PET Six-Month Monitoring Report 2023-2

Evidence from Primary Studies and Systematic Reviews and Recommendations from Clinical Practice Guidelines July to December 2023

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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 26th 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 2023 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

Sixty-two studies published between July and December 2023 met the inclusion criteria. A summary of the evidence from the 62 studies can be found in **Appendix 1: Summary of studies from July to December 2023**.

Breast Cancer

Five studies met the inclusion criteria [1-5]. Two retrospective studies investigated the role of FDG PET/CT in the preoperative evaluation of axillary lymph node metastases and the reported sensitivity and specificity were 41.7% to 82.4% and 69.7% to 93.2%, respectively [1,2]. In the PET ABC trial, patients with stage IIB or III invasive ductal carcinoma being considered for curative combined modality treatment were randomized to receive FDG PET/CT or conventional staging (e.g., bone scan, contrast-enhanced CT). FDG PET/CT upstaged more patients to stage IV disease than conventional imaging (23.4% vs. 11.4%; relative risk, 2.4; 95% confidence interval [CI], 1.4 to 4.2, p=0.002). Correspondingly, 19.0% of FDG PET/CT-staged patients did not receive combined modality treatment compared with 10.8% of conventionally staged patients (absolute difference, 8.2%; 95% CI, 0.1 to 15.4, p=0.03) [3]. Overall, FDG PET/CT impacted management decisions in 78.8% of patients across different clinical scenarios. These changes translated to a five-year overall survival (OS) rate of 72.3% with a mean of 82.2 months [4]. As for the detection of bone metastases, FDG PET/magnetic resonance imaging (MRI) was found to exhibit superior patient-level (pooled estimate, 99.0% vs. 73.0%, p=0.04) and lesion-level (pooled estimate, 99.0% vs. 89.0%, p<0.01) sensitivity over FDG PET/CT. However, both imaging modalities possessed a similar level of specificity [5].

Esophageal Cancer

Two studies met the inclusion criteria [6,7]. FDG PET/CT outperformed endoscopic ultrasound (US) in the preoperative T-staging of patients with esophageal squamous cell carcinoma who received neoadjuvant chemoradiotherapy (accuracy, 65.1% vs. 18.6%, p<0.01) [6]. In patients with high-grade dysplasia or early esophageal adenocarcinoma, the accuracies of preoperative T- and N-staging for FDG PET/CT (11.0% to 30.0%), CT (28.6% to 43.3%), and endoscopic US (29.6% to 59.7%) were all unreliably low [7].

Gastrointestinal Cancer

Four studies met the inclusion criteria [8-11]. In the preoperative staging of patients with colorectal cancer, FDG PET/CT allowed for a more precise evaluation of distant metastatic disease (accuracy, 98.4% vs. 93.8%), particularly for liver metastases (accuracy, 93.1% vs. 79.3%), than contrast-enhanced CT. As a consequence, additional FDG PET/CT findings altered the treatment planning in 15.4% of cases [8]. In surgically treated patients, FDG PET/CT detected recurrent or metastatic disease with higher sensitivity (95.0% vs. 58.0%) but lower specificity (73.0% vs. 96.0%) than serum carcinoembryonic antigen (CEA) [9]. For the preoperative TNM staging of patients with hilar cholangiocarcinoma, FDG PET/MRI outperformed FDG PET/CT in T (accuracy, 72.4% vs. 58.6%, p=0.0022) and N (accuracy, 84.5% vs. 67.2%, p=0.002) staging, while showing similar performance in M staging (accuracy, 98.3% vs. 94.8%, p=0.5) [10]. In patients with anal canal cancer, results from a meta-analysis showed that FDG PET or FDG PET/CT have excellent diagnostic value in primary tumour (pooled sensitivity, 98.0%), lymph node metastases (pooled sensitivity, 99.0%; pooled specificity, 93.0%), distant metastases (pooled sensitivity, 99.0%) and recurrence (pooled sensitivity, 90.0%; pooled specificity, 97.0%) detection, as well as therapy response assessment (pooled sensitivity, 96.0%; pooled specificity, 86.0%) [11].

Genitourinary Cancer

Four studies met the inclusion criteria [12-15]. In the initial staging of bladder cancer with or without muscle invasion, FDG PET/CT displayed poor sensitivity but high specificity for the detection of localized disease (sensitivity, 51.7%; specificity, 96.2%) and lymph node metastases (sensitivity, 40.0% to 54.3%; specificity, 85.0% to 98.9%) [12,13]. On the other hand, FDG PET/CT was better at detecting distant metastases (sensitivity, 76.8%; specificity, 96.9%). Overall, the management approach and intent to treat changed in 26.3% of patients [13]. FDG PET/CT was also found to be impactful by altering the intended mode of therapeutic intervention in 41.9% of patients with germ cell tumours. Furthermore, the need for surgical biopsy and additional diagnostic imaging was reduced by 18.6% and 58.1%, respectively [14]. For the characterization of adrenal mass seen on conventional imaging, FDG PET/CT proved to be reliable in differentiating benign from malignant tumours (pooled sensitivity, 87.3%; pooled specificity, 84.7%) [15].

Gynecologic Cancer

Six studies met the inclusion criteria [16-21]. Four studies examined the clinical utility of FDG PET/CT in ovarian cancer. In the initial staging and restaging of patients, FDG PET/CT (area under the curve [AUC], 0.96) offered the highest patient-based diagnostic performance for primary tumour and/or metastases identification, followed by MRI (AUC, 0.90) and CT (AUC, 0.84) [16]. In patients with suspected recurrent disease, FDG PET/CT demonstrated exceptional sensitivity (95.5% to 96.3%) and moderate to high specificity (75.0% to 92.3%) for the detection of recurrence [17-19], including the evaluation of peritoneal involvement (sensitivity, 97.1%; specificity, 93.3%) [19]. In patients with suspected recurrent cervical cancer, FDG PET/CT was also better than contrast-enhanced CT in detecting recurrence or residual disease (accuracy, 90.0% versus 70.0%). On the basis of FDG PET/CT findings, treatment planning was revised in 35.2% of cases [20]. Taken together, FDG PET/CT had a significant impact on the management (pooled proportion, 42.0%) of patients with various gynecological cancers, including cervical, uterine, and ovarian [21].

Head and Neck Cancer

Seven studies met the inclusion criteria [22-28]. In patients with head and neck squamous cell carcinoma, treatment with FDG PET/CT response-guided radiotherapy with dose escalation led to comparable three-year local control rates as standard 70 Gy radiotherapy (74% vs.78%; hazard ratio [HR], 0.8; 95% CI, 0.25 to 2.52, p=0.7) but at the cost of increased late grade 3 toxicity (35% vs. 18%; OR, 5.09; 95% CI, 1.64 to 15.8, p=0.005) [22]. For the post-treatment follow-up of clinically asymptomatic patients, those who received FDG PET/CT had a significantly improved three-year OS rate (72.5% vs.64.3%, p=0.002) and a lower risk of death (OR, 0.71; 95% CI, 0.57 to 0.88, p=0.002) in comparison to those who received only chest CT [23]. In the staging or restaging of patients without distant metastases, FDG PET/CT uncovered additional malignancies in 6.1% of cases [24]. In patients with laryngeal squamous cell carcinoma, FDG PET/CT provided superior accuracy over neck MRI in the preoperative detection of lymph node metastases (75.8% vs. 63.6%, p=0.03). As a result, therapy intent was changed in 10.6% of cases [25]. On the contrary, FDG PET/CT was found to be more sensitive (74.2% vs. 26.7%, p=0.0001) but less specific (60.0% vs. 88.4%, p=0.001) than neck MRI for nodal disease detection in patients with T1-T2 oral squamous cell carcinoma [26]. Results from a meta-analysis showed high diagnostic accuracy (AUC, 0.88) for FDG PET/CT in detecting recurrence in patients with differentiated thyroid cancer who have negative radioiodine whole-body scan and elevated thyroglobulin or thyroglobulin antibody levels. The pooled rate of treatment change following FDG PET/CT was 40.0% [27]. However, FDG PET/CT was not particularly useful

in the surveillance of patients with oropharyngeal squamous cell carcinoma when evaluating treatment failure or disease recurrence (accuracy, 68.8%) [28].

