Limitations of 18FDG-PET/TC in oncology: False positive and false negative findings

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Learning objectives

To review the spectrum of potential pitfalls and limitations of whole body 18f-fluorodeoxyglucose (18FDG) positron emission/computed tomography (PET/CT) scans in oncologic patients with emphasis on false positive and false negative interpretations, and learn them and how some of them can be avoided or appropriately interpreted.

Background

Cancer is one of the leading causes of death worldwide. Accurate diagnosis and staging are essential for an adequate management of oncologic patients. Conventional imaging techniques, such as computed tomography (CT) and magnetic resonance rely on anatomic alterations and abnormal contrast enhancement, with limitations to detect infiltration in normal-sized structures and characterization of residual lesions. Positron emission tomography (PET) provides valuable functional information based on the increased glucose uptake and glycolysis of cancer cells. The radiotracer most commonly used in oncology diagnosis is 18FDG, a radiopharmaceutical analogue of glucose that is taken up by metabolically active tumor cells using facilitated transport similar to that used by glucose. 18FDG cannot enter glycolysis and becomes trapped intracellularly, emitting positrons. Therefore, PET has the ability to depict metabolic abnormalities before morphologic alterations occur. The main drawback of PET is the limited spatial resolution.

The hybrid PET/CT modality acquires PET and CT data in the same imaging session and allows accurate coregistration of metabolic and anatomic data. The combined PET/CT is a more sensitive and specific test than either of its constituents obtained separately with an increased diagnostic and staging accuracy in numerous cancers. Limitations of FDG-PET/CT in the evaluation of cancer have been documented as well. 18FDG is not a cancer-specific tracer and accumulates in areas of increased metabolism such as several normal organs. On the other hand, there are limitations related to the variability in FDG uptake of several types of cancers. There are also several pitfalls related to technical factors.

In this exhibit, we review the spectrum of potential pitfalls and limitations of whole body 18FDG-PET/CT scans in oncologic patients with emphasis on false positive and false negative interpretations.

Imaging findings OR Procedure details
18FDG is physiologically taken up by various organs difficulting identification of lesions in these localisations. There are also benign pathologic causes of 18FDG uptake that can mimic malignant neoplasm (infectious and inflammatory processes; benign tumors). Exclusion of malignancy may be impossible based on 18FDG -PET/CT images only, and correlation with clinical data, the morphologic findings on the CT and an experience interpreter, is essential to the correct interpretation of scans. Other limitations are related to the variable 18FDG avidity of several types of cancers. Tumors exhibiting very low 18FDG uptake may lead to false negative interpretations. In addition, there are potential pitfalls related to technical factors or the timing of the study that can compromise the sensitivity of 18FDG-PET/CT for detecting tumours.

**FALSE POSITIVES**

In malignant tissues, 18FDG uptake depends on the metabolic activity of the lesion, and it is proportional to the number of malignant cells and their proliferative activity. 18FDG uptake in neoplastic tissues is a function of increased expression and activity of glucose transporter proteins on their cell surface, as well as enhanced rates of glycolisis.

**NORMAL VARIANTS AND ARTIFACTS**

There are sites of variable physiologic 18FDG uptake and benign pathologic 18FDG uptake that could be confused with malignant neoplasms and may yield false-positives findings. This reflects the fact that the use of glucose, and hence uptake of 18FDG, is not specific to malignant tumours. Some of these sites of variable physiological 18FDG, such as larynx, thyroid, brown fat or gastrointestinal tract may be potential causes of false positive interpretations on PET scans, but are less likely to be misinterpreted as pathology on fused PET/CT images.

**Larynx**: laryngeal muscles normally show mild uptake. Talking following radiotracer injection causes higher 18FDG accumulation in the muscles of phonation and vocal cords. Asymmetric superphysiologic 18FDG uptake is observed due to previous surgery or laryngeal nerve palsy with higher tracer accumulation in the normal vocal cord simulating laryngeal neoplasm. Patients are asked not to talk during the uptake phase.

**Thyroid**: diffuse increased uptake in the thyroid gland occurs in up to 4% of the PET/CT studies, more frequently in women, representing a normal variant. The mechanism is not well understood.

