PET Six-Month Monitoring Report 2022-2

Evidence from Primary Studies and Systematic Reviews and Recommendations from Clinical Practice Guidelines

July to December 2022

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QUESTION

What is the role of positron emission tomography (PET) in the clinical management of patients with cancer, sarcoidosis, epilepsy, or dementia with respect to:

- Diagnosis and staging
- Assessment of treatment response
- Detection and restaging of recurrence
- Evaluation of metastasis

Outcomes of interest are survival, quality of life, prognostic indicators, time until recurrence, safety outcomes (e.g., avoidance of unnecessary surgery), and change in clinical management.

INTRODUCTION

In 2010, the Ontario PET Steering Committee (the Committee) requested that the Program in Evidence-Based Care (PEBC) provide regular updates to the Committee of recently published literature reporting on the use of PET in patients with cancer, sarcoidosis, epilepsy, or dementia. The PEBC recommended a regular monitoring program be implemented, with a systematic review of recent evidence conducted every six months. The Committee approved this proposal, and this is the 24th issue of the six-month monitoring reports. This report is

intended to be a high-level, brief summary of the identified evidence, and not a detailed evaluation of its quality and relevance.

METHODS

Literature Search Strategy

Full-text articles published between July and December 2022 were systematically searched through MEDLINE and EMBASE for evidence from primary studies and systematic reviews. The search strategies used are available upon request to the PEBC.

Inclusion Criteria for Clinical Practice Guidelines

Any clinical practice guidelines that contained recommendations with respect to PET were included. Study design was not a criterion for inclusion or exclusion.

Pediatric studies were included in this report and will be included in subsequent reports. The decision to include them was made by the Committee based on the formation of a Pediatric PET Subcommittee that will explore and report on indications relating to PET in pediatric cancer.

Inclusion Criteria for Primary Studies

Articles were selected for inclusion in the systematic review of the evidence if they were fully published, English-language reports of studies that met the following criteria:

1. Studied the use of 18-fluorodeoxyglucose (FDG) PET in cancer, sarcoidosis, or epilepsy in humans.
2. Evaluated the use of the following radiopharmaceutical tracers:
    - ^{68}Ga-DOTA-NOC, ^{68}Ga-DOTATOC, ^{68}Ga DOTATATE
    - ^{18}F-choline, ^{11}C-choline
    - ^{18}F-FET ([^{18}F]fluoroethyl-L-tyrosine) (brain)
    - ^{18}F-FLT ([^{18}F]3-deoxy-^{3}F-fluorothymidine) (various)
    - ^{18}F-MISO ([^{18}F]fluoromisonidazole) (hypoxia tracer)
    - ^{18}F-FAZA ([^{18}F]fluoroazomycin arabinoside) (hypoxia tracer)
    - ^{18}F-fluoride (more accurate than bone scanning)
    - ^{18}F-flurpiridaz (cardiac)
    - ^{18}F-florbetapir/^{18}F-flutemetamol (dementia imaging)
    - ^{18}F-FDOPA
    - ^{68}Ga-PSMA/^{18}F-DCFPyL (prostate-specific membrane antigen)
    - ^{18}F-FACBC (fluciclovine)
    - ^{68}Ga-FAPI
3. Published as a full-text article in a peer-reviewed journal.
4. Reported evidence related to change in patient clinical management or clinical outcomes or reported diagnostic accuracy of PET compared with an alternative diagnostic modality.
5. Used a suitable reference standard (pathological and clinical follow-up) when appropriate.
6. Included ≥12 patients for a prospective study/randomized controlled trial (RCT) or ≥50 patients (≥25 patients for sarcoma) for a retrospective study with the disease of interest.

Inclusion Criteria for Systematic Reviews

1. Reviewed the use of FDG PET/computed tomography (CT) in cancer, sarcoidosis, or epilepsy.
2. Contained evidence related to diagnostic accuracy; change in patient clinical management, clinical outcomes, or treatment response; survival; quality of life; prognostic indicators; time until recurrence; or safety outcome (e.g., avoidance of unnecessary surgery).

Exclusion Criteria

1. Letters and editorials.

RESULTS

Literature Search Results

Primary Studies and Systematic Reviews

Seventy-five studies published between July and December 2022 met the inclusion criteria. A summary of the evidence from the 75 studies can be found in **Appendix 1: Summary of studies from July to December 2022**.

Breast Cancer

Three studies met the inclusion criteria [1-3]. In the preoperative staging of patients with early-stage breast cancer, FDG PET/CT performed suboptimally (sensitivity, 68.6%; specificity, 72.3%) when detecting axillary lymph node metastases [1]. For locally advanced cases, FDG PET/CT appeared to be more sensitive (100% versus 65.2%) but less specific (72.2% to 75.7% versus 80.7%) than magnetic resonance imaging (MRI) in predicting pathological response to neoadjuvant chemotherapy [2,3]. Patients with a complete FDG PET/CT response were observed to have a longer three-year disease-free survival (84.4% versus 60.0%, p=0.001) than those with a non-complete response [3].

Epilepsy

Two studies met the inclusion criteria [4,5]. In the presurgical evaluation of patients with refractory temporal lobe or extratemporal lobe epilepsy, FDG PET/CT was able to localize the epileptogenic zone with a sensitivity of 62.7% [4]. With respect to temporal epilepsy only, FDG PET/CT (74.6%) was the most accurate in determining the surgical field, followed by cortical thickness (66.7%) and quantitative anisotropy (55.6%) abnormalities on MRI. Furthermore, FDG PET/CT had the highest sensitivity (89.4%) for predicting seizure freedom whereas quantitative anisotropy had the highest specificity (87.5%). Taken together, the proportion of patients free of seizure was 96.4% when congruous localization was achieved between all three methods (odds ratio [OR], 19.57; 95% confidence interval [CI], 2.38 to 161.25, p=0.006) [5].

Gastrointestinal Cancer

Eight studies met the inclusion criteria [6-13]. In the preoperative staging of patients with rectal or colorectal cancer, one retrospective study found FDG PET/CT (100%) to be more sensitive than CT (37.5%) in the detection of lymph node involvement [6], while a meta-analysis found FDG PET/CT (pooled estimate, 54.0%) to be less sensitive than MRI (pooled estimate, 77.0%) [7]. Nevertheless, the specificity for all three imaging modalities was consistently high (FDG PET/CT, 94.3% to 95.0%; CT, 100%; MRI, 85.0%) [6,7]. For identification of liver and lung metastases, FDG PET/CT and CT performed comparably well [6]. In the postoperative setting, FDG PET/CT (accuracy, 82.9%) was inferior to MRI (accuracy, 100%) in the assessment of extension to nearby organs [8], but when compared to carcinoembryonic antigen (CEA) level, circulating tumour DNA level, and CT scan, FDG PET/CT (pooled estimate, 95.0%) offered the highest sensitivity for detecting recurrence, whereas circulating tumour DNA had the highest specificity (pooled estimate, 95.0%) [9]. Additionally, the area under the receiver operating characteristic curve (AUC) of FDG PET/CT improved from 0.88 in patients with normal CEA levels to 0.97 in those with elevated CEA [10]. In general, postoperative FDG PET/CT findings changed the treatment strategy of 11.8% of cases [6]. In the staging of patients with hepatocellular carcinoma, FDG PET/CT appeared to provide an improvement in sensitivity (92.3% versus 51.3%) and accuracy (88.7% versus 64.8%) over triphasic CT for detecting

extrahepatic metastases [11]. FDG PET/CT also demonstrated added benefit in gastric cancer staging by changing the initial management of 3% to 29% of patients [12]. For response assessment of patients with anal squamous cell carcinoma treated with curative-intent chemoradiotherapy, the diagnostic performance of FDG PET/CT and MRI were broadly similar except for sensitivity, which favoured MRI (86.7% versus 73.3%, p=0.04) [13].

Genitourinary Cancer

Four studies met the inclusion criteria [14-17]. Three studies examined the clinical utility of FDG PET/CT in patients with renal cell carcinoma. Preoperative FDG PET/CT was able to reveal venous tumour thrombus with exceptional sensitivity (96.7%), specificity (99.1%), and accuracy (98.3%) [14]. For patients who underwent initial staging or restaging after surgery, FDG PET/CT presented better specificity (100% versus 81.2%, p<0.0001) and negative predictive value (NPV) (100% versus 37.1%, p<0.0001) than contrast-enhanced CT in detecting metastases and recurrence [15]. Postoperative FDG PET/CT alone achieved 95.0% for both sensitivity and specificity in the evaluation of recurrent disease [16]. During active surveillance/follow-up of testicular seminoma, FDG PET/CT offered positive predictive values (PPVs) of 100% and 77.1% for identifying recurrence in stage 1 and advanced stage patients, respectively. In both cases, FDG PET/CT was able to accurately rule out recurrent disease (NPV, 90.9% to 91.1%) within 24 months [17].

Gynecologic Cancer

Six studies met the inclusion criteria [18-23]. Two retrospective studies and one meta-analysis looked at FDG PET/CT in the evaluation of recurrent or persistent ovarian cancer. Results were consistently high across the studies with sensitivity ranging from 88.0% to 98.0% and specificity ranging from 80.0% to 100% [18-20]. For the detection of recurrent cervical cancer, FDG PET/CT showed high sensitivity (97.6%) but low specificity (61.9%), yet still exceeded the diagnostic performance of MRI [21]. Conversely, FDG PET/CT displayed low sensitivity (53.9%) but high specificity (90.5%) for the preoperative detection of lymph node metastases in patients with early-stage cervical cancer [22]. As for endometrial cancer, FDG PET/MRI (86.0%) had a higher staging accuracy than that of FDG PET/CT (77.2%), with a clear advantage in detecting myometrial invasion (accuracy, 93.0% versus 73.7%). Overall, FDG PET/MRI overstaged 8.8% and understaged 5.3% of patients, whereas FDG PET/CT overstaged 15.8% and understaged 7.0% of patients [23].

Head and Neck Cancer

Twelve studies met the inclusion criteria [24-35]. In the preoperative staging of patients with head and neck squamous cell carcinoma, FDG PET/CT can reliably rule out nodal metastases due to its high NPV (patient-based, 94.1%; neck side-based, 92.5%; nodal level-based, 90.5%) [24]. In the follow-up of patients after 12 weeks of chemoradiotherapy treatment, FDG PET/MRI proved to be superior to FDG PET/CT for detecting locoregional recurrence in terms of sensitivity (100% versus 67.0%, p<0.05), NPV (100% versus 87.0%, p<0.05), and AUC (0.997 versus 0.890, p=0.0017) [25]. On the contrary, FDG PET/CT and FDG PET/MRI performed similarly for detecting distant metastases and distant second primary cancers [26]. Collectively, FDG PET or PET/CT or PET/MRI was highly effective (pooled sensitivity, 91.7%; pooled specificity, 92.4%) in the detection of perineural spread [27]. With respect to oropharyngeal squamous cell carcinoma, the addition of preoperative FDG PET/CT to conventional workup led to remarkably lower risk of all-cause mortality in stage IVA to IVB (hazard ratio [HR], 1.82; 95% CI, 1.47 to 2.26, p<0.0001) but not stage I to III (HR, 1.12; 95% CI, 0.86 to 1.48, p=0.4028) patients [28]. However, early-stage patients may benefit from preoperative FDG PET/CT to help inform suitability for transoral robotic surgery [29]. In the

response assessment of patients treated with definitive radiotherapy with or without chemotherapy, FDG PET/CT using Hopkins score 1 to 3 was associated with prolonged three-year overall survival (OS) (94.0% versus 69.4%, p=0.001) and three-year progression-free survival (PFS) (86.6% versus 55.4%, p<0.001) [30]. Likewise, negative FDG PET/CT scan was associated with considerably better three-year OS (83% versus 30%, p<0.001) and three-year PFS (79.0% versus 17.0%, p<0.001) when considering only human papillomavirus (HPV)-negative cases [31]. In the primary staging of oral squamous cell carcinoma, FDG PET/CT detected synchronous upper aerodigestive tract malignancies with diagnostic measures comparable to that of panendoscopy [32]. Patients who underwent postoperative FDG PET/CT rather than CT/MRI before adjuvant radiotherapy or chemoradiotherapy had significantly improved median disease-specific survival (not reached versus 4.9 years, p=0.049; HR, 2.46; 95% CI: 1.83 to 7.63, p=0.032) and media OS (5.4 years vs. 4.3 years, p=0.024; HR, 1.60; 95% CI, 1.04 to 4.66, p=0.011) [33]. For the assessment of cervical lymph node metastases in patients with differentiated thyroid cancer, FDG PET/CT offered greater specificity (80.0% versus 60.0%) than diffusion-weighted MRI, while maintaining equal sensitivity (84.0% for both) [34]. In patients with suspicious laryngeal findings after organ preservation treatment, a negative FDG PET/CT scan (NPV, 100%) can safely obviate the need for direct laryngoscopy and biopsy. However, FDG PET/CT do suffer from substantial false-positive results due to very poor PPV (55.6%) [35].

Hematologic Cancer

Two studies met the inclusion criteria [36-37]. In the initial staging of patients with extranodal natural killer/T-cell lymphoma, FDG PET/CT (accuracy, 90.6% to 93.2%) performed comparably to bone marrow aspiration (accuracy, 91.9%) in the detection of bone marrow involvement [36,37]. FDG PET/CT examination did not change the clinical stage or initial treatment plan of any patients [37].