Hematologic Cancer

Five studies met the inclusion criteria [29-33]. In patients with Hodgkin or non-Hodgkin lymphoma (HL or NHL), FDG PET/CT detected bone marrow involvement with sensitivity that ranged from 67.0% to 92.3% and specificity that ranged from 82.0% to 93.4% [29-31]. For one of the studies, the diagnostic accuracy of FDG PET/CT was reported to be equivalent to that of MRI [31]. Long-term analysis of the EORTC/LYSA/FIL H10 trial for localized HL confirmed that the omission of involved-node radiotherapy from additional cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) was associated with lower 10-year progression-free survival (PFS) rates in both favourable (HR, 13.2; 95% CI, 3.1 to 55.8, noninferiority test, p=0.9735; difference test, p<0.0001) and unfavourable (HR, 1.52; 95% CI, 0.84 to 2.75, noninferiority test, p=0.8577; difference test, p=0.1628) interim-PET-negative patients. However, the difference in terms of PFS between standard ABVD and intensification with bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone ($BEACOPP_{escalated}$) was no longer significant for interim-PET-positive patients (HR, 0.67; 95% CI, 0.37 to 1.20; p=0.1777) [32]. In the extended follow-up of the RATHL trial for patients with advanced-stage HL, the lower confidence interval for the 1.3% difference in three-year PFS (95% CI, –3.0 to 4.7) between ABVD and the omission of bleomycin after negative findings on interim FDG PET/CT now falls within the predefined noninferiority margin [33].

Melanoma

Two studies met the inclusion criteria [34,35]. In the primary staging of patients with melanoma, FDG PET/CT detected lymph node and distant metastases with high specificity (93.2%) but suboptimal sensitivity (66.0%). Nonetheless, the imaging results led to a change in diagnostic or therapeutic procedure in 42.6% of cases, with 28.7% of lymph node biopsies no longer necessary [34]. Similar findings were observed in the evaluation of regional nodal status (sensitivity, 41.4%; specificity, 88.5%) and distant disease (sensitivity, 60.0%; specificity, 81.3%) in the Asian population [35].

Non-FDG Tracers

Eighteen studies met the inclusion criteria [36-53]. In patients with differentiated neuroendocrine tumours (NETs), ^{68}Ga-DOTA-TATE/TOC PET/CT was able to confirm liver metastases with high positive predictive value (95.5%) [36]. Across two studies, ^{18}F-FET PET or PET/CT or PET/MRI demonstrated high diagnostic potential for distinguishing between true progression and treatment-related changes in patients with glioma (sensitivity, 80.0% to 88.0%; specificity, 81.0% to 83.0%) [37,38] or brain metastases (sensitivity, 80.0%; specificity, 88.0%) [38]. Altogether, clinical management was impacted in 51.3% of cases [38]. Numerous studies investigated the role of ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT in prostate cancer. In patients who underwent preoperative staging, ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT detected lymph node metastases with high specificity (96.0% to 96.9%) but low sensitivity (57.0% to 63.2%) [39,40]. Furthermore, ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT was able to identify extraprostatic extension (73.0% to 82.8%) and seminal vesicle invasion (87.0% to 90.6%) with moderate to high accuracy [41,42]. Overall, 38.5% of patients had their disease stage modified as a result of ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT, leading to a change in therapy decisions in 28.0% to 32.3% of cases [39,43]. In the follow-up of patients treated with definitive therapy, ^{68}Ga-PSMA or ^{18}F-DCFPyL PET/CT displayed high sensitivity (84.0% to 100%) and specificity (95.0% to 97.0%) for the detection of recurrent disease [39,44]. The proportion of patients who had their management changed was 54.0% [39]. Specifically, patients imaged with ^{18}F-DCFPyL PET/CT were more likely to undergo

pelvic node basin treatment at the time of salvage radiotherapy than those who received conventional imaging (e.g., CT, bone scan) (61.4% vs. 20.0%, p<0.001). Nevertheless, the addition of nodal irradiation did not translate to improvement in biochemical failure-free survival (p=0.662), event-free survival (p=0.675), or metastasis-free survival (p=0.083) [45]. For patients with oligometastatic recurrence who received ^{68}Ga-PSMA PET-directed stereotactic body radiotherapy, the five-year biochemical failure-free survival was 15.0% (95% CI, 9.2% to 25.0%). At five years, 39.0% of the patients had not received any androgen deprivation therapy and 55.0% had not started palliative androgen deprivation therapy [46]. One meta-analysis compared the diagnostic performance of ^{18}F-NaF PET/CT to that of ^{99m}Tc-MDP/HDP SPECT for bone metastases. In both patient-based (AUC, 0.98 vs. 0.92, p<0.05) and lesion-based (AUC, 0.99 vs. 0.94, p<0.05) analysis, ^{18}F-NaF PET/CT came out on top [47]. In mild cognitive impairment or dementia, two ancillary studies enrolled participants from the IDEAS trial. For clinically ambiguous cases of cognitive impairment, amyloid PET provided information that guided a change in diagnosis in 35.9% of patients [48]. However, results from the other study showed that the use of amyloid PET was not associated with a significant rate reduction in 12-month hospitalization or 12-month emergency department visit. Moreover, the mean 12-month cost of care was $1,720 per person higher in patients who received amyloid PET scanning [49]. For the staging or restaging of various types of solid tumours, ^{68}Ga-FAPI PET/CT findings impacted the TNM stage and clinical management of 42.0% and 56.3% of patients, respectively [50]. In particular, ^{68}Ga-FAPI PET/CT detected primary tumour and/or metastases in patients with proven or suspected pancreatic ductal adenocarcinoma with high accuracy (patient-based, 94.8%; region-based, 95.1%), which prompted intended management changes in 56.3% of cases [51]. The clinical utility of PET/CT with tracer ^{18}F-FDOPA was examined in two studies, one in pheochromocytomas and paragangliomas, and the other in suspected recurrent high-grade glioma. Regarding the initial diagnosis or detection of recurrence/metastases of pheochromocytomas and paragangliomas, ^{18}F-FDOPA PET/CT demonstrated superior region-level sensitivity (86.2% vs. 65.5%, p=0.031) and accuracy (AUC, 0.93 vs. 0.82, p=0.004) in comparison to ^{123}I-MIBG SPECT/CT [52]. In the second study, ^{18}F-FDOPA PET/CT added valuable information that led to a change in proposed management for 22.5% of glioma recurrences [53].

Pancreatic Cancer

One study met the inclusion criteria [54]. In newly diagnosed patients, the accuracy of FDG PET/MRI in T staging was significantly higher than that of FDG PET/CT (85.2% versus 63.6%, p<0.05). For N and M staging, the diagnostic accuracies were comparable between the two modalities (p>0.05).

Sarcoma

One study met the inclusion criteria [55]. In the initial staging of soft-tissue or bone sarcoma, or restaging of patients with presumed limited recurrence, additional information provided by FDG PET/CT changed the treatment intent and treatment type in 37.4% and 31.6% of patients, respectively. The presence of metastases on FDG PET/CT was associated with shorter median PFS at initial staging (p=0.04) as well as median OS at the time of recurrence (p=0.002).

Thoracic Cancer

Three studies met the inclusion criteria [56-58]. In the preoperative staging of patients with stage I and II non-small cell lung cancer (NSCLC), the addition of FDG PET/CT to contrast-enhanced CT was associated with greater disease-free survival (12.6 years vs. 6.9 years; HR, 0.67, 95% CI, 0.53 to 0.83, p<0.001) and OS (13.9 years vs. 10.5 years; HR, 0.64, 95% CI, 0.50 to 0.81, p<0.001) [56]. In the same way, patients with stage III disease who received

pretreatment FDG PET/CT had longer OS (17.0 months vs. 11.0 months, p<0.001) and five-year OS rate (22.0% vs. 14.0%, p<0.001) than those who did not undergo the scan. FDG PET/CT also led to more patients being treated with curative-intent chemoradiotherapy (23.0% vs. 13.0%, p<0.001) and surgery (23.0% vs. 10.0%, p<0.001) [57]. For the assessment of mediastinal lymph node involvement after neoadjuvant chemoimmunotherapy, FDG PET/CT showed a sensitivity of 66.7% and a specificity of 83.9% [58].

CLINICAL EXPERT REVIEW

Breast Cancer

Current Indications for Breast Cancer

- For the staging of patients with histologically confirmed clinical stage 2b or stage 3 breast cancer being considered for curative-intent combined modality treatment; and/or repeat PET on completion of neoadjuvant therapy, prior to surgery (when there is clinical suspicion of progression); or for re-staging of patients with locoregional recurrence, after primary treatment, being considered for ablative or salvage therapy.
- For staging or re-staging of patients with oligometastatic disease (4 or fewer metastases) on conventional imaging prior to radical intent or ablative therapy.