**Brown fat**: 18FDG uptake in the neck, supraclavicular, axillar and paraspinal regions and surrounding mediastinal large vessels caused by metabolically active brown fat is sometimes seen on PET scans and may mimic lymphadenopathies. It is more common in children, young patients, and those with a low body mass index. Brown adipocytes involved in the non-shivering thermoregulation become activated through sympathetic stimulation and have increased glycolisis. It has also been suggested that can be caused by a high level of circulating catecholamines in anxious patients. On PET/CT brown fat uptake is easily recognized as an intense
symmetric pattern of uptake in the regions mentioned above which is localised to areas of fat on the CT component (**Figure 1**). However, brown fat may hamper evaluation of lymph nodes of these regions. Premedication with a small dose of benzodiazepine and keeping the injection room at warmer temperature can help prevent brown fat uptake.

**Physiological gastrointestinal uptake:** the gastrointestinal tract shows variable $^{18}$FDG uptake due to smooth muscle activity, metabolically active mucosa and lymphoid tissue or colonic bacterial uptake. It is usually more noticeable in the right colon. The typical location, often linear pattern diffuse or segmental and correlation with a morphologically normal digestive tract on CT images usually allow identification of this physiological uptake (**Figure 2**). However, when it is intense or focal it may be confused with inflammatory conditions (oesophagitis, inflammatory bowel disease) or neoplasia.

**Metallic objects** (prostheses, pacemakers, dental devices) may lead to artifactual overestimation of FDG activity because of the differences in the attenuation properties of the highly attenuation object when the transmission data from CT images are used for attenuation correction. The PET/CT software "overcorrects" photopenic areas adjacent to hyperattenuating objects at CT, falsely appearing as hypermetabolic on the attenuation-correct PET and fused PET/CT images. Reviewing the non-attenuation corrected PET images allows for identification of these artifacts: the artifactual uptake area on corrected images appears as a photopenic area on the non-corrected PET images, whereas a true lesion remains with increased tracer uptake (**figure 3**).

**INFECTION**

Activated macrophages and neutrophils in inflammatory tissue use glucose as an energy source for chemotaxis and phagocytosis, and fibroblasts use glucose for proliferation. Therefore, these cells show avid $^{18}$FDG uptake on PET, resulting in enhanced uptake in sites of active inflammation and tissue repair.

In **immunocompromised patients**, such as cancer patients, where atypical and unusual infections are more common, it is often necessary to be more cautious in diagnosing malignancy at sites of $^{18}$FDG accumulation.

False positive findings have been described in **viral** (**Figure 4**), **fungal** and **bacterial infections** with variable uptake of FDG.

**Pneumonia** typically causes diffuse, relatively uniform $^{18}$FDG activity, which together with the lobular, segmental or lobar pattern and morphologic findings on CT is easily recognized (**figure 5**). These findings are atypical for cancer and suggest benign disease on PET/CT. But when the uptake is focal or intense, or there is necrosis, cavitation (fig. 6) or a masslike consolidation, it may be impossible to differentiate pneumonia from malignant neoplasms.

**Active tuberculosis, tuberculous pneumonias, adenitis** (**figure 8**) and **granulomas** (**figure 9**) may show avid $^{18}$FDG uptake on PET because these
lesions are mainly composed of lymphocytes and macrophages, which use $^{18}$FDG as an energy source. Tuberculomas are not an infrequent cause of false positive result on PET/CT studies performed for solitary pulmonary nodule evaluation (Figure 10) on page 40 especially in geographic areas with a high prevalence of granulomatous disease. In addition tuberculous involvement of hilar lymph nodes can take up $^{18}$FDG mimicking lymphatic metastatic disease.

**Abscesses** also show increased $^{18}$FDG uptake in the surrounding inflammatory tissue with no uptake in the central necrotic area. Abscesses can be indistinguishable from cavitating neoplasms such as squamous carcinoma (Figure 7A on page 36, figure 7B on page 37).

