; this was confirmed by clinical evolution of the
patients. As was mentioned in the introduction, a mild segmental uptake in the distal esophagus can be considered a physiological variant (figure 1). A diffuse moderate colon uptake was also interpreted as a physiological variant since no focal uptake was identified (figure 2). None of these patients presented morphological alterations in CT and both were sent for evaluation of a solitary pulmonary nodule.

We presented 4 cases of moderate segmental uptake patterns, which were interpreted as 

inflammatory 
lesions, when CT alterations and patients' medical history were taken into account. Chart 1.

<table>
<thead>
<tr>
<th>Topography of primary lesions</th>
<th>Total of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophagus</td>
<td>6</td>
<td>19%</td>
</tr>
<tr>
<td>Stomach</td>
<td>6</td>
<td>19%</td>
</tr>
<tr>
<td>Colorectal</td>
<td>15</td>
<td>47%</td>
</tr>
<tr>
<td>Anal canal</td>
<td>5</td>
<td>15%</td>
</tr>
<tr>
<td>Total</td>
<td>32</td>
<td>100%</td>
</tr>
</tbody>
</table>

Chart 2. Frequency of primary tumoral lesions of digestive tract

Figure 4. Diverticulitis- 57 years old, CBP. A) Coronal PET: moderate focal uptake in sigmoid colon (arrow), B-C) Axial and coronal reconstruction CT: Sigmoid colon diverticula and increase in fat density (arrows), D) Axial fusion: focal uptake in sigmoid colon (arrow).

Figure 5. Radic rectitis- 60 years old, female. RT, cervical neoplasm. PET/CT- A) Sagittal PET: Diffuse moderate uptake in rectum (arrow), B-C) CT axial plane and sagittal reconstruction: diffuse thickening of rectum and alteration of fat density (arrows), D-E) Sagittal and axial fusion: diffuse moderate uptake in rectum.
In patients with esophagitis, a moderate segmental uptake can be seen in the distal esophagus, which is the case of one patient with a history of gastro esophageal reflux, which was being studied for lymphoma. In the stomach of a patient with seminoma, a J-shaped, moderate to intense uptake associated with diffuse parietal thickening was observed. This patient had a history of nicotine poisoning and gastritis confirmed with endoscopy (figure 3).

Another patient with a broncho-pulmonary carcinoma presented a moderate focal uptake in the left iliac fossa, at sigmoid level. Diverticula and increased fat density, were demonstrated, which suggested the diagnosis of diverticulitis, that was confirmed by clinical evolution (figure 4).

In a patient with cervix cancer stage IIIb who received RT, a moderate diffused uptake was observed in the rectum and an increase in perirectal fat density, interpreted as radio-rectitis, confirmed by clinical evolution (figure 5).

Figure 6: Esophageal carcinoma - 55 years old, male. Esophageal carcinoma moderately differentiated in middle third. Staging PET/CT: A-B-C Coronal CT reconstruction, fusion and PET respectively; hypermetabolic focal lesion (SUV 11) in esophageal middle third associated to circumferential parietal thickening (arrows in B and C), E-F-G) Axial plane in CT, fusion and PET respectively with the same findings (arrows).

Figure 7. Gastric adenocarcinoma. 60 years old, female. Staging. PET/CT: A-B-C Coronal CT reconstruction, fusion and PET respectively; parietal thickening of gastric body with focal and intense uptake (arrows). D-E-F) Axial plane in CT, fusion and PET respectively; parietal thickening of gastric body with focal and increase of metabolism (SUV 11). Peritoneal carcinomatosis with hypermetabolic peritoneal nodules in hepatic surface (arrows).
From a total of 32 patients with known tumors in the digestive tract, the distribution according to localization and frequency was as follows: colorectal carcinoma (47%), esophagus cancer 19%, gastric cancer 19%, and 15% cancer of anal canal as shown on Chart 2. All of them presented focal uptake, moderate to intense in the different referred topographies correlated to parietal alterations in CT.

We had exemplified some of these cases.

**Figure 6**: Patient with esophageal carcinoma of the middle third diagnosed by endoscopy and biopsy. An intense focal uptake (SUV max: 11) associated with circumferential parietal thickening of approximately 4 cm in length was visualized.

**Figure 7**: Patient with gastric adenocarcinoma diagnosed by endoscopy and biopsy in whom an intense focal uptake associated to circumferential parietal thickening of the gastric body was evidenced, the patient also showed peritoneal carcinomatosis evident in the hepatic dome where an intense FDG uptake associated to peritoneal nodules was observed.