Reviewer's Comments

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

Esophageal Cancer

Current Indications for Esophageal Cancer

- For baseline staging assessment of patients diagnosed with esophageal/ gastroesophageal junction cancer being considered for curative therapy and/or repeat PET/CT scan on completion of preoperative/neoadjuvant therapy, prior to surgery; or for re-staging of patients with locoregional recurrence, after primary treatment, being considered for definitive salvage therapy.

Reviewer's Comments

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

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).

Current Indication for Gynecologic Malignancies

- For re-staging of patients with recurrent gynecologic malignancies under consideration for radical salvage surgery (e.g., pelvic exenteration).

Reviewer's Comments (Dr. Ji-Hyun Jang)

Given the increasing evidence supporting the use of PET/CT in recurrent ovarian cancer, PET/CT should be indicated when conventional imaging is equivocal, and biopsy is not feasible for tissue diagnosis.

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 (human papillomavirus 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 (human papillomavirus 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 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 (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.

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 (Dr. Tara Baetz)

The current recommendations for the utilization of PET/CT in melanoma remain valid and no changes are required. However, there needs to be clarification on the definition of staging of "high-risk" melanoma to include stage IIB/C and stage III patients.

Non-FDG Tracers

Current Indications for Gallium-68 PET/CT in NETs

- For the evaluation of a pancreatic, small bowel or mesenteric mass with findings suggestive of a NET (e.g., hypervascular pancreatic mass, desmoplastic mesenteric mass) on conventional imaging.
- For the evaluation of extra-adrenal mass (e.g., carotid body nodule), with conventional imaging and/or elevated biomarkers suggestive of a pheochromocytoma/paraganglioma (PPGL).
- For the evaluation of patients with a genetic syndrome predisposing to NETs and a biochemical and/or morphological suspicion of a NET in whom PET results would measurably impact management.

  Special Considerations for Diagnosis
  - For the evaluation of patients with a suspicious mass in another anatomical location (e.g., lung) without elevated biochemical markers should be considered for further workup and/or biopsy before the PET. PET could be considered after a failed biopsy or if a biopsy is not feasible.
  - For the evaluation of patients with a pancreatic tail mass suggestive of a NET should have a Tc-99m Sulpha Colloid or Red Blood Cell scan to exclude intrapancreatic accessory spleen as both can present Ga-68 DOTATATE avid.
- For the initial staging of histologically proven well-differentiated NET (G1-G3), including unknown primary, or PPGL.
- For the initial staging of histologically proven medullary thyroid cancer being considered for curative intent therapy.

  Note: Initial staging PET scans should be requested within one year from the initial diagnosis.

  Special Considerations for Initial Staging
  - PET is not appropriate for patients with Type 1 Gastric NET, neuroendocrine carcinomas and adenocarcinomas with NET features.
  - Unless there are unique clinical and/or structural concerns, PET is not routinely appropriate for patients with diffuse idiopathic pulmonary neuroendocrine cell hyperplasia.
  - Initial staging of patients with an appendiceal NET should be considered when there are positive lymph nodes, the tumour is greater than 1 cm, and/or the tumour is invading through the serosa into the mesoappendix.
  - Initial staging of patients with medullary thyroid cancer should be considered when the patient has yet to have a thyroidectomy or following it when biomarkers are positive with negative or equivocal structural imaging.

- For the re-staging of patients with progressive NETs disease who are being considered for publicly funded peptide receptor radionuclide therapy (PRRT).
  Note: For PRRT consideration, a PET scan should be completed within 12 months. However, a more recent PET scan should be considered if there are concerning clinical features (e.g., de-differentiation).
- New baseline PET scan for patients with new metastatic disease on conventional imaging and/or clinical suspicion of de-differentiation.
- For the re-staging of patients with NETs disease when surgery (e.g., de-bulking, focal ablation, liver-directed therapy) is being considered.
- For the re-staging of patients with NETs disease where conventional imaging is negative or equivocal at the time of clinical and/or biochemical progression.
- For the re-staging of patients with medullary thyroid cancer when 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.
  Special Considerations for Routine Surveillance
    - Requests for routine surveillance when there is no clinical or biochemical suspicion of recurrence or progression are not eligible.

Current Indications for PSMA PET/CT in Prostate Cancer

- For the initial staging of patients with a new diagnosis of high-risk prostate cancer being considered for radical (curative) therapy.
- For the re-staging of patients with post-prostatectomy node-positive disease or persistently detectable prostate-specific antigen (PSA).
- For the re-staging of patients with biochemical failure post-prostatectomy.
- For the re-staging of patients with failure following radical prostatectomy followed by adjuvant or salvage radiotherapy.
- For the re-staging of patients with rising PSA post-prostatectomy despite salvage hormone therapy.
- For the re-staging of patients with biochemical failure following treatment for oligometastatic disease.
- For the re-staging of patients with biochemical failure following primary radiotherapy.
- For the re-staging of patients with rising PSA and/or progression on conventional imaging despite prior second-line hormone therapy or chemotherapy for castrate-resistant prostate cancer.
- 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 (Dr. Derek Jonker)

There is insufficient evidence to recommend the utilization of PET/CT in pancreatic cancer.

Sarcoma

Current Indications for Sarcoma

- For the initial staging of patients with histologically confirmed high grade (≥ Grade 2), or ungradable, soft tissue or bone sarcomas, when conventional work-up is negative or equivocal for metastatic disease, prior to curative intent therapy.
- For re-staging of patients with suspicion of, or histologically confirmed, recurrent sarcoma (local recurrence of limited metastatic disease) when radical salvage therapy is being considered.

Current Indication for Plexiform Neurofibromas

- For patients with suspicion of malignant transformation of plexiform neurofibromas.

Reviewer's Comments (Dr. Gina Di Primio)

The current recommendations for the utilization of PET/CT in sarcoma 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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DISCLAIMER

Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Ontario Health (Cancer Care Ontario) makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

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APPENDIX 1: SUMMARY OF STUDIES FROM JULY TO DECEMBER 2023.

Breast Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Gupta et al, 2023 [1]	Retrospective	128 patients underwent staging prior to axillary lymph node dissection (operable, early-stage breast cancer)	FDG PET/CT	Mammography supplemented with ultrasonography	Histopathology, sentinel lymph node biopsy	**Axillary lymph node metastases** Sens: 41.7% Spec: 93.2% PPV: 92.1% NPV: 45.6% AUC: 0.76	**Axillary lymph node metastases** Sens: 84.5% Spec: 54.5% PPV: 78.0% NPV: 68.6%	NA
Cetindag et al, 2023 [2]	Retrospective	67 patients who underwent preoperative staging and did not receive neoadjuvant therapy (breast cancer)	FDG PET/CT	NA	Histopathology	**Axillary lymph node metastases** Sens: 82.4% Spec: 69.7% PPV: 73.7% NPV: 79.3% Accu: 76.1%	NA	NA
Dayes et al, 2023 [3]	RCT (PET ABC trial)	369 patients randomized 1:1 to PET/CT or conventional staging and were being considered for curative combined modality treatment (stage IIb or III invasive ductal carcinoma of the breast)	FDG PET/CT (n=184)	CeCT of the chest/abdomen and pelvis, bone scan (n=185)	Biopsy, clinical and imaging follow-up	NA	NA	FDG PET/CT upstaged 23.4% (43/184) of patients to stage IV compared with 11.4% (21/185) conventionally staged patients (RR, 2.4; 95% CI, 1.4 to 4.2, p=0.002). Subsequently, 19.0% (35/184) of FDG PET/CT-staged patients did not receive combined modality treatment compared with 10.8% (20/185) of conventionally staged patients (absolute difference, 8.2%; 95% CI, 0.1 to 15.4, p=0.03).
Werner et al, 2023 [4]	Prospective	47 patients who underwent primary staging, restaging, or evaluation of suspected recurrence (breast cancer)	FDG PET/CT	CT, MRI, US, bone scintigraphy, tumour marker	Pre- and post-PET questionnaires	NA	NA	Management changes occurred after 78.8% (41/52) of FDG PET/CT scans, of which 18 were major and 23 were minor (6—palliative to curative, 3—initiated systemic therapy, 2—cancelled