**INFLAMMATION**

**Sarcoidosis** can lead to a false positive interpretation on PET/CT. $^{18}$FDG in sarcoid lesions is related to disease activity and depends on the presence of actively dividing inflammatory cells, particularly the macrophages, lymphocytes and epithelioid monocytes that comprise sarcoid granulomas.

Patients with chronic pulmonary diseases, such as pneumoconiosis may show increased FDG uptake, making it difficult to distinguish from lung cancer. In addition, lymph nodes with chronic inflammatory changes such as anthracosis take up $^{18}$FDG simulating metastatic lymphadenopathies leading to false overstaging of lung cancer (Figure 11A on page 41, figure 11B on page 42).

**Healing** involves an inflammatory reaction even in the absence of infection. Leukocytic infiltration is present in the granulation tissue associated with wound repair and the resorption of necrotic debris and hematoma.

**Post-surgical inflammatory tissue** takes up FDG. For this reason, FDG-PET/CT imaging should be delayed at least 3-4 months after completion of radiotherapy and 1-2 months after surgery in order to avoid false positives results caused by post-therapy inflammation (figure 12). on page 43

In oncology, the inflammatory reaction associated with radiotherapy can be responsible for increased FDG activity and it may be difficult to differentiate post-radiotherapy changes from residual active tumor. Radiotherapy induced changes may last for 6 months or more and has been described in head and neck, rectal and lung tumours.

A **flare response**, with increased uptake of FDG, has been described following chemotherapy, occurring a few days after therapy and it is possibly related to an influx of inflammatory cells as a response to tumour cell death. This phenomenon may be associated with a better response.

**BENIGN TUMORS**

A number of benign tumours have been described as showing FDG activity that may be mistaken for malignancy including:
**Thyroid adenomas.**

**Benign tumors in the head and neck,** such as Warthin’s tumor of the salivary glands.

**Colonic adenomas** (Fig.13), on page 44

**Uterine fibroids.**

**Adrenal adenoma** (5%).

**Sclerosing hemangioma of the lung.**

**Inflammatory pseudotumor.**

**OTHER CONDITIONS THAT CAN LEAD TO A FALSE-POSITIVE INTERPRETATION, ESPECIALLY IN RESTAGING STUDIES**

**Thymic hyperplasia:** thymic activity is commonly seen in children and can also be seen in adolescents and young adults after chemotherapy, as a result of the thymic rebound phenomenon. This can persist for a few months after chemotherapy is completed. The typical pattern is of low to moderate uptake in the shape of an inverted "V" in the anterior mediastinum corresponding to the anatomic bi-lobed figure of the thymus on CT (Figure 15) on page 46 and should not be confused with uptake due to lymphoma in this location.

**Bone marrow hyperplasia:** physiologically, the bone marrow shows a modest $^{18}$FDG similar to liver activity. Increased bone marrow uptake can be seen in patients with haematopoietic hyperplasia, eg: patients with severe bleeding, undergoing treatment with granulocyte colony-stimulating factor (G-CSF) or who have recently received chemotherapy may also demonstrate diffuse increased bone marrow uptake of FDG. It is usually a moderate diffuse symmetric pattern of uptake within the axial and proximal appendicular skeleton. However, it can be intense and simulate diffuse bone marrow neoplastic involvement or mask osseous metastatic disease. Increased FDG uptake is often seen in spleen during and after G-CSF therapy and suggests the correct diagnosis (Figure 16), on page 47. In addition, the diffuse uniform pattern may be altered by previous conditions such as treated bone marrow or bone metastases, radiation therapy, old vertebral compression fractures. In these cases areas of sclerotic bone may produce a heterogeneous pattern of bone marrow $^{18}$FDG which can be mistaken for metastases.

**FALSE NEGATIVES**

**FALSE NEGATIVES RELATED TO TECHNICAL FACTORS**

Given the **spatial resolution** of PET scanners, it is not possible to detect very small volumes or microscopic disease. The diagnostic accuracy of FDG-PET/TC depends on the size of the lesion and its avidity for FDG. Lesions below its spatial resolution (6 mm) and those with low FDG uptake can be missed on PET. More active lesions can be detected down to a smaller size than
less active ones and false negative studies have been reported in lung nodules smaller than 8-10 mm (Figure 17).

