www.rcr.ac.uk

Evidence-based indications for the use of PET-CT in the United Kingdom 2022

July 2022

Contents

Foreword

These guidelines mark the 30th anniversary of clinical positron emission tomography (PET) in the UK.

Since its introduction into the UK clinical practice in 1992 by Professor Michael Maisey, PET, followed by positron emission tomography-computed tomography (PET-CT), has become a key multimodality molecular imaging technique in the assessment of a wide range of medical conditions.

The Inter-Collegiate Standing Committee on Nuclear Medicine (ICSCNM) supported the development of PET-CT in the UK through several initiatives including the 2003 document, *'Positron emission tomography – A strategy for provision in the UK'* and the 2005 document *'PET-CT in the UK: A strategy for development and integration of a leading edge technology within routine clinical practice'*.

The publication of the first version of '*Evidence-based indications for the use of PET-CT in the United Kingdom*' in 2012 and its third edition in 2016, authored by Sally Barrington and Andrew Scarsbrook, provided a guide for the use of PET-CT in clinical practice and the evidence base on which this was founded. The first version was used to inform the commissioning of PET-CT services in the UK and beyond. Now in its fourth edition, the 2022 document provides updated indications with key references underpinning the use of fluorodeoxyglucose (FDG) and non-FDG PET-CT tracers in malignant and non-malignant diseases in clinical practice.

The ICSCNM wishes to thank the multidisciplinary team of nuclear medicine (NM) physicians, radionuclide radiologists and oncologists for updating this invaluable reference guide.

Sabina Dizdarevic,

Chair of the Intercollegiate Standing Committee on Nuclear Medicine (ICSCNM)

Preface

A document prepared for the Intercollegiate Standing Committee on Nuclear Medicine, by members of The Royal College of Radiologists and the Royal College of Physicians.

Lead authors (for current edition):

Sabina Dizdarevic, Andrew Scarsbrook, Sally Barrington.

List of co-authors and contributors (for current edition) *:

Asim Afaq, Parthiban Arumugam, Tara Barwick, Clare Beadsmoore, Lorenzo Biassoni, Jamshed Bomanji, John Buscombe, Amarnath Challapalli, Greg Chambers, Gary Cook, Stephen Daw, Amy Eccles, Sameer Gangoli, Gopinath Gnanasegaran, Deepa Gopalan, Richard Graham, Prasad Guntur, Sai Han, Athar Haroon, Iain Lyburn, Sergejs Magers, Vanessa Morris, Shaunak Navalkissoor, Bob Philips, Eliana Reyes, Rebecca Roylance, Ananth Shankar, Nitasha Singh, Teresa Szyszko, Sharlini Varatharajah, Sobhan Vinjamuri, Stefan Vöö, Kshama Wechalekar, Zarni Win, Wai Lup Wong, Lyn Zimmo.

These guidelines comprise an up-to-date summary of relevant indications for the use of PET-CT, where there is good evidence that patients will benefit from improved disease assessment resulting in altered management and improved outcomes. This document supersedes the previous '*Evidence-based indications for the use of PET-CT in the United Kingdom*' guidelines published by The Royal College of Radiologists in 2016.

The document will be updated at regular intervals.

The indications are divided into oncological and non-oncological applications then body area/system. This list is not exhaustive and there are cases where PET-CT may be helpful in patients who have equivocal or definite abnormalities on other imaging where PET-CT may alter the management strategy if found to be 'positive' or 'negative'; for example, radical or high-risk surgery. PET-CT would be appropriate in such patients at the discretion of the local Administration of Radioactive Substances Advisory Committee (ARSAC) licence holder as a problem-solving tool when other imaging modalities have been inconclusive.

General references

1. Hillner BE, Siegel BA, Liu D et al. Impact of Positron Emission Tomography/Computed Tomography and Positron Emission Tomography (PET) Alone on Expected Management of Patients with Cancer: Initial Results From the National Oncologic PET Registry. *J Clin Oncol 2008*; **26**: 2155–2161.
2. Royal College of Radiologists (Great Britain). iRefer: Making the best use of clinical radiology. 7th ed. The Royal College of Radiologists: London, 2017.
3. U.S. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) - Positron Emission Tomography (PET) Scans. *https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=211* (accessed 2021-11-22).
4. Lynch C, Reguilon I, Langer DL et al. A comparative analysis: international variation in PET-CT service provision in oncology-an International Cancer Benchmarking Partnership study. *Int J Qual Health Care* 2021; **33**: mzaa166.

* For a more detailed list of authors and contributors, please refer to appendix 'Authors and contributors' on page 74.

1 Indications for 2-[^{18}F]fluoro-2-deoxy-D-glucose ([^{18}F]FDG) PET-CT

Oncological applications

Brain[a]

- Assist in decision-making and target selection for biopsy by identifying the grade of malignancy where there is uncertainty on anatomical imaging.[1,2]
- Suspected relapse where magnetic resonance imaging (MRI) is equivocal to inform decisions regarding surgery or radiotherapy planning.[3]
  See below for alternative PET imaging with ^{11}C-methionine or [^{18}F]fluoroethyltyrosine (FET).
- Assessment of suspected high-grade transformation in low-grade glioma.[1,4]
- To differentiate recurrent glioma from post-treatment effects when MRI is unhelpful.[1,4,5]
- Differentiation between glioma and primary central nervous system lymphoma limited to the brain in combination with MRI in highly selected cases.[4]
- Differentiation of cerebral tumour from atypical infection in immuno-compromised patients with indeterminate lesions on MRI/CT.[6]

References

1. Chen W. Clinical applications of PET in brain tumors. *J Nucl Med* 2007; **48**: 1468–1481.
2. Hillner BE, Siegel BA, Shields AF et al. Impact of dedicated brain PET on intended patient management in participants of the national oncologic PET Registry. *Mol Imaging Biol* 2011; **13**: 161–165.
3. Van Laere K, Ceyssens S, Van Calenbergh F et al. Direct comparison of 18F-FDG and 11C-methionine PET in suspected recurrence of glioma: sensitivity, inter-observer variability and prognostic value. *Eur J Nucl Med Mol Imaging* 2005; **32**: 39–51.
4. Quartuccio N, Laudicella R, Vento A et al. The Additional Value of 18F-FDG PET and MRI in Patients with Glioma: A Review of the Literature from 2015 to 2020. *Diagnostics (Basel) 2020*; **10**: E357.
5. Gómez-Río M, Rodríguez-Fernández A, Ramos-Font C, López-Ramírez E, Llamas-Elvira JM. Diagnostic accuracy of 201Thallium-SPECT and 18F-FDG-PET in the clinical assessment of glioma recurrence. *Eur J Nucl Med Mol Imaging 2008*; **35**: 966–975.
6. O'Doherty MJ, Barrington SF, Campbell M, Lowe J, Bradbeer CS. PET scanning and the human immunodeficiency virus-positive patient. *J Nucl Med* 1997; **38**: 1575–1583.

a Emerging evidence for use of [^{18}F]FDG PET in prognostication of treatment response in primary glioma including predicting MGMT (O6-methyl-guanine-DNA methyltransferase) promoter methylation status as described in 'Kong Z, Lin Y, Jiang C et al. ^{18}F-FDG-PET-based Radiomics signature predicts MGMT promoter methylation status in primary diffuse glioma. *Cancer Imaging* 2019; **19**: 58'.

Head and neck tumours

- Staging of patients where staging is difficult clinically; for example, where there is uncertainty on other imaging or equivocal findings that would preclude radical treatment.[1-8]
- 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 nasophayngeal and hypopharyngeal cancer.[3-10]
- To identify the primary site in patients presenting with metastatic squamous cell carcinoma in cervical lymph nodes, with no primary site identified on other imaging.[7,11,12]
- Response assessment three to six months' post chemoradiotherapy in head and neck cancer with advanced locoregional or metastatic disease.[7,8,13-17 a]
- To differentiate relapse from treatment effects in patients suspected to have tumour recurrence where MRI is uncertain or equivocal.[7,8,13,15–17]

References

1. Rohde M, Dyrvig A-K, Johansen J et al. 18F-fluoro-deoxy-glucose-positron emission tomography/computed tomography in diagnosis of head and neck squamous cell carcinoma: a systematic review and meta-analysis. *Eur J Cancer Oxf Engl* 1990 2014; **50**: 2271–2279.
2. Kim SY, Roh J-L, Yeo N-K et al. Combined 18F-fluorodeoxyglucose-positron emission tomography and computed tomography as a primary screening method for detecting second primary cancers and distant metastases in patients with head and neck cancer. *Ann Oncol Off J Eur Soc Med Oncol* 2007; **18**: 1698–1703.
3. Krabbe CA, Pruim J, van der Laan BFAM, Rödiger LA, Roodenburg JLN. FDG-PET and detection of distant metastases and simultaneous tumors in head and neck squamous cell carcinoma: a comparison with chest radiography and chest CT. *Oral Oncol* 2009; **45**: 234–240.
4. Kubicek GJ, Champ C, Fogh S et al. FDG-PET staging and importance of lymph node SUV in head and neck cancer. *Head Neck Oncol* 2010; **2**: 19.
5. Lonneux M, Hamoir M, Reychler H et al. Positron emission tomography with [18F]fluorodeoxyglucose improves staging and patient management in patients with head and neck squamous cell carcinoma: a multicenter prospective study. *J Clin Oncol Off J Am Soc Clin Oncol* 2010; **28**: 1190–1195.
6. Scott AM, Gunawardana DH, Bartholomeusz D, Ramshaw JE, Lin P. PET changes management and improves prognostic stratification in patients with head and neck cancer: results of a multicenter prospective study. *J Nucl Med Off Publ Soc Nucl Med* 2008; **49**: 1593–1600.
7. The National Institute for Health and Care Excellence. Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. 2016. *https://www.nice.org.uk/guidance/ng36* (accessed 2021-11-22).
8. Wong WL. PET-CT for Staging and Detection of Recurrence of Head and Neck Cancer. *Semin Nucl Med* 2021; **51**: 13–25.
9. Cacicedo J, Fernandez I, Del Hoyo O et al. Should PET/CT be implemented in the routine imaging work-up of locally advanced head and neck squamous cell carcinoma? A prospective analysis. *Eur J Nucl Med Mol Imaging* 2015; **42**: 1378–1389.
10. Senft A, de Bree R, Hoekstra OS et al. Screening for distant metastases in head and neck cancer patients by chest CT or whole body FDG-PET: A prospective multicenter trial. *Radiother Oncol* 2008; **87**: 221–229.

a Baseline PET-CT may be required in this group of patients as chemoradiotherapy is typically used for their treatment.

11. Zhu L, Wang N. 18F-fluorodeoxyglucose positron emission tomography-computed tomography as a diagnostic tool in patients with cervical nodal metastases of unknown primary site: a meta-analysis. *Surg Oncol* 2013; **22**: 190–194.
12. Smith KA, Dort JC, Hall SF, Rudmik L. Cost-effectiveness of positron emission tomography-CT in the evaluation of cancer of unknown primary of the head and neck. *Head Neck* 2015; **37**: 1781–1787.
13. Porceddu SV, Pryor DI, Burmeister E et al. Results of a prospective study of positron emission tomography-directed management of residual nodal abnormalities in node-positive head and neck cancer after definitive radiotherapy with or without systemic therapy. *Head Neck* 2011; **33**: 1675–1682.
14. Yao M, Smith RB, Hoffman HT et al. Clinical significance of postradiotherapy [18F]-fluorodeoxyglucose positron emission tomography imaging in management of head-and-neck cancer-a long-term outcome report. *Int J Radiat Oncol Biol Phys* 2009; **74**: 9–14.
15. Shah K, Te Marvelde L, Collins M et al. Safety and cost analysis of an (18)FDG-PET-CT response based follow-up strategy for head and neck cancers treated with primary radiation or chemoradiation. *Oral Oncol* 2015; **51**: 529–535.
16. Sheikhbahaei S, Taghipour M, Ahmad R et al. Diagnostic Accuracy of Follow-Up FDG PET or PET/CT in Patients With Head and Neck Cancer After Definitive Treatment: A Systematic Review and Meta-Analysis. *AJR Am J Roentgenol* 2015; **205**: 629–639.
17. Mehanna H, Wong W-L, McConkey CC et al. PET-CT Surveillance versus Neck Dissection in Advanced Head and Neck Cancer. *N Engl J Med* 2016; **374**: 1444–1454.

Thyroid carcinoma

- Assessment of patients with elevated thyroglobulin levels and negative iodine scintigraphy with suspected recurrent disease.[1-3]
- To evaluate disease in treated medullary thyroid carcinoma associated with elevated calcitonin levels with equivocal or normal cross-sectional imaging, bone and octreotide scintigraphy.[1,4]
  See below for alternative PET imaging with Gallium-68 [^{68}Ga]Ga-DOTA-TATE (DOTA-TATE), [^{68}Ga]Ga-DOTA-1-Nal3- octreotide (DOTA-NOC) or [^{68}Ga]Ga-DOTA-octreotide (DOTA-TOC).
- Monitor response to tyrosine kinase inhibitor (TKI) therapy in patients with FDG-avid and non-iodine-avid disease.[5-7]
- Evaluation of anaplastic thyroid cancer in highly selected cases based on a multidisciplinary decision where impact on clinical management is expected.[8-11]

References

1. Abraham T, Schöder H. Thyroid cancer--indications and opportunities for positron emission tomography/computed tomography imaging. *Semin Nucl Med* 2011; **41**: 121–138.
2. Caetano R, Bastos CRG, de Oliveira IAG et al. Accuracy of positron emission tomography and positron emission tomography-CT in the detection of differentiated thyroid cancer recurrence with negative (131) I whole-body scan results: A meta-analysis. *Head Neck* 2016; **38**: 316–327.
3. Haugen BR, Alexander EK, Bible KC et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2016; **26**: 1–133.
4. Giovanella L, Treglia G, Iakovou I, Mihailovic J, Verburg FA, Luster M. EANM practice guideline for PET/CT imaging in medullary thyroid carcinoma. *Eur J Nucl Med Mol Imaging* 2020; **47**: 61–77.
5. Ahmaddy F, Burgard C, Beyer L et al. 18F-FDG-PET/CT in Patients with Advanced, Radioiodine Refractory Thyroid Cancer Treated with Lenvatinib. *Cancers (Basel)* 2021; **13**: 317.
6. Valerio L, Guidoccio F, Giani C et al. [18F]-FDG-PET/CT Correlates With the Response of Radiorefractory Thyroid Cancer to Lenvatinib and Patient Survival. *J Clin Endocrinol Metab* 2021; **106**: 2355–2366.
7. Ferrari C, Santo G, Ruta R et al. Early Predictive Response to Multi-Tyrosine Kinase Inhibitors in Advanced Refractory Radioactive-Iodine Differentiated Thyroid Cancer: A New Challenge for [18F] FDG PET/CT. *Diagnostics (Basel)* 2021; **11**: 1417.
8. Khan N, Oriuchi N, Higuchi T, Endo K. Review of fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography (FDG-PET) in the follow-up of medullary and anaplastic thyroid carcinomas. *Cancer Control* 2005; **12**: 254–260.
9. Bogsrud TV, Karantanis D, Nathan MA et al. 18F-FDG PET in the management of patients with anaplastic thyroid carcinoma. *Thyroid* 2008; **18**: 713–719.
10. Poisson T, Deandreis D, Leboulleux S et al. 18F-fluorodeoxyglucose positron emission tomography and computed tomography in anaplastic thyroid cancer. *Eur J Nucl Med Mol Imaging* 2010; **37**: 2277–2285.
11. Kim HJ, Chang H-S, Ryu YH. Prognostic Role of Pre-Treatment [18F]FDG PET/CT in Patients with Anaplastic Thyroid Cancer. *Cancers (Basel)* 2021; **13**: 4228.

Lung carcinoma

- Staging of patients considered for radical treatment of non-small cell lung cancer.[1,4,9,10]
  - Specifically, National Institute of Clinical Excellence (NICE) guidelines 2019 recommend PET-CT is used for intrathoracic lymph node staging in patients who could potentially have treatment with curative intent, such as those with a low probability of nodal malignancy (lymph nodes below 10 millimetre (mm) maximum short axis on CT) or in patients with enlarged intrathoracic lymph nodes (lymph nodes greater than or equal to 10 mm short axis on CT), and for confirming the presence of isolated distant metastases/synchronous tumours.[3,13]
- Characterisation of a solid solitary pulmonary nodule with an initial risk of malignancy of >10% (Brock model) where the nodule size is greater than local PET-CT detection threshold (8–10 mm) below which the influence of the partial volume effect is substantial and precludes adequate sensitivity.[2,5,6,7,9,15]
  - 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.
  - Smaller nodules in the upper lobes may be considered after multidisciplinary team (MDT) discussion or discussion with the local ARSAC licence holder if biopsy and/or CT follow-up are not appropriate.
- Assessment of response to chemotherapy and/or radiation treatment in selected patients who have had an apparently very good response on conventional imaging and surgery is being considered.[8]
- Assessment of suspected disease recurrence:
  - To differentiate between treatment effects and recurrent cancer.[8,11]
- Staging of patients with small-cell lung cancer with limited disease on CT being considered for radical therapy.[12,14]

References

1. Antoch G, Stattaus J, Nemat AT et al. Non-small cell lung cancer: dual-modality PET/CT in preoperative staging. *Radiology* 2003; **229**: 526–533.
2. Bryant AS, Cerfolio RJ. The maximum standardized uptake values on integrated FDG-PET/CT is useful in differentiating benign from malignant pulmonary nodules. *Ann Thorac Surg* 2006; **82:** 1016–1020.
3. Cerfolio RJ, Bryant AS, Eloubeidi MA. Routine mediastinoscopy and esophageal ultrasound fine-needle aspiration in patients with non-small cell lung cancer who are clinically N2 negative: a prospective study. *Chest* 2006; **130**: 1791–1795.
4. Lardinois D, Weder W, Hany TF et al. Staging of non-small-cell lung cancer with integrated positron-emission tomography and computed tomography. *N Engl J Med* 2003; **348**: 2500–2507.
5. Gould MK, Maclean CC, Kuschner WG, Rydzak CE, Owens DK. Accuracy of positron emission tomography for diagnosis of pulmonary nodules and mass lesions: a meta-analysis. *JAMA* 2001; **285**: 914–924.
6. Baldwin DR, Callister MEJ, Guideline Development Group. The British Thoracic Society guidelines on the investigation and management of pulmonary nodules. *Thorax* 2015; **70**: 794–798.
7. McWilliams A, Tammemagi MC, Mayo JR et al. Probability of cancer in pulmonary nodules detected on first screening CT. *N Engl J Med* 2013; **369**: 910–919.
8. Keidar Z, Haim N, Guralnik L et al. PET/CT using 18F-FDG in suspected lung cancer recurrence: diagnostic value and impact on patient management. *J Nucl Med* 2004; **45**: 1640–1646.

9. Shon IH, O'Doherty MJ, Maisey MN. Positron emission tomography in lung cancer. *Semin Nucl Med* 2002; **32**: 240–271.
10. Toloza EM, Harpole L, McCrory DC. Noninvasive staging of non-small cell lung cancer: a review of the current evidence. *Chest* 2003; **123**: 137S-146S.
11. He Y-Q, Gong H-L, Deng Y-F, Li W-M. Diagnostic efficacy of PET and PET/CT for recurrent lung cancer: a meta-analysis. *Acta Radiol* 2014; **55**: 309–317.
12. Lu Y-Y, Chen J-H, Liang J-A, Chu S, Lin W-Y, Kao C-H. 18F-FDG PET or PET/CT for detecting extensive disease in small-cell lung cancer: a systematic review and meta-analysis. *Nucl Med Commun* 2014; **35**: 697–703.
13. The National Institute for Health and Care Excellence. Lung cancer: diagnosis and management. 2019. *https://www.nice.org.uk/guidance/ng122* (accessed 2021-11-22).
14. Martucci F, Pascale M, Valli MC et al. Impact of 18F-FDG PET/CT in Staging Patients With Small Cell Lung Cancer: A Systematic Review and Meta-Analysis. *Front Med (Lausanne)* 2019; **6**: 336.
15. Weir-McCall JR, Harris S, Miles KA et al. Impact of solitary pulmonary nodule size on qualitative and quantitative assessment using 18F-fluorodeoxyglucose PET/CT: the SPUTNIK trial. *Eur J Nucl Med Mol Imaging* 2021; **48**: 1560–1569.

Pleural malignancy

- To guide biopsy in patients with suspected pleural malignancy with pleural thickening.
  - FDG is less likely to be useful in patients presenting with a pleural effusion only or with a history of previous pleurodesis.[1-4 a]
- To exclude extra-thoracic disease in proven mesothelioma in patients considered for multimodality treatment including radical surgery/decortication.[2,5,6]
- Response assessment to therapy where there is uncertainty on conventional imaging.[2,7,8]

References

1. Porcel JM, Hernández P, Martínez-Alonso M, Bielsa S, Salud A. Accuracy of fluorodeoxyglucose-PET imaging for differentiating benign from malignant pleural effusions: a meta-analysis. *Chest* 2015; **147**: 502–512.
2. Kitajima K, Doi H, Kuribayashi K. Present and future roles of FDG-PET/CT imaging in the management of malignant pleural mesothelioma. *Jpn J Radiol* 2016; **34**: 537–547.
3. Pinelli V, Roca E, Lucchini S et al. Positron Emission Tomography/Computed Tomography for the Pleural Staging of Malignant Pleural Mesothelioma: How Accurate Is It? *Respiration* 2015; **89**: 558–564.
4. Treglia G, Sadeghi R, Annunziata S et al. Diagnostic accuracy of 18F-FDG-PET and PET/CT in the differential diagnosis between malignant and benign pleural lesions: a systematic review and meta-analysis. *Acad Radiol* 2014; **21**: 11–20.
5. Flores RM. The role of PET in the surgical management of malignant pleural mesothelioma. *Lung Cancer* 2005; **49** (Suppl 1): S27-32.
6. Truong MT, Marom EM, Erasmus JJ. Preoperative evaluation of patients with malignant pleural mesothelioma: role of integrated CT-PET imaging. *J Thorac Imaging* 2006; **21**: 146–153.
7. Niccoli Asabella A, Di Palo A, Altini C et al. 18F-FDG PET/CT in therapy response and in predicting responders or non-responders in malignant pleural mesothelioma patients, by using semi-quantitative mRECIST and EORTC criteria. Hell *J Nucl Med* 2018; **21**: 191–197.
8. Kitajima K, Maruyama M, Yokoyama H et al. Response to Immune Checkpoint Inhibitor Therapy in Patients with Unresectable Recurrent Malignant Pleural Mesothelioma Shown by FDG-PET and CT. *Cancers (Basel)* 2021; **13**: 1098.

a FDG PET-CT may demonstrate false positive appearances in patients with history of pleurodesis, however, in this clinical context FDG PET-CT may still be useful for assessment of potential mediastinal lymph node involvement, peritoneal extension of disease and in cases of progressive pleural disease suspected on CT.

Thymic tumours

- Staging of patients considered for surgical resection.[1]
- Assessment of indeterminate thymic lesions if being considered for radical treatment.[2-4]
- Response assessment to therapy where there is uncertainty on conventional imaging.[5]

References

1. Benveniste MFK, Moran CA, Mawlawi O et al. FDG PET-CT aids in the preoperative assessment of patients with newly diagnosed thymic epithelial malignancies. *J Thorac Oncol* 2013; **8**: 502–510.
2. Nakagawa K, Takahashi S, Endo M, Ohde Y, Kurihara H, Terauchi T. Can 18F-FDG PET predict the grade of malignancy in thymic epithelial tumors? An evaluation of only resected tumors. *Cancer Manag Res* 2017; **9**: 761–768.
3. Hephzibah J, Shanthly N, Oommen R. Diagnostic Utility of PET CT in Thymic Tumours with Emphasis on 68Ga-DOTATATE PET CT in Thymic Neuroendocrine Tumour - Experience at a Tertiary Level Hospital in India. *J Clin Diagn Res* 2014; **8**: QC01-03.
4. Lee J, Cho YS, Kim J, Shim YM, Lee K-H, Choi JY. Prognostic Significance of Metabolic Parameters by 18F-FDG PET/CT in Thymic Epithelial Tumors. *Cancers (Basel)* 2021; **13**: 712.
5. Segreto S, Fonti R, Ottaviano M et al. Evaluation of metabolic response with 18F-FDG PET-CT in patients with advanced or recurrent thymic epithelial tumors. *Cancer Imaging* 2017; **17**: 10.

Breast tumours

Indeterminate or equivocal breast lesions

- In case of an FDG-avid intramammary incidental abnormality on a FDG PET-CT scan (performed for reasons other than breast cancer), it is recommended to evaluate on further investigations to exclude breast cancer, including correlation with dedicated breast imaging and, not infrequently, histological confirmation.[1]

Primary staging

- To be performed when standard staging imaging studies are equivocal or suspicious (*problem-solving*)[2-4,*] and particularly when required to guide management decisions such as pre-operative systemic therapy.[4,‡]
- Staging of inflammatory or non-inflammatory locally advanced breast cancers (LABC) – *instead of* and *not* in addition to CT scan and bone scan.[3,**]
- Replacing or complementing standard staging imaging studies in high-risk patients, such as patients with:[3],
  - High tumour burden:[***]
    - Large tumours (e.g. > 5 cm, T3) and/or;
    - Clinically positive axillary nodes (cN+);
  - Aggressive tumour biology, e.g. triple-negative breast carcinoma;[†]
  - Clinical signs, symptoms or laboratory values suggesting the presence of metastases.
- To identify occult primary breast cancers in *a highly selected group of patients* with proven lymph nodal (particularly axillary) or distant metastatic disease but undetected lesions on dedicated breast imaging.[5-10]
- Replacing standard staging imaging studies in patients with proven or suspected allergy to CT or MRI contrast agents.

Notes:

** FDG PET-CT is less informative in cases of lobular cancers and low-grade tumour;[2]*

***For the purpose of these recommendations, LABC means inoperable, non-metastatic locally advanced breast cancer;*

****In the initial staging, FDG PET-CT imaging has been suggested in patients with clinical stage IIA (T1N1 or T2N0) and strongly recommended in patients with clinical stage >=IIB breast cancer, and is better when performed before surgery;*

†Other aggressive breast cancer phenotypes which are known to be FDG-avid include grade 3 ductal cancer, high Ki67, ER/PR-negative, luminal B cancers.[11-15]

‡Bone scan or sodium fluoride PET-CT may not be needed if FDG PET-CT is performed.[4]

Recurrence assessment

- To be performed in patients in which standard imaging studies are equivocal or suspicious of recurrent disease (*problem-solving*).[2-4,*,**]
- For restaging of patients with confirmed locoregional recurrence or clinical suspicion of relapsed disease (e.g. chest wall tenderness, elevated tumour markers*** and so on) equivocal on standard imaging.[16,17]
- Differentiation of treatment-induced brachial plexopathy from tumour infiltration in symptomatic patients with an equivocal or normal MRI.
- Replacing standard restaging imaging studies in patients with proven or suspected allergy to CT or MRI contrast agents.