								systemic treatment, 1—additional radiotherapy, 2—surgery to systemic therapy, 4—additional surgery, 13—avoided unnecessary biopsy, 10—modified systemic therapy). FDG PET/CT-induced changes resulted in a 5-year OS of 72.3% (mean, 82.2 months, 95% CI, 70.7 to 93.7).
Xia et al, 2023 [5]	Meta-analysis	16 studies (1261 patients with breast cancer)	FDG PET/CT, FDG PET/MRI	NA	Pathology, imaging follow-up	**Bone metastases (patient-based)** ***PET/CT*** Pooled Sens: 73.0%‡ Pooled Spec: 100% ***PET/MRI*** Pooled Sens: 99.0%‡ Pooled Spec: 100% **(lesion-based)** ***PET/CT*** Pooled Sens: 89.0%‡ Pooled Spec: 99.0% ***PET/MRI*** Pooled Sens: 99.0%‡ Pooled Spec: 99.0%	NA	NA
Esophageal Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Huang et al, 2023 [6]	Retrospective	100 patients who underwent preoperative staging with or without neoadjuvant chemoradiotherapy (esophageal squamous cell carcinoma)	FDG PET/CT	EUS	Pathology	**T-staging** ***Without neoadjuvant chemoradiotherapy*** Accu: 71.9% ***With neoadjuvant chemoradiotherapy*** Accu: 65.1%*	**T-staging** ***Without neoadjuvant chemoradiotherapy*** Accu: 56.1% ***With neoadjuvant chemoradiotherapy*** Accu: 18.6%*	NA
Reyhani et al, 2023 [7]	Prospective	297 patients who underwent staging prior to endoscopic mucosal resection and/or esophagectomy (high-grade	FDG PET/CT	Endoscopy, CT, EUS	Histopathology	**T- and N-staging** Accu: 11.0%-30.0%	**T- and N-staging** ***CT*** Accu: 28.6%-43.3% ***EUS*** Accu: 29.6%-59.7%	NA

		dysplasia or early esophageal adenocarcinoma)						
Gastrointestinal Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Mogollon-Gonzalez et al, 2023 [8]	Retrospective	195 patients who underwent preoperative staging (colorectal cancer)	FDG PET/CT	CeCT, colonoscopy	Surgical exploration, histopathology, biopsy, imaging follow-up	**N staging** Sens: 40.0% Spec: 91.0% PPV: 80.1% NPV: 61.4% Accu: 66.1% **Distant metastases** Sens: 93.1% Spec: 99.4% PPV: 96.4% NPV: 98.8% Accu: 98.4% **Liver metastases** Sens: 94.0% Spec: 90.1% PPV: 94.0% NPV: 90.1% Accu: 93.1%	**N staging** ***CeCT*** Sens: 63.1% Spec: 85.0% PPV: 80.0% NPV: 79.2% Accu: 74.3% **Distant metastases** ***CeCT*** Sens: 75.8% Spec: 96.9% PPV: 81.4% NPV: 95.8% Accu: 93.8% **Liver metastases** ***CeCT*** Sens: 72.2% Spec: 90.0% PPV: 92.8% NPV: 66.0% Accu: 79.3%	Additional findings from FDG PET/CT altered the treatment planning of 15.4% (30/195) patients (14—modified surgical approach, 7—additional resection of second malignancy, 5—resection of metastatic disease, 4—prevented unnecessary resection).
Milardovic et al, 2023 [9]	Retrospective	100 surgically treated patients with rising CEA (suspected recurrent colorectal cancer)	FDG PET/CT	CEA tumour marker	Histopathology, clinical follow-up	**Recurrence or metastatic disease** Sens: 95.0% Spec: 73.0% PPV: 70.0% NPV: 95.0%	**Recurrence or metastatic disease** Sens: 58.0% Spec: 96.0% PPV: 91.0% NPV: 78.0%	NA
Pang et al, 2023 [10]	Retrospective	58 patients who underwent initial staging (hilar cholangiocarcinoma)	FDG PET/CT, FDG PET/MRI	NA	Histopathology, correlative imaging results and/or imaging follow-up	**T staging** ***PET/CT*** Accu: 58.6%‡ ***PET/MRI*** Accu: 72.4%‡ **N staging** ***PET/CT*** Accu: 67.2%‡ ***PET/MRI*** Accu: 84.5%‡ **M staging** ***PET/CT*** Accu: 94.8%	NA	NA

						PET/MRI Accu: 98.3% **Bismuth-Corlette classification** ***PET/CT*** Accu: 79.3%‡ ***PET/MRI*** Accu: 89.7‡		
Mirshahvalad et al, 2023 [11]	Meta-analysis	28 studies (1448 patients with anal canal cancer)	FDG PET or PET/CT	CT, MRI	Histopathology, clinical follow-up, multimodality imaging composite	**Primary tumour** Pooled Sens: 98.0% **Distinguishing T3-4 from other T-stages** Pooled Sens: 91.0% Pooled Spec: 96.0% **Lymph node metastases** Pooled Sens: 99.0% Pooled Spec: 93.0% **Distant metastases** Pooled Spec: 99.0% **Recurrence** Pooled Sens: 90.0% Pooled Spec: 97.0% Pooled +LR: 26.8 Pooled -LR: 0.10 **Response assessment** Pooled Sens: 96.0% Pooled Spec: 86.0%	NA	NA
Genitourinary Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Richters et al, 2023 [12]	Retrospective	550 patients who underwent preoperative staging without neoadjuvant chemotherapy (newly diagnosed muscle-invasive bladder cancer)	FDG PET/CT + CT	CT	Histopathology	**Lymph node metastases** Sens: 40.0% Spec: 85.0% PPV: 50.0% NPV: 80.0%	**Lymph node metastases** Sens: 7.1% Spec: 96.0% PPV: 39.0% NPV: 73.0%	NA
Shahait et al, 2023 [13]	Retrospective	133 patients who underwent initial staging (bladder cancer)	FDG PET/CT	CeCT	Consensus from multidisciplinary team, imaging follow-up	**Localized disease** Sens: 51.7% Spec: 96.2% PPV: 79.1% NPV: 87.6% Accu: 86.4%	NA	FDG PET/CT findings changed the intent of treatment in 26.3% (35/133) of patients (16—curative to

						Pelvic lymph node metastases Sens: 54.3% Spec: 98.9% PPV: 96.2% NPV: 82.2% Accu: 84.7% **Distant metastases** Sens: 76.8% Spec: 96.9% PPV: 96.4% NPV: 79.4% Accu: 86.4%		palliative, 19—palliative to curative).
Liang et al, 2023 [14]	Prospective	43 patients who underwent primary staging, restaging, or evaluation of suspected relapse (germ cell tumours)	FDG PET/CT	CT, MRI	Pre- and post-PET questionnaires	NA	NA	FDG PET/CT caused a change in the intended mode of therapeutic intervention in 41.9% (18/43) of patients (8—switched to chemotherapy, 1—switched to radiotherapy, 9—surgical resection to non-invasive treatment). FDG PET/CT also reduced the need for surgical biopsy in 18.6% (8/43) and additional diagnostic imaging in 58.1% (25/43).
Schaafsma et al, 2023 [15]	Meta-analysis	17 studies (1227 patients with an adrenal mass on CT or MRI)	FDG PET/CT	CT, MRI	Histopathology, clinical and imaging follow-up	**Differentiating benign from malignant adrenal tumours** Pooled Sens: 87.3% Pooled Spec: 84.7% Pooled DOR: 9.20 AUC: 0.92	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**
Li et al, 2023 [16]	Meta-analysis	61 studies (4284 patients with ovarian cancer)	FDG PET/CT	CT, MRI	Histopathology, clinical and/or imaging follow-up	**Primary tumour and/or metastases (patient-based)** Pooled Sens: 92.0% Pooled Spec: 88.0% Pooled +LR: 7.9	**Primary tumour and/or metastases (patient-based)** ***CT*** Pooled Sens: 83.0% Pooled Spec: 69.0% Pooled +LR: 2.7	NA