False negatives due to **micrometastases** have been described. These false negatives in the localization of lymph node metastases can occur in up to 8% of patients with lung cancer due to micrometastases, although these patients have a better prognosis.

Lesion detection also depends on the tissular **background activity**. Organs that show high normal uptake or excretion of $^{18}$FDG may have a diminished sensitivity for detection of primary tumours or metastases. $^{18}$FDG is excreted through the urinary tract and therefore, not generally suitable for imaging renal or urothelial tumours. Variable physiologic uptake of $^{18}$FDG in normal structures such as the mucosa and the lymphoid tissue in the Waldeyer ring reduces its effectiveness. Sensitivity decreases with decreasing size of lesions and small flat mucosal lesions of the pharynx may go undetected. Relative small brain metastases can also be missed on $^{18}$FDG-PET/CT owing to the high background activity. Hence, symptomatic patients with negative scans or those at high risk for brain metastases will require further imaging with MRI or contrast-enhanced CT.

Patient **respiratory motion** during imaging acquisition may produce misregistration on the fused images and cause confusion or mistakes regarding the correct localization of the FDG uptake. This is a common problem described in lesions less than 1 cm especially in the bases of the lung near the diaphragmatic surface, and may lead to misregistration of lung nodules or to apparent mispositioning of liver metastases into the lung base. These mismatches are readily identified by carefully reviewing both sets of images and acquiring the CT in normal expiratory phase.

**Elevated blood glucose levels** have a major influence on the distribution of $^{18}$FDG in the body since serum glucose is competitive with $^{18}$FDG, leading to less tracer uptake and potentially compromising the sensitivity of $^{18}$FDG-PET/CT in detecting tumours. A glucose level <150 mg/dl is desirable.

Regarding the **timing of PET/CT**, scans performed within 1 month of chemotherapy, may yield false negative results because neoplastic tissue might not be metabolically active (figure 18).

**FALSE NEGATIVES RELATED TO HISTOLOGY TUMOUR**

There are a number of neoplasms that are not hypermetabolic and thus not $^{18}$FDG avid that can lead to false negatives findings on FDG-PET/CT. Well differentiated, hypocellular, and mucin-producing tumours (and their metastases) may exhibit poor accumulation of $^{18}$FDG. The anatomic information provided by the diagnostic CT component of PET/CT is extremely valuable in situations in which tumours are not $^{18}$FDG avid. Contrast-enhanced CT facilitates tumour detection and characterization, although differentiation from benign processes is not always
possible. Detection of $^{18}$FDG uptake is also impaired in lesions with extensive necrosis and only a thin rim of viable neoplastic tissue.

Some of the neoplasms with reduced $^{18}$FDG uptake that can simulate benignancy are:

**Adenocarcinomas:** mucinous and nonmucinous bronchioloalveolar carcinoma (Figure 19), on page 50 colonic mucinous adenocarcinomas, pancreatic cancer and cholangiocarcinomas (Figure 20), on page 51 parotid adenocarcinoma (Figure 14). on page 45

**Well differentiated tumours:** neuroendocrine tumours, tubular and ductal in situ breast cancer, and hepatocarcinoma.

**Lobular breast cancer.**

**Some subtypes of non Hodgkin’s lymphoma (NHL), especially of low grade:** MALT (mucosa associated lymphoid tissue) NHL, peripheral T cell NHL, small lymphocytic lymphoma and marginal zone lymphoma (Figure 21). on page 52

Images linked within the text of this section:
**FIGURE 2: PHYSIOLOGIC BOWEL UPTAKE.**

Axial PET (B), coronal PET (D) and PET/CT in a patient undergoing reevaluation of NHL show uptake in a linear configuration corresponding on CT (A) and PET/CT (C) with morphologically normal large (arrows) and small (open arrows) bowel.
FIGURE 3. METALIC OBJECTS
Staging PET/CT study in a 77 year-old female with NHL. A mild pseudoFDG uptake adjacent to the right hip prosthesis is noted on corrected PET/CT (A) and PET(B) images due to inappropriate attenuation correction in the region of the metallic implant. Uncorrected PET (C).

