PET Six-Month Monitoring Report 2016-1

Evidence from Primary Studies and Systematic Reviews and Recommendations from Clinical Practice Guidelines January to June 2016

R. Poon and the Program in Evidence-Based Care Disease Site Group Reviewers

Program in Evidence-Based Care (PEBC), Cancer Care Ontario (CCO)

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QUESTION

What is the role of positron emission tomography (PET) in the clinical management of patients with cancer, sarcoidosis, or epilepsy 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, or epilepsy. 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 11th 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 articles published between January and June 2016 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 (prostate cancer)
    - ^{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 (Amyvid) (dementia imaging)
    - ^{18}F-FDOPA
    - ^{68}Ga-PSMA (prostate-specific membrane antigen)
3. Published as a full 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 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

7. Letters and editorials.

RESULTS

Literature Search Results

Primary Studies and Systematic Reviews

One hundred twelve studies published between January and June 2016 met the inclusion criteria. A summary of the evidence from the 112 studies can be found in **Appendix 1: Summary of studies from January to June 2016**.

Breast Cancer

Thirteen studies met the inclusion criteria [1-13]. Several studies evaluated the use of FDG PET/CT in detecting metastases in biopsy-proven breast cancer. Overall, FDG PET/CT demonstrated high specificity (95.8% to 100%) but poor sensitivity (28.6% to 78.0%) in detecting lymph node metastasis [1-4]. One particular study reported that both the sensitivity (51.8% to 55.4% vs. 41.1%; p=0.013 to 0.041) and accuracy (84.5% vs. 79.5%; p=0.0044) were significantly higher for FDG PET/CT than for CT [2]. With regard to distant metastases, a meta-analysis of six studies showed that the pooled sensitivity and specificity of FDG PET or PET/CT were 99% and 95%, respectively, compared with 57% and 88%, respectively, for conventional imaging [5]. Furthermore, FDG PET/CT was found to be significantly more sensitive (97.6% vs. 86.9%; p<0.05) than bone scintigraphy in detecting bone metastases [6]. Similarly, FDG PET/CT was superior or comparable to contrast-enhanced CT (CeCT) and/or bone scintigraphy in detecting recurrence [7]. In patients receiving neoadjuvant chemotherapy, FDG PET/CT was able to predict pathologic complete response with a pooled sensitivity of 86% and a pooled specificity of 72%, both of which were significantly higher than that of magnetic resonance imaging (MRI) (65% and 88%, respectively) [8]. Another prospective study also reported a high sensitivity (88%) but a suboptimal specificity (50%) for prediction of response [9]. The diagnostic performance for differentiating between benign and malignant lesions and detecting additional malignant lesions was similar between FDG PET/CT and MRI [10,11]. The clinical impact of FDG PET/CT was shown in a few studies. FDG PET/CT upstaged the disease in 19% to 33% of patients [1,9,12] and identified unknown synchronous breast cancer in 2% of patients [1]. FDG PET/CT findings led to a change in therapeutic management in 11% of patients on initial staging [1], 14% of patients on response assessment [9], and 21.1% on fourth and subsequent follow-up scans [13].

Epilepsy

Two studies met the inclusion criteria [14,15]. In a prospective study of surgically treated patients, PET was significantly associated with complete seizure control (p<0.05) but the combination of MRI and high-density electric source imaging offered the highest predictive value for favourable postoperative outcome [14]. Based on PET/CT results, 31.6% of patients were selected for surgery and 10.3% of patients were selected for intracranial monitoring [15].

Esophageal Cancer

One study met the inclusion criteria [16]. In a randomized controlled trial of 157 patients with operable squamous cell cancer of middle-to-lower esophagus, FDG PET/CT displayed significantly better sensitivity (86.5% vs. 76.3%; p=0.006) and accuracy (92.2% vs. 87.2%; p=0.024) than CT in the detection of nodal metastasis. Additionally, the PET/CT-guided surgical approach enabled the removal of significantly more involved lymph nodes (2.83 vs. 1.76; p=0.039) and their stations (1.65 vs. 1.08; p=0.042), which led to a longer disease-free survival.

Gastrointestinal Cancer

Thirteen studies met the inclusion criteria [17-29]. Seven of the studies looked at FDG PET/CT in the evaluation of colorectal cancer. FDG PET/CT detected recurrence with sensitivity of 85.7% to 96.6%, specificity of 67.4% to 94.7%, and accuracy of 64.1% to 95.5% [17-19]. Moreover, a meta-analysis reported a pooled sensitivity and specificity of 94% for detecting local recurrence [20]. In preoperative staging of primary colorectal cancer, one meta-analysis concluded that FDG PET or PET/CT had good performance in tumour detection rate, and T and M staging when compared with CT. However, the diagnostic value of FDG PET or PET/CT in N staging was less than ideal [21]. In restaging of patients with rectal cancer after preoperative chemoradiation, FDG PET/CT had the most impact on patient management (11%), followed by CT and MRI, each with 4% [22]. High pretreatment standardized uptake value (SUV) of FDG PET/CT and nonresponders were predictive of survival outcomes in patients with liver metastases [23]. When diagnosing malignant hepatic lesions, FDG PET/CT was found to be comparable to diffusion-weighted MRI and ultrasonography, but more useful than CeCT [24,25]. In patients with suspected metastases on CT, the addition of FDG PET/CT changed the management of 39.8% of patients. FDG PET/CT was significantly more specific in detecting hepatic and extrahepatic metastases, whereas CT was significantly more sensitive in detecting hepatic metastases [26]. Post-operative FDG PET or PET/CT showed good diagnostic ability for detecting recurrence in patients with gastric cancer [27,28] and periampullary carcinoma [29]. In the latter case, FDG PET/CT had a significantly higher accuracy than CeCT (area under the curve [AUC]: 0.94 vs. 0.76; p=0.034).