Melanoma

Two studies met the inclusion criteria [38-39]. In the diagnosis of patients with Merkel cell carcinoma, FDG PET or PET/CT demonstrated high sensitivity (pooled estimate, 91.0%) and specificity (pooled estimate, 92.0%) [38]. For staging or restaging of patients with malignant melanoma, FDG PET/CT was more sensitive but less specific than ultrasound in both examination-based (sensitivity, 80.0% versus 63.0%, p=0.0018; specificity, 96.0% versus 98.0%, p=0.014) and lesion-based analysis (sensitivity, 83.0% versus 61.0%, p<0.001; specificity, 91.0% versus 98.0%, p<0.001) [39].

Neuro-Oncology

One study met the inclusion criteria [40]. Pooled estimates from a meta-analysis signified high sensitivity (91.0%) and specificity (88.0%) for FDG PET/CT in the differential diagnosis of primary central nervous system lymphoma and high-grade gliomas.

Non-FDG Tracers

Twenty-six studies met the inclusion criteria [41-66]. Summary data from a meta-analysis showed that 36.0% of patient management for confirmed or suspected neuroendocrine tumours (NETs) were guided by ^{68}Ga-DOTA-TATE/NOC/TOC PET/CT findings [41]. However, the use of ^{68}Ga-DOTA-TOC PET/CT or PET/MRI was less impactful in the preoperative staging of patients specifically with non-functioning pancreatic NETs. The sensitivity of ^{68}Ga-DOTA-TOC PET/CT or PET/MRI for assessing nodal metastases was exceedingly low (11.9%), despite a high specificity (94.8%) [42]. In patients with suspicious tumour recurrence after gross total resection of glioma, ^{18}F-Fluorocholine PET/CT (accuracy, 87.5%) performed better than MRI (accuracy, 70.8%) in the definitive diagnosis of recurrent disease [43]. ^{68}Ga-PSMA PET/CT or

PET/MRI was also evaluated in patients with high-grade glioma and demonstrated high sensitivity (pooled estimate, 98.2%) and specificity (pooled estimate, 91.2%) for differential diagnosis or recurrence [44]. Likewise, ^{68}Ga-PSMA PET/CT or PET/MRI can effectively reveal hepatic and extrahepatic lesions (detection rate, 85.1%) during staging or restaging of patients with hepatocellular carcinoma [45]. Numerous studies evaluated the clinical utility of ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT in prostate cancer. The sensitivity (79.0% to 96.7%) and specificity (54.0% to 87.0%) of ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT in the diagnosis of primary prostate cancer varied between studies [46-48] but appeared to be superior to multiparametric MRI [46]. In the same manner, ^{68}Ga-PSMA PET/CT targeted biopsy maybe a better choice over multiparametric MRI targeted biopsy in the diagnosis of clinically significant prostate cancer [49,50]. For primary staging, ^{68}Ga-PSMA PET/CT detected lymph node metastases with high specificity (91.5%) but low sensitivity (60.0%) [51]. Despite this limitation, the five-year recurrence-free survival rate (71.1% versus 56.4%, p=0.003; HR, 0.58; 95% CI, 0.41 to 0.83, p=0.004) was significantly higher in patients staged by ^{68}Ga-PSMA PET/CT as compared to conventional imaging, which likely due to improved selection in surgical candidacy [52]. Similarly, ^{18}F-DCFPyL PET/CT outperformed conventional imaging in the detection of nodal (sensitivity, 89.0% versus 25.0%, p<0.001) and distant (sensitivity, 92.0% versus 23.0%, p<0.001) metastases. As a result, the N and M staging were altered in 39.8% of patients and a shift in treatment strategy in 22.2% of cases [53]. In the setting of biochemical recurrence after definitive therapy, ^{68}Ga-PSMA PET/CT influenced the therapeutic management of 25.0% to 42.9% of patients [54-56]. ^{18}F-DCFPyL PET/CT too had a significant impact on treatment intent (43.8%), whereas only 16.8% of cases were affected by CT [57]. This is in line with the high PPV (89.0%) reported for ^{18}F-DCFPyL PET/CT in detecting sites of recurrence [58]. In terms of bone metastases evaluation, ^{68}Ga-PSMA PET/CT (pooled sensitivity, 97.0% to 98.0%; pooled specificity, 97.0% to 100%) [59,60] proved to be far superior to ^{99m}Tc-MDP bone scintigraphy (pooled sensitivity, 83.0%; pooled specificity, 68.0%) [59]. ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT was also shown to be useful in the staging of patients with suspected metastatic renal cell carcinoma, where it guided management in 49.2% of cases [61]. PET imaging with ^{18}F-DOPA was investigated in two small prospective studies, one in recurrent medullary thyroid carcinoma and the other in recurrent high-grade glioma. In the former, ^{18}F-DOPA PET/CT findings led to changes in management in 38.9% of patients [62], while in the latter, ^{18}F-DOPA PET expanded the MRI-defined gross target volume by 43% during re-irradiation and subsequently improved the three-month PFS against historical control [63]. ^{18}F-FET PET or PET/MRI was also examined in patients with suspected recurrent high-grade glioma. In this study, ^{18}F-FET PET or PET/MRI (AUC, 0.89 to 0.96) provided higher overall diagnostic accuracy than dynamic contrast-enhanced perfusion MRI (AUC, 0.79 to 0.84) in the differentiation of tumour progression from treatment-related changes [64]. Results from a multicentre, phase 3 trial (MITNEC-A1) suggested that ^{18}F-sodium fluoride PET/CT has the potential to supplant ^{99m}Tc-MDP SPECT as the preferred bone imaging modality (accuracy, 84.3% versus 77.4%, p=0.016) in patients with high-risk breast or prostate cancer [65]. Similar outcomes were observed in morbidly obese patients (body mass index >40 kg/m^2) where ^{18}F-sodium fluoride PET/CT (patient-based, 95.7%; lesion-based, 97.7%) showed superior accuracy over ^{99m}Tc-MDP whole-body scintigraphy (patient-based, 64.1%; lesion-based, 48.9%), ^{99m}Tc-MDP SPECT (patient-based, 73.5%; lesion-based, 56.0%), and ^{99m}Tc-MDP SPECT/CT (patient-based, 82.1%; lesion-based, 67.3%) in the detection of bone metastases (p<0.0001 for all pairwise comparisons) [66].

Pancreatic Cancer

One study met the inclusion criteria [67]. FDG PET/CT showed a pooled sensitivity of 89.0% and a pooled specificity of 88.0% for detecting local and/or distant disease recurrence following definitive treatment.

Pediatric Cancer

One study met the inclusion criteria [68]. In patients with Hodgkin lymphoma (HL), FDG PET/CT assessment after two cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) was more likely to indicate a satisfactory response as compared with contrast-enhanced CT assessment and thereby, significantly reducing the need for radiotherapy (38.7% versus 50.0%, p=0.017). However, the five-year OS (94.1% versus 91.8%, p=0.391) and event-free survival (85.5% versus 86.7%, p=0.724) were comparable between the two response-based treatment protocols.

Thoracic Cancer

Five studies met the inclusion criteria [69-73]. In the preoperative staging of non-small cell lung cancer (NSCLC) with FDG PET/CT, one meta-analysis that comprised of patients from Asia demonstrated high specificity (pooled estimate, 93.0%) but subpar sensitivity (pooled estimate, 68.0%) for identifying lymph node metastases [69]. Similar results (specificity, 88.9%; sensitivity, 50.0%) were observed from a retrospective study conducted in Germany. The authors also reported that FDG PET/CT findings downstaged 13.8% and upstaged 8.0% of patients [70]. Nonetheless, endobronchial ultrasound-guided transbronchial needle aspiration should be the preferred method over FDG PET/CT for evaluating the status of mediastinal lymph nodes due to superior diagnostic accuracy (96.4% versus 64.3%, p<0.001) [71]. In terms of OS, the use of preoperative FDG PET/CT was associated with a lower all-cause mortality in stage IIIA (HR, 0.90; 95% CI, 0.79 to 0.94, p=0.02) and IIIB (HR, 0.80; 95% CI, 0.71 to 0.90, p<0.01) patients, but not in stage I and II patients (HR, 1.19; 95% CI, 0.89 to 1.30, p=0.65) [72]. Likewise for patients with stage IV extracranial oligometastatic disease, FDG PET/CT-guided thorax radiotherapy (p<0.001) was associated with improved median survival time while CT-guided radiotherapy (p=0.236) was not [73].

CLINICAL EXPERT REVIEW

Breast Cancer

Current Eligibility Criteria for the PET ABC Trial

- For the staging of patients with clinical stage III breast cancer.

Reviewer's Comments

A review was not completed by a clinical expert in breast cancer.

Epilepsy

Current Indications for Epilepsy

- For patients with medically intractable epilepsy being assessed for epilepsy surgery.

Reviewer's Comments (Dr. Jorge Burneo)

The current recommendation for the utilization of PET/CT in epilepsy remains valid and no changes are required.

Gastrointestinal Cancer

Current Indications for Colorectal Cancer

- For the staging or re-staging of patients with apparent limited metastatic disease (e.g., organ-restricted liver or lung metastases) or limited local recurrence, who are being considered for radical intent therapy.

  Note: as chemotherapy may affect the sensitivity of the PET scan, it is strongly recommended to schedule PET at least six weeks after last chemotherapy, if possible.

- Where recurrent disease is suspected on the basis of an elevated and/or rising CEA level(s) during follow-up after surgical resection but standard imaging tests are negative or equivocal.

Current Indication for Anal Canal Cancer

- For the initial staging of patients with T2-4 (or node-positive) squamous cell carcinoma of the anal canal with or without evidence of nodal involvement on conventional anatomical imaging.

Reviewer's Comments (Dr. Aamer Mahmud)

The current recommendations for the utilization of PET/CT in gastrointestinal cancer remain valid and no changes are required.

Genitourinary Cancer

Current Indications for Germ Cell Tumours

- Where recurrent disease is suspected on the basis of elevated tumour marker(s) (beta human chorionic gonadotropin and/or alpha fetoprotein) and standard imaging tests are negative; or where persistent disease is suspected on the basis of the presence of a residual mass after primary treatment for seminoma when curative surgical resection is being considered.

Current Indication for Bladder Cancer

- For the staging of patients with newly diagnosed muscle-invasive urothelial carcinoma of the bladder being considered for curative intent treatment with either radical cystectomy or radiation-based bladder preservation therapy; TNM stage T2a-T4a, N0-3, M0.

Reviewer's Comments (Dr. Glenn Bauman)

The current recommendations for the utilization of PET/CT in genitourinary cancer remain valid and no changes are required.

Gynecologic Cancer

Current Indications for Cervical Cancer

- For the staging of locally advanced cervical cancer when CT/MRI shows positive or indeterminate pelvic nodes (>7 mm and/or suspicious morphology), borderline or suspicious para-aortic nodes, or suspicious or indeterminate distant metastases (e.g., chest nodules).
- For re-staging of patients with recurrent gynecologic malignancies under consideration for radical salvage surgery (e.g., pelvic exenteration).

Reviewer's Comments

A review was not completed by a clinical expert in gynecologic cancer.

Head and Neck Cancer

Current Indications for Head and Neck Cancer

- For the baseline staging of node-positive (N1-N3) head and neck cancer where PET will impact radiation therapy (e.g., radiation volume or dose).
- To assess patients with N1-N3 metastatic squamous cell carcinoma of the head and neck after chemoradiation (HPV negative); or who have residual neck nodes equal to or

greater than 1.5 cm on re-staging CT performed 10 to 12 weeks post therapy (HPV positive).

Current Indication for Unknown Primary

- For the evaluation of metastatic squamous cell carcinoma in neck nodes when the primary disease site is unknown after standard radiologic and clinical investigation.
  Note: a panendoscopy is not required prior to the PET scan.

Current Indication for Nasopharyngeal Cancer

- For the staging of nasopharyngeal cancer.

Current Indications for Thyroid Cancer

- Where recurrent or persistent disease is suspected on the basis of an elevated and/or rising tumour markers (e.g., thyroglobulin) with negative or equivocal conventional imaging work-up.
- For the staging of histologically proven anaplastic thyroid cancer with negative or equivocal conventional imaging work-up.
- For the baseline staging of histologically proven medullary thyroid cancer being considered for curative intent therapy or where recurrent disease is suspected on the basis of elevated and/or rising tumour markers (e.g., calcitonin) with negative or equivocal conventional imaging work-up.

Reviewer's Comments (Dr. Amit Singnurkar)

The current recommendations for the utilization of PET/CT in head and neck cancer remain valid and no changes are required.

Hematologic Cancer

Current Indications for Lymphoma

- For the baseline staging of patients with HL or non-Hodkin lymphoma (NHL).
- For the assessment of response in HL following two or three cycles of chemotherapy when curative therapy is being considered.
- For the evaluation of residual mass(es) or lesion(s) (e.g., bone) following chemotherapy in a patient with HL or NHL when further potentially curative therapy (such as radiation or stem cell transplantation) is being considered.
- To assess response to chimeric antigen receptor T-cell therapy, 90 days post transfusion.