Notes:

**When feasible/available, FDG PET-CT could be performed with a high-resolution diagnostic, contrast-enhanced CT, according to the imaging pathway algorithms of individual institutions;[4]*

***Bone scan or sodium fluoride PET-CT may not be needed if FDG PET-CT is performed and clearly indicates bone metastases;*

****Elevated CA-125, CEA or CA 15-3 markers;[17]*

Response to treatment

- For early evaluation of response to neoadjuvant therapy, particularly in triple negative or Her2+ disease.[4,*]
- Assessing response to systemic treatment, as clinically indicated, particularly in patients whose disease is not well demonstrated using other diagnostic techniques (for example, bone metastases)[4] or in complex patients with multisystemic disease (for identifying differential response and guide clinical management).[*]

Note:

** Baseline FDG PET-CT is recommended.*

References

1. Aarstad EM, Nordhaug P, Naghavi-Behzad M, Larsen LB, Gerke O, Hildebrandt MG. Prevalence of focal incidental breast uptake on FDG-PET/CT and risk of malignancy: a systematic review and meta-analysis. *Eur J Hybrid Imaging* 2019; **3**: 16.
2. Cardoso F, Kyriakides S, Ohno S et al. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2019; **30**: 1674.
3. Cardoso F, Paluch-Shimon S, Senkus E et al. 5th ESO-ESMO international consensus guidelines for advanced breast cancer (ABC 5). *Ann Oncol 2020*; **31**: 1623–1649.
4. Gradishar WJ, Moran MS, Abraham J et al. NCCN Guidelines® Insights: Breast Cancer, Version 4.2021. *J Natl Compr Canc Netw* 2021; **19**: 484–493.
5. Fizazi K, Greco FA, Pavlidis N et al. Cancers of unknown primary site: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2015; **26** (Suppl 5): v133-138.

6. NCCN Guidelines®: Occult Primary (Cancer of Unknown Primary), Version 2.2021. *https://www.nccn.org/guidelines/guidelines-detail?category=1&id=1451* (accessed 2021-11-22).
7. Kwee TC, Kwee RM. Combined FDG-PET/CT for the detection of unknown primary tumors: systematic review and meta-analysis. *Eur Radiol* 2009; **19**: 731–744.
8. Takabatake D, Taira N, Aogi K et al. Two cases of occult breast cancer in which PET-CT was helpful in identifying primary tumors. *Breast Cancer* 2008; **15**: 181–184.
9. Liu M, Liu B, Song Y, Ding L, Dong L. FDG PET/CT reveals the primary tumor in a patient with occult breast carcinoma undetected by other modalities. *Clin Nucl Med* 2014; **39**: 755–757.
10. Soundararajan R, Naswa N, Karunanithi S, Walia R, Kumar R, Bal C. Occult breast primary malignancy presenting as isolated axillary lymph node metastasis - early detection of primary site by 18F-FDG PET/CT. *Nucl Med Rev Cent East Eur* 2016; **19**: 5–7.
11. Bos R, van Der Hoeven JJM, van Der Wall E et al. Biologic correlates of (18)fluorodeoxyglucose uptake in human breast cancer measured by positron emission tomography. *J Clin Oncol* 2002; **20**: 379–387.
12. Buck A, Schirrmeister H, Kühn T et al. FDG uptake in breast cancer: correlation with biological and clinical prognostic parameters. *Eur J Nucl Med Mol Imaging* 2002; **29**: 1317–1323.
13. Humbert O, Berriolo-Riedinger A, Cochet A et al. Prognostic relevance at 5 years of the early monitoring of neoadjuvant chemotherapy using (18)F-FDG PET in luminal HER2-negative breast cancer. *Eur J Nucl Med Mol Imaging* 2014; **41**: 416–427.
14. Groheux D, Giacchetti S, Moretti J-L et al. Correlation of high 18F-FDG uptake to clinical, pathological and biological prognostic factors in breast cancer. *Eur J Nucl Med Mol Imaging* 2011; **38**: 426–435.
15. Groheux D, Hindie E. Breast cancer: initial workup and staging with FDG PET/CT. *Clin Transl Imaging* 2021; 1–11.
16. Aukema TS, Straver ME, Peeters M-JTFDV et al. Detection of extra-axillary lymph node involvement with FDG PET/CT in patients with stage II-III breast cancer. *Eur J Cancer* 2010; **46**: 3205–3210.
17. Chang H-T, Hu C, Chiu Y-L, Peng N-J, Liu R-S. Role of 2-[18F] fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography in the post-therapy surveillance of breast cancer. PLoS One 2014; **9**: e115127.

Oesophageal and oesophago-gastric junction cancers

- For staging/re-staging patients with oesophageal or oesophago-gastric carcinoma, particularly if considered at risk of metastases, suitable for radical treatment, including patients who have received neo-adjuvant treatment.[1-8,*, **, ***, †]
- Evaluation of suspected recurrence of oesophago-gastric tumours when other imaging is negative or equivocal.[1,3-8,‡]
- For radiotherapy planning/volume delineation of oesophageal and oesophago-gastric junction cancers.[1,3]
- To evaluate response assessment after primary treatment in patients with oesophageal or oesophago-gastric junction cancers.[1,3,9-14]

Notes:

**FDG PET-CT outperforms morphological imaging for the detection of distant metastases in oesophageal cancer;* [4-8]

***FDG PET-CT performs well and better than morphological imaging, in detecting regional or distant lymph node involvement;* [4,6,8,15-18]

****FDG PET-CT evaluation could be reserved for patients with no evidence of M1 disease on CT;* [1]

†Review of CT and FDG PET-CT scans prior EUS is recommended to become familiar with the nodal distribution for FNA biopsy; [1]

‡FDG PET-CT shows a good sensitivity for the diagnosis of recurrent disease, but lacks specificity, which means that histological proof of local FDG-avidity appears necessary. [4-8]

References

1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Esophageal and Esophagogastric Cancers, version 2.2021.
2. Kim TJ, Kim HY, Lee KW, Kim MS. Multimodality assessment of esophageal cancer: preoperative staging and monitoring of response to therapy. *Radiographics* 2009; **29**: 403–421.
3. Lordick F, Mariette C, Haustermans K, Obermannová R, Arnold D, ESMO Guidelines Committee. Oesophageal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2016; **27**: v50–v57.
4. Salaün P-Y, Abgral R, Malard O et al. Good clinical practice recommendations for the use of PET/CT in oncology. *Eur J Nucl Med Mol Imaging* 2020; **47**: 28–50.
5. Tirumani H, Rosenthal MH, Tirumani SH, Shinagare AB, Krajewski KM, Ramaiya NH. Esophageal Carcinoma: Current Concepts in the Role of Imaging in Staging and Management. *Can Assoc Radiol J* 2015; **66**: 130–139.
6. Findlay JM, Bradley KM, Maile EJ et al. Pragmatic staging of oesophageal cancer using decision theory involving selective endoscopic ultrasonography, PET and laparoscopy. *Br J Surg* 2015; **102**: 1488–1499.
7. Omloo JMT, Sloof GW, Boellaard R et al. Importance of fluorodeoxyglucose-positron emission tomography (FDG-PET) and endoscopic ultrasonography parameters in predicting survival following surgery for esophageal cancer. *Endoscopy* 2008; **40**: 464–471.

8. van Westreenen HL, Heeren PAM, van Dullemen HM et al. Positron emission tomography with F-18-fluorodeoxyglucose in a combined staging strategy of esophageal cancer prevents unnecessary surgical explorations. *J Gastrointest Surg* 2005; **9**: 54–61.
9. Swisher SG, Erasmus J, Maish M et al. 2-Fluoro-2-deoxy-D-glucose positron emission tomography imaging is predictive of pathologic response and survival after preoperative chemoradiation in patients with esophageal carcinoma. *Cancer* 2004; **101**: 1776–1785.
10. Bruzzi JF, Swisher SG, Truong MT et al. Detection of interval distant metastases: clinical utility of integrated CT-PET imaging in patients with esophageal carcinoma after neoadjuvant therapy. *Cancer* 2007; **109**: 125–134.
11. Higuchi I, Yasuda T, Yano M et al. Lack of fludeoxyglucose F 18 uptake in posttreatment positron emission tomography as a significant predictor of survival after subsequent surgery in multimodality treatment for patients with locally advanced esophageal squamous cell carcinoma. *J Thorac Cardiovasc Surg* 2008; **136**: 205–212, 212.e1–3.
12. Malik V, Lucey JA, Duffy GJ et al. Early repeated 18F-FDG PET scans during neoadjuvant chemoradiation fail to predict histopathologic response or survival benefit in adenocarcinoma of the esophagus. *J Nucl Med* 2010; **51**: 1863–1869.
13. Smithers BM, Couper GC, Thomas JM et al. Positron emission tomography and pathological evidence of response to neoadjuvant therapy in adenocarcinoma of the esophagus. *Dis Esophagus* 2008; **21**: 151–158.
14. van Heijl M, Omloo JM, van Berge Henegouwen MI et al. Fluorodeoxyglucose positron emission tomography for evaluating early response during neoadjuvant chemoradiotherapy in patients with potentially curable esophageal cancer. *Ann Surg* 2011; **253**: 56–63.
15. Cuellar SLB, Carter BW, Macapinlac HA et al. Clinical staging of patients with early esophageal adenocarcinoma: does FDG-PET/CT have a role? *J Thorac Oncol* 2014; **9**: 1202–1206.
16. Little SG, Rice TW, Bybel B et al. Is FDG-PET indicated for superficial esophageal cancer? *Eur J Cardiothorac Surg* 2007; **31**: 791–796.
17. Munden RF, Macapinlac HA, Erasmus JJ. Esophageal cancer: the role of integrated CT-PET in initial staging and response assessment after preoperative therapy. *J Thorac Imaging* 2006; **21**: 137–145.
18. Takizawa K, Matsuda T, Kozu T et al. Lymph node staging in esophageal squamous cell carcinoma: a comparative study of endoscopic ultrasonography versus computed tomography. *J Gastroenterol Hepatol* 2009; **24**: 1687–1691.

Gastric cancer

- To identify primary gastric tumours in case of equivocal findings on conventional imaging for patients which are eligible for radical treatment.[1,***]
- For staging and re-staging of confirmed gastric cancer if there is a curative treatment intent.[1-4*]
- Assessment of suspected relapsed or disease progression in patients who are candidates for further chemotherapy or radiotherapy.[1]
- To identify recurrent disease in gastric bed, near anastomoses or stumps.[2,***]
- For treatment response assessment (particularly in cases of renal insufficiency or allergy to CT contrast).[2,5]

Notes:

** FDG PET-CT may be less informative in patients with mucinous or diffuse/non-intestinal types tumours[1];*

*** Baseline clinical staging FDG PET-CT evaluation is recommended in >T1 suspected disease, particularly if nodal and/or metastatic disease is equivocal on initial CT chest+abdomen+pelvis imaging.[1-3]*

**** Although CT chest+abdomen+pelvis with oral and IV contrast is the preferred imaging for follow-up/surveillance of patients with p stage II/III or yp stage I-III (treated with neoadjuvant ± adjuvant chemotherapy), FDG PET-CT can be considered in addition or replacing the CT, as above.[2]*

References

1. Smyth EC, Verheij M, Allum W et al. Gastric cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2016; **27**: v38–v49.
2. Ajani JA, D'Amico TA, Almhanna K et al. Gastric Cancer, Version 3.2016, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2016; **14**: 1286–1312.
3. Bosch KD, Chicklore S, Cook GJ et al. Staging FDG PET-CT changes management in patients with gastric adenocarcinoma who are eligible for radical treatment. *Eur J Nucl Med Mol Imaging* 2020; **47**: 759–767.
4. Ajani JA, Winter K, Okawara GS et al. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic response. *J Clin Oncol* 2006; **24**: 3953–3958.
5. Smyth E, Schöder H, Strong VE et al. A prospective evaluation of the utility of 2-deoxy-2-[18 F]fluoro-D -glucose positron emission tomography and computed tomography in staging locally advanced gastric cancer. *Cancer* 2012; **118**: 5481–5488.

Gastrointestinal stromal tumours

- Staging prior to treatment in patients who are likely to require systemic therapy.[1,2]
- Response assessment to systemic therapy.[1,3]
- Early treatment response (six to eight weeks) to imatinib.[4]

References

1. Gayed I, Vu T, Iyer R et al. The role of 18F-FDG PET in staging and early prediction of response to therapy of recurrent gastrointestinal stromal tumors. *J Nucl Med Off Publ Soc Nucl Med* 2004; **45**: 17–21.
2. Kwon HR, Pahk K, Park S, Kwon HW, Kim S. Prognostic Value of Metabolic Information in Advanced Gastric Cancer Using Preoperative 18F-FDG PET/CT. *Nucl Med Mol Imaging* 2019; **53**: 386–395.
3. Dimitrakopoulou-Strauss A, Ronellenfitsch U, Cheng C et al. Imaging therapy response of gastrointestinal stromal tumors (GIST) with FDG PET, CT and MRI: a systematic review. *Clin Transl Imaging* 2017; **5**: 183–197.
4. Antoch G, Kanja J, Bauer S et al. Comparison of PET, CT, and dual-modality PET/CT imaging for monitoring of imatinib (STI571) therapy in patients with gastrointestinal stromal tumors. *J Nucl Med Off Publ Soc Nucl Med* 2004; **45**: 357–365.

Hepatopancreatobiliary disease

Pancreatic cancer

- Staging of patients with localised pancreatic cancer on CT before they have surgery, radiotherapy or systemic therapy to help in planning appropriate treatment.[1-8]
- Suspected recurrence of pancreatic cancer, where cross-sectional imaging is equivocal or negative, taking into consideration that up to 30% of pancreatic adenocarcinomas may not be FDG avid.[2,4,6,8,9]
- Diagnosis of primary pancreatic cancer when other imaging is non-diagnostic.[6]

Hepatocellular carcinoma

- Suspected recurrence of hepatocellular carcinoma (HCC), where cross-sectional imaging is equivocal or negative, taking into consideration that that up to 50% of HCC may not be FDG avid.[10]
- Identification of poor prognosis HCC.[11-13]
- Predicting probability of early recurrence after liver transplantation for HCC.[13]

Other tracers (e.g., ^{18}F-choline/^{11}C-choline, ^{11}C-acetate) can be useful in imaging HCC. See section ***Choline PET for other tumours*** *for more details.*

References

1. Garcea G, Ong SL, Maddern GJ. The current role of PET-CT in the characterization of hepatobiliary malignancies. *HPB (Oxford)* 2009; **11**: 4–17.
2. Pakzad F, Groves AM, Ell PJ. The role of positron emission tomography in the management of pancreatic cancer. *Semin Nucl Med* 2006; **36**: 248–256.
3. The National Institute for Health and Care Excellence. Pancreatic cancer. 2018. *https://www.nice.org.uk/guidance/qs177/* (accessed 2021-11-22).
4. Dibble EH, Karantanis D, Mercier G, Peller PJ, Kachnic LA, Subramaniam RM. PET/CT of cancer patients: part 1, pancreatic neoplasms. *AJR Am J Roentgenol* 2012; **199**: 952–967.
5. Wartski M, Sauvanet A. 18F-FDG PET/CT in pancreatic adenocarcinoma: A role at initial imaging staging? *Diagn Interv Imaging* 2019; **100**: 735–741.
6. Sahani DV, Bonaffini PA, Catalano OA, Guimaraes AR, Blake MA. State-of-the-art PET/CT of the pancreas: current role and emerging indications. *Radiographics* 2012; **32**: 1133–1158; discussion 1158-1160.
7. Que R, Chen Y, Tao Z et al. Diffusion-weighted MRI versus FDG-PET/CT for diagnosing pancreatic cancer: an indirect comparison meta-analysis. *Acta Radiol* 2020; **61**: 1473–1483.
8. Ghaneh P, Hanson R, Titman A et al. PET-PANC: multicentre prospective diagnostic accuracy and health economic analysis study of the impact of combined modality 18fluorine-2-fluoro-2-deoxy-d-glucose positron emission tomography with computed tomography scanning in the diagnosis and management of pancreatic cancer. *Health Technol Assess* 2018; **22**: 1–114.
9. Daamen LA, Groot VP, Goense L et al. The diagnostic performance of CT versus FDG PET-CT for the detection of recurrent pancreatic cancer: a systematic review and meta-analysis. *Eur J Radiol* 2018; **106**: 128–136.
10. Hu J-H, Tang J-H, Lin C-H, Chu Y-Y, Liu N-J. Preoperative staging of cholangiocarcinoma and biliary carcinoma using 18F-fluorodeoxyglucose positron emission tomography: a meta-analysis. *J Investig Med* 2018; **66**: 52–61.Na SJ, Oh JK, Hyun SH et al. 18F-FDG PET/CT Can Predict Survival of Advanced

Hepatocellular Carcinoma Patients: A Multicenter Retrospective Cohort Study. *J Nucl Med* 2017; **58**: 730–736.

11. Lim C, Salloum C, Chalaye J et al. 18F-FDG PET/CT predicts microvascular invasion and early recurrence after liver resection for hepatocellular carcinoma: A prospective observational study. *HPB (Oxford)* 2019; **21**: 739–747.
12. Lv J, Yin H, Mao W, Shi H. Investigating the value of pre-treatment 18F-FDG PET/CT in predicting the pathological characteristic of hepatocellular carcinoma and recurrence after liver transplantation. *Abdom Radiol (NY)* 2021; **46**: 2490–2497.
13. Na SJ, Oh JK, Hyun SH et al. 18F-FDG PET/CT Can Predict Survival of Advanced Hepatocellular Carcinoma Patients: A Multicenter Retrospective Cohort Study. *J Nucl Med* 2017; **58**: 730–736.**66**: 52–61.

Gallbladder cancer

- Pre-operative staging.[1,2]

References

1. Ramos-Font C, Gómez-Rio M, Rodríguez-Fernández A, Jiménez-Heffernan A, Sánchez Sánchez R, Llamas-Elvira JM. Ability of FDG-PET/CT in the detection of gallbladder cancer. *J Surg Oncol* 2014; **109**: 218–224.
2. Goel S, Aggarwal A, Iqbal A, Gupta M, Rao A, Singh S. 18-FDG PET-CT should be included in preoperative staging of gall bladder cancer. *Eur J Surg Oncol* 2020; **46**: 1711–1716.

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.[1-4,6]
- Restaging of patients with recurrence being considered for radical treatment and/or invasive targeted techniques (for example, metastatectomy/selective internal radiation therapy [SIRT]).[1,5,6]
- Assessment of treatment response in patients with rectal carcinoma post (chemo) radiotherapy with indeterminate findings on other imaging.[7-9]
- Evaluation of indeterminate pre-sacral masses post-treatment.[7-9]
- Assessment of treatment response following targeted therapy (ablative techniques for liver or lung metastases, selective internal radiotherapy for liver metastases) in metastatic colorectal carcinoma when findings on other imaging are inconclusive.[10,11]
- PET-CT follow up after liver metastasis ablation.[12-14]
- Detection of recurrence in patients with rising tumour markers and/or clinical suspicion of recurrence with normal or equivocal findings on other imaging.[15]
- Monitoring metabolic response in patients with metastatic colorectal cancer being treated with oral multikinase and immune checkpoint inhibitors.[16]

References

1. Brush J, Boyd K, Chappell F et al. The value of FDG positron emission tomography/computerised tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation. *Health Technol Assess* 2011; **15**: 1–192, iii–iv.
2. Llamas-Elvira JM, Rodríguez-Fernández A, Gutiérrez-Sáinz J et al. Fluorine-18 fluorodeoxyglucose PET in the preoperative staging of colorectal cancer. *Eur J Nucl Med Mol Imaging* 2007; **34**: 859–867.
3. Lake ES, Wadhwani S, Subar D et al. The influence of FDG PET-CT on the detection of extrahepatic disease in patients being considered for resection of colorectal liver metastasis. *Ann R Coll Surg Engl* 2014; **96**: 211–215.
4. Maffione AM, Lopci E, Bluemel C, Giammarile F, Herrmann K, Rubello D. Diagnostic accuracy and impact on management of (18)F-FDG PET and PET/CT in colorectal liver metastasis: a meta-analysis and systematic review. *Eur J Nucl Med Mol Imaging* 2015; **42**: 152–163.
5. Moulton C-A, Gu C-S, Law CH et al. Effect of PET before liver resection on surgical management for colorectal adenocarcinoma metastases: a randomized clinical trial. *JAMA* 2014; **311**: 1863–1869.
6. The National Institute for Health and Care Excellence. Colorectal cancer: diagnosis and management. 2014. *https://www.nice.org.uk/guidance/ng151* (accessed 2022-05-23).
7. Calvo FA, Sole CV, de la Mata D et al. 18F-FDG PET/CT-based treatment response evaluation in locally advanced rectal cancer: a prospective validation of long-term outcomes. *Eur J Nucl Med Mol Imaging* 2013; **40**: 657–667.
8. Huh JW, Kwon SY, Lee JH, Kim HR. Comparison of restaging accuracy of repeat FDG-PET/CT with pelvic MRI after preoperative chemoradiation in patients with rectal cancer. *J Cancer Res Clin Oncol* 2015; **141**: 353–359.
9. Maffione AM, Marzola MC, Capirci C, Colletti PM, Rubello D. Value of (18)F-FDG PET for Predicting Response to Neoadjuvant Therapy in Rectal Cancer: Systematic Review and Meta-Analysis. *AJR Am J Roentgenol* 2015; **204**: 1261–1268.

10. Bonichon F, Palussière J, Godbert Y et al. Diagnostic accuracy of 18F-FDG PET/CT for assessing response to radiofrequency ablation treatment in lung metastases: a multicentre prospective study. *Eur J Nucl Med Mol Imaging* 2013; **40**: 1817–1827.
11. Sabet A, Meyer C, Aouf A et al. Early post-treatment FDG PET predicts survival after 90Y microsphere radioembolization in liver-dominant metastatic colorectal cancer. *Eur J Nucl Med Mol Imaging* 2015; **42**: 370–376.
12. Zheng J-H, Chang Z-H, Han C-B et al. Detection of residual tumor following radiofrequency ablation of liver metastases using 18F-FDG PET/PET-CT: a systematic review and meta-analysis. *Nucl Med Commun* 2014; **35**: 339–346.
13. Nielsen K, van Tilborg AAJM, Scheffer HJ et al. PET-CT after radiofrequency ablation of colorectal liver metastases: suggestions for timing and image interpretation. *Eur J Radiol* 2013; **82**: 2169–2175.
14. Schnitzer ML, Froelich MF, Gassert FG et al. Follow-Up 18F-FDG PET/CT versus Contrast-Enhanced CT after Ablation of Liver Metastases of Colorectal Carcinoma-A Cost-Effectiveness Analysis. *Cancers* (Basel) 2020; **12**: E2432.
15. Lu Y-Y, Chen J-H, Chien C-R et al. Use of FDG-PET or PET/CT to detect recurrent colorectal cancer in patients with elevated CEA: a systematic review and meta-analysis. *Int J Colorectal Dis* 2013; **28**: 1039–1047.
16. Woff E, Hendlisz A, Garcia C et al. Monitoring metabolic response using FDG PET-CT during targeted therapy for metastatic colorectal cancer. *Eur J Nucl Med Mol Imaging* 2016; **43**: 1792–1801.

Anal carcinoma

- For staging in patients with T2-T4 anal tumours suitable for radical treatment.[1,2,4,6-9]
- For re-staging/re-assessment in patients treated with radical chemoradiotherapy.[1-5,7,8]

References

1. Nguyen BT, Joon DL, Khoo V et al. Assessing the impact of FDG-PET in the management of anal cancer. *Radiother Oncol* 2008; **87**: 376–382.
2. Jones M, Hruby G, Solomon M, Rutherford N, Martin J. The Role of FDG-PET in the Initial Staging and Response Assessment of Anal Cancer: A Systematic Review and Meta-analysis. *Ann Surg Oncol* 2015; **22**: 3574–3581.
3. Goldman KE, White EC, Rao AR, Kaptein JS, Lien WW. Posttreatment FDG-PET-CT response is predictive of tumor progression and survival in anal carcinoma. *Pract Radiat Oncol* 2016; **6**: e149–e154.
4. Teagle AR, Gilbert DC, Jones JR, Burkill GJ, McKinna F, Dizdarevic S. Negative 18F-FDG-PET-CT may exclude residual or recurrent disease in anal cancer. *Nucl Med Commun* 2016; **37**: 1038–1045.
5. Houard C, Pinaquy J-B, Mesguich C et al. Role of 18F-FDG PET/CT in Posttreatment Evaluation of Anal Carcinoma. *J Nucl Med* 2017; **58**: 1414–1420.
6. Mahmud A, Poon R, Jonker D. PET imaging in anal canal cancer: a systematic review and meta-analysis. *Br J Radiol* 2017; **90**: 20170370.
7. Geh I, Gollins S, Renehan A et al. Association of Coloproctology of Great Britain & Ireland (ACPGBI): Guidelines for the Management of Cancer of the Colon, Rectum and Anus (2017) - Anal Cancer. Colorectal Dis 2017; **19** (Suppl 1): 82–97.
8. Benson AB, Venook AP, Al-Hawary MM et al. Anal Carcinoma, Version 2.2018, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw* 2018; **16**: 852–871.
9. Stewart DB, Gaertner WB, Glasgow SC et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for Anal Squamous Cell Cancers (Revised 2018). *Dis Colon Rectum* 2018; **61**: 755–774.

Urological malignancy

Renal cancer

- Assessment of metastatic renal or ureteric carcinoma in staging and restaging of extra-renal or extra-ureteric disease in selected cases with equivocal imaging (recognising that ~ 50% of renal cell carcinomas may not be FDG-avid and that the radiotracer is excreted into the urinary tract, however, it's useful in cases when disease is FDG-avid and for potential problem solving).[1,2,4-6,8]
- Assessment of disease recurrence within the nephrectomy bed.[2,3,5,7]
- Monitoring response to treatment if previously FDG-avid metastatic disease.[2,4,5]

References

1. Ma H, Shen G, Liu B, Yang Y, Ren P, Kuang A. Diagnostic performance of 18F-FDG PET or PET/CT in restaging renal cell carcinoma: a systematic review and meta-analysis. *Nucl Med Commun* 2017; **38**: 156–163.
2. Liu Y. The Place of FDG PET/CT in Renal Cell Carcinoma: Value and Limitations. *Front Oncol* 2016; **6**: 201.
3. Kumar R, Shandal V, Shamim SA, Jeph S, Singh H, Malhotra A. Role of FDG PET-CT in recurrent renal cell carcinoma. *Nucl Med Commun* 2010; **31**: 844–850.
4. Kitajima K, Yamamoto S, Fukushima K, Minamimoto R, Kamai T, Jadvar H. Update on advances in molecular PET in urological oncology. *Jpn J Radiol* 2016; **34**: 470–485.
5. Lindenberg L, Mena E, Choyke PL, Bouchelouche K. PET imaging in renal cancer. *Curr Opin Oncol* 2019; **31**: 216–221.
6. Wang H-Y, Ding H-J, Chen J-H, Chao C-H, Lu Y-Y, Lin W-Y et al. Meta-analysis of the diagnostic performance of [18F]FDG-PET and PET/CT in renal cell carcinoma. *Cancer Imaging* 2012; **12**: 464–474.
7. Park S, Lee H-Y, Lee S. Role of F-18 FDG PET/CT in the follow-up of asymptomatic renal cell carcinoma patients for postoperative surveillance: based on conditional survival analysis. *J Cancer Res Clin Oncol* 2021. doi:10.1007/s00432-021-03688-2.
8. Hou G, Zhao D, Jiang Y, Zhu Z, Huo L, Li F et al. Clinical utility of FDG PET/CT for primary and recurrent papillary renal cell carcinoma. *Cancer Imaging* 2021; **21**: 25.

Bladder cancer

- Staging – In the setting of proven muscle invasive bladder cancer or high-risk non-muscle-invasive bladder cancer before radical treatment if there are indeterminate findings on CT or MRI, or a high-risk of metastatic disease (e.g., T3b disease).[3-5,7,9-12]
- Re-staging following treatment or in suspected extra-vesical recurrence (nodal or visceral).[1 3,5,6,8,12]

References

1. Güney İB, Küçüker KA, İzol V, Kibar M. The role and effect of FDG-PET/CT on patient management and restaging of bladder carcinoma. *Turk J Urol* 2019; **45**: 423–430.
2. Zattoni F, Incerti E, Dal Moro F et al. 18F-FDG PET/CT and Urothelial Carcinoma: Impact on Management and Prognosis-A Multicenter Retrospective Study. *Cancers (Basel)* 2019; **11**: E700.
3. Chakraborty D, Mittal BR, Kashyap R et al. Role of fluorodeoxyglucose positron emission tomography/computed tomography in diagnostic evaluation of carcinoma urinary bladder: comparison with computed tomography. *World J Nucl Med* 2014; **13**: 34–39.
4. The National Institute for Health and Care Excellence. Bladder cancer: diagnosis and management. 2015. *https://www.nice.org.uk/guidance/ng2* (accessed 2021-11-22).
5. Girard A, Vila Reyes H, Shaish H et al. The Role of 18F-FDG PET/CT in Guiding Precision Medicine for Invasive Bladder Carcinoma. *Front Oncol* 2020; **10**: 565086.
6. Kitajima K, Yamamoto S, Fukushima K et al. FDG-PET/CT as a post-treatment restaging tool in urothelial carcinoma: Comparison with contrast-enhanced CT. *Eur J Radiol* 2016; **85**: 593–598.
7. Mertens LS, Fioole-Bruining A, Vegt E, Vogel WV, van Rhijn BW, Horenblas S. Impact of (18) F-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) on management of patients with carcinoma invading bladder muscle. *BJU Int* 2013; **112**: 729–734.
8. Zattoni F, Incerti E, Colicchia M et al. Comparison between the diagnostic accuracies of 18F-fluorodeoxyglucose positron emission tomography/computed tomography and conventional imaging in recurrent urothelial carcinomas: a retrospective, multicenter study. *Abdom Radiol (NY)* 2018; **43**: 2391–2399.
9. Goodfellow H, Viney Z, Hughes P et al. Role of fluorodeoxyglucose positron emission tomography (FDG PET)-computed tomography (CT) in the staging of bladder cancer. *BJU Int* 2014; **114**: 389–395.
10. Girard A, Rouanne M, Taconet S et al. Integrated analysis of 18F-FDG PET/CT improves preoperative lymph node staging for patients with invasive bladder cancer. *Eur Radiol* 2019; **29**: 4286–4293.
11. Apolo AB, Riches J, Schöder H et al. Clinical value of fluorine-18 2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography in bladder cancer. *J Clin Oncol* 2010; **28**: 3973–3978.
12. Lodde M, Lacombe L, Friede J, Morin F, Saourine A, Fradet Y. Evaluation of fluorodeoxyglucose positron-emission tomography with computed tomography for staging of urothelial carcinoma. *BJU Int* 2010; **106**: 658–663.

Prostate malignancy

- Positive FDG PET is a poor prognostic marker in prostate malignancy and can be used in combination with multitracer imaging (e.g., prostate-specific membrane antigen (PSMA) tracer imaging, DOTATATE, Na[^{18}F]F) in highly selected patients based on MDT approach.[1-3]
  See below for alternative PET imaging with non-FDG tracers in prostate malignancy.

References

1. Wang B, Liu C, Wei Y et al. A Prospective Trial of 68Ga-PSMA and 18F-FDG PET/CT in Nonmetastatic Prostate Cancer Patients with an Early PSA Progression During Castration. *Clin Cancer Res* 2020; **26**: 4551–4558.
2. Bakht MK, Lovnicki JM, Tubman J et al. Differential Expression of Glucose Transporters and Hexokinases in Prostate Cancer with a Neuroendocrine Gene Signature: A Mechanistic Perspective for 18F-FDG Imaging of PSMA-Suppressed Tumors. *J Nucl Med* 2020; **61**: 904–910.
3. Hofman MS, Emmett L, Violet J et al. TheraP: a randomized phase 2 trial of 177 Lu-PSMA-617 theranostic treatment vs cabazitaxel in progressive metastatic castration-resistant prostate cancer (Clinical Trial Protocol ANZUP 1603). *BJU Int* 2019; **124** (Suppl 1): 5–13.

Testicular malignancy

- In selected cases of primary staging of testicular germ cell tumours with equivocal findings on conventional work-up.[1,2]
- Assessment of recurrent disease in seminoma patients with elevated or rising tumour markers and equivocal or normal anatomical imaging.[3-8]
- Post chemotherapy assessment of residual masses in patients with metastatic seminoma (note high NPV especially for masses > 3 cm but false positives can occur secondary to inflammation and desmoplastic reaction so ideally perform at least eight weeks post chemotherapy).[3-8]
  Note for non-seminomatous germ cell tumours, teratomas have variable, low or no FDG uptake, so FDG PET is not reliable to distinguish disease versus fibrosis or necrosis.

References

1. Cook GJ, Sohaib A, Huddart RA, Dearnaley DP, Horwich A, Chua S. The role of 18F-FDG PET/CT in the management of testicular cancers. *Nucl Med Commun* 2015; **36**: 702–708.
2. Honecker F, Aparicio J, Berney D et al. ESMO Consensus Conference on testicular germ cell cancer: diagnosis, treatment and follow-up. *Ann Oncol* 2018; **29**: 1658–1686.
3. De Santis M, Becherer A, Bokemeyer C et al. 2-18fluoro-deoxy-D-glucose positron emission tomography is a reliable predictor for viable tumor in postchemotherapy seminoma: an update of the prospective multicentric SEMPET trial. *J Clin Oncol* 2004; **22**: 1034–1039.
4. Oechsle K, Hartmann M, Brenner W et al. [18F]Fluorodeoxyglucose positron emission tomography in nonseminomatous germ cell tumors after chemotherapy: the German multicenter positron emission tomography study group. *J Clin Oncol* 2008; **26**: 5930–5935.
5. Ambrosini V, Zucchini G, Nicolini S et al. 18F-FDG PET/CT impact on testicular tumours clinical management. *Eur J Nucl Med Mol Imaging* 2014; **41**: 668–673.

6. Bachner M, Loriot Y, Gross-Goupil M et al. 2-18fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) for postchemotherapy seminoma residual lesions: a retrospective validation of the SEMPET trial. *Ann Oncol* 2012; **23**: 59–64.
7. Calabrò D, Telo S, Ambrosini V. PET imaging in testicular tumours. Curr Opin Urol 2020; 30: 665–671.
8. European Association of Urology. Testicular Cancer Guidelines. *https://uroweb.org/guideline/testicular-cancer/* (accessed 2021-11-22).

Penile carcinoma

- Staging of high-risk penile carcinoma.[1-4]

References

1. Graafland NM, Leijte JAP, Valdés Olmos RA, Hoefnagel CA, Teertstra HJ, Horenblas S. Scanning with 18F-FDG-PET/CT for detection of pelvic nodal involvement in inguinal node-positive penile carcinoma. *Eur Urol* 2009; **56**: 339–345.
2. Leijte JAP, Graafland NM, Valdés Olmos RA, van Boven HH, Hoefnagel CA, Horenblas S. Prospective evaluation of hybrid 18F-fluorodeoxyglucose positron emission tomography/computed tomography in staging clinically node-negative patients with penile carcinoma. *BJU Int* 2009; **104**: 640–644.
3. Ottenhof SR, Djajadiningrat RS, Versleijen MWJ et al. F-18 Fluorodeoxyglucose Positron Emission Tomography with Computed Tomography Has High Diagnostic Value for Pelvic and Distant Staging in Patients with High-risk Penile Carcinoma. *Eur Urol Focus* 2021; S2405-4569(21)00055–9.
4. Jakobsen JK, Frahm Nielsen T, Ipsen P et al. DaPeCa-7: comparative assessment of fluorodeoxyglucose positron emission tomography/computed tomography (CT) and conventional diagnostic CT in diagnosis of lymph node metastases, distant metastases and incidental findings in patients with invasive penile cancer. *BJU Int* 2021; **127**: 254–262.

Gynaecological malignancy

- Staging of patients with locally advanced cervical cancer being considered for radical chemoradiotherapy.[1-4]
- Response assessment of locally advanced cervical cancer after chemoradiotherapy if felt clinically warranted.[1-4]
- Suspected recurrence of vulval, endometrial or cervical carcinoma when other imaging is equivocal.[5]
- Staging or restaging of patients with vulval or uterine (cervix/endometrium) carcinoma considered for exenterative surgery.[6]
- Detection of tumour in selected patients with ovarian carcinoma who have rising CA125 levels and equivocal or negative imaging.[7]
- Staging of high-risk endometrial cancer with equivocal findings on conventional work-up.[8,9]

References

1. Adam JA, van Diepen PR, Mom CH, Stoker J, van Eck-Smit BLF, Bipat S. [18F]FDG-PET or PET/CT in the evaluation of pelvic and para-aortic lymph nodes in patients with locally advanced cervical cancer: A systematic review of the literature. *Gynecol Oncol* 2020; **159**: 588–596.
2. Reed N, Balega J, Barwick T et al. British Gynaecological Cancer Society (BGCS) cervical cancer guidelines: Recommendations for practice. *Eur J Obstet Gynecol Reprod Biol* 2021; **256**: 433–465.
3. Woo S, Atun R, Ward ZJ, Scott AM, Hricak H, Vargas HA. Diagnostic performance of conventional and advanced imaging modalities for assessing newly diagnosed cervical cancer: systematic review and meta-analysis. *Eur Radiol* 2020; **30**: 5560–5577.
4. Adam JA, Loft A, Chargari C et al. EANM/SNMMI practice guideline for [18F]FDG PET/CT external beam radiotherapy treatment planning in uterine cervical cancer v1.0. *Eur J Nucl Med Mol Imaging* 2021; **48**: 1188–1199.
5. Rao YJ, Grigsby PW. The Role of PET Imaging in Gynecologic Radiation Oncology. *PET Clin* 2018; **13**: 225–237.
6. Lakhman Y, Nougaret S, Miccò M et al. Role of MR Imaging and FDG PET/CT in Selection and Follow-up of Patients Treated with Pelvic Exenteration for Gynecologic Malignancies. *Radiographics* 2015; **35**: 1295–1313.
7. Soussan M, Wartski M, Cherel P et al. Impact of FDG PET-CT imaging on the decision making in the biologic suspicion of ovarian carcinoma recurrence. *Gynecol Oncol* 2008; **108**: 160–165.
8. Garau LM, Niccoli-Asabella A, Ferrari C, Sardaro A, Pisani A, Rubini G. The role of 18F-FDG PET/CT in endometrial adenocarcinoma: a review of the literature and recent advances. *Clin Transl Imaging* 2020; **8**: 357–364.
9. Rockall AG, Barwick TD, Wilson W et al. Diagnostic Accuracy of FEC-PET/CT, FDG-PET/CT, and Diffusion-Weighted MRI in Detection of Nodal Metastases in Surgically Treated Endometrial and Cervical Carcinoma. *Clin Cancer Res* 2021; **27**: 6457–6466.

Lymphoma

- Staging and restaging of FDG-avid lymphoma (including indolent lymphoma and post-transplant lymphoproliferative disorder (PTLD) in patients being for considered for active treatment.[1-11]
- Response assessment using Deauville criteria and Lugano classification.[1,4-8,12-24] Semi-quantitative evaluation should be performed using iterative reconstruction rather than advanced reconstructions employing point spread function compensation or penalised likelihood reconstruction.[25]
- In cases where there is a high index of clinical suspicion for high grade transformation to identify a suitable biopsy site in low grade lymphoma. Re-biopsy is not required prior to immunochemotherapy based on standardised uptake value (SUV) alone.[1,26]
- Evaluation of suspected relapse for FDG-avid lymphomas in symptomatic patients. Surveillance imaging is not recommended.[1,7,27-29]
- Prior to bone marrow transplant to assess remission status and residual volume of disease and suitability for transplant.[1,5,30,31]

References

1. Barrington SF, Mikhaeel NG, Kostakoglu L et al. Role of imaging in the staging and response assessment of lymphoma: consensus of the International Conference on Malignant Lymphomas Imaging Working Group. *J Clin Oncol Off J Am Soc Clin Oncol* 2014; **32**: 3048–3058.
2. Barrington SF, Kirkwood AA, Franceschetto A et al. PET-CT for staging and early response: results from the Response-Adapted Therapy in Advanced Hodgkin Lymphoma study. *Blood* 2016; **127**: 1531–1538.
3. Brady JL, Binkley MS, Hajj C et al. Definitive radiotherapy for localized follicular lymphoma staged by 18F-FDG PET-CT: a collaborative study by ILROG. *Blood* 2019; **133**: 237–245.
4. Cheson BD, Fisher RI, Barrington SF et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol Off J Am Soc Clin Oncol* 2014; **32**: 3059–3068.
5. Eichenauer DA, Engert A, André M et al. Hodgkin's lymphoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol Off J Eur Soc Med Oncol* 2014; **25**: iii70-75.
6. Follows GA, Ardeshna KM, Barrington SF et al. Guidelines for the first line management of classical Hodgkin lymphoma. Br J Haematol 2014; **166**: 34–49.
7. Hoppe RT, Advani RH, Ai WZ et al. Hodgkin Lymphoma Version 1.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Cancer Netw JNCCN* 2017; **15**: 608–638.
8. Mehta-Shah N, Ito K, Bantilan K et al. Baseline and interim functional imaging with PET effectively risk stratifies patients with peripheral T-cell lymphoma. *Blood Adv* 2019; **3**: 187–197.
9. Metser U, Prica A, Hodgson DC et al. Effect of PET/CT on the Management and Outcomes of Participants with Hodgkin and Aggressive Non-Hodgkin Lymphoma: A Multicenter Registry. *Radiology* 2019; **290**: 488–495.
10. Specht L, Yahalom J, Illidge T et al. Modern radiation therapy for Hodgkin lymphoma: field and dose guidelines from the international lymphoma radiation oncology group (ILROG). Int *J Radiat Oncol Biol Phys* 2014; **89**: 854–862.
11. Voltin C-A, Goergen H, Baues C et al. Value of bone marrow biopsy in Hodgkin lymphoma patients staged by FDG PET: results from the German Hodgkin Study Group trials HD16, HD17, and HD18. *Ann Oncol Off J Eur Soc Med Oncol* 2018; **29**: 1926–1931.
12. André MPE, Girinsky T, Federico M et al. Early Positron Emission Tomography Response-Adapted Treatment in Stage I and II Hodgkin Lymphoma: Final Results of the Randomized EORTC/LYSA/FIL H10 Trial. *J Clin Oncol Off J Am Soc Clin Oncol* 2017; **35**: 1786–1794.

13. Barrington SF, Kluge R. FDG PET for therapy monitoring in Hodgkin and non-Hodgkin lymphomas. *Eur J Nucl Med Mol Imaging* 2017; **44**: 97–110.
14. Borchmann P, Goergen H, Kobe C et al. PET-guided treatment in patients with advanced-stage Hodgkin's lymphoma (HD18): final results of an open-label, international, randomised phase 3 trial by the German Hodgkin Study Group. *Lancet Lond Engl* 2017; **390**: 2790–2802.
15. Borchmann P, Plütschow A, Kobe C et al. PET-guided omission of radiotherapy in early-stage unfavourable Hodgkin lymphoma (GHSG HD17): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol* 2021; **22**: 223–234.
16. Casasnovas R-O, Bouabdallah R, Brice P et al. PET-adapted treatment for newly diagnosed advanced Hodgkin lymphoma (AHL2011): a randomised, multicentre, non-inferiority, phase 3 study. *Lancet Oncol* 2019; **20**: 202–215.
17. Eertink JJ, Burggraaff CN, Heymans MW et al. Optimal timing and criteria of interim PET in DLBCL: a comparative study of 1692 patients. *Blood Adv* 2021; **5**: 2375–2384.
18. Engert A, Haverkamp H, Kobe C et al. Reduced-intensity chemotherapy and PET-guided radiotherapy in patients with advanced stage Hodgkin's lymphoma (HD15 trial): a randomised, open-label, phase 3 non-inferiority trial. *Lancet Lond Engl* 2012; **379**: 1791–1799.
19. Freeman CL, Savage KJ, Villa DR et al. Long-term results of PET-guided radiation in patients with advanced-stage diffuse large B-cell lymphoma treated with R-CHOP. *Blood* 2021; **137**: 929–938.
20. Fuchs M, Goergen H, Kobe C et al. Positron Emission Tomography-Guided Treatment in Early-Stage Favorable Hodgkin Lymphoma: Final Results of the International, Randomized Phase III HD16 Trial by the German Hodgkin Study Group. *J Clin Oncol Off J Am Soc Clin Oncol* 2019; **37**: 2835–2845.
21. Johnson P, Federico M, Kirkwood A et al. Adapted Treatment Guided by Interim PET-CT Scan in Advanced Hodgkin's Lymphoma. *N Engl J Med* 2016; **374**: 2419–2429.
22. Mamot C, Klingbiel D, Hitz F et al. Final Results of a Prospective Evaluation of the Predictive Value of Interim Positron Emission Tomography in Patients With Diffuse Large B-Cell Lymphoma Treated With R-CHOP-14 (SAKK 38/07). *J Clin Oncol Off J Am Soc Clin Oncol* 2015; **33**: 2523–2529.
23. Radford J, Illidge T, Counsell N et al. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. *N Engl J Med* 2015; **372**: 1598–1607.
24. Trotman J, Barrington SF, Belada D et al. Prognostic value of end-of-induction PET response after first-line immunochemotherapy for follicular lymphoma (GALLIUM): secondary analysis of a randomised, phase 3 trial. *Lancet Oncol* 2018; **19**: 1530–1542.
25. Rogasch JMM, Boellaard R, Pike L et al. Moving the goalposts while scoring-the dilemma posed by new PET technologies. *Eur J Nucl Med Mol Imaging* 2021; **48**: 2696–2710.
26. Mir F, Barrington SF, Brown H et al. Baseline SUVmax did not predict histological transformation in follicular lymphoma in the phase 3 GALLIUM study. *Blood* 2020; **135**: 1214–1218.
27. Dann EJ, Berkahn L, Mashiach T et al. Hodgkin lymphoma patients in first remission: routine positron emission tomography/computerized tomography imaging is not superior to clinical follow-up for patients with no residual mass. *Br J Haematol* 2014; **164**: 694–700.
28. Huntington SF, Svoboda J, Doshi JA. Cost-effectiveness analysis of routine surveillance imaging of patients with diffuse large B-cell lymphoma in first remission. *J Clin Oncol Off J Am Soc Clin Oncol* 2015; **33**: 1467–1474.
29. El-Galaly TC, Mylam KJ, Bøgsted M et al. Role of routine imaging in detecting recurrent lymphoma: A review of 258 patients with relapsed aggressive non-Hodgkin and Hodgkin lymphoma. *Am J Hematol* 2014; **89**: 575–580.
30. Moskowitz CH, Matasar MJ, Zelenetz AD et al. Normalization of pre-ASCT, FDG-PET imaging with second-line, non-cross-resistant, chemotherapy programs improves event-free survival in patients with Hodgkin lymphoma. *Blood* 2012; **119**: 1665–1670.
31. Sauter CS, Matasar MJ, Meikle J et al. Prognostic value of FDG-PET prior to autologous stem cell transplantation for relapsed and refractory diffuse large B-cell lymphoma. *Blood* 2015; **125**: 2579–2581.

Myeloma[a]

- Work-up of patients with newly diagnosed, relapsed or refractory multiple myeloma [b,c] .[1-5]
- Work-up of patients with a solitary extramedullary plasmacytoma, as well as in cases of solitary bone plasmacytoma if whole-body MRI is not available or contraindicated.[5]
- Distinguish between smouldering and active myeloma.[1,5]
- Monitor the effects of treatment.[1,5-8]

References

1. Cavo M, Terpos E, Nanni C et al. Role of 18F-FDG PET/CT in the diagnosis and management of multiple myeloma and other plasma cell disorders: a consensus statement by the International Myeloma Working Group. *Lancet Oncol* 2017; **18**: e206–e217.
2. Lecouvet FE, Boyadzhiev D, Collette L et al. MRI versus 18F-FDG-PET/CT for detecting bone marrow involvement in multiple myeloma: diagnostic performance and clinical relevance. *Eur Radiol* 2020; **30**: 1927–1937.
3. Mesguich C, Hulin C, Latrabe V et al. Prospective comparison of 18-FDG PET/CT and whole-body diffusion-weighted MRI in the assessment of multiple myeloma. *Ann Hematol* 2020; **99**: 2869–2880.
4. The National Institute for Health and Care Excellence. Myeloma: diagnosis and management. 2018. *https://www.nice.org.uk/guidance/ng35* (accessed 2021-02-15).
5. Hillengass J, Usmani S, Rajkumar SV et al. International myeloma working group consensus recommendations on imaging in monoclonal plasma cell disorders. *Lancet Oncol* 2019; **20**: e302–e312.
6. Moreau P, Attal M, Caillot D et al. Prospective Evaluation of Magnetic Resonance Imaging and [18F] Fluorodeoxyglucose Positron Emission Tomography-Computed Tomography at Diagnosis and Before Maintenance Therapy in Symptomatic Patients With Multiple Myeloma Included in the IFM/DFCI 2009 Trial: Results of the IMAJEM Study. *J Clin Oncol Off J Am Soc Clin Oncol* 2017; **35**: 2911–2918.
7. Stolzenburg A, Lückerath K, Samnick S et al. Prognostic value of [18F]FDG-PET/CT in multiple myeloma patients before and after allogeneic hematopoietic cell transplantation. E*ur J Nucl Med Mol Imaging* 2018; **45**: 1694–1704.
8. Jung S-H, Kwon SY, Min J-J et al. 18F-FDG PET/CT is useful for determining survival outcomes of patients with multiple myeloma classified as stage II and III with the Revised International Staging System. *Eur J Nucl Med Mol Imaging* 2019; **46**: 107–115.
9. Basha MAA, Hamed MAG, Refaat R et al. Diagnostic performance of 18F-FDG PET/CT and whole-body MRI before and early after treatment of multiple myeloma: a prospective comparative study. Jpn J *Radiol* 2018; **36**: 382–393.
10. Messiou C, Porta N, Sharma B et al. Prospective Evaluation of Whole-Body MRI versus FDG PET/CT for Lesion Detection in Participants with Myeloma. *Radiol Imaging Cancer* 2021; **3**: e210048.

a According to the International Myeloma Working Group recommendations.
b In accordance with NICE guidance on 'Myeloma: diagnosis and management' (NG35) for cases of suspected myeloma whole-body MRI is the preferred first-line imaging method, but for cases of already diagnosed myeloma, whole-body imaging with either CT, MRI or [^{18}F]FDG PET-CT (depending on local availability) should be considered.
c Whole-body MRI is more sensitive than [^{18}F]FDG PET-CT in the diagnosis of multiple myeloma before treatment, however, [^{18}F]FDG PET-CT is more specific than whole-body MRI in detecting residual disease in treated patients.[9,10]

Skin tumours

- Staging of patients with known disseminated melanoma to assess extent of disease prior to treatment.[1-13]
- To assess for distant disease in patients with melanoma when radical dissection is contemplated (nodal or metastatic disease).[2]
- To assess response to isolated limb infusion for malignant melanoma.[13]
- [^{18}F]FDG PET-CT is a useful non-invasive tool in the work-up of locally advanced (unresectable) and metastatic Merkel cell carcinoma, providing information for initial staging, therapy response evaluation, and monitoring of recurrent disease.[14-20]
- To exclude systemic involvement in skin lymphomas and exclude large cell transformation in mycosis fungoides.[21,22,23]
- To exclude primary malignancy where dermatomyositis suspected to represent a paraneoplastic manifestation.[24]
- Response assessment to immunomodulatory therapy for melanoma.[25,26]
  Not indicated for early-stage patients who should undergo sentinel node biopsy.[27]

References

1. Steinert HC. PET and PET/CT of Malignant Melanoma. In: Dummer R, Pittelkow MR, Iwatsuki K, Green A, Elwan NM (eds). Skin Cancer - A World-Wide Perspective. Springer Berlin Heidelberg: Berlin, *Heidelberg,* 2010, pp 379–390.
2. Aukema TS, Valdés Olmos RA, Wouters MWJM et al. Utility of preoperative 18F-FDG PET/CT and brain MRI in melanoma patients with palpable lymph node metastases. *Ann Surg Oncol* 2010; **17**: 2773–2778.
3. Friedman KP, Wahl RL. Clinical use of positron emission tomography in the management of cutaneous melanoma. *Semin Nucl Med* 2004; 34: 242–253.
4. Mijnhout GS, Hoekstra OS, van Tulder MW, Teule GJ, Devillé WL. Systematic review of the diagnostic accuracy of (18)F-fluorodeoxyglucose positron emission tomography in melanoma patients. *Cancer* 2001; **91**: 1530–1542.
5. Strobel K, Dummer R, Husarik DB, Pérez Lago M, Hany TF, Steinert HC. High-risk melanoma: accuracy of FDG PET/CT with added CT morphologic information for detection of metastases. *Radiology* 2007; **244**: 566–574.
6. Xing Y, Bronstein Y, Ross MI et al. Contemporary diagnostic imaging modalities for the staging and surveillance of melanoma patients: a meta-analysis. *J Natl Cancer Inst* 2011; **103**: 129–142.
7. Bastiaannet E, Uyl-de Groot CA, Brouwers AH et al. Cost-effectiveness of adding FDG-PET or CT to the diagnostic work-up of patients with stage III melanoma. *Ann Surg* 2012; **255**: 771–776.
8. Subesinghe M, Marples M, Scarsbrook AF, Smith JT. Clinical impact of (18)F-FDG PET-CT in recurrent stage III/IV melanoma: a tertiary centre Specialist Skin Cancer Multidisciplinary Team (SSMDT) experience. *Insights Imaging* 2013; **4**: 701–709.
9. Bisschop C, de Heer EC, Brouwers AH, Hospers G a. P, Jalving M. Rational use of 18F-FDG PET/CT in patients with advanced cutaneous melanoma: A systematic review. *Crit Rev Oncol Hematol* 2020; **153**: 103044.
10. Groen LC, Lazarenko SV, Schreurs HW, Richir MC. Evaluation of PET/CT in patients with stage III malignant cutaneous melanoma. *Am J Nucl Med Mol Imaging* 2019; **9**: 168–175.
11. Howard MD. Melanoma Radiological Surveillance: A Review of Current Evidence and Clinical Challenges. *Yale J Biol Med* 2020; **93**: 207–213.

12. Dinnes J, Ferrante di Ruffano L, Takwoingi Y et al. Ultrasound, CT, MRI, or PET-CT for staging and re-staging of adults with cutaneous melanoma. *Cochrane Database Syst Rev* 2019; **7**: CD012806.
13. Beasley GM, Parsons C, Broadwater G et al. A multicenter prospective evaluation of the clinical utility of F-18 FDG-PET/CT in patients with AJCC stage IIIB or IIIC extremity melanoma. *Ann Surg* 2012; **256**: 350–356.
14. Concannon R, Larcos GS, Veness M. The impact of (18)F-FDG PET-CT scanning for staging and management of Merkel cell carcinoma: results from Westmead Hospital, Sydney, Australia. *J Am Acad Dermatol* 2010; **62**: 76–84.
15. Treglia G, Kakhki VRD, Giovanella L, Sadeghi R. Diagnostic performance of fluorine-18-fluorodeoxyglucose positron emission tomography in patients with Merkel cell carcinoma: a systematic review and meta-analysis. *Am J Clin Dermatol* 2013; **14**: 437–447.
16. Hawryluk EB, O'Regan KN, Sheehy N et al. Positron emission tomography/computed tomography imaging in Merkel cell carcinoma: a study of 270 scans in 97 patients at the Dana-Farber/Brigham and Women's Cancer Center. *J Am Acad Dermatol* 2013; **68**: 592–599.
17. Siva S, Byrne K, Seel M et al. 18F-FDG PET provides high-impact and powerful prognostic stratification in the staging of Merkel cell carcinoma: a 15-year institutional experience. *J Nucl Med Off Publ Soc Nucl Med* 2013; **54**: 1223–1229.
18. Byrne K, Siva S, Chait L et al. 15-Year Experience of 18F-FDG PET Imaging in Response Assessment and Restaging After Definitive Treatment of Merkel Cell Carcinoma. *J Nucl Med Off Publ Soc Nucl Med* 2015; **56**: 1328–1333.
19. Singh N, Alexander NA, Lachance K et al. Clinical benefit of baseline imaging in Merkel cell carcinoma: Analysis of 584 patients. *J Am Acad Dermatol* 2021; **84**: 330–339.
20. Sachpekidis C, Sidiropoulou P, Hassel JC, Drakoulis N, Dimitrakopoulou-Strauss A. Positron Emission Tomography in Merkel Cell Carcinoma. *Cancers* 2020; **12**: E2897.
21. Feeney J, Horwitz S, Gönen M, Schöder H. Characterization of T-cell lymphomas by FDG PET/CT. *AJR Am J Roentgenol* 2010; **195**: 333–340.
22. Spaccarelli N, Gharavi M, Saboury B, Cheng G, Rook AH, Alavi A. Role of (18)F-fluorodeoxyglucose positron emission tomography imaging in the management of primary cutaneous lymphomas. *Hell J Nucl Med* 2014; **17**: 78–84.
23. Duncan JR, Carr D, Kaffenberger BH. The utility of positron emission tomography with and without computed tomography in patients with nonmelanoma skin cancer. *J Am Acad Dermatol* 2016; **75**: 186–196.
24. Sheikhbahaei S, Marcus CV, Fragomeni RS, Rowe SP, Javadi MS, Solnes LB. Whole-Body 18F-FDG PET and 18F-FDG PET/CT in Patients with Suspected Paraneoplastic Syndrome: A Systematic Review and Meta-Analysis of Diagnostic Accuracy. *J Nucl Med Off Publ Soc Nucl Med* 2017; **58**: 1031–1036.
25. Lang D, Wahl G, Poier N et al. Impact of PET/CT for Assessing Response to Immunotherapy-A Clinical Perspective. *J Clin Med* 2020; **9**: E3483.
26. Dimitrakopoulou-Strauss A. Monitoring of patients with metastatic melanoma treated with immune checkpoint inhibitors using PET-CT. *Cancer Immunol Immunother CII* 2019; **68**: 813–822.
27. Singh B, Ezziddin S, Palmedo H et al. Preoperative 18F-FDG-PET/CT imaging and sentinel node biopsy in the detection of regional lymph node metastases in malignant melanoma. *Melanoma Res* 2008; **18**: 346–352.

Musculoskeletal tumours

- Staging of high-grade sarcomas (e.g., Ewing's sarcoma, rhabdomyosarcoma, osteosarcoma), unless already proven to have metastatic disease.[1–4]
- In the pre-amputation setting of a high-grade sarcoma where detection of distant disease will alter the surgical management.[5]
- Staging of 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.[1,6]
- Treatment response assessment in high-grade sarcomas.[1,2,7,8]
- Follow-up assessment post surgical treatment (ie, operative bed surveillance for local recurrence), particularly in cases where metallic orthopaedic implants preclude or complicate conventional imaging.[9]
- Aid in differentiation of equivocal findings from conventional imaging in selected cases[a].[1,6]
- Assessment of suspected malignant transformation within plexiform neurofibromas in patients with neurofibromatosis type 1, particularly with dual-time-point imaging[b].[10,11]

References

1. Lakkaraju A, Patel CN, Bradley KM, Scarsbrook AF. PET/CT in primary musculoskeletal tumours: a step forward. *Eur Radiol* 2010; **20**: 2959–2972.
2. Nanni C, Marzola MC, Rubello D, Fanti S. Positron emission tomography for the evaluation of soft-tissue sarcomas and bone sarcomas. *Eur J Nucl Med Mol Imaging* 2009; **36**: 1940–1943.
3. Strauss SJ, Frezza AM, Abecassis N et al. Bone sarcomas: ESMO–EURACAN–GENTURIS–ERN PaedCan Clinical Practice Guideline for diagnosis, treatment and follow-up. *Ann Oncol* 2021; **32**: 1520–1536.
4. Zhang Q, Xi Y, Li D, Yuan Z, Dong J. The utility of 18F-FDG PET and PET/CT in the diagnosis and staging of chondrosarcoma: a meta-analysis. *J Orthop Surg* 2020; **15**: 229.
5. Sambri A, Bianchi G, Longhi A et al. The role of 18F-FDG PET/CT in soft tissue sarcoma. *Nucl Med Commun* 2019; **40**: 626–631.
6. Gronchi A, Miah AB, Dei Tos AP et al. Soft tissue and visceral sarcomas: ESMO-EURACAN-GENTURIS Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol Off J Eur Soc Med Oncol* 2021; **32**: 1348–1365.
7. Fendler WP, Lehmann M, Todica A et al. PET response criteria in solid tumors predicts progression-free survival and time to local or distant progression after chemotherapy with regional hyperthermia for soft-tissue sarcoma. *J Nucl Med Off Publ Soc Nucl Med* 2015; **56**: 530–537.
8. Palmerini E, Colangeli M, Nanni C et al. The role of FDG PET/CT in patients treated with neoadjuvant chemotherapy for localized bone sarcomas. *Eur J Nucl Med Mol Imaging* 2017; **44**: 215–223.
9. Garner HW, Kransdorf MJ. Musculoskeletal Sarcoma: Update on Imaging of the Post-treatment Patient. *Can Assoc Radiol J J Assoc Can Radiol* 2016; **67**: 12–20.
10. Warbey VS, Ferner RE, Dunn JT, Calonje E, O'Doherty MJ. [18F]FDG PET/CT in the diagnosis of malignant peripheral nerve sheath tumours in neurofibromatosis type-1. Eur J Nucl Med Mol Imaging 2009; **36**: 751–757.
11. Chirindel A, Chaudhry M, Blakeley JO, Wahl R. 18F-FDG PET/CT qualitative and quantitative evaluation in neurofibromatosis type 1 patients for detection of malignant transformation: comparison of early to delayed imaging with and without liver activity normalization. *J Nucl Med Off Publ Soc Nucl Med* 2015; **56**: 379–385.

a While [^{18}F]FDG PET-CT may be helpful for differentiating between benign and malignant findings, there can be considerable overlap.
b Additional delayed imaging recommended at four hours when there is initial [^{18}F]FDG uptake at 60–90 minutes.

Neuroendocrine tumours

- Staging or restaging (including pre-operative assessments) of selected patients with poorly differentiated neuroendocrine tumours (NETs) including phaeochromocytoma and paraganglioma (in particular those with succinate dehydrogenase mutations) prior to treatment with negative somatostatin receptor imaging with single photon techniques or [^{68}Ga]Ga-DOTA-TOC or [^{68}Ga]Ga-DOTA-TATE PET-CT.[1-8]
- Staging of well-differentiated neuroendocrine tumour with lesion(s) showing rapid progression.[1-8]
- Staging of well-differentiated neuroendocrine tumour with lesion(s) on cross-sectional imaging that is negative on SSR imaging to evaluate for secondary pathology or dedifferentiation.[1-8]
- Identify patients who are unlikely to respond to ^{177}Lu-DOTATATE therapy (ie, discordant lesions that are SSR negative and FDG positive).[9-11]
- Risk stratification of well-differentiated NETs for treatment planning.[5,7,9,10-14]
- Assessment of possible multifocal disease in patients with paraganglioma considered for surgery in combination with [^{68}Ga]Ga-DOTA-TOC or [^{68}Ga]Ga-DOTA-TATE PET-CT.[4,5,15]
- Assessment of selected patients with adrenocortical carcinoma being considered for invasive treatment where cross-sectional imaging is inconclusive.[16]

References

1. Binderup T, Knigge U, Loft A et al. Functional imaging of neuroendocrine tumors: a head-to-head comparison of somatostatin receptor scintigraphy, 123I-MIBG scintigraphy, and 18F-FDG PET. *J Nucl Med* 2010; **51**: 704–712.
2. Sato A, Masui T, Yogo A et al. Usefulness of 18 F-FDG-PET/CT in the diagnosis and prediction of recurrence of pancreatic neuroendocrine neoplasms. *J Hepatobiliary Pancreat Sci* 2020; **27**: 414–420.
3. Cingarlini S, Ortolani S, Salgarello M et al. Role of Combined 68Ga-DOTATOC and 18F-FDG Positron Emission Tomography/Computed Tomography in the Diagnostic Workup of Pancreas Neuroendocrine Tumors: Implications for Managing Surgical Decisions. *Pancreas* 2017; **46**: 42–47..
4. Nockel P, El Lakis M, Gaitanidis A et al. Preoperative 18F-FDG PET/CT in Pheochromocytomas and Paragangliomas Allows for Precision Surgery. *Ann Surg* 2019; **269**: 741–747
5. Kornaczewski ER, Pointon OP, Burgess JR. Utility of FDG-PET imaging in screening for succinate dehydrogenase B and D mutation-related lesions. *Clin Endocrinol (Oxf)* 2016; **85**: 172–179.
6. Panagiotidis E, Alshammari A, Michopoulou S et al. Comparison of the Impact of 68Ga-DOTATATE and 18F-FDG PET/CT on Clinical Management in Patients with Neuroendocrine Tumors. *J Nucl Med* 2017; **58**: 91–
7. Pencharz D, Gnanasegaran G, Navalkissoor S. Theranostics in neuroendocrine tumours: somatostatin receptor imaging and therapy. *Br J Radiol* 2018; **91**: 20180108
8. Jiang Y, Hou G, Cheng W. The utility of 18F-FDG and 68Ga-DOTA-Peptide PET/CT in the evaluation of primary pulmonary carcinoid: A systematic review and meta-analysis. *Medicine (Baltimore)* 2019; **98**: e14769.
9. Sansovini M, Severi S, Ianniello A et al. Long-term follow-up and role of FDG PET in advanced pancreatic neuroendocrine patients treated with 177Lu-D OTATATE. *Eur J Nucl Med Mol Imaging* 2017; **44**: 490–499.

10. Binderup T, Knigge U, Johnbeck CB et al. 18F-FDG PET is Superior to WHO Grading as a Prognostic Tool in Neuroendocrine Neoplasms and Useful in Guiding PRRT: A Prospective 10-Year Follow-up Study. *J Nucl Med* 2021; **62**: 808–815.
11. Adnan A, Sampathirao N, Basu S. Implications of fluorodeoxyglucose uptake in low-intermediate grade metastatic neuroendocrine tumors from peptide receptor radionuclide therapy outcome viewpoint: A semi-quantitative standardized uptake value-based analysis. World *J Nucl Med* 2019; **18**: 389–395.
12. Panagiotidis E, Alshammari A, Michopoulou S et al. Comparison of the Impact of 68Ga-DOTATATE and 18F-FDG PET/CT on Clinical Management in Patients with Neuroendocrine Tumors. *J Nucl Med* 2017; **58**: 91–96.
13. Zhang J, Liu Q, Singh A, Schuchardt C, Kulkarni HR, Baum RP. Prognostic Value of 18F-FDG PET/CT in a Large Cohort of Patients with Advanced Metastatic Neuroendocrine Neoplasms Treated with Peptide Receptor Radionuclide Therapy. *J Nucl Med* 2020; **61**: 1560–1569.
14. Binderup T, Knigge U, Johnbeck CB et al. 18F-FDG PET is Superior to WHO Grading as a Prognostic Tool in Neuroendocrine Neoplasms and Useful in Guiding PRRT: A Prospective 10-Year Follow-up Study. *J Nucl Med* 2021; **62**: 808–815.
15. Jha A, de Luna K, Balili CA et al. Clinical, Diagnostic, and Treatment Characteristics of SDHA-Related Metastatic Pheochromocytoma and Paraganglioma. *Front Oncol* 2019; **9**: 53.
16. Takeuchi S, Balachandran A, Habra MA et al. Impact of 18F-FDG PET/CT on the management of adrenocortical carcinoma: analysis of 106 patients. *Eur J Nucl Med Mol Imaging* 2014; **41**: 2066–2073.

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.[1-8]

References

1. Bannas P, Weber C, Derlin T et al. 18F-FDG-PET/CT in the diagnosis of paraneoplastic neurological syndromes: a retrospective analysis. *Eur Radiol* 2010; **20**: 923–930.
2. Hadjivassiliou M, Alder SJ, Van Beek EJR et al. PET scan in clinically suspected paraneoplastic neurological syndromes: a 6-year prospective study in a regional neuroscience unit. *Acta Neurol Scand* 2009; **119**: 186–193.
3. Patel RR, Subramaniam RM, Mandrekar JN, Hammack JE, Lowe VJ, Jett JR. Occult malignancy in patients with suspected paraneoplastic neurologic syndromes: value of positron emission tomography in diagnosis. *Mayo Clin Proc* 2008; **83**: 917–922.
4. Younes-Mhenni S, Janier MF, Cinotti L et al. FDG-PET improves tumour detection in patients with paraneoplastic neurological syndromes. *Brain* 2004; **127**: 2331–2338.
5. Vaidyanathan S, Pennington C, Ng CY, Poon FW, Han S. 18F-FDG PET-CT in the evaluation of paraneoplastic syndromes: experience at a regional oncology centre. *Nucl Med Commun* 2012; **33**: 872–880.
6. Schramm N, Rominger A, Schmidt C et al. Detection of underlying malignancy in patients with paraneoplastic neurological syndromes: comparison of 18F-FDG PET/CT and contrast-enhanced CT. *Eur J Nucl Med Mol Imaging* 2013; **40**: 1014–1024.
7. Kristensen SB, Hess S, Petersen H, Høilund-Carlsen PF. Clinical value of FDG-PET/CT in suspected paraneoplastic syndromes: a retrospective analysis of 137 patients. *Eur J Nucl Med Mol Imaging* 2015; **42**: 2056–2063.
8. Sheikhbahaei S, Marcus CV, Fragomeni RS, Rowe SP, Javadi MS, Solnes LB. Whole-Body 18F-FDG PET and 18F-FDG PET/CT in Patients with Suspected Paraneoplastic Syndrome: A Systematic Review and Meta-Analysis of Diagnostic Accuracy. *J Nucl Med* 2017; **58**: 1031–1036.

Carcinoma of unknown primary

- Detection of the primary site when imaging and histopathology has failed to show a primary site, where the site of tumour will influence choice of chemotherapy.[1-5]

References

1. Kwee TC, Basu S, Cheng G, Alavi A. FDG PET/CT in carcinoma of unknown primary. E*ur J Nucl Med Mol Imaging* 2010; **37**: 635–644.
2. Fencl P, Belohlavek O, Skopalova M, Jaruskova M, Kantorova I, Simonova K. Prognostic and diagnostic accuracy of [18F]FDG-PET/CT in 190 patients with carcinoma of unknown primary. *Eur J Nucl Med Mol Imaging* 2007; **34**: 1783–1792.
3. Wang G, Wu Y, Zhang W, Li J, Wu P, Xie C. Clinical value of whole-body F-18 fluorodeoxyglucose positron emission tomography/computed tomography in patients with carcinoma of unknown primary. *J Med Imaging Radiat Oncol* 2013; **57**: 65–71.
4. Elboga U, Kervancioğlu S, Sahin E, Basibuyuk M, Celen YZ, Aktolun C. Utility of F-18 fluorodeoxyglucose posıtron emıssıon tomography/computed ın carcınoma of unknown primary. *Int J Clin Exp Pathol* 2014; **7**: 8941–8946.
5. Li Y, Li F, Li X, Qu L, Han J. Value of 18F-FDG PET/CT in patients with hepatic metastatic carcinoma of unknown primary. *Medicine (Baltimore)* 2020; **99**: e23210.

Non-oncological applications

Neurological indications

Dementia and other neurodegenerative disorders[a]

- To assess progressive cognitive decline where Alzheimer's dementia (AD) or frontotemporal dementia (FTD) are possible diagnoses if structural imaging (e.g., MRI, CT) has been inconclusive and clinical suspicion for dementia remains high, particularly in cases of early symptom onset or atypical presentation.[1-8]
- Aid differential diagnosis of dementia types (e.g, AD versus FTD) and subtypes based on disease-specific patterns of glucose hypometabolism with the understanding that diagnostic overlap may still persist.[1, 3, 4, 6-11]
- Monitor progression of neurodegenerative diseases in highly selected cases (e.g., borderline abnormal scans), as an adjunct to clinical evaluation and cognitive assessment tools [b.1, 10]
- Adjunct in differentiation of degenerative parkinsonism, particularly if associated with cognitive impairment in combination with dopamine transporter radionuclide imaging methods and/or ^{123}I-metaiodobenzylguanidine (mIBG).[12-17]
- Consider when conventional neuroimaging (ie, MRI, CT) is inconclusive, but the clinical impression of an underlying neurodegenerative disorder warrants further assessment, namely in progressive speech disorders (e.g., primary progressive aphasia)[6], differential diagnosis between depressive pseudo-dementia and neurodegeneration disorders[6], HIV-associated neurocognitive disorder (HAND)[18,19] and so on.

See below for amyloid imaging which may be helpful in highly selected patients with suspected dementia.

References

1. Berti V, Pupi A, Mosconi L. PET/CT in diagnosis of dementia. *Ann N Y Acad Sci* 2011; 1228: 81–92.
2. Daniela P, Orazio S, Alessandro P et al. A Survey of FDG- and Amyloid-PET Imaging in Dementia and GRADE Analysis. *Biomed Res* Int 2014; 2014: 1–22.
3. Shivamurthy VKN, Tahari AK, Marcus C, Subramaniam RM. Brain FDG PET and the Diagnosis of Dementia. *AJR Am J Roentgenol* 2015; **204**: W76–W85.
4. Iaccarino L, Sala A, Caminiti SP, Perani D. The emerging role of PET imaging in dementia. F1000Res 2017; **6**: 1830.
5. Arbizu J, Festari C, Altomare D et al. Clinical utility of FDG-PET for the clinical diagnosis in MCI. *Eur J Nucl Med Mol Imaging* 2018; **45**: 1497–1508.
6. Nobili F, Arbizu J, Bouwman F et al. European Association of Nuclear Medicine and European Academy of Neurology recommendations for the use of brain 18 F-fluorodeoxyglucose positron emission tomography in neurodegenerative cognitive impairment and dementia: Delphi consensus. *Eur J Neurol* 2018; **25**: 1201–1217.
7. Tripathi SM, Murray AD. Alzheimer's Dementia: The Emerging Role of Positron Emission Tomography. *Neuroscientist 2021*; 107385842199703.

a FDG PET-CT is indicated if structural brain imaging with MRI (or CT if MRI is contraindicated) is normal or inconclusive and clinical suspicion for a neurodegenerative disorder remains high.
b Based on established clinical practice functional neuroimaging at intervals of 12-24 months is suggested for monitoring progression of neurodegeneration.

8. Perini G, Rodriguez-Vieitez E, Kadir A, Sala A, Savitcheva I, Nordberg A. Clinical impact of 18F-FDG-PET among memory clinic patients with uncertain diagnosis. *Eur J Nucl Med Mol Imaging* 2021; **48**: 612–622.
9. Foster NL, Heidebrink JL, Clark CM et al. FDG-PET improves accuracy in distinguishing frontotemporal dementia and Alzheimer's disease. *Brain* 2007; **130**: 2616–2635.
10. Herholz K, Carter SF, Jones M. Positron emission tomography imaging in dementia. *BJR 2007*; **80**: S160–S167.
11. Varrone A, Asenbaum S, Vander Borght T et al. EANM procedure guidelines for PET brain imaging using [18F]FDG, version 2. *Eur J Nucl Med Mol Imaging* 2009; **36**: 2103–2110.
12. Berti V, Pupi A, Mosconi L. PET/CT in diagnosis of movement disorders. *Ann N Y Acad Sci* 2011; **1228**: 93–108.
13. Garibotto V, Montandon ML, Viaud CT et al. Regions of Interest–Based Discriminant Analysis of DaTSCAN SPECT and FDG-PET for the Classification of Dementia. *Clin Nucl Med* 2013; **38**: e112–e117.
14. Kang SW, Jeon S, Lee Y et al. Implication of metabolic and dopamine transporter PET in dementia with Lewy bodies. *Sci Rep* 2021; **11**: 14394.
15. Meyer PT, Frings L, Rücker G, Hellwig S. 18F-FDG PET in Parkinsonism: Differential Diagnosis and Evaluation of Cognitive Impairment. *J Nucl Med* 2017; **58**: 1888–1898.
16. McKeith IG, Boeve BF, Dickson DW et al. Diagnosis and management of dementia with Lewy bodies: Fourth consensus report of the DLB Consortium. *Neurology* 2017; **89**: 88–100.
17. Minoshima S, Mosci K, Cross D, Thientunyakit T. Brain [F-18]FDG PET for Clinical Dementia Workup: Differential Diagnosis of Alzheimer's Disease and Other Types of Dementing Disorders. *Semin Nucl Med* 2021; **51**: 230–240.
18. Vera JH, Ridha B, Gilleece Y, Amlani A, Thorburn P, Dizdarevic S. PET brain imaging in HIV-associated neurocognitive disorders (HAND) in the era of combination antiretroviral therapy. *Eur J Nucl Med Mol Imaging* 2017; **44**: 895–902.
19. Sinharay S, Hammoud DA. Brain PET Imaging: Value for Understanding the Pathophysiology of HIV-associated Neurocognitive Disorder (HAND). *Curr HIV/AIDS Rep* 2019; **16**: 66–75.

Epilepsy

- Localisation of epileptogenic focus (especially when co-registered with MRI[a]), both in the paediatric and adult population.[1-4]
- Pre-surgical assessment of drug resistant focal epilepsy and complex partial seizures.[3-8]

References

1. Desarnaud S, Mellerio C, Semah F et al. 18F-FDG PET in drug-resistant epilepsy due to focal cortical dysplasia type 2: additional value of electroclinical data and coregistration with MRI. *Eur J Nucl Med Mol Imaging* 2018; **45**: 1449–1460.
2. Niu N, Xing H, Wu M et al. Performance of PET imaging for the localization of epileptogenic zone in patients with epilepsy: a meta-analysis. *Eur Radiol* 2021; **31**: 6353–6366.
3. Tian M, Watanabe Y, Kang KW et al. International consensus on the use of [18F]-FDG PET/CT in pediatric patients affected by epilepsy. *Eur J Nucl Med Mol Imaging* 2021; **48**: 3827–3834.
4. Guedj E, Varrone A, Boellaard R et al. EANM procedure guidelines for brain PET imaging using [18F] FDG, version 3. *Eur J Nucl Med Mol Imaging* 2021.
5. Jayakar P, Gaillard WD, Tripathi M et al. Diagnostic test utilization in evaluation for resective epilepsy surgery in children. *Epilepsia* 2014; **55**: 507–518.
6. Tóth M, Barsi P, Tóth Z et al. The role of hybrid FDG-PET/MRI on decision-making in presurgical evaluation of drug-resistant epilepsy. *BMC Neurol* 2021; **21**: 363.
7. Willmann O, Wennberg R, May T, Woermann FG, Pohlmann-Eden B. The contribution of 18F-FDG PET in preoperative epilepsy surgery evaluation for patients with temporal lobe epilepsy A meta-analysis. *Seizure* 2007; **16**: 509–520.
8. O'Brien TJ, Miles K, Ware R, Cook MJ, Binns DS, Hicks RJ. The cost-effective use of 18F-FDG PET in the presurgical evaluation of medically refractory focal epilepsy. *J Nucl Med Off Publ Soc Nucl Med* 2008; **49**: 931–937.

Encephalitis

- Diagnosis of autoimmune encephalitis and differentiation of its subtypes.[1,2]

References

1. Bordonne M, Chawki MB, Doyen M et al. Brain 18F-FDG PET for the diagnosis of autoimmune encephalitis: a systematic review and a meta-analysis. *Eur J Nucl Med Mol Imaging* 2021; **48**: 3847–3858.
2. Guedj E, Varrone A, Boellaard R et al. EANM procedure guidelines for brain PET imaging using [18F] FDG, version 3. *Eur J Nucl Med Mol Imaging* 2021.

a PET-MRI if available is preferable to PET-CT.

Cardiological indications[a]

- ***Assessment of myocardial hibernation and viability*** in patients with ischaemic heart failure and poor left ventricular function being considered for revascularisation, usually in combination with perfusion imaging with sestamibi/tetrofosmin or ammonia/rubidium. Preparation with glucose loading and short-acting insulin titrated according to blood glucose level enhances FDG delivery to the chronically ischaemic myocardium.[1,2]
  - ***Cardiac Inflammation*** - The cardiological applications are increasing due to wider awareness and complex clinical scenarios in inflammation and infection imaging requirements. FDG PET-CT can provide important information that may not be evident on other non-invasive imaging techniques but requires specific pre-procedural preparation and careful interpretation[9] with knowledge of possible artifacts in a multi-disciplinary team environment.

    To suppress normal physiological FDG uptake in normal myocardium specific dietary manipulation (high fat, no carbohydrate diet) for 12-24 hours and prolonged fast (12-18 hours) with or without Heparin before FDG scan is recommended whenever inflammation/infection in the myocardium is suspected.
  - ***Sarcoidosis diagnosis*** - FDG PET-CT aids in the diagnostic process of sarcoidosis, especially when conventional tests are inconclusive. In addition, FDG PET-CT reveals treatable active disease, particularly in heart, lungs and other extra-cardiac sites such as lymph nodes which help to get tissue diagnosis.[3-5] This may be performed in combination with resting perfusion imaging to assess perfusion metabolism mismatch which is of prognostic importance in cardiac sarcoidosis. Important pre-requisites are exclusion of coronary artery disease.
  - ***Treatment Response*** – FDG PET with SUV quantitation and in conjunction with myocardial perfusion imaging is useful to detect myocardial inflammation and monitor progression of scar and inflammation and assess response to active immunosuppressive therapies in cardiac sarcoidosis.[4]
  - ***Myocarditis*** - Assessment of suspected myocarditis in difficult cases where other modalities such as cardiac MRI are uncertain and where diagnosis is likely to impact patient management, e.g. viral, drug induced myocarditis.[6]
- ***Cardiac Infection***
- ***Infective Endocarditis (IE)*** – PET-CT is a useful adjunctive diagnostic tool in the evaluation of diagnostically challenging cases of IE, particularly in prosthetic valve endocarditis.[7,8] It also has the potential to detect clinically relevant extra-cardiac foci of infection, malignancy and other sources of inflammation leading to more appropriate treatment regimens and surgical intervention.[8]

  Caution must be exercised when interpreting [^{18}F]FDG PET-CT results in patients who have recently undergone cardiac surgery, as a postoperative inflammatory response may result in non-specific FDG uptake in the immediate postoperative period. Furthermore, several pathological conditions can mimic the pattern of focally increased uptake that is typically observed in IE, such as active thrombi, soft atherosclerotic plaques, vasculitis, primary cardiac tumours and metastasis, post-surgical inflammation and foreign body reactions.

a PET-CT may also be helpful as a complementary imaging tool for assessment of cardiac masses and extra-cardiac involvement in cases of suspected rheumatological cardiac conditions, but evidence in this area is still evolving.

Septic emboli appear as focal areas of FDG uptake and are typically located in the spleen, liver, lungs and kidneys. Uptake at the inter-vertebral disks and/or the vertebral bone (spondylodiscitis) suggests metastatic infection, which can also be observed in muscles and joints.

- ***Cardiac Implantable device Infection*** - FDG PET-CT is useful to identify infection in generator pocket of pacemaker, defibrillator and left ventricular assist devices and its components.[9,10,11] Diet and fasting are necessary when normal myocardial uptake is likely to interfere with interpretation or infection is suspected within the heart. Caution should be exercised in interpretation for about two months post implantation due to inflammatory response. Attenuation corrected and non-corrected images should be viewed concurrently.

References

1. Ghosh N, Rimoldi OE, Beanlands RSB, Camici PG. Assessment of myocardial ischaemia and viability: role of positron emission tomography. *Eur Heart J* 2010; **31**: 2984–2995.
2. Schinkel AFL, Bax JJ, Delgado V, Poldermans D, Rahimtoola SH. Clinical relevance of hibernating myocardium in ischemic left ventricular dysfunction. *Am J Med* 2010; **123**: 978–986.
3. Keijsers RGM, Grutters JC. In Which Patients with Sarcoidosis Is FDG PET/CT Indicated? *J Clin Med* 2020; **9**: E890.
4. Chareonthaitawee P, Beanlands RS, Chen W et al. Joint SNMMI-ASNC expert consensus document on the role of 18F-FDG PET/CT in cardiac sarcoid detection and therapy monitoring. *J Nucl Cardiol* 2017; **24**: 1741–1758.
5. Slart RHJA, Glaudemans AWJM, Lancellotti P et al. A joint procedural position statement on imaging in cardiac sarcoidosis: from the Cardiovascular and Inflammation & Infection Committees of the European Association of Nuclear Medicine, the European Association of Cardiovascular Imaging, and the American Society of Nuclear Cardiology. *J Nucl Cardiol 2018*; **25**: 298–319.
6. Nensa F, Kloth J, Tezgah E et al. Feasibility of FDG-PET in myocarditis: Comparison to CMR using integrated PET/MRI. *J Nucl Cardiol* 2018; **25**: 785–794.
7. Mahmood M, Kendi AT, Ajmal S et al. Meta-analysis of 18F-FDG PET/CT in the diagnosis of infective endocarditis. *J Nucl Cardiol* 2019; **26**: 922–935.
8. Habib G, Lancellotti P, Antunes MJ et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015; **36**: 3075–3128.
9. Salomäki SP, Saraste A, Kemppainen J et al. 18F-FDG positron emission tomography/computed tomography of cardiac implantable electronic device infections. *J Nucl Cardiol* 2020. DOI:10.1007/s12350-020-02256-4.
10. Mahmood M, Kendi AT, Farid S et al. Role of 18F-FDG PET/CT in the diagnosis of cardiovascular implantable electronic device infections: A meta-analysis. *J Nucl Cardiol* 2019; **26**: 958–970.
11. Slart RHJA, Glaudemans AWJM, Gheysens O et al. Procedural recommendations of cardiac PET/CT imaging: standardization in inflammatory-, infective-, infiltrative-, and innervation- (4Is) related cardiovascular diseases: a joint collaboration of the EACVI and the EANM: summary. *Eur Heart J Cardiovasc Imaging* 2020; **21**: 1320–1330.

Vasculitis

- ***Suspicion of vasculitis***
  - To determine the presence, extent and distribution of active extracranial disease in patients with suspected medium or large vessel vasculitis.[1,4*]
  - To exclude other pathological processes which could result in atypical clinical presentation mimicking vasculitis, such as infection, multisystemic inflammatory disease, malignancies and potential paraneoplatic phenomenon.[5,6]
  - To confirm active extracranial vascular disease in patient with clinical suspicion of vasculitis in which conventional imaging (ultrasonography, CT angiography or magnetic resonance angiography) is negative or equivocal.[1,2,4,**,***]

Notes:

** Withdraw or delay of glucocorticoid (GC) therapy until after FDG PET-CT is suggested, unless there is risk of ischaemic complications, as in the case of GCA with temporal artery involvement. FDG PET-CT within 3 days after start of GC is suggested.*

*** Normal blood glucose levels during FDG PET-CT are desirable, but glucose levels below 7 mmol/L (126 mg/dL) are preferable.*

- **Suspicion of vasculitis relapse (during glucocorticoid taper and/or immunosuppressive therapy)**

  In case of suspicion of vasculitis relapse (vasculitis-related inflammation of the aorta and/or its proximal branches), investigation with FDG PET-CT imaging should be considered.[2]

References

1. Slart RHJA, Writing group, Reviewer group et al. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PIG), and endorsed by the ASNC. *Eur J Nucl Med Mol Imaging* 2018; **45**: 1250–1269.
2. Mackie SL, Dejaco C, Appenzeller S et al. British Society for Rheumatology guideline on diagnosis and treatment of giant cell arteritis. *Rheumatology (Oxford)* 2020; **59**: e1–e23.
3. Basu N, Watts R, Bajema I et al. EULAR points to consider in the development of classification and diagnostic criteria in systemic vasculitis. *Ann Rheum Dis* 2010; **69**: 1744–1750.
4. Hellmich B, Agueda A, Monti S et al. 2018 Update of the EULAR recommendations for the management of large vessel vasculitis. *Ann Rheum Dis* 2020; **79**: 19–30.
5. Sharma AM, Singh S, Lewis JE. Diagnostic approach in patients with suspected vasculitis. *Tech Vasc Interv Radiol* 2014; 17: 226–233.
6. Maningding E, Kermani TA. Mimics of vasculitis. *Rheumatology (Oxford)* 2021; **60**: 34–47.

Infection and inflammatory disorders (excluding sarcoidosis and vasculitis)

- Specific indications where FDG PET-CT may offer advantages over other forms of imaging include the following:
  - suspected implantable cardiac device related infection in selected cases provided sufficient time has elapsed since surgery;[1-3]
  - suspected central or peripheral vascular graft infection; [4-6, a]
  - bone and soft tissue infections in the feet of patients with diabetes mellitus;[5,7]
  - detection of focal site(s) of infection in immunocompromised patients;[5,8]
  - spinal infections;[9]
  - possible multi-resistant tuberculosis especially in HIV positive or otherwise immunocompromised patients;[10-12]
  - post-fracture osteomyelitis.[5,13]
- For diagnosis and prognostication of idiopathic retroperitoneal fibrosis.[14,15]
- May be considered as a problem-solving tool in complex cases of autoimmune disease.[16]

References

1. Graziosi M, Nanni C, Lorenzini M et al. Role of 18F-FDG PET/CT in the diagnosis of infective endocarditis in patients with an implanted cardiac device: a prospective study. *Eur J Nucl Med Mol Imaging* 2014; **41**: 1617–1623.
2. Ahmed FZ, James J, Cunnington C et al. Early diagnosis of cardiac implantable electronic device generator pocket infection using 18F-FDG-PET/CT. *Eur Heart J Cardiovasc Imaging* 2015; **16**: 521–530.
3. Ten Hove D, Treglia G, Slart RHJA et al. The value of 18F-FDG PET/CT for the diagnosis of device-related infections in patients with a left ventricular assist device: a systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging* 2021; **48**: 241–253.
4. Rojoa D, Kontopodis N, Antoniou SA, Ioannou CV, Antoniou GA. 18F-FDG PET in the Diagnosis of Vascular Prosthetic Graft Infection: A Diagnostic Test Accuracy Meta-Analysis. *Eur J Vasc Endovasc Surg* 2019; **57**: 292–301.
5. Basu S, Chryssikos T, Moghadam-Kia S, Zhuang H, Torigian DA, Alavi A. Positron emission tomography as a diagnostic tool in infection: present role and future possibilities. *Semin Nucl Med* 2009; **39**: 36–51.
6. Chakfé N, Diener H, Lejay A et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2020 Clinical Practice Guidelines on the Management of Vascular Graft and Endograft Infections. *Eur J Vasc Endovasc Surg* 2020; **59**: 339–384.
7. Lauri C, Tamminga M, Glaudemans AWJM et al. Detection of Osteomyelitis in the Diabetic Foot by Imaging Techniques: A Systematic Review and Meta-analysis Comparing MRI, White Blood Cell Scintigraphy, and FDG-PET. *Diabetes Care* 2017; **40**: 1111–1120.
8. O'Doherty MJ, Barrington SF, Klein JL. Opportunistic infection and nuclear medicine. *Semin Nucl Med* 2009; **39**: 88–102.
9. Kim S-J, Pak K, Kim K, Lee JS. Comparing the Diagnostic Accuracies of F-18 Fluorodeoxyglucose Positron Emission Tomography and Magnetic Resonance Imaging for the Detection of Spondylodiscitis: A Meta-analysis. *Spine* 2019; **44**: E414–E422.
10. Sánchez-Montalvá A, Barios M, Salvador F et al. Usefulness of FDG PET/CT in the management of tuberculosis. *PloS One* 2019; **14**: e0221516.

a If radiolabelled leukocyte studies are not available.

11. Bomanji J, Sharma R, Mittal BR et al. PET/CT features of extrapulmonary tuberculosis at first clinical presentation: a cross-sectional observational 18F-FDG imaging study across six countries. *Eur Respir J* 2020; **55**: 1901959.
12. Bomanji J, Sharma R, Mittal BR et al. Sequential 18F-fluorodeoxyglucose positron emission tomography (18F-FDG PET) scan findings in patients with extrapulmonary tuberculosis during the course of treatment-a prospective observational study. *Eur J Nucl Med Mol Imaging* 2020; **47**: 3118–3129.
13. Zhang Q, Dong J, Shen Y, Yun C, Zhou D, Liu F. Comparative diagnostic accuracy of respective nuclear imaging for suspected fracture-related infection: a systematic review and Bayesian network meta-analysis. *Arch Orthop Trauma Surg* 2021; **141**: 1115–1130.
14. Fofi C, Prosperi D, Pettorini L et al. Diagnosis and follow-up of idiopathic retroperitoneal fibrosis: role of (18)F-FDG-PET/CT and biochemical parameters in patients with renal involvement. I*ntern Emerg Med* 2016; **11**: 809–816.
15. Fernando A, Pattison J, Horsfield C, D'Cruz D, Cook G, O'Brien T. [18F]-Fluorodeoxyglucose Positron Emission Tomography in the Diagnosis, Treatment Stratification, and Monitoring of Patients with Retroperitoneal Fibrosis: A Prospective Clinical Study. *Eur Urol* 2017; **71**: 926–933.
16. Signore A, Anzola KL, Auletta S et al. Current Status of Molecular Imaging in Inflammatory and Autoimmune Disorders. *Curr Pharm Des* 2018; **24**: 743–753.

Pyrexia of unknown origin

- To identify the cause of pyrexia of unknown origin where conventional investigations have not revealed a source.[1-10]

References

1. Jasper N, Däbritz J, Frosch M, Loeffler M, Weckesser M, Foell D. Diagnostic value of [(18)F]-FDG PET/CT in children with fever of unknown origin or unexplained signs of inflammation. *Eur J Nucl Med Mol Imaging* 2010; **37**: 136–145.
2. Keidar Z, Gurman-Balbir A, Gaitini D, Israel O. Fever of unknown origin: the role of 18F-FDG PET/CT. *J Nucl Med* 2008; **49**: 1980–1985.
3. Dong M, Zhao K, Liu Z, Wang G, Yang S, Zhou G. A meta-analysis of the value of fluorodeoxyglucose-PET/PET-CT in the evaluation of fever of unknown origin. *Eur J Radiol* 2011; **80**: 834–844.
4. Jamar F, Buscombe J, Chiti A et al. EANM/SNMMI guideline for 18F-FDG use in inflammation and infection. *J Nucl Med* 2013; **54**: 647–658.
5. Hao R, Yuan L, Kan Y, Li C, Yang J. Diagnostic performance of 18F-FDG PET/CT in patients with fever of unknown origin: a meta-analysis. *Nucl Med Commun* 2013; **34**: 682–688.
6. Schönau V, Vogel K, Englbrecht M et al. The value of 18F-FDG-PET/CT in identifying the cause of fever of unknown origin (FUO) and inflammation of unknown origin (IUO): data from a prospective study. A*nn Rheum Dis* 2018; **77**: 70–77.
7. Bharucha T, Rutherford A, Skeoch S et al. Diagnostic yield of FDG-PET/CT in fever of unknown origin: a systematic review, meta-analysis, and Delphi exercise. *Clin Radiol* 2017; **72**: 764–771.
8. Kan Y, Wang W, Liu J, Yang J, Wang Z. Contribution of 18F-FDG PET/CT in a case-mix of fever of unknown origin and inflammation of unknown origin: a meta-analysis. *Acta Radiol* 2019; **60**: 716–725.
9. Georga S, Exadaktylou P, Petrou I et al. Diagnostic Value of 18F-FDG-PET/CT in Patients with FUO. J *Clin Med* 2020; **9**: E2112.
10. Kubota K, Tanaka N, Miyata Y et al. Comparison of 18F-FDG PET/CT and 67Ga-SPECT for the diagnosis of fever of unknown origin: a multicenter prospective study in Japan. *Ann Nucl Med* 2021; **35**: 31–46.

2 Non-FDG tracers for clinical practice

The role of FDG in a range of malignancies is established, but there are limitations to using FDG for imaging some tumours. Non-FDG tracers can be used to image a limited number of tumours, which are important for patient care. The exceptions are the potential use of choline derivatives for imaging prostate cancer and the use of amyloid tracers for assessment of patients with cognitive impairment/dementia.

Fluorinated tracers can be produced in a regional cyclotron and transported, such as FDG and fluoro-choline. Generators that are used to produce radionuclides such as ^{68}Ga can be purchased and the tracers produced in nuclear medicine department radiopharmacies. Other short-lived tracers such as ^{13}N-ammonia and ^{11}C-labelled compounds are produced in a cyclotron which needs to be on the same site as the scanner.

It is recognised that cyclotron and generator-produced tracers are available in a few specialist centres and that fluorinated tracers and generator-produced tracers may become more widely available. The rationale for using alternative tracers to FDG for these indications is highlighted in italics.

Indications for non-FDG tracers

Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer

1. **PET tracers**
   a. Prostate-specific membrane antigen (PSMA) tracers are considered the first-line PET tracer for prostate cancer.[1] However, this may not be accessible at all sites in the UK. Radiolabelled fluciclovine and Choline may be used as an alternative as documented below:
   b. There are several different types of PSMA being used for diagnostic evaluation of Prostate Cancer. Currently in the UK, this includes [^{68}Ga]Ga-PSMA-11 (also known as [^{68}Ga]Ga-HBED PSMA), [^{68}Ga]Ga-THP-PSMA and [^{18}F]PSMA-1007. Although the target is the same, each of these have slightly different imaging characteristics. For the purposes of this document, PSMA PET may refer to any of these types of PSMA agents.[2]
   c. There is only one type of fluciclovine PET tracer available for clinical use, [^{18}F]fluciclovine. This has a different mechanism, protocol and imaging characteristics to the PSMA tracers. The uptake of [^{18}F]fluciclovine is mediated by sodium-dependent (Na^+) and independent (Na^-) amino acid transport systems.[3]
   d. Radiolabelled choline [^{18}F (methyl or ethyl) or ^{11}C5[a]] PET have similar physiological distribution pattern and cellular retention reflects activity of choline kinase (a rate limiting enzyme in the Kennedy pathway to generate cell membrane lipids).[4]

2. **Biochemical relapse post radical prostatectomy[3,5-13]**

Offer PET in patients with biochemical recurrence after radical prostatectomy and if the results will influence subsequent treatment decisions.

2.1 PSMA

- Recommended if the PSA ≥ 0.2 ng/ml.

a ^{11}C-choline is not excreted in urine and, therefore, is more suitable for imaging prostate cancer than ^{18}F choline but has extremely limited availability.

2.2 Fluciclovine

- Fluciclovine is considered a suitable alternative PET tracer where PSMA is unavailable.

2.3 Radiolabelled Choline

- Radiolabelled Choline is considered a suitable alternative PET tracer where PSMA is unavailable, if PSA levels are ≥ 1.0 ng/ml and the patient is not being considered for prostate bed RT. Sensitivity of Choline is very low with PSA levels <1.0 ng/ml, where prostate bed RT is more efficacious.

It should be noted that there is evidence to suggest superior diagnostic performance of PSMA over fluciclovine for the detection of biochemically recurrent prostate cancer, although in some cases there may be potential benefit for evaluation of the prostatectomy bed (due to lack of urinary excretion/ bladder accumulation).[14] There is no recommended threshold PSA value above which fluciclovine is favoured. A recent metanalysis of the performance of all PSMA radiotracers and [^{18}F]fluciclovine in the setting of biochemical recurrence showed superior performance of PSMA radiotracers for patients with PSA values of 1.0-1.9 ng/ml.[12] At lower levels of PSA the pooled detection rates were equivalent between PSMA and fluciclovine. It should be noted that there has been variation in imaging protocols which may have influenced image quality in some studies using fluciclovine.[3]

PSMA is superior to choline in detection of recurrence.[15] It has been reported that sequential imaging approach designed to limit ^{68}Ga PSMA imaging to patients with negative choline scans resulted in high detection rates.16 ^{68}Ga PSMA PET-CT identified sites of recurrent disease in 43.8% of the patients with negative ^{18}F-choline PET-CT scans.[16]

3. Detectable PSA post-prostatectomy [3,5,9,13,17]

3.1 PSMA PET

May be performed in the setting of persistent elevation of PSA (≥ 0.2 ng/ml) post prostatectomy, to assess for residual or otherwise occult disease, not identified in the pre-operative setting.

3.2 Fluciclovine

Fluciclovine is considered a suitable alternative PET tracer where PSMA is unavailable.

3.3 Radiolabelled choline

Radiolabelled choline is considered a suitable alternative PET tracer where PSMA is unavailable, when PSA levels are ≥ 1.0 ng/ml.

4. Biochemical Relapse post radical prostatectomy and prostate bed radiotherapy [3,5,9,13,18]

Offer PET in patients with biochemical recurrence after surgery and salvage radiotherapy where there is intent for further salvage therapy (e.g., SABR).[18]

4.1 PSMA PET

Recommended if the PSA ≥ 0.2ng/ml.

4.2 Fluciclovine

Fluciclovine is considered a suitable alternative PET tracer where PSMA is unavailable.

4.3 Radiolabelled choline

Radiolabelled choline is considered a suitable alternative PET tracer where PSMA is unavailable, when PSA levels ≥ 1.0 ng/ml.

5. **Biochemical relapse post radical radiotherapy** [5-7,11]

5.1 PSMA PET

Offer PSMA PET in patients with biochemical recurrence after radical radiotherapy/brachytherapy (PSA nadir + 2 ng/ml) in patients fit for salvage local therapy (salvage prostatectomy. Note multi-parametric prostate MRI should be performed for local staging if PSMA PET shows no metastatic disease.

5.2 Fluciclovine

Fluciclovine is considered a suitable alternative PET tracer where PSMA is unavailable.

5.3 Radiolabelled choline

Radiolabelled choline is considered a suitable alternative PET tracer where PSMA is unavailable.

6. **Non-metastatic castrate-resistant prostate cancer (nmCRPC)**

a. PET is not recommended routinely in patients with nmCRPC as the clinical benefit and impact on management in detecting metastases in disease thought to be non-metastatic by conventional imaging remains unclear.[19]

7. **Metastatic prostate cancer**

a. Patients being considered for ^{177}Lu-labelled PSMA-ligand therapy, a PSMA PET should be performed. Consider paired [^{18}F]FDG PET to optimise patient selection.[20]

b. Increased [^{18}F]FDG uptake seems to be more frequent in aggressive forms, aberrant histology (e.g., neuroendocrine), and advanced cases of metastatic castration-resistant PCa (mCRPC).

8. **Staging in high-risk prostate cancer**

8.1 Equivocal lesions: Consider PSMA PET in selected patients with equivocal lesions on baseline conventional staging investigations where management will be directly influenced by the PSMA result, after discussion in the MDT.[5,21,22] It should be noted that no currently available PET tracer can replace lymph node dissection and histopathologic confirmation.[23,24] [^{18}F]fluciclovine or ^{18}F/^{11}C-radiolabelled choline may identify disease sites which were occult or equivocal on standard of care imaging. However, there is insufficient data to recommend the routine use in this setting.[25]

8.2 Discordant biopsy or contraindications to biopsy: [26-28]

Consider PSMA PET in high-risk patients who have discordant biopsy results (ie, negative repeated biopsy, patient refusal, or contraindication to biopsy due to comorbidities) where exclusion of nodal or visceral metastatic disease is required. This includes patients with high clinical suspicion of occult metastatic disease provided decision has been made at MDT level. [26-28]

References

1. Jadvar H, Calais J, Fanti S et al. Appropriate Use Criteria for Prostate-Specific Membrane Antigen PET Imaging. *J Nucl Med* 2021; : jnumed.**121**.263262.
2. Zippel C, Ronski SC, Bohnet-Joschko S, Giesel FL, Kopka K. Current Status of PSMA-Radiotracers for Prostate Cancer: Data Analysis of Prospective Trials Listed on ClinicalTrials.gov. *Pharmaceuticals (Basel)* 2020; **13**: E12.

3. Rais-Bahrami S, Efstathiou JA, Turnbull CM et al. ^{18}F-Fluciclovine PET/CT performance in biochemical recurrence of prostate cancer: a systematic review. *Prostate Cancer Prostatic Dis* 2021; **24**: 997–1006.
4. Calabria F, Gallo G, Schillaci O, Cascini GL. Bio-Distribution, Imaging Protocols and Diagnostic Accuracy of PET with Tracers of Lipogenesis in Imaging Prostate Cancer: a Comparison between ^{11}C-Choline, ^{18}FFluoroethylcholine and ^{18}F-Methylcholine. *Curr Pharm Des* 2015; **21**: 4738–4747.
5. European Association of Urology. Prostate Cancer Guidelines. https://uroweb.org/guideline/prostate-cancer/ (accessed 2021-11-22).
6. Ceci F, Castellucci P, Graziani T et al. 68Ga-PSMA-11 PET/CT in recurrent prostate cancer: efficacy in different clinical stages of PSA failure after radical therapy. *Eur J Nucl Med Mol Imaging* 2019; **46**: 31–39.
7. Fanti S, Minozzi S, Castellucci P et al. PET/CT with (11)C-choline for evaluation of prostate cancer patients with biochemical recurrence: meta-analysis and critical review of available data. *Eur J Nucl Med Mol Imaging* 2016; **43**: 55–69.
8. Giesel FL, Knorr K, Spohn F et al. Detection Efficacy of 18F-PSMA-1007 PET/CT in 251 Patients with Biochemical Recurrence of Prostate Cancer After Radical Prostatectomy. *J Nucl Med* 2019; **60**: 362–368.
9. Graziani T, Ceci F, Castellucci P et al. (11)C-Choline PET/CT for restaging prostate cancer. Results from 4,426 scans in a single-centre patient series. *Eur J Nucl Med Mol Imaging* 2016; **43**: 1971–1979.
10. Nanni C, Zanoni L, Bach-Gansmo T et al. [18F]Fluciclovine PET/CT: joint EANM and SNMMI procedure guideline for prostate cancer imaging-version 1.0. *Eur J Nucl Med Mol Imaging* 2020; **47**: 579–591.
11. Perera M, Papa N, Roberts M et al. Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer-Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avid Lesions: A Systematic Review and Meta-analysis. *Eur Urol* 2020; **77**: 403–417.
12. Tan N, Oyoyo U, Bavadian N et al. PSMA-targeted Radiotracers versus 18F Fluciclovine for the Detection of Prostate Cancer Biochemical Recurrence after Definitive Therapy: A Systematic Review and Meta-Analysis. *Radiology* 2020; **296**: 44–55.
13. Wang R, Shen G, Huang M, Tian R. The Diagnostic Role of 18F-Choline, 18F-Fluciclovine and 18F-PSMA PET/CT in the Detection of Prostate Cancer With Biochemical Recurrence: A Meta-Analysis. *Front Oncol* 2021; **11**: 684629.
14. Calais J, Ceci F, Eiber M et al. 18F-fluciclovine PET-CT and 68Ga-PSMA-11 PET-CT in patients with early biochemical recurrence after prostatectomy: a prospective, single-centre, single-arm, comparative imaging trial. *The Lancet Oncology* 2019; **20**: 1286–1294.
15. Schwenck J, Rempp H, Reischl G et al. Comparison of 68Ga-labelled PSMA-11 and 11C-choline in the detection of prostate cancer metastases by PET/CT. *Eur J Nucl Med Mol Imaging* 2017; **44**: 92–101.
16. Bluemel C, Krebs M, Polat B et al. 68Ga-PSMA-PET/CT in Patients With Biochemical Prostate Cancer Recurrence and Negative 18F-Choline-PET/CT. *Clin Nucl Med* 2016; **41**: 515–521.
17. Meijer D, Donswijk ML, Bodar YJL et al. Biochemical Persistence of Prostate-Specific Antigen After Robot-Assisted Laparoscopic Radical Prostatectomy: Tumor Localizations Using PSMA PET/CT Imaging. *J Nucl Med* 2021; **62**: 961–967.
18. Byrne K, Eade T, Kneebone A et al. Delineating sites of failure following post-prostatectomy radiation treatment using 68Ga-PSMA-PET. *Radiother Oncol* 2018; **126**: 244–248.
19. Weber M, Hadaschik B, Ferdinandus J et al. Prostate-specific Membrane Antigen-based Imaging of Castration-resistant Prostate Cancer. *Eur Urol Focus* 2021; **7**: 279–287.
20. Kratochwil C, Fendler WP, Eiber M et al. EANM procedure guidelines for radionuclide therapy with 177Lu-labelled PSMA-ligands (177Lu-PSMA-RLT). *Eur J Nucl Med Mol Imaging* 2019; **46**: 2536–2544.
21. Corfield J, Perera M, Bolton D, Lawrentschuk N. 68Ga-prostate specific membrane antigen (PSMA) positron emission tomography (PET) for primary staging of high-risk prostate cancer: a systematic review. World *J Urol* 2018; **36**: 519–527.

22. Hofman MS, Lawrentschuk N, Francis RJ et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. *The Lancet* 2020; **395**: 1208–1216.
23. Hope TA, Eiber M, Armstrong WR et al. Diagnostic Accuracy of 68Ga-PSMA-11 PET for Pelvic Nodal Metastasis Detection Prior to Radical Prostatectomy and Pelvic Lymph Node Dissection: A Multicenter Prospective Phase 3 Imaging Trial. *JAMA Oncol* 2021; **7**: 1635–1642.
24. Wu H, Xu T, Wang X et al. Diagnostic Performance of 68Gallium Labelled Prostate-Specific Membrane Antigen Positron Emission Tomography/Computed Tomography and Magnetic Resonance Imaging for Staging the Prostate Cancer with Intermediate or High Risk Prior to Radical Prostatectomy: A Systematic Review and Meta-analysis. *World J Mens Health* 2020; **38**: 208–219.
25. Zanoni L, Bianchi L, Nanni C et al. [18F]-Fluciclovine PET/CT for preoperative nodal staging in high-risk primary prostate cancer: final results of a prospective trial. *Eur J Nucl Med Mol Imaging* 2021. DOI:10.1007/s00259-021-05429-6.
26. Amin A, Blazevski A, Thompson J et al. Protocol for the PRIMARY clinical trial, a prospective, multicentre, cross-sectional study of the additive diagnostic value of gallium-68 prostate-specific membrane antigen positron-emission tomography/computed tomography to multiparametric magnetic resonance imaging in the diagnostic setting for men being investigated for prostate cancer. *BJU Int* 2020; **125**: 515–524.
27. Zhang L-L, Li W-C, Xu Z et al. 68Ga-PSMA PET/CT targeted biopsy for the diagnosis of clinically significant prostate cancer compared with transrectal ultrasound guided biopsy: a prospective randomized single-centre study. *Eur J Nucl Med Mol Imaging* 2021; **48**: 483–492.
28. Liu C, Liu T, Zhang Z et al. 68Ga-PSMA PET/CT Combined with PET/Ultrasound-Guided Prostate Biopsy Can Diagnose Clinically Significant Prostate Cancer in Men with Previous Negative Biopsy Results. *J Nucl Med* 2020; **61**: 1314–1319.

Choline (^{18}F/^{11}C-radiolabelled) PET in tumour imaging

Choline PET in parathyroid adenoma

- For parathyroid gland localisation indications prior to surgery when, despite first line imaging (ultrasonography, sestamibi SPECT-CT, 4D-CT), the location of the parathyroid adenoma(s) cannot be confidently determined[a].[1-5]
- In persistent (post surgery) / recurrent primary hyperparathyroidism (PHPT) when conventional imaging fails to localise parathyroid adenoma[b].[5]

Note that ^{11}C-methionine has been reported to have better sensitivity for localising parathyroid tumour than FDG in difficult cases.[6]

References

1. Treglia G, Piccardo A, Imperiale A et al. Diagnostic performance of choline PET for detection of hyperfunctioning parathyroid glands in hyperparathyroidism: a systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging* 2019; **46**: 751–765.
2. Petranović Ovčariček P, Giovanella L, Carrió Gasset I et al. The EANM practice guidelines for parathyroid imaging. *Eur J Nucl Med Mol Imaging* 2021; **48**: 2801–2822.
3. Lee S-W, Shim SR, Jeong SY, Kim S-J. Direct Comparison of Preoperative Imaging Modalities for Localization of Primary Hyperparathyroidism: A Systematic Review and Network Meta-analysis. *JAMA Otolaryngol Head Neck Surg* 2021; **147**: 692–706.
4. Broos WAM, van der Zant FM, Knol RJJ, Wondergem M. Choline PET/CT in parathyroid imaging: a systematic review. *Nucl Med Commun* 2019; **40**: 96–105.
5. Boccalatte LA, Higuera F, Gómez NL et al. Usefulness of 18F-Fluorocholine Positron Emission Tomography-Computed Tomography in Locating Lesions in Hyperparathyroidism: A Systematic Review. *JAMA Otolaryngol Head Neck Surg* 2019; **145**: 743–750.
6. Weber T, Maier-Funk C, Ohlhauser D et al. Accurate preoperative localization of parathyroid adenomas with C-11 methionine PET/CT. *Ann Surg* 2013; **257**: 1124–1128.

a Selective venous sampling of parathyroid hormone levels can be considered before choline PET when available and if clinically appropriate.
b Functional parathyroid imaging cannot distinguish between parathyroid adenoma and the rare occurrence of carcinoma.

Choline PET for other tumours

- Assessment of patients with HCC being considered for transplant or other radical treatment where the results would directly influence patient management[1-4]
- Delineation of brain tumours where ^{11}C-methionine and [^{18}F]fluoroethyltyrosine are not available and to guide biopsy.[5]

References

1. Filippi L, Schillaci O, Bagni O. Recent advances in PET probes for hepatocellular carcinoma characterization. *Expert Rev Med Devices* 2019; **16**: 341–350.
2. Mertens K, Slaets D, Lambert B, Acou M, De Vos F, Goethals I. PET with (18)F-labelled choline-based tracers for tumour imaging: a review of the literature. *Eur J Nucl Med Mol Imaging* 2010; **37**: 2188–2193.
3. Talbot J-N, Fartoux L, Balogova S et al. Detection of hepatocellular carcinoma with PET/CT: a prospective comparison of 18F-fluorocholine and 18F-FDG in patients with cirrhosis or chronic liver disease. *J Nucl Med* 2010; **51**: 1699–1706.
4. Bertagna F, Bertoli M, Bosio G et al. Diagnostic role of radiolabelled choline PET or PET/CT in hepatocellular carcinoma: a systematic review and meta-analysis. Hepatol Int 2014; **8**: 493–500.
5. Vetrano IG, Laudicella R, Alongi P. Choline PET/CT and intraoperative management of primary brain tumors. New insights for contemporary neurosurgery. *Clin Transl Imaging* 2020; **8**: 401–404.

^{11}C-metomidate[a]

- The diagnosis of adrenal Conn's tumours pre-surgery.[1]

References

1. Mendichovszky I, Powlson A, Manavaki R et al. Targeted Molecular Imaging in Adrenal Disease—An Emerging Role for Metomidate PET-CT. Diagnostics 2016; **6**: 42.

a Cyclotron-produced, short-lived tracer.

[^{82}Rb]RbCl and ^{13}N-ammonia in myocardial perfusion imaging

- While single-photon emission computed tomography (SPECT[a]) imaging continues to be the most widely available functional imaging modality in patients with suspected or known coronary artery disease (CAD), there is increasing use of perfusion PET as endorsed by the guidelines published by the American Society of Nuclear Cardiology and European Association of Nuclear Medicine and Molecular Imaging.[1 4] Cardiac PET has significant advantages over SPECT – lower radiation burden to patients and staff, accurate attenuation correction, better diagnostic accuracy and the only modality that allows routine measurement of myocardial blood flow during stress and rest. Where there is access to perfusion PET, it is preferred to SPECT under the following clinical conditions:[3]
  - Previous poor quality SPECT images; equivocal other functional imaging or CT coronary angiography (CTCA); functional imaging results discordant with clinical assessment or coronary angiogram findings.
  - Body characteristics where artefacts are likely to affect image quality, e.g., in high-body mass patients where significant attenuation of the inferior and anterior walls limits assessment.
  - High-risk patients (e.g., significant CAD on coronary angiogram including left main or proximal epicardial disease, cardiac transplant vasculopathy, severe left ventricular dysfunction).
  - In view of the lower radiation burden, young patients with established CAD or those with suspected CAD who cannot undergo non radiation functional imaging to exclude ischaemia.
  - Patients in who myocardial blood flow would be helpful to exclude multivessel disease causing ischaemia or patients with suspected microvascular dysfunction.
  - Assessment of perfusion in selected patients with coronary anomalies with congenital disease, after surgery and with Kawasaki's disease.

^{13}N-ammonia allows quantitative assessment of myocardial perfusion to be performed and is better used to assess disease in patients with balanced three vessel disease. Rubidium has improved image quality compared to technetium ^{99m}Tc and may be cost-effective compared to ^{99m}Tc when there is a large throughput of patients (around five cases per day Monday to Friday).

References

1. Lortie M, Beanlands RSB, Yoshinaga K, Klein R, Dasilva JN, DeKemp RA. Quantification of myocardial blood flow with 82Rb dynamic PET imaging. *Eur J Nucl Med Mol Imaging* 2007; **34**: 1765–1774.
2. Nandalur KR, Dwamena BA, Choudhri AF, Nandalur SR, Reddy P, Carlos RC. Diagnostic performance of positron emission tomography in the detection of coronary artery disease: a meta-analysis. *Acad Radiol* 2008; **15**: 444–451.
3. American Society of Nuclear Cardiology and Society of Nuclear Medicine and Molecular Imaging Joint Position Statement on the Clinical Indications for Myocardial Perfusion PET. *J Nucl Cardiol* 2016; **23**: 1227–1231.
4. Sciagrà R, Lubberink M, Hyafil F et al. EANM procedural guidelines for PET/CT quantitative myocardial perfusion imaging. *Eur J Nucl Med Mol Imaging* 2021; **48**: 1040–1069.

a ^{99}mTc-labelled tracers (sestamibi, tetrofosmin) are widely available and have high sensitivity and specificity for the evaluation of CAD with single-photon emission computed tomography (SPECT).

^{68}Ga-labelled somatostatin receptor imaging ([^{68}Ga]Ga-DOTA-TATE, [^{68}Ga]Ga-DOTA-NOC)[a]

Assessment of neuroendocrine tumours

- Localisation of primary tumour in patients with known metastatic disease but unknown primary.[1,2]
  - Selection of patients for somatostatin receptor-targeted peptide receptor radionuclide therapy PRRT of G1 and G2 neuroendocrine tumour, especially if negative on ^{111}In or ^{99m}Tc somatostatin receptor imaging.[3-22]
- Staging of NETs before planned 'curative' surgery.[1-22]
- Evaluation of mass suggestive of NET not amenable to endoscopic or percutaneous biopsy (e.g., ileal lesion, hypervascular pancreatic mass, mesenteric mass).[1-16,21,22]
- Monitoring of NETs seen predominantly on SSTR PET though interval of scanning needs careful thought. For most patients a gap of 12 months between studies should be sufficient unless rapidly progressive or in active treatment phase or determining progression pre-PRRT.[12]
- Evaluation of patients with biochemical evidence and symptoms of NET without evidence on cross-sectional imaging and without prior histologic diagnosis of NET.[1,2,12]
- Imaging phaeochromocytomas and paragangliomas with succinate dehydrogenase (SADHD) mutation.[23,24]

  Imaging with [^{68}Ga]Ga-DOTA-TATE should be undertaken after discussion with local or network specialist NET MDT and all subsequent scans should be discussed within that MDT to ensure optimal therapy options.

Most NETs have low uptake of FDG; however, tracers that bind to somatostatin receptors, which are expressed by these tumours have high uptake. Somatostatin receptor (SSR) scintigraphy using SPECT tracers, for example ^{111}In-octreotide, have been in clinical use for a number of years. Newer peptides labelled with ^{68}Ga such as DOTATOC and DOTATATE show much higher affinity for NETs. Recently radionuclide treatments using SSR agents have resulted in improved quality of life and an 82% increase in progression free survival for patients with NETs and SSR imaging helps to select and manage patients for radionuclide therapy.

References

1. Menda Y, O'Dorisio TM, Howe JR et al. Localization of Unknown Primary Site with 68Ga-DOTATOC PET/CT in Patients with Metastatic Neuroendocrine Tumor. *J Nucl Med* 2017; **58**: 1054–1057.
2. Sadowski SM, Neychev V, Millo C et al. Prospective Study of 68Ga-DOTATATE Positron Emission Tomography/Computed Tomography for Detecting Gastro-Entero-Pancreatic Neuroendocrine Tumors and Unknown Primary Sites. *J Clin Oncol* 2016; **34**: 588–596
3. Ambrosini V, Tomassetti P, Castellucci P et al. Comparison between 68Ga-DOTA-NOC and 18F-DOPA PET for the detection of gastro-entero-pancreatic and lung neuro-endocrine tumours. *Eur J Nucl Med Mol Imaging* 2008; **35**: 1431–1438.
4. Ambrosini V, Campana D, Bodei L et al. 68Ga-DOTANOC PET/CT clinical impact in patients with neuroendocrine tumors. *J Nucl Med* 2010; **51**: 669–673.
5. Baum RP, Prasad V, Hommann M, Hörsch D. Receptor PET/CT imaging of neuroendocrine tumors. *Recent Results Cancer Res* 2008; **170**: 225–242.

a Generator-produced, short-lived, but transportable for up to one hour.

6. Breeman WAP, de Blois E, Sze Chan H, Konijnenberg M, Kwekkeboom DJ, Krenning EP. (68)Ga-labeled DOTA-peptides and (68)Ga-labeled radiopharmaceuticals for positron emission tomography: current status of research, clinical applications, and future perspectives. *Semin Nucl Med* 2011; **41**: 314–321.
7. Kayani I, Bomanji JB, Groves A et al. Functional imaging of neuroendocrine tumors with combined PET/CT using 68Ga-DOTATATE (DOTA-DPhe1,Tyr3-octreotate) and 18F-FDG. *Cancer* 2008; **112**: 2447–2455.
8. Kowalski J. Evaluation of Positron Emission Tomography Imaging Using [68Ga]-DOTA-D Phe1-Tyr3-Octreotide in Comparison to [111In]-DTPAOC SPECT. First Results in Patients with Neuroendocrine Tumors. *Molecular Imaging & Biology* 2003; **5**: 42–48.
9. Virgolini I, Ambrosini V, Bomanji JB et al. Procedure guidelines for PET/CT tumour imaging with 68Ga-DOTA-conjugated peptides: 68Ga-DOTA-TOC, 68Ga-DOTA-NOC, 68Ga-DOTA-TATE. *Eur J Nucl Med Mol Imaging* 2010; **37**: 2004–2010.
10. Geijer H, Breimer LH. Somatostatin receptor PET/CT in neuroendocrine tumours: update on systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging* 2013; **40**: 1770–1780.
11. Herrmann K, Czernin J, Wolin EM et al. Impact of 68Ga-DOTATATE PET/CT on the management of neuroendocrine tumors: the referring physician's perspective. *J Nucl Med 2015;* **56**: 70–75.
12. Hope TA, Bergsland EK, Bozkurt MF et al. Appropriate Use Criteria for Somatostatin Receptor PET Imaging in Neuroendocrine Tumors. *J Nucl Med* 2018; **59**: 66–74.
13. Barrio M, Czernin J, Fanti S et al. The Impact of Somatostatin Receptor-Directed PET/CT on the Management of Patients with Neuroendocrine Tumor: A Systematic Review and Meta-Analysis. *J Nucl Med* 2017; **58**: 756–761.
14. Skoura E, Michopoulou S, Mohmaduvesh M et al. The Impact of 68Ga-DOTATATE PET/CT Imaging on Management of Patients with Neuroendocrine Tumors: Experience from a National Referral Center in the United Kingdom. *J Nucl Med* 2016; **57**: 34–40.
15. Deppen SA, Blume J, Bobbey AJ et al. 68Ga-DOTATATE Compared with 111In-DTPA-Octreotide and Conventional Imaging for Pulmonary and Gastroenteropancreatic Neuroendocrine Tumors: A Systematic Review and Meta-Analysis. *J Nucl Med* 2016; **57**: 872–878.
16. Ambrosini V, Kunikowska J, Baudin E et al. Consensus on molecular imaging and theranostics in neuroendocrine neoplasms. *Eur J Cancer* 2021; **146**: 56–73.
17. Sanli Y, Garg I, Kandathil A et al. Neuroendocrine Tumor Diagnosis and Management: 68Ga-DOTATATE PET/CT. *AJR Am J Roentgenol* 2018; **211**: 267–277.
18. Ambrosini V, Kunikowska J, Baudin E et al. Consensus on molecular imaging and theranostics in neuroendocrine neoplasms. Eur J Cancer 2021; **146**: 56–73.
19. Skoura E, Michopoulou S, Mohmaduvesh M et al. The Impact of 68Ga-DOTATATE PET/CT Imaging on Management of Patients with Neuroendocrine Tumors: Experience from a National Referral Center in the United Kingdom. *J Nucl Med* 2016; **57**: 34–40.
20. Deppen SA, Blume J, Bobbey AJ et al. 68Ga-DOTATATE Compared with 111In-DTPA-Octreotide and Conventional Imaging for Pulmonary and Gastroenteropancreatic Neuroendocrine Tumors: A Systematic Review and Meta-Analysis. *J Nucl Med* 2016; **57**: 872–878.
21. Van Binnebeek S, Vanbilloen B, Baete K et al. Comparison of diagnostic accuracy of (111)In-pentetreotide SPECT and (68)Ga-DOTATOC PET/CT: A lesion-by-lesion analysis in patients with metastatic neuroendocrine tumours. *Eur Radiol* 2016; **26**: 900–909.
22. Manoharan P, Lamarca A, Navalkissoor S et al. Safety, tolerability and clinical implementation of 'ready-to-use' 68gallium-DOTA0-Tyr3-octreotide (68Ga-DOTATOC) (SomaKIT TOC) for injection in patients diagnosed with gastroenteropancreatic neuroendocrine tumours (GEP-NETs). *ESMO Open* 2020; **5**: e000650.
23. Archier A, Varoquaux A, Garrigue P et al. Prospective comparison of (68)Ga-DOTATATE and (18) F-FDOPA PET/CT in patients with various pheochromocytomas and paragangliomas with emphasis on sporadic cases. *Eur J Nucl Med Mol Imaging* 2016; **43**: 1248–1257
24. Han S, Suh CH, Woo S, Kim YJ, Lee JJ. Performance of 68Ga-DOTA-Conjugated Somatostatin Receptor-Targeting Peptide PET in Detection of Pheochromocytoma and Paraganglioma: A Systematic Review and Metaanalysis. *J Nucl Med* 2019; **60**: 369–376.

In meningioma imaging

- Meningioma delineation prior to resection and defining optimal radiotherapy target volume.[1-3]

References

1. Rachinger W, Stoecklein VM, Terpolilli NA et al. Increased 68 Ga-DOTATATE Uptake in PET Imaging Discriminates Meningioma and Tumor-Free Tissue. *J Nucl Med* 2015; **56**: 347–353.
2. Mahase SS, Roth O'Brien DA, No D et al. [68Ga]-DOTATATE PET/MRI as an adjunct imaging modality for radiation treatment planning of meningiomas. *Neurooncol Adv* 2021; **3**: vdab012.
3. Galldiks N, Albert NL, Sommerauer M et al. PET imaging in patients with meningioma—report of the RANO/PET Group. *Neuro Oncol* 2017; **19**: 1576–1587.

[^{18}F]fluorodopa imaging

In tumour assessment

- To identify locoregional and/or distant metastases in medullary thyroid cancer.[1-4]
- For imaging of primary brain tumours of all grades of differentiation (for primary assessment, radiotherapy planning, diagnosis of tumour recurrence, therapy monitoring and assessment of prognosis).[5-8]
- For assessing suspected congenital hyperinsulinism and other hypoglycaemic syndromes.[9-11]
- In the assessment of pheocromocytoma/parangliomas.[12,13]
- In the assessment of selected cases of NETs.[14,15]

References

1. Filetti S, Durante C, Hartl D et al. Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up†. *Ann Oncol* 2019; **30**: 1856–1883.
2. Giovanella L, Treglia G, Iakovou I, Mihailovic J, Verburg FA, Luster M. EANM practice guideline for PET/CT imaging in medullary thyroid carcinoma. *Eur J Nucl Med Mol Imaging* 2020; **47**: 61–77.
3. Meintjes M, Endozo R, Dickson J et al. 18F-DOPA PET and enhanced CT imaging for congenital hyperinsulinism: initial UK experience from a technologist's perspective. *Nucl Med Commun* 2013; **34**: 601–608.
4. Yang J, Hao R, Zhu X. Diagnostic role of 18F-dihydroxyphenylalanine positron emission tomography in patients with congenital hyperinsulinism: a meta-analysis. *Nucl Med Commun* 2013; **34**: 347–353.
5. Law I, Albert NL, Arbizu J et al. Joint EANM/EANO/RANO practice guidelines/SNMMI procedure standards for imaging of gliomas using PET with radiolabelled amino acids and [18F]FDG: version 1.0. *Eur J Nucl Med Mol Imaging* 2019; **46**: 540–557.
6. Albert NL, Weller M, Suchorska B et al. Response Assessment in Neuro-Oncology working group and European Association for Neuro-Oncology recommendations for the clinical use of PET imaging in gliomas. *Neuro Oncol* 2016; **18**: 1199–1208.
7. Galldiks N, Lohmann P, Albert NL, Tonn JC, Langen K-J. Current status of PET imaging in neuro-oncology. *Neurooncol Adv* 2019; 1: vdz010.
8. Somme F, Bender L, Namer IJ, Noël G, Bund C. Usefulness of 18F-FDOPA PET for the management of primary brain tumors: a systematic review of the literature. *Cancer Imaging* 2020; **20**: 70.
9. Pattison DA, Hicks RJ. Molecular imaging in the investigation of hypoglycaemic syndromes and their management. *Endocr Relat Cancer* 2017; **24**: R203–R221.
10. Padidela R, Fiest M, Arya V et al. Insulinoma in childhood: clinical, radiological, molecular and histological aspects of nine patients. *Eur J Endocrinol* 2014; **170**: 741–747.
11. de Herder WW, Niederle B, Scoazec J-Y et al. Well-differentiated pancreatic tumor/carcinoma: insulinoma. *Neuroendocrinology* 2006; **84**: 183–188.
12. Fassnacht M, Assie G, Baudin E et al. Adrenocortical carcinomas and malignant phaeochromocytomas: ESMO-EURACAN Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2020; **31**: 1476–1490.
13. Janssen I, Chen CC, Millo CM et al. PET/CT comparing (68)Ga-DOTATATE and other radiopharmaceuticals and in comparison with CT/MRI for the localization of sporadic metastatic pheochromocytoma and paraganglioma. *Eur J Nucl Med Mol Imaging* 2016; **43**: 1784–1791.
14. Koopmans KP, Neels OC, Kema IP et al. Improved staging of patients with carcinoid and islet cell tumors with 18F-dihydroxy-phenyl-alanine and 11C-5-hydroxy-tryptophan positron emission tomography. *J Clin Oncol* 2008; **26**: 1489–1495.
15. Schiesser M, Veit-Haibach P, Muller MK et al. Value of combined 6-[18F]fluorodihydroxyphenylalanine PET/CT for imaging of neuroendocrine tumours. *Br J Surg* 2010; **97**: 691–697.

In movement disorders

- Assessment of movement disorders.[1]

References

1. Ibrahim N, Kusmirek J, Struck AF et al. The sensitivity and specificity of F-DOPA PET in a movement disorder clinic. *Am J Nucl Med Mol Imaging* 2016; **6**: 102–109.

[^{18}F]fluoride[a] bone imaging

- Assessment of benign and malignant bone diseases in selected patients.[1-7]

Sodium [^{18}F]fluoride produces very high-quality images of the skeleton with high uptake in bone and rapid clearance from blood. [^{18}F]fluoride has been evaluated against [^{99m}Tc]Tc-MDP planar and SPECT imaging in patients with suspected or known metastatic bone disease. These studies show it to be more sensitive and specific than [^{99m}Tc]Tc-MDP scintigraphy, and the addition of CT increases further the specificity of the test.

Uptake times are shorter than conventional bone scintigraphy, 15-30 minutes versus three-four hours, and imaging times are shorter 15-30 minutes versus 30-60 minutes suggesting that [^{18}F]fluoride imaging for some patients with bone disease may be an appropriate use of PET-CT.

References

1. Segall G, Delbeke D, Stabin MG et al. SNM practice guideline for sodium 18F-fluoride PET/CT bone scans 1.0. *J Nucl Med Off Publ Soc Nucl Med* 2010; **51**: 1813–1820.
2. Beheshti M, Mottaghy FM, Paycha F et al. (18)F-NaF PET/CT: EANM procedure guidelines for bone imaging. *Eur J Nucl Med Mol Imaging* 2015; **42**: 1767–1777.
3. Hillner BE, Siegel BA, Hanna L, Duan F, Quinn B, Shields AF. 18F-fluoride PET used for treatment monitoring of systemic cancer therapy: results from the National Oncologic PET Registry. *J Nucl Med Off Publ Soc Nucl Med* 2015; **56**: 222–228.
4. Shen C-T, Qiu Z-L, Han T-T, Luo Q-Y. Performance of 18F-fluoride PET or PET/CT for the detection of bone metastases: a meta-analysis. *Clin Nucl Med* 2015; **40**: 103–110.
5. Jadvar H, Desai B, Conti PS. Sodium 18F-fluoride PET/CT of bone, joint, and other disorders. Semin *Nucl Med* 2015; **45**: 58–65.
6. Beheshti M. 18F-Sodium Fluoride PET/CT and PET/MR Imaging of Bone and Joint Disorders. *PET Clin* 2018; **13**: 477–490.
7. Liu Y, Sheng J, Dong Z et al. The diagnostic performance of 18F-fluoride PET/CT in bone metastases detection: a meta-analysis. *Clin Radiol* 2019; **74**: 196–206.

a Cyclotron-produced, but transportable.

^{18}F-labelled amyloid tracer[a] (florbetapir, florbetaben, flutemetamol) brain imaging

Amyloid PET imaging detects the presence of human amyloid deposition in the brain. A negative PET amyloid scan can reliably exclude amyloid pathology, as confirmed by histopathology.[1-7] While presence of amyloid plaques is one of the defining pathological features of Alzheimer's dementia (AD), it is not specific and can be present as part of the normal ageing process and in other clinical syndromes.[8-10] Therefore, it is essential that this test is only used in patients who have been fully assessed by an expert clinician. It is considered that amyloid imaging cannot diagnose AD but can contribute to diagnosis in combination with clinical assessment and other factors and more importantly, can exclude AD type pathology.

Amyloid brain PET is used according to the Appropriate Use Criteria (AUC), which were developed by the Society of Nuclear Medicine and Molecular Imaging and the Alzheimer's Association.[11,12] It is indicated in highly selected patients with cognitive impairment where

- AD is a possible diagnosis, but this remains uncertain after comprehensive evaluation by a dementia expert and conventional imaging work-up[b] and;
- where knowledge of the presence or absence of amyloid is expected to increase diagnostic certainty and influence patient management.

Inappropriate scenarios for use would include:

- patients 65 years or older who meet standard definitions and tests for AD;
- where there is no clinical evidence of memory impairment (that is, as a screening tool);
- to assess the severity of dementia;
- in asymptomatic patients with a family history of dementia;
- for non-medical reasons such as pre-employment screening.

There is now sufficient evidence to support the use of this technique in the scenarios defined above by the AUC, where the patient has persistent or progressive unexplained memory impairment not confirmed by standard medical tests, an unusual clinical presentation and/or an atypically early age of onset (usually defined as 65 years or less in age)[11,13]

It has been demonstrated that the introduction of amyloid brain PET in the investigative pathway has led to significant change in management and diagnosis therefore reducing the need for additional diagnostic testing.[14-17] These findings are even more pertinent with the recent regulatory approval of the disease modifying drug aducanumab[c].[18]

References

1. Ossenkoppele R, Jansen WJ, Rabinovici GD et al. Prevalence of amyloid PET positivity in dementia syndromes: a meta-analysis. *JAMA* 2015; **313**: 1939–1949.

a Cyclotron-produced, but transportable.

b In patients older than 70 years with clinical suspicion for a possible AD, [^{18}F]FDG PET-CT should be considered after inconclusive structural conventional imaging (CT, MRI) and before amyloid imaging. However, in younger patients with an early onset of dementia (65 years and younger, as well as in selected cases of 65-70 year old patients) and progressive decline that has features of AD dementia as well as of a non-AD dementia, where the presence of absence of amyloid plaque depositions and AD type pathology is a critical component of the initial differential diagnosis, ^{18}F-labelled amyloid tracer imaging, if available, may be considered in a dementia multidisciplinary meeting after inconclusive structural brain imaging (CT, MRI) and prior to [^{18}F]FDG PET-CT.

c Aducanumab is not yet approved for use by MHRA or EMA but has been approved by FDA.

2. Clark CM, Pontecorvo MJ, Beach TG et al. Cerebral PET with florbetapir compared with neuropathology at autopsy for detection of neuritic amyloid-β plaques: a prospective cohort study. *Lancet Neurol* 2012; **11**: 669–678.
3. Sabri O, Sabbagh MN, Seibyl J et al. Florbetaben PET imaging to detect amyloid beta plaques in Alzheimer's disease: phase 3 study. *Alzheimers Dement J Alzheimers Assoc* 2015; **11**: 964–974.
4. Thal DR, Beach TG, Zanette M et al. [(18)F]flutemetamol amyloid positron emission tomography in preclinical and symptomatic Alzheimer's disease: specific detection of advanced phases of amyloid-β pathology. *Alzheimers Dement J Alzheimers Assoc* 2015; **11**: 975–985.
5. Clark CM, Schneider JA, Bedell BJ et al. Use of florbetapir-PET for imaging beta-amyloid pathology. *JAMA* 2011; **305**: 275–283.
6. Clark CM, Pontecorvo MJ, Beach TG et al. Cerebral PET with florbetapir compared with neuropathology at autopsy for detection of neuritic amyloid-β plaques: a prospective cohort study. *Lancet Neurol* 2012; **11**: 669–678.
7. Wong DF, Rosenberg PB, Zhou Y et al. In vivo imaging of amyloid deposition in Alzheimer disease using the radioligand 18F-AV-45 (florbetapir [corrected] F 18). *J Nucl Med Off Publ Soc Nucl Med* 2010; **51**: 913–920.
8. Wolk DA, Sadowsky C, Safirstein B et al. Use of Flutemetamol F 18-Labeled Positron Emission Tomography and Other Biomarkers to Assess Risk of Clinical Progression in Patients With Amnestic Mild Cognitive Impairment. *JAMA Neurol* 2018; **75**: 1114–1123.
9. Landau SM, Horng A, Fero A, Jagust WJ, Alzheimer's Disease Neuroimaging Initiative. Amyloid negativity in patients with clinically diagnosed Alzheimer disease and MCI. *Neurology* 2016; **86**: 1377–1385.
10. Fantoni ER, Chalkidou A, O' Brien JT, Farrar G, Hammers A. A Systematic Review and Aggregated Analysis on the Impact of Amyloid PET Brain Imaging on the Diagnosis, Diagnostic Confidence, and Management of Patients being Evaluated for Alzheimer's Disease. *J Alzheimers Dis JAD* 2018; **63**: 783–796.
11. Johnson KA, Minoshima S, Bohnen NI et al. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. *J Nucl Med Off Publ Soc Nucl Med* 2013; **54**: 476–490.
12. Minoshima S, Drzezga AE, Barthel H et al. SNMMI Procedure Standard/EANM Practice Guideline for Amyloid PET Imaging of the Brain 1.0. *J Nucl Med Off Publ Soc Nucl Med* 2016; **57**: 1316–1322.
13. Carswell CJ, Win Z, Muckle K, Kennedy A, Waldman A, Dawe G et al. Clinical utility of amyloid PET imaging with (18)F-florbetapir: a retrospective study of 100 patients. *J Neurol Neurosurg Psychiatry* 2018; **89**: 294–299.
14. Shea Y-F, Barker W, Greig-Gusto MT, Loewenstein DA, Duara R, DeKosky ST. Impact of Amyloid PET Imaging in the Memory Clinic: A Systematic Review and Meta-Analysis. *J Alzheimers Dis JAD* 2018; **64**: 323–335.
15. de Wilde A, van der Flier WM, Pelkmans W et al. Association of Amyloid Positron Emission Tomography With Changes in Diagnosis and Patient Treatment in an Unselected Memory Clinic Cohort: The ABIDE Project. *JAMA Neurol* 2018; **75**: 1062–1070.
16. Petersen RC, Lopez O, Armstrong MJ et al. Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. *Neurology* 2018; **90**: 126–135.
17. Rabinovici GD, Gatsonis C, Apgar C et al. Association of Amyloid Positron Emission Tomography With Subsequent Change in Clinical Management Among Medicare Beneficiaries With Mild Cognitive Impairment or Dementia. *JAMA* 2019; **321**: 1286–1294.
18. Sevigny J, Chiao P, Bussière T et al. The antibody aducanumab reduces Aβ plaques in Alzheimer's disease. *Nature* 2016; **537**: 50–56.

[^{18}F]fluoroethyltyrosine, [^{18}F]fluciclovine and ^{11}C-methionine[a] in brain tumours[b]

^{11}C-methionine, [^{18}F]fluoroethyltyrosine (FET) and [^{18}F]fluciclovine are superior in defining the extent of tumour in low and intermediate grade gliomas compared to FDG which has limited use because of high uptake in normal brain. Uptake tends to occur in lower grade tumours with a better prognosis. Also, the low uptake in normal brain makes these agents ideal in finding small post-treatment recurrence and separating progression form pseudo-progression.

- Assessment of tumour grade and extent in some patients with glioma for staging target biopsy or plan treatment.[1-9]
- To differentiate between post-treatment progression and pseudo progression.[10-12]
- Identify the site of a pituitary adenoma pre-surgery or find post-surgical residual tumour (^{11}C- methionine only).[13-14]
- Assessment of tumour grade.[15-21]

References

1. De Witte O, Goldberg I, Wikler D et al. Positron emission tomography with injection of methionine as a prognostic factor in glioma. *J Neurosurg* 2001; **95**: 746–750.
2. Herholz K, Hölzer T, Bauer B et al. 11C-methionine PET for differential diagnosis of low-grade gliomas. *Neurology* 1998; **50**: 1316–1322.
3. Pirotte B, Goldman S, Dewitte O et al. Integrated positron emission tomography and magnetic resonance imaging-guided resection of brain tumors: a report of 103 consecutive procedures. *J Neurosurg* 2006; **104**: 238–253.
4. Pirotte BJM, Levivier M, Goldman S et al. Positron emission tomography-guided volumetric resection of supratentorial high-grade gliomas: a survival analysis in 66 consecutive patients. *Neurosurgery* 2009; **64**: 471–481; discussion 481.
5. Pirotte BJM, Lubansu A, Massager N et al. Clinical impact of integrating positron emission tomography during surgery in 85 children with brain tumors. *J Neurosurg Pediatr* 2010; **5**: 486–499.
6. Smits A, Westerberg E, Ribom D. Adding 11C-methionine PET to the EORTC prognostic factors in grade 2 gliomas. *Eur J Nucl Med Mol Imaging* 2008; **35**: 65–71.
7. Yamane T, Sakamoto S, Senda M. Clinical impact of (11)C-methionine PET on expected management of patients with brain neoplasm. *Eur J Nucl Med Mol Imaging* 2010; **37**: 685–690.
8. Falk Delgado A, Falk Delgado A. Discrimination between primary low-grade and high-grade glioma with 11C-methionine PET: a bivariate diagnostic test accuracy meta-analysis. *Br J Radiol* 2018; **91**: 20170426.
9. Treglia G, Muoio B, Trevisi G et al. Diagnostic Performance and Prognostic Value of PET/CT with Different Tracers for Brain Tumors: A Systematic Review of Published Meta-Analyses. *Int J Mol Sci* 2019; **20**: E4669.
10. Castello A, Riva M, Fernandes B, Bello L, Lopci E. The role of 11C-methionine PET in patients with negative diffusion-weighted magnetic resonance imaging: correlation with histology and molecular biomarkers in operated gliomas. *Nucl Med Commun* 2020; **41**: 696–705.
11. Hotta M, Minamimoto R, Miwa K. 11C-methionine-PET for differentiating recurrent brain tumor from radiation necrosis: radiomics approach with random forest classifier. *Sci Rep* 2019; **9**: 15666.

a Cyclotron-produced, short-lived tracer.
b Please, also note that choline (18F/11C) is used for brain tumour imaging. See section *Choline* (^{18}F/^{11}C-radiolabelled) *PET in tumour imaging* on page 54.

12. Wang Y, Rapalino O, Heidari P et al. C11 Methionine PET (MET-PET) Imaging of Glioblastoma for Detecting Postoperative Residual Disease and Response to Chemoradiation Therapy. *Int J Radiat Oncol Biol Phys* 2018; **102**: 1024–1028.
13. Feng Z, He D, Mao Z et al. Utility of 11C-Methionine and 18F-FDG PET/CT in Patients With Functioning Pituitary Adenomas. *Clin Nucl Med* 2016; **41**: e130-134.
14. Bashari WA, Senanayake R, Fernández-Pombo A et al. Modern imaging of pituitary adenomas. *Best Pract Res Clin Endocrinol Metab* 2019; **33**: 101278.
15. Michaud L, Beattie BJ, Akhurst T et al. 18F-Fluciclovine (18F-FACBC) PET imaging of recurrent brain tumors. Eur J Nucl Med Mol Imaging 2020; **47**: 1353–1367.
16. Parent EE, Patel D, Nye JA et al. [18F]-Fluciclovine PET discrimination of recurrent intracranial metastatic disease from radiation necrosis. *EJNMMI Res* 2020; **10**: 148.
17. Albano D, Tomasini D, Bonù M, Giubbini R, Bertagna F. 18F-Fluciclovine (18F-FACBC) PET/CT or PET/MRI in gliomas/glioblastomas. *Ann Nucl Med* 2020; **34**: 81–86.
18. Tsuyuguchi N, Terakawa Y, Uda T, Nakajo K, Kanemura Y. Diagnosis of Brain Tumors Using Amino Acid Transport PET Imaging with 18F-fluciclovine: A Comparative Study with L-methyl-11C-methionine PET Imaging. Asia Ocean *J Nucl Med Biol* 2017; **5**: 85–94.
19. Huang X, Bai H, Zhou H, Tang H, Yang L. Performance of 18F-FET-PET versus 18F-FDG-PET for the diagnosis and grading of brain tumors: inherent bias in meta-analysis not revealed by quality metrics. *Neuro Oncol* 2016; **18**: 1028.
20. Grosu A-L, Astner ST, Riedel E et al. An interindividual comparison of O-(2-[18F]fluoroethyl)-L-tyrosine (FET)- and L-[methyl-11C]methionine (MET)-PET in patients with brain gliomas and metastases. *Int J Radiat Oncol Biol Phys* 2011; **81**: 1049–1058.
21. Rapp M, Heinzel A, Galldiks N et al. Diagnostic performance of 18F-FET PET in newly diagnosed cerebral lesions suggestive of glioma. *J Nucl Med* 2013; **54**: 229–235.

3 PET-CT in paediatrics

Oncological applications[a]

Hodgkin's lymphoma

- Baseline staging (routine).[1,2,4,8]
- Interim response assessment after two cycles of OEPA (routine)[1,2,17]
- End of treatment assessment (consider).[17]
- Clinical suspicion of relapse (consider).[17]

Non-Hodgkin's lymphoma

- Staging.[1,17]
- Response assessment in selected cases.[17]
- Suspicion of relapse.[17]

Leukaemia

- Cross-sectional imaging performed in case of suspected extra-medullary disease (EMD); 20%-40% of patients with acute myeloid leukaemia have EMD at diagnosis; this is associated with high relapse rates.
- FDG PET-CT aids in detecting EMD, especially in the case of subclinical multifocal disease; however, the lack of definitive treatment options limits the clinical use of PET.[17]

Osteosarcoma

- FDG PET/CT is the most accurate imaging technique for staging apart from the lungs (superior accuracy for bone metastases).
- Thin slice chest CT in full inspiration required for lung metastases.
- End-of-treatment FDG PET-CT usually not done, assessment based on histology. However, initial reports suggest decreased FDG avidity in primary osteosarcoma correlates with histological response.[17,18]
- Value of interim FDG PET-CT not proven (no alternative chemotherapy alters outcome in poorly responding osteosarcomas).
- Possible role of FDG PET-CT in relapse to define extent of disease (probably more accurate than CT, especially in peri-prosthetic recurrence).

Ewing's sarcoma

- At staging, FDG PET-CT more sensitive to detect metastatic disease, apart from the lungs (chest CT required).[1,17]
- Conflicting results on the use of PET-CT in predicting response to chemotherapy; further research is needed.

Soft tissue sarcoma

- Rhabdomyosarcoma (RMS, four histological subtypes) includes over 50% of soft tissue sarcomas.
- Sites of metastatic disease: lungs, loco-regional lymph nodes, bone marrow and cortical bone.

a There is evolving evidence for the use of PET-MRI in the management of children with cancer as per Baratto *L, Hawk KE, States L et al. PET/MRI Improves Management of Children with Cancer. J Nucl Med 2021; 62: 1334–1340.*

- Outcome linked to site and number of metastases - routine FDG PET-CT at staging (lymph nodes, bone marrow and cortical bone) recommended, more sensitive than CT[3,5,6;] dedicated thin slice chest CT for assessment of possible lung disease required.
- Parametric PET factors (SUVmax, MTV, TLG) not predictive of poor prognosis.[11]

Malignant peripheral nerve sheath tumours (MPNST)

- Malignant transformation in previously benign plexiform neurofibromata in neurofibromatosis type 1 patients.
- High NPV of FDG PET-CT (a positive PET-CT scan has low specificity).[17]
- Strong reliance on histological sampling when malignant transformation based on clinical symptoms is suspected.
- Possible role of FDG PET-CT in predicting malignant change in asymptomatic patients or in children with difficulty in verbally expressing symptomatology, for earlier diagnosis and improved overall survival.[17]

Brain tumours

- FDG PET-CT currently used as a problem-solving tool.[1,17]
  - To improve diagnostic yield from biopsy to assess the histological grade
    - Glioblastomas and medulloblastomas show high grade FDG uptake
    - Brain stem gliomas have low-grade uptake
    - Ependymomas have low-grade uptake
  - FDG PET can improve tumour delineation when co-registered with MRI
  - To distinguish between residual disease or recurrence
    - Superior accuracy of amino-acid analogue PET-CT (e.g. choline, L-dihydroxyphenylalanine ([^{18}F]fluorodopa), [^{18}F]F-fluoroethyl-L-tyrosine, ^{11}C-methionine), with a higher tumour-to-background ratio than FDG.[7,12,16]

Neuroblastoma

- Valuable role of FDG PET-CT in mIBG negative neuroblastoma.[1]
- FDG PET-CT: higher sensitivity but lower specificity than mIBG: biopsy may be needed for soft tissue lesions.
- Small volume bone marrow involvement may be missed with both FDG PET-CT and mIBG SPECT-CT: bone marrow biopsy needed.
- FDG PET-CT may be a better predictor of PFS than mIBG.[13]
- ^{123}I-mIBG still gold standard after chemotherapy (FDG PET-CT less sensitive and specific for bone/bone marrow disease).
- mIBG positive neuroblastomas can become mIBG negative; problem-solving role of FDG PET-CT in these cases.[17]
- [^{18}F]F-fluorophenyl-alanine (F-DOPA) and [^{68}Ga]Ga-somatostatin receptor (SSR) analogues are alternative PET tracers, not widely available yet, with higher sensitivity compared to FDG PET-CT and ^{123}I-mIBG SPECT-CT.[14,15]
- [^{18}F]F-meta-fluorobenzylguanidine (MFBG) new promising tracer.

Wilms' tumour

- Limited data on FDG PET-CT
  - May predict tumour viability after neoadjuvant chemotherapy
  - May detect more sites of disease at relapse versus MRI
- Current, problem-solving role for restaging relapsed patients.[17]

Langerhans cell histiocytosis (LCH)

- Single or several lesions (involving a single or multiple body systems).[9]
- Prognosis determined by organ involvement and treatment response.
- FDG PET-CT appears to be highly sensitive for staging and response assessment with a low false-positive rate.[10]

Germ cell tumour

- As a problem-solving tool at staging, biopsy guidance, assessment of residual metabolic activity and recurrence detection.[17]

Hepatoblastoma

- Currently limited role for FDG PET-CT in the detection of suspected tumour relapse with negative conventional imaging and rising blood serum alpha-fetoprotein.[1,17]

References

1. Vali R, Alessio A, Balza R et al. SNMMI Procedure Standard/EANM Practice Guideline on Pediatric 18F-FDG PET/CT for Oncology 1.0. *J Nucl Med* 2021; **62**: 99–110.
2. Spijkers S, Littooij AS, Kwee TC et al. Whole-body MRI versus an FDG-PET/CT-based reference standard for staging of paediatric Hodgkin lymphoma: a prospective multicentre study. *Eur Radiol* 2021; **31**: 1494–1504.
3. van Ewijk R, Schoot RA, Sparber-Sauer M et al. European guideline for imaging in paediatric and adolescent rhabdomyosarcoma - joint statement by the European Paediatric Soft Tissue Sarcoma Study Group, the Cooperative Weichteilsarkom Studiengruppe and the Oncology Task Force of the European Society of Paediatric Radiology. *Pediatr Radiol* 2021; **51**: 1940–1951.
4. Kim K, Kim S-J. Diagnostic performance of F-18 FDG PET/CT in the detection of bone marrow involvement in paediatric hodgkin lymphoma: A meta-analysis. *Leuk Res* 2021; **102**: 106525.
5. Tal AL, Doshi H, Parkar F et al. The Utility of 18FDG PET/CT Versus Bone Scan for Identification of Bone Metastases in a Pediatric Sarcoma Population and a Review of the Literature. *J Pediatr Hematol Oncol* 2021; **43**: 52–58.
6. Mercolini F, Zucchetta P, Jehanno N et al. Role of 18F-FDG-PET/CT in the staging of metastatic rhabdomyosarcoma: a report from the European paediatric Soft tissue sarcoma Study Group. *Eur J Cancer* 2021; **155**: 155–162.
7. Bag AK, Wing MN, Sabin ND et al. [11C]-Methionine PET for Identification of Pediatric High-Grade Glioma Recurrence. *J Nucl Med* 2021; : jnumed.120.261891.
8. Rauf MS, Khan ZA, Zahir MN et al. Comparison of 18F-labelled fluoro-2-deoxyglucose-PET with conventional computed tomography for staging and response assessment in paediatric and adult patients with nodular lymphocyte-predominant Hodgkin's lymphoma. *Nucl Med Commun* 2021; **42**: 899–906.
9. Rajakulasingam R, Siddiqui M, Michelagnoli M, Saifuddin A. Skeletal staging in Langerhans cell histiocytosis: a multimodality imaging review. *Skeletal Radiol* 2021; **50**: 1081–1093.

10. Jessop S, Crudgington D, London K, Kellie S, Howman-Giles R. FDG PET-CT in pediatric Langerhans cell histiocytosis. *Pediatr Blood Cancer* 2020; **67**: e28034.
11. Harrison DJ, Chi Y-Y, Tian J et al. Metabolic response as assessed by 18 F-fluorodeoxyglucose positron emission tomography-computed tomography does not predict outcome in patients with intermediate- or high-risk rhabdomyosarcoma: A report from the Children's Oncology Group Soft Tissue Sarcoma Committee. *Cancer Med* 2021; **10**: 857–866.
12. Marner L, Lundemann M, Sehested A et al. Diagnostic Accuracy and Clinical Impact of [18F]FET PET in Childhood CNS tumors. *Neuro Oncol* 2021; noab096.
13. Sung AJ, Weiss BD, Sharp SE, Zhang B, Trout AT. Prognostic significance of pretreatment 18F-FDG positron emission tomography/computed tomography in pediatric neuroblastoma. *Pediatr Radiol* 2021; **51**: 1400–1405.
14. Piccardo A, Morana G, Puntoni M et al. Diagnosis, Treatment Response, and Prognosis: The Role of 18F-DOPA PET/CT in Children Affected by Neuroblastoma in Comparison with 123I-mIBG Scan: The First Prospective Study. *J Nucl Med* 2020; **61**: 367–374.
15. McElroy KM, Binkovitz LA, Trout AT et al. Pediatric applications of Dotatate: early diagnostic and therapeutic experience. *Pediatr Radiol* 2020; 50: 882–897.
16. Morana G, Tortora D, Bottoni G et al. Correlation of multimodal 18F-DOPA PET and conventional MRI with treatment response and survival in children with diffuse intrinsic pontine gliomas. *Theranostics* 2020; **10**: 11881–11891.
17. Chambers G, Frood R, Patel C, Scarsbrook A. 18F-FDG PET-CT in paediatric oncology: established and emerging applications. *Br J Radiol* 2019; **92**: 20180584.
18. Davis JC, Daw NC, Navid F et al. 18F-FDG uptake during early adjuvant chemotherapy predicts histologic response in pediatric and young adult patients with osteosarcoma. *J Nucl Med* 2018; **59**:25-30.

Non-oncological applications

Epilepsy

Please, refer to the general epilepsy section (on page 42).

Paediatric dystonia

- Evaluation of dystonia in children and young adults, particularly secondary dystonias and prior to deep brain stimulation therapy.[1-5]

References

1. Szyszko TA, Dunn JT, O'Doherty MJ, Reed L, Lin J-P. Role of 18F-FDG PET imaging in paediatric primary dystonia and dystonia arising from neurodegeneration with brain iron accumulation. *Nucl Med Commun* 2015; **36**: 469–476.
2. Gimeno H, Lin J-P. The International Classification of Functioning (ICF) to evaluate deep brain stimulation neuromodulation in childhood dystonia-hyperkinesia informs future clinical & research priorities in a multidisciplinary model of care. *Eur J Paediatr Neurol* 2017; **21**: 147–167.
3. Hutchinson M, Nakamura T, Moeller JR et al. The metabolic topography of essential blepharospasm: a focal dystonia with general implications. *Neurology* 2000; **55**: 673–677.
4. Trost M, Carbon M, Edwards C et al. Primary dystonia: is abnormal functional brain architecture linked to genotype? *Ann Neurol* 2002; **52**: 853–856.
5. Carbon M, Su S, Dhawan V, Raymond D, Bressman S, Eidelberg D. Regional metabolism in primary torsion dystonia: effects of penetrance and genotype. *Neurology* 2004; **62**: 1384–1390.

Childhood hyperinsulinaemia/insulinoma

- Insulinoma localisation and staging prior to surgery
  - [^{18}F]fluorodopa and [^{68}Ga]Ga-DOTA-TOC or [^{68}Ga]Ga-DOTA-TATE PET-CT may be used as a complementary diagnostic study for insulinoma localisation and staging prior surgery when standard imaging studies are equivocal or suspicious (*problem-solving*).[1, a, b, c, d]
- Assessment of the extent of metastatic disease in malignant insulinomas
  - Somatostatin receptor imaging can be used as a complementary diagnostic study for assessing the extent of metastatic disease in malignant insulinomas, particularly in cases when PRRT (suitability assessment). [2,d]

References

1. de Herder WW, Niederle B, Scoazec J-Y et al. Well-differentiated pancreatic tumor/carcinoma: insulinoma. *Neuroendocrinology* 2006; **84**: 183–188.
2. Pattison DA, Hicks RJ. Molecular imaging in the investigation of hypoglycaemic syndromes and their management. *Endocr Relat Cancer* 2017; **24**: R203–R221.
3. Orlefors H, Sundin A, Garske U et al. Whole-body (11)C-5-hydroxytryptophan positron emission tomography as a universal imaging technique for neuroendocrine tumors: comparison with somatostatin receptor scintigraphy and computed tomography. *J Clin Endocrinol Metab* 2005; **90**: 3392–3400.
4. Eriksson B, Orlefors H, Oberg K, Sundin A, Bergström M, Långström B. Developments in PET for the detection of endocrine tumours. *Best Pract Res Clin Endocrinol Metab* 2005; **19**: 311–324.
5. Barthlen W, Blankenstein O, Mau H et al. Evaluation of [18F]fluoro-L-DOPA positron emission tomography-computed tomography for surgery in focal congenital hyperinsulinism. *J Clin Endocrinol Metab 2008*; **93**: 869–875.
6. Wild D, Christ E, Caplin ME et al. Glucagon-like peptide-1 versus somatostatin receptor targeting reveals 2 distinct forms of malignant insulinomas. *J Nucl Med* 2011; **52**: 1073–1078.
7. Meintjes M, Endozo R, Dickson J et al. 18F-DOPA PET and enhanced CT imaging for congenital hyperinsulinism: initial UK experience from a technologist's perspective. *Nucl Med Commun* 2013; **34**: 601–608.
8. Sadowski SM, Neychev V, Cottle-Delisle C et al. Detection of insulinoma using (68)Gallium-DOTATATE PET/CT: a case report. *Gland Surg* 2014; **3**: E1-5.
9. Antwi K, Fani M, Nicolas G et al. Localization of Hidden Insulinomas with 68Ga-DOTA-Exendin-4 PET/CT: A Pilot Study. *J Nucl Med* 2015; **56**: 1075–1078.
10. Luo Y, Pan Q, Yao S et al. Glucagon-Like Peptide-1 Receptor PET/CT with 68Ga-NOTA-Exendin-4 for Detecting Localized Insulinoma: A Prospective Cohort Study. *J Nucl Med* 2016; **57**: 715–720.
11. Antwi K, Nicolas G, Fani M et al. 68Ga-Exendin-4 PET/CT Detects Insulinomas in Patients With Endogenous Hyperinsulinemic Hypoglycemia in MEN-1. *J Clin Endocrinol Metab* 2019; **104**: 5843–5852.
12. Grant CS. Insulinoma. *Best Pract Res Clin Gastroenterol* 2005; **19**: 783–798.
13. Pattison DA, Hofman MS. Role of Fluorodeoxyglucose PET/Computed Tomography in Targeted Radionuclide Therapy for Endocrine Malignancies. *PET Clin* 2015; **10**: 461–476.

a The most used imaging modalities are gadolinium-enhanced dynamic magnetic resonance imaging (MRI), 3-phase computed tomography (CT) and endoscopic ultrasound.

b Promising results have been obtained with [^{18}F]fluorodopa PET-CT and [^{68}Ga]Ga-exendin-4 PET-CT; other imaging includes [^{11}C]-5-hydroxytryptophan PET-CT, somatostatin receptor imaging, including ^{68}Ga-DOTA-TOC or ^{68}Ga-DOTA-TATE PET-CT[2-11]

c There is a wide variability with regard to the results for localisation between different centres for each of these imaging studies presumably reflecting the specialist expertise and the availability of tracer and equipment. It is, therefore, recommended that any proposed imaging algorithm would take into account cost, sensitivity, availability and local expertise.[12]

d [^{18}F]FDG PET -CT is not recommended for insulinoma imaging, with the exception of patients with metastatic insulinoma.[1, 13]

Contributors

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Asim Afaq	Clinical Associate Professor of Radiology, Division of Body Imaging, Department of Radiology, Carver College of Medicine, University of Iowa Hospitals and Clinics; Honorary Consultant Radiologist, Institute of Nuclear Medicine, University College London Hospitals	▪ Prostate malignancy; ▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer
Dr Parthiban Arumugam	Clinical Director, Nuclear Medicine Department, Manchester University NHS Foundation Trust	▪ Cardiological Indications (within Indications for 18F-fluorodeoxyglucose (FDG) PET-CT); ▪ 82-Rubidium chloride and 13N-ammonia in myocardial perfusion imaging (within Non-FDG tracers for clinical practice)
Prof. Sally Barrington[1]	Professor of PET Imaging and NIHR Research Professor, School of Biomedical Engineering and Imaging Sciences, King's College London and Guy's and St Thomas' PET Centre	▪ Lymphoma; ▪ PET-CT in paediatrics
Prof. Tara Barwick	Consultant Radiologist and Nuclear Medicine Physician, Imperial College Healthcare NHS Trust; Professor of Practice (Cancer Imaging), Imperial College London	▪ Urological malignancy; ▪ Renal cancer; ▪ Bladder cancer; ▪ Prostate malignancy; ▪ Testicular malignancy; ▪ Gynaecological malignancy; ▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer; ▪ Choline PET in parathyroid adenoma

1 *Please, see Acknowledgements on page 82 for additional details.*

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Clare Beadsmoore	Consultant Radiologist and Radionuclide Radiologist, Norfolk and Norwich University Hospital	▪ Colorectal carcinoma; ▪ Lymphoma; ▪ Myeloma; ▪ Carcinoma of unknown primary
Dr Lorenzo Biassoni	Consultant in Nuclear Medicine, Great Ormond Street Hospital for Children NHS Foundation Trust	▪ Paediatric Oncological applications
Prof. Jamshed Bomanji	Consultant in Nuclear Medicine and Clinical Lead and Head of Clinical Department, Institute of Nuclear Medicine, University College London Hospitals NHS Foundation Trust	▪ 18F-DOPA imaging ▪ Childhood hyperinsulinaemia (insulinoma)
Dr John Buscombe	Locum Consultant in Nuclear Medicine, Barts Health NHS Trust	▪ Brain; ▪ Oesophageal and oesophago-gastric junction cancers; ▪ Gastric cancer ▪ Gastrointestinal stromal tumours; ▪ Hepatopancreatobiliary disease; ▪ Neuroendocrine tumours; ▪ Paraneoplastic syndromes; ▪ Carcinoma of unknown primary; ▪ Infection and inflammatory disorders (excluding sarcoidosis and vasculitis); ▪ Pyrexia of unknown origin; ▪ 18F-fluoroethyltyrosine (FET), 18F-fluciclovine and 11C-methionine in brain tumours
Dr Amarnath Challapalli	Consultant Clinical Oncologist, Bristol Haematology and Oncology Centre, University Hospitals Bristol and Weston NHS Foundation Trust	▪ Prostate malignancy; ▪ Skin tumours; ▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Greg Chambers	Consultant Radiologist in Paediatric Radiology and Nuclear Medicine, Leeds Teaching Hospitals NHS Trust	▪ PET-CT in paediatrics
Prof. Gary Cook	Professor of Molecular Imaging, Department of Cancer Imaging and King's College London and Guy's and St Thomas' PET Centre, School of Biomedical Engineering and Imaging Sciences	▪ Breast tumours; ▪ Gastric cancer
Dr Stephen Daw	Consultant Paediatric and Adolescent Haemato-Oncologist, University College London Hospitals	▪ PET-CT in paediatrics
Prof. Sabina Dizdarevic	Principal Lead Consultant in Imaging and Nuclear Medicine, University Hospitals Sussex NHS Foundation Trust; Honorary Clinical Professor / Clinical PET-CT Lead, Clinical Imaging Sciences Centre, Brighton and Sussex Medical School	▪ Thyroid carcinoma; ▪ Gastric cancer; ▪ Anal carcinoma; ▪ Urological malignancy; ▪ Bladder cancer; ▪ Prostate malignancy; ▪ Testicular malignancy; ▪ Penile carcinoma; ▪ Musculoskeletal tumours; ▪ Dementia and other neurodegenerative disorders; ▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer; ▪ 68Ga-DOTATE in meningioma; ▪ 18F-labelled amyloid tracer brain imaging; ▪ 18F-fluoroethyltyrosine (FET), 18F-fluciclovine and 11C-methionine in brain tumours ▪ PET-CT in paediatrics

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Amy Eccles	Consultant Radionuclide Radiologist, Imperial College Healthcare NHS Trust	▪ Prostate malignancy; ▪ Skin tumours; ▪ Neuroendocrine tumours; ▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer; ▪ 68Ga-labelled somatostatin receptor (SSR) imaging for neuroendocrine tumours
Dr Sameer Gangoli	Consultant Radiologist, University Hospitals Sussex NHS Foundation Trust	▪ Head and neck tumours
Dr Gopinath Gnanasegaran	Consultant In Nuclear Medicine, Royal Free London NHS Foundation Trust	▪ Hepatopancreatobiliary disease
Dr Deepa Gopalan	Consultant Cardiac Radiologist, Imperial College Healthcare NHS Trust and Cambridge University Hospitals NHS Foundation Trust	▪ Cardiological Indications; ▪ 82-Rubidium chloride and 13N-ammonia in myocardial perfusion imaging
Prof. Richard Graham	Deputy Medical Director and Consultant Radiologist, Royal United Hospitals Bath NHS Foundation Trust; Head of School of Radiology, Health Education England South West-Severn Deanery; President of British Nuclear Medical Society	▪ Myeloma; ▪ Musculoskeletal tumours; ▪ Dementia and other neurodegenerative disorders; ▪ Vasculitis; ▪ Choline PET in parathyroid adenoma

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Prasad Guntur	Consultant Radiologist, Ninewells Hospital and Medical School, NHS Tayside; Honorary Senior Clinical Lecturer and Co-Director of Clinical Research Imaging Facility, University of Dundee	▪ Lung carcinoma; ▪ Pleural malignancy; ▪ Thymic tumours; ▪ Prostate malignancy; ▪ Paraneoplastic syndromes; ▪ Carcinoma of unknown primary; ▪ Pyrexia of unknown origin; ▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer
Dr Sai Han	Consultant in Nuclear Medicine and PET-CT, NHS Greater Glasgow and Clyde	▪ Lung carcinoma; ▪ Pleural malignancy; ▪ Thymic tumours
Dr Athar Haroon	Consultant Radionuclide Radiologist, St Bartholomew's Hospital, London	▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer
Dr Iain Lyburn	Consultant Radiologist, Gloucestershire Hospitals NHS Foundation Trust; Visiting Professor, Cranfield University; Medical Director, Cobalt Medical Charity	▪ Breast tumours
Dr Sergejs Magers	Clinical Fellow in Nuclear Medicine, University Hospitals Sussex NHS Foundation Trust	▪ Thyroid carcinoma; ▪ Musculoskeletal tumours; ▪ Dementia and other neurodegenerative disorders
Dr Vanessa Morris	Consultant Rheumatologist, University College London Hospitals NHS Foundation Trust	▪ Vasculitis

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Shaunak Navalkissoor	Consultant In Nuclear Medicine, Royal Free London NHS Foundation Trust	▪ Neuroendocrine tumours; ▪ 68Ga-labelled somatostatin receptor (SSR) imaging for neuroendocrine tumours
Dr Bob Phillips	Consultant in Paediatric (Teenage and Young-Adult) Oncology, Leeds Teaching Hospitals NHS Trust	▪ Paediatric; ▪ Oncological applications
Dr Eliana Reyes	Consultant Nuclear Cardiologist, Barts Health NHS Trust; Clinical Lecturer in Cardiac PET Imaging, King's College London	▪ Cardiological Indications
Dr Rebecca Roylance	Consultant Medical Oncologist, University College London Hospitals NHS Foundation Trust; Honorary Associate Professor, University College London	▪ Breast tumours
Prof. Andrew Scarsbrook	Consultant Radiologist and Nuclear Medicine Physician, Leeds Teaching Hospitals NHS Trust; Professor of Radiology, University of Leeds	▪ Anal carcinoma; ▪ Penile carcinoma; ▪ PET-CT in paediatrics
Dr Ananth Shankar	Consultant Paediatric and Adolescent Oncologist, University College London Hospitals NHS Foundation Trust	▪ PET-CT in paediatrics

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Nitasha Singh	Lead Consultant in Nuclear Medicine, University Hospitals Sussex NHS Foundation Trust	▪ Thyroid carcinoma; ▪ Anal carcinoma; ▪ Urological malignancy; ▪ Renal cancer; ▪ Bladder cancer; ▪ Testicular malignancy; ▪ Dementia and other neurodegenerative disorders
Dr Teresa Szyszko	Consultant in Nuclear Medicine, Royal Free London NHS Foundation Trust; Honorary Associate Professor, University College London	▪ Brain; ▪ Pleural malignancy; ▪ Oesophageal and oesophago-gastric junction cancers; ▪ Gastric cancer; ▪ Epilepsy; ▪ Choline PET for other tumours; ▪ 68Ga-labelled somatostatin receptor (SSR) imaging for neuroendocrine tumours; ▪ 18F-DOPA imaging; ▪ 18F-fluoroethyltyrosine (FET), 18F-fluciclovine and 11C-methionine in brain tumours; ▪ Paediatric; ▪ Non-oncological applications
Miss Sharlini Varatharajah	Medical Student, Brighton and Sussex Medical School	▪ Bladder cancer
Prof. Sobhan Vinjamuri	Lead Consultant in Nuclear Medicine, Royal Liverpool and Broadgreen University Hospitals NHS Trust	▪ Colorectal carcinoma

Co-author/contributor	Medical role(s) and affiliation(s)	Sections
Dr Stefan Vöö	Consultant in Nuclear Medicine, University College London Hospitals NHS Foundation Trust; Clinical Lead in Nuclear Medicine, Whittington Hospital; Research Associate, NIHR Biomedical Research Centre at University College London Hospitals NHS Foundation Trust and University College London	▪ Breast tumours; ▪ Oesophageal and oesophago-gastric junction cancers; ▪ Gastric cancer;Vasculitis; ▪ 18F-DOPA imaging;Childhood hyperinsulinaemia (insulinoma)
Dr Kshama Wechalekar	Cross-site Lead for Nuclear Medicine and PET, Royal Brompton and Harefield Hospitals; Honorary Senior Lecturer, National Heart and Lung Institute, Imperial College London	▪ Cardiological Indications
Dr Zarni Win	Consultant Radiologist and Nuclear Medicine Physician, Head of Service Nuclear Medicine, Imperial College Healthcare NHS Trust	▪ 18F-labelled amyloid tracer brain imaging
Dr Wai Lup Wong	Consultant Radiologist (Nuclear Medicine), East and North Hertfordshire NHS Trust; Honorary Senior Lecturer and Clinical Guardian, University College London; National Specialty Advisor [PET-CT], NHS England	▪ Head and neck tumours; ▪ Prostate malignancy; ▪ Multitracer (PSMA and other relevant tracer) PET-CT imaging of prostate cancer

Acknowledgements

These guidelines have been updated on behalf of the RCR by members of the ICSCNM (in alphabetical order):

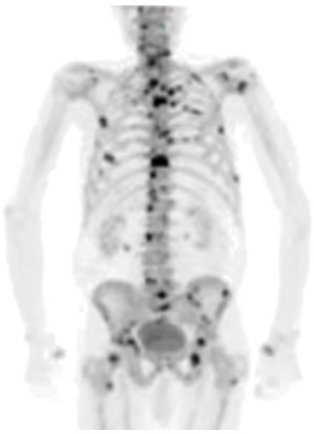
- Dr Clare Beadsmoore, *Consultant Radiologist and Radionuclide Radiologist, Norfolk and Norwich University Hospital;*
- Dr John Buscombe, *Imminent Past President of the British Nuclear Medicine Society*;
- Dr Jeanette Dickson, *President, RCR;*
- Prof Sabina Dizdarevic, *Intercollegiate Standing Committee for Nuclear Medicine Chair and Principal Lead Consultant in Imaging and Nuclear Medicine, University Hospitals Sussex NHS Foundation Trust;*
- Dr Amy Eccles, *Consultant in Nuclear Medicine, Guy's and St. Thomas' Hospitals; RCR radionuclide radiology advisor;*
- Dr Cathryn Edwards, *Registrar, RCP*;
- Dr Charlotte Fowler, *Guy's and St. Thomas' Hospitals, Nuclear Medicine Specialty Advisory Committee Chair;*
- Ms Louise Fraser, *UK Health Security Agency representative;*
- Dr Mark Gaze, *Clinical Oncology representative, RCR*;
- Prof Andrew Goddard, *President, RCP;*
- Prof Richard Graham, *Deputy Medical Director and Consultant Radiologist, Royal United Hospitals Bath NHS Foundation Trust; Current President of the British Nuclear Medicine Society;*
- Dr Prasad Guntur, *Consultant Radiologist/Nuclear Medicine/PETCT, Ninewells Hospital and Medical School, Dundee;*
- Dr Sai Han, *RCPSG/RCPE representative and Consultant in Nuclear Medicine, Glasgow Royal Infirmary;*
- Dr Stephen Harden, *Medical Director for Education and Training, RCR;*
- Prof Geeta Menon, *Lead Dean for Nuclear Medicine/Postgraduate Dean for Health Education England South London;*
- Ms Sue Mitchell, *PET-CT Lead, Cancer Programme of Care – Specialised Commissioning, NHSE/I*;
- Dr Shaunak Navalkissoor, *Consultant Physician in Nuclear Medicine, Royal Free London Foundation NHS Trust;*
- Dr William Ramsden, *Vice-President, Clinical Radiology, RCR;*
- Prof Sobhan Vinjamuri, *Joint Specialty Committee for Nuclear Medicine at the Royal College of Physicians (Chair) and Consultant in Nuclear Medicine, Royal Liverpool University Hospital;*
- Dr Wai Lup Wong, *Consultant Radiologist (Nuclear Medicine), East and North Hertfordshire NHS Trust – PET-CT guardian*

Professor Barrington acknowledges support from the National Institute for Health and Care Research (NIHR) [RP-2-16-07-001]. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

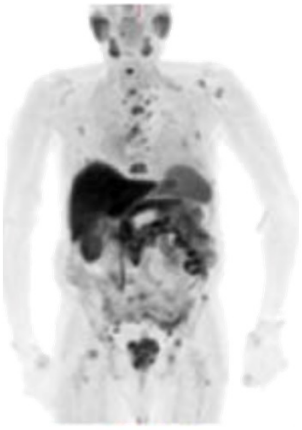
The ICSCNM wishes to acknowledge Dr Sergejs Magers for his significant contribution in co-editing the document.

Furthermore, we would like to thank Emma Burgum (RCR), as well as Louise Abrahams and Heidi Shuttle (University Hospitals Sussex NHS Foundation Trust), for their administrative support.

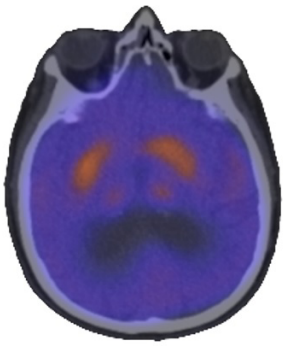
Appendix.
PET-CT illustrations



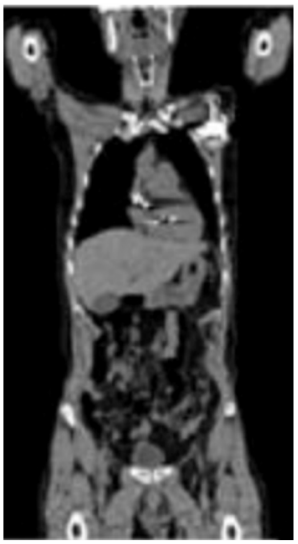
[^{18}F]fluoride in prostate cancer.

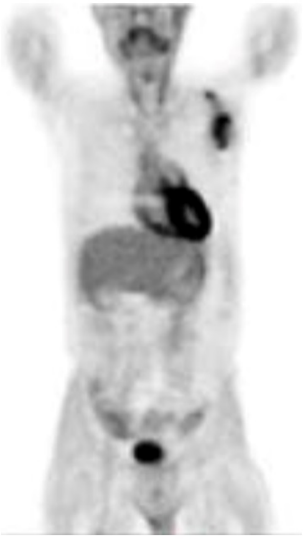


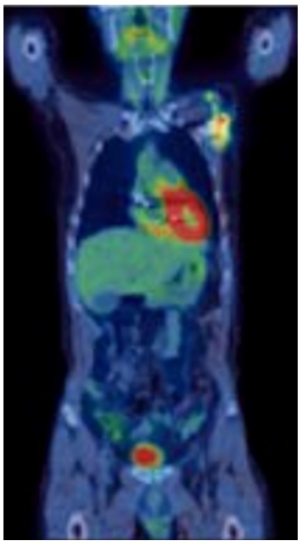
[^{18}F]choline in prostate cancer.



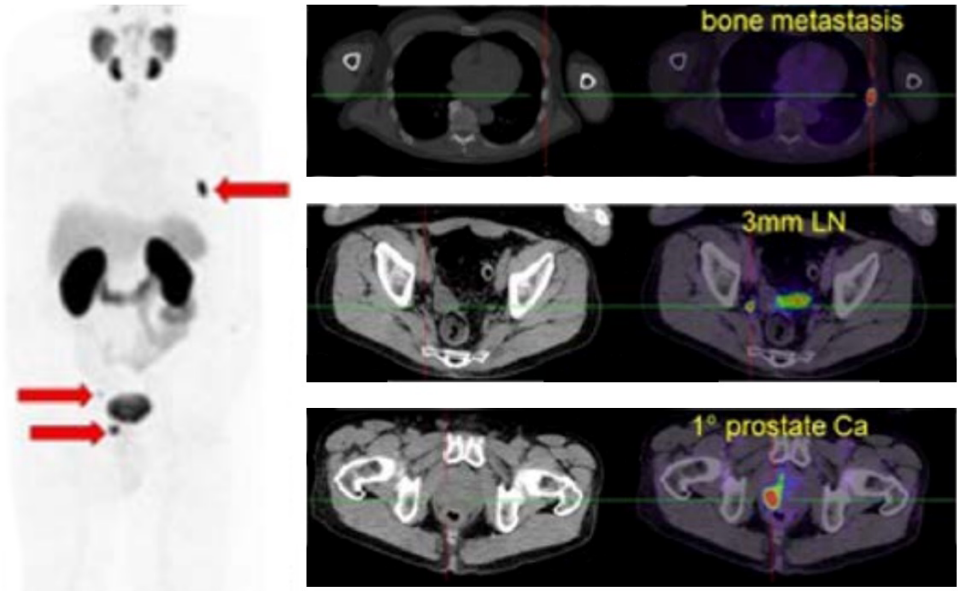
[^{18}F]FDG in limbic encephalitis.



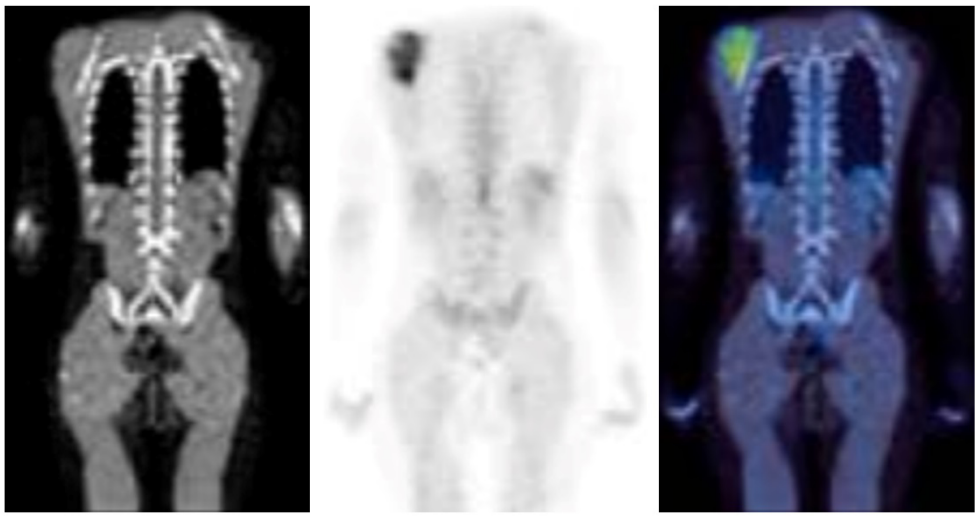




[^{18}F]FDG PET-CT in assessment of infected cardiac pacemaker



^{68}Ga-labelled PSMA ligand PET-CT in prostate cancer.



[^{18}F]FDG PET-CT in paediatric soft tissue sarcoma.

The Royal College of Radiologists
63 Lincoln's Inn Fields
London WC2A 3JW

+44 (0)20 7405 1282
enquiries@rcr.ac.uk
www.rcr.ac.uk
@RCRadiologists

The Royal College of Radiologists, Royal College of Physicians, British Nuclear Medicine Society, Administration of Radioactive Substances Advisory Committee. *Evidence-based indications for the use of PET-CT in the United Kingdom 2022*. London: The Royal College of Radiologists, 2022.