Genitourinary Cancer

Nine studies met the inclusion criteria [30-38]. In bladder cancer, FDG PET/CT offered no advantage over CT in the detection of lymph node metastasis [30-32]. In renal cell carcinoma, FDG PET/CT was shown to be a valuable tool in the restaging of patients after definitive surgery [33,34]. Specifically, FDG PET/CT findings influenced therapeutic management in 43.3% of patients that included treatment being switched from palliative to curative, new chemotherapy or immunotherapy being initiated, and observational approach being adopted [33]. The sensitivity of FDG PET/CT for the diagnosis of bone metastasis in patients with suspected recurrence of urothelial carcinoma (93.8% vs. 25.0%; p=0.0026) was significantly better than that of CeCT, but there was no significant difference in detecting overall metastatic disease between the two imaging modalities [35]. FDG PET/CT was significantly more sensitive than CT for the detection of metastases in patients with recurrent upper urinary tract cancer (85% vs. 50%; p=0.0001). On account of FDG PET/CT findings, the extent of disease of 32.1% of patients was changed as was the management plan of 19.6% of patients [36]. In contrast, FDG PET/CT was found to be significantly less sensitive than CT (50% vs. 80%; p=0.047) in diagnosing liver recurrence in patients with adrenocortical carcinoma. Diagnosis of recurrence in the peri-renal space, abdomen, thorax, bone, and other sites were comparable between the two imaging modalities. Overall, the management strategy was changed due to FDG PET/CT in 21.1% of patients [37]. In one prospective study, FDG PET/CT provided helpful information in the preoperative staging of testicular tumours (sensitivity: 88.9%; specificity: 87.5% [38].

Gynecologic Cancer

Nine studies met the inclusion criteria [39-47]. For the assessment of patients with endometrial cancer, FDG PET/CT displayed consistently high accuracy of greater than 90% in detecting lymph node and distant metastases [39,40]. In fact, comparison with MRI showed that FDG PET/CT was significantly more accurate on a per-patient basis (91.3% vs. 84.3%; $p<0.001$) but not on a per-lesion basis (94.8% vs. 92.5%; $p>0.05$) [39]. FDG PET/CT was also

very accurate in detecting recurrence (AUC: 0.97) [41] and had a high impact on management in 28.0% of patients with recurrent disease [42]. Among patients referred for adjuvant radiation, PET/CT findings had a high impact on management in 20.8% of patients [42]. In patients with newly diagnosed cervical cancer, FDG PET/CT compared favourably well to pathological staging (accuracy: 94.7%) [43]. A positive impact on clinical management was seen in 18.6% of patients [44]. In the presurgical characterization of ovarian masses, FDG PET/CT demonstrated high sensitivity (91.3%) but subpar specificity (67%). However, FDG PET/CT was instrumental in identifying limiting factors for optimal cytoreductive surgery in 28.6% of patients [45]. For post-treatment detection of residual or recurrent ovarian tumours, FDG PET/CT significantly outperformed CeCT in both study-based and site-based analyses [46]. One prospective study reported that following FDG PET/CT, a change in planned management occurred in 36.1% of studies performed on patients with vulvar and vagina cancer [47].