						Pooled -LR: 0.09 Pooled DOR: 11 AUC: 0.96 **(lesion-based)** Pooled Sens: 82.0% Pooled Spec: 94.0% Pooled +LR: 12.6 Pooled -LR: 0.20 Pooled DOR: 64 AUC: 0.95	Pooled -LR: 0.25 Pooled DOR: 11 AUC: 0.84 ***MRI*** Pooled Sens: 95.0% Pooled Spec: 81.0% Pooled +LR: 4.9 Pooled -LR: 0.07 Pooled DOR: 72 AUC: 0.90 **(lesion-based)** ***CT*** Pooled Sens: 69.0% Pooled Spec: 88.0% Pooled +LR: 5.8 Pooled -LR: 0.35 Pooled DOR: 17 AUC: 0.86	
Ali et al, 2023 [17]	Prospective	76 patients presented with rising tumour marker CA125 after treatment (suspected recurrent ovarian cancer)	FDG PET/CT	Tumour marker CA125	Histopathology, clinical or imaging follow-up	**Recurrence** Sens: 96.3% Spec: 92.3% PPV: 85.7% NPV: 96.1% Accu: 98.4%	NA	NA
Kosinska et al, 2023 [18]	Prospective	84 patients who underwent cytoreductive surgery (suspected recurrent ovarian cancer)	FDG PET/CT	NA	Histology, clinical or imaging follow-up	**Recurrence** Sens: 95.5% Spec: 77.8% PPV: 94.0% NPV: 82.4%	NA	NA
Sami et al, 2023 [19]	Prospective	50 patients with rising CA-125 levels after receiving chemotherapy or surgical intervention (suspected recurrent ovarian cancer)	FDG PET/CT	CA-125 tumour marker	Histopathology, clinical and imaging follow-up	**Recurrence** Sens: 95.7% Spec: 75.0% PPV: 97.8% NPV: 60.0% Accu: 94.0% **Peritoneal metastases** Sens: 97.1% Spec: 93.3% PPV: 97.1% NPV: 93.3% Accu: 96.0%	NA	NA
Jain et al, 2023 [20]	Retrospective	386 patients who underwent restaging after radiotherapy,	FDG PET/CT	CeCT	Histopathology, clinical or imaging follow-up	**Recurrence or residual disease** Sens: 89.4% Spec: 65.0%	**Recurrence or residual disease** Sens: 66.4% Spec: 40.7%	Based on FDG PET/CT findings, clinical management was altered

		chemotherapy, and surgery, either alone or in combination (suspected recurrent cervical cancer)				PPV: 78.3% NPV: 81.3% Accu: 80.0%	PPV: 71.8% NPV: 34.8% Accu: 70.0%	in 35.2% (136/386) of patients.
Pak and Yoon, 2023 [21]	Meta-analysis	19 studies (6191 patients with recurrent gynecologic cancers)	FDG PET/CT	NA	Pre- and post-PET information	NA	NA	The pooled proportion of management change due to FDG PET/CT findings was 42.0%.
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**
Al-Mamgani et al, 2023 [22]	Prospective (The ADMIRE study)	87 patients who received adaptive FDG PET/CT response-guided radiotherapy with dose escalation or the current standard of 70 Gy radiotherapy (stage II to IV head and neck squamous cell carcinoma)	FDG PET/CT-guided dose escalation with 2 planned adaptations (at the end of week 2 and 4 treatment)	Current standard of 70 Gy radiotherapy	Clinical follow-up	NA	NA	The 3-year local control rates were similar between patients who received FDG PET/CT-guided dose escalation and those who received standard radiotherapy (74% versus 78%, respectively; HR, 0.8; 95% CI, 0.25 to 2.52, p=0.70). Likewise, the 3-year locoregional control rates (69% versus 73%, respectively, p=0.76), disease-free survival (50% versus 61%, respectively, p=0.31) and OS (60% versus 72%, respectively, p=0.21) were similar between the two groups. However, FDG PET/CT-guided dose escalation was associated with higher odds of any late grade 3 toxicity (OR, 5.09; 95% CI, 1.64 to 15.8, p=0.005), any late grade ≥2 toxicity (OR, 3.67; 95% CI, 1.2 to 11.17, p=0.02), persistent laryngeal edema (OR, 10.95; 95%

								CI, 2.71 to 44.29, p=0.001), persistent mucosal ulcers (OR, 4.67; 95% CI, 1.23 to 17.7, p=0.02), and late grade 3 radionecrosis (OR, 15.69; 95% CI, 2.43 to 101.39, p=0.004).
Leclere et al, 2023 [23]	Retrospective	782 patients who are clinically asymptomatic after curative intent treatment and underwent surveillance imaging (head and neck squamous cell carcinoma)	FDG PET/CT (n=497)	Chest CT (n=285)	Clinical follow-up	NA	NA	Patients who received posttreatment FDG PET/CT had a significantly improved 3-year OS when compared with those who received chest CT (72.5% versus 64.3%, p=0.002). FDG PET/CT was associated with a lower risk of death (OR, 0.71; 95% CI, 0.57 to 0.88, p=0.002).
Zwittag et al, 2023 [24]	Retrospective	114 patients without distant metastases who underwent staging or restaging (head and neck cancer)	FDG PET/CT	MRI	Histopathology	**Cervical lymph node metastases** Sens: 80.4% Spec: 87.3% PPV: 83.7% NPV: 84.6%	**Cervical lymph node metastases** Sens: 80.4% Spec: 85.7% PPV: 82.0% NPV: 84.4%	FDG PET/CT uncovered additional malignancies in 6.1% (7/114) of patients.
Al-Ibraheem et al, 2023 [25]	Retrospective	66 patients who underwent nodal staging prior to total laryngectomy with unilateral or bilateral neck dissection (Laryngeal squamous cell carcinoma)	FDG PET/CT	Neck MRI	Histopathology	**Lymph node metastases** Sens: 89.7% Spec: 64.9% PPV: 66.7% NPV: 88.9% Accu: 75.8%*	**Lymph node metastases** Sens: 65.5% Spec: 62.2% PPV: 57.6% NPV: 69.7% Accu: 63.6%*	FDG PET/CT results changed the therapy intent of 10.6% (7/66) of patients.
Madsen et al, 2023 [26]	Prospective	76 patients who underwent staging prior to sentinel node biopsy or elective neck dissection (T1-T2 oral squamous cell carcinoma)	FDG PET/CT	Neck MRI	Histopathology	**Cervical lymph node metastases** Sens: 74.2%* Spec: 60.0%* PPV: 56.1% NPV: 77.1% Accu: 65.8%	**Cervical lymph node metastases** Sens: 26.7%* Spec: 88.4%* PPV: 61.5% NPV: 63.3% Accu: 63.0%	NA
Bang et al, 2023 [27]	Meta-analysis	24 studies (1988 patients with differentiated	FDG PET/CT	Iodine whole-body scan	Histopathology, clinical follow-up	**Recurrence** Pooled Sens: 87.0% Pooled Spec: 84.0%	NA	The pooled rate of treatment change

		thyroid cancer who have negative radioiodine whole-body scan and elevated serum thyroglobulin or thyroglobulin antibody levels)				AUC: 0.88		following FDG PET/CT was 40.0%.
Liu et al, 2023 [28]	Retrospective	224 patients who underwent surveillance within 10 to 20 weeks post-treatment (oropharyngeal squamous cell carcinoma)	FDG PET/CT	NA	Histology	**Treatment failure or disease recurrence** Sens: 52.3% Spec: 72.8% PPV: 31.9% NPV: 86.2% Accu: 68.8%	NA	NA
Hematologic Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Zheng et al, 2023 [29]	Meta-analysis	9 studies (1119 patients with follicular lymphoma)	FDG PET or PET/CT	NA	BMB	**Bone marrow involvement** Pooled Sens: 67.0% Pooled Spec: 82.0% Pooled +LR: 3.7 Pooled -LR: 0.4 Pooled DOR: 9 AUC: 0.83	NA	NA
Guo et al, 2023 [30]	Retrospective	102 newly diagnosed patients (DLBCL)	FDG PET/CT	NA	BMB	**Bone marrow involvement** Sens: 92.3% Spec: 93.4% YI: 0.857	NA	NA
Shah et al, 2023 [31]	Meta-analysis	24 studies (2969 patients with HL and NHL)	FDG PET/CT	MRI	Histopathology, BMB	**Bone marrow involvement** Pooled Sens: 77.1% Pooled Spec: 89.7% Pooled +LR: 6.72 Pooled -LR: 0.19 Pooled DOR: 39.05	**Bone marrow involvement** Pooled Sens: 77.8% Pooled Spec: 88.6% Pooled +LR: 6.97 Pooled -LR: 0.19 Pooled DOR: 39.18	NA
Federico et al, 2023 [32]	RCT (10-year follow-up of the EORTC/LYSA/ FIL H10 trial)	1419 patients who underwent interim-PET response evaluation after	FDG PET/CT	NA	Clinical follow-up	NA	NA	In PET-positive patients, the 10-year PFS rates were 79.2% for standard ABVD + INRT and 85.1% for BEACOPPesc + INRT

