### **Review Article**

### Role fluorodeoxglucose (FDG)-positron emission tomography imaging for Hodgkin and Diffuse Large B-Cell Lymphoma

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#### Abstract

The use of 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET) in conjunction with computed tomography has recently become important in the initial staging, evaluation of response, and treatment of malignant lymphomas. PET has shown high sensitivity in early and late response assessment during treatment, and early diagnosis of lymphoma manifestations. PET is most helpful in evaluating how well DLBCL and Hodgkin's lymphoma patients are responding to treatment. PET- CT in staging is extremely sensitive at identifying lymphoma lesions, and it is used to help doctors decide on treatment options, resulting in better therapy selection this imaging technique is often used to assess individual chemo sensitivity and adjust treatment accordingly. FDG-PET may also be used to assess residual masses after treatment is over. Patients with a negative FDG-PET scan should be considered in full remission, according to a recent update. FDG-PET/CT is no longer used in routine follow-up following a full metabolic response to treatment, but it is still a useful tool for excluding recurrence if patients experience clinical symptom suggestive of disease relapse.

**Keywords:** Hodgkin lymphoma; diffuse large B-cell lymphoma; positron emission tomography; staging; response assessment; treatments

#### Introduction

Hodgkin lymphoma is a common lymphoid tumor, representing 11% of all lymphomas, it a neoplastic disease of B- cell origin, classical Hodgkin lymphoma is characterized by the Reed-Sternberg presence of cells and inflammatory background that is composed of group of cells as lymphocytes, histiocytes, and monocytes but nodular lymphocyte predominance type is characterized by lymphocyte predominant cells in group of histiocytes and lymphocytes, Reed-Sternberg cells are positive for CD30 and CD15 but lymphocyte predominant cells positive for CD20 and CD45, While the cause of Hodgkin lymphoma is unclear, Epstein-Barr virus is thought to play a role in the pathogenesis of classical Hodgkin lymphoma. , smoking and family history increases the risk of Hodgkin lymphoma, the most common clinical features include lymphadenopathy particularly supradiaphragmatic, chronic pruritus, chest symptoms related to mediastinal adenopathy and B symptoms as unexplained Wight loss, fever and night sweat. Excisional biopsy of enlarged lymph node is strongly recommended for initial diagnosis and

other laboratory tests and radiological studies as computed tomography of chest, abdomen and pelvis, whole body FDG-PET scan is an important diagnostic tool. Hodgkin disease is a hematological tumor that has one of the best long-term outcomes following first-line treatment, with a 5-year relative survival rate of around 90% for patients diagnosed between the ages of 20 and 64.<sup>[1]</sup>

Chemotherapy accompanied by irradiation or chemotherapy alone are the options for treatment, depending on a variety of factors. Restaging after two or four cycles of chemotherapy to evaluate the response to treatment and restaging should be repeated 3 months after the of treatment<sup>[2]</sup> Non-Hodgkin lymphoma is a term used to describe a group of lymphoproliferative diseases including B cells, T cells, and NK cells. The cause of most cases of NHL is unknown; although several genetic diseases, environmental agents, and infectious agents have been associated with the development of lymphoma, the process of lymphagenesis in of non Hodgkin lymphoma involves a complex interplay between genetic mutations that disrupt

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the normal cellular pathways of proliferation, differentiation, and apoptosis. Excision lymph node biopsy remains the gold standard for diagnosis of suspected lymphoma. Patients should be asked about systemic symptoms and their performance status measured during a thorough history and physical assessment during the initial work up and staging evaluation of non Hodgkin lymphoma. Prior cancer, chemotherapy], or radiation therapy, as well as autoimmune or immunodeficiency disorder. Infection or exposure to pathogens such as HIV, hepatitis C, or HTLV-1 should be taken into account. As a whole body FDG-PET scan, a clinical laboratory and radiological evaluation is performed. Pathological categorizing of non Hodgkin lymphoma includes B cell, T cell, indolent or aggressive type. The most common form of non-Hodgkin lymphoma is diffuse large B-cell lymphoma (DLBCL), which accounts for 30 to 40% of all new cases.<sup>[3]</sup> Despite major treatment advancements, the cure rate for this tumor is substantially lower than that of Hodgkin lymphoma by about one-third of all patients relapsing after first-line therapy. The use of FDG-PET to diagnose patients with DLBC is strongly recommended because of its high sensitivity in detecting lymphoma manifestations, nodal and extranodal<sup>[4]</sup> FDG-PET/CT is used to evaluate response after chemotherapy and can identify a subgroup that will benefit from consoldative radiotherapy. FDG-PET/CT is no longer used in routine follow-up following a full metabolic response to treatment, but it is still a valuable method for excluding recurrence if patients experience clinical symptoms that indicate disease relapse.

# FDG-PET/CT application in initial staging of lymphoma

In Hodgkin lymphoma and DLBCL, accurate staging is critical for determining the most appropriate treatment options.FDG-PET has been the gold standard for testing all FDG-avid lymphoma because of its high sensitivity for compromised lymph nodes and non-nodal cancer. To assess glycolytic activity, researchers used a glucose analogue (2-fluoro-2deoxy-D-glucose [FDG]) radio labeled with the positron emitter fluorine-18. Glycolytic activity is elevated in malignancies, including lymphoma. For initial staging and follow-up, PET

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offers responsive functional imaging of lymphomas.

