

IAEA HUMAN HEALTH SERIES No. 45

PET-CT for the Management of Cancer Patients: a Review of the Existing Evidence



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PET–CT FOR THE MANAGEMENT OF CANCER PATIENTS

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IAEA HUMAN HEALTH SERIES No. 45

PET-CT FOR THE MANAGEMENT OF CANCER PATIENTS

A REVIEW OF THE EXISTING EVIDENCE

INTERNATIONAL ATOMIC ENERGY AGENCY VIENNA, 2023

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FOREWORD

The global incidence of cancer is increasing in both developed and developing countries and will become an increasing health burden in the coming decades. This rise in the cancer rate will bring with it challenges for health care systems, clinicians, and patients and their families. Technologies that improve the decision making process and optimize treatment have the potential to benefit society as a whole.

The purpose of this publication, predominantly aimed at policy makers, is to develop a consensus — based on the existing evidence — on the value and the main indications of hybrid imaging using positron emission tomography (PET) combined with computed tomography (CT) in the management of patients affected by cancer. Indeed, PET-CT is considered to be a growing part of the health care landscape due to the rising prevalence of non-communicable diseases, the need for early and accurate diagnostic methods, the technological developments in both hardware and software, the availability of new tracers and its acceptance in emerging markets. Fluorodeoxyglucose (FDG) PET-CT has earned global recognition as a significant tool in the modern management of cancer patients. However, FDG has limitations in its ability to assess several prevalent tumours, such as those produced by prostate cancer. In addition, new therapeutic options available today in the management of cancer have underscored the need to assess tumour characteristics other than metabolism. Therefore, there has been a pressing need for the development and clinical assessment of additional PET radiopharmaceuticals that can enable the imaging and precise characterization of various aspects of a wide range of malignant tumours.

While the use of PET–CT is a standard of care in oncological practice in many developed countries, it is still limited in many low to middle income nations. Based on these considerations, the IAEA recognizes the need to make reliable information widely available to support Member States in the use of PET–CT.

To achieve this goal, the IAEA convened an expert consultant group to review the previous publication, Appropriate Use of FDG PET for the Management of Cancer Patients, IAEA Human Health Series No. 9, in view of the most recent evidence. In the present publication, we focus our attention on highlighting the main indications of FDG and non-FDG radiopharmaceuticals in the management of cancer patients, based on the current clinical evidence.

The recommendations included here to promote the optimal use of PET-CT imaging procedures in oncology considered the most recent developments of PET radiopharmaceuticals. These broad recommendations cannot be applied rigidly to all patients in all clinical settings, but might be considered as a valid basis for tumour board discussions.

The IAEA officer responsible for this publication was F. Giammarile of the Division of Human Health.

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1. INTRODUCTION

1.1. BACKGROUND

A multidisciplinary approach to cancer management is increasingly required to provide personalized evidence based patient care. Appropriateness is a guiding principle to justify any new health care intervention: from the use of new drugs or new treatment modalities to the implementation of new diagnostic procedures. The concept of appropriateness, with a decision aid for its assessment, provides clinicians and policy makers with a tool to determine which diagnostic investigations and therapies ought to be implemented.

Appropriateness of diagnostic investigations has been defined in terms of clinical utility and may also be used to assist in the allocation of limited resources in health care. There is, however, a definite risk that new interventions will be underutilized because they are viewed by policy makers as inappropriate or inappropriately expensive. This could be due to a narrow interpretation of appropriateness that is based solely on the cost of the intervention, isolated from the potential cost savings derived from its use. Therefore, there might be a series of interventions, services and health services of proven effectiveness that are widely underutilized, whose necessary implementation requires, at least in the short and medium terms, an increase in costs.

Policy makers need to accept that the main aim of appropriateness is not cost reduction, but rather optimization of health resource allocation, recognizing the unfavourable consequences of failure to implement innovations of proven effectiveness. It is only through acceptance of this perspective that innovations of proven effectiveness will be introduced for the benefit of both individuals and society.

In nuclear medicine, positron emission tomography (PET) technology has emerged as an integral part of patient management in oncology and is now the standard of care for most tumour types. While not a new concept, in recent years theranostics, the combination of diagnostic and therapy using similar molecules, has enjoyed a revival. This is largely owing to the integration of new PET tracers with radionuclide agents for therapy [1–4].

1.2. OBJECTIVE

The purpose of this publication is to revise and update previous guidelines through consensus based on current evidence, in order to make health care providers and policy makers aware of the value and the recommended use of positron emission tomography combined with computed tomography (PET–CT) in the management of cancer patients [5]. Guidance provided here, describing good practices, represents expert opinion but does not constitute recommendations made on the basis of a consensus of Member States.

1.3. SCOPE

This publication provides a good overview of all the common indications of PET–CT in clinical oncology. It is hoped that this publication will be beneficial to medical professionals from IAEA Member States for learning and teaching purposes.

1.4. STRUCTURE

Indications for the use of PET–CT in the management of multiple cancers are outlined in Section 2 and presented in more detail in subsequent sections. Several possible indications are considered for each type of cancer, with recommendations given for each indication in Section 3.

2. CLINICAL SCENARIOS FOR PET-CT INDICATIONS

2.1. SEARCH STRATEGY

A search of the available scientific publications was initially confined to systematic reviews on the use of PET–CT in oncology published prior to 2009 for Human Health Series No. 9 [5]. This version will incorporate additional literature relevant to recent improvements in the availability of newer PET radiopharmaceuticals and updated indications for 2-fluoro-2-deoxy-D-glucose (FDG) PET [4].

2.2. LIST OF INCLUDED RADIOPHARMACEUTICALS

2.2.1. Acetate: [¹¹C]acetate

Acetate is integrated into the intracellular phosphatidylcholine membrane microdomains (dominant pathway in cancer cells).

2.2.2. Choline: [¹¹C]choline chloride, [¹⁸F]fluoroethylcholine or [¹⁸F]fluoromethylcholine

Choline is an important component of phospholipids in cell membranes. Tissues with increased cell turnover frequently exhibit increased uptake of choline.

2.2.3. Somatostatin analogues such as [⁶⁸Ga]DOTA-NOC, -TOC or -TATE

Synthetic somatostatin peptides with a long biological half-life display high specific affinity for somatostatin receptors expressed on the cellular surface of neuroendocrine tumours.

2.2.4. FDOPA: 6-[¹⁸F]fluoro-L-DOPA

The fate of radiolabelled fluoro-l-dihydroxyphenylalanine (FDOPA) mirrors all stages of native dihydroxyphenylalanine (DOPA) transport, storage and metabolism.