**Figure 8**: Patient bearing sigmoid carcinoma diagnosed by endoscopy and biopsy, (which also showed a pulmonary nodule), moderate focal uptake in the sigmoid colon associated to focal parietal thickening of approximately 3 cm in length was observed. According to some series (12,13), in up to 3% of cases, a focal lesion in colon of patients on whom the study was carried out for other reasons can be observed as a finding. These patients had a second tumor.

![Figure 8: Sigmoid adenocarcinoma.](image)
Figure 9: Right colon Adenocarcinoma-67 years old. Lymphoma staging. PET/CT: A) Coronal PET: Focal lesion with intense metabolism in the right hypochondrium (arrow). B) Axial CT: eccentric parietal thickening of the ascending colon (arrow). C) Axial fusion: focal lesion with intense metabolism in ascending colon (arrow). Endoscopy confirms adenocarcinoma of right colon.

Figure 10: Sigmoid colon carcinoma relapse-65 years old. Postoperative carcinoma control of sigmoid colon with mechanical suture. PET/CT: A) Coronal PET: focal area of intense metabolism in the left lateral sector of the pelvis (arrow). B) Axial CT: mechanical suture (yellow arrows) and mild parietal thickening in adjacent sigmoid colon (blue arrow). C) Axial fusion: focal lesion with intense metabolism close to suture: local relapse.

Figure 9: Patient sent to be monitored for lymphoma. Two intense punctual focal uptakes in the ascending colon with no clear correlation in CT were observed, the suggested endoscopic study showed a vegetant lesion, which corresponded to adenocarcinoma.

Figure 10: Patient with sigmoid carcinoma for the last 6 months, with colo-rectal anastomosis, in whom relapse due to elevation in tumor markers is suspected. No alterations were found on CT or in endoscopy, which was partially due to low tolerance. In PET-CT study a punctual
intense focal uptake was observed in distal colon, close to mechanic suture with no clear morphological alterations in CT. It was suggested it might correspond to relapse but because there was recent surgery it was not discarded that it could be a suture granuloma. The patient was submitted to re-intervention and relapse in the anastomosis was shown.

4- Discussion

Hypermetabolic lesions in the digestive tract in the different studied sectors may be characterized by PET-CT and there were elements as the uptake pattern: focal, segmental or diffuse. Metabolic activity in pre-malignant or malignant lesions is generally focal or short segmental and in inflammatory processes it is diffuse, segmental diffuse or multi-focal.

We will proceed to analyze the different uptake patterns distinguished by organ.

**Esophagus:** There could exist a weak physiological uptake in the distal part of the esophagus. In patients with gastro esophageal reflux a slight to moderate diffuse uptake may be shown in the distal third associated to reflux esophagitis. The most intense diffuse uptake has been described in Barret’s esophagus. In patients with radiotherapy history, in the radiation area there may exist an increase in the uptake (4). If a focal absorption of FDG is identified it is important to recommend endoscopic correlation, to exclude malignant or pre-malignant causes. (5).

**Stomach:** Uptake of FDG in the stomach is generally mild with a J-shaped configuration. A diffuse increase in gastric uptake combined with thickening of the wall in a distended stomach can indicate an underlying inflammatory process or infectious gastritis. In these cases correlation with endoscopic results or with clinic elements may be useful. If a focal absorption in the stomach is identified, PET-CT images must be carefully evaluated in search of a gastric mass. It has been shown that PET-CT is sensitive to detection of a primary lesion, as well as in metastases or recurrence of adenocarcinoma. (5).

**Small intestine:** The small intestine shows a mild and heterogeneous uptake pattern, however this uptake might appear more focally intense in the pelvis. One limitation in the images interpretation can be the lack of distention that can simulate the appearance of parietal thickening. Infectious or inflammatory processes can show a diffuse or segmental uptake. In patients with Crohn’s disease, PET-CT is sensitive and specific in detecting active sites of the disease. Malignant primary and metastatic tumors can affect the small intestine and both can show a greater uptake of FDG. (5).

**Colon:** FDG activity within the colon is typically heterogeneous and its distribution can vary, it can be focal or
diffuse. Frequently there is a greater absorption in the ascending colon, the caecum and sigmoid colon, due to a greater amount of lymphocytes in this region. An intense uptake of FDG has been documented in non-malignant processes such as acute enterocolitis, pseudomembranous colitis, Crohn’s disease and ulcerous colitis. (5). There is also an intense uptake of FDG in primary colon neoplasia as well as in recurrences. (11,12).