*: normal FDG activity in the bladder as a result of urinary excretion.
Fig. 4. False positive FDG-uptake in viral infection. A 47-year-old woman referred for staging of T-cell non-Hodgkin’s lymphoma. FDG PET and FDG PET/CT fusion scans show abnormal foci of FDG uptake in the left axilla and the skin overlying the left breast (arrows). The findings were misinterpreted as cutaneous and nodal lymphomatous infiltration. Skin and axillary node biopsies demonstrated herpes virus infection and benign reactive follicle hyperplasia respectively. There was no evidence for malignancy.
**FIGURE 5: PNEUMONIA.**
Axial FDG PET/CT in a patient with lung consolidation and partial response to antibiotic treatment. A segmental consolidation with air bronchograma and increased FDG uptake is observed. The lesion dissapeared after wide spectrum antibiotic therapy.
FIGURE 6. NECROTIZING PNEUMONIA.

62-year-old male evaluated because of suspected lung malignancy. Axial, coronal and sagittal enhanced CT, PET and PET/CT images showed heterogeneous cavitating consolidation with low attenuation areas and increased FDG uptake in right lower lobe. A right pleural effusion was also noted. Percutaneous needle biopsy did not obtain malignant cells and complete resolution was achieved after intensive antibiotic treatment.
FIGURE 7. A/ LUNG ABSCESS. Axial enhanced CT, PET and fused FDG PET/TC images of a patient referred for evaluation of suspected pulmonary carcinoma. There is a mass in the right upper lobe with a central area of low attenuation and enhancing wall. At PET/CT the lesion shows a rim of increased glucose metabolic activity and a central photopenic area suggesting necrosis. Cytological study showed inflammatory tissue without evidence of malignancy. Patient responded to antibiotic therapy.
FIGURE 7/B.
LUNG NEOPLASM
58 year old man with a mass in the posterior segment of the right lower lobe that exhibits peripheral hypermetabolic activity and central photopenia. Percutaneous needle biopsy of the lesion demonstrated large-cell carcinoma. Similar findings to figure 4A.
FIGURE 8. TUBERCULOUS ADENITIS. FDG PET/CT study of a 37 year old woman with diffuse-large-B-cell NHL undergoing initial staging. FDG PET/CT images demonstrate jugular and submandibular lymph nodes with increased FDG uptake that were misinterpreted as nodal lymphomatous infiltration. The patient was classified as stage III. Biopsies demonstrated tuberculosis, being the correct staging II (infradiaphragmatic disease).
FIGURE 9. Coronal FDG PET/CT scan demonstrates multiple areas of increased FDG uptake in spleen. Patient presented active tuberculosis and the spleen lesions corresponded to tuberculous lesions.

Fig.
**Figure 10. False Positive FDG Uptake for Tuberculoma.**

68 years old woman that presented with a pulmonary node at chest radiograph. A nodule with pleura tail and increased FDG uptake is observed in the right upper lobe at FDG PET/CT scan. The histologic study demonstrated tuberculosis.
**FIGURE 11/A:** FDG PET/CT study in a patient undergoing initial staging for lung neoplasm and silicosis history. Mediastinal and hilar lymph nodes with increased glucose metabolism were observed, but histological examination demonstrated granulomatous changes only and no neoplastic infiltration.
**FIGURE 11/8:** FDG PET/CT study in a patient undergoing initial staging for lung squamous carcinoma. There is a mass in right lower lobe with increased peripheral uptake and a central area of necrosis. Markedly increased FDG uptake in prevascular lymph node is noticed. Histological examination of the lymph node was negative for metastatic disease and demonstrated inflammatory cells, histiocytes and macrophages with anthracotic pigmentation.
FIGURE 12. POST-SURGICAL INFLAMMATORY UPTAKE.
PET/CT study performed shortly after surgical resection of adenocarcinoma of the right parotid gland. FDG PET/CT (A) and PET(B) images show a moderate uptake at surgical site (arrows) related to inflammatory response and granulation tissue. There was no evidence of residual tumour in this location.
**FIGURE 13. COLONIC ADENOMA.** FDG PET/CT study in a 47 year old woman with an ovarian cancer stage IIIc, referred for reevaluation. FDG PET/CT scan reveals increased FDG uptake in left external iliac lymph nodes, suggesting tumoral infiltration. Another focal intense accumulation of FDG was observed in sigma. Colonoscopy examination demonstrated colonic adenoma.
FIGURE 14. FALSE NEGATIVE: PAROTID GLAND ADENOCARCINOMA. PET/CT study of a 50-year-old man, status postsurgery of right parotid gland adenocarcinoma. There is a left submandibular lymph node without increased FDG uptake (arrow), which was histologically proved to be metastatic. Notice FDG uptake related to postsurgical inflammatory changes (open arrows) on PET/CT (A) and PET(B). Same patient as in figure 12.
**FIGURE 15. THYMIC REBOUND.**