Current Indications for Multiple Myeloma or Plasmacytoma

- For patients with presumed solitary plasmacytoma who are candidates for curative-intent radiotherapy (to determine whether solitary or multifocal/extensive disease).
- For work-up of patients with smoldering myeloma and negative or equivocal skeletal survey (to determine whether smoldering or active myeloma).
- For baseline staging and response assessment of patients with nonsecretory myeloma, oligosecretory myeloma, or POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal protein, skin changes).
- For work-up of patients with newly diagnosed secretory multiple myeloma and negative or equivocal skeletal survey.

Reviewer's Comments

A review was not completed by a clinical expert in hematologic cancer.

Melanoma

Current Indications for Melanoma

- For the staging of patients with localized "high-risk" melanoma, or for the evaluation of patients with isolated melanoma metastases, when surgery or other ablative therapies are being considered.
- For the staging of patients before starting immunotherapy.
- For early response assessment of patients with metastatic melanoma currently receiving immunotherapy after two to four cycles.
- For response assessment of patients with metastatic melanoma at end of immunotherapy.

Reviewer's Comments

A review was not completed by a clinical expert in melanoma.

Neuro-Oncology

Current Indications for Paraneoplastic Syndrome

- For the evaluation of patients with suspected paraneoplastic neurologic syndromes with negative conventional imaging, with or without positive onconeuronal antibodies.

Reviewer's Comments (Dr. Amit Singnurkar)

The current recommendations for the utilization of PET/CT in neuro-oncology remain valid and no changes are required.

Non-FDG Tracers

Current Indications for Gallium-68 PET/CT in NETs

- For identification of primary tumour when there is clinical suspicion of NETs and primary tumour site is unknown or uncertain. Patients should have elevated biochemical markers (e.g., 5-HIAA ± elevated chromogranin A) and no definitive evidence of disease on CT.
- For the staging of patients upon initial diagnosis of NETs.
- For the re-staging of patients with NETs when clinical intervention is being considered.
- As a problem-solving tool in patients with NETs when confirmation of site of disease and/or disease extent may impact clinical management.

Current Indications for PSMA PET/CT in Prostate Cancer

- For patients with post-prostatectomy node-positive disease or persistently detectable prostate-specific antigen (PSA).
- For patients with biochemical failure post-prostatectomy.
- For patients with failure following radical prostatectomy followed by adjuvant or salvage radiotherapy.
- For patients with rising PSA post-prostatectomy despite salvage hormone therapy.
- For patients with biochemical failure following treatment for oligometastatic disease.
- For patients with biochemical failure following primary radiotherapy.
- Where confirmation of site of disease and/or disease extent may impact clinical management over and above the information provided by conventional imaging.

Reviewer's Comments (Dr. Amit Singnurkar)

The current recommendations for the utilization of PET/CT with non-FDG tracers remain valid and no changes are required.

Pancreatic Cancer

No indication currently exists for the utilization of PET/CT in pancreatic cancer.

Reviewer's Comments

A review was not completed by a clinical expert in pancreatic cancer.

Pediatric Cancer

Current Indications for Pediatric Cancer (patients must be <18 years of age)

- For the following cancer types (International Classification for Childhood Cancer):
  - Bone/cartilage – osteosarcoma, Ewing sarcoma
  - Connective/other soft tissue – rhabdomyosarcoma, other
  - Kidney – renal tumour
  - Liver – hepatic tumour
  - Lymphoma/post-transplant lymphoproliferative disorder – HL and NHL
  - Primary brain – astrocytoma, medulloblastoma, ependymoma, other
  - Reproductive – germ cell tumour
  - Sympathetic nervous system - neuroblastoma MIBG-negative
  - Other – Langerhans cell histiocytosis, melanoma of the skin, thyroid
- For the following indications:
  - Initial staging
  - Monitoring response during treatment/determine response-based therapy
  - Rule out progression prior to further therapy
  - Suspected recurrence/relapse
  - Rule out persistent disease
  - Select optimal biopsy site
- For the assessment of response in HL or NHL after a minimum of two cycles of chemotherapy when curative therapy is being considered.

Reviewer's Comments (Dr. Amer Shammas)

The current recommendations for the utilization of PET/CT in pediatric cancer remain valid and no changes are required.

Thoracic Cancer

Current Indications for Solitary Pulmonary Nodule

- For a semi-solid or solid lung nodule for which a diagnosis could not be established by a needle biopsy due to unsuccessful attempted needle biopsy; the solitary pulmonary nodule is inaccessible to needle biopsy; or the existence of a contraindication to the use of needle biopsy.

Current Indications for NSCLC

- For initial staging of patients with NSCLC (clinical stage I–III) being considered for potentially curative therapy.
- For re-staging of patients with locoregional recurrence, after primary treatment, being considered for definitive salvage therapy.
  Note: Histological proof is not required prior to PET if there is high clinical suspicion for NSCLC (e.g., based on patient history and/or prior imaging).
  Note: PET is appropriate for patients with either histological proof of locoregional recurrence or strong clinical and radiological suspicion of recurrence who are being considered for definitive salvage therapy.

Current Indication for Small Cell Lung Cancer

- For initial staging of patients with limited-disease small cell lung cancer where combined modality therapy with chemotherapy and radiotherapy is being considered.

Current Indication for Mesothelioma

- For the staging of patients with histologic confirmation of malignant mesothelioma.

Reviewer's Comments (Dr. Donna Maziak)

The current recommendations for the utilization of PET/CT in thoracic cancer remain valid and no changes are required.

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REFERENCES

1. Dulgeroglu O, Arikan A, Kara H, Uras C. Impact of preoperative PET/CT for axillary staging in patients with early breast cancer. Ann Ital Chir. 2022;93:504-9.
2. Baysal H, Serdaroglu AY, Ozemir IA, Baysal B, Gungor S, Erol CI, et al. Comparison of magnetic resonance imaging With positron emission tomography/computed tomography in the evaluation of response to neoadjuvant therapy of breast cancer. J Surg Res. 2022;278:223-32.
3. Goktas Aydin S, Bilici A, Olmez OF, Oven BB, Acikgoz O, Cakir T, et al. The Role of 18F-FDG PET/CT in predicting the neoadjuvant treatment response in patients with locally advanced breast cancer. Breast Care. 2022;17(5):470-9.
4. Carvalho MS, Alvim MKM, Etchebehere E, Santos AO, Ramos CD, Argenton JLP, et al. Interictal and postictal18F-FDG PET/CT in epileptogenic zone localization. Radiologia Brasileira. 2022;55(5):273-9.
5. Wang ZM, Wei PH, Wang C, Hou Y, Guo K, Cui B, et al. Combined [(18)F]FDG-PET with MRI structural patterns in predicting post-surgical seizure outcomes in temporal lobe epilepsy patients. Eur Radiol. 2022;32(12):8423-31.
6. Omarov N, Uymaz DS, Kulle CB, Ozkan ZG, Azamat S, Keskin M, et al. The Role of FDG positron emission tomography/contrast--enhanced computed tomography in preoperative staging and postoperative follow-up in rectal cancer surgery. Pol Przegl Chir. 2022;94(6):10-6.
7. Rooney S, Meyer J, Afzal Z, Ashcroft J, Cheow H, DePaepe K, et al. The Role of preoperative imaging in the detection of lateral lymph node metastases in rectal cancer: a systematic review and diagnostic test meta-analysis. Dis Colon Rectum. 2022;65(12):1436-46.
8. Faheem MH, Nathan E, Youssef AF. Role of PET/CT in the follow-up of postoperative and/or post-therapy cancer rectum: comparison with pelvic MRI. Egypt J Radiol Nucl Med. 2022;53(1):161.
9. Dawood ZS, Alaimo L, Lima HA, Moazzam Z, Shaikh C, Ahmed AS, et al. Circulating Tumor dna, imaging, and carcinoembryonic antigen: comparison of surveillance strategies among patients who underwent resection of colorectal cancer-a systematic review and meta-analysis. Ann Surg Oncol. 2023;30(1):259-74.
10. Yao J, Zhang S, Liang J, Li H. The diagnostic performance of 2-[18F]FDG PET/CT for the recurrent colorectal cancer in patients with elevated CEA versus normal CEA: a systematic review and meta-analysis. Clin Transl Imaging. 2022.
11. Barakat MMK, Badran EM, Allam YEAH, Alsabbagh ZA, Abdelrahman AS. The role of triphasic CT imaging and 18F FDG PET CT on detection of extrahepatic metastases and proper staging of HCC: a comparative study. Egypt J Radiol Nucl Med. 2022;53(1):137.
12. Foley KG, Coomer W, Coles B, Bradley KM. The impact of baseline (18)F-FDG PET-CT on the management and outcome of patients with gastric cancer: a systematic review. Br J Radiol. 2022;95(1139):20220437.
13. Adusumilli P, Elsayed N, Theophanous S, Samuel R, Cooper R, Casanova N, et al. Combined PET-CT and MRI for response evaluation in patients with squamous cell anal carcinoma treated with curative-intent chemoradiotherapy. Eur Radiol. 2022;32(8):5086-96.
14. Chen S, Zhao Y, Tang Q, Wu C, Wang A, Ma L, et al. Diagnostic performance and prognostic value of preoperative 18F-FDG PET/CT in renal cell carcinoma patients with venous tumor thrombus. Cancer Imaging. . 2022;22(1):65.
15. Pereira M, Punatar CB, Singh N, Sagade SN. Role of 18F-FDG PET/CT for detection of recurrence and metastases in renal cell carcinoma-are we underusing PET/CT? Diagn Interv Radiol. 2022;28(5):498-502.
16. Fan L, Xu Y, Zhao J, Tang W, Zhang Z, Zhang Y, et al. The diagnostic performance of 18F-FDG PET/CT in recurrent renal cell carcinoma: a systematic review and meta-analysis. Clin Transl Imaging. 2022.

17. Conduit C, Koh TT, Hofman MS, Toner GC, Goad J, Lawrentschuk N, et al. Two decades of FDG-PET/CT in seminoma: exploring its role in diagnosis, surveillance and follow-up. Cancer Imaging. 2022;22(1):58.
18. Dondi F, Albano D, Bertagna F, Giubbini R. [18F]FDG PET/CT and CA-125 in the evaluation of ovarian cancer relapse or persistence: is there any correlation? Nucl Med Rev Cent East Eur. 2022;25(2):78-84.
19. Amer MIES, Monib AM, Chalabi NAM, Othman AIA. Role of 18F FDG PET/CT in evaluation of post-operative ovarian carcinoma. Egypt J Radiol Nucl Med. 2022;53(1):199.
20. Wang X, Yang L, Wang Y. Meta-analysis of the diagnostic value of (18)F-FDG PET/CT in the recurrence of epithelial ovarian cancer. Front Oncol. 2022;12:1003465.
21. Stojiljkovic M, Sobic Saranovic D, Odalovic S, Popovic M, Petrovic J, Rankovic N, et al. FDG PET-CT as an important diagnostic tool and prognostic marker in suspected recurrent cervical carcinoma after radiotherapy: comparison with MRI. Radiol Oncol. 2022;56(4):453-60.
22. Maheshwari A, Gupta S, Deodhar K, Chopra S, Rangarajan V, Purandare N, et al. Preoperative imaging with positron emission tomography and computed tomography (18F-FDG PET/CT) or contrast-enhanced computed tomography (CECT) scan in operable cervical cancer: a prospective study. Eur J Gynaecol Oncol. 2022;43(4):32-9.
23. Yu Y, Zhang L, Sultana B, Wang B, Sun H. Diagnostic value of integrated 18F-FDG PET/MRI for staging of endometrial carcinoma: comparison with PET/CT. BMC Cancer. 2022;22(1):947.
24. Piotrowicz O, Jia HN, Blazak J. F18-FDG PET/CT accuracy in nodal staging of head and neck squamous cell carcinoma and correlation of SUV(max) to the likelihood of a confirmed nodal metastasis. J Med Imaging Radiat Sci. 2022;53(4):599-604.
25. Murtojarvi S, Malaspina S, Kinnunen I, Tuokkola T, Honka M-J, Saunavaara V, et al. Diagnostic accuracy of 18F-FDG-PET/CT and 18F-FDG-PET/MRI in Detecting locoregional recurrence of HNSCC 12 Weeks after the end of chemoradiotherapy: single-center experience with PET/MRI. Contrast Media Mol Imaging. 2022;2022:8676787.
26. Katirtzidou E, Rager O, Varoquaux AD, Poncet A, Lenoir V, Dulguerov N, et al. Detection of distant metastases and distant second primary cancers in head and neck squamous cell carcinoma: comparison of [18F]FDG PET/MRI and [18F]FDG PET/CT. Insights Imaging. 2022;13(1):121.
27. Nie X, Zhou J, Zeng J, Sun J, Chen W, Niu J. Does PET scan have any role in the diagnosis of perineural spread associated with the head and neck tumors? Adv Clin Exp Med. 2022;31(8):827-35.
28. Chen TM, Chen WM, Chen M, Shia BC, Wu SY. Use of preoperative PET-CT and survival of p16-negative oropharyngeal cancer. Am J Cancer Res. 2022;12(10):4775-88.
29. Tapia M, Manji J, Dhillon K, Kleid S, Flatman S, Prasad J, et al. The negative predictive value of FDG PET/CT staging in early oropharyngeal squamous cell carcinoma and implications to transoral robotic surgery patient selection. Oral Oncol. 2022;135:106213.
30. Miller JA, Moradi F, Sundaram V, Liang R, Zhang C, Nguyen NK, et al. Posttreatment FDG-PET/CT Hopkins criteria predict locoregional recurrence after definitive radiotherapy for oropharyngeal squamous cell carcinoma. Head Neck. 2022;44(11):2491-504.
31. Iyizoba-Ebozue Z, Billingsley S, Frood R, Vaidyanathan S, Scarsbrook A, Prestwich RJD. Accuracy of response assessment FDG PET-CT post (chemo)radiotherapy in HPV negative oropharynx squamous cell carcinoma. Cancers. 2022;14(19):4680.
32. Linz C, Brands RC, Hackenberg S, Hartmann S, Iring T, Hohm J, et al. [(18)F]FDG-PET/CT improves the detection of synchronous malignancies at primary staging of oral squamous cell carcinoma - A retrospective study. J Craniomaxillofac Surg. 2022;50(8):671-6.
33. Li M, Xuan G, Gu H, Wu J, Wang Y. Survival benefit associated with postoperative PET-CT before adjuvant radiotherapy or chemoradiotherapy in patients with oral squamous cell carcinoma. Int J Oral Maxillofac Surg. 2022;51(11):1382-8.