In the study that was performed, it was not possible to determine the frequency of physiological uptake since only a few cases in which the type of uptake was confirmed by monitoring were cited. In the same way, we presented cases of patients in whom a malignant or inflammatory lesion was suspected, which was confirmed by endoscopy, biopsy or clinical history.

Finally, from the series of patients who attended for staging their malignant pathology, already confirmed by endoscopy and biopsy, all presented focal uptake, moderate to intense with positive findings in the correlation with CT images.

Combination of PET-CT can sometimes help identify the cause of focal or segmental intestinal absorption. The presence in a PET image of FDG uptake of lineal or tubular morphology in the digestive tract is very frequent and allows it to be distinguished from other focuses of pathological uptake, but occasionally physiological uptake is focal or nodular in character and very intense (as in the gastric fundus or in the cecum). Without a precise anatomic correlation, the abovementioned intense and focal FDG uptakes (non-pathological) may be confused with uptakes of a tumoral origin, however in these cases we must consider differential diagnosis and suggest performing other studies to make progress in the diagnosis. This was the case of the patient in figure 9, in whom the presence of a second tumor in the ascendant colon was suspected.

Regarding the use of contrast media, it has been suggested that oral iodine contrast can produce an overestimation of uptake and therefore cause a false focus of metabolic hyperactivity in the abdomen, although several recent articles conclude that the mentioned effect is not frequent and not significant clinically (6,9,15). The formation mechanism of this group of artifacts related to the use of oral contrast is due to the fact that the correction of attenuation of PET images is based on CT images and if these present foci of high attenuation in the interior of the intestine, these can be misinterpreted as false areas of metabolic hyperactivity in the process of attenuation correction. Fusion of CT and PET images allows localizing false focus of FDG uptake by proving that they correspond to oral contrast. Another way to confirm the artifactual nature of false focus of metabolic hyperactivity consists in visualizing uncorrected PET images (without correction of CT attenuation), in which
only the emission information is represented.

Postoperative absorption can be intense, especially after recent surgery. It is common to visualize absorption associated to ostomies, as well as in resection edges, correlation with surgery data and the report of the pathological anatomy (for example the presence or absence of a positive margin), will help to distinguish. Postoperative absorption will decrease with time and will be equal to values close to background intensity. It is recommended to wait between 4 to 6 weeks after surgery before obtaining images with PET, but a certain degree of consumption may persist beyond this time. Surgical clips can generate granulomas in adjacent tissues, which generate foci of hyper-uptake adjacent to the same, which can persist for a long time. This was the case with patient in Figure 10 in which differential diagnosis between relapse and post-surgical inflammatory alterations (suture granuloma) was suggested. Endoscopic methods were negative and finally surgery confirmed a relapse).

This is why an exhaustive clinical history is important, considering the clinical situation, which motivates exploration, all the patient’s history, received treatments (QT, RT and surgeries performed), which allow us to identify physiological uptakes, which can emulate pathology. Sometimes correlation with other imaging methods can be necessary and endoscopy with eventual biopsy can contribute with anatomo-pathological data.

**Conclusions**

The correct interpretation of PET-CT images requires, apart from a physio-pathologic understanding of cancer and the behavior of different types of neoplasias, a deep knowledge of FDG physiological distribution, its variants, and possible causes of non-malignant FDG pathological uptake.

Most errors in interpretation can be avoided if PET-CT technical factors and basic physio-pathological aspects of the behavior of different tumors are taken into account and if PET images are directly compared with the corresponding CT images.

PET-CT is sensitive in showing primary neoplastic processes in the intestine but is not very specific due to physiological uptake and inflammatory causes. PET-CT is useful in localizing and characterizing foci of increased FDG uptake in the intestine. Fusion with CT can sometimes help to identify the cause. It is recommended that foci with greater uptake in the intestine should be evaluated with endoscopy, especially punctual ones with a moderate or intense grade of uptake.
Bibliography


8. Wahl RL. Why nearly all PET of abdominal and pelvic cancers will be performed as PET/CT. J Nucl Med. 2004; 45:82S-95S.


12. Ora Israel, MD; NikolayYefremov, MD; Rachel Bar-Shalom, MD, et al. PET/CT Detection of Unexpected Gastrointestinal Foci of 18F-FDG Uptake: Incidence, Localization, Patterns, and Clinical Significance. The journal of nuclear medicine 2005; 46, 758-76.