2.2.5. FDG: [¹⁸F]fluorodeoxyglucose

Uptake of the glucose analogue FDG is closely correlated with cancer metabolism and proliferation rate.

2.2.6. FES: [¹⁸F]fluoroestradiol

FES binds to the oestrogen receptors on the tumour cell surface as well as intratumoural receptors in oestrogen receptor positive tumours

2.2.7. FET: [¹⁸F]fluoroethyltyrosine

FET is a radiolabelled amino acid but is not incorporated into proteins and remains trapped in cells after uptake. Certain tumour subtypes exhibit high uptake of FET.

2.2.8. Fluoride: [¹⁸F]sodium fluoride

The intensity of deposition of fluoride ions in the bone matrix reflects bone remodelling and blood flow. Note that fluoride PET is not covered in this guideline because its use is universally relevant to all bone seeking tumours.

2.2.9. Methionine: [¹¹C]methionine

Methionine is an essential amino acid involved in angiogenesis and demonstrates high uptake in certain tumour types.

2.2.10. PSMA: [⁶⁸Ga]-ligand for the prostate specific membrane antigen

Prostate specific membrane antigen (PSMA), a tumour associated antigen and type II transmembrane protein, is overexpressed on prostate tumour cells and is avidly bound by this tracer.

2.3. DEFINITIONS

2.3.1. Recommendation criteria for the use of PET

Based on the review of the literature, the use of PET for clinical indications is classified as recommended, potentially recommended, possibly recommended, or not recommended. These criteria are defined as follows.

2.3.1.1. Recommended (all conditions below need to be met)

- (a) There is evidence of improved diagnostic performance (higher sensitivity and specificity) compared with other current techniques.
- (b) The information derived from PET influences clinical practice.
- (c) The information derived from PET has a plausible impact on the patient's outcome, either through adoption of more effective therapeutic strategies or through non-adoption of futile, ineffective or harmful practices.

2.3.1.2. Potentially recommended (potentially useful)

There is evidence of improved diagnostic performance (greater sensitivity and specificity) compared with other current techniques, but evidence of an impact on treatment and outcome is lacking.

2.3.1.3. Possibly recommended (appropriateness not yet documented)

There is insufficient evidence for assessment, although there is a strong rationale for an expected clinical benefit from PET.

2.3.1.4. Not recommended

Improved accuracy of tumour staging will not alter management, or the performance of PET is poorer than that of other current techniques.

2.3.2. Indications for PET

Different indications for PET are considered here:

- (a) Diagnosis;
- (b) Staging;
- (c) Monitoring response to multimodality therapy;
- (d) Detection/restaging of suspected recurrence;
- (e) Follow-up (i.e. planned at regular intervals post-treatment in the absence of any signs/symptoms);
- (f) Radiotherapy planning.

When relevant, refinements to these definitions are made in the respective tumour type sections [4].

2.4. SUMMARY OF RESULTS

While only cancer types for which PET has an established role have been included in this publication, it is not intended to be exhaustive in covering all possible pathologies in which PET may add value to management. Cancers in the following organ systems have been considered [3]:

- (a) Central nervous system:
 - (i) Primary tumours of the central nervous system.
- (b) Head and neck:
 - (i) Head and neck cancer.
- (c) Thoracic:
 - (i) Non-small cell lung cancer;
 - (ii) Small cell lung cancer;
 - (iii) Mesothelioma.

- (d) Breast:
 - (i) Breast cancer.
- (e) Gastrointestinal:
 - (i) Oesophageal cancer;
 - (ii) Gastric cancer;
 - (iii) Colorectal cancer;
 - (iv) Anal cancer;
 - (v) Pancreatic adenocarcinoma;
 - (vi) Hepatocellular carcinoma;
 - (vii) Cholangio- and gall bladder carcinomas.
- (f) Genitourinary:
 - (i) Renal cancer;
 - (ii) Urothelial and bladder cancers;
 - (iii) Germinal cancer;
 - (iv) Prostate cancer.
- (g) Gynaecological:
 - (i) Ovarian cancer;
 - (ii) Endometrial cancer;
 - (iii) Cervical cancer;
 - (iv) Vulvar cancer.
- (h) Bone and soft tissue:
 - (i) Bone and soft tissue sarcomas.
- (i) Cutaneous:
 - (i) Melanoma.
- (j) Haematological:
 - (i) Lymphomas;
 - (ii) Myeloma.
- (k) Endocrine:
 - (i) Thyroid cancer;
 - (ii) Adrenal cancer.
- (l) Neuroendocrine:
 - (i) Bronchial carcinoid;
 - (ii) Gastroenteropancreatic neuroendocrine tumours (GEP-NETs);
 - (iii) Paraganglioma, pheochromocytoma and neuroblastoma;
 - (iv) Medullary thyroid carcinoma.
- (m) Unknown primary:
 - (i) Cancer of unknown primary.

Table 1 summarizes the current evidence for PET in the conditions and indications covered by this publication. Recommendations in several cases refer to radiotracers other than FDG. For full details see the relevant sections.

TABLE 1. INDICATIC	ONS FOR PET						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Primary tumours of the	Recommended						
	Potentially recommended				>		
	Possibly recommended			>			>
	Not recommended	>	>		>	>	
Head and neck cancer	Recommended			>	>		>
	Potentially recommended		>				
	Possibly recommended						
	Not recommended	>				>	

TABLE 1. INDICATIO	ONS FOR PET (cont.	Ć.					
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Non-small cell lung	Recommended	>	>	>	>		
	Potentially recommended						>
	Possibly recommended						
	Not recommended					>	
Small cell lung cancer	Recommended	>					
	Potentially recommended						
	Possibly recommended		>				>
	Not recommended			>	>	>	

TABLE 1. INDICATIONS FOR PET (cont.)

