ELSEVIER

Seminars in
NUCLEAR
MEDICINE

FDG-PET/CT Variants and Pitfalls in Haematological Malignancies

Patrick Pilkington, MD,* Egesta Lopci, MD, PhD,† Judit A. Adam, MD,‡ Carsten Kobe, MD,§ Karolien Goffin, MD, PhD,‖ and Ken Herrmann, MD¶

Hematologic malignancies represent a vast group of hematopoietic and lymphoid cancers that typically involve the blood, the bone marrow, and the lymphatic organs. Due to extensive research and well defined and standardized response criteria, the role of [^{18}F]FDG-PET/CT is well defined in these malignancies. Never the less, the reliability of visual and quantitative interpretation of PET/CT may be impaired by several factors including inconsistent scanning protocols and image reconstruction methods. Furthermore, the uptake of [^{18}F]FDG not only reflects tissue glucose consumption by malignant lesions, but also in other situations such as in inflammatory lesions, local and systemic infections, benign tumors, reactive thymic hyperplasia, histiocytic infiltration, among others; or following granulocyte colony stimulating factors therapy, radiation therapy, chemotherapy or surgical interventions, all of which are a potential source of false-positive or negative interpretations. Therefore it is of paramount importance for the Nuclear Medicine Physician to be familiar with, not only the normal distribution of [^{18}F]FDG in the body, but also with the most frequent findings that may hamper a correct interpretation of the scan, which could ultimately alter the patients management.

In this review, we describe these myriad of situations so the interpreting physician can be familiar with them, providing tools for their correct identification and interpretation when possible.

Semin Nucl Med 51:554-571

Introduction

Background

Hematologic malignancies represent a vast group of hematopoietic and lymphoid cancers that typically involve the blood, the bone marrow, and the lymphatic organs. The WHO classification of these tumors, lastly revised in 2016,[1,2,3] includes various types of acute and chronic leukemia, multiple myeloma and lymphomas, the later ones conventionally divided into Hodgkin's (HL) and non-Hodgkin's (NHL). Malignancies affecting the blood, that is, leukemia, can be furthermore divided based on the level of cell differentiation and maturity into acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL) and chronic myeloid leukemia (CML). Acute lymphoblastic leukemia typically derives from malignant lymphoid cells blocked at an early stage of differentiation, which invade both hematopoietic organs (blood and bone marrow), as well as extramedullary sites.[4] Commonly affecting healthy individuals, ALL tends to be more frequent in children, by showing a conventional peak at 1-4 years of age.[5] Acute myeloid leukemia, on counterpart, derives from malignant cells of myeloid lineage and is mostly diagnosed in older patients, aged ≥60 years.[6,7] The presence of recurrent genetic abnormalities is a primary criteria for AML classification, which decreases with age, while other AML types due to myelodysplasia-related changes or therapy-related AML,

*Department of Nuclear Medicine, University Hospital 12 de Octubre, Madrid, Spain.
†Nuclear Medicine Unit, IRCCS—Humanitas Research Hospital, Rozzano (Milano), Italy.
‡Department of Radiology and Nuclear Medicine, Amsterdam University Medical Center, University of Amsterdam, Amsterdam, The Netherlands.
§Department of Nuclear Medicine, Faculty of Medicine and University Hospital Cologne, University of Cologne, Cologne, Germany.
‖Department of Nuclear Medicine, University Hospital Leuven, Division of Nuclear Medicine and Molecular Imaging, KU Leuven, Leuven, Belgium.
¶Department of Nuclear Medicine, University of Duisburg-Essen and German Cancer Consortium (DKTK)-University Hospital Essen, Essen Germany; West German Cancer Center.
Address reprint requests to Patrick Pilkington, MD, Nuclear Medicine Department, University Hospital 12 de Octubre, Av. de Cordoba s/n, 28041, Madrid, Spain. E-mail: johnpatrick.pilkington@madrid.salud.org

 https://doi.org/10.1053/j.semnuclmed.2021.06.014
0001-2998/

tend to increase.[7,8,9] Chronic lymphocytic leukemia represents instead the most frequent B cell leukemia in elderly patients and the commonest form in Western countries, typically diagnosed at a median age of 72 years.[10,11] Family members of patients affected by CLL tend to have an increased risk of CLL and other non-Hodgkin lymphomas, which in case of mantle cell lymphoma (MCL), leukemic marginal zone lymphoma (MZL) and lymphoplasmacytic lymphoma requires a differential diagnosis with CLL.[10,12] Chronic myeloid leukemia is another hematopoietic malignancy arising from myeloid lineage, which is characterized by a typical genetic alteration leading to the translocation t (9;22)(q34;q11), with the shortened chromosome 22, also known as Philadelphia chromosome.[13,14] The traslocation determines a BCR−ABL1 fusion gene that codes for BCR−ABL1 transcripts, which can be used for peripheral blood and bone marrow diagnosis of CML together with the detection of Philadelphia chromosome. CML rarely affects children, while it is mostly present in older population, with a median age at diagnosis 60-65 years.[14] Multiple myeloma (MM) represents the second most common hematological malignancy in high-income countries, accounting for almost 1% of the tumors.[15,16] It derives from monoclonal plasma cells that accumulate in the bone marrow and produce M-protein, leading to a variety of manifestations starting with subtle asymptomatic conditions such as monoclonal gammopathy of undetermined significance (MGUS) or smouldering multiple myeloma up to bone fractures and complicated organ dysfunction.[16] Along inherited genetic variants, other risk factors have been associated to MM development, including obesity, chronic inflammation, as well as exposure to pesticides, organic solvents, or radiation.[17,18] The introduction of autologous stem-cell transplantation (ASCT) along systemic treatment and novel drugs, has improved patients outcome, especially at younger age,[19] with median overall survival rising up from 4 to 10 years.[20,21] Lymphomas represent instead a large group of malignancies affecting the lymphoid organs. The majority are encompassed into non-Hodgkin lymphomas, while 10% of them are represented by Hodgkin Lymphoma.[22,23] Based on the cell types, NHL can be characterized into B-cell lymphomas (85%-90% of the cases), T-cell and natural killer (NK)-cell lymphomas,[1,23,24] whereas HL can be conventionally divided into classical or nodular lymphocyte-predominant and non-classical forms.[1] The key elements identifying in any case HL on a histopathological level are the Reed-Sternberg (HRS) cells, also known to be of B-cell origin.[24] On a clinical point of view, HL and most B-cell representatives of NHL, that is, Diffuse Large B-Cell Lymphoma (DLBCL), Burkitt lymphoma (BL), are defined as aggressive malignancies. While is it also possible for more indolent forms, that is, Follicular lymphoma (FL), to transform into more aggressive lymphomas, typically DLBCL. Of note, the aggressive switch known as Richter's transformation, is also documented for chronic lymphocytic leukemia.[25,26] The variegate nature of the different lymphoma subtypes determines a large spectrum of clinical presentations and outcome, which very much depend on the type of cell-origin and disease extent. Once based on the Ann Arbor classification,[27] the staging system for lymphomas has markedly changed following the embedment of diagnostic imaging into the clinical work-up,[28,29,30] reaching up to the current Lugano classification[31] used for both HL and NHL.

Indications of [^{18}F]FDG-PET/CT in Haematological Malignancies

Haematological malignancies were one of the first indications to perform [^{18}F]FDG-PET/CT and up to date a substantial amount of patients who are referred for [^{18}F]FDG-PET/CT are suspected for a hematological malignancy. Due to extensive research and well defined and standardized response criteria, the role of [^{18}F]FDG-PET/CT is well defined in hematological malignancies and summarized in European and American guidelines.[32,33,34,35,36,37,38,39]. A summary of the current recommendations of different types of lymphomas and leukemias are presented in Table 1.

Technical Considerations

The reliability of visual and quantitative PET/CT interpretation in hematological malignancies may be impaired by several factors including inconsistent scanning protocols and image reconstruction methods of PET/CT.

Imaging artifacts may occur due to technical and physical factors on the imaging system, such as follows:

i) The limited spatial resolution of PET scanners may result in a reduced sensitivity, especially when it comes to small lesions. Here we have to keep in mind, that PET interpretation is validated on scanners with limited resolution, and over-interpretation must be avoided. This is why an improved scanner quality should be handled with care. Improved PET images obtained e.g. by using point spread function might improve tumor detectability, but does not necessarily improve patients outcome. In contrast, the rate of PET positive patients during response assessment might increase, and may lead in on overtreatment including acute toxicities and long-term sequelae such as 2nd malignancies.[40,41]

ii) Misalignment between PET and CT data sets can lead to localization errors and incorrect attenuation correction. One major reason for misalignment is the respiratory movement, when using diagnostic CT in deep inspiration for attenuation correction. In order to avoid such errors, restriction on quality of CT imaging would be accepted.[42]

iii) Furthermore CT contrast agents can cause artifacts leading to subsequent overestimation of attenuation and artificially elevated regions of PET activity. Previous studies reported that SUVs increase less strongly in tumor tissue than in background locations such as the liver or mediastinal blood pool.[43,44,45,46]

This observation could be of clinical significance, as reference regions are nowadays increasingly used for

Table 1 Current Guideline Recommendations on the Routine Clinical Use of [^{18}F]FDG-PET/CT in Lymphomas, Multiple Myeloma and Leukemias

	Staging	Interim Evaluation	End of Treatment Evaluation	Routine Follow-Up	Suspected recurrence
Lymphoma type					
Hodgkin lymhoma (HL)					
Classical HL	X	X	X		X
Nodular HL	X	X	X		X
Non-Hodgkin lymphoma (NHL)					
DLBCL	X	X	X		X
Follicular lymphoma	X (st I and II)		X		
T-cell lymhomas	X	X	X		X
Mantle cell lymphomas	X		X		X
Multiple myeloma	X		X	X	X
Transformation	X				
Biopsy localization	X				
Leukemias					
ALL extramedullair disease	X		X		X
AML extramedullary disease	X		X		X

quantitative PET interpretation, not only in hematological malignancies. Uptake values in lesions and reference locations show significant changes when contrast-enhanced CT is used for attenuation. Hereby, tumor SUVs increase to a lesser degree than SUVs particular in the liver and mediastinal blood pool, especially in situations with a lower lesional [^{18}F]FDG uptake.[47]

The following procedures may be affected in particular: (1) Evaluation of residual tissue using reference regions (eg, assessment of the Deauville score with or without support of SUV measurements) (2) Calculation of ratios between tumor and background SUVs (eg, tumor-to-blood-pool ratio) (3) Measurement of percentage changes between the SUV in the patient's most intense lesion at baseline as well as on follow-up scans (eg, ΔSUV_{max}). However, the role of CT contrast media in the management of patients with hematological malignancies is still under discussion. According to the international consensus recommendations contrast-enhanced CT exclusively should be used for specific issues, for instance to obtain more accurate measurements of nodal size in clinical studies, to distinguish bowel from lymphadenopathy, to assess compression or thrombosis of central vessels and for radiotherapy planning.[31]

Standardization of image reconstruction methods and the use of comparable SUV measurements are therefore crucial when using PET/CT in hematological malignancies. It should always be considered whether a patient might additionally benefit from contrast-enhanced CT and whether this examination can be integrated into a planned PET/CT. Ideally, the attenuation correction CT should be performed without enhancement through a contrast fluid, and additional diagnostic CT with i.v. contrast should be restricted to body part of clinical relevance.

Normal [^{18}F]FDG Distribution and its Variants

Before being able to detect abnormalities on an [^{18}F]FDG PET-CT scan performed in patients with hematological malignancies, or any other indication, it is of paramount importance to know the normal distribution of this tracer within the body.

For this, PET-CT scans should be performed following the recommendations of procedure guidelines such as those published by the European Society of Nuclear Medicine (EANM) or the Society of Nuclear Medicine and Molecular Imaging (SNMMI).[48,49]

In this section, we present a basic description of normal [^{18}F]FDG distribution together with typical variants found in routine [^{18}F]FDG PET-CT examinations.