Head and Neck Cancer

Nineteen studies met the inclusion criteria [48-66]. Four studies assessed the role of FDG PET/CT in thyroid cancer. FDG PET/CT showed a high sensitivity and a high negative predictive value (NPV) for identifying malignancy in thyroid nodules with indeterminate cytology [48,49]. The sensitivity (94% vs. 50%, p=0.02 and 56%, p=0.01, respectively) and NPV (98% vs. 80%, p=0.01 and 82%, p=0.03, respectively) of FDG PET/CT were significantly higher than those of both multiparametric neck ultrasonography and ^{99}mTc-MIBI-scan [49]. In the detection of differentiated thyroid cancer recurrence, one prospective study found FDG PET/CT to be significantly more accurate than ^{131}I whole-body scintigraphy (^{131}I WBS) (91.4% vs. 61.7%, p<0.001) [50] whereas a meta-analysis that included only patients with a negative ^{131}I WBS reported a pooled sensitivity of 93% and a pooled specificity of 81% for FDG PET/CT [51]. Results from FDG PET/CT altered the staging and therapeutic management of 25.9% and 38.3% of patients, respectively [50]. In the follow-up of human papillomavirus-related oropharyngeal squamous cell carcinoma after primary treatment, FDG PET/CT detected recurrent or residual disease with high sensitivity (92.0% to 97.0%) and good specificity (85.1% to 92.5%) [52,53]. Subsequently, there was a change in management plan from no treatment to new treatment after 12.6% of scans [52]. FDG PET/CT was found to be very accurate in identifying cervical nodal metastasis in patients with laryngeal squamous cell carcinoma (90.8%) [54], but inadequate in patients with oral squamous cell carcinoma (66%) [55]. Pooled estimates from a meta-analysis of 23 studies confirmed high sensitivity (93%) and specificity (87%) for FDG PET or PET/CT in the diagnosis of residual or recurrent nasopharyngeal carcinoma [56]. In a randomized controlled trial, patients with stage N2 or N3 head and neck cancer who had received chemoradiotherapy for primary treatment were assigned to undergo either a planned neck dissection or FDG PET/CT-guided surveillance. Survival was similar between the two groups but surveillance resulted in substantially fewer neck operations and significant cost savings [57]. In the staging of head and neck cancer, FDG PET/CT was shown to be significantly more sensitive and more accurate than CT/MRI for detecting cervical lymph node metastasis [58]. Results from a retrospective study reported a much lower specificity (44.8%) for FDG PET/CT in detecting regional cervical metastasis [59]. Nevertheless, FDG PET/CT changed the staging of 15.5% of patients and modified management in 26.2% of patients [60]. Regarding diagnosis of extracapsular spread, the authors from a systematic review and meta-analysis concluded that evidence was lacking for the use of FDG PET/CT [61]. In the assessment of patients previously treated with radical radiotherapy with or without chemotherapy for advanced head and neck squamous cell carcinoma, FDG PET/CT performed at six weeks (94%) and three months (98.3%) after therapy was associated with a high NPV for excluding residual disease (62,63). In patients who underwent surgical resection

as primary treatment, FDG PET/CT within six months after completion of treatment also had a high NPV (94.4%) and influenced subsequent management in 20.4% of patients [64]. Pertaining to suspected recurrent head and neck squamous cell carcinoma, FDG PET/CT with or without intravenous contrast medium displayed significantly higher accuracy for diagnosing overall recurrence relative to CeCT [65]. The use of FDG PET/CT in head and neck squamous cell carcinoma of unknown primary was investigated in one retrospective. FDG PET/CT alone appeared to be insufficient in ruling out primary malignant site [66].

Hematologic Cancer

Seven studies met the inclusion criteria [67-73]. In advanced Hodgkin lymphoma (HL), interim FDG PET/CT performed after two cycles of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) showed that patients with a positive scan, as opposed to those with a negative scan, have worst progression-free survival (PFS) at two years (64% vs. 82%) [67] and significantly inferior event-free survival (50% vs. 82%; p=0.013) despite escalation of therapy to bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisolone (BEACOPP) [68]. Escalated BEACOPP was significantly more toxic than ABVD (grade 4/5 toxicities: 85.7% vs. 36.7%; p<0.001) [67]. In addition, one randomized controlled trial demonstrated that the omission of bleomycin from the ABVD regimen after negative findings on interim FDG PET/CT reduced the incidence of grade 3/4 respiratory events but did not significantly lower efficacy in terms of three-year PFS and overall survival [69]. With regard to staging, FDG PET/CT findings upstaged 13.6% and downstaged 6.3% of advanced HL patients [70]. In diffuse large B-cell lymphoma (DLBCL), patients with a negative interim FDG PET/CT scan after two to four cycles of rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP) or CHOP have significantly better survival than PET-positive patients. Patients with a negative end-of-treatment FDG PET/CT also had significantly higher survival rates [71]. For the follow-up of patients with non-Hodgkin lymphoma (NHL) who had completed primary treatment, the fourth and subsequent post-treatment FDG PET/CT scans altered the management of 36.4% and 9.2% of patients with and without previous clinical suspicion of recurrence, respectively [72]. In follicular lymphoma, FDG PET/CT was able to rule out bone marrow involvement with high certainty (NPV: 100%) but at the expense of a high false positive rate (positive predictive value [PPV]: 48.5%) [73].

Melanoma

Three studies met the inclusion criteria [74-76]. In patients with stage III/IV melanoma, FDG PET/CT was able to detect inguinal lymph node (97%) and distant metastases (90.6%) with high sensitivity but one-third of patients with iliac lymph node involvement (sensitivity: 67%) would be missed by FDG PET/CT [74,75]. Taken together, additional information provided by FDG PET/CT changed the initial CT-based treatment decisions of 54.7% of patients [74]. Results from the Ontario PET registry revealed significant upstaging of patients (17.6%) with advanced or high-risk disease following FDG PET/CT. This led to more frequent surgical interventions to resect distant metastases (p=0.034) [76].