34. Shalash AM, Elahmadawy MA, Heikal SY, Amin AA, Youssef AA. Value of diffusion MRI versus [18F]FDG PET/CT in detection of cervical nodal metastases in differentiated thyroid cancer patients. Nucl Med Rev Cent East Eur. 2022;25(2):112-8.
35. Warshavsky A, Holan A, Muhanna N, Oestraicher Y, Nachalon Y, Kampel L, et al. Diagnostic efficacy of positron emission computerized tomography scans in suspicious laryngeal findings postorgan preservation treatment. Head Neck. 2023;45(1):207-11.
36. Yang Y, Wang J-J, Zhao R-Z, Huang C, Shi G-Q, Zheng H, et al. The value of routine bone marrow examination in patients with extranodal NK/T-cell lymphoma staged with PET/CT. Cancer. 2022;128(22):3943-50.
37. Yang C, Wu W, Zhou H, Zhao S, Tian R, Xiang M, et al. 18F-FDG PET/CT plays a limited role in replacing bone marrow biopsy for newly diagnosed advanced-stage patients with extranodal natural killer/T-cell lymphoma. Front Oncol. 2022;12:894804.
38. Shim SR, Kim SJ. Diagnostic test accuracy of 18 F-FDG PET or PET/CT in Merkel cell carcinoma. Clin Nucl Med. 2022;47(10):843-8.
39. Weber P, Arnold A, Hohmann J. Comparison of 18F-FDG PET/CT and ultrasound in staging of patients with malignant melanoma. Medicine. 2022;101(42):e31092.
40. Zhang G, Li J, Hui X. Use of 18F-FDG-PET/CT in differential diagnosis of primary central nervous system lymphoma and high-grade gliomas: A meta-analysis. Front Neurol. 2022;13:935459.
41. Lee ONY, Tan KV, Tripathi V, Yuan H, Chan WW, Chiu KWH. The role of 68 Ga-DOTA-SSA PET/CT in the management and prediction of peptide receptor radionuclide therapy response for patients with neuroendocrine tumors: a systematic review and meta-analysis. Clin Nucl Med. 2022;47(9):781-93.
42. Partelli S, Muffatti F, Andreasi V, Giannone F, Rossi G, Palumbo D, et al. A single-center prospective observational study investigating the accuracy of preoperative diagnostic procedures in the assessment of lymph node metastases in nonfunctioning pancreatic neuroendocrine tumors. Ann Surg. 2022;276(5):921-8.
43. Garcia Vicente AM, Amo-Salas M, Sandoval Valencia H, Lozano Setien E, Soriano Castrejon AM. Early recurrence detection of glioma using 18 F-Fluorocholine PET/CT: GliReDe Pilot Study. Clin Nucl Med. 2022;47(10):856-62.
44. Muoio B, Albano D, Dondi F, Bertagna F, Garibotto V, Kunikowska J, et al. Diagnostic accuracy of PET/CT or PET/MRI using PSMA-targeting radiopharmaceuticals in high-grade gliomas: a systematic review and a bivariate meta-analysis. Diagnostics. 2022;12(7):1665.
45. Rizzo A, Racca M, Albano D, Dondi F, Bertagna F, Annunziata S, et al. Can PSMA-targeting radiopharmaceuticals be useful for detecting hepatocellular carcinoma using positron emission tomography? An updated systematic review and meta-analysis. Pharmaceuticals. 2022;15(11):1368.
46. Zhao Y, Simpson BS, Morka N, Freeman A, Kirkham A, Kelly D, et al. Comparison of multiparametric magnetic resonance imaging with prostate-specific membrane antigen positron-emission tomography imaging in primary prostate cancer diagnosis: a systematic review and meta-analysis. Cancers. 2022;14(14):3497.
47. Hu X, Wu Y, Yang P, Wang J, Wang P, Cai J. Performance of 68Ga-labeled prostate-specific membrane antigen ligand positron emission tomography/computed tomography in the diagnosis of primary prostate cancer: a systematic review and meta-analysis. Int Braz J Urol. 2022;48(6):891-902.
48. Parathithasan N, Perry E, Taubman K, Hegarty J, Talwar A, Wong L-M, et al. Combination of MRI prostate and 18F-DCFPyl PSMA PET/CT detects all clinically significant prostate cancers in treatment-naive patients: An international multicentre retrospective study. J Med Imaging Radiat Oncol. 2022;66(7):927-35.

49. Pepe P, Pepe L, Tamburo M, Marletta G, Pennisi M, Fraggetta F. Targeted prostate biopsy: 68Ga-PSMA PET/CT vs. mpMRI in the diagnosis of prostate cancer. Arch Ital Urol Andro. 2022;94(3):274-7.
50. Pepe P, Roscigno M, Pepe L, Panella P, Tamburo M, Marletta G, et al. Could 68Ga-PSMA PET/CT evaluation reduce the number of scheduled prostate biopsies in men enrolled in active surveillance protocols? J Clin Med. 2022;11(12):3473.
51. Kubilay E, Akpinar C, Oguz ES, Araz MS, Soydal C, Baltaci S, et al. Significance of metabolic tumor volume and total lesion uptake measured using Ga-68 labelled prostate-specific membrane antigen PET/CT in primary staging of prostate cancer. Urol Oncol. 2022;40(9):408 e19- e25.
52. Klingenberg S, Fredsoe J, Sorensen KD, Ulhoi BP, Borre M, Jochumsen MR, et al. Recurrence rate after radical prostatectomy following primary staging of high-risk prostate cancer with (68)Ga-PSMA PET/CT. Acta Oncol. 2022;61(10):1289-94.
53. Basso Dias A, Finelli A, Bauman G, Veit-Haibach P, Berlin A, Ortega C, et al. Impact of (18)F-DCFPyL PET on Staging and treatment of unfavorable intermediate or high-risk prostate cancer. Radiology. 2022;304(3):600-8.
54. Ceci F, Rovera G, Iorio GC, Guarneri A, Chiofalo V, Passera R, et al. Event-free survival after 68 Ga-PSMA-11 PET/CT in recurrent hormone-sensitive prostate cancer (HSPC) patients eligible for salvage therapy. Eur J Nucl Med Mol Imaging. 2022;49(9):3257-68.
55. Davies A, Foo M, Gan CL, Kourambas J, Redgrave N, Donnellan S, et al. (68) Ga-prostate-specific membrane antigen (PSMA) PET/CT as a clinical decision-making tool in biochemically recurrent prostate cancer. Asia Pac J Clin Oncol. 2022;18(5):e204-e10.
56. Ong S, Pascoe C, Kelly BD, Ballok Z, Webb D, Bolton D, et al. PSMA PET-CT imaging predicts treatment progression in men with biochemically recurrent prostate cancer-a prospective study of men with 3 year follow up. Cancers. 2022;14(11):2717.
57. Ng M, Guerrieri M, Wong LM, Taubman K, Sutherland T, Benson A, et al. Changes in management After (18)F-DCFPyL PSMA PET in patients undergoing postprostatectomy radiotherapy, with early biochemical response outcomes. J Nucl Med. 2022;63(9):1343-8.
58. Ulaner GA, Thomsen B, Bassett J, Torrey R, Cox C, Lin K, et al. (18)F-DCFPyL PET/CT for initially diagnosed and biochemically recurrent prostate cancer: prospective trial with pathologic confirmation. Radiology. 2022;305(2):419-28.
59. Zhao G, Ji B. Head-To-Head Comparison of (68)Ga-PSMA-11 PET/CT and (99m)Tc-MDP Bone scintigraphy for the detection of bone metastases in patients with prostate cancer: a meta-analysis. AJR Am J Roentgenol. 2022;219(3):386-95.
60. Zhou J, Wu R, Wang W, Zhao Y, Liu X. (68)Ga-PSMA PET/CT for the evaluation of metastasis in patients with prostate cancer: A systematic review and meta-analysis. Hell J Nucl Med. 2022;25(3):297-311.
61. Udovicich C, Callahan J, Bressel M, Ong WL, Perera M, Tran B, et al. Impact of Prostate-specific Membrane Antigen Positron Emission Tomography/Computed Tomography in the Management of Oligometastatic Renal Cell Carcinoma. Eur Urol Open Sci. 2022;44:60-8.
62. Califano I, Pitoia F, Chirico R, De Salazar A, Bastianello MJ. Prospective study on the clinical relevance of 18F-DOPA positron emission tomography/computed tomography in patients with medullary thyroid carcinoma. Endocrine. 2022;77(1):143-50.
63. Breen WG, Youland RS, Giri S, Jacobson SB, Pafundi DH, Brown PD, et al. Initial results of a phase II trial of 18F-DOPA PET-guided re-irradiation for recurrent high-grade glioma. J Neuro-oncol. 2022;158(3):323-30.
64. Henriksen OM, Hansen AE, Muhic A, Marner L, Madsen K, Moller S, et al. Diagnostic yield of simultaneous dynamic contrast-enhanced magnetic resonance perfusion measurements and [18F]FET PET in patients with suspected recurrent anaplastic astrocytoma and glioblastoma. Eur J Nucl Med Mol Imaging. 2022;49(13):4677-91.

65. Benard F, Harsini S, Wilson D, Zukotynski K, Abikhzer G, Turcotte E, et al. Intra-individual comparison of (18)F-sodium fluoride PET-CT and (99m)Tc bone scintigraphy with SPECT in patients with prostate cancer or breast cancer at high risk for skeletal metastases (MITNEC-A1): a multicentre, phase 3 trial. Lancet Oncol. 2022;23(12):1499-507.
66. Usmani S, Ahmed N, Gnanasegaran G, Al Kandari F, Marafi F, Bani-Mustafa A, et al. Prospective study of Na[(18)F]F PET/CT for cancer staging in morbidly obese patients compared with [(99m)Tc]Tc-MDP whole-body planar, SPECT and SPECT/CT. Acta Oncol. 2022;61(10):1230-9.
67. Gu A, Shan Y, Huo H, Ding C, Sun C. The Diagnostic Performance of 18F-FDG PET/CT in Recurrent Pancreatic Cancer: A Systematic Review and Meta-analysis. Appl Bionics Biomech. 2022;2022:3655225.
68. Kalra M, Bakhshi S, Singh M, Seth R, Verma N, Jain S, et al. Response assessment by positron emission tomography-computed tomography as compared with contrast-enhanced computed tomography in childhood Hodgkin lymphoma can reduce the need for radiotherapy in low- and middle-income countries. Pediatr Blood Cancer. 2023;70(2):e30091.
69. Sun J, Li Y, Gong F, Xu S, Wu J, Wang H, et al. The diagnostic value of PET/CT for the lymph node metastasis in Asian patients with non-small cell lung cancer: A meta-analysis. Hell J Nucl Med. 2022;25(2):196-204.
70. Bedetti B, Schnorr P, May S, Ruhlmann J, Ahmadzadehfar H, Essler M, et al. Multidisciplinary Postoperative Validation of 18F-FDG PET/CT Scan in Nodal Staging of Resected Non-Small Cell Lung Cancer. Journal of Clinical Medicine. 2022;11(23):7215.
71. Nie S, Yu W, Hu X, Xu H, Wen R, Jiao W, et al. Positron emission tomography/computed tomography and endobronchial ultrasound-guided transbronchial needle aspiration to evaluate the status of N2 in preoperative non-small cell lung cancer: a diagnostic test. J ThoracDis. 2022;14(6):2122-30.
72. Chen WM, Chen M, Hsu JG, Lee TS, Shia BC, Wu SY. Use of preoperative FDG PET/CT and survival of patients with resectable non-small cell lung cancer. Radiology. 2022;305(1):219-27.
73. Liu CS, Song YQ, Wang RZ, Wang Z, He R, Xu K, et al. Thorax radiotherapy using (18)F-positron emission tomography/computed tomography-guided precision radiotherapy is a prognostic factor for survival in patients with extracranial oligometastatic non-small cell lung cancer:A two-center propensity score-matched analysis. Front Oncol. 2022;12:991378.
74. Bera S, Jamilloux Y, Gerfaud-Valentin M, Durupt S, Nove-Josserand R, Lega JC, et al. Inflammation of unknown origin: Evaluation and prognosis of 57 cases. J Clin Med. 2022;11(1):32.
75. Ly KH, Costedoat-Chalumeau N, Liozon E, Dumonteil S, Ducroix JP, Sailler L, et al. Diagnostic Value of 18F-FDG PET/CT vs. chest-abdomen-pelvis CT scan in management of patients with fever of unknown origin, inflammation of unknown origin or episodic fever of unknown origin: a comparative multicentre prospective study. J Clin Med. 2022;11(2):386.