Head and Neck

The brain has the highest [^{18}F]FDG accumulation in the whole body due to the exclusive use of glucose as a metabolic substrate. High uptake is routinely seen within the cortical grey matter and basal ganglia. Because of this high baseline uptake, [^{18}F]FDG is not the ideal tracer for tumor brain imaging. In spite of this, a recent meta-analysis by Park HY et al[50] and a recent guideline from the European Association for Neuro-Oncology,[51] suggest the use of [^{18}F]FDG PET-CT over whole-body contrast enhanced CT in suspected primary central nervous system lymphoma, as it usually presents as a highly hypermetabolic brain lesion, with uptake higher than the surrounding tissue. Furthermore, current guidelines for staging of primary CNS lymphoma from the "International Primary CNS Lymphoma Collaborative Group" and the "National Comprehensive Cancer Network" (NCCN)

recommend whole body imaging with [^{18}F]FDG PET-CT or contrast enhanced CT to exclude systemic involvement.[52,53]

Lymphoid tissue in the head and neck, especially involving the Waldeyer's Ring, is often seen and is usually symmetrical. Nevertheless, a slight degree of asymmetry can be accepted as non-pathological.[54] Seasonal variations have been described and related to upper respiratory tract infections.[55] Particular caution should be taken when interpreting these findings in the context of patients with lymphoma. Involvement of the Waldeyer's Ring may be considered if a significant asymmetry is seen on PET images and this correlates with CT images.[56] Nevertheless, confirmation is recommended if this involvement changes patient management. In our experience, bilateral cervical lymph nodes (mainly in level II) can sometimes be found together with the previously described findings, which in the context of lymphoma patients it raises a particular challenge (Fig. 1). Ideally, these findings should be biopsied for confirmation if they change patient's management, but if not, the activity of the lymph nodes can be compared with the activity or location of the other involved lymph nodes for a better diagnostic approach.

Even though the salivary glands can show varied degrees of tracer accumulation, it is usually mild, homogeneous and symmetric.[57,58]

Thyroid uptake is usually absent or mild with a diffuse and homogeneous distribution.

Thorax

The thymus can be frequently seen in children, but sometimes also in young adults. It can usually be identified as an anterior mediastinal soft tissue with an inverted "V" shape in a coronal plane showing a mild [^{18}F]FDG uptake. Care should be taken when interpreting these findings in patients with hematological malignancies, as the thymus can hypertrophy and increase its uptake after chemotherapy (thymic rebound),[59] becoming a potential source of false positive findings (Fig. 2).

Breast tissue usually shows low levels of uptake that can get higher in patient in the postovulatory phase of the menstrual cycle or depending on the amount of active glandular tissue.[60] For example, lactating breast usually show bilateral high levels of heterogeneous uptake. On the other hand, uptake decreases with increasing age and lower breast density.[61]

Mediastinal physiologic activity is largely dependent on blood pool activity of [^{18}F]FDG. In contrast, myocardial activity is variable and depends on fasting state. In normal conditions, the heart primarily uses glucose metabolism as a source of energy, therefore, increased myocardial uptake will be found. On the other hand, when fasting, the myocardium will decrease its uptake, as it will turn to a fatty acid metabolism. In general, the most frequent finding is a homogeneous left ventricular myocardial uptake.

Other variants that can cause a false positive interpretation due to increased [^{18}F]FDG are the lipomatous hypertrophy[62] of the atrial septum and the crista terminalis.[63]

The lung and pleural usually show very low uptake if there is no associated pathology.

Abdomen

Gastrointestinal (GI) tract [^{18}F]FDG activity is common and often benign. The mechanism of physiologic uptake is not

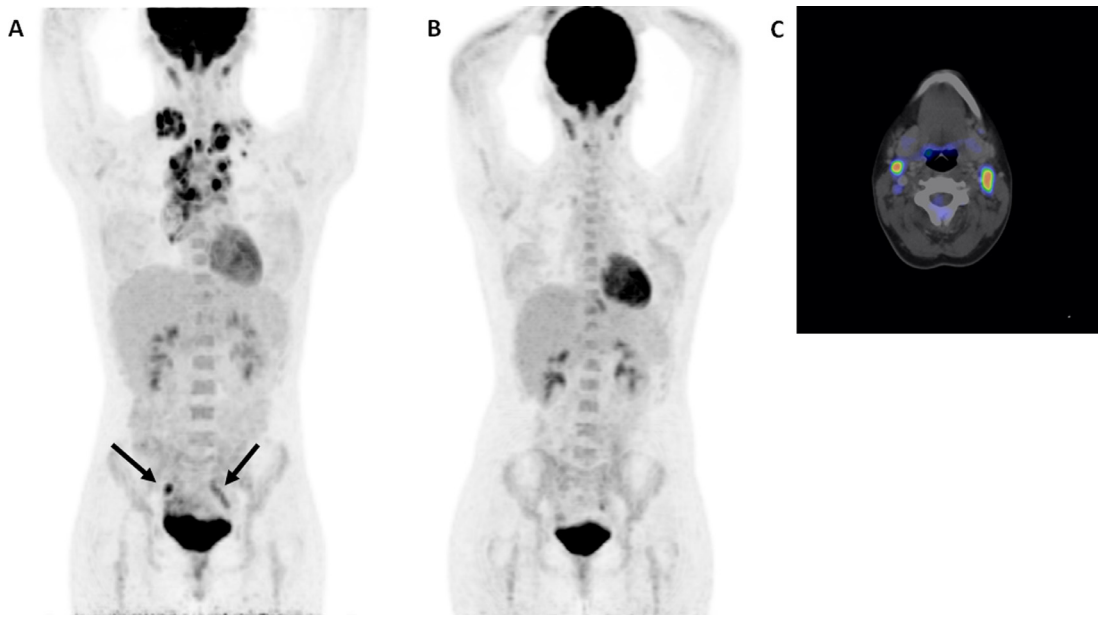

Figure 1 This is the case of a 22-year-old patient with Hodgkin's Lymphoma, Nodular Sclerosis subtype. (A) Staging PET-CT show cervical and mediastinal lymph node involvement (Stage II). Arrows show bilaterally increase uptake in ovaries due to menstrual cycle. (B) PET-CT after 4 cycles of ABVD treatment shows a complete metabolic response of most of the mediastinal and cervical lymph nodes, (C) while the superior cervical lymph nodes (bilateral level II) show persistent increased metabolic activity. Due to the discordant findings, ultrasound guided core needle biopsy of both cervical lymph nodes is performed. Histopathological examination of both cervical lymph nodes shows reactive follicular lymphoid hyperplasia with no signs of infiltration by lymphoma, therefore no change in management was needed.

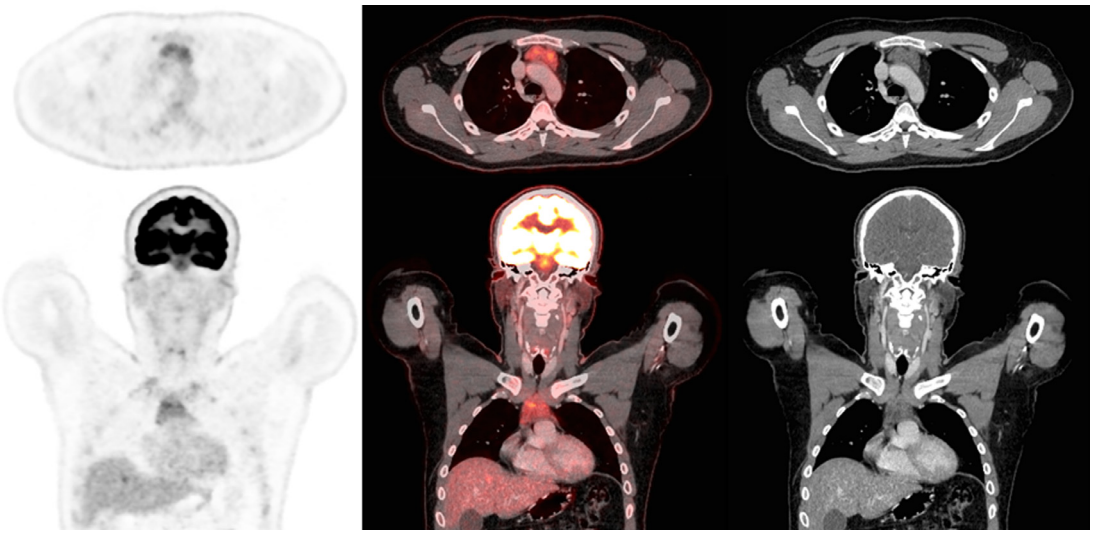

Figure 2 Transverse and coronal slices of FDG-PET/CT, fusion and CT in a 22- year-old male patient with common variable immune deficiency and weight loss in whom malignant disease needed to be excluded. FDG-PET/CT showed moderately to strongly increased FDG-uptake in the anterior mediastinum, representing thymus hyperplasia. This physiological entity is a pitfall of FDG-PET imaging and should not be interpreted as a malignant finding. No malignant lesions were detected in this patient.

fully understood, but it is thought to be a combination of mucosal and smooth muscle uptake, microbial overgrowth and [^{18}F]FDG excretion.[64] It can be variable, but is typically mild to moderate in intensity and diffuse in distribution.[65] Focal activity in the GI tract can also be a normal variant (ie, polyps, inflamed diverticula, focal colitis) (Fig. 3), but should be further evaluated to discard malignancy. This can be done by correlating with underlying CT abnormalities, the use of dual-time-point images[66] or by recommending a colonoscopy. Furthermore, intense colonic activity with diffuse distribution can be seen in patients with colitis, inflammatory vowel disease or when the patient is using oral antidiabetic drugs such as metformin.[67]

Physiologic [^{18}F]FDG activity in solid abdominal organs such as liver, spleen, pancreas and adrenal glands, without an underlying CT abnormality is usually mild, diffuse and homogeneous, with a higher pool activity in the liver when compared to the other organs.[68]

[^{18}F]FDG is excreted by the kidneys, therefore, uptake is seen in calyces, ureters and bladder. The activity seen within the ureters can be heterogeneous depending on peristalsis.

Pelvis

In pre-menopausal women, endometrial and ovarian uptake depends on the menstrual cycle. Increased endometrial uptake can be seen during the flow phase (typically within the first 4 days of the menstrual cycle) and during ovulation (typically day 14 of the menstrual cycle).[69] Physiologic ovarian uptake can be seen during ovulation (Fig 1) and in relation to a corpus luteal cyst.[70]

On the other hand, in post-menopausal women, neither endometrial or ovarian uptake should be seen. If any [^{18}F]FDG uptake is seen in this group of patients, it should be regarded as suspicious, and further work-up should be recommended. This is why it is so important to document the date of the last menstrual period to aid interpretation.

In men, prostate activity is usually mild and homogeneous, even in benign prostate hyperplasia. Any site of focal or diffuse increased uptake should be further investigated.

Skeletal and Muscular System

Uptake in muscles (eg, ocular, tongue, mastication and phonation muscles) can be frequently seen and is usually due to activation before or during the uptake period. Recent insulin injection or food intake will also give rise to increased [^{18}F]FDG muscular uptake.[71] It is usually symmetric, but in some cases such as surgery, irradiation, muscle contraction or unilateral palsy, they can show an asymmetric pattern that should be interpreted with caution.[72] The elongated shape of the uptake can also suggest a physiological uptake, nevertheless, focal uptake at the genioglossus insertion in the oral cavity can be frequently seen and relates to muscle activity to maintain the upper airway in the supine position.[73]

Activity in cortical bone is usually mild and homogeneous if there are no underlying bone abnormalities. On the other hand, bone marrow activity is lower than that of the bone, except in some particular cases, which are described on section 4.6.