		2 cycles of ABVD (localized HL)						(HR, 0.67; 95% CI, 0.37 to 1.20; p=0.1777). The 10-year OS rates were 90.4% and 92.0% for ABVD + INRT and BEACOPPesc + INRT, respectively (HR, 0.92; 95% CI, 0.43 to 1.97; p=0.8370). In PET-negative patients, the 10-year PFS rates favoured ABVD + INRT in both favourable risk (98.8% versus 85.4%; HR, 13.2; 95% CI, 3.1 to 55.8, noninferiority test, p=0.9735; difference test, p<0.0001) and unfavourable risk (91.4% versus 86.5%; HR, 1.52; 95% CI, 0.84 to 2.75, noninferiority test, p=0.8577; difference test, p=0.1628) patients. However, there were no differences in 10-year OS rates between ABVD + INRT and ABVD only for both favourable risk (100% versus 98.0%, respectively; HR, 2.80; 95% CI, 0.29 to 26.9, p=0.3522) and unfavourable risk (94.3% versus 94.8%, respectively; HR, 0.84; 95% CI, 0.36 to 1.98, p=0.6908) patients.
Luminari et al, 2023 [33]	RCT (long-term follow-up of the RATHL trial)	1201 patients who underwent interim-PET response evaluation after 2 cycles of ABVD (advanced HL)	FDG PET/CT	NA	Clinical follow-up	NA	NA	In PET-negative patients, the 3-year PFS was 85.5% in the ABVD group and 84.3% in the AVD group (HR, 1.10; 95% CI, 0.82 to 1.47). The lower CI for the 1.3% difference (95% CI, -3.0 to 4.7) is within the predefined noninferiority margin of 5%. The 7-year PFS and OS rates were 81.0% and

								93.2%, respectively with ABVD and 79.2% and 93.5%, respectively with AVD. In PET-positive patients, the 7-year PFS and OS rates were 65.9% and 83.2%, respectively.
Melanoma								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Mayer et al, 2023 [34]	Retrospective	94 patients who underwent primary staging (melanoma)	FDG PET/CT	NA	Histology, clinical and imaging follow-up	**Lymph node and distant metastases** Sens: 66.0% Spec: 93.2% PPV: 91.2% NPV: 73.2%	NA	FDG PET/CT results altered the subsequent diagnostic or therapeutic procedure in 42.6% (40/94) of patients (26—surgical procedure change, 4—received neoadjuvant immunotherapy, 2—surgical procedure declined, 8—uncovered secondary malignancy). FDG PET/CT also made sentinel lymph node biopsy unnecessary in 28.7% (27/94) of cases.
Chen et al, 2023 [35]	Retrospective	90 patients who underwent staging prior to surgical treatment (cutaneous melanoma)	FDG PET/CT	NA	Histopathology, imaging follow-up	**Regional lymph node metastases** Sens: 41.4% Spec: 88.5% PPV: 63.2% NPV: 76.1% Accu: 73.3% **Distant metastases** Sens: 60.0% Spec: 81.3% PPV: 28.6% NPV: 94.2% Accu: 78.9%	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**

Fabritius et al, 2023 [36]	Retrospective	119 patients who underwent staging (differentiated neuroendocrine tumours)	^{68}Ga-DOTA-TATE/TOC PET/CT	Liver MRI	Histopathology	**Liver metastases (lesion-based)** Sens: 95.5% Spec: 0% PPV: 95.5% NPV: 0% Accu: 91.4%	NA	NA
^{18}F-FET								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Ouyang et al, 2023 [37]	Meta-analysis	14 studies (774 patients with glioma)	^{18}F-FET PET or PET/CT or PET/MRI	MRI	Pathology, imaging follow-up	**Distinguishing pseudoprogression from true progression** Pooled Sens: 80.0% Pooled Spec: 81.0% AUC: 0.86	NA	NA
Smith et al, 2023 [38]	Retrospective	80 patients with equivocal brain MRI findings following surgery, radiation, and/or chemotherapy (42 high-grade glioma or 38 brain metastases)	^{18}F-FET PET/MRI	MRI	Pathology, clinical follow-up	**Distinguishing true progression from treatment-related changes (High-grade glioma)** Sens: 88.0% Spec: 83.0% PPV: 93.0% NPV: 67.0% +LR: 4.4 -LR: 0.16 Accu: 86.0% **(Brain metastases)** Sens: 80.0% Spec: 88.0% PPV: 73.0% NPV: 93.0% +LR: 7.5 -LR: 0.22 Accu: 87.0%	NA	Clinical management changed as a consequence of ^{18}F-FET PET/MRI in 61.9% (26/42) of patients with high-grade glioma (15—change in chemotherapy agent, 4—performed surgery, 4—performed radiotherapy, 2—implemented electric tumour treatment field therapy, 1—performed surgery and US) and 39.5% (15/38) of patients with brain metastases (3—change in chemotherapy agent, 7—performed surgery, 3—performed radiotherapy, 1—transitioned to hospice care, 1—planned surgery but not performed).
^{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**

Jeet et al, 2023 [39]	Meta-analysis	111 studies (11378 patients with intermediate- or high-risk prostate cancer)	^{68}Ga-PSMA-11 or ^{18}F-DCFPyL or ^{18}F-PSMA-1007 or ^{64}Cu-PSMA or ^{18}F-rhPSMA-7 or ^{68}Ga-THP-PSMA PET/CT	NA	Histopathology, pre- and post-PET information	**Primary tumour** Pooled Sens: 71.0% Pooled Spec: 92.0% Pooled +LR: 8.7 Pooled -LR: 0.3 Pooled DOR: 27.5 AUC: 0.90 **Lymph node metastases** Pooled Sens: 57.0% Pooled Spec: 96.0% Pooled +LR: 15.5 Pooled -LR: 0.5 Pooled DOR: 34.8 AUC: 0.90 **Recurrence** Pooled Sens: 84.0% Pooled Spec: 97.0% Pooled +LR: 29.9% Pooled -LR: 0.2 Pooled DOR: 179.4 AUC: 0.95	NA	In the setting of primary staging, the pooled proportion of management change as a result of PSMA PET/CT was 28%. In the setting of biochemical recurrence, the pooled proportion of change in therapy decisions was 54.0%.
Rajwa et al, 2024 [40]	Retrospective	165 patients who underwent staging prior to radical prostatectomy and extended pelvic lymph node dissection (high-risk, nonmetastatic prostate cancer)	^{68}Ga-PSMA PET/CT	NA	Histopathology	**Pelvic lymph node metastases** Sens: 63.2% Spec: 96.9% PPV: 93.5% NPV: 78.8% Accu: 82.9%	NA	NA
Gossili et al, 2023 [41]	Meta-analysis	23 studies (969 patients with prostate cancer who underwent preoperative staging)	^{68}Ga-PSMA or ^{18}F-DCFPyL or ^{18}F-PSMA-1007 or ^{64}Cu-PSMA or ^{18}F-DCFBC PET/CT or PET/MRI	NA	Histopathology	**Intraprostatic tumour** ***PET/CT*** Pooled Accu: 86.0% ***PET/MRI*** Pooled Accu: 97.0% **Extraprostatic extension** ***PET/CT*** Pooled Accu: 73.0% ***PET/MRI*** Pooled Accu: 77.0% **Seminal vesicle involvement** ***PET/CT*** Pooled Accu: 87.0% ***PET/MRI***	NA	NA

						Pooled Accu: 90.0%		
Stasiak et al, 2023 [42]	Retrospective	65 patients who underwent staging prior to prostatectomy with or without lymphadenectomy (prostate cancer)	^{68}Ga-PSMA-11 PET/CT	mpMRI	Histopathology, biopsy	**Primary tumour** Sens: 95.0% **Bilateral disease** Sens: 53.0% Spec: 79.0% Accu: 51.0% **Extraprostatic extension** Sens: 14.3% Spec: 91.2% Accu: 82.8% **Seminal vesicle invasion** Sens: 57.1% Spec: 100% Accu: 90.6%	**Primary tumour** Sens: 91.0% **Bilateral disease** Sens: 59.0% Spec: 83.0% Accu: 56.0% **Extraprostatic extension** Sens: 28.6% Spec: 70.2% Accu: 65.6% **Seminal vesicle invasion** Sens: 78.6% Spec: 98.0% Accu: 93.8%	NA
Yasmin et al, 2023 [43]	Prospective	65 patients who underwent initial staging (high-risk prostate cancer)	^{68}Ga-PSMA-11 PET/CT	CT, MRI, US, bone scan	Histopathology, imaging follow-up	NA	NA	^{68}Ga-PSMA-11 PET/CT modified the disease stage of 38.5% (25/65) of patients (20 upstaged, 5 downstaged). A change in therapeutic decision making was observed in 32.3% (21/65) of patients (4—hormonal therapy to surgery, 2—surgery to hormonal therapy and chemotherapy, 10—radiotherapy and hormonal therapy to surgery followed by radiotherapy and hormonal therapy, 5—additional cycles of chemotherapy or continuation of hormonal treatment).
Lu et al, 2023 [44]	Retrospective	93 patients with low PSA level of ≤0.2 ng/mL after definitive treatment (suspected recurrent prostate cancer)	^{18}F-DCFPyL PET/CT	NA	Biopsy, clinical and imaging follow-up	**Recurrence (scan-based)** ***PSA ≤0.1 ng/mL*** Sens: 100% Spec: 95.0% PPV: 96.0% NPV: 100% ***PSA 0.2 ng/mL*** Sens: 100% Spec: 97.0% PPV: 95.0% NPV: 100%	NA	NA