Neuro-oncology

One study met the inclusion criteria [77]. A meta-analysis of 23 studies revealed no statistical difference in diagnostic accuracy (AUC: 0.866 vs. 0.933, respectively; p=0.9886) between FDG PET or PET/CT and magnetic resonance spectroscopy (MRS) in detecting tumour recurrence of gliomas, although the pooled sensitivity of FDG PET or PET/CT (70%) was lower than that of MRS (87%).

Non-FDG Tracers

Sixteen studies met the inclusion criteria [78-93]. In the diagnosis of patients with prostate cancer, one prospective found that ^{11}C-choline PET/CT (100%) was more sensitive than MRI (46%) [78] while a meta-analysis of 77 studies reported a higher pooled sensitivity for ^{11}C-choline PET/CT (78.3%) than for transrectal real-time elastosonography (TRTE) (69.7%). Nonetheless, ^{11}C-choline PET/CT and ^{18}F-choline PET/CT were both less sensitive and less specific than shear-wave elastography. ^{18}F-choline (90.1%) did have a higher pooled specificity than TRTE (75.7%) [79]. In the evaluation of hepatocellular carcinoma, ^{11}C-choline PET/CT was shown to be significantly more accurate than that of CT and/or MRI (79% vs. 64%, p=0.003). ^{11}C-choline PET/CT provided information that modified the therapeutic strategy of 24.4% of patients [80]. Another prospective study suggested that combining FDG and ^{11}C-choline PET/CT increased the sensitivity of detecting hepatocellular carcinoma [81]. The utility of ^{68}Ga-DOTA-TATE and –TOC PET/CT in neuroendocrine tumours (NETs) were evaluated in several studies. ^{68}Ga-DOTA-TATE PET/CT was found to be superior to CeCT in the detection of extra-hepatic metastases [82] and prompted treatment changes in 40.9% of patients due to new and unexpected findings [83]. In patients with pulmonary or gastroenteropancreatic NETs, the addition of ^{68}Ga-DOTA-TATE PET/CT changed treatment plans in 32.8% to 35.9% of patients [84,85]. Overall diagnostic accuracy for ^{68}Ga-DOTA-TATE PET/CT was significantly higher than for ^{111}In-pentetreotide single photon emission computed tomography (SPECT) or SPECT/CT (94% vs. 82%, p=0.02) [85]. Furthermore, a meta-analysis reported high summary estimates of sensitivity (90.9%) and specificity (90.6%) for the diagnosis or staging of these tumours [86]. As for ^{68}Ga-DOTA-TOC PET/CT, it was shown to be significantly more sensitive than ^{111}In-pentetreotide SPECT in detecting metastatic NETs [87]. PET/CT imaging with ^{68}Ga-PSMA was investigated in one prospective study. In patients with biochemical recurrence of prostate cancer being considered for salvage radiation therapy, results from ^{68}Ga-PSMA PET/CT led to a major management change in 28.6% of patients [88]. The diagnostic performance of ^{18}F-FLT and FDG PET or PET/CT was compared in various malignancies. ^{18}F-FLT PET or PET/CT showed significantly better specificity than FDG PET or PET/CT in the diagnosis of pulmonary [89], pancreatobillary [90], and adrenal tumours [91]. However, FDG PET or PET/CT was significantly more sensitive in pulmonary lesion diagnosis [89]. In the treatment response assessment of patients with DLBCL, early interim FLT PET/CT (91%) displayed a significantly higher PPV than standardized FDG PET/CT-based interpretation using International Harmonization Project (IHP) (42%, p<0.001), European Organization for Research and Treatment of Cancer (EORTC) (42%, p<0.001), PET Response Criteria in Solid Tumours (PERCIST) (46%, p<0.008), and Deauville criteria (44%, p<0.001) [92]. Compared with CeCT, FLT PET/CT proved to be superior for identifying regional metastatic nodes in the preoperative staging of gastric cancer (AUC: 0.958 vs. 0.708, p=0.0033) [93].

Non-Small Cell Lung Cancer and Other Lung Cancer

Five studies met the inclusion criteria [94-98]. The authors from a meta-analysis of 28 studies concluded that FDG PET/CT had a high specificity (node-based: 92%; patient-based: 87%) but low sensitivity (node-based: 62%; patient-based: 67%) for detecting lymph node metastasis in patients with non-small cell lung cancer (NSCLC) [94]. Conversely, FDG PET/CT was highly sensitive (pooled estimate: 98.7%) but not very specific (pooled estimate: 58.2%) in the diagnosis of lung cancer in patients with pulmonary lesions [95]. For postoperative surveillance of lung adenocarcinoma manifesting as ground-glass opacity, CT showed significantly higher accuracy than FDG PET/CT in detecting recurrence (98.2% vs. 90.1%; p=0.0188) [96]. Furthermore, post-therapy assessment using the Hopkins criteria generated good accuracy (86.7%) and resulted in starting a new treatment plan in 70.8% of patients with

residual small cell lung cancer (SCLC) or NSCLC [97]. The SUV_{max} of lung adenocarcinoma was shown to be a potential predictor of lymphovascular invasion [98].