APPENDIX 1: SUMMARY OF STUDIES FROM JULY TO DECEMBER 2022.

Breast Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Dulgeroglu et al, 2022 [1]	Retrospective	223 patients who underwent nodal staging prior to surgery with SLNB and/or ALND (early breast cancer)	FDG PET/CT	Physical examination, breast US, mammography, breast MRI	Histopathology	**Axillary lymph node metastases** Sens: 68.6% Spec: 72.3% PPV: 60.8% NPV: 78.6% Accu: 70.9%	NA	NA
Baysal et al, 2022 [2]	Retrospective	88 operated patients who underwent evaluation of response to neoadjuvant therapy (breast cancer)	FDG PET/CT	MRI	Histopathology	**Predicting pathological complete response** Sens: 100% Spec: 75.7% PPV: 57.9% NPV: 100%	**Predicting pathological complete response** Sens: 65.2% Spec: 80.7% PPV: 75.0% NPV: 72.4%	NA
Goktas Aydin et al, 2022 [3]	Retrospective	186 patients who underwent evaluation of response to neoadjuvant chemotherapy (locally advanced breast cancer)	FDG PET/CT	NA	Histopathology	**Predicting pathological complete response** Sens: 100% Spec: 72.2% PPV: 75.2% NPV: 100% Accu: 85.0%	NA	The 3-year DFS rate was significantly longer in patients with a pathological complete response after neoadjuvant chemotherapy treatment than in patients with a non-pathological complete response (84.4% vs. 60.0%, p=0.001).
Epilepsy								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Carvalho et al, 2022 [4]	Prospective	110 patients who are candidates for surgery (refractory local epilepsy)	FDG PET/CT	Seizure semiology, serial EEG, long-term video EEG, MRI, functional MRI, neuropsychological tests,	Histopathology, clinical and imaging follow-up, consensus from multidisciplinary team	**Localization** Sens: 62.7%	NA	NA

				ictal and interictal SPECT				
Wang et al, 2022 [5]	Retrospective	63 patients who underwent presurgical evaluation (refractory temporal lobe epilepsy)	FDG PET/CT	MRI (cortical thickness), MRI (diffusion spectrum imaging quantitative anisotropy)	Engel classification, site of surgical resection	**Surgical field** Accu: 74.6% **Seizure freedom** Sens: 89.4% Spec: 68.8%	**Surgical field** ***MRI (cortical thickness)*** Accu: 66.7% ***MRI (diffusion spectrum imaging quantitative anisotropy***) Accu: 55.6% **Seizure freedom** ***MRI (cortical thickness)*** Sens: 72.3% Spec: 50.0% ***MRI (diffusion spectrum imaging quantitative anisotropy***) Sens: 68.1% Spec: 87.5%	FDG PET/CT (OR, 29.03; 95% CI, 5.30 to 158.95, p<0.001) and diffusion spectrum imaging quantitative anisotropy (OR, 14.64; 95% CI, 2.90 to 73.80, p=0.001) but not cortical thickness (OR, 2.56; 95% CI, 0.79 to 8.32, p=0.118) were significantly predictors of seizure freedom. The proportion of patients achieving seizure freedom was 96.4% (27/28) for congruous localization between all three methods covered by the surgical field (OR, 19.57; 95% CI, 2.38 to 161.25, p=0.006).
Gastrointestinal Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Omarov et al, 2022 [6]	Retrospective	170 patients who underwent preoperative staging and postoperative follow-up (rectal cancer)	FDG PET/CT	CT	Pathology, intraoperative findings, biopsy, follow-up	**Staging** ***Liver metastases*** Sens: 100% Spec: 94.2% ***Lung metastases*** Sens: 100% Spec: 91.8% ***Lymph node involvement*** Sens: 100% Spec: 94.3% **Recurrence** ***Liver metastases*** Sens: 100% Spec: 98.0% ***Lung metastases*** Sens: 100% Spec: 96.0% ***Pelvic relapse*** Sens: 100% Spec: 76.7%	**Staging** ***Liver metastases*** Sens: 88.8% Spec: 100% ***Lung metastases*** Sens: 85.1% Spec: 100% ***Lymph node involvement*** Sens: 37.5% Spec: 100% **Recurrence** ***Liver metastases*** Sens: 93.1% Spec: 100% ***Lung metastases*** Sens: 90.4% Spec: 100% ***Pelvic relapse*** Sens: 60.5% Spec: 100%	Postoperative FDG PET/CT changed the treatment modality in 11.8% (15/127) of patients (12—referred for more treatment, 3—referred for surgery).

Rooney et al, 2022 [7]	Meta-analysis	20 studies (1827 patients with rectal cancer who underwent preoperative staging)	FDG PET/CT or PET/MRI	Pelvic MRI	Histopathology	**Lateral lymph node metastases** ***FDG PET/CT*** Pooled Sens: 54.0% Pooled Spec: 95.0% Pooled DOR: 24 AUC: 0.83 ***FDG PET/MRI*** Pooled Sens: 72.0% Pooled Spec: 90.0%	**Lateral lymph node metastases** Pooled Sens: 77.0% Pooled Spec: 85.0% Pooled DOR: 19 AUC: 0.88	NA
Faheem et al, 2022 [8]	Prospective	35 patients who underwent restaging after neoadjuvant chemoradiotherapy or surgery (locally advanced rectal cancer)	FDG PET/CT	Pelvic MRI	Imaging follow-up	**Local tumour** Sens: 94.7% Spec: 100% PPV: 100% NPV: 94.1% Accu: 97.1% **Lymph node metastases** Sens: 78.6% Spec: 95.2% PPV: 91.7% NPV: 87.0% Accu: 88.6% **Extension to nearby structures** Sens: 53.8% Spec: 100% PPV: 100% NPV: 78.6% Accu: 82.9%	**Local tumour** Sens: 94.7% Spec: 100% PPV: 100% NPV: 94.1% Accu: 97.1% **Lymph node metastases** Sens: 100% Spec: 76.2% PPV: 73.7% NPV: 100% Accu: 85.7% **Extension to nearby structures** Sens: 100% Spec: 100% PPV: 100% NPV: 100% Accu: 100%	NA
Dawood et al, 2022 [9]	Meta-analysis	30 studies (3839 patients who underwent surveillance following resection of colorectal cancer)	FDG PET or PET/CT	CEA, CtDNA, CT	Follow-up	**Recurrence** Pooled Sens: 95.0% Pooled Spec: 87.0% Pooled +LR: 7.15 Pooled -LR: 0.06 Pooled DOR: 120.68	**Recurrence** ***CEA*** Pooled Sens: 52.0% Pooled Spec: 88.0% Pooled +LR: 4.13 Pooled -LR: 0.55 Pooled DOR: 7.45 ***CtDNA*** Pooled Sens: 68.0% Pooled Spec: 95.0% Pooled +LR: 12.83 Pooled -LR: 0.34 Pooled DOR: 37.60 ***CT*** Pooled Sens: 77.0% Pooled Spec: 84.0% Pooled +LR: 4.78 Pooled -LR: 0.27 Pooled DOR: 17.42	NA

Yao et al, 2022 [10]	Meta-analysis	18 studies (1406 patients with suspected recurrent colorectal cancer presenting with normal or elevated CEA level)	FDG PET/CT	Not specified	Pathology, clinical follow-up	**Recurrence** ***Elevated CEA level*** Pooled Sens: 95.0% Pooled Spec: 84.0% AUC: 0.97 ***Normal CEA level*** Pooled Sens: 97.0% Pooled Spec: 87.0% AUC: 0.88	NA	NA
Barakat et al, 2022 [11]	Prospective	40 patients who underwent staging (hepatocellular carcinoma)	FDG PET/CT	Triphasic CT	Histopathology, clinical and imaging follow-up	**Extrahepatic metastases (lesion-based)** Sens: 92.3% Spec: 84.4% PPV: 87.8% NPV: 90.0% Accu: 88.7%	**Extrahepatic metastases (lesion-based)** Sens: 51.3% Spec: 81.3% PPV: 76.9% NPV: 57.8% Accu: 64.8%	NA
Foley et al, 2022 [12]	Systematic review	11 studies (2101 patients with gastric cancer who underwent staging)	FDG PET/CT	NA	Pre- and post-PET information	NA	NA	FDG PET/CT was reported to have changed the initial management of 3% to 29% of cases.
Adusumilli et al, 2022 [13]	Retrospective	75 patients who underwent response evaluation 3 months post curative-intent chemoradiotherapy (anal squamous cell carcinoma)	FDG PET/CT	MRI	Biopsy, clinical and imaging follow-up	**Response assessment** Sens: 73.3%* Spec: 68.3% PPV: 36.7% NPV: 91.1% Accu: 69.3%	**Response assessment** Sens: 86.7%* Spec: 73.3% PPV: 44.8% NPV: 95.7% Accu: 76.0%	PFS was significantly different between responders and non-responders as stratified by FDG PET/CT (p=0.007) and MRI (p=0.005).
Genitourinary Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Chen et al, 2022 [14]	Retrospective	174 patients who underwent preoperative evaluation (renal cell carcinoma)	FDG PET/CT	NA	Histopathology	**Venus tumour thrombus** Sens: 96.7% Spec: 99.1% PPV: 98.3% NPV: 98.2% Accu: 98.3%	NA	NA
Pereira et al, 2022 [15]	Retrospective	76 patients who underwent initial staging or	FDG PET/CT	CeCT	Histopathology, imaging follow-up	**Metastases and recurrence** Sens: 100% Spec: 100%*	**Metastases and recurrence** Sens: 87.5% Spec: 81.2%*	NA

		restaging (renal cell carcinoma)				PPV: 100% NPV: 100%* Accu: 100%	PPV: 98.0% NPV: 37.1%* Accu: 86.9%	
Fan et al, 2022 [16]	Meta-analysis	11 studies (1307 patients treated for renal cell carcinoma)	FDG PET/CT	NA	Histopathology, imaging follow-up	**Recurrence** Pooled Sens: 95.0% Pooled Spec: 95.0% AUC: 0.99	NA	NA
Conduit et al, 2022 [17]	Retrospective	249 treated patients who underwent follow-up or active surveillance (testicular seminoma)	FDG PET/CT	NA	Histology, clinical or imaging follow-up	**Recurrence (scan-based)** ***Stage 1*** PPV: 100% NPV: 91.1% ***Advanced stage*** PPV: 77.1% NPV: 90.9%	NA	NA
Gynecologic Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Dondi et al, 2022 [18]	Retrospective	61 patients who underwent restaging or follow-up after therapy (ovarian cancer)	FDG PET/CT	NA	Histopathology, clinical and imaging follow-up	**Recurrence or residual disease (scan-based)** Sens: 94.0% Spec: 80.0% PPV: 93.0% NPV: 83.0% +LR: 4.70 -LR: 0.07 Accu: 90.0%	NA	NA
Amer et al, 2022 [19]	Retrospective	50 patients treated by combined surgery and chemotherapy or chemotherapy alone with complete radiographic responses to treatment (suspected recurrent ovarian cancer)	FDG PET/CT	CA-125	Histopathology, clinical and imaging follow-up	**Recurrence** Sens: 98.0% Spec: 100% PPV: 100% NPV: 83.0% Accu: 98.0%	**Recurrence** Sens: 47.0% Spec: 80.0% PPV: 95.0% NPV: 14.0% Accu: 50.0%	NA
Wang et al, 2022 [20]	Meta-analysis	17 studies (920 patients with suspected recurrent ovarian cancer)	FDG PET/CT	CT, MRI, tumor markers, US	Pathology, clinical follow-up	**Recurrence** Pooled Sens: 88.0% Pooled Spec: 89.0% Pooled +LR: 7.73 Pooled -LR: 0.14	NA	NA

						Pooled DOR: 4.02 AUC: 0.94		
Stojiljkovic et al, 2022 [21]	Retrospective	84 patients previously treated with radiation with or without surgery and chemotherapy (suspected recurrent cervical cancer)	FDG PET/CT	MRI	Histopathology, clinical and imaging follow-up	**Recurrence** Sens: 97.6% Spec: 61.9% PPV: 71.9% NPV: 96.3% Accu: 79.8%	**Recurrence** Sens: 80.1% Spec: 52.4% PPV: 63.0% NPV: 73.3% Accu: 66.7%	NA
Maheshwari et al, 2022 [22]	Prospective	57 patients who underwent preoperative staging (early-stage cervical cancer)	FDG PET/CT	CeCT	Histopathology	**Paraaortic and pelvic lymph node metastases** Sens: 53.9% Spec: 90.5% PPV: 63.6% NPV: 86.4% FPR: 7.3% FNR: 14.6%	**Paraaortic and pelvic lymph node metastases** Sens: 69.2% Spec: 95.0% PPV: 81.8% NPV: 90.5% FPR: 3.8% FNR: 9.4%	NA
Yu et al, 2022 [23]	Retrospective	57 patients who underwent preoperative staging (endometrial carcinoma)	FDG PET/CT, FDG PET/MRI	NA	Histopathology, clinical follow-up	**FIGO staging** ***FDG PET/CT*** Accu: 77.2% ***FDG PET/MRI*** Accu: 86.0% **Myometrial invasion** ***FDG PET/CT*** Sens: 61.1% Spec: 79.5% Accu: 73.7% ***FDG PET/MRI*** Sens: 88.9% Spec: 94.9% Accu: 93.0% **Cervical invasion** ***FDG PET/CT*** Sens: 81.3% Spec: 92.7% Accu: 89.5% ***FDG PET/MRI*** Sens: 81.3% Spec: 95.1% Accu: 91.2% **Pelvic lymph node metastases** ***FDG PET/CT*** Sens: 87.5%	NA	FDG PET/MRI overstaged 8.8% (5/57) and understaged 5.3% (3/57) of patients. FDG PET/CT overstaged 15.8% (9/57) and understaged 7.0% (4/57) of patients.