Arifin et al, 2023 [45]	Retrospective	124 patients who received salvage therapy following biochemical failure post-radical prostatectomy (suspected persistent or recurrent prostate cancer)	^{18}F-DCFPyL PET/CT (n=44)	CT, bone scan (n=80)	Clinical and imaging follow-up	NA	NA	^{18}F-DCFPyL PET/CT was associated with more patients receiving pelvic radiation in addition to the prostate bed (61.4% versus 20.0%, p<0.001). However, the biochemical failure-free survival (p=0.662), event-free survival (p=0.675), and metastasis-free survival (p=0.083) were not significantly different between those who received ^{18}F-DCFPyL PET/CT and those who did not.
Mohan et al, 2023 [46]	Retrospective	103 patients treated with SBRT (oligometastatic recurrent prostate cancer)	^{68}Ga-PSMA PET-directed SBRT	NA	Clinical follow-up	NA	NA	The 5-year biochemical failure-free survival was 15.0% (95% CI, 9.2% to 25.0%) with a median time to biochemical failure of 1.1 years. At 5 years, 39.0% (95% CI, 30.0% to 49.0%) of the patients had not received any androgen deprivation therapy and 55.0% (95% CI, 46.0% to 66.0%) had not started palliative androgen deprivation therapy.
^{18}F-NaF								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Fan et al, 2023 [47]	Meta-analysis	11 studies (1085 patients with bone metastases)	^{18}F-NaF PET/CT	^{99m}Tc-MDP/HDP SPECT	Not specified	**Bone metastases (patient-based)** Pooled Sens: 92.0% Pooled Spec: 96.0% Pooled +LR: 23.2 Pooled -LR: 0.09 Pooled DOR: 270 AUC: 0.98* **(lesion-based)** Pooled Sens: 96.0% Pooled Spec: 98.0% Pooled +LR: 59.0	**Bone metastases (patient-based)** Pooled Sens: 80.0% Pooled Spec: 90.0% Pooled +LR: 8.2 Pooled -LR: 0.23 Pooled DOR: 36 AUC: 0.92* **(lesion-based)** Pooled Sens: 76.0% Pooled Spec: 94.0% Pooled +LR: 12.2	NA

						Pooled -LR: 0.04 Pooled DOR: 1627 AUC: 0.99*	Pooled -LR: 0.26 Pooled DOR: 48 AUC: 0.94*	
Amyloid								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Pletnikova et al, 2023 [48]	Prospective	112 patients who were enrolled in the IDEAS study (clinically ambiguous cases of cognitive impairment)	Amyloid PET	Not specified	Pre- and post-PET questionnaires	NA	NA	Amyloid PET resulted in a change in diagnosis in 35.9% (33/92) of patients.
Rabinovici et al, 2023 [49]	Retrospective	25,368 patients who were Medicare beneficiaries (mild cognitive impairment or dementia)	Amyloid PET in the IDEAS study (n=12684)	No Amyloid PET (n=12684)	Clinical follow-up	NA	NA	The 12-month hospitalization rates were 24.0% in the IDEAS study cohort and 25.1% in the control cohort (relative difference, -4.49%; 97.5%CI, -9.09% to 0.34%). The 12-month emergency department visit rates were 44.5% for both cohorts (relative difference, -0.12%; 97.5% CI, -3.19% to 3.05%). Both outcomes did not meet the prespecified effect size of 10% or greater relative reduction. The mean 12-month cost of care was $1720 per person higher in the IDEAS study cohort.
^{68}Ga-FAPI								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Koerber et al, 2023 [50]	Retrospective	226 patients who underwent staging or restaging (77 pancreatic ductal adenocarcinoma; 29 head and neck	^{68}Ga-FAPI PET/CT	CeCT, CeMRI	Pre- and post-PET information, consensus	NA	NA	^{68}Ga-FAPI PET/CT findings led to a change in TNM staging of 42.0% (86/205) of patients. A change in management occurred in 56.3% (117/208) of cases.

		cancer; 23 lung cancer; 21 glioma; 20 colorectal cancer; 11 sarcoma; 10 esophageal cancer; 3 prostate cancer; 5 thyroid cancer; 4 ovarian cancer; 4 hepatic cancer; 4 cholangiocellular carcinoma; 15 other cancers)						
Kessler et al, 2023 [51]	Prospective	62 patients who underwent staging or restaging (proven or suspected pancreatic ductal adenocarcinoma)	^{68}Ga-FAPI PET/CT	CeCT, FDG PET/CT	Histopathology, clinical and imaging follow-up, pre- and post-PET questionnaires	**Primary tumour and/or metastases (patient-based)** Sens: 100% Spec: 40.0% PPV: 94.6% NPV: 100% Accu: 94.8% **(region-based)** Sens: 98.0% Spec: 92.7% PPV: 91.7% NPV: 98.3% Accu: 95.1%	NA	Therapeutic changes occurred in 8.5% (5/59) of patients after ^{68}Ga-FAPI PET/CT imaging (2—change in systemic treatments, 2—biopsies cancelled and chemotherapy initiated, 1—active surveillance to chemotherapy).
^{18}F-DOPA								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Sung et al, 2024 [52]	Prospective	32 patients who underwent initial diagnosis or restaging (suspected PPGL or suspected recurrence and/or metastases of known PPGL)	^{18}F-FDOPA PET/CT	^{123}I-MIBG SPECT/CT	Histopathology, clinical and imaging follow-up	**Diagnosis or recurrence and metastases (patient-based)** Sens: 95.7% Spec: 88.9% **Recurrence and metastases (region-based)** Sens: 86.2%* Spec: 100% AUC: 0.93*	**Diagnosis or recurrence and metastases (patient-based)** Sens: 91.3% Spec: 88.9% **Recurrence and metastases (region-based)** Sens: 65.5%* Spec: 98.6% AUC: 0.82*	NA
Darcourt et al, 2023 [53]	Prospective	107 patients who received initial	^{18}F-FDOPA PET + MRI	MRI	Pathology, clinical and	**Progression or recurrence**	**Progression or recurrence**	Proposed management was changed after the

		standard of care treatment (suspected recurrent high-grade glioma)			imaging follow-up, consensus from multidisciplinary neuro-oncology board	Sens: 84.0% Spec: 63.0% Accu: 71.0%	Sens: 83.0% Spec: 58.0% Accu: 66.0%	results of 22.5% (31/138) of ^{18}F-FDOPA PET scans (14—new chemotherapy, 10—continue same treatment, 3—performed surgery, 2—reirradiation, 2—stop all curative treatment).
Pancreatic Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Zhang et al, 2024 [54]	Retrospective	88 patients who underwent initial staging (newly diagnosed pancreatic cancer)	FDG PET/CT, FDG PET/MRI	NA	Pathology, biopsy, imaging follow-up	**T staging** ***PET/CT*** Sens: 63.6% Spec: 90.9% Accu: 63.6%‡ ***PET/MRI*** Sens: 85.2% Spec: 89.0% Accu: 85.2%‡ **N staging** ***PET/CT*** Sens: 28.6% Spec: 96.6% Accu: 74.4% ***PET/MRI*** Sens: 57.1% Spec: 93.1% Accu: 81.4% **M staging** ***PET/CT*** Sens: 77.3% Spec: 97.0% Accu: 92.1% ***PET/MRI*** Sens: 90.9% Spec: 98.5% Accu: 96.6%	NA	NA
Sarcoma								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Metser et al, 2023 [55]	Retrospective	171 patients who underwent initial staging or restaging due to local tumour	FDG PET/CT	CeCT, MRI	Clinical follow-up, pre- and post-PET information	NA	NA	FDG PET/CT findings led to a change in treatment intent in 37.4% (64/171) of patients. A change in the offered treatment