Patient with a history of Hodgkin disease who was referred for post-therapy evaluation. FDG PET/CT scan reveals a moderate uptake in the shape of an inverted “v” in the anterior mediastinum, as a result of the thymic rebound phenomenon after chemotherapy.
Figure 16. Bone marrow hyperplasia. 38 year old man with small lymphocytic lymphoma that presented bone marrow infiltration at the initial diagnosis. Mid-therapy reevaluation fused PET/CT showed intense FDG activity in both the axial and proximal appendicular skeleton. An increased FDG uptake was observed in the spleen as well, slightly higher than in the liver. Patient had been treated with chemotherapy and with colony-stimulating factors. Bone marrow biopsy ruled out tumoral infiltration.
17-year-old patient, recipient of a liver transplant five years ago as treatment for hepatocarcinoma who was referred for evaluation of a pulmonary solitary nodule of recent apparition in a routine control. PET/CT fusion images revealed a pulmonary nodule, smaller than 1 cm, in the left lower lobe. The nodule was surgically removed and proved to be metastatic disease. Peripheral lung nodes smaller than 1 cm are a PET limitation.
**FIGURE 18**: False negative FDG uptake in an early reevaluation post-chemotherapy study.

**13A**: Early reevaluation PET/CT scan in a patient treated with chemotherapy for rhabdomyosarcoma, showed a residual retroperitoneal mass (arrow), adjacent to the left psoas muscle, with no FDG uptake, interpreted as a residual fibrotic lesion.

**13B**: Follow up CT study showed a marked increase in size of the mass (arrow). Percutaneous needle biopsy demonstrated tumoral disease progression.
FIGURE 19.
BRONCHIOLOALVEOLAR CARCINOMA

49 year old man with cough and a persistent lesion on chest radiographies. FDG PET/CT study shows a lower left lobe lesion with air bronchogram and with no FDG uptake. Histological examination demonstrated bronchioloalveolar carcinoma.
Recurrence of cholangiocarcinoma in a patient who had undergone surgical tumor resection. The CT scan (A) shows a mass at the site of previous surgery in contact with the pancreatic head. The lesion shows minimal FDG uptake on FDG PET (B) and FDG PET/CT (C) fusion images.
**FIGURE 21. MARGINAL ZONE NHL.**

70 year old woman who underwent FDG PET/CT for initial staging of marginal zone NHL. Images show retroperitoneal lymph nodes with no FDG uptake.

Fig.

Additional images for this section:
FIGURE 1. BROWN FAT UPTAKE. 30-year-old woman referred for restaging of NHL after therapy. FDG PET and FDG PET/CT fusion scans show symmetric diffuse increased uptake in the fat of cervical, supraclavicular regions and around mediastinal large vessels corresponding to brown fat (arrows). A right upper paratracheal lymph node shows no uptake (open arrow).
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Axial PET (B), coronal PET (D) and PET/CT in a patient undergoing reevaluation of NHL show uptake in a linear configuration corresponding on CT (A) and PET/CT (C) with morphologically normal large (arrows) and small (open arrows) bowel.