IABLE I. INDICATIC	NNS FUK PET (CONL)						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Mesothelioma	Recommended						
	Potentially recommended						
	Possibly recommended		>	>			>
	Not recommended	>			>	>	
Breast cancer	Recommended						
	Potentially recommended		>		>		
	Possibly recommended			>			
	Not recommended					>	>

TABLE 1. INDICATIC	ONS FOR PET (cont.)						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Oesophageal cancer	Recommended		>	>	>		
	Potentially recommended						>
	Possibly recommended						
	Not recommended	>				>	
Gastric cancer	Recommended						
	Potentially recommended						
	Possibly recommended		>	>			
	Not recommended	>			>	>	>

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TABLE 1. INDICATIO	NS FOR PET (cont.)						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Colorectal cancer	Recommended				>		
	Potentially recommended						
	Possibly recommended		>	>		>	>
	Not recommended	>					
Anal cancer	Recommended				>		>
	Potentially recommended		>				
	Possibly recommended						
	Not recommended	>				>	

TABLE 1. INDICATIC	ONS FOR PET (cont.)						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Pancreatic adenocarcinoma	a Recommended						
	Potentially recommended				>		
	Possibly recommended		>	>			>
	Not recommended	>				>	
Hepatocellular carcinoma	Recommended						
	Potentially recommended						
	Possibly recommended	>		>			
	Not recommended		>		~	>	>

TABLE 1. INDICATIO	ONS FOR PET (cont.	(
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Cholangio- and gall bladder carcinomas	Recommended						
	Potentially recommended						
	Possibly recommended		>				
	Not recommended	>		>	>	>	>
Urothelial and bladder	Recommended						
CallCels	Potentially recommended						
	Possibly recommended		>	>	>		
	Not recommended	>				>	>

TABLE 1. INDICATIC	NNS FOR PET (cont.)						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Germinal tumours	Recommended			>			
	Potentially recommended						
	Possibly recommended				>		
	Not recommended	>	>			>	>
Prostate cancer	Recommended				>		
	Potentially recommended		>				
	Possibly recommended			>			
	Not recommended	>				>	>

TABLE 1. INDICATIC	NS FOR PET (cont.)						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Ovarian cancer	Recommended				>		
	Potentially recommended						
	Possibly recommended		>	>			
	Not recommended	>				>	>
Endometrial cancer	Recommended						
	Potentially recommended		>		>		
	Possibly recommended						
	Not recommended	~		>		>	>

TABLE 1. INDICATIC	ONS FOR PET (cont.)						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Cervical cancer	Recommended		>	>	>		>
	Potentially recommended						
	Possibly recommended						
	Not recommended	>			>	>	
Vulvar cancer	Recommended						
	Potentially recommended		>		>		
	Possibly recommended						
	Not recommended	>		>		>	>

TABLE 1. INDICATIO	INS FOR PET (cont.						
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Bone and soft tissue	Recommended						
	Potentially recommended			>	>		
	Possibly recommended	>	>				
	Not recommended					>	>
Lymphoma	Recommended		>	>	>		
	Potentially recommended						
	Possibly recommended	>					>
	Not recommended					>	

TABLE 1. INDICATIC	ONS FOR PET (cont.	<u> </u>					
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Melanoma ^b	Recommended						
	Potentially recommended		>	>	>		
	Possibly recommended					>	
	Not recommended						>
Myeloma	Recommended						
	Potentially recommended	>	>	>	>		
	Possibly recommended						
	Not recommended					>	>

TABLE 1. INDICATIC	ONS FOR PET (cont.	~					
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Thyroid cancer	Recommended				>		
	Potentially recommended						
	Possibly recommended		>				
	Not recommended	>		>		>	>
Adrenocortical cancer	Recommended						
	Potentially recommended						
	Possibly recommended		>	>	>		
	Not recommended	>				>	>

TABLE 1. INDICATIC	INS FOR PET (cont.	 					
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Bronchial carcinoid	Recommended					>	
	Potentially recommended	>					
	Possibly recommended		>	>	>		
	Not recommended	>					>
Gastrointestinal and	Recommended		>		>	>	
participants (OLD) neuroendocrine tumour (NET)	Potentially recommended	>		>			
	Possibly recommended						
	Not recommended						>
TABLE 1. INDICATIO	ONS FOR PET (cont.)	(
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Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
Paraganglioma, nheochromocytoma and	Recommended		>	>			
processiona and neuroblastoma	Potentially recommended					>	
	Possibly recommended	>			>		
	Not recommended			>			>
Medullary thyroid carcinoma	Recommended						
	Potentially recommended						
	Possibly recommended				>		
	Not recommended	>	>	>		>	>
Cancer of unknown primary	Recommended	>					

		(
Type of cancer	Recommendation	Diagnosis	Staging	Response evaluation	Recurrence	Follow-up	RT planning
	Potentially recommended						
	Possibly recommended		>	>	>		
	Not recommended					>	>
^a In diagnosis tha indi	insticn is only valid for an	oluation of the co	litery nulmone	elula Modula			

TABLE 1. INDICATIONS FOR PET (cont.)

In diagnosis, the indication is only valid for evaluation of the solitary pulmonary nodule. Not recommended in low risk patients.

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3. PRIMARY TUMOURS OF THE CENTRAL NERVOUS SYSTEM

Useful PET tracers for central nervous system tumours include FDG and amino acid tracers such as acetate, methionine, FET and DOPA. Amino acid tracers are preferable because their distribution is characterized by lower background activity in the brain. Final choice of the tracer depends on local availability [6].

3.1. DIAGNOSIS

Recommendation: Not recommended

There is insufficient evidence for the use of PET in this indication. In addition, the correlation between PET tracer uptake and tumour grade is insufficient to support a role for PET in tumour grading [6].

3.2. STAGING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication. Magnetic resonance imaging (MRI) provides excellent anatomic definition to determine the local extent of the tumour [6] and distant metastases from primary central nervous system tumours are exceedingly rare.

3.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

Although a strong rationale exists for this indication, there are few reports regarding the use of PET tracers to assess tumour response to multimodality therapy [7].

3.4. RECURRENCE

3.4.1. Suspected recurrence

Recommendation: Possibly recommended

PET may provide additional information to that provided by MRI or CT for the detection of recurrence following resection or radiotherapy and may identify the region most likely to yield a representative biopsy.

3.4.2. Confirmed recurrence

Recommendation: Not recommended

There is generally no requirement to further define the tumour using PET when recurrence has been confirmed by other imaging modalities.

3.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for PET. MRI is adequate for this indication [8].

3.6. RADIATION THERAPY PLANNING

Recommendation: Possibly recommended

PET currently has no role in defining radiation fields or doses. However, there is a rationale for using PET for dose escalation to the metabolically intense region within the tumour [8].

Note: For central nervous system lymphoma, see the discussion on lymphomas in Section 26.

4. HEAD AND NECK CANCERS

The following discussion does not include thyroid cancer, which is considered in Section 28.

4.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication. The diagnosis of primary head and neck cancers is based on clinical examination, endoscopy with biopsies and imaging with CT, MRI and/or ultrasound. See Section 34 for cervical lymph node metastasis of tumours from unknown origin [9].

4.2. STAGING

Recommendation: Potentially recommended

Use of CT or MRI remains the standard of care for tumoural and nodal staging in this setting. FDG PET is accurate in detecting regional nodal disease, distant metastases and synchronous tumours [6].

4.3. RESPONSE EVALUATION

Recommendation: Recommended

If performed at least 12 weeks after multimodality treatment, FDG PET is accurate in detecting residual disease. If performed earlier, false positive results due to inflammatory changes are possible. Persistently enlarged FDG negative lymph nodes require close clinical monitoring [6].

4.4. RECURRENCE

Recommendation: Recommended

Since scarring with distortion of tissue structures following surgery and radiation therapy may limit the diagnostic performance of anatomic imaging techniques, the use of FDG PET in both suspected and confirmed recurrence is recommended [6].

4.5. FOLLOW-UP

Recommendation: Not recommended

There is insufficient evidence that FDG PET is useful in asymptomatic patients after presumed complete remission [6].

4.6. RADIATION THERAPY PLANNING

Recommendation: Recommended

Data demonstrate that target volumes and doses may be modified on the basis of FDG PET findings. FDG PET is helpful for the inclusion or exclusion of lymph nodes in the radiation field, although no data on patient outcome are available [10].

5. NON-SMALL CELL LUNG CANCER (NSCLC)

5.1. DIAGNOSIS (CHARACTERIZATION OF SOLITARY PULMONARY NODULES)

Recommendation: Recommended

Solitary pulmonary nodules (SPNs) are common and present a diagnostic challenge, particularly in persons with chronic pulmonary disease or any other condition where biopsy may be risky. FDG PET may be used to stratify SPNs 1 cm or larger as being of high or low risk for malignancy. SPNs with high FDG uptake ought to be considered malignant until proven otherwise, whereas lesions with low or no uptake ought to be considered for surveillance using CT scanning. The use of PET for characterization of SPNs is cost effective [11].

5.2. STAGING

Recommendation: Recommended

The use of FDG PET represents the standard of care for staging non-small cell lung cancer (NSCLC), with meta-analyses indicating a higher sensitivity and specificity for PET than for CT scanning. PET is especially valuable in the detection of mediastinal lymph node metastases that are equivocal or negative on CT. In this context, the role of FDG PET is in identifying nodal lesions requiring biopsy for confirmation [12]. Brain metastases are not detected adequately using FDG PET.

5.3. RESPONSE EVALUATION

Recommendation: Recommended

After multimodality treatment, FDG PET response may be used to select candidates for subsequent potentially life extending therapies. Survival following multimodality treatment is strongly predicted by FDG PET, with improved survival in patients whose tumours show no uptake on post-treatment PET. This predictive value is much greater than that based on CT response [13].

5.4. RECURRENCE

Recommendation: Recommended

The value of FDG PET in proven or suspected recurrence has been confirmed, allowing the selection of appropriate therapy [13].

5.5. FOLLOW-UP

Recommendation: Not recommended

While recurrence can probably be detected earlier by PET than by clinical examination or by other imaging modalities, there is no evidence that patient management or survival would be affected [14].

5.6. RADIATION THERAPY PLANNING

Recommendation: Potentially recommended

The information provided by FDG PET alters the size of radiation therapy treatment fields in over one third of the cases. In most cases, the field size is increased to incorporate FDG positive areas, while in some cases the field size is reduced to avoid unnecessary radiation to adjacent normal tissues, especially in the proximity of critical anatomical structures [14].

6. SMALL CELL LUNG CANCER (SCLC)

6.1. DIAGNOSIS

Recommendation: Recommended

See Section 5.1, as well as Ref. [11].

6.2. STAGING

Recommendation: Possibly recommended

Management of SCLC is based on staging derived predominantly from CT findings, although FDG PET may be used to confirm limited stage disease. MRI or CT ought to be used to assess metastasis to the brain [15].

6.3. RESPONSE EVALUATION

Recommendation: Not recommended

As SCLC shrinks rapidly in response to effective treatment, it is unlikely that FDG PET would contribute significantly to the assessment of treatment response [16].

6.4. SUSPECTED RECURRENCE

Recommendation: Not recommended

The high FDG uptake of SCLC suggests that PET is a sensitive tool for identifying recurrence, although there is no evidence that PET in this context would alter clinical management [17].

6.5. FOLLOW-UP

Recommendation: Not recommended

Recurrence of SCLC is considered not to be amenable to potentially curative treatments, with CT providing adequate detection of recurrence [17].

6.6. RADIATION THERAPY PLANNING

Recommendation: Possibly recommended

It is likely that FDG PET would have the same benefit for SCLC as has been demonstrated for NSCLC, resulting in a modification of the radiation therapy field definition in a high proportion of cases [16].

7. MESOTHELIOMA

7.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication, as diagnosis is based on pleural biopsies [18].

7.2. STAGING

Recommendation: Possibly recommended

Staging of patients with malignant pleural mesothelioma is to assess whether they are candidates for surgical resection. Contrast enhanced CT of the chest and abdomen is the standard for imaging for this purpose. Nonetheless, FDG PET–CT may be useful in identifying distant metastases. When utilized, PET ought to be performed prior to pleurodesis [18].

7.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

FDG PET may play a role in assessing response to multimodality therapy [19]. Its utility following talc pleurodesis, however, is limited.

7.4. RECURRENCE

Recommendation: Not recommended

Although the high FDG uptake suggests that PET is a sensitive tool for identifying recurrence, there is no evidence that FDG PET alters clinical management [18].

7.5. FOLLOW-UP

Recommendation: Not recommended

Recurrence is considered not to be amenable to potentially curative treatments, with CT providing adequate detection of recurrence [20].

7.6. RADIATION THERAPY PLANNING

Recommendation: Possibly recommended

There are several reports that FDG PET influences target volume delineation in intensity modulated radiation therapy [21].

8. BREAST CANCER

8.1. DIAGNOSIS

Recommendation: Not recommended

The uptake of FDG in primary breast cancers is related to tumour size, histology and grade. Multiple prospective studies have shown a low sensitivity (25%) for primary tumours 1 cm or smaller in diameter. There is good correlation between FES uptake and oestrogen receptor expression [22].

8.2. STAGING

Recommendation: Potentially recommended

FDG PET allows the detection of extra-axillary nodes and distant metastases with higher sensitivity than other diagnostic imaging methods. An exception is brain metastases, where MRI is the method of choice. The relative role of bone scans using ^{99m}Tc labelled compounds or FDG PET in the detection of bone metastases remains undefined. Nevertheless, bone metastases from breast cancer tend to be osteolytic, and such lesions are known to be detected by FDG PET with higher sensitivity than sclerotic bone metastases. The negative predictive

value of FDG PET is too low to stage the axilla reliably, as micrometastases may be missed. FDG PET cannot replace sentinel node biopsy [23]. The sensitivity of FDG PET may be suboptimal in lobular carcinoma [24].

8.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

FDG PET is most helpful when the results of standard imaging are equivocal or suspicious [25].

8.4. RECURRENCE

Recommendation: Potentially recommended

Due to its high sensitivity for distant metastases, particularly lymph node and skeletal metastases, FDG PET is helpful in establishing the extent of recurrent disease. There is a role for FDG PET in the detection of suspected recurrence, especially in patients with rising tumour associated markers. So far, however, prospective trials that also address the issues of management changes, outcome and cost efficiency are lacking [25].

8.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG or FES PET in this indication, including patients on long term therapy [22].

8.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [22].

9. OESOPHAGEAL CANCER

9.1. DIAGNOSIS

Recommendation: Not recommended

There is currently no evidence that the addition of FDG PET improves the diagnostic accuracy of endoscopic ultrasound and biopsy [26].

9.2. STAGING

Recommendation: Recommended

FDG PET is the imaging modality of choice for pre-therapy assessment of disease, especially when the presence of metastatic disease is unknown. In this context, PET may be especially valuable in preventing futile surgery or guiding multimodality therapy [27].

9.3. RESPONSE EVALUATION

Recommendation: Recommended

FDG PET identifies locoregional disease that is unresponsive to neoadjuvant therapy and interval metastases prior to planned surgery. The endoscopic findings ought to be taken into consideration, as oesophagitis may mimic residual disease on PET [28].

9.4. RECURRENCE

Recommendation: Recommended

This recommendation is particularly relevant for lower stage tumours treated with local techniques that have recurred locally and remain amenable to potentially curative locoregional therapy [29].

9.5. FOLLOW-UP

Recommendation: Not recommended

There are no data indicating a role for FDG PET in follow-up of oesophageal cancer [29].

9.6. RADIATION THERAPY PLANNING

Recommendation: Potentially recommended

There is a strong rationale for the use of FDG PET in radiation therapy planning, although clinical outcome data are lacking. Whenever available, 4-D CT, or other motion management methods, ought to be employed to allow better delineation of target volumes [26].

10. GASTRIC CANCER

The following discussion refers to distal gastric cancers. Tumours involving the gastroesophageal junction are generally considered to be distal oesophageal carcinomas.

10.1. DIAGNOSIS

Recommendation: Not recommended

There is currently no evidence that the addition of FDG PET to endoscopy and biopsy improves diagnostic performance. The normal gastric mucosa shows some level of physiological FDG uptake, as do several benign conditions [15].

10.2. STAGING

Recommendation: Possibly recommended

There are limited data on the value of FDG PET in detecting locoregional lymph node and distant metastatic disease [27].

10.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

FDG PET may identify response to neoadjuvant therapy. There are, however, no data to determine the impact of PET on clinical outcome [30].

10.4. RECURRENCE

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [31].

10.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [31].

10.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication. Palliative radiation therapy is targeted at the CT defined mass; curative post-operative radiation therapy (usually associated with chemotherapy) is targeted at the surgical bed. **Note:** FDG PET may have reduced sensitivity in mucinous and diffuse adenocarcinomas [30].

11. COLORECTAL CANCER

11.1. DIAGNOSIS

Recommendation: Not recommended

Any symptoms suggestive of colorectal cancer need to be investigated by endoscopy, with biopsy of suspicious lesions. Incidental focal FDG avid colorectal lesions are associated with a high risk of pre-malignancy or malignancy and ideally ought to be investigated further [32].

11.2. STAGING

Recommendation: Possibly recommended

FDG PET has not shown superiority to CT and/or MRI in T or N staging, or in the evaluation of hepatic metastases [33]. In high risk, therapy naive patients being considered for hepatic resection, FDG PET may be superior to other imaging modalities for the detection of extrahepatic metastases [34]. In the context of recent neoadjuvant therapy, FDG PET–CT is less reliable than CT and MRI.

11.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

FDG PET may be useful in excluding local disease progression in the liver after ablative therapy (superior to CT, complementary to MRI) [35]. In other contexts, FDG PET has little or no additional benefit to CT or MRI assessment [36].

11.4. RECURRENCE

Recommendation: Recommended

FDG PET is valuable in the evaluation of patients with suspected recurrence (e.g. due to elevated carcinoembryonic antigen levels). Evidence suggests that in this context FDG PET is more sensitive than CT [36].

11.5. FOLLOW-UP

Recommendation: Possibly recommended

In patients with contraindications for iodine contrast medium, FDG PET may be considered as an alternative to CT [37].

11.6. RADIATION THERAPY PLANNING

Recommendation: Possibly recommended

In rectal cancer there are limited data to support the use of FDG PET in assisting with the definition of radiation fields.

Note: Although mucinous adenocarcinomas are usually not FDG avid, there is in fact evidence that FDG uptake by rectal cancer is similar in mucinous and nonmucinous histological subtypes [38].

12. ANAL CANCER

12.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [39].

12.2. STAGING

Recommendation: Potentially recommended

In high risk patients, FDG PET is superior to other imaging modalities for detecting locoregional lymph node and distant metastases [39].

12.3. RESPONSE EVALUATION

Recommendation: Recommended

In high risk patients for whom salvage surgery is considered, FDG PET provides a sensitive assessment of response to chemoradiation [39].

12.4. RECURRENCE

Recommendation: Recommended

The exam is required in high risk patients for whom salvage surgery is considered [40].

12.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [41].

12.6. RADIATION THERAPY PLANNING

Recommendation: Recommended

For anal cancer there are data to support the use of FDG PET in assisting with the placement of radiation fields [41].

13. PANCREATIC ADENOCARCINOMA

13.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication: FDG PET cannot replace diagnostic CT and ultrasound with biopsy [42].

13.2. STAGING

Recommendation: Possibly recommended

FDG PET may be recommended for high risk patients who are candidates for therapies with curative intent. For metastatic staging, FDG PET may complement conventional imaging modalities [31].

13.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

There is a rationale for the use of FDG PET for the assessment of response to systemic therapy [43].

13.4. RECURRENCE

Recommendation: Potentially recommended

The degree of FDG avidity may help distinguish recurrence from post-treatment changes [44].

13.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [45].

13.6. RADIATION THERAPY PLANNING

Recommendation: Possibly recommended

FDG PET data may be useful for target volume delineation and dose intensification [45].

14. HEPATOCELLULAR CARCINOMA

14.1. DIAGNOSIS

Recommendation: Possibly recommended

FDG PET alone has no role in diagnosis. Several studies have suggested its usefulness in combination with acetate to detect well differentiated tumours. A similar role has been described for choline [46].

14.2. STAGING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [47].

14.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

Limited data suggest that persistent FDG uptake after chemotherapy is a negative prognostic feature in patients considered for liver transplantation [48].

14.4. RECURRENCE

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [49].

14.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [47].

14.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [47].

15. CHOLANGIO- AND GALLBLADDER CARCINOMAS

15.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET alone in this indication. Several studies have suggested its usefulness in combination with acetate to detect well differentiated tumours. A similar role has been described for choline [50].

15.2. STAGING

Recommendation: Potentially recommended

In limited series, FDG PET is more accurate than CT scanning for identifying extrahepatic lesions in patients being considered for surgical resection [50].

15.3. RESPONSE EVALUATION

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [51].

15.4. RECURRENCE

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [51].

15.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [52].

15.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [52].

16. RENAL CANCER

While FDG PET is sensitive in the detection of extrarenal metastasis in renal cell carcinoma, there is currently insufficient evidence for the value of FDG PET in the management of this cancer [53].

17. UROTHELIAL AND BLADDER CANCERS

17.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [54].

17.2. STAGING

Recommendation: Possibly recommended

FDG PET may be useful in patients with muscle invasive or suspected metastatic bladder cancer. There are no data supporting the use of FDG PET for urethral and ureteral carcinomas, which have a poor detection rate [54].

17.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

FDG PET may be useful for evaluation of patients with invasive bladder cancer following systemic therapy [55].

17.4. RECURRENCE

Recommendation: Possibly recommended

In cases of CT findings that are equivocal for metastatic recurrence, FDG PET may be useful to detect recurrence [55].

17.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [56].

17.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [56].

18. GERMINAL TUMOUR

18.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [57].

18.2. STAGING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication. The negative predictive value is not high enough to avoid adjuvant therapies in the case of negative results [57].

18.3. RESPONSE EVALUATION

Recommendation: Recommended

FDG PET is superior to CT in patients affected by seminoma. Except for mature teratoma, PET can distinguish residual tumour mass >3 cm from necrosis and/or fibrosis [57].

18.4. RECURRENCE

Recommendation: Possibly recommended

In cases of equivocal CT findings and/or elevation of serum tumour markers, FDG PET can be used to detect recurrence [58].

18.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [58].

18.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

Radiation therapy has a minimal role in non-seminomatous germ cell tumours, and there are currently insufficient data to support a role for FDG PET in this indication. For early stage seminomas, for which the patterns of failure are well described, there are no data to suggest that PET may influence radiation fields [57].

19. PROSTATE CANCER

The role of FDG PET in patients with prostate cancer is somewhat limited because of the intrinsically low glucose transporter expression of these tumours, except for poorly differentiated types. Other PET tracers such as PSMA ligands and choline are superior for imaging prostate cancer. When available, PSMA ligands (most notably the PSMA-11 ligand) constitute the tracers of choice in this tumour type [59].

19.1. DIAGNOSIS

Recommendation: Not recommended

There are insufficient data to support a role for PET in this indication. MRI remains the modality of choice after inconclusive biopsy [60].

19.2. STAGING

Recommendation: Potentially recommended

In high risk patients, PET has superior sensitivity for lymph node and distant metastatic disease as compared to CT, MRI and bone scan. For local staging, there are insufficient data to support PET use [61].

19.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

Limited data are available to support a role for PET for this indication [61].

19.4. RECURRENCE

Recommendation: Recommended

The use of PSMA ligand PET for localization of prostate cancer in the setting of biochemical recurrence is especially recommended in patients with low prostate specific antigen (PSA) values (0.2–10 ng/mL) who may be candidates for salvage therapy. For choline PET, PSA values ought to be \geq 1.0 ng/mL [60].

19.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [62].

19.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication. Pelvic MRI remains the modality of choice [63].

19.7. THERANOSTIC PLANNING

Recommendation: Recommended

Documentation of PSMA expression with ⁶⁸Ga-PSMA ligand PET is required prior to treatment with radiolabelled PSMA ligand [64].

20. OVARIAN CANCER

20.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [65].

20.2. STAGING

Recommendation: Possibly recommended

Staging of ovarian cancers is usually performed surgically with the support of conventional imaging. There is limited evidence that FDG PET may be useful in patients with suspected stage IV disease or when indeterminate lymph nodes are identified on conventional imaging [65].

20.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

FDG PET may be used for assessing response in patients with known metastatic disease after multimodality therapy [66].

20.4. RECURRENCE

Recommendation: Recommended

Most studies show that FDG PET is superior to CT and complementary to MRI in patients with suspected recurrence [65].

20.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [65].

20.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication. Radiation therapy has a very limited role in the management of ovarian carcinoma. When used for palliation, radiation therapy is directed at symptomatic masses identified by CT.

Note: Mucinous adenocarcinomas may be non-FDG avid, and PET in this particular subgroup may be less sensitive [65].

21. ENDOMETRIAL CANCER

21.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication. The incidental finding of uterine activity in post-menopausal patients requires further workup to exclude uterine malignancy [67].

21.2. STAGING

Recommendation: Potentially recommended

In advanced disease FDG PET may be recommended to exclude distant metastasis [67].

21.3. RESPONSE EVALUATION

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [67].

21.4. RECURRENCE

Recommendation: Potentially recommended

FDG PET may be used in the workup for patients considered for surgery and/or locoregional therapy [67].

21.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [67].

21.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [68].

22. CERVICAL CANCER

22.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [69].

22.2. STAGING

Recommendation: Recommended

In stage IB–IV cervical cancer, FDG PET is a valuable adjunct to conventional imaging methods, namely CT and MRI. Although MRI is the preferred method for evaluation of local extension, PET is superior for the evaluation of lymph node involvement and sensitive for the detection of distant metastases [69].

22.3. RESPONSE EVALUATION

Recommendation: Recommended

In high risk cervical cancer, FDG PET ought to be performed 3–6 months after the completion of chemoradiation [66].

22.4. RECURRENCE

Recommendation: Recommended

In cervical cancer recurrence, FDG PET is recommended for patients where metastasis is suspected [69].

22.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [70].

22.6. RADIATION THERAPY PLANNING

Recommendation: Recommended

For locally advanced tumours, the detection of metastasis in para-aortic lymph nodes by FDG PET may lead to modification of the treatment fields. This is particularly important in cervical cancer [70].

23. VULVAR CANCER

23.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [71].

23.2. STAGING

Recommendation: Potentially recommended

In advanced disease FDG PET may be used to exclude distant metastasis [71].

23.3. RESPONSE EVALUATION

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [71].

23.4. RECURRENCE

Recommendation: Potentially recommended

FDG PET may be used in the workup for patients considered for salvage surgery and/or locoregional therapy [71].

23.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [71].

23.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [71].

24. BONE AND SOFT TISSUE SARCOMAS

24.1. DIAGNOSIS

Recommendation: Possibly recommended

There are limited data to suggest that FDG PET may direct biopsy to identify malignant transformation in pre-existing benign mesenchymal lesions. Gastrointestinal stromal tumours (GISTs) are usually diagnosed by endoscopy and/or biopsy [72].

24.2. STAGING

Recommendation: Possibly recommended

Sarcomas have a particular propensity for early metastatic spread to the lungs. High resolution CT is more effective than FDG PET for detecting small lung metastases. However, PET may be more useful for detecting extrapulmonary metastases. With GIST patients, a baseline FDG PET may be used to determine tumour avidity for subsequent treatment and response evaluation [73].

24.3. RESPONSE EVALUATION

Recommendation: Potentially recommended

There are data supporting the use of FDG PET to monitor the response to multimodality therapy. In GIST, FDG avid tumours may be assessed for early response (e.g. after two days) to treatment [73].

24.4. RECURRENCE

Recommendation: Potentially recommended

Suspected recurrence will usually require biopsy for confirmation, which can be directed by FDG PET [74].

24.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [74].

24.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication.

25. MELANOMA

25.1. DIAGNOSIS

Recommendation: Not recommended

The diagnosis of melanoma requires biopsy and histopathological examination. FDG PET does not reliably distinguish between benign and malignant pigmented skin lesions [75].

25.2. STAGING

25.2.1. Stages I and II: Low pre-test probability of metastases

Recommendation: Not recommended

FDG PET is less sensitive than sentinel node biopsy for staging regional lymph nodes. In patients with low pre-test probability of distant metastases, the sensitivity of FDG PET for distant metastases has been reported to be low. Very small metastases are common in melanoma and may be beyond the resolution of PET, despite the usually high avidity of these tumours for FDG [76].

25.2.2. Stages I and II: High pre-test probability of metastases

Recommendation: Recommended

In patients with intermediate or high risk of distant metastases (melanoma of the head, neck and trunk, Breslow index >4 mm, ulceration, high mitotic rate), FDG PET is recommended for detecting potentially operable metastases [76].

25.2.3. Stage III or potential stage IV

Recommendation: Potentially recommended

There is a role for FDG PET in assessing locoregional or distant disease to guide appropriate therapy [76].

25.3. RESPONSE EVALUATION

Recommendation: Potentially recommended

Recent data support a role for FDG PET in assessing response to immunotargeted therapy [77].

25.4. RECURRENCE

Recommendation: Potentially recommended

In the case of a suspicious lesion that is not readily amenable to biopsy, high uptake of FDG is strongly suggestive of recurrent melanoma [78].

25.5. FOLLOW-UP

Recommendation: Possibly recommended

FDG PET may be used as an alternative to CT in high risk patients [79].

25.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [75].

Note: Squamous and Merkel cell carcinomas will not be discussed in this publication due to the limited role of FDG PET in their treatment [75].

26. LYMPHOMA

26.1. DIAGNOSIS

Recommendation: Possibly recommended

There is a rationale to support the use of FDG PET for the diagnosis of high grade transformation of low grade lymphoma, including chronic lymphocytic leukaemia and/or small lymphocytic lymphoma [80].
26.2. STAGING

Recommendation: Recommended

FDG PET is the modality of choice for baseline staging but does not necessarily replace the need for contrast enhanced CT. Owing to its superior sensitivity and specificity for most types of lymphomas, FDG PET is recommended for staging of lymphomas known to demonstrate FDG avidity [81]. Bone marrow biopsy is unnecessary in patients with Hodgkin's disease when staged with FDG PET and may be obviated in patients with high grade non-Hodgkin's lymphoma, when positive [82].

26.3. RESPONSE EVALUATION

Recommendation: Recommended

FDG PET is the method of choice for the assessment of response (including interim PET, when performed) in FDG avid lymphomas. FDG PET has prognostic value in patients who are candidates for bone marrow transplant [80].

26.4. RECURRENCE

Recommendation: Recommended

FDG PET is the modality of choice for suspected recurrence [83].

26.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [83].

26.6. RADIATION THERAPY PLANNING

Recommendation: Possibly recommended

There are limited data to support the use of FDG PET for radiation therapy planning in patients treated for Hodgkin's disease and non-Hodgkin's lymphoma [84].

Note: The above recommendations also apply to primary central nervous system lymphomas [7].

27. MYELOMA

27.1. DIAGNOSIS

Recommendation: Potentially recommended

There is a rationale to support the use of FDG PET to distinguish monoclonal gammopathy of uncertain significance, from plasmacytoma, multiple myeloma and smouldering myeloma [85].

27.2. STAGING

Recommendation: Potentially recommended

FDG PET is useful for risk stratification to identify FDG avid medullary and extramedullary disease. FDG PET is also useful for confirming solitary skeletal plasmacytoma [86].

27.3. RESPONSE EVALUATION

Recommendation: Potentially recommended

FDG PET is useful for the assessment of response to therapy. FDG PET has prognostic value in patients who are candidates for bone marrow transplant [85].

27.4. RECURRENCE

Recommendation: Potentially recommended

FDG PET is useful for suspected recurrence [86].

27.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [87].

27.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [88].

28. THYROID CANCER

28.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication. FDG avid incidental nodules need to be evaluated with ultrasound guided fine needle aspiration cytology [89].

28.2. STAGING

Recommendation: Possibly recommended

There is increasing evidence for the use of FDG PET in locally advanced differentiated thyroid cancers. For poorly differentiated or anaplastic cancers, the evidence supporting the use of FDG PET is more established [90].

28.3. RESPONSE EVALUATION

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication, except for poorly differentiated and anaplastic cancers [91].

28.4. RESTAGING AND SUSPECTED RECURRENCE

Recommendation: Recommended

In patients with rising thyroglobulin levels and a negative ¹³¹I iodide whole body scan, FDG PET provides useful data [92].

28.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication, except for poorly differentiated and anaplastic cancers [93].

28.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [94].

29. ADRENOCORTICAL CARCINOMAS

29.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [95].

29.2. STAGING

Recommendation: Possibly recommended

There is evidence for the use of FDG PET in staging adrenocortical carcinomas [95].

29.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

Limited data are available to support a role for FDG PET in this indication [95].

29.4. RECURRENCE

Recommendation: Possibly recommended

In patients with equivocal findings on conventional imaging, FDG PET may be considered in identifying recurrence [95].

29.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [95].

29.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [95].

30. BRONCHIAL CARCINOID

In general, ⁶⁸Ga-DOTA labelled somatostatin analogues are the tracers of choice for bronchial carcinoid. However, in patients with poorly differentiated forms, FDG may also be considered [96].

30.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [97].

30.2. STAGING

Recommendation: Possibly recommended

In suspected advanced stage disease DOTA-SSA PET shows high sensitivity in detecting metastasis [97].

30.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

DOTA-SSA may be used to assess treatment response [97].

30.4. RECURRENCE

Recommendation: Possibly recommended

The high sensitivity of DOTA-SSA allows for the detection of local recurrence and possible metastatic disease [97].

30.5. FOLLOW-UP

Recommendation: Recommended

Due to the long natural history of these tumours, imaging incorporating DOTA-SSA PET is a sensitive means of detecting disease recurrence and/or progression [97].

30.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [97].

30.7. THERANOSTIC PLANNING

Recommendation: Potentially recommended

While there are limited data for the application of peptide receptor radionuclide therapy (PRRT) in bronchial carcinoid, when such therapy is considered, DOTA-SSA PET is an important part of the patient's workup [98].

31. GASTROINTESTINAL AND PANCREATIC NEUROENDOCRINE TUMOURS (GEP-NETs)

In general, ⁶⁸Ga-DOTA labelled somatostatin analogues are the tracers of choice for GEP-NETs (except for insulinoma). FDOPA, when available, is an alternative tracer for these tumours. In poorly differentiated NETs, FDG may be recommended [96].

31.1. DIAGNOSIS

Recommendation: Potentially recommended

In patients in whom there is a high clinical suspicion, DOTA-SSA PET is helpful for identifying disease and assessing surgical resectability [99].

31.2. STAGING

Recommendation: Recommended

DOTA-SSA PET is the most accurate modality for identifying the true extent of disease. MRI imaging of the liver ought to be considered for accurate assessment of intrahepatic disease burden [99].

31.3. RESPONSE EVALUATION

Recommendation: Potentially recommended

DOTA-SSA PET may be used to assess treatment response to somatostatin receptor based therapy [99].

31.4. RECURRENCE

Recommendation: Recommended

The high sensitivity of DOTA-SSA PET allows for the detection of local recurrence and possible metastatic disease [99].

31.5. FOLLOW-UP

Recommendation: Recommended

Due to the long natural history of these tumours, imaging incorporating DOTA-SSA PET is a sensitive means of detecting disease recurrence and/or progression [99].

31.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [99].

31.7. THERANOSTIC PLANNING

Recommendation: Recommended

DOTA-SSA PET is an important part of the patient's workup, as it identifies potentially suitable candidates for PRRT [98].

32. PARAGANGLIOMA, PHAEOCHROMOCYTOMA AND NEUROBLASTOMA

For these neuroectodermal NETs, FDG, FDOPA and DOTA labelled somatostatin analogues may be recommended, depending on the level of differentiation and the clinical context [100].

32.1. DIAGNOSIS

Recommendation: Possibly recommended

In patients in whom there is a high clinical suspicion, PET may be helpful in identifying disease and surgical resectability [101].

32.2. STAGING

Recommendation: Recommended

In suspected advanced stage disease PET shows high sensitivity in detecting metastasis. For neuroblastoma, it should be noted that radioiodinated metaiodobenzylguanidine (mIBG) remains the recommended tracer [101].

32.3. RESPONSE EVALUATION

Recommendation: Recommended

PET is used to assess treatment response. For mIBG avid neuroblastoma, see the note above [101].

32.4. RECURRENCE

Recommendation: Possibly recommended

The high sensitivity of PET allows for the detection of local recurrence and possible metastatic disease [101].

32.5. FOLLOW-UP

Recommendation: Potentially recommended

There are not sufficient data to support this application outside of neuroblastoma [101].

32.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [101].

32.7. THERANOSTIC PLANNING

Recommendation: Potentially recommended

While there are limited data for the application of PRRT in these diseases, when such therapy is considered, PET, using the corresponding theranostic agent, is an important part of the patient's workup [102].

33. MEDULLARY THYROID CARCINOMA

For medullary thyroid carcinoma, FDG and DOPA are utilized, depending on the clinical context [103].

33.1. DIAGNOSIS

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [104].

33.2. STAGING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [104].

33.3. RESPONSE EVALUATION

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [104].

33.4. RECURRENCE

Recommendation: Possibly recommended

While CT, MRI and ultrasound remain the modalities of choice for identifying the site(s) of recurrence, PET has potential utility in patients with rising calcitonin or carcinoembryonic antigen levels [104].

33.5. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [104].

33.6. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for PET in this indication [104].

34. CANCER OF UNKNOWN PRIMARY

For neuroendocrine tumours of unknown origin, depending on the level of differentiation, either FDG, DOTA-SSA or FDOPA may be recommended.

34.1. DIAGNOSIS

34.1.1. Cervical adenopathy with occult primary

Recommendation: Recommended

FDG PET has a primary tumour detection rate of approximately 31–58% when other tests fail to identify a primary [9].

34.1.2. Other metastases of unknown origin

Recommendation: Possibly recommended

For raised tumour markers, paraneoplastic syndromes and metastases outside the neck, FDG PET may be used if the conventional workup has failed to identify the primary tumour [105].

34.2. STAGING

Recommendation: Possibly recommended

FDG PET may be recommended for evaluation of the extent of disease [106].

34.3. RESPONSE EVALUATION

Recommendation: Possibly recommended

FDG PET may be recommended for evaluation of treatment response where clinically relevant [107].

34.4. FOLLOW-UP

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [107].

34.5. RADIATION THERAPY PLANNING

Recommendation: Not recommended

There are currently insufficient data to support a role for FDG PET in this indication [107].

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ABBREVIATIONS

CT	computed tomography
DOPA	dihydroxyphenylalanine
DOTA	dodecane tetra-acetic acid
FDG	fluorodeoxyglucose
FDOPA	fluoro-l-dihydroxyphenylalanine
FES	fluoroestradiol
FET	fluoroethyltyrosine
GEP-NET	gastroenteropancreatic neuroendocrine tumours
MRI	magnetic resonance imaging
NET	neuroendocrine tumour
NSCLC	non-small cell lung carcinoma
PET	positron emission tomography
PRRT	peptide receptor radionuclide therapy
PSMA	prostate specific membrane antigen
SCLC	small cell lung carcinoma
SSA	somatostatin analogue

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While the use of positron emission tomography-computed tomography (PET-CT) is a standard of care in oncological practice in many developed countries, it is still limited in many low to middle income nations. To make reliable information more widely available, the IAEA convened an expert consultant group to review, based on the most recent developments of PET radiopharmaceuticals, the appropriate use of FDG-PET for the management of cancer patients. The resulting publication provides up to date recommendations on the optimal use of PET-CT imaging procedures in oncology. It is written for policy makers and decision makers who allocate resources dedicated to the healthcare system, a critical issue in the development of nuclear medicine in low and middle income countries. It will also benefit medical imaging practitioners as well as referring physicians.

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