Brown Fat

Brown fat uptake has a variable incidence, being more often seen in young[74] female patients.[71] It is due to locally increased metabolic activity from a cold stimulus that results in local thermogenesis.[75] Brown fat uptake can be typically seen in head and neck region (mostly in the posterior aspect), the suprasternal notch, the upper axilla, the mediastinum, the paraspinal regions, the cardiac apex and the pararenal

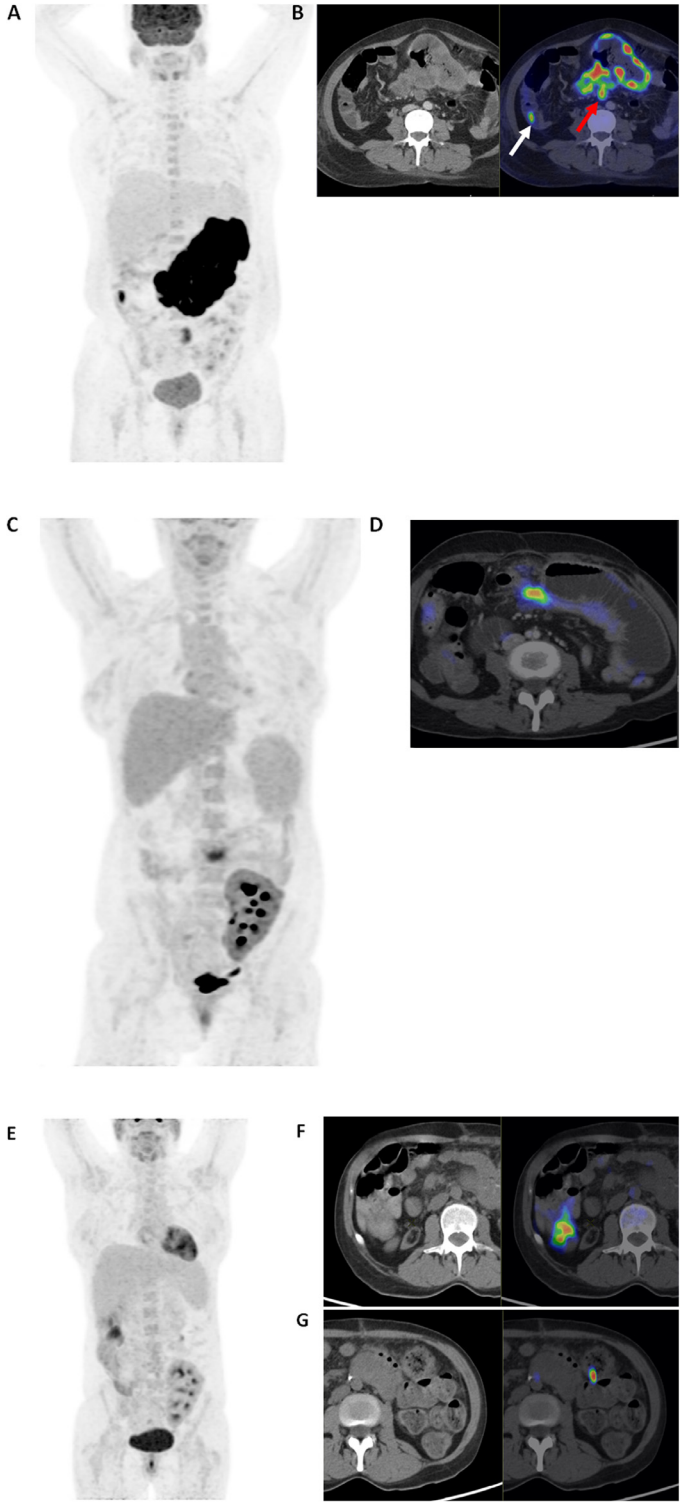

Figure 3 Forty-two- year-old patient with renal transplant and the diagnosis of intestinal non-Hodgkin's lymphoma, diffuse large beta cell subtype. (A and B) Staging PET-CT shows extensive involvement of the small intestine with wall thickening that shows increased metabolic activity. At least two necrotic mesenteric lymph nodes are noted (red arrow). Also, another two sites of focally increased uptake are noted near the hepatic angle of the colon (white arrow) and in the terminal ileum, which are also considered as lymphoma involvement. (C) PET-CT after four cycles of R-CHOP shows a very good response, nevertheless, there is persistent uptake in the lesion at the terminal ileum (D) which causes intestinal obstruction. (E) PET-CT after completing 6 cycles of the treatment, shows response of all previously visualized lesions, but 2 new sites of increase metabolic uptake are seen in the (F) hepatic angle of the colon and (G) in the proximal transverse colon. Due to the paradoxical findings, colonoscopy was performed and biopsies were taken from both lesions, with a final histopathological result of: (F) tubular adenoma with low grade epithelial dysplasia and (G) hyperplasic polyp.

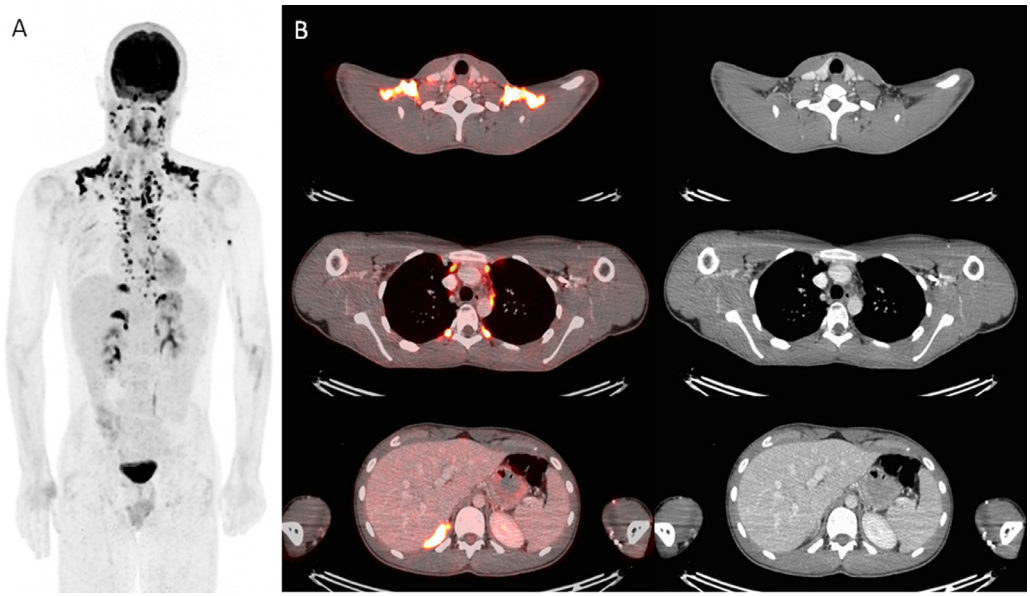

Figure 4 Maximum-intensity projection (MIP) (A) and transverse slices of fusion of FDG-PET/CT and CT (B) demonstrating physiological high FDG-uptake in brown fat in cervical, paraclavicular, paravertebral, mediastinal, parasternal, retrocrural and pararenal regions in a 17-year old male patient with suspicion of lymphoma due to eosinophylic fasciitis. No lesions suspicious of lymphoma were diagnosed on FDG-PET/CT.

space.[71] The correct interpretation of this kind of uptake used to be very challenging in the PET era, nevertheless, the incorporation of hybrid imaging has dramatically reduced this problem. In lymphoma patients these uptakes can be a potential source of false positive or false negative findings, therefore, a careful assessment is required when found (Fig. 4). This can be done by carefully going through the CT images to identify underlying lymph nodes within the activated brown fat. On the other hand, brown fat uptake can be minimized by ensuring that the patient is warm and rested during the uptake period, avoiding medication such as nicotine or adrenergic agents, diet and also by the use of beta-blockade or diazepam.[71,76]

Pitfalls of [^{18}F]FDG in Haematological Malignancies

Usually, it is accepted that, in cancer patients such as those with hematological malignancies, finding foci of increased [^{18}F]FDG uptake can be considered as indicative of active disease. Nevertheless, it is known that [^{18}F]FDG not only accumulates in malignant lesions, but also in other types of lesions such as benign tumors, sites of infection and inflammation, among others.

Therefore, knowledge of patients history, symptoms, laboratory findings (such as tumor markers, etc) and physical examination findings can be very important in accurately interpreting foci of increased uptake. Furthermore, as differences in [^{18}F]FDG activity can overlap among benign and malignant lesions, CT and other conventional imaging characteristics can also be of help for a correct interpretation. Finally, if the findings can potentially alter patients management, confirmation by biopsy should be pursued.

In this section we describe the most common sources of potential pitfalls while performing [^{18}F]FDG PET-CT in patients with hematological malignancies.

Brain

[^{18}F]FDG PET-CT is recommended for the detection and systemic staging of primary CNS lymphoma. For other hematological malignancies, [^{18}F]FDG PET-CT is useful detecting extramedullary disease. Therefore, potential pitfalls have to be taken into consideration for a correct interpretation. For example:

False negative findings:

- Lymphomatosis cerebri and intravascular brain lymphoma may show, in some cases, a normal pattern of brain [^{18}F]FDG distribution.[77]
- Meningeal involvement in extramedullary leukemia might be difficult to assess due to lesion size and superficial extension.[78]

False positive findings:

- Acute cerebral infarction.[79]
- Infection, especially in leukemia patients that can have post-treatment immunosuppression.

Head and Neck

Head and neck involvement by hematological malignancies is mainly due to lymph node or lymphoid tissue involvement; therefore, it will be treated in section 4.7. Lymphatic system.

Thorax

Thoracic involvement, mainly lung involvement (as mediastinal lymphadenopathy will be addressed in section 4.7. Lymphatic system), can occur throughout the whole spectrum of hematological malignancies. For example, most patients with lymphoma (85% of HL and 66% of NHL)[80] may have pulmonary findings. On the other hand, primary involvement of the lung by lymphoma is rarer.

There is a myriad of presentations of lung involvement due to hematological malignancies, the most common being:[81]

- Bronchovascular or lymphangitic: due to direct invasion from lymph nodes or bronchopulmonary lymphatics.
- Nodular: which can be single or multiple. In the context of AML (but also myelodisplasic syndrome and myeloproliferative neoplasms)[82] if a lung mass is found, myeloid sarcoma should be suspected.
- Pneumonic (alveolar): indistinguishable from bacterial pneumonia
- Miliary

Endobronquial disease and pleural effusion have also been described. Vascular complications such as (but not limited to) superior vena cava syndrome and thromboembolic disease, are not rare and should be taken into consideration.

On the other hand, there are various findings that could hamper the interpretation of these studies. For example, infectious processes of the lungs are common (Fig. 5), some of them due to immunosuppression, were opportunist pathogens can be frequently found. Noninfectious lesions, such as drug-induced lung injury by cytokines, immunotherapeutic drugs or transfusion of blood products, have to be taken into consideration as they account for up to half of the lung manifestations found. Primary lung cancer is another common differential diagnosis that should be taken into consideration.

Abdomen

Gastrointestinal Tract

The gastrointestinal (GI) tract is one of the most common extranodal sites involved in hematological malignancies,[83,84] but it can be particularly challenging to identify on imaging, mainly due to the higher incidence of other pathologies and due to the high physiologic GI uptake seen on [^{18}F]FDG PET-CT images.

Primary GI tract lymphomas account for only 1-8% of all GI malignancies, nevertheless, it is one of the most common sites for extranodal lymphomas, accounting for 30%-40% of extranodal NHL,[84,85] while it is extremely rare to see it in HL patients.[86,87] Furthermore, secondary GI involvement by

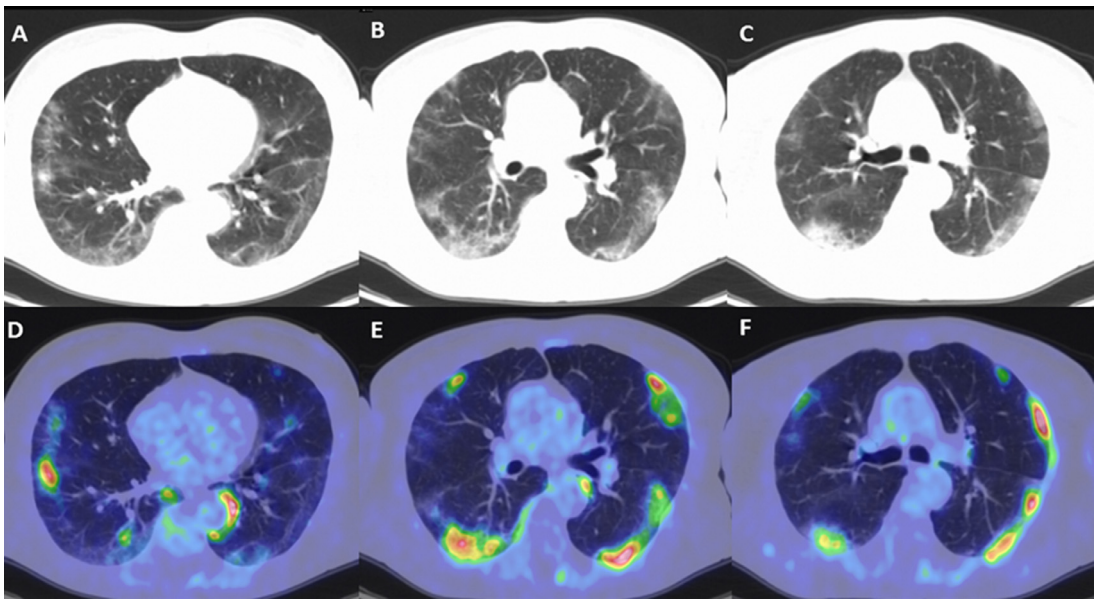

Figure 5 Herein we report on a 62 year-old male referred for restaging ^{18}F-FDG PET/CT during Non-Hodgkin lymphoma treatment. The patient had no history of pulmonary disease and was overall asymptomatic, that is, no fever or cough prior to the scan. An unexpected diffuse lung parenchyma involvement with inflammatory infiltrate was seen (A-C). Fused ^{18}F-FDG PET/CT images (D-F) documented an associated intense hypermetabolism in all subpleural and periaortic lung opacities; in addition, the presence of some residual lymphoma was seen in the abdominal region. Given the pandemic situation, the imaging findings required a differential diagnosis with COVID-19. The patient was therefore immediately tested by reverse transcriptase- polymerase chain reaction (RT-PCR), which confirmed positive for COVID-19. In the subsequent weeks, the patient was hospitalized and treated. After a period of quarantine and two consecutive negative nasal swabs, the patient was considered recovered. Subsequent lymphoma restaging, two months after initial diagnosis, documented some minor residual subpleural ocapities on CT. with no evidence of residual metabolism in the lungs on restaging ^{18}F-FDG PET/CT, confirming the complete recovery of pulmonary inflammation.

lymphoma is found in up to 50% of patients at autopsy.[83,88] The stomach is the most common site, with a reported incidence of 47%-75%, followed by the small intestine (mainly the ileum) and the colon.[83,86]

Imaging patterns have been described as diffuse infiltration (usually seen as a homogeneous wall thickening), focal lesions,[89] or multifocal (also known as "lymphomatous polyps"), all of which show moderate to high [^{18}F]FDG uptake that depends on the histology.

Gastrointestinal tract involvement by multiple myeloma is uncommon, but when it happens, the most frequent sites involved are usually the stomach and small bowel.[90,91] In general, these lesions may appear as large masses or as wall thickening, with a moderate to intense [^{18}F]FDG uptake.[92] Extramedullary plasmacytomas of the gastrointestinal tract are rare, with an incidence of only 4%,[93,94] and usually present as masses.

Autopsy reports have suggest an incidence of up to 25% of GI involvement in patients with leukemia, being more common in acute than in chronic leukemia. Lesions have been described as nodules, plaques, diffuse infiltration, polyps and convoluted in appearance.[95,96]

Common sources of false positive findings are:

- Primary GI malignancies, mainly adenocarcinomas, which usually presents with less wall thickening and less lymphatic involvement.[97]
- Diverticulitis, that typically presents as a focal uptake together with common inflammatory CT characteristics.
- Colonic polyp or primary colonic neoplasm.
- Physiologic [^{18}F]FDG uptake that can be diffuse or focal.

Liver

Hepatic involvement is a common extranodal manifestation of hematological malignancies,[98,99] but Imaging findings are mostly nonspecific.

In lymphomas, primary hepatic involvement is rare, accounting for <1% of all non-Hodgkin lymphomas, while secondary involvement has been reported in at least 50% of patients at autopsy.[100] It is important to differentiate between both, as they have different management and prognosis. Liver involvement by lymphoma has been described on imaging to manifest as: Focal liver mass or masses, diffuse infiltration and multifocal and/or military.[101,102,103]

In multiple myeloma, the liver (together with lymph nodes, spleen, kidneys and pleura) is one of the most common sites of extramedullary disease. Autopsy studies have reported liver involvement in about 30% of myeloma patients. As in lymphoma, imaging findings are usually presented as unifocal, multifocal or diffuse involvement, with a moderate to intense [^{18}F]FDG uptake.[104,105]

Liver involvement on [^{18}F]FDG PET-CT by leukemia has been reported to show a diffuse pattern in ALL and CML, and a multifocal pattern on AML.[106]

The most common differential diagnoses that should be taken into account are the following:

- Hepatocellular carcinoma, usually shows a low [^{18}F]FDG.
- Infection, usually opportunistic, such as fungal microabscesses
- Hemangioma
- Drug toxicity may show a diffuse increased [^{18}F]FDG uptake
- Septic emboli
- Metastases

Spleen

The most common hematological malignancy to affect the spleen is lymphoma. Its infiltration is found in approximately 30 – 40% of patients,[107] with an uptake pattern that can been focal, miliary or diffuse. Also, spleen infiltration should be considered when the CT shows a homogeneous splenomegaly with no focal [^{18}F]FDG lesions, even though splenomegaly can happen without any tumor involvement.[108]

In leukemia, spleen involvement is mostly seen as a diffusely increased uptake[78] and splenomegaly, but focal/military lesions have also been described.[109]

Spleen involvement in Multiple Myeloma can be seen in approximately 1/3 of patients at autopsy.[110] As in lymphoma, involvement can be present as splenomegaly with or without focal lesions with increased uptake.[111]

Common pitfalls have been described, mainly due to false positive findings. For example:

- Focal hypermetabolic lesions: Infection, infarction, extramedullary hematopoiesis.[107]
- Miliary hypermetabolic lesions: Infection, fungal microabsceses[109] (specially in leukemia patients due to immune suppression after treatment),
- Diffusely increased uptake: Response to infection, post-therapy period (Fig. 6), hematopoietic proliferation (which is usually associated with increased symmetric uptake in bone marrow of axial skeleton).

Pancreas

Primary involvement of the pancreas by lymphoma accounts for less than 2% of all pancreatic neoplasms, most of them being of B cell type.[112] In contrast, secondary involvement is much more frequent and has been reported in up to 30% of non-hodgkin lymphoma patients in autopsy.[113]

The following uptake patterns have been described for pancreatic involvement with lymphoma:

1. On morphological images:[114,115,116,117]
   a. Diffuse homogeneous enlargement of the pancreas
   b. Segmental enlargement of the pancreas
2. On [^{18}F]FDG PET:[118]
   a. Solitary: most common form. Usually involving the head.
   b. Diffuse
   c. Multiple
   d. Segmental

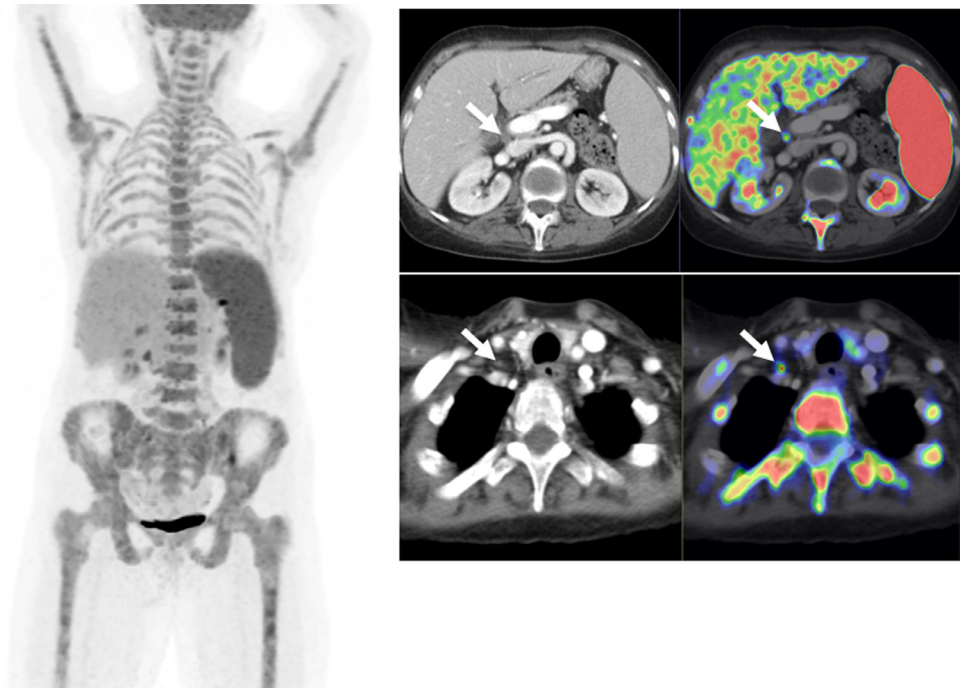

Figure 6 Diffuse bone marrow and spleen uptake (with splenomegaly) in a patient with diffuse large beta cell lymphoma after receiving granulocyte colony-stimulating factor. Persistent lymph nodes (white arrows) present an uptake that is lower than the hepatic pool uptake (Deauville score: 3).

Pancreatic involvement by multiple myeloma is rare, with a reported incidence rate of 2.3% based on autopsy studies.[119] Obstructive jaundice and abdominal pain have been described as the most common symptoms.[120] On imaging, some have reported a focal or diffuse infiltration of the gland as the most common findings.[115]

In leukemia, pancreatic infiltration is very rare, with only a few cases reported in the literature for acute lymphoblastic leukemia (ALL), both in adults and pediatric patients.[121,122] To our knowledge, no patterns of involvement have been described, only the findings of case reports that show focal disease.

In general, the following differential diagnoses should be taken into consideration when finding abnormal [^{18}F]FDG uptake in the pancreas in patients with hematological malignancies:

1. Focal uptake with a solid mass
   a. Pancreatic Adenocarcinoma: Responsible for approximately 95% of pancreatic cancers.[123] It usually shows more aggressive features than lymphoma, like infiltration or obstruction of adjacent structures.[124] On contrast enhanced CT, early enhancement similar to that of unaffected pancreatic tissue can be seen in Myeloma and Lymphoma, in contrast to what is seen in pancreatic adenocarcinoma.[125] Also, the metastatic pattern of adenocarcinoma can help orient diagnosis, being the most frequent sites of involvement the liver, peripancreatic lymph nodes, peritoneum, lung and pleura.[126] Also, lymphomas are usually larger and bulkier than adenocarcinomas.[124] [^{18}F]FDG uptake intensity is not useful to differentiate diagnosis.
   b. Neuroendocrine tumor (NET): They account for only 1-3% of all pancreatic cancers.[127] Well differentiate NET, especially if they have a low proliferative activity, usually show low [^{18}F]FDG uptake, conversely to what is seen in lymphomas.
   c. Focal acute/chronic pancreatitis: It is usually difficult to differentiate. Clinical history and laboratory findings may help guide diagnosis. Chronic pancreatitis usually show low [^{18}F]FDG uptake and upstream atrophy of the pancreas.[115]
   d. Cystic tumors
   e. Focal autoimmune pancreatitis: Might be difficult to differentiate based on uptake, but usually presents upstream atrophy.[115]
   f. Infection: Usually preceded by a history of sever acute pancreatitis.
2. Diffuse uptake with diffuse enlargement:
   a. Autoimmune pancreatitis: Usually shows relatively low [^{18}F]FDG uptake.[128] Abnormal uptake in other organs such as salivary glands, retroperitoneum or kidneys[129] can help diagnosis of autoimmune disease. Even though both may present lymphadenopathy, if they are large and below the level of renal veins it is more indicative of lymphoma.[115]
   b. Acute pancreatitis: Is usually accompanied by severe abdominal symptoms and characteristic laboratory findings, like elevated amylase, that can help differentiate from lymphoma.
   c. Multiple foci:
   d. NET: Especially in multiple endocrine neoplasia syndromes.

Pancreatic metastases can present with a focal (solitary), multiple or diffuse pattern,[129,130] which makes it very difficult to interpret. We recommend a correlation with the clinical history, serum tumor markers and other imaging findings to correctly pose a differential diagnosis.

Adrenal Glands

Usually, lesions found in the adrenal gland are benign in nature, mostly adenomas. Nevertheless, adrenal glands are a frequent site of metastasis in patients with cancer, with a rate of approximately 25%-75% depending on the site of the primary tumor.[131] The most common tumors with adrenal metastasis are lung, kidneys, melanoma, breast, colon and rectal, among others.

There are a very few case reports of adrenal involvement by hematological malignancies, mostly by lymphoma and less frequently by myeloma. Therefore, the finding of metabolically increase adrenal lesions should give rise to the following differential diagnosis:

- Adenomas: if using a non-contrast enhanced CT, an attenuation of <10HU has been described correctly identify adrenal adenomas with a sensitivity of 71% and a specificity of 98%.[132]
- Metastases
- Primary adrenal tumor like adrenal carcinoma or pheocromocytomas.

Genitourinary System

Renal involvement is usually found in hematological malignancies due to hematogenous or lymphatic spread,[133] and is usually seen in the context of other concomitant sites of extramedullary involvement.

Primary involvement of the kidneys by lymphoma is rare, accounting for less than 1% of extranodal lymphoma.[134] On the other hand, secondary renal involvement by lymphoma has been reported to be found in approximately 30-60% of patients with non-Hodgkin lymphoma. Bilateral involvement is seen in 10 − 20% of the cases.[135]

The most common imaging finding, seen on approximately 50%-60% of patients, is the presence of multiple parenchymal nodular masses of different sizes.[136] A solitary mass can be seen in approximately 10%-25% of patients.[134,136] Renal lymphomas are intensively [^{18}F]FDG avid, nevertheless, physiological accumulation and excretion of the tracer at the parenchyma and collecting systems can make it difficult to identify.[137] In these cases, delayed PET-CT images, with or without administration of a diuretic drug and intravenous hydration, may be of help.[138] Correlation with contrast enhanced CT images may also be of use.[136,137]

On autopsy series, renal involvement by multiple myeloma has been reported in approximately 10-30% of patients, but this rarely manifests on imaging.[139] The most common imaging patterns described have been the presence of perinephric nodules or masses, and less frequently, focal renal masses.[140] Renal plasmocytomas have also been reported

Renal involvement by leukemia is rarely detected by imaging (less than 5%), nevertheless, on autopsy, involvement has been reported to be found in 60-90% of patients.[135,141] It usually presents as nephromegaly, which can be unilateral o bilateral, but also focal lesions have been describe.[135,142] As renal involvement is rare on imaging, detection of a lesion should raise other more common possibilities as differential diagnosis.

Common differential diagnoses that should be taken into consideration:

- Renal cell carcinoma: Tends to show only mild [^{18}F] FDG uptake.
- Metastases: common primary tumor with renal metastases are melanoma, lung, colon and breast.[143]
- Abscess
- Acute pyelonephritis
- Angiomiolipoma
- Bladder cancer
- Chronic pyelonephritis
- Renal adenoma
- Renal cyst
- Renal infarction
- Wilms disease

Pelvis

Involvement of pelvic organs (ie, cervix, uterus, ovary and prostate) by hematological malignancies is rare, except for lymphoma, were cases of primary a secondary involvement has been described, and some anecdotal cases of gynecological plasmocytomas.

Due to the low incidence of involvement, further work-up should be recommended when finding abnormal [^{18}F]FDG uptake in these organs.

Common causes of increased [^{18}F]FDG uptake:[144]

- Primary malignancies
- Metastases
- Benign prostate hyperplasia, usually has a mild uptake
- Pelvic inflammatory disease
- Endometriomas and/or endometriosis
- Benign cystadenomas
- Teratomas
- Miomas
- Abscesses
- Schwannomas
- Benign uterine leiomiomas (uterine fibroids)

Skeleton and Bone Marrow

Bone marrow involvement is one of the most important prognostic factors in patients with lymphoma. [^{18}F]FDG PET-CT has a great accuracy in discarding and detecting bone marrow involvement in patients with diffuse large B cell lymphoma (DLBCL) and Hodgkin's lymphoma (HL)

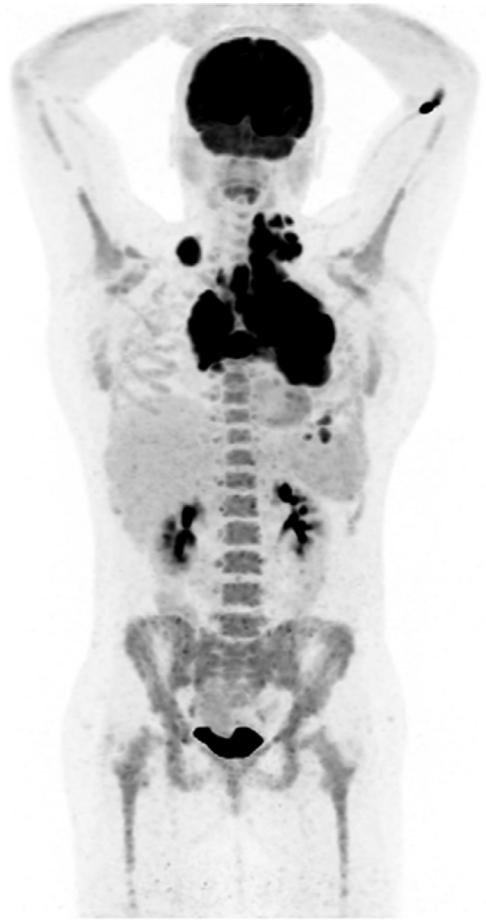

Figure 7 Staging PET-CT in a 25 year-old patient with Hodgkin Lymphoma, nodular sclerosis subtype extensive supra diaphragmatic lymph node involvement. Diffusely increased metabolic uptake is seen in the bone marrow with negative bone marrow biopsy. Care should be taken when interpreting bone marrow uptake in HL patients, as a diffusely increased bone marrow activity should not be regarded as lymphoma involvement.

(Fig. 7), with a pooled sensitivity and specificity of 88,7% and 99.8% for DLBCL,[145] and 96.9% and 99.7% for HL.[146]

Due to these excellent results, [^{18}F]FDG PET-CT has replaced bone marrow biopsy in these lymphoma subtypes.[30] Nevertheless, it has been reported to miss diffuse bone marrow involvement in 10-20% of DLBCL patients,[147] therefore, a negative PET does not firmly rule out bone marrow involvement in clinically advanced DLBCL. Consequently, bone marrow biopsy is still necessary in this scenario if relevant for patient management.

In other subtypes of NHL, mainly indolent NHL, bone marrow biopsy with immunohistochemistry and flow cytometry are still considered as gold standard for the detection of bone marrow involvement.[148]

In multiple myeloma, bone disease occurs in virtually all patients during the course of the disease. A recent consensus statement by the International Myeloma Working Group recommends incorporating [^{18}F]FDG PET-CT into the diagnostic work-up of this hematological malignancy.[149]

[^{18}F]FDG PET-CT is not regularly used in the assessment of leukemia. However, several case reports have demonstrated its potential in diagnosis and follow-up of leukemic bone marrow infiltration,[150] nevertheless, further research is needed before acceptances in clinical guidelines. Patterns of uptake have been described as focal or diffuse on [^{18}F]FDG PET-CT imaging.[151]

Common sources of false-positive findings:

- Diffusely increased [^{18}F]FDG uptake:
- Following the administration of granulocyte stimulating factors (G-CSF) (Fig. 6). It is recommended to delay imaging for up to 4-6 week after administration.
- Reactive hyperplasia due to previous chemotherapy. It is also recommended to delay images for up to 4-6 weeks after chemotherapy.[152]
- Hypercellular bone marrow due to anemia, infection, alcohol, autoimmune disorders.
- Metabolic disorders; such as renal osteodystrophy and parathyroid carcinoma.[153]
- Other malignant disorders (ie, diffuse metastatic involvement from prostate cancer)[154,155]
- Focal or regional [^{18}F]FDG uptake:
- Bone remodeling or fractures
- Postsurgical or biopsy areas
- Due to metallic implants
- Degenerative bone cysts
- Primary bone malignancy (ie, Fibrosarcoma)
- Benign bone lesions (ie, eosinophilic granuloma)
- Joint surfaces
- Inflammation - Infection

Most of these differential diagnoses can be narrowed by the careful evaluation of the TC component. For example, if a sclerotic component is seen within a focal avid lesion, this is less likely to be due to myeloma infiltration. On the other hand, if there is infiltration of the medullary cavity and erosion of the inner cortical bone, this increases the likelihood of myeloma infiltration.

False negative findings have been describe in hyperglycemic patients, after a recent administration of high-dose of steroids (which should be suspended at least 5 days before scanning)[156] and in small sub-centimetric lytic lesions. It can also be negative in patients with multiple myeloma with a low concentration of plasma-cell infiltration.[157]

Lymphatic System

Lymph node involvement can be seen in most hematological malignancies, especially in lymphoma, but also in cases of extramedullary multiple myeloma and leukemia.

One of the great strengths of [^{18}F]FDG PET-CT imaging is its ability to detect tumor involvement in lymph nodes that are not enlarged, which is one of the reasons it is the modality of choice when evaluating these malignancies.

However, [^{18}F]FDG uptake is not exclusive of malignant cells. Neutrophils and activated macrophages also show and increased uptake which results in and increased metabolic activity in a variety of benign processes such as granulomatous disease (such as sarcoidosis) (Fig. 8), tuberculosis,

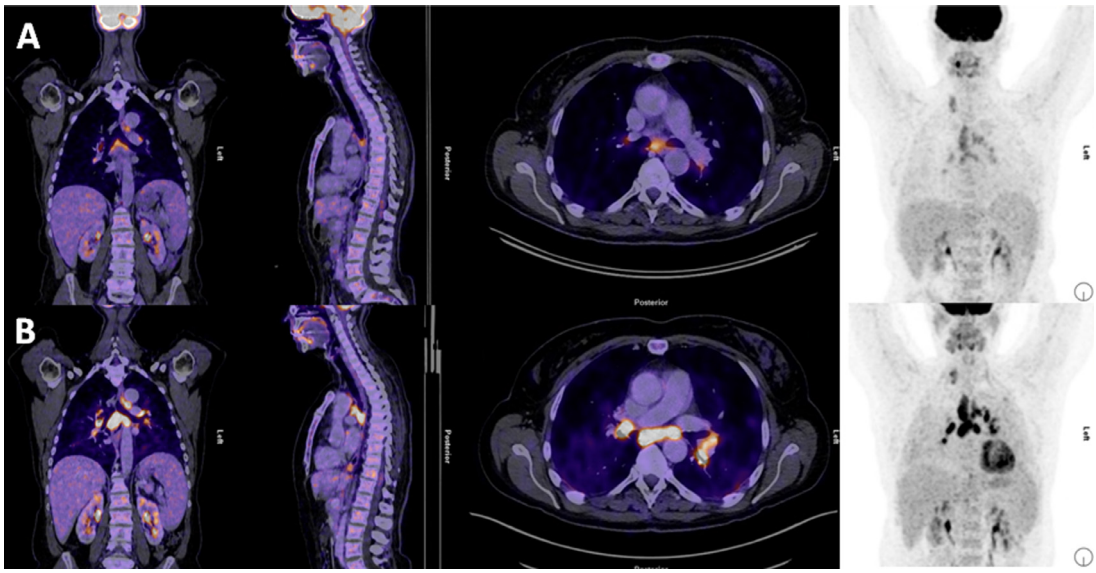

Figure 8 Fifty-five year-old female with Mantel cell lymphoma of the milt in the history, presenting with B symptoms (fever and weight loss) and high suspicion of transformed NHL. [A] [^{18}F]FDG-PET/CT shows multiple enlarged and highly [^{18}F]FDG-avide lymph nodes in the mediastinum and right supraclavicular. Due to the symmetrical uptake sarcoid like reaction was part of the differential diagnosis but recurrent lymphoma could not be ruled out. Pathology results of lymph nodes 4R and 11R (via EBUS) showed granulomatous inflammation. [B] Follow-up scan 10 weeks later show decreased [^{18}F]FDG-uptake in all nodes, confirming self-limiting sarcoid like reaction.

inflammatory lymph nodes, systemic infections like HIV, among others.

Special care should be taken when evaluating axillary lymph nodes in patients who have recently received the SARS-CoV-2 vaccine, as these may present lymph nodes with increased uptake in the same side where the vaccine was injected.

Pitfalls During and/or After Treatment

The correct interpretation of [^{18}F]FDG PET-CT during (interim) or following completion of therapy of hematological malignancies is of critical importance, as misdiagnosis may lead to a major impact on patient management. Pitfalls related to many diseases that can mimic a progression or refractory disease have to be taken into consideration. Also, the timing from surgery, administration of G-CSF, chemotherapy, external beam radiotherapy or radioinmunotherapy[48,49] has to be taken into account to avoid potential sources of false positive findings.

Infection and/or Inflammation

These are the most common pitfalls during and after treatment evaluation, as patients are more prone to infections due to treatment-induced neutropenia, anemia and thrombocytopenia.

In this context, infections are mainly found in the lungs, presenting as a mild and diffuse increased uptake with typical CT findings. Care should be taken when interpreting these findings, and should not be considered as disease progression, especially if there was no lung involvement before treatment. CT evaluation after completing antibiotic treatment should be recommended.

In patients with systemic infections, diffusely increased uptake in bone marrow and spleen can be seen, and should also not be considered as progressive disease.

Granulomatous disease, mainly due to sarcoidosis but also induced by different immunotherapy agents (see section 4.8.3), should be considered when persistent mediastinal and/or hilar lymph nodes are found. An early control should be done to confirm non-progression.[158]

Various Treatment Induced Pitfalls

The effects of G-CSF and chemotherapy in spleen and bone marrow activity are a very common source of potential pitfalls and should always be considered.

Interstitial lung disease due to drug toxicity can be seen after treatment with rituximab or bleomycin, and should be recognized on CT findings.[159]

Thymic hyperplasia or rebound, caused by a suppression of thymic activity during chemotherapy,[160] can be seen for up to 2 years, but is more frequent in the first 6 months following treatment.[161] In patients with mediastinal involvement on initial staging this finding can be challenging to differentiate for residual disease. In doubtful cases, biopsy or diffusion-weight MRI should be performed.[158]

Radiotherapy can induce inflammation of tissues or organs involved in the radiation field causing, for example, pneumonitis, esophagitis or pharyngitis, which could potentially be sources of false positive findings.

The most common post-surgical causes of false positive findings are due to inflammation, infection, abscess, fistula, fat necrosis (which can also be a chemotherapy induced

finding) and reactive lymphadenitis,[162] which can be found on, or near, the surgical area.

Immunotherapy

Special attention should be given to immunomodulatory regimens. Typically, immunotherapeutic drugs aim to foster the anti-tumoral activity of the immune system by inhibiting blockage mechanisms mediated by immune checkpoints such as PD-1 (programmed cell death-1) and its ligand (PD-L1), or by conveying anti-tumoral activity through chimeric antigen receptor T (CAR-T) cell therapy.[163,164,165] Along the desirable effect on tumor masses, immunotherapy promotes the appearance of atypical response patterns, such as pseudoprogression or dissociated response, and is associated to the development of immune-related adverse events (irAEs).[166,167,168] Pseudoprogression is characterized by a transient increase in tumor size, followed by stabilization or shrinkage on subsequent imaging. To overcome the occurrence of pseudoprogression and allow its proper classification, new response criteria have been proposed in 2016 for immunotherapy response assessment, that is, LYRIC (Lymphoma response to immunomodulatory therapy criteria).[169] Hence, indeterminate responses (IR) have been contemplated to classify lymphoma patients treated with immunotherapy. Quite variegate can be instead the presentation of irAEs, which tend to be more frequent after the first months of treatment, affecting 10% to 11% of the patients.[166,170] The advantage of [^{18}F]FDG PET-CT is that it can depict early in time the presentation of irAEs, including those having the major impact in patient safety, i.e. pneumonitis, colitis, pancreatitis, hypophysitis, hepatitis, and so forth. On the other hand, particularly for sarcoidosis-like reactions to immunotherapy, the real challenge can be the differential diagnosis with lymphoma progression. In this case, the pattern of distribution, typically involving the mediastinum and lung hila, can be of help, particularly when the new sites of FDG uptake do not correspond to previous sites of lymphoma involvement.

Others

Technical and physical factors regarding the scanner, as those mentioned in section 2, can induce important artifacts and limit the comparison of images for response assessment. This is especially relevant when evaluating response with Deauville criteria and also when using a semi-quantitative evaluation.

Never the less, even though Deauville scoring might be limited,[171] it remains as the Standard Scoring for Response assessment.[172] Maybe, in the near future, the use of the metabolic tumor volume will help to avoid uncertainties when applying the Deauville scoring system.

Summary

[^{18}F]FDG PET-CT is the imaging modality of choice for [^{18}F]FDG avid lymphomas and can be of great help providing additional information in other hematological malignancies. Nevertheless, [^{18}F]FDG uptake not only reflects tissue glucose consumption by malignant lesions, but also in inflammatory lesions, local and systemic infections, benign tumors, reactive thymic hyperplasia, histiocytic infiltration, or following G-CSF therapy, radiation therapy, or surgical interventions, all of which could result in false-positive findings.[173]

Being familiar with the most frequent differential diagnosis for lesions in each location where hematological malignancies are found can be helpful. On the other hand, sometimes the amount of possible differential diagnosis is too big. Therefore, knowing the clinical history of the patient, their symptoms, the results of laboratory findings (including tumor markers) and physical examination, can help narrow down the possible diagnosis. Also, CT characteristics and those of other conventional imaging modalities have been described and can be of help, nevertheless these characteristics usually overlap among different lesions. In the end, if lesion detection is prone to change the clinical management of the patient, the nuclear medicine physician should recommend further work up, like biopsy, to confirm the findings.

Acknowledgments

Nothing to declare

References

1. Swerdlow SH, Campo E, Pileri SA, et al: The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 127:2375, 2016
2. Swerdlow SH, Campo E, Harris NL, et al: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues World Health Organization Classification of Tumours. (Revised 4th ed.). Lyon, France: International Agency for Research on Cancer (IARC), 2017
3. Arber DA, Orazi A, Hasserjian R, et al: The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 127:2391, 2016
4. Malard F, Mohty M: Acute lymphoblastic leukemia. Lancet 395:1146-1162, 2020
5. Howlader N, Noone AM, Krapcho M, et al: SEER cancer statistics review. Bethesda, MD: National Cancer Institute, 2017 1975−2014 https://seer.cancer.gov/csr/1975_2014/(accessed Feb 7, 2020
6. Roman E, Smith A, Appleton S, et al: Myeloid malignancies in the real-world: Occurrence, progression and survival in the UK's population-based Haematological Malignancy Research Network 2004-15. Cancer Epidemiol 42:186-198, 2016
7. Heuser M, Ofran Y, Boissel N, et al: Acute myeloid leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 31:697-712, 2020
8. Bullinger L, Dohner K, Dohner H: Genomics of acute myeloid leukemia diagnosis and pathways. J Clin Oncol 35:934e946, 2017
9. Granfeldt Ostgard LS, Medeiros BC, Sengeløv H, et al: Epidemiology and clinical significance of secondary and therapy-related acute myeloid leukemia: a national population-based cohort study. J Clin Oncol 33:3641-3649, 2015.
10. Eichhorst B, Robak T, Montserrat E, et al: Chronic lymphocytic leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 32:23-33, 2021
11. Zenz T, Mertens D, Küppers R, et al: From pathogenesis to treatment of chronic lymphocytic leukaemia. Nat Rev Cancer 10:37-50, 2010
12. Goldin LR, Slager SL, Caporaso NE: Familial Chronic Lymphocytic Leukemia. Curr Opin Hematol 17:350-355, 2010
13. Hehlmann R, Hochhaus A, Baccarani M: Chronic myeloid leukaemia. Lancet 370:342-350, 2007

14. Hochhaus A, Saussele S, Rosti G, et al: Chronic myeloid leukaemia: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 28(Suppl_4):iv41-iv51, 2017
15. Cowan AJ, Allen C, Barac A, et al: Global burden of multiple myeloma: A systematic analysis for the Global Burden of Disease Study 2016. JAMA Oncol 4:1221-1227, 2018
16. Van de Donk NWCJ, Pawlyn C, Yong KL: Multiple Myeloma. Lancet 397:410-427, 2021
17. Went M, Sud A, Försti A, et al: Identification of multiple risk loci and regulatory mechanisms influencing susceptibility to multiple myeloma. Nat Commun 9:3707, 2018
18. Vachon CM, Kyle RA, Therneau TM, et al: Increased risk of monoclonal gammopathy in first-degree relatives of patients with multiple myeloma or monoclonal gammopathy of undetermined significance. Blood 114:785-790, 2009
19. Kumar SK, Dimopoulos MA, Kastritis E, et al: Natural history of relapsed myeloma, refractory to immunomodulatory drugs and proteasome inhibitors: A multicenter IMWG study. Leukemia 31:2443-2448, 2017
20. Rosinol Dachs L, Oriol A, Teruel AI, et al: VTD (bortezomib/thalidomide/dexamethasone) as pretransplant induction therapy for multiple myeloma: definitive results of a randomized phase 3 PETHEMA/GEM study. Blood 132(suppl 1):126, 2018
21. Tacchetti P, Dozza L, Di Raimondo F, et al: Bortezomib−thalidomide−dexamethasone versus thalidomide−dexamethasone before and after double autologous stem cell transplantation for newly diagnosed multiple myeloma: Final analysis of phase 3 Gimema-MMY-3006 study and prognostic score for survival outcomes. Blood 132(suppl 1):125, 2018
22. Almitage JO, Gascoyne RD, Lunning MA, et al: Non-Hodgkin lymphoma. Lancet 390:298-310, 2017
23. Townsend W, Linch D: Hodgkin's lymphoma in adults. Lancet 380:836-847, 2012
24. Mugnaini EN, Ghosh N: Lymphoma. Prim Care Clin Office Pract 43, 2016. 661-675
25. Richter MN: Generalized reticular cell sarcoma of lymph nodes associated with lymphatic leukemia. Am J Pathol 4:285-292, 1928
26. Jain P, O'Brien S: Richter's transformation in chronic lymphocytic leukemia. Oncology (Williston Park, N.Y.). 26: 1146−52.
27. Rosenberg SA: Validity of the Ann Arbor staging classification for the non-Hodgkin's lymphomas. Cancer Treat Rep 61:1023-1027, 1977
28. Juweid ME, Wiseman GA, Vose JM, et al: Response assessment of aggressive non-Hodgkin's lymphoma by integrated international workshop criteria and fluorine-18-fluorodeoxyglucose positron emission tomography. J Clin Oncol 23:4652-4661, 2005
29. Cheson BD, Pfistner B, Juweid ME, et al: Revised response criteria for malignant lymphoma. J Clin Oncol 25:579-586, 2007
30. Barrington SF, Mikhaeel NG, Kostakoglu L, et al: Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. J Clin Oncol 32:3048-3058, 2014
31. Cheson BD, Fisher RI, Barrington SF, et al: Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 32:3059-3068, 2014
32. Eichenauer DA, Alerman BMP, André M, et al: Hodgkin Lymphoma: ESMO Clinical Practice Guidelines. Ann Oncol 29(Suppl 4):iv19-iv29, 2018
33. Tilly H, Gomes da Silva M, Vitolo U, et al: Diffuse large B-cel lymphoma: ESMO clinical practice guidelines. Ann Oncol 26(suppl 5): v116-v125, 2015
34. Dreyling M, Ghielmini M, Rule S, et al: Newly Diagnosed and Relapsed Follicular Lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 32:298-308, 2021
35. Dreyling M, Campo E, Hermine O, et al: Newly diagnosed and relapsed mantle cell lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 28(Supplement 4):iv62-iv71, 2017
36. e Zucca, L Arcaini, Buske C, et al: Marginal zone lymphomas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 31:17-29, 2020
37. Dimopoulos MA, Moreau P, Terpos E, et al: Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 32:309-332, 2021
38. Heuser M, Ofran Y, Boissel N, et al: Acute myeloid leukaemia in adult patients: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol 31:697-712, 2020
39. National Comprehensive Cancer Network. https://www.nccn.org/professionals/physician_gls/default.aspx. Accessed March 31, 2021.
40. Kadrmas DJ, Casey ME, Conti M, et al: Impact of time-of-flight on PET tumor detection. J Nucl Med 50:1315-1323, 2009
41. Kuhnert G, Boellaard R, Sterzer S, et al: Impact of PET/CT image reconstruction methods and liver uptake normalization strategies on quantitative image analysis. Eur J Nucl Med Mol Imaging 43:249-258, 2016
42. Osman MM, Cohade C, Nakamoto Y, et al: Respiratory motion artifacts on PET emission images obtained using CT attenuation correction on PET-CT. Eur J Nucl Med Mol Imaging 30:603-606, 2003
43. Berthelsen AK, Holm S, Loft A, et al: PET/CT with intravenous contrast can be used for PET attenuation correction in cancer patients. Eur J Nucl Med Mol Imaging 32:1167-1175, 2005
44. Yau YY, Chan WS, Tam YM, et al: Application of intravenous contrast in PET/CT: Does it really introduce significant attenuation correction error? J Nucl Med 46:283-291, 2005
45. Mawlawi O, Erasmus JJ, Munden RF, et al: Quantifying the effect of IV contrast media on integrated PET/CT: Clinical evaluation. Am J Roentgenol 186:308-319, 2006
46. Vera P, Ouvrier MJ, Hapdey S, et al: Does chemotherapy influence the quantification of SUV when contrastenhanced CT is used in PET/CT in lymphoma? Eur J Nucl Med Mol Imaging 34:1943-1952, 2007
47. Voltin CA, Mettler J, Boellaard R, et al: Quantitative assessment of 18F-FDG PET in patients with Hodgkin lymphoma: Is it significantly affected by contrast-enhanced computed tomography attenuation correction? Nucl Med Commun 40:249-257, 2019
48. Boellaard R, Delgado-Bolton R, Oyen WJ, et al: FDG PET/CT: EANM procedure guidelines for tumour imaging: Version 2.0. Eur J Nucl Med Mol Imaging 42:328-354, 2015
49. Delbeke D, Coleman RE, Guiberteau MJ, et al: Procedure guideline for tumor imaging with 18F-FDG PET/CT 1.0. J Nucl Med 47:885-895, 2006
50. Park HY, Suh CH, Huang RY, et al: Diagnostic Yield of Body CT and Whole-Body FDG PET/CT for Initial Systemic Staging in Patients with Suspected Primary Central System Lymphoma: A Systematic Review and Meta-analysis. AJR Am J Roentgenol 216:1172-1182, 2021.
51. Hoang-Xuan K, Bessell E, Bromberg J, et al: Diagnosis and treatment of primary CNS lymphoma in immunocompetent patients: guidelines from the European Association for Neuro-Oncology. The Lancet Oncology 16:e322-e332, 2015
52. National Comprehensive Cancer Network. Central Nervous System Cancers (Version 2.2020). https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed May 9, 2020.
53. Abrey LE, Batchelor TT, Ferreri AJ, et al: Report of an international workshop to standardize baseline evaluation and response criteria for primary CNS lymphoma. Journal of clinical oncology 23:5034-5043, 2005
54. Heusner TA, Hahn S, Hamami ME, et al: Incidental head and neck 18F-FDG uptake on PET/CT without corresponding morphological lesion: Early predictor of cancer development. Eur J Nucl Med Mol Imaging 36:1397-1406, 2009
55. Lewis PJ, Salama A: Uptake of fluorine-18-fluorodeoxyglucose in sarcoidosis. J Nucl Med 35:1-3, 1994
56. Kluge R, Kurch L, Georgi T, et al: Current Role of FDG-PET in Pediatric Hodgkin's Lymphoma, 47. Semin Nucl Med, 242-257, 2017
57. Nakamoto Y, Tatsumi M, Hammoud D, et al: Normal FDG distribution patterns in the head and neck: PET/CT evaluation. Radiology 234:879-885, 2005
58. Yiyan L, Nasrin V, Lionel S: Physiology and pathophysiology of incidental findings detected on FDG-PET scintigraphy. Semin Nucl Med 40:294-315, 2010

59. Chen CH, Hsiao CC, Chen YC, et al: Rebound thymic hyperplasia after chemotherapy in children with lymphoma. Pediatr Neonatol 58:151-157, 2017
60. Vranjesevic D, Schiepers C, Silverman DH, et al: Relationship between 18F-FDG uptake and breast density in women with normal breast tissue. J Nucl Med 44:1238-1242, 2003
61. Wachsmann JW, Gerbaudo VH: Thorax: Normal and benign pathologic patterns in FDG-PET/CT imaging. PET Clin 9:147-168, 2014
62. Zingas AP, Carrera JD, Murray CA, et al: Lipoma of the myocardium. J Comput Assist Tomogr 7:1098-1100, 1983
63. D'Amato N, Pierfelice O, D'Agostino C: Crista terminalis bridge: A rare variant mimicking right atrial mass. Eur J Echocardiogr 10:444-445, 2009
64. Abouzied MM, Crawford ES, Nabi HA: 18F-FDG imaging: Pitfalls and artifacts. J Nucl Med Technol 33:145-155, 2005
65. Jadvar H: Colonic FDG uptake pattern in subjects receiving oral contrast with no known or suspected colonic disease. Clin Nucl Med 36:754-756, 2011
66. Naganawa S, Yoshikawa T, Yasaka K, et al: Role of delayed-time-point imaging during abdominal and pelvic cancer screening using FDG-PET/CT in the general population. Medicine (Baltimore) 96:e8832, 2017
67. Bybel B, Greenberg ID, Paterson J, et al: Increased F-18 FDG intestinal uptake in diabetic patients on metformin: A matched case-control analysis. Clin Nucl Med 36:452-456, 2011
68. Zukotynski K, Kim CK: Abdomen: Normal variations and benign conditions resulting in uptake on FDG-PET/CT. PET Clin 9:169-183, 2014
69. Lerman H, Metser U, Grisaru D, et al: Normal and abnormal 18F-FDG endometrial and ovarian uptake in pre- and postmenopausal patients: Assessment by PET/CT. J Nucl Med 45:266-271, 2004
70. Nishizawa S, Inubushi M, Okada H: Physiological 18F-FDG uptake in the ovaries and uterus of healthy female volunteers. Eur J Nucl Med Mol Imaging 32:549-556, 2005
71. Cohade C: Altered biodistribution on FDG-PET with emphasis on brown fat and insulin effect. Semin Nucl Med 40:283-293, 2010
72. Højgaard L, Berthelsen AK, Loft A: Head and neck: normal variations and benign findings in FDG positron emission tomography/computed tomography imaging. PET Clin 9:141-145, 2014
73. Abouzied M, Crawford E, Nabi H: 18F-FDG imaging: Pitfalls and artifacts. J Nucl Med Technol 33:145-155, 2005
74. Yeung HW, Grewal RK, Gonen M, et al: Patterns of (18)F-FDG uptake in adipose tissue and muscle: A potential source of false-positives for PET. J Nucl Med 44:1789-1796, 2003
75. Cypess A, Lehman S, Williams G, et al: Identification and importance of brown adipose tissue in adult humans. N Engl J Med 360:1509-1517, 2009
76. Barrington SF, Maisey MN: Skeletal muscle uptake of Fluorine-18-FDG: Effect of oral diazepam. J Nucl Med 37:1127-1129, 1996
77. Tomura N, Saginoya T, Goto H: PET findings in lymphomatosis and gliomatosis of the brain: A comparison of C-11 methionine PET/CT and F-18 FDG PET/CT. Acta Radiol 2020:284185120966710. Oct 20
78. Zhou WL, Wu HB, Wang LJ, et al: Usefulness and pitfalls of F-18-FDG PET/CT for diagnosing extramedullary acute leukemia. Eur J Radiol 85:205-210, 2016
79. Fernández-Rodríguez P, Tamayo D, Fernández R, et al: Acute brain stroke evolution detected by 18F-FDG PET/CT and MRI justifies the discordance of lesions in a patient with lymphoproliferative syndrome. Clin Nucl Med 46:e171-e172, 2021
80. Berkman N, Breuer R, Kramer MR, et al: Pulmonary involvement in lymphoma. Leuk Lymphoma 20:229-237, 1996
81. Bashoura L, Eapen GA, Faiz SA: Pulmonary Manifestations of Lymphoma and Leukemia. Clin Chest Med 38:187-200, 2017
82. Paydas S, Zorludemir S, Ergin M: Granulocytic sarcoma: 32 cases and review of the literature. Leuk Lymphoma 47:2527-2541, 2006
83. Herrmann R, Panahon AM, Barcos MP, et al: Gastrointestinal involvement in non-Hodgkin's lymphoma. Cancer 46:215-222, 1980
84. Ghimire P, Wu GY, Zhu L: Primary gastrointestinal lymphoma. World j gastroenterol 17:697-707, 2011
85. Bautista-Quach MA, Ake CD, Chen M, et al: Gastrointestinal lymphomas: Morphology, immunophenotype and molecular features. J gastrointestinal oncol 3:209-225, 2012
86. Howell JM, Auer-Grzesiak I, Zhang J, et al: Increasing incidence rates, distribution and histological characteristics of primary gastrointestinal non-Hodgkin lymphoma in a North American population. Canadian J gastroenterol = Journal canadien de gastroenterology 26:452-456, 2012
87. Shi Z, Ding H, Shen QW, et al: The clinical manifestation, survival outcome and predictive prognostic factors of 137 patients with primary gastrointestinal lymphoma (PGIL): Strobe compliant. Medicine (Baltimore) 97(1):e9583, 2018
88. Levine MS, Rubesin SE, Pantongrag-Brown L, et al: Non-Hodgkin's lymphoma of the gastrointestinal tract: radiographic findings. Am J Roentgenol 168:165-172, 1997
89. Lo Re G, Federica V, Midiri F, et al: Radiological Features of Gastrointestinal Lymphoma. Gastroenterol res and pract 2016:2498143, 2016
90. Zhou HB: A case of multiple myeloma initially presenting as hematemesis. The Turkish J gastroenterol: the off j Turkish Soc Gastroenterol 29:108-111, 2018
91. Khan Z, Darr U, Renno A, et al: Massive Upper and Lower GI Bleed from Simultaneous Primary (AL) Amyloidosis of the Stomach and Transverse Colon in a Patient with Multiple Myeloma. Case Rep Gastroenterol 11:625-631, 2017
92. Bailly C, Leforestier R, Jamet B, et al: PET imaging for initial staging and therapy assessment in multiple myeloma patients. Int j molecular sci 18:445, 2017.
93. Glasbey JC, Arshad F, Almond LM, et al: Gastrointestinal manifestations of extramedullary plasmacytoma: a narrative review and illustrative case reports. Ann Royal College of Surgeons of England 100:371-376, 2018
94. Dores GM, Landgren O, McGlynn KA, et al: Plasmacytoma of bone, extramedullary plasmacytoma, and multiple myeloma: Incidence and survival in the United States 1992-2004 Br J Haematol 144:86-94, 2009
95. Cornes JS, Jones TG: Leukaemic lesions of the gastrointestinal tract. J Clin Pathol 15:305-313, 1962
96. Prolla JC, Kirsner JB: The gastrointestinal lesions and complications of leukemias. Ann Intern Med 61:1084-1103, 1964
97. Lewis RB, Mehrotra AK, Rodriguez P, et al: From the Radiologic pathology archives: Gastrointestinal lymphoma: Radiologic and pathologic findings. Radiographics: A Rev Publ of the Radiol Soc N Am, Inc 34:1934-1953, 2014
98. Leite NP, Kased N, Hanna RF, et al: Cross-sectional imaging of extranodal involvement in abdominopelvic lymphoproliferative malignancies. RadioGraphics 27:1613-1634, 2007
99. Walz-Mattmüller R, Horny HP, Ruck P, et al: Incidence and pattern of liver involvement in haematological malignancies. Pathol Res Pract 194:781-789, 1998
100. Freeman C, Berg JW, Cutler SJ: Occurrence and prognosis of extranodal lymphomas. Cancer 29:252-260, 1972
101. Elsayes KM, Menias CO, Willatt JM, et al: Primary hepatic lymphoma: imaging findings. J Med Imaging Radiat Oncol 53:373-379, 2009
102. Noronha V, Shafi NQ, Obando JA, et al: Primary non-Hodgkin's lymphoma of the liver. Crit Rev Oncol Hematol 53:199-207, 2005
103. Bach AG, Behrmann C, Holzhausen HJ, et al: Prevalence and imaging of hepatic involvement in malignant lymphoproliferative disease. Clin Imaging 36:539-546, 2012
104. Oshima K, Kanda Y, Nannya Y, et al: Clinical and pathologic findings in 52 consecutively autopsied cases with multiple myeloma. Am J Hematol 67:1-5, 2001
105. Philips S, Menias C, Vikram R, et al: Abdominal manifestations of extraosseous myeloma: cross-sectional imaging spectrum. J Comput Assist Tomogr 36:207-212, 2012
106. Du B, Li X, Li N, et al: 18F-FDG hepatic superscan in a patient with chronic myeloid leukemia. Clin Nucl Med 39:835-836, 2014
107. Saboo SS, Krajewski KM, O`Regan KN, et al: Spleen in haematological malignancies: Spectrum of imaging findings. Br J Radiol 85:81-92, 2012

108. De Jong PA, van Ufford HM, Baarslag HJ, et al: CT and 18F-FDG PET for noninvasive detection of splenic involvement in patients with malignant lymphoma. AJR Am J Roentgenol 192:745-753, 2009
109. Heiberg E, Wolverson MK, Sundaram M, et al: CT findings in leukemia. AJR AmJ Roentgenol 143:1317-1323, 1984
110. Oshima K, Kanda Y, Nannya Y, et al: Clinical and pathologic findings in 52 consecutively autopsied cases with multiple myeloma. Am J Hematol 67:1-5, 2001
111. Hall MN, Jagannathan JP, Ramaiya NH, et al: Imaging of extraosseous myeloma: CT, PET/CT, and MRI Features. AJR Am J Roentgenol 195:1057-1065, 2010
112. Nayer H, Weir EG, Sheth S, et al: Primary pancreatic lymphomas: A cytopathologic analysis of a rare malignancy. Cancer 102:315-321, 2004
113. Rosenberg SA, Diamond HD, Jaslowitz B, et al: Lymphosarcoma: A review of 1269 cases. Medicine (Baltimore) 40:31-84, 1961.
114. Merkle EM, Bender GN, Brambs HJ: Imaging findings in pancreatic lymphoma: Differential aspects. AJR Am J Roentgenol 174:671-675, 2000
115. Sandrasegaran K, Tomasian A, Elsayes KM, et al: Hematologic malignancies of the pancreas. Abdom Imaging 40:411-423, 2015
116. Battula N, Srinivasan P, Prachalias A, et al: Primary pancreatic lymphoma: Diagnostic and therapeutic dilemma. Pancreas 33:192-194, 2006
117. Fujinaga Y, Lall C, Patel A, et al: MR features of primary and secondary malignant lymphoma of the pancreas: A pictorial review. Insights Imaging 4:321-329, 2013
118. Dong A, Cui Y, Gao L, et al: Patterns of FDG uptake in pancreatic non-Hodgkin's lymphoma lesions. Abdom Imaging 39:175-186, 2014
119. Pasmantier MW, Azar HA: Extraskeletal spread in multiple plasma cell myeloma. Cancer 23:167-174, 1969
120. Davidson BS, Lee JE, Dood LG, et al: Extramedullary plasmacytoma of the pancreas. Am J Clin Oncol 16:363-368, 1993
121. Choi EK, Byun JH, Lee SJ, et al: Imaging findings of leukemic involvement of the pancreaticobiliary system in adults. AJR Am J Roentgenol 188:1589-1595, 2007
122. Ikawa Y, Saikawa Y, Horisawa T, et al: Pancreatic and renal involvement in pediatric acute lymphoblastic leukemia/lymphoma. J Clin Oncol 25:451-453, 2007
123. Grassetto G, Rubello D: Role of FDG-PET/CT in diagnosis, staging, response to treatment, and prognosis of pancreatic cancer. Am J Clin Oncol 34:111-114, 2011.
124. Yoon SH, Lee JM, Cho JY, et al: Small (≤20 mm) pancreatic adenocarcinomas: analysis of enhancement patterns and secondary signs with multiphasic multidetector CT. Radiology 259:442-452, 2011
125. Bhosale PR, Menias CO, Balachandran A, et al: Vascular pancreatic lesions: Spectrum of imaging findings of malignant masses and mimics with pathologic correlation. Abdom Imaging 38:802-817, 2013
126. Blastik M, Plavecz E, Zalatnai A: Pancreatic carcinomas in a 60-year, institute-based autopsy material with special emphasis of metastatic pattern. Pancreas 40:478-480, 2011
127. Oberg K, Eriksson B: Endocrine tumours of the pancreas. Best Pract Res Clin Gastroenterol 19:753-781, 2005.
128. Zhang J, Shao C, Wang J, et al: Autoimmune pancreatitis: Whole-body 18F-FDG PET/CT findings. Abdom Imaging 38:543-549, 2013
129. Ozaki Y, Oguchi K, Hamano H, et al: Differentiation of autoimmune pancreatitis from suspected pancreatic cancer by fluorine-18 fluorodeoxyglucose positron emission tomography. J Gastroenterol 43:144-151, 2008.
130. Tsitouridis I, Diamantopoulou A, Michaelides M, et al: Pancreatic metastases: CT and MRI findings. Diagn Interv Radiol 16:45-51, 2010
131. McLean K, Lilienfeld H, Caracciolo JT, et al: Management of isolated adrenal lesions in cancer patients. Cancer Control 18:113-126, 2011
132. Boland GW, Lee MJ, Gazelle GS, et al: Characterization of adrenal masses using unenhanced CT: An analysis of the CT literature. AJR Am J Roentgenol 171:201-204, 1998
133. Leung N: Hematologic manifestations of kidney disease. Semin Hematol 50:207-215, 2013
134. Chen L, Richendollar B, Bunting S, et al: Lymphomas and lymphoproliferative disorders clinically presenting as renal carcinoma: A clinicopathological study of 14 cases. Pathology 45:657-663, 2013
135. Bach AG, Behrmann C, Holzhausen HJ, et al: Prevalence and patterns of renal involvement in imaging of malignant lymphoproliferative diseases. Acta Radiol 53:343-348, 2012
136. Sheth S, Ali S, Fishman E: Imaging of renal lymphoma: Patterns of disease with pathologic correlation. RadioGraphics 26:1151-1168, 2006
137. Zukotynski K, Lewis A, O'Regan K, et al: PET/CT and renal pathology: A blind spot for radiologists? II. Lymphoma, leukemia, and metastatic disease. AJR Am J Roentgenol 199:W168-W174, 2012.
138. Purysko AS, Westphalen AC, Remer EM, et al: Imaging manifestations of hematologic diseases with renal and perinephric involvement. Radiographics 36:1038-1054, 2016
139. Oshima K, Kanda Y, Nannya Y, et al: Clinical and pathologic findings in 52 consecutively autopsied cases with multiple myeloma. Am J Hematol 67:1-5, 2001
140. Birjawi GA, Jalbout R, Musallam KM, et al: Abdominal manifestations of multiple myeloma: A retrospective radiologic overview. Clin Lymphoma Myeloma 8:348-351, 2008
141. Barcos M, Lane W, Gomez GA, et al: An autopsy study of 1206 acute and chronic leukemias (1958 to 1982). Cancer 60:827-837, 1987
142. Hilmes MA, Dillman JR, Mody RJ, et al: Pediatric renal leukemia: Spectrum of CT imaging findings. Pediatr Radiol 38:424-430, 2008
143. Patel U, Ramachandran N, Halls J, et al: Synchronous renal masses in patients with a nonrenal malignancy: Incidence of metastasis to the kidney versus primary renal neoplasia and differentiating features on CT. AJR Am J Roentgenol 197:W680-W686, 2011
144. Lakhani A, Khan SR, Bharwani N, et al: FDG PET/CT pitfalls in gynecologic and genitourinary oncologic imaging. Radiographics 37:577-594, 2017
145. Adams HJ, Kwee TC, de Keizer B, et al: FDG PET/CT for the detection of bone marrow involvement in diffuse large B-cell lymphoma: Systematic review and meta-analysis. Eur J Nucl Med Mol Imaging 41:565-574, 2014
146. Adams HJ, Kwee TC, de Keizer B, et al: Systematic review and meta-analysis on the diagnostic performance of FDG-PET/CT in detecting bone marrow involvement in newly diagnosed Hodgkin lymphoma: Is bone marrow biopsy still necessary? Ann Oncol 25:921-927, 2014
147. Berthet L, Cochet A, Kanoun S, et al: In newly diagnosed diffuse large B-cell lymphoma, determination of bone marrow involvement with 18F-FDG PET/CT provides better diagnostic performance and prognostic stratification than does biopsy. J Nucl Med 54:1244-1250, 2013
148. Pelosi E, Penna D, Douroukas A, et al: Bone marrow disease detection with FDG-PET/CT and bone marrow biopsy during the staging of malignant lymphoma: Results from a large multicentre study. Q J Nucl Med Mol Imaging 55:469-475, 2011
149. Cavo M, Terpos E, Nanni C, et al: Role of (18)F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: A consensus statement by the International Myeloma Working Group. Lancet Oncol 18:e206-e217, 2017
150. Endo T, Sato N, Koizumi K, et al: Localized relapse in bone marrow of extremities after allogeneic stem cell transplantation for acute lymphoblastic leukemia. Am J Hematol 76:279-282, 2004
151. Arimoto MK, Nakamoto Y, Nakatani K, et al: Increased bone marrow uptake of 18F-FDG in leukemia patients: Preliminary findings. Springerplus 4:521, 2015
152. Jerusalem G, Beguin Y: The place of positron emission tomography imaging in the management of patients with malignant lymphoma. Haematologica 91:442-444, 2006
153. Ghesani N, Jung J, Patel S, et al: Superscan caused by renal osteodystrophy: Observed on 18F FDG PET/CT scan. Indian J Nucl Med 28:251-2, 2013
154. Su HY, Liu RS, Liao SQ, et al: F-18 FDG PET superscan. Clin Nucl Med 31:28-9, 2006
155. Bailly M, Besse H, Kerdraon R, et al: 18F-FDG PET/CT superscan in prostate cancer. Clin Nucl Med 39:912-4, 2014

156. Hanrahan CJ, Vhristensen CR, Crim JR: Current concepts in the evaluation of multiple myeloma with MR imaging and FDG PET/CT. Radiographics 30:127-142, 2010
157. Sachpekidis C, Mai EK, Goldschmidt H, et al: (18)F-FDG dynamic PET/CT in patients with multiple myeloma: Patterns of tracer uptake and correlation with bone marrow plasma cell infiltration rate. Clin Nucl Med 40:e300-e307, 2015
158. Dubreuil J, Salles G, Bozzetto J, et al: Usual and unusual pitfalls of 18F-FDG-PET/CT in lymphoma after treatment: A pictorial review. Nucl Med Commun 38:563-576, 2017
159. Wagner SA, Mehta AC, Laber DA: Rituximab-induced interstitial lung disease. Am J Hematol 82:916-919, 2007
160. Choyke PL, Zeman RK, Gootenberg JE, et al: Thymic atrophy and regrowth in response to chemotherapy: CT evaluation. Am J Roentgenol 149:269-272, 1987
161. Jerushalmi J, Frenkel A, Bar-Shalom R, et al: Physiologic thymic uptake of 18F-FDG in children and young adults: A PET/CT evaluation of incidence, patterns, and relationship to treatment. J Nucl Med 50:849-853, 2009
162. Garg G, Benchekroun MT, Abraham T: FDG-PET/CT in the postoperative period: Utility, expected findings, complications, and pitfalls. Semin Nucl Med 47:579-594, 2017
163. Ansell SM, Lesophin AM, Borrello I, et al: PD-1 blockade with nivolumab in relapsed or refractory Hodgkin's lymphoma. N Engl J Med 372:311-319, 2015
164. Armand P, Shipp M, Ribrag V, et al: Programmed death-1 blockade with pembrolizumab in patients with classical Hodgkin lymphoma after brentuximab vedotin failure. J Clin Oncol 34:3733-3739, 2016
165. Neelapu SS, Locke FL, Bartlett NL, et al: Axicabtagene ciloleucel CAR T-cell therapy in refractory large B-cell lymphoma. N Engl J Med 377:2531-2544, 2017
166. Lopci E, Meignan M: Current evidence on PET response assessment to immunotherapy in lymphomas. PET Clin 15:23-34, 2020
167. Humbert O, Chardin D: Dissociated response in metastatic cancer: An atypical pattern brought into the spotlight with immunotherapy. Front Oncol 10:566297, 2020
168. Ferrari C, et al: Early evaluation of immunotherapy response in lymphoma patients by 18F-FDG PET/CT: A literature overview. J. Pers. Med. 11:217, 2021
169. Cheson BD, Ansell S, Schwartz L, et al: Refinement of the Lugano classification response criteria for lymphoma in the era of immunomodulatory therapy. Blood 128:2489-2496, 2016
170. Brave M, Liu J, Przepiorka D, et al: Analysis of immune-related adverse reactions in patients with classical Hodgkin lymphoma (cHL) on programmed death-1 (PD-1) inhibitors therapy. Blood 132:1652, 2018
171. Rekowski J, Hüttmann A, Schmitz C, et al: Interim PET evaluation in diffuse large B-Cell lymphoma using published recommendations: Comparison of the deauville 5-point scale and the ΔSUVmax method. J Nucl Med 62:37-42, 2021
172. Barrington S, Eertink JJ, de Vet HC, et al: Not yet time to abandon the Deauville criteria in diffuse large B cell lymphoma. J Nucl Med 2021. Apr 23;jnumed.121.262317. Online ahead of print
173. Valls L, Badve C, Avril S, et al: FDG-PET imaging in hematological malignancies. Blood Rev 30:317-331, 2016