Fig. 2
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(*) normal FDG activity in the bladder as a result of urinary excretion.
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Fig. 5

**FIGURE 5: PNEUMONIA.**
Axial FDG PET/CT in a patient with lung consolidation and parcial response to antibiotic treatment. A segmental consolidation with air bronchograma and increased FDG uptake is observed. The lesion dissapeared after wide spectrum antibiotic therapy.
Fig. 6

62-year-old male evaluated because of suspected lung malignancy. Axial, coronal and sagittal enhanced CT, PET and PET/CT images showed heterogeneous cavitating consolidation with low attenuation areas and increased FDG uptake in right lower lobe. A right pleural effusion was also noted. Percutaneous needle biopsy did not obtain malignant cells and complete resolution was achieved after intensive antibiotic treatment.
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**FIGURE 7/B. LUNG NEOPLASM**

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Fig. 11
**FIGURE 11/A:** FDG PET/CT study in a patient undergoing initial staging for lung neoplasm and silicosis history. Mediastinal and hilar lymph nodes with increased glucose metabolism were observed, but histological examination demonstrated granulomatous changes only and no neoplastic infiltration.
Fig. 13

**FIGURE 11/12:** FDG PET/CT study in a patient undergoing initial staging for lung squamous carcinoma. There is a mass in right lower lobe with increased peripheral uptake and a central area of necrosis. Markedly increased FDG uptake in prevascular lymph node is noticed. Histological examination of the lymph node was negative for metastatic disease and demonstrated inflammatory cells, histiocytes and macrophages with anthracotic pigmentation.
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Fig. 17
Fig. 18

**Fig. 16. Bone Marrow Hyperplasia.** 38 year old man with small lymphocytic lymphoma that presented bone marrow infiltration at the initial diagnosis. Mid-therapy reevaluation fused PET/CT showed intense FDG activity in both the axial and proximal appendicular skeleton. An increased FDG uptake was observed in the spleen as well, slightly higher than in the liver. Patient had been treated with chemotherapy and with colony-stimulating factors. Bone marrow biopsy ruled out tumoral infiltration.
17-year-old patient, recipient of a liver transplant five years ago as treatment for hepatocarcinoma who was referred for evaluation of a pulmonary solitary nodule of recent apparition in a routine control. PET/CT fusion images revealed a pulmonary node, smaller than 1 cm, in the left lower lobe. The nodule was surgically removed and proved to be metastatic disease. Peripheral lung nodes smaller than 1 cm are a PET limitation.

Fig. 19
**FIGURE 1A:** False negative FDG uptake in an early reevaluation post-chemotherapy study.

13A: Early reevaluation PET/CT scan in a patient treated with chemotherapy for rhabdomyosarcoma, showed a residual retroperitoneal mass (arrow), adjacent to the left psoas muscle, with no FDG uptake, interpreted as a residual fibrotic lesion.

13B: Follow up CT study showed a marked increased in size of the mass (arrow). Percutaneous needle biopsy demonstrated tumoral disease progression.

Fig. 20
Fig. 21
**Figure 20. Cholangiocarcinoma.**
Recurrence of cholangiocarcinoma in a patient who had undergone surgical tumor resection. The CT scan (A) shows a mass at the site of previous surgery in contact with the pancreatic head. The lesion shows minimal FDG uptake on FDG PET (B) and FDG PET/CT (C) fusion images.
Fig. 23

**FIGURE 21. MARGINAL ZONE NHL.**

70 year old woman who underwent FDG PET/CT for initial staging of marginal zone NHL. Images show retroperitoneal lymph nodes with no FDG uptake.
Conclusion

$^{18}$FDG-PET/CT has emerged as a powerful imaging tool for diagnosing, staging and follow up of cancer patients. Despite its benefits, $^{18}$FDG-PET/CT has recognized limitations. There are a number of benign lesions with increased FDG uptake that simulate malignant lesions and tumours that lead to false negatives due to little FDG uptake on integrated PET/CT images. Misinterpretations can be reduced with careful attention to technical factors, knowledge of a patient's clinical history and a proper patient preparation. However, sometimes exclusion of malignancy can be impossible based on $^{18}$FDG-PET/CT only. It is important that readers are aware of these potential pitfalls so that the study is interpreted in the most accurate manner.

Personal Information

If you have any question, you can contact me in aureadiez@yahoo.es. Thank you.

References