Introduction

The purpose of these guidelines is to provide a broad framework for clinicians considering the use of positron emission tomography (PET) scanning for their patients. PET imaging is a rapidly evolving field, with ongoing developments in imaging technology, radiochemistry, isotope production, animal research and clinical applications. There is a need for regular review of these guidelines, to incorporate new evidence and results of scientific research.

Like most diagnostic tests, meta-analyses or systematic reviews are not available for PET in every clinical application. Nonetheless, clinical practice should be guided by the best available evidence. Whilst some of the following recommendations are based on mature scientific evidence, others simply represent the current consensus of experts in this field.

Most of the published data on PET scanning refer to studies using traditional PET scanners. Combined PET-computed tomography (CT) scanners became commercially available in 2002, and a wealth of new data will emerge over the next few years on the incremental value of fusing PET with CT images. Preliminary experience suggests a further enhancement of diagnostic accuracy, impact on patient management and outcome, and extension of useful clinical applications, particularly in oncology practice. As clinical PET services were introduced in Singapore only in mid-2003, all the currently installed scanners are PET-CT devices.

New PET radiotracer compounds will also emerge from experimental use into routine clinical application. Future updates to these guidelines will need to keep pace with these developments. In addition, as PET technology has spread more recently in Asian countries, more scientific data relevant to our disease context will need to be sought, e.g. for hepatocellular and nasopharyngeal carcinoma. Local research into these areas should therefore be encouraged.

It is not possible to be dogmatic or prescriptive about the role of PET in a given clinical situation, as this may depend on clinical factors, socio-economic circumstances, patient attitudes and other factors. These recommendations should therefore not be interpreted as mandatory for compliance in every stated clinical situation. For ease of reference, the recommendations have been classified into 3 categories:

** Useful application for clinical PET imaging.

* Potentially useful application – not indicated routinely, but may be helpful in individual cases, or there is currently limited data to prove cost-effectiveness.

# Not recommended at present.

Unless otherwise stated, routine clinical PET imaging is deemed to be performed with the glucose analog $^{18}$F-FDG. However, in certain situations, other PET radiotracers are needed, to visualise other metabolic processes. These are not yet routinely available at most clinical PET sites (including those in Singapore).

The following recommendations are intended as a guide for physician referral and patient selection for clinical PET imaging. For more details on the scientific evidence, the reader is advised to refer to the publications in the references section.

Oncology

Brain and Spinal Cord Tumours

(PET scanning using both $^{18}$F-FDG and $^{11}$C-methionine is recommended.)

- Distinguishing residual or recurrent disease from post-therapy scarring or radionecrosis, when anatomical imaging is difficult or equivocal.**

- Benign versus malignant lesions, where there is uncertainty on anatomical imaging and a relative contraindication to biopsy, e.g. intra-cranial lymphoma versus toxoplasmosis.**

- Grading of primary brain tumours.*

- Evaluation of response to therapy.*

- Identifying site of recurrent brain tumour for biopsy.*

- PET is not recommended as a primary imaging tool for suspected brain metastases.#
Head and Neck Cancers (other than nasopharyngeal, thyroid cancer, or brain tumours)

- Staging.*
- Restaging.**
- Evaluation of suspected recurrence.**
- Evaluation of response to therapy.*
- Search for unknown primary tumour in patients with cervical nodal metastases.**
- For parotid tumours, however, PET is not helpful for distinguishing benign from malignant pathology.#

Nasopharyngeal Cancer

- Staging.*
- Restaging.**
- Localising or differentiating recurrence from therapy-induced radiological changes.**
- Evaluation of response to therapy.*

Thyroid Cancer

- Detection of recurrent or residual tumour (follicular or papillary cancer), when serum thyroglobulin is elevated but radiiodine scan is negative or appears to underestimate the extent of disease.**
- Not recommended for routine assessment of thyroglobulin-positive recurrence with radiiodine uptake.#
- Assessment of tumour recurrence in medullary carcinoma of the thyroid.*

Parathyroid Adenoma

- Preoperative localisation of parathyroid adenoma using 11C-methionine, when other investigations are negative.*

Solitary Pulmonary Nodule

- Characterisation of a newly discovered indeterminate lung nodule, or a nodule that shows interval increase in size on chest X-ray or CT scan.**

Non-small Cell Lung Cancer

- Staging.**
- Restaging.**
- Assessment of recurrent disease in previously treated areas where anatomical imaging is unhelpful.**
- Evaluation of response to therapy.*

Small Cell Lung Cancer

- Staging.*

Breast Cancer

- Staging.*
- Restaging.*
- Evaluation of suspected recurrence, e.g. brachial plexopathy (radiation effects versus malignant infiltration), when anatomical imaging results are non-diagnostic or equivocal.*
- Evaluation of response to therapy.*

Oesophageal Cancer

- Staging and restaging.**
- Suspected recurrent disease – useful for distant lymph nodes and distant metastases, but of limited value for detection of locoregional disease near to the primary tumour.**
- Evaluation of response to therapy.*

Gastric Cancer

- Staging and restaging.*

Gastrointestinal Stromal Tumour

- Evaluation of response to therapy.*

Hepatocellular Carcinoma

- Staging.*
- Evaluation of response to therapy.*

Pancreatic Carcinoma

- Staging of known primary pancreatic carcinoma.*
- Differentiation between benign and malignant pathology, e.g. chronic pancreatitis from pancreatic cancer.*

Colorectal Cancer

- Staging.*
- Restaging.**
- Suspected recurrence, e.g. elevated serum markers, suspicious radiological changes, abnormal physical exam or clinical symptoms of recurrence.**

Renal Cancer, Transitional Cell Carcinoma and Bladder Cancer

- Limited data available for 18F-FDG PET in diagnosis and staging. A negative 18F-FDG PET does not rule out active malignancy.
- Possible role for 11C-methionine and 11C-acetate PET.
Prostate Cancer
- 18F-FDG PET is of limited value. Lower histologic grade tumours may not show FDG uptake.
- PET imaging with 11C-acetate, 11C-choline, 18F-fluoroacetate, or 18F-choline show promise for detection of recurrence and metastases from prostate cancer.