Pancreatic Cancer

Three studies met the inclusion criteria [99-101]. In the setting of operable pancreatic, ampullary, or distal bile duct cancers, FDG PET/CT spared 10.9% to 16.1% of patients from surgery as a result of identifying unexpected metastases [99,100]. However, 7.5% of patients with metastases were missed by FDG PET/CT [99]. In the follow-up of curatively resected pancreatic cancer patients, FDG PET/CT and CT showed comparable diagnostic accuracy in detecting recurrence [101].

Pediatric Cancer

One study met the inclusion criteria [102]. In pediatric patients diagnosed with high-grade osteosarcoma, FDG PET/CT demonstrated superior sensitivity in a lesion-based analysis (93.2% vs. 74.6%; p=0.013) over bone scintigraphy for detecting osseous metastases. Examination-based analysis did not yield significant differences.

Sarcoma

Two studies met the inclusion criteria [103,104]. FDG PET/CT with SUV_{max} of 2.2 achieved high sensitivity (94.7%), specificity (94.1%), and accuracy (94.4%) for differentiating chondroma from chondrosarcoma in patients with cartilaginous bone lesions in the extremities [103]. In patients with uterine carcinosarcoma, FDG PET/CT was comparable to MRI in detecting primary lesions, but was more sensitive (77.8% vs. 51.9%; p=0.016) and less specific (90.2% vs. 100%; p=0.025) than MRI for predicting lymph node metastases [104].

Unknown Primary Cancer

Two studies met the inclusion criteria [105,106]. FDG PET/CT was able to identify the primary site in 50% to 73% of patients with unknown primary tumours whose conventional imaging test results were negative [105,106].

CLINICAL EXPERT REVIEW

Breast Cancer

No recommendations currently exist for the utilization of PET/CT in breast cancer.

Reviewer's Comments (Dr. Muriel Brackstone)

This year marks the first where there have been a number of publications supporting some indications for PET scans in the management of breast cancer. Thirteen studies were published between January and June, 2016. These can be broken down into the indications for which they were studied (specific to breast cancer and contrasted to conventional imaging):

Diagnostic of malignancy in breast

With regard to diagnosis, PET imaging was found to be slightly inferior to standard imaging for suspicious breast lesions. Compared with current methods, mammography, ultrasound, and biopsy, plus or minus MRI should remain the standard recommended breast imaging. PET imaging does not appear to add significantly to in-breast diagnoses, and although it does seem to be slightly superior at identifying contralateral or multicentric disease, there is no evidence that this would lead to a superior clinical outcome. For this reason, MRI is not routinely recommended for diagnostic breast imaging since a higher rate of

multicentricity and/or contralateral disease by MRI has upstaged the amount of treatment required (most notably increasing the mastectomy rate), but has not resulted in an increased survival. High sensitivity by MRI has been problematic and not clinically helpful, and I suspect that increased PET sensitivity at identifying synchronous disease would result in more surgery and morbidity without improved survival.

Predictive of regional axillary nodal disease

PET and PET/CT imaging appears to have improved sensitivity in the diagnosis of regional axillary nodal disease when compared with CT; however, it should be noted that axillary disease is not routinely diagnosed by CT. When compared with the gold standard, sentinel lymph node procedure performed in the operating room, PET imaging had a lower sensitivity (78%), which is too low to be clinically useful. Therefore, sentinel lymph node biopsy should remain the gold standard method for diagnosing regional axillary lymph node disease.

Diagnostic for distant metastases

PET/CT appears to outperform conventional imaging (CT and bone scan) for the diagnosis of 'suspicious lesions'. Although it is likely that PET/CT imaging is superior to conventional imaging for the detection of distant metastases, it remains unclear from these studies whether this would remain the case in prospectively conducted trials with blinded reviewers and in all patients, rather than those with pre-identified suspicious lesions. This is the area where I recommend the committee consider revaluating whether PET/CT could be recommended for the diagnosis of distant metastases over bone scan and CT chest/abdomen/pelvis.

Predictive of response to neoadjuvant chemotherapy

PET/CT scanning for residual disease as a marker of complete pathological response after neoadjuvant chemotherapy showed a sensitivity and specificity of 72% to 86% and 50% to 72%, respectively. Although there may be some research utility in PET/CT imaging to predict pathological complete response in specific subsets of patients, this result is not clinically useful. With these low sensitivity and specificity rates, complete excision remains the gold standard and should not be supplanted by any imaging modalities. Even if PET/CT outperforms MRI for predicting complete pathological response, this remains a research tool, as there is no clinical surrogate for complete excision of the prior tumour bed/area of residual disease.

