Role of PET scan in Clinical Practice

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ABSTRACT
PET scan is an emerging image modality in clinical practice and especially useful for cancer cases. The principal clinical applications, benefits and shortcomings of this imaging technique are reviewed here.

INTRODUCTION
Noninvasive imaging is of fundamental and increasing importance in the daily management of the patient in clinical practice. This especially holds true in cancer patients as morbidity is more in such patients and objective imaging tests are required to be used at different times during the course of the disease to monitor disease staging, prognosis, efficacy (or lack of efficacy) of treatment. PET scan is a newer modality of imaging with increasingly newer applications more so in cancer patients.

Principles of operation
Positron emission tomography (PET) is a nuclear medical imaging technique that produces a three-dimensional image or picture of functional processes in the body. The system detects pairs of gamma rays emitted indirectly by a positron-emitting radionuclide (tracer), which is introduced into the body on a biologically active molecule. Three-dimensional images of tracer concentration within the body are then constructed by computer analysis. In modern scanners, three dimensional imaging is often accomplished with the aid of a CT scan performed on the patient during the same session, in the same machine.

If radiotracer chosen for PET is FDG, an analogue of glucose, the concentrations of tracer imaged will indicate tissue metabolic activity by virtue of the regional glucose uptake. Using this tracer to explore the possibility of cancer metastasis (i.e., spreading to other sites) is the most common type of PET scan in standard medical care (90%). Now, many other radiotracers are used in PET to image the tissue concentration of many other types of molecules of interest.

Clinical Applications
PET is both a medical and research tool. Main clinical fields of PET scan are oncology, cardiology, and neurology.

Non oncological applications:
Neurological applications
Presurgical assessment of medically refractory complex partial seizures where MR is normal, equivocal or conflicts with EEG localization
Evaluation of memory loss/neurological signs suggestive of dementia and differentiation of types of dementia in selected patients.
Cardiological indications:
- Assessment of myocardial viability in patients with ischemic heart failure and poor left ventricular function being considered for revascularization, usually in combination with perfusion imaging with sestamibi/tetrofosmin or ammonia/rubidium.
Infection imaging:
- Detection of site of focal infection in immune compromised patients or problematic cases of infection
- Evaluation of vascular graft infection in selected cases
Pyrexia of unknown origin (PUO):
- To identify the cause of a PUO where conventional investigations have not revealed a source.

Oncology applications:
Brain
- To differentiate between tumor recurrence and radiation necrosis in patients treated previously with cranial irradiation.
- Identifying the grade of malignancy where there is uncertainty on anatomical imaging and functional assessment would assist biopsy.

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• Assessment of suspected high grade transformation in low grade glioma.
• Differentiation of cerebral tumor from atypical infection in immunocompromised patients with indeterminate lesions on MR/CT.

Head and neck tumors
• Staging of patients where staging is difficult clinically or where there is uncertainty on other imaging or equivocal findings that would preclude radical treatment
• Staging or restaging of patients with a high risk of disseminated disease such as advanced loco regional disease and primary sites with a high propensity for disseminated disease such as nasopharyngeal cancer.
• To identify the primary site in patients presenting with metastatic carcinoma in cervical lymph nodes, with no primary site identified on other imaging.
• Response assessment 3-6 months post chemoradiotherapy in patients with residual masses following treatment.
• To differentiate between radiation induced edematous changes versus active tumor tissue.
• To rule out metastatic disease in locally advanced cancer before major operative procedure.

Lymphoma
• Staging of patients with Hodgkin’s disease (HD) and Non Hodgkin’s lymphoma (NHL) and as baseline for comparison with treatment response scan.
• Interim and end of treatment response assessment of patients with HD and aggressive NHL.
• Evaluation of suspected relapse for FDG avid lymphomas in symptomatic patient.
• Staging of suspected post transplant lymphoproliferative disorder (PTLD).
• Prior to bone marrow transplant to assess volume of disease and suitability for transplant
• To determine extent and identify a suitable biopsy site in patients with low grade lymphomas in whom there is suspected high grade transformation.

Lung carcinoma
• Staging of patients considered for radical treatment of non-small cell lung cancer especially mediastinal nodes <1 cm on CT or mediastinal nodes between 1–2 cm on CT or equivocal lesions that might represent metastases such as adrenal enlargement.
• Characterization of a solitary pulmonary nodule
• Especially in the case of failed biopsy, a technically difficult biopsy or where there is a significant risk of a pneumothorax in patients with medical co morbidities
• Assessment of suspected disease recurrence
• To differentiate between treatment effects and recurrent cancer
• Staging of patients with small cell lung cancer with limited disease on CT being considered for radical therapy.
• Pleural malignancy
• To guide biopsy in patients with suspected pleural malignancy
• To exclude extra-thoracic disease in proven mesothelioma in patients considered for multimodality treatment including radical surgery/decortication.

Breast carcinoma
• Assessment of multi focal disease or suspected recurrence in breast cancer.
• Differentiation of treatment induced brachial plexopathy from tumour infiltration in symptomatic patients with an equivocal or normal MR.
• Assessment of extent of disease in selected patients with disseminated breast cancer before therapy.
• Assessment of response to chemotherapy in patients whose disease is not well demonstrated using other techniques; for example, bone metastases

Hepatopancreaticobiliary cancers
• Staging of potentially operable primary hepatobiliary or pancreatic malignancy (choangiocarcinoma, gallbladder carcinoma or hepatocellular carcinoma) where cross sectional imaging is equivocal for metastatic disease, who are fit for resection and a positive PET-CT would lead to a decision not to operate.
• Suspected recurrence of hepato-pancreatico-biliary cancer in selected patients, where other imaging is equivocal or negative.

Colorectal carcinoma
• Staging of patients with synchronous metastases at presentation suitable for resection or patients with equivocal findings on other imaging; for example, pulmonary or liver lesions.
• Restaging of patients with recurrence being considered for radical treatment and/or metastatectomy
• Detection of recurrence in patients with rising tumour markers and/or clinical suspicion of recurrence
• Evaluation of indeterminate presacral masses post treatment.

Thymic carcinoma
• Staging of patients considered for surgical resection
• Assessment of indeterminate thymic lesions if being considered for radical treatment

Oesophagogastric carcinoma
• Staging/restaging of patients with oesophageal or oesophago gastric carcinoma, suitable for radical treatment, including patients who have received neo adjuvant treatment.¹⁰
• Evaluation of suspected recurrence of oesophago gastric tumours when other imaging is negative or equivocal

Gastrointestinal stromal tumours
• Staging prior to treatment in patients who are likely to require systemic therapy
• Response assessment to systemic therapy

Kidney and ureter
• Assessment of metastatic renal and ureteric carcinoma in difficult management situations or when standard imaging is inconclusive
• Assessment of renal carcinoma at staging in selected cases with equivocal findings on other imaging (recognizing that ~50% of renal cell carcinoma may not be FDG avid and that the tracer is excreted into the urinary tract)

Gynaecological malignancy
• Staging or restaging of patients with uterine carcinoma (cervix/endometrium)considered for exenterative surgery
• Staging of patients with cervical cancer suspected of having locally advanced disease with suspicious findings such as abnormal pelvic nodes on MR or at high risk of paraaortic nodal or distant metastatic disease.¹¹
• Suspected recurrence of endometrial and/or cervical carcinoma when other imaging is inconclusive.

Myeloma
• Assessment of patients with apparently solitary plasmacytoma or patients with ambiguous lytic lesions on skeletal survey.¹²
• Suspected relapse in patients with non-secretory myeloma or predominantly extramedullary disease.

Skin tumours
• Staging and assessment for distant disease in patients with melanoma when radical dissection is contemplated (nodal or metastatic disease).
• To exclude primary malignancy where dermatomyositis is suspected to represent paraneoplastic manifestation.

Musculoskeletal tumours
• Assessment of suspected malignant transformation within plexiform neurofibromas in patients with neurofibromatosis type 1
• Staging of high grade sarcomas, unless already proven to have metastatic disease, especially Ewing’s sarcoma, rhabdomyosarcoma, leiomyosarcoma, osteosarcoma, malignant fibrous histiocytoma, synovial sarcoma and myxoid liposarcoma.¹³
• Preamputation in the setting of a high grade sarcoma where the detection of distant disease will alter the surgical management
• To stage patients with metastatic sarcoma considered for liver or lung metastatectomy where anatomical imaging has not identified any extra thoracic or extra hepatic disease which would preclude surgery
• Response assessment in high grade sarcomas

Paraneoplastic syndromes
• To detect an occult primary tumour in selected patients with non metastatic manifestations of neoplastic disease when other imaging is negative or equivocal

Carcinoma of unknown primary
• Detection of the primary site when imaging and histopathology has failed to show a primary site, where the site of tumor will influence choice of chemotherapy.

Neuroendocrine tumours
• Staging or restaging of selected patients with poorly differentiated neuroendocrine tumours prior to treatment with negative or normal metaiodobenzylguanidine (MIBG) and octreotide scans.¹⁴
• Assessment of possible multifocal disease in patients with paraganglioma considered for surgery
• Staging and response assessment of osteosarcoma and Ewing's sarcoma in patients with negative bone scintigraphy

PET CT may be helpful in paediatric or adolescent patients with Wilms' tumours, MIBG negative neuroblastoma, Hepatoblastoma, Langerhans' cell histiocytosis.

Benefits and shortcomings

MRI and FDG-PET scan imaging serve to identify primary or metastatic or paraneoplastic disease and monitor response to therapy.

For most malignancies, FDG-PET will be helpful in the setting of suspected or proven recurrence. Its utility in the primary setting depends on the availability and information derived from structural imaging studies.

Some primary malignancies show relatively low uptake of FDG, which reflects their low glucose metabolism, lower expression of glucose transporters, a high rate of FDG dephosphorylation (e.g., hepatocellular carcinoma), and the histologic composition of the lesion.

Most well-differentiated malignant tumors, including differentiated, iodine-avid thyroid cancer, many primary prostate and renal cancers, also show low FDG uptake. Indolent lymphomas also show relatively low FDG uptake. As these malignancies become more aggressive and clinical disease progresses, they will become detectable on FDG PET, and it can then help in monitoring the response to chemotherapy or experimental therapies (e.g., in castration-resistant metastatic prostate cancer) and also provide prognostic information.

As the normal brain metabolizes glucose almost exclusively as a fuel, FDG uptake will be high. Thus, tumors with glucose metabolism lower than or even equal to that in normal cortex (e.g., low-grade astrocytomas) may not be detected on FDG PET.

False-positive findings may occur due to increased glucose metabolism and FDG uptake within brown adipose tissue, a normal variant, in various granulomatous diseases such as sarcoidosis, in some benign tumors (e.g., paragangliomas, benign bone lesions such as eosinophilic granuloma, nonossifying fibroma, Paget's disease), at sites of infection, or in nonspecific inflammation. The latter sometimes presents a problem when PET imaging is done too early (earlier than 10 weeks) after the end of radiation or chemoradiation therapy.

PET scan with its widespread applications has emerged as an indispensable tool in the detection, staging, treatment monitoring, and identification of recurrent disease in a large number of malignancies.

REFERENCES