						Spec: 95.9% Accu: 94.7% ***FDG PET/MRI*** Sens: 87.5% Spec: 95.9% Accu: 94.7%		
Head and Neck Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Piotrowicz et al, 2022 [24]	Retrospective	73 patients who underwent nodal staging prior to neck dissection (head and neck squamous cell carcinoma)	FDG PET/CT	NA	Histopathology	**Lymph node metastases (patient-based)** Sens: 93.8% Spec: 76.2% PPV: 76.9% NPV: 94.1% Accu: 84.9% **(neck side-based)** Sens: 91.2% Spec: 77.1% PPV: 73.8% NPV: 92.5% Accu: 82.9% **(nodal level-based)** Sens: 68.8% Spec: 85.1% PPV: 59.9% NPV: 90.5% Accu: 81.5%	NA	NA
Murtojarvi et al, 2022 [25]	Retrospective	104 patients who underwent restaging 12 weeks after treatment with chemoradiotherapy (head and neck squamous cell carcinoma)	FDG PET/CT (n=52), FDG PET/MRI (n=52)	NA	Histopathology, imaging follow-up	**Recurrence (patient-based)** ***FDG PET/CT*** Sens: 67.0%‡ Spec: 92.0% PPV: 77.0% NPV: 87.0%‡ AUC: 0.890‡ ***FDG PET/MRI*** Sens: 100%‡ Spec: 97.0% PPV: 94.0% NPV: 100%‡ AUC: 0.997‡ **(lesion-based)** ***FDG PET/CT*** Sens: 68.0% Spec: 94.0%	NA	NA

						PPV: 76.0% NPV: 92.0% AUC: 0.899‡ ***FDG PET/MRI*** Sens: 87.0% Spec: 98.0% PPV: 95.0% NPV: 95.0% AUC: 0.989‡		
Katirtzidou et al, 2022 [26]	Prospective	82 patients who underwent primary staging, follow-up of suspected locoregional recurrence, or search for the unknown primary (head and neck squamous cell carcinoma)	FDG PET/CT; FDG PET/MRI	NA	Histology, clinical and imaging follow-up	**Distant metastases and distant synchronous cancers** ***FDG PET/CT*** **(patient-based)** Sens: 94.0% Spec: 91.0% PPV: 71.0% NPV: 98.0% +LR: 10.31 -LR: 0.07 Accu: 91.0% AUC: 0.975 **(examination-based)** Sens: 96.0% Spec: 93.0% PPV: 79.0% NPV: 99.0% +LR: 12.75 -LR: 0.05 Accu: 93.0% AUC: 0.968 **(lesion-based)** Sens: 90.0% Spec: 86.0% PPV: 83.0% NPV: 92.0% +LR: 6.46 -LR: 0.12 Accu: 88.0% AUC: 0.944 ***FDG PET/MRI*** **(patient-based)** Sens: 94.0% Spec: 88.0% PPV: 65.0% NPV: 98.0% +LR: 7.73 -LR: 0.07	NA	NA

						Accu: 89.0% AUC: 0.947 **(examination-based)** Sens: 96.0% Spec: 90.0% PPV: 73.0% NPV: 99.0% +LR: 9.57 -LR: 0.05 Accu: 91.0% AUC: 0.965 **(lesion-based)** Sens: 95.0% Spec: 85.0% PPV: 84.0% NPV: 96.0% +LR: 6.40 -LR: 0.06 Accu: 90.0% AUC: 0.957		
Nie et al, 2022 [27]	Meta-analysis	14 studies (977 patients with head and neck cancer)	FDG PET or PET/CT or PET/MRI	NA	Not specified	**Perineural spread** Pooled Sens: 91.7% Pooled Spec: 92.4% Pooled PPV: 92.3% Pooled NPV: 91.1% Pooled +LR: 7.45 Pooled -LR: 0.28 Pooled Accu: 91.5%	NA	NA
Chen et al, 2022 [28]	Retrospective	1543 patients who underwent preoperative staging (nonmetastatic, p16-negaive oropharyngeal squamous cell carcinoma)	FDG PET/CT + Convention al imaging (n=1133)	MRI, CeCT, US, whole-body bone scan, chest X-ray (n=410)	Clinical follow-up	NA	NA	The addition of preoperative FDG PET/CT was associated with a significantly lower risk of all-cause mortality in patients staged IVA-IVB (HR, 1.82; 95% CI, 1.47 to 2.26, p<0.0001) but not in patients staged I-III (HR, 1.12; 95% CI, 0.86 to 1.48, p=0.4028).
Tapia et al, 2022 [29]	Retrospective	88 patients suitable for transoral robotic surgery who underwent preoperative staging (clinical stage T1-2N0-1 oropharyngeal	FDG PET/CT	Staging neck dissection	Histopathology	**Occult nodal metastases** NPV: 70.2% FPR: 4.5% FNR: 28.4%	NA	NA

		squamous cell carcinoma)						
Miller et al, 2022 [30]	Retrospective	259 patients treated with definitive radiotherapy with or without induction/concurrent chemotherapy (node-positive oropharyngeal squamous cell carcinoma)	FDG PET/CT	Endoscopy, CT, MRI	Pathology, imaging follow-up	**Response assessment (Hopkins scores 4-5 vs. 1-3)** Sens: 67.6% Spec: 88.0% PPV: 46.0% NPV: 94.7% Accu: 85.3% **(Hopkins scores 3-5 vs. 1-2)** Sens: 79.4% Spec: 36.4% PPV: 15.9% NPV: 92.1% Accu: 42.1%	NA	The 3-year OS (94.0% vs. 69.4%, p=0.001) and PFS (86.6% vs. 55.4%, p<0.001) were significantly longer for patients with Hopkins scores 1-3 than for patients with Hopkins scores 4-5. The 3-year cumulative incidence of locoregional recurrence/persistence (44.7% vs. 4.8%, p<0.001) and distant metastasis (22.4% vs. 9.6%, p=0.02) were also significantly greater in patients with Hopkins scores 4-5.
Iyizoba-Ebozue et al, 2022 [31]	Retrospective	96 patients who underwent response assessment after treatment with definitive radiotherapy with or without concurrent chemotherapy (HPV-negative oropharynx squamous cell carcinoma)	FDG PET/CT	Clinical examination, nasoendoscopy	Pathology, clinical and imaging follow-up	**Response assessment** Sens: 79.4% Spec: 75.4% PPV: 73.8% NPV: 85.2% Accu: 80.2%	NA	The 3-year OS (83.0% versus 30.0%, p<0.001) and PFS (79.0% versus 17.0%, p<0.001) were significantly longer for patients with negative FDG PET/CT scans versus those with equivocal and positive scans.
Linz et al, 2022 [32]	Retrospective	182 patients who underwent primary staging (oral squamous cell carcinoma)	FDG PET/CT	Panendoscopy	Histopathology, clinical and imaging follow-up	**Synchronous upper aerodigestive tract malignancies** Sens: 100% Spec: 99.4% PPV: 88.9% NPV: 100%	**Synchronous upper aerodigestive tract malignancies** Sens: 87.5% Spec: 100% PPV: 100% NPV: 99.4%	NA
Li et al, 2022 [33]	Retrospective	268 patients who underwent postoperative imaging prior to adjuvant radiotherapy or chemoradiotherapy (oral	FDG PET/CT (n=123)	CT/MRI (n=145)	Pathology, clinical follow-up	NA	NA	The median DSS (not reached vs. 4.9 years, p=0.049; HR, 2.46; 95% CI, 1.83 to 7.63, p=0.032) and OS (5.4 years vs. 4.3 years, p=0.024; HR, 1.60; 95% CI, 1.04 to 4.66,

		squamous cell carcinoma)						p=0.011) were significantly longer in patients who received FDG PET/CT than those who received CT/MRI.
Shalash et al, 2022 [34]	Prospective	30 patients who underwent initial nodal staging or follow-up due to suspected nodal recurrence (differentiated thyroid caner).	FDG PET/CT	DW-MRI	Pathology, clinical and imaging follow-up	**Cervical lymph node metastases** Sens: 84.0% Spec: 80.0% PPV: 95.0% NPV: 50.0% Accu: 83.0%	**Cervical lymph node metastases** Sens: 84.0% Spec: 60.0% PPV: 91.3% NPV: 42.8% Accu: 80.0%	NA
Warshavsky et al, 2022 [35]	Retrospective	72 patients who received organ preservation treatment (suspected recurrent laryngeal cancer)	FDG PET/CT	Direct laryngoscopy	Biopsy, follow-up	**Recurrence** Sens: 100%* Spec: 81.4* PPV: 55.6%* NPV: 100%*	**Recurrence** Sens: 56.3%* Spec: 100%* PPV: 100%* NPV: 83.7%*	The mean number of negative biopsies was significantly lower in patients who were initially investigated with FDG PET/CT than those who received direct laryngoscopy (0.27 ± 0.08 vs. 1.43 ± 1.14, p<0.001).
Hematologic Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Yang et al, 2022 [36]	Retrospective	186 patients who underwent initial staging (newly diagnosed nasal-type extranodal natural killer/T-cell lymphoma)	FDG PET/CT	Bone marrow aspiration	BMB	**Bone marrow involvement** Sens: 81.5% Spec: 92.9% PPV: 73.3% NPV: 95.4% Accu: 90.6%	**Bone marrow involvement** Sens: 66.7% Spec: 100% PPV: 100% NPV: 90.4% Accu: 91.9%	NA
Yang et al, 2022 [37]	Retrospective	356 patients who underwent initial staging (newly diagnosed extranodal natural killer/T-cell lymphoma)	FDG PET/CT	BMB	Bone marrow histology	**Bone marrow involvement** Sens: 46.2% Spec: 96.9% PPV: 54.5% NPV: 95.8% +LR: 15.2 -LR: 0.6 Accu: 93.2%	NA	FDG PET/CT examination did not change the clinical stage or initial treatment strategy of any patients.
Melanoma								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**

Shim and Kim, 2022 [38]	Meta-analysis	9 studies (259 patients with Merkel cell carcinoma)	FDG PET or PET/CT	NA	Histopathology	**Diagnosis** Pooled Sens: 91.0% Pooled Spec: 93.0% Pooled +LR: 14.0 Pooled -LR: 0.09 Pooled DOR: 153 AUC: 0.97	NA	NA
Weber et al, 2022 [39]	Retrospective	258 patients who underwent primary staging or restaging (suspected or confirmed malignant melanoma)	FDG PET/CT	US	Histopathology, imaging follow-up	**Staging or restaging (patient-based)** Sens: 71.0% Spec: 96.0% PPV: 92.0% NPV: 82.0% Accu: 85.0% **(examination-based)** Sens: 80.0%* Spec: 96.0%* PPV: 91.0% NPV: 90.0% Accu: 90.0% **(lesion-based)** Sens: 83.0%* Spec: 91.0%* PPV: 91.0% NPV: 83.0% Accu: 87.0%	**Staging or restaging (patient-based)** Sens: 48.0% Spec: 97.0% PPV: 79.0% NPV: 90.0% Accu: 89.0% **(examination-based)** Sens: 63.0%* Spec: 98.0%* PPV: 85.0% NPV: 95.0% Accu: 94.0% **(lesion-based)** Sens: 61.0%* Spec: 98.0%* PPV: 85.0% NPV: 93.0% Accu: 92.0%	NA
Neuro-Oncology								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Zhang et al, 2022 [40]	Meta-analysis	9 studies (151 patients with primary central nervous system lymphoma and 281 patients with high-grade glioma)	FDG PET/CT	NA	Histopathology	**Differential diagnosis** Pooled Sens: 91.0% Pooled Spec: 88.0% Pooled +LR: 7.83 Pooled -LR: 0.10 Pooled DOR: 77.36 AUC: 0.95	NA	NA
Non-FDG Tracers ^{68}Ga-DOTA-(TATE, NOC, TOC)								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**

Lee et al, 2022 [41]	Meta-analysis	24 studies (2266 patients with confirmed or suspected neuroendocrine tumours)	^{68}Ga-DOTA-TATE, NOC, TOC PET/CT	^{111}In-pentetreotide scintigraphy, ^{99m}Tc-octreotide SPECT/CT, ^{99m}Tc-HYNICTOC scintigraphy	Pre- and post-PET questionnaire	NA	NA	The pooled proportion of patients with a management change after ^{68}Ga-DOTA-TATE, NOC, TOC PET/CT was 36.0%.
Partelli et al, 2022 [42]	Prospective	100 patients who underwent preoperative staging (non-functioning pancreatic neuroendocrine tumours)	^{68}Ga-DOTA-TOC PET/CT or PET/MRI	CeCT, EUS	Pathology	**Lymph node metastases** Sens: 11.9% Spec: 94.8% PPV: 62.5% NPV: 59.8% Accu: 60.0%	**Lymph node metastases** ***CeCT*** Sens: 26.2% Spec: 94.8% PPV: 78.6% NPV: 64.0% Accu: 66.0% ***EUS*** Sens: 19.0% Spec: 98.3% PPV: 88.9% NPV: 62.6% Accu: 65.0%	NA
^{11}C/^{18}F-Choline								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Garcia Vicente et al, 2022 [43]	Prospective	21 patients with a previous gross total resection and first suspicious or doubtful MRI for tumour recurrence (glioma)	^{18}F-Fluorocholine PET/CT	MRI	Histology, clinical and imaging follow-up	**Recurrence** Sens: 100% PPV: 87.0% Accu: 87.5%	**Recurrence** Sens: 70.0% PPV: 93.3% Accu: 70.8%	NA
^{68}Ga-PSMA/^{18}F-DCFPyL								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Muoio et al, 2022 [44]	Meta-analysis	6 studies (157 patients with suspicious high-grade glioma at diagnosis or suspicious	^{68}Ga-PSMA PET/CT or PET/MRI	MRI	Histology, clinical or imaging follow-up	**Differential diagnosis or recurrence** Pooled Sens: 98.2% Pooled Spec: 91.2% Pooled +LR: 4.5	NA	NA

		recurrence after treatment)				Pooled -LR: 0.07 Pooled DOR: 70.1		
Rizzo et al, 2022 [45]	Meta-analysis	6 studies (126 patients with hepatocellular carcinoma who underwent staging or restaging)	^{68}Ga-PSMA PET/CT or PET/MRI	MRI, CeCT	Composite, not specified	**Hepatic and extrahepatic lesions** Pooled DR: 85.1%	NA	NA
Zhao et al, 2022 [46]	Meta-analysis	10 studies (918 patients with prostate cancer)	^{68}Ga-PSMA-11 or ^{68}Ga-PSMA-617 or ^{18}F-PSMA-1007 PET/CT	mpMRI	Histopathology	**Diagnosis (patient-based)** Pooled Sens: 93.0%* Pooled Spec: 54.0% AUC: 0.91 **(lesion-based)** Pooled Sens: 79.0%* Pooled Spec: 71.0%* AUC: 0.84	**Diagnosis (patient-based)** Pooled Sens: 87.0%* Pooled Spec: 47.0% AUC: 0.84 **(lesion-based)** Pooled Sens: 63.0%* Pooled Spec: 88.0%* AUC: 0.83	NA
Hu et al, 2022 [47]	Meta-analysis	9 studies (547 patients and 443 lesion segments with prostate cancer)	^{68}Ga-PSMA PET/CT	NA	Histopathology	**Diagnosis** Pooled Sens: 93.0% Pooled Spec: 87.0% Pooled +LR: 7.4 Pooled -LR: 0.08 Pooled DOR: 89 AUC: 0.95	NA	NA
Parathithasan et al, 2022 [48]	Retrospective	65 treatment-naive patients who underwent primary diagnosis (clinically suspected or biopsy-proven prostate cancer)	^{18}F-DCFPyL PET/CT	mpMRI	Histopathology	**Diagnosis** Sens: 96.7% PPV: 93.7% +LR: 0.97	**Diagnosis** Sens: 93.4% PPV: 93.4% +LR: 0.93	NA
Pepe et al, 2022 [49]	Prospective	100 patients with negative digital rectal examination underwent transperineal prostate biopsy for abnormal PSA values (prostate cancer)	^{68}Ga-PSMA PET/CT targeted biopsy	mpMRI targeted biopsy	Histology	**Diagnosis** Sens: 95.4% Spec: 80.0% PPV: 73.4% NPV: 96.5% Accu: 84.7%	**Diagnosis** Sens: 81.8% Spec: 71.8% PPV: 54.5% NPV: 87.5% Accu: 76.9%	NA
Pepe et al, 2022 [50]	Prospective	30 patients submitted to scheduled biopsy (very low-risk prostate cancer)	^{68}Ga-PSMA PET/CT targeted biopsy	mpMRI targeted biopsy	Histology	**Diagnosis** NPV: 85.7% FPR: 16.7%	**Diagnosis** NPV: 57.1% FPR: 43.3%	NA

Kubilay et al, 2022 [51]	Retrospective	77 patients who underwent primary staging prior to radical prostatectomy with extended pelvic lymph node dissection (prostate cancer)	^{68}Ga-PSMA PET/CT	NA	Histopathology	**Lymph node metastases** Sens: 60.0% Spec: 91.5% PPV: 81.8% NPV: 78.2% Accu: 79.2%	NA	NA
Klingenberg et al, 2022 [52]	Retrospective	384 patients who underwent primary staging prior to radical prostatectomy (high-risk prostate cancer)	^{68}Ga-PSMA PET/CT (n=247)	^{99m}Tc bone scintigraphy and CT (n=137)	Clinical follow-up	NA	NA	The 5-year RFS rate was significantly higher in patients staged by ^{68}Ga-PSMA PET/CT than those staged by conventional imaging (71.1% vs. 56.4%, p=0.003; HR, 0.58; 95% CI, 0.41 to 0.83, p=0.004).
Basso Dias et al, 2022 [53]	Prospective	108 patients who underwent primary staging (untreated, unfavourable intermediate or high-risk prostate cancer)	^{18}F-DCFPyL PET/CT	CeCT, bone scintigraphy, mpMRI	Histopathology, correlative imaging, clinical and/or imaging follow-up, consensus from multidisciplinary team	**Pelvic nodal metastases** Sens: 89.0%* **Distant metastases** Sens: 92.0%*	**Pelvic nodal metastases** Sens: 25.0%* **Distant metastases** Sens: 23.0%*	^{18}F-DCFPyL PET/CT altered the N and M staging of 39.8% (43/103) (36 upstaged, 7 downstaged). Treatment was changed in 22.2% (24/108) of cases (10—systemic therapy to local-regional therapy, 9—local-regional therapy to systemic therapy, 2—local-regional therapy to metastases-directed therapy, 1—local-regional therapy to observation, 1—metastases-directed therapy to local-regional therapy, 1—metastases-directed therapy to systemic therapy).
Ceci et al, 2022 [54]	Prospective	176 patients who were eligible for salvage therapy and underwent follow-up after radical treatment (hormone-sensitive, hormone-free, recurrent prostate cancer)	^{68}Ga-PSMA-11 PET/CT	NA	Clinical and imaging follow-up, consensus from multidisciplinary tumour board	NA	NA	^{68}Ga-PSMA-11 PET/CT changed the therapeutic management of 30.1% (53/176) of cases. The event-free survival was 78.8% at 1 year, 65.2% at 2 years, and 52.2% at 3 years. There were no significant differences in event rates between patients who received a

								change in therapy and those who did not (p=0.258).
Davies et al, 2022 [55]	Prospective	70 patients who received definitive therapy (biochemically recurrent prostate cancer)	^{68}Ga-PSMA-11 PET/CT	NA	Pre- and post-PET questionnaire	NA	NA	^{68}Ga-PSMA-11 PET/CT changed the intended management of 42.9% (30/70) of patients (7—watchful waiting to salvage radiotherapy, 6—watchful waiting to stereotactic radiotherapy, 4—watchful waiting to androgen deprivation therapy, 1—watchful waiting to salvage surgery, 4—salvage radiotherapy to watchful waiting, 2—salvage radiotherapy to stereotactic radiotherapy, 1—salvage radiotherapy to further investigation, 1—salvage radiotherapy to androgen deprivation therapy, 2—androgen deprivation therapy to watchful waiting, 1—androgen deprivation therapy to systemic chemotherapy, 1—stereotactic ablative body radiotherapy to watchful waiting).
Ong et al, 2022 [56]	Prospective	96 patients who underwent restaging (biochemically recurrent prostate cancer)	^{68}Ga-PSMA PET/CT	Not specified	Clinical and imaging follow-up, consensus from multidisciplinary team	NA	NA	^{68}Ga-PSMA PET/CT findings led to treatment additions or changes in 25.0% (24/96) of patients. Of the patients who did not have a change in treatment based on ^{68}Ga-PSMA PET/CT findings, 9.7% (7/72) of cases were found to have disease progression.
Ng et al, 2022 [57]	Prospective	96 patients with a rising PSA level of 0.2 to 2.0 ng/mL after	^{18}F-DCFPyL PET/CT	CT of the chest, abdomen, and pelvis	Pre- and post-PET questionnaire	NA	NA	^{18}F-DCFPyL PET/CT impacted management intent in 43.8% (42/96) of patients. Conversely,

		radical prostatectomy being considered for salvage radiotherapy (biochemically recurrent prostate cancer)						CT altered management intent in 16.8% (16/95) of patients. There were significantly more patients with major (12.5% vs. 3.2%, p=0.01) and moderate (31.3% vs. 13.7%, p=0.001) changes after ^{18}F-DCFPyL PET/CT than after CT.
Ulaner et al, 2022 [58]	Prospective	184 patients who underwent initial staging or follow-up (92 newly diagnosed high-risk prostate cancer; 92 biochemically recurrent prostate cancer)	^{18}F-DCFPyL PET/CT	CT, bone scan	Histopathology	**Distant metastases** PPV: 74.0% **Recurrence** PPV: 89.0%	NA	NA
Zhao and Ji, 2022 [59]	Meta-analysis	6 studies (546 patients with prostate cancer who underwent initial staging, restaging or follow-up)	^{68}Ga-PSMA-11 PET/CT	^{99m}Tc-MDP bone scintigraphy	Clinical and/or imaging follow-up	**Bone metastases** Pooled Sens: 98.0%* Pooled Spec: 97.0%* AUC: 0.99	**Bone metastases** Pooled Sens: 83.0%* Pooled Spec: 68.0%* AUC: 0.85	From 5 studies, the pooled proportion of patients with a management change after ^{68}Ga-PSMA-11 PET/CT was 28.0%.
Zhou et al, 2022 [60]	Meta-analysis	16 studies (1567 patients with prostate cancer who underwent primary staging or follow-up for disease recurrence)	^{68}Ga-PSMA PET/CT	Bone scintigraphy, MRI, CT, SPECT/CT	Histopathology, biopsy, clinical or imaging follow-up	**Lymph node metastases (patient-based)** Pooled Sens: 61.0% Pooled Spec: 96.0% Pooled +LR: 14.4 Pooled -LR: 0.41 Pooled DOR: 35 AUC: 0.95 **(lesion-based)** Pooled Sens: 74.0% Pooled Spec: 99.0% Pooled +LR: 76.0 Pooled -LR: 0.26 Pooled DOR: 289 AUC: 0.99 **Bone metastases (patient-based)** Pooled Sens: 97.0% Pooled Spec: 100% Pooled +LR: 1100.1 Pooled -LR: 0.03 Pooled DOR: 37490	NA	NA

						AUC: 0.98		
Udovicich et al, 2022 [61]	Retrospective	61 patients who underwent staging (suspected metastatic renal cell carcinoma)	^{68}Ga-PSMA-11 or ^{18}F-DCFPyL PET/CT	CeCT	Histopathology, consensus from multidisciplinary meeting	NA	NA	^{68}Ga-PSMA-11 or ^{18}F-DCFPyL PET/CT impacted management in 49.2% (30/61) of patients (8—metastasis-directed therapy to surveillance, 7—metastasis-directed therapy to systemic therapy, 4—metastasis-directed therapy to additional sites, 2—metastasis-directed therapy to fewer sites, 6—surveillance to metastasis-directed therapy, 3—systemic therapy to metastasis-directed therapy).
^{18}F-DOPA								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Califano et al, 2022 [62]	Prospective	36 patients with calcitonin level ≥150 pg/ml after initial treatment (recurrent medullary thyroid carcinoma)	^{18}F-DOPA PET/CT	Neck US, chest CT, liver MRI, abdominal CT, bone scan	Histology or cytology	NA	NA	^{18}F-DOPA PET/CT findings led to management changes in 38.9% (14/36) patients (4—surgical strategy modified, 4—initiated surgery, 3—started treatment with a multikinase inhibitor, 1—received liver chemoembolization, 1—submitted to cervical external beam radiotherapy, 1—multikinase inhibitor to cervicomediastinal lymphadenectomy).
Breen et al, 2022 [63]	Prospective	20 patients previously treated with radiotherapy and were planned to receive re-irradiation	^{18}F-DOPA PET	CeMRI	Clinical and imaging follow-up	NA	NA	MRI-defined GTV were expanded by a median of 43% by incorporating ^{18}F-DOPA PET. PFS at 3 months was 85%, which met the primary endpoint of a 20% improvement from

		(recurrent high-grade glioma)						historical control. No grade 4 or 5 toxicities were observed.
^{18}F-FET								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Henriksen et al, 2022 [64]	Retrospective	60 patients who received prior standard therapy (suspected progressive grade III or IV gliomas)	^{18}F-FET PET or PET/MRI	DCE perfusion MRI	Histopathology, clinical or imaging follow-up	**Tumour progression (patient-based)** ***^{18}F-FET PET TBR_{max} of 2.27*** Sens: 88.4% Spec: 100% PPV: 100% NPV: 76.2% AUC: 0.96 ***^{18}F-FET PET/MRI TBR_{max} of 2.27 + nBV_{max} of 5.33*** Sens: 86.0% Spec: 100% PPV: 100% NPV: 72.7% AUC: 0.96 **(lesion-based)** ***^{18}F-FET PET TBR_{max} of 2.27*** Sens: 86.4% Spec: 87.5% PPV: 90.5% NPV: 82.4% AUC: 0.89 ***^{18}F-FET PET/MRI TBR_{max} of 2.27 + nBV_{max} of 10.43*** Sens: 72.7% Spec: 90.6% PPV: 91.4% NPV: 70.7% AUC: 0.90	**Tumour progression (patient-based)** ***DCE perfusion MRI BV_{max} of 10.43*** Sens: 69.8% Spec: 87.5% PPV: 93.8% NPV: 51.9% AUC: 0.84 ***DCE perfusion MRI nBV_{max} of 5.33*** Sens: 90.7% Spec: 68.8% PPV: 88.6% NPV: 73.3% AUC: 0.82 **(lesion-based)** ***DCE perfusion MRI BV_{max} of 10.43*** Sens: 70.5% Spec: 90.6% PPV: 91.2% NPV: 69.0% AUC: 0.80 ***DCE perfusion MRI nBV_{max} of 6.23*** Sens: 81.8% Spec: 71.9% PPV: 80.0% NPV: 74.2% AUC: 0.79	NA
^{18}F-sodium fluoride								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**

Benard et al, 2022 [65]	Prospective (Phase 3)	261 patients with high clinical suspicion of bone metastases who underwent initial staging or restaging (high-risk breast or prostate cancer)	^{18}F-sodium fluoride PET/CT	^{99m}Tc-MDP SPECT	Histopathology, correlative imaging results, clinical and imaging follow-up	**Bone metastases** Sens: 78.9%* Spec: 88.2% PPV: 82.7% NPV: 85.4%* Accu: 84.3%*	**Bone metastases** Sens: 63.3%* Spec: 87.5% PPV: 78.4% NPV: 76.9%* Accu: 77.4%*	NA
Usmani et al, 2022 [66]	Prospective	117 morbidly obese patients with BMI > 40kg/m^2 who underwent skeletal staging or restaging (98 breast cancer, 15 prostate cancer, 4 others)	^{18}F-sodium fluoride PET/CT	^{99m}Tc-MDP whole-body scintigraphy, ^{99m}Tc-MDP SPECT, ^{99m}Tc-MDP SPECT/CT	Clinical and imaging follow-up	**Bone metastases (patient-based)** Sens: 95.5%* Spec: 95.9%* PPV: 93.3%* NPV: 97.2%* +LR: 23.2* -LR: 0.05* Accu: 95.7* AUC: 0.957* **(lesion-based)** Sens: 97.7%* Spec: 97.9%* PPV: 98.8%* NPV: 95.8%* +LR: 45.9* -LR: 0.02* Accu: 97.7%* AUC: 0.978*	**Bone metastases (patient-based)** ***^{99m}Tc-MDP whole-body scintigraphy*** Sens: 52.3%* Spec: 71.2%* PPV: 52.3%* NPV: 71.2%* +LR: 1.8* -LR: 0.67* Accu: 64.1%* AUC: 0.618* ***^{99m}Tc-MDP SPECT*** Sens: 61.4%* Spec: 80.8%* PPV: 65.9%* NPV: 77.6%* +LR: 3.2* -LR: 0.48* Accu: 73.5%* AUC: 0.711* ***^{99m}Tc-MDP SPECT/CT*** Sens: 65.9%* Spec: 91.8% PPV: 82.9%* NPV: 81.7%* +LR: 8.02* -LR: 0.37* Accu: 82.1%* AUC: 0.788* **(lesion-based)** ***^{99m}Tc-MDP whole-body scintigraphy*** Sens: 39.0%* Spec: 67.0%* PPV: 68.4%* NPV: 37.5%* +LR: 1.2* -LR: 0.91* Accu: 48.9%*	NA

						AUC: 0.538* ***^{99m}Tc-MDP SPECT*** Sens: 44.8%* Spec: 76.6%* PPV: 77.8%* NPV: 43.1%* +LR: 1.9* -LR: 0.72* Accu: 56.0%* AUC: 0.607* ***^{99m}Tc-MDP SPECT/CT*** Sens: 52.9%* Spec: 93.6% PPV: 93.8%* NPV: 52.1%* +LR: 8.3* -LR: 0.50* Accu: 67.3%* AUC: 0.733*	
Pancreatic Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Gu et al, 2022 [67]	Meta-analysis	7 studies (263 patients with recurrent pancreatic cancer)	FDG PET/CT	NA	Pathology, imaging follow-up	**Recurrence** Pooled Sens: 89.0% Pooled Spec: 88.0% AUC: 0.94	NA	NA
Pediatric Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Kalra et al, 2022 [68]	Prospective	382 patients who underwent early response assessment after 2 cycles of ABVD; those with bulky disease or inadequate response received radiotherapy (HL)	FDG PET/CT (n=186)	CeCT (n=196)	Clinical follow-up	NA	NA	Patients who underwent FDG PET/CT assessment were significantly less likely to receive radiotherapy than those who underwent CeCT assessment (38.7% vs. 50.0%, p=0.017). However, the 5-year OS (94.1% vs. 91.8%, p=0.391) and EFS (85.5% vs. 86.7%, p=0.724) did not differ significantly between the two groups.

Thoracic Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Sun et al, 2022 [69]	Meta-analysis	25 studies (2458 Asian patients with NSCLC)	FDG PET/CT	NA	Pathology	**Lymph node metastases** Pooled Sens: 68.0% Pooled Spec: 93.0% Pooled +LR: 9.4 Pooled -LR: 0.34 Pooled DOR: 28 AUC: 0.88	NA	NA
Bedetti et al, 2022 [70]	Retrospective	87 patients who underwent preoperative staging (nonmetastatic NSCLC)	FDG PET/CT	EBUS	Histopathology	**Lymph node metastases** Sens: 50.0% Spec: 88.9% PPV: 63.2% NPV: 82.4% Accu: 78.2%	NA	FDG PET/CT findings downstaged 13.8% (12/87) and upstaged 8.0% (7/87) of patients.
Nie et al, 2022 [71]	Retrospective	112 patients who underwent preoperative staging (NSCLC)	FDG PET/CT	EBUS-TBNA	Pathology	**Lymph node metastases** Sens: 71.4%* Spec: 60.0%* PPV: 51.7%* NPV: 77.8%* Accu: 64.3%* AUC: 0.636	**Lymph node metastases** Sens: 90.5%* Spec: 100%* PPV: 100%* NPV: 94.6%* Accu: 96.4%* AUC: 0.954	NA
Chen et al, 2022 [72]	Retrospective	13,508 patients who underwent staging prior to thoracic surgery and adjuvant treatments (nonmetastatic, resectable stage I-IIIB NSCLC)	FDG PET/CT + CI (n=6754)	Chest-abdomen-pelvis CT, brain CeMRI, brochoscopy	Clinical follow-up	NA	NA	The addition of FDG PET/CT to preoperative staging was associated with a lower risk of all-cause mortality in stage IIIA (HR, 0.90; 95% CI, 0.79 to 0.94, p=0.02) and stage IIIB (HR, 0.80; 95% CI, 0.71 to 0.90, p<0.01) patients. However, preoperative FDG PET/CT was not associated with a lower all-cause mortality in stage I-II patients (HR, 1.19; 95% CI, 0.89 to 1.30, p=0.65).
Liu et al, 2022 [73]	Retrospective	122 patients who underwent staging prior to	FDG PET/CT (n=61)	CT (n=61)	Clinical follow-up	NA	NA	The median survival time was significantly better in patients who received

		thorax radiotherapy with systemic therapy or systemic therapy alone (stage IV extracranial oligometastatic NSCLC)						FDG PET/CT than those who received CT (19 months vs. 6 months, p<0.001). Among the patients who received FDG PET/CT examination, thorax radiotherapy was associated with significantly longer median survival time (27 months vs. 11 months, p<0.001). However, there was no significant difference in median survival time between thorax radiotherapy or no thorax radiotherapy in patients who received CT examination (7 months vs. 5 months, p=0.236).
Various Sites								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Bera et al, 2022 [74]	Retrospective	42 patients with elevated inflammatory markers and no diagnosis after at least 3 outpatient visits or 3 days of hospitalization (inflammation of unknown origin)	FDG PET/CT	Clinical examination, C-reactive protein level or erythrocyte sedimentation rate, laboratory tests, chest X-ray, abdominal and pelvic US, thoracic-abdominal CT, endoscopy	Biopsy, clinical follow-up	NA	NA	FDG PET/CT was contributory to the diagnosis in 28.6% (12/42) of patients.
Ly et al, 2022 [75]	Prospective	103 patients who underwent diagnostic workup (fever/inflammation/episodic	FDG PET/CT	Chest-abdomen-pelvis CT	Biopsy, clinical and imaging follow-up	**Diagnostic contribution** Sens: 36.4% Spec: 81.2%	**Diagnostic contribution** Sens: 10.5% Spec: 95.6%	FDG PET/CT provided a higher diagnostic orientation (28.2% vs. 7.8%, p=0.0003) and diagnostic contribution (19.4% vs. 5.8%,

	fever of unknown origin)		p<0.0001) than chest-abdomen-pelvis CT. Delay in diagnosis was slightly reduced for patients with FDG PET/CT-related orientation diagnosis compared to patients with chest-abdomen-pelvic CT-related orientation (2.2 vs. 3.8 months, p=0.25).

*p<0.05

‡Significant difference with PET/MRI (p<0.05)

Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; Accu, accuracy; ALND, axillary lymph node dissection; AUC, area under the curve; BMB, bone marrow biopsy; BMI, body mass index; ^{11}C, carbon-11; CEA, carcinoembryonic antigen; CeCT, contrast-enhanced computed tomography; CeMRI, contrast-enhanced magnetic resonance imaging; CI, confidence interval; CT, computed tomography; CtDNA, circulating tumour DNA; DCE, dynamic contrast enhanced; DFS, disease-free survival; DOR, diagnostic odds ratio; DR, detection rate; DSS, disease-specific survival; DW-MRI, diffusion-weighted magnetic resonance imaging; EBUS, endobronchial ultrasound; EEG, electroencephalography; EFS, event-free survival; EUS, endoscopic ultrasound; ^{18}F, fluorine-18; 18F-DCFPyL (2-(3-{1-carboxy-5-[(6-18F-fluoropyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid; FDG, fluorodeoxyglucose; ^{18}F-DOPA, 3,4-dihydroxy-6-[18F]-fluoro-l-phenylalanine; ^{18}F-FET, O-(2[^{18}F]-fluoroethyl)-L-tyrosine; FFS, failure-free survival; FIGO, Federation of Gynecology and Obstetrics; FNR, false negative rate; FPR, false positive rate; ^{68}Ga-DOTA-NOC, Gallium-68-1,4,7,10-tetraazacyclododecane-1,4,7,10-tet-raacetic acid-1-Nal3-octreotide; ^{68}Ga-DOTA-TATE, Gallium-68-dodecanetetraacetic acid-Tyr3-octreotate; ^{68}Ga-DOTA-TOC, Gallium-68-edotretide; ^{68}Ga-PSMA, Gallium-68-labelled prostate-specific membrane antigen; GTV, gross target volume; HL, Hodgkin lymphoma; HR, hazard ratio; ^{31}In, indium 111; –LR, negative likelihood ratio; +LR, positive likelihood ratio; mpMRI, multiparametric magnetic resonance imaging; MRI, magnetic resonance imaging; NA, not applicable; nBVmax, normalized maximal blood volume; NPV, negative predictive value; NSCLC, non-small-cell lung carcinoma; OR, odds ratio; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; PPV, positive predictive value; PSA, prostate-specific antigen; RFS, recurrence-free survival; Sens, sensitivity; SLNB, sentinel lymph node biopsy; Spec, specificity; SPECT, single-photon emission CT; TBRmax, maximal tumour-to-background [18F]FET uptake; ^{99m}Tc, Technetium 99m; ^{99m}Tc-HYNICTOC, ^{99m}Tc-Hydrazinonicotinyl-Tyr3-Octreotide; ^{99m}Tc-MDP, Technetium 99m-methyl diphosphonate; US, ultrasonography