Predictive of disease recurrence/survival

A number of studies published over this period have reported a superior sensitivity and specificity for PET/CT in detecting disease recurrence when compared with CT and bone scan. There are no good data to date to suggest whether using PET/CT, under any circumstance, has resulted in an improved survival. The authors of one of these studies identified that patients without recurrence have improved survival over patients with recurrence, that statement being obvious but not related to the use of PET/CT for imaging. It is likely that PET/CT detects recurrence sooner than would be evident by conventional imaging. Since patients with distant metastases from breast cancer are considered, with the rarest of exceptions, incurable, the earlier detection of distant metastatic disease is not likely to be of clinical benefit to patients other than increase lead-time bias. For this reason, routine imaging to screen for distant disease is not performed for breast cancer. Should treatments for metastatic disease become mainstream, early detection of distant disease would be very useful and PET/CT would have a role here.

Epilepsy

Current Registry Indication

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

Current Recommendations for the Utilization of PET in Epilepsy

- ^{18}F-FDG PET is recommended for the presurgical evaluation of adult and pediatric patients with medically intractable focal or partial epilepsy in the setting of a comprehensive epilepsy surgery program within a Regional Epilepsy Surgery Centre of Excellence.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of ^{18}F-FDG PET in the detection of cortical malformations in patients with intractable infantile spasms when MRI or CT fails to show structural abnormalities.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of ^{18}F-FDG PET/MRI coregistration in the presurgical evaluation of patients with medically intractable epilepsy.

Reviewer's Comments (Dr. Jorge Burneo)

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

Esophageal Cancer

Current Insured Indication

- For baseline staging assessment of those patients diagnosed with esophageal cancer who are being considered for curative therapy and/or repeat PET/CT scan on completion of preoperative/neoadjuvant therapy, prior to surgery.

Current Recommendations for the Utilization of PET/CT in Esophageal Cancer

- For the staging workup of patients with esophageal cancer who are potential candidates for curative therapy, PET is recommended to improve the accuracy of M staging.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET (post-therapy or neoadjuvant therapy) for the purpose of predicting response to neoadjuvant therapy.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET for the evaluation of suspected recurrence.

Reviewer's Comments (Dr. Rebecca Wong)

The current recommendations for the utilization of PET/CT in esophageal cancer remain valid and no changes are required. Liu et al. [16] described the results in a way that focused on the impact of PET/CT on surgical approach and yield of nodal dissection. This study supports the recommendation for the use of PET/CT in preoperative staging.

Gastrointestinal Cancer

Current Insured Indication (Colorectal Cancer)

- Where recurrent disease is suspected on the basis of elevated and/or rising carcinoembryonic antigen level(s) during follow-up after surgical resection but standard imaging tests are negative or equivocal; or prior to surgery for liver metastases from colorectal cancer when the procedure is high risk (e.g., multiple-staged liver resection or vascular reconstruction); or where the patient is at high risk for surgery (e.g., American Society of Anesthesiology score ≥4).

Current Recommendations for the Utilization of PET/CT in Colorectal Cancer

- The routine use of PET is not recommended for the diagnosis or staging of clinical stage I to III colorectal cancers.
- PET is recommended for determining management and prognosis if conventional imaging is equivocal for the presence of metastatic disease.
- The routine use of PET is not recommended for the measurement of treatment response in locally advanced rectal cancer before and after preoperative chemotherapy.
- PET is not recommended for routine surveillance in patients with colorectal cancer treated with curative surgery who are at high risk for recurrence.
- PET is recommended to determine the site of recurrence in the setting of rising carcinoembryonic antigen levels, when a conventional workup fails to unequivocally identify metastatic disease.
- PET is recommended in the preoperative assessment of colorectal cancer liver metastasis prior to surgical resection.

Reviewer's Comments (Dr. Anand Swaminath)

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

Genitourinary Cancer

Current Recommendations for the Utilization of PET/CT in Testicular Cancer

- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET in the routine staging of patients with testicular cancer.
- PET is recommended for the assessment of treatment response in patients with seminoma and residual masses after chemotherapy.
- PET is not recommended for the assessment of treatment response in patients with nonseminoma.
- Due to insufficient evidence, a recommendation cannot be made for or against the routine use of PET for evaluation of recurrence.

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. In the Kitajima et al. [6] study, comparison with CT was not appropriate for bone metastases, PET/CT should be compared with ^{99m}Tc bone scan instead. Overall, the balance of evidence still does not support PET/CT for staging or restaging of bladder cancer. Some preliminary data for kidney seem promising and this may be a specific site worth watching out for more data. Other sites have little data to evaluate.

Gynecologic Cancer

Current Recommendations for the Utilization of PET/CT in Cervical Cancer

- PET is not recommended for diagnosis of cervical cancer.
- PET is not recommended for staging early-stage cervical cancer.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET for staging advanced-stage cervical cancer. However, ongoing studies will clarify the role of PET in advanced disease.
- PET is not recommended (following or early during therapy) for the purpose of predicting response to chemoradiation therapy.

- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET for evaluation of suspected recurrence.
- PET is recommended for women with recurrence who are candidates for pelvic exenteration or chemoradiation with curative intent.

Current Recommendations for the Utilization of PET/CT in Ovarian Cancer

- PET is not recommended in the diagnosis of ovarian cancer.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET in the evaluation of asymptomatic ovarian mass.
- PET is not recommended for staging of ovarian cancer.
- PET is not recommended for detecting recurrence or restaging patients not being considered for surgery.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET for patients being considered for secondary cytoreduction.