Ovarian Cancer
- Evaluation of suspected recurrence.*

Cervical Cancer
- Staging.*
- Restaging.*
- Evaluation of suspected recurrence.*

Testicular Tumours
- Staging.*
- Restaging.*
- Evaluation of suspected recurrence.*
- Evaluation of response to therapy.*

Lymphoma
- Staging.**
- Restaging.**
- Evaluation of response to therapy.**
- Evaluation of suspected tumour recurrence, e.g. tumour versus post-therapy fibrosis in a residual mass.**
- Assessing bone marrow involvement.*

Malignant Melanoma
- Staging (Breslow >1.5 mm or known lymph node involvement).**
- Restaging.**
- Follow-up of patients with high-risk primary lesions.**

Soft Tissue Sarcomas
- Diagnosis and grading.*
- Restaging.*

Metastatic Cancer of Unknown Primary Cancer
- Detection of occult malignant disease.*
- Not indicated in widespread metastatic disease if PET result will not influence management.#

Paraneoplastic Syndrome
- Detection of unknown primary cancer.*

Cardiology

Myocardial Viability
- Cardiac FDG-PET imaging is recommended for assessment of myocardial viability in selected patients with coronary artery disease and severely impaired left ventricular function, who are being considered for coronary revascularisation or heart transplantation, especially in patients with equivocal or inconclusive results for viability based on myocardial perfusion SPECT, dobutamine stress echocardiography or cardiac magnetic resonance imaging (MRI).**

Myocardial Perfusion
(Myocardial blood flow studies using 13N-ammonia or 82Rb.)
- Diagnosis for coronary artery disease when myocardial perfusion SPECT or other tests are equivocal.*
- Distinguishing ischaemic cardiomyopathy from other types of dilated cardiomyopathy.*

Neurology

Refractory Epilepsy
- Inter-ictal FDG-PET is recommended for lateralisation of epileptogenic foci prior to surgical intervention in patients with medically refractory epilepsy and where inconclusive localising information is provided by a standard assessment, including seizure pattern, electroencephalography and MRI.**
- 11C-flumezanil may be helpful for localisation of epileptogenic foci.*

Dementia
- In the work-up of patients with dementia, FDG-PET is helpful in identification of early Alzheimer’s disease before the onset of cerebral atrophy, especially in younger patients with dementia and normal MRI or CT.*

Parkinson’s Disease
- Confirmation of Parkinson’s disease using 18F-DOPA when symptoms are atypical or mild.*

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REFERENCES

Comprehensive Reviews – PET in Oncology

Brain and Central Nervous System Tumours

Diagnosis of Tumour Recurrence, Benign versus Malignant

Grading and Prognosis

Evaluating Response to Therapy

Guiding Biopsy

Head and Neck Cancer

Nasopharyngeal Cancer
Clinical Indications for PET Scanning

Non-small Cell Lung Cancer


Small Cell Lung Cancer


Breast Cancer


10. Samson DJ, Flam CR, Pisano ED, Aronson N. Should FDG PET be used to decide whether a patient with an abnormal mammogram or breast finding at physical examination should undergo biopsy? Acad Radiol 2002;9:773-83.


Oesophageal Cancer


Gastric Cancer


Gastrointestinal Stromal Tumour


Hepatocellular Carcinoma


Pancreatic Cancer


Colorectal Cancer


Renal, Transitional Cell and Bladder Cancer

1. Hain SF, Maisey MN. Positron emission tomography for urological tumours. BJU Int 2003;92:159-64.


Prostate Cancer


Ovarian Cancer


4. Chang WC, Hung YC, Kao CH, Yen RF, Shen YY, Lin CC. Usefulness of whole body positron emission tomography (PET) with 18F-fluoro-2-deoxyglucose (FDG) to detect recurrent ovarian cancer based on symptomatically elevated serum levels of tumor marker. Neoplasma 2002;49:329-33.


Cervical Cancer


3. Lin WC, Hng YC, Yeh LS, Kao CH, Yen RF, Shen YY. Usefulness of (18)F-fluorodeoxyglucose positron emission tomography to detect para-aortic lymph nodal metastasis in advanced cervical cancer with negative computed tomography findings. Gynecol Oncol 2003;89:73-6.


Testicular Tumours


4. Spermon JR, De Geus-Oei LF, Klimeney LA, Witjes JA, Oyen WI. The role of 18F-fluoro-2-deoxyglucose positron emission tomography in initial staging and re-staging after chemotherapy for testicular germ cell tumours. BJU Int 2002;89:549-56.


Lymphoma


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Cardiac PET Imaging


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