# **FDG-PET/CT** application in early response assessment

Treatment response should be asses by evaluate all physical findings, abnormal tests should be repeated as CT scan and bone marrow biopsy if positive previously. Final treatment evaluation is usually don 3 to 6 weeks after end of therapy unless progression occurs early; FDG-PET scans during and/or after therapy have also been shown to have prognostic value. PET is most useful in evaluate response to therapy of DLBCL and Hodgkin's lymphoma. A recent update recommended that patients considered in complete remission if they have a negative FDG-PET scan .FDG-PET is also useful for the evaluation of residual masses at the completion of therapy. In case of suspected disease relapse to initial therapy, repeated biopsy should be performed to exclude non malignant causes of abnormal imaging and evaluate possible disease transformation. The so-called Deauville score was first used in 2009 to aid in the application of clear and repeatable PET in the context of early response evaluation<sup>[5]</sup> It assigns a score of 1 to 5 to residual tissue centered on a direct visual contrast of lesional FDG uptake with the mediastinal blood pool and liver. Multiple studies have shown that using the Deauville criteria enhanced the quality of PET-based lymphoma response evaluation, and since this criteria allows the cut-off between positive and negative results to be adjusted based on the clinical outcome, graded evaluation allowed for more flexibility in interpretation.

### FDG-PET/CT application in late response assessment

CT imaging was used as the normal method of follow-up during chemotherapy before FDG-PET but CT scans, on the other hand, were unable to distinguish between fibrosis disease and active viable lymphoma, resulting in unconfirmed diagnoses.<sup>[6]</sup> In 37 patients with follicular lymphoma, 72 patients with Hodgkin lymphoma, and 72 patients with DLBCL, The diagnostic effectiveness of CT and FDG-PET/ CT was contrasted by Spanish researchers<sup>[4]</sup> FDG-PET/CT was highly sensitive and more accurate than CT in evaluate viable tissue in 97.8% in comparison with 78% for CT. There is

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no role for PET in follow up for patients in remission, unless anatomic imaging changes or patients experience clinical signs and symptoms that point to a disease relapse.

### False Positive and False Negative FDG-PET Scan

FDG is not a cancer-specific agent, and false positive results have been identified in benign diseases as infectious diseases (mycobacterial, fungal, and bacterial infection), sarcoidosis, radiation pneumonitis, and post-operative surgical conditions showed high absorption but adenomas, bronchioloalveolar carcinomas, and carcinoid tumours, on the other hand, have low glycolytic activity, low grade lymphomas and small sized tumors have revealed false negative findings on PET scan. So FDG-PET should be complemented with other imaging modalities to confirm results and to minimize false negative findings.

### Conclusions

PET has been the gold standard for diagnosis, and treatment assessment in DLBCL and Hodgkin's lymphoma. PET imaging at the start and halfway through a patient's recovery will provide useful details about the prognosis of their illness. PET effective at identifying lymphoma lesions and it is used to help determine treatment options resulting in more successful treatment. PET can be done 6 to 8 weeks after chemotherapy or 8 to 12 weeks after radiation after treatment is finished. Although FDG-PET/CT has no role in routine follow-up after a full metabolic response to therapy, it is still a valuable tool for excluding recurrence if patients develop clinical features that indicate disease relapse.

#### References

- Howlader, N.; Noone, A.M.; Krapcho, M.; Miller, D.; Brest, A.; Yu, M.; Ruhl, J.; Tatalovich, Z.; Mariotto, A.; Lewis, D.R.; et al. SEER Cancer Statistics Review, 1975–2016; National Cancer Institute: Bethesda, MD, USA,2019
- Eichenauer, D.A.; Aleman, B.M.P.; André, M.P.E.; Federico, M.; Hutchings, M.; Illidge, T.; Engert, A.; Ladetto, M. Hodgkin lymphoma: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann. Oncol. 2018, 29, iv19– iv29.
- Swerdlow, S.H.; Campo, E.; Harris, N.L.; Ja\_e, E.S.; Pileri, S.A.; Stein, H.; Thiele, J.; Arber, D.A.; Hasserjian, R.P.;Le Beau, M.M.; et al., WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues, Review, 4<sup>th</sup> ed.; International Agency for Research on Cancer: Lyon, France, 2017.
- Gómez León, N.; Delgado-Bolton, R.C.; Del Campo Del Val, L.; Cabezas, B.; Arranz, R.; García, M.; Cannata, J.; González Ortega, S.; Pérez Sáez, M.Á.; López-Botet, B.; et al., Multicenter comparison of contrast-enhanced FDG PET/CT and 64-slice multi-detector-row CT for initial staging and response evaluation at the end of treatment in patients with lymphoma. Clin. Nucl. Med. 2017, 42, 595–602.
- Meignan, M.; Gallamini, A.; Haioun, C. Report on the First International Workshop on Interim-PET-Scan inLymphoma. Leuk. Lymphoma 2009, 50, 1257–1260.
- Canellos, G.P. Residual mass in lymphoma may not be residual disease. J. Clin. Oncol. 1988, 6, 931–933.