Reviewer's Comments (Dr. Anthony Fyles)

There should be recommendations added for the utilization of PET/CT in endometrial cancer.

Head and Neck Cancer

Current Insured Indications

- Head and neck cancer:
    - For the evaluation of metastatic squamous cell carcinoma in neck nodes when the primary disease site is unknown after standard radiological and clinical investigation; or for the staging of nasopharyngeal cancer.
- Thyroid cancer:
    - Where recurrent or persistent disease is suspected on the basis of an elevated and/or rising thyroglobulin level, but standard imaging studies, including I-131 scan and/or neck ultrasound, are negative or equivocal.

Current Recommendations for the Utilization of PET/CT in Head and Neck Cancer

- PET is recommended in the M and bilateral nodal staging of all patients with head and neck squamous cell carcinoma where conventional imaging is equivocal, or where treatment may be significantly modified.
- PET is recommended in all patients after conventional imaging and in addition to, or prior to, diagnostic panendoscopy where the primary site is unknown.
- PET is recommended for staging and assessment of recurrence of patients with nasopharyngeal carcinoma if conventional imaging is equivocal.
- PET is recommended for restaging patients who are being considered for major salvage treatment, including neck dissection.

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 Registry Indication (Lymphoma Staging)

- PET for the staging of HL or NHL being treated with curative intent:

    - For the staging of limited disease as per conventional imaging, or
    - When imaging results are equivocal for differentiating between limited- and advanced-stage disease.
- PET for apparent limited-stage nodal follicular lymphoma or other indolent NHL where curative radiation therapy is being considered for treatment.

Current Insured Indication (Lymphoma)

- For the evaluation of residual mass(es) following chemotherapy in a patient with HL or NHL when further potentially curative therapy (such as radiation or stem cell transplantation) is being considered; or for the assessment of response in early-stage HL following two or three cycles of chemotherapy when chemotherapy is being considered as the definitive single modality therapy.

Current Recommendations for the Utilization of PET/CT in Hematologic Cancer

- When functional imaging is considered to be important in situations where anatomical imaging is equivocal and/or in potentially curable cases, a FDG PET/CT scan is recommended.
- When functional imaging is considered to be important in situations where anatomical imaging is equivocal and treatment choices may be affected in limited-stage indolent lymphomas, a FDG PET/CT scan is recommended.
- An FDG PET/CT scan is recommended for the assessment of early response in early stage (I or II) HL following two or three cycles of chemotherapy when chemotherapy is being considered as the definitive single modality therapy, to inform completion of therapy or to determine whether more therapy is warranted.
- In potentially curable cases, when functional imaging is considered to be important and conventional imaging is equivocal, a FDG PET/CT scan is recommended to investigate recurrence of HL or NHL.
- An FDG PET/CT scan is recommended for the evaluation of residual mass(es) following chemotherapy in a patient with HL or NHL when further potentially curative therapy (such as radiation or stem cell transplantation) is being considered and when biopsy cannot be safely or readily performed.
- An FDG PET/CT scan is not recommended for the routine monitoring and surveillance of lymphoma.

Reviewer's Comments (Dr. Marc Freeman)

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

Melanoma

Current Registry Indication

- For the staging of melanoma patients with localized "high-risk" tumours with potentially resectable disease; or for the evaluation of patients with melanoma and isolated metastasis at the time of recurrence when metastasectomy is being contemplated.

Current Recommendations for the Utilization of PET/CT in Melanoma

- PET is recommended for staging of high-risk patients with potentially resectable disease.
- PET is not recommended for the diagnosis of sentinel lymph node micrometastatic disease or for staging of I, IIa, or IIb melanoma.
- The routine use of PET or PET/CT is not recommended for the diagnosis of brain metastases.
- The routine use of PET is not recommended for the detection of primary uveal malignant melanoma.
- A recommendation cannot be made for or against the use of PET for the assessment of treatment response in malignant melanoma due to insufficient evidence.
- A recommendation cannot be made for or against the use of PET for routine surveillance due to insufficient evidence.
- PET is recommended for isolated metastases at time of recurrence or when contemplating metastectomy.

Reviewer's Comments (Dr. Tara Baetz)

The current recommendations for the utilization of PET/CT in melanoma remain valid and no changes are required. Both the Schule et al. [74] and Singnurkar et al. [76] studies support the use of PET/CT in the staging of high-risk patients and prior to planned mestastectomy. The van Wissen et al. [75] study is interesting but would not change the current practice.

Neuro-oncology

Current Recommendations for the use of PET/CT in Neuro-oncology

- PET is not recommended for the determination of diagnosis or grading in gliomas.
- A recommendation cannot be made for or against the use of PET for the assessment of treatment response in gliomas due to insufficient evidence.
- A recommendation cannot be made for or against the use of PET or PET/CT in the assessment of patients with recurrent gliomas due to insufficient evidence.