		recurrence or limited metastases (soft-tissue or bone sarcoma)						type was seen in 31.6% (54/171) of patients. The presence of metastases on FDG PET/CT was associated with shorter median PFS at initial staging (18.3 months vs. 29.1 months, p=0.04) and shorter median OS at the time of recurrence (60.7 months vs. not reached, p=0.002).
Thoracic Cancer								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Lin et al, 2024 [56]	Retrospective	659 patients who underwent staging prior to curative-intent complete resection with systematic mediastinal lymphadenectomy or sampling (clinical stage I and II NSCLC)	FDG PET/CT + CeCT (n=392)	CeCT (n=267)	Clinical and imaging follow-up	NA	NA	Patients who received FDG PET/CT after CeCT had superior median DFS (12.6 years vs. 6.9 years; HR, 0.67, 95% CI, 0.53 to 0.83, p<0.001) and OS (13.9 years vs. 10.5 years; HR, 0.64, 95% CI, 0.50 to 0.81, p<0.001) than those who received only CeCT. The 5- and 10-year DFS rates for FDG PET/CT were 70.8% and 54.5%, respectively vs. 57.1% and 43.7%, respectively for CeCT. Similarly, the 5- and 10-year OS rates for FDG PET/CT were 78.1% and 62.4%, respectively vs. 65.7% and 50.7%, respectively for CeCT.
Beers et al, 2023 [57]	Retrospective	13796 patients who underwent pretreatment staging (stage III NSCLC)	FDG PET/CT	Not specified	Clinical follow-up	NA	NA	More patients with pretreatment FDG PET/CT scans received curative-intent chemoradiotherapy (23.0% vs. 13.0%, p<0.001) and surgery (23.0% vs. 10.0%, p<0.001) than those without. Both median OS (17.0 months vs. 11.0

								months, p<0.001) and 5-year OS rate (22.0% vs. 14.0%, p<0.001) were longer in patients with FDG PET/CT scans prior to treatment.
Zhang et al, 2023 [58]	Retrospective	181 patients who underwent preoperative assessment of mediastinal lymph node disease after neoadjuvant chemotherapy or chemoimmunotherapy (resectable NSCLC)	FDG PET/CT	NA	Pathology	**Mediastinal lymph node metastases** Sens: 66.7% Spec: 83.9% PPV: 66.7% NPV: 83.5% Accu: 77.9% AUC: 0.751	NA	NA
Various Sites								
Citation	**Study Type**	**Population**	**PET Type**	**Conventional Intervention**	**Reference Standard**	**Diagnostic Performance (PET)**	**Diagnostic Performance (Conventional Intervention)**	**Change in Patient Management**
Chan et al, 2023 [59]	Meta-analysis	11 studies (2227 patients with brain metastases)	FDG PET or PET/CT or PET/MRI	MRI, CeCT	Correlative imaging, clinical follow-up	**Brain metastases** Pooled Sens: 44.0% Pooled Spec: 99.7% Pooled +LR: 143.5 Pooled -LR: 0.561 Pooled DOR: 256.0	NA	NA
Chen et al, 2023 [60]	Prospective	163 patients who underwent differential diagnosis (classical fever of unknown origin accompanied by lymphadenopathy)	FDG PET/CT	Physical examination, complete blood count, aspartate aminotransferase, alanine aminotransferase, LDH, C-reactive protein, creatine, total protein, protein electrophoresis, ESR, serum ferritin, procalcitonin, antinuclear antibodies, rheumatoid	Histopathology, clinical and imaging follow-up	**Diagnosing lymphoma** Sens: 81.0% Spec: 47.6% PPV: 59.3% NPV: 72.7%	NA	NA

				factor, urinalysis, interferon gamma release assay, blood culture, urine culture, chest CT, US				
Luo et al, 2023 [61]	Retrospective	53 patients with suspected spinal leptomeningeal metastases (various primary tumour)	FDG PET/CT	CeMRI	Clinical and imaging follow-up	**Spinal leptomeningeal metastases** Sens: 87.5% Spec: 89.2% Accu: 88.7%	**Spinal leptomeningeal metastases** Sens: 75.0% Spec: 100% Accu: 92.5%	NA
Zheng et al, 2023 [62]	Retrospective	60 patients who underwent screening for underlying malignancy (clinically suspected paraneoplastic dermatoses)	FDG PET/CT	NA	Pathology, international diagnostic standard, follow-up	**Diagnosis** DR: 30.0%	NA	FDG PET/CT findings led to a change in management in 15.0% (9/60) of patients (2—change in therapeutic strategy due to altering of tumour staging or restaging, 7—monitoring to active treatment due to identifying previously undetected tumour or hot spot for biopsy).

*p<0.05

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

Abbreviations: ABVD, doxorubicin, bleomycin, vinblastine, dacarbazine; Accu, accuracy; AUC, area under the curve; AVD, doxorubicin, vinblastine, and dacarbazine; BEACOPPesc, bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisone; BMB, bone marrow biopsy; CEA, carcinoembryonic antigen; CeCT, contrast-enhanced computed tomography; CeMRI, contrast-enhanced magnetic resonance imaging; CI, confidence interval; CT, computed tomography; ^{64}Cu-PSMA, ^{64}Cu labelled prostate-specific membrane antigen; DFS, disease-free survival; DLBCL, diffuse large B-cell lymphoma; DOR, diagnostic odds ratio; ESR, erythrocyte sedimentation rate; EUS, endoscopic ultrasound; ^{18}F, fluorine-18; ^{18}F-DCFBC, N-[N-[(S)-1,3-dicarboxypropyl]carbamoyl]-4-[18F]fluorobenzyl-L-cysteine; ^{18}F-DCFPyL, (2-(3-{1-carboxy-5-[(6-18F-fluoropyridine-3-carbonyl)-amino]-pentyl}-ureido)-pentanedioic acid; FDG, fluorodeoxyglucose; ^{18}F-FDOPA, L-3,4-Dihydroxy-6-[^{18}F]fluorophenylalanine; ^{18}F-FET, O-(2[^{18}F]-fluoroethyl)-L-tyrosine; ^{18}F-NaF, ^{18}F labelled sodium fluoride; ^{18}F-PSMA-1007, ^{18}F labelled prostate-specific membrane antigen 1007; ^{18}F-rhPSMA-7, ^{18}F labelled radiohybrid prostate-specific membrane antigen; ^{68}Ga-DOTA-TATE, Gallium-68-dodecanetetraacetic acid-Tyr3-octreotate; ^{68}Ga-DOTA-TOC, Gallium-68-edotretide; ^{68}Ga-FAPI, ^{68}Ga-labelled fibroblast activation protein inhibitors; ^{68}Ga-PSMA, Gallium-68-labelled prostate-specific membrane antigen; ^{68}Ga-PSMA-11, ^{68}Ga labelled prostate-specific membrane antigen 11; ^{68}Ga-THP-PSMA, ^{68}Ga labelled tetrahydropyran-2,6-dicarboxylate prostate-specific membrane antigen; HL, Hodgkin lymphoma; HR, hazard ratio; ^{123}I-MIBG, meta-[radioiodinated]iodobenzylguanidine; INRT, involved-node radiotherapy; LDH, lactate dehydrogenase; –LR, negative likelihood ratio; +LR, positive likelihood ratio; mpMRI, multiparametric magnetic resonance imaging; MRI, magnetic resonance imaging; NA, not available; NHL, non-Hodgkin lymphoma; NPV, negative predictive value; NSCLC, non-small-cell lung cancer; OR, odds ratio; OS, overall survival; PET, positron emission tomography; PFS, progression-free survival; PPGL, pheochromocytoma and paraganglioma; PPV, positive predictive value; PSA, prostate-specific antigen; PSMA, prostate-specific membrane antigen; RCT, randomized controlled trial; SBRT, stereotactic body radiotherapy; Sens, sensitivity; Spec, specificity; SPECT, single-photon emission CT; ^{99m}Tc, Technetium 99m; ^{99m}Tc-HDP, ^{99m}Tc-hydroxymethylene diphosphonate; ^{99m}Tc-MDP, Technetium 99m-methyl diphosphonate; TNM, tumour, node, metastasis; US, ultrasonography; YI, Youden index