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

No recommendations currently exist for the utilization of PET/CT with non-FDG tracers.

Reviewer's Comments (Dr. Amit Singnurkar)

There is currently not enough evidence to support making appropriate recommendations for the use of PET/CT with non-FDG tracers.

Non-Small Cell Lung Cancer and Other Lung Cancer

Current Insured Indications

- Solitary pulmonary nodule:
    - A 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.

- NSCLC:
    - Where curative surgical resection is being considered based on negative standard imaging tests; or clinical stage III NSCLC where potentially curative combined modality therapy with radiotherapy and chemotherapy is being considered.
- Limited-disease SCLC:
    - Where combined modality therapy with chemotherapy and radiotherapy is being considered.

Current Recommendations for the Utilization of PET/CT in Small Cell Lung Cancer

- PET is recommended for staging in patients with SCLC who are potential candidates for the addition of thoracic radiotherapy to chemotherapy.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET for the assessment of treatment response in SCLC.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET for evaluation of recurrence or restaging.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET when metastasectomy or stereotactic body radiation therapy is being contemplated for solitary metastases.

Current Recommendations for the Utilization of PET/CT in Radiation Treatment Planning for Lung Cancer

- Combination PET/CT imaging data may be used as part of research protocols in radiation treatment planning. Current evidence does not support the routine use of PET/CT imaging data in radiation treatment planning at this time outside of a research setting.

Reviewer's Comments (Dr. Donna Maziak)

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

Pancreatic Cancer

Current Registry Indication

- For staging if the patient is a candidate for potentially curative surgical resection (pancreatectomy) as determined by conventional staging.

Current Recommendations for the Utilization of PET/CT in Pancreatic Cancer

- PET is not recommended for primary diagnosis of pancreatic cancer.
- PET is recommended for staging if a patient is a candidate for potentially curative surgical resection as determined by conventional staging.
- Due to insufficient evidence, a recommendation cannot be made for or against the use of PET to guide clinical management based on assessment of treatment response.
- Due to insufficient evidence and lack of effective therapeutic options, PET is not recommended for clinical management of suspected recurrence, nor for restaging at the time of recurrence.

- A recommendation cannot be made for or against the use of PET for staging if a solitary metastasis is identified at recurrence because there are no trials that identify the utility of PET scanning in this setting.

Reviewer's Comments

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

Pediatric Cancer

Current Registry Indications (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, 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

Reviewer's Comments

A review was not completed by a clinical expert in pediatric oncology.

Sarcoma

No recommendations currently exist for the utilization of PET/CT in sarcoma.

Reviewer's Comments (Dr. Gina Diprimio)

There is now additional evidence to support the use of PET/CT in bone or soft tissue sarcoma. The prospective study by Jesus-Garcia et al. [103] showed that PET/CT is of value in differentiating chondroma from chondrosarcoma.

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Contact Information

For information about the PEBC and the most current version of all reports,
please visit the CCO website at http://www.cancercare.on.ca/ or contact the PEBC office at:
Phone: 905-527-4322 ext. 42822 Fax: 905-526-6775 E-mail: ccopgi@mcmaster.ca

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Appendix 1: Summary of studies from January to June 2016.

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
Breast Cancer								
Krammer et al, 2015 [1]	Prospective	101 patients (biopsy-proven first diagnosis of invasive breast cancer)	FDG PET/CT	Abdominal US, chest X-ray, bone scan	Histopathology, clinical and imaging follow-up, consensus from an expert group	**Axillary lymph node involvement** Sens: 78% Spec: 100% PPV: 100% NPV: 57% **Distant metastasis** NPV: 100%	NA	PET/CT led to an upgrade of the N and/or M stage in 19% (19/101) of patients and identified unknown synchronous breast cancer in 2% (2/101) of patients. Overall, PET/CT findings caused a significant change of therapeutic management in 11% (11/101) of patients.
Kitajima et al, 2016 [2]	Retrospective	196 patients (biopsy-proven breast cancer)	FDG PET/CT	CT	Histopathology, clinical follow-up	**Axillary lymph node metastasis** ***Visual analysis*** Sens: 55.4%* Spec: 95.8% PPV: 83.8% NPV: 84.7% Accuracy: 84.5%* ***SUV_{max} of 1.50*** Sens: 51.8%* Spec: 97.2% PPV: 87.9% NPV: 83.8% Accuracy: 84.5%*	**Axillary lymph node metastasis** Sens: 41.1%* Spec: 94.4% PPV: 74.2% NPV: 80.5% Accuracy: 79.5%*	NA
Fujii et al, 2016 [3]	Retrospective	179 patients (primary breast cancer)	FDG PET/CT	NA	Pathology	**Lymph node metastasis** Sens: 47.9% Spec: 98.5% Accuracy: 84.9%	NA	NA
Fujii et al, 2016 [4]	Retrospective	156 patients (primary breast cancer)	FDG PET/CT	SLN biopsy	Pathology	**SLN metastasis** Sens: 28.6% Spec: 99.2% Accuracy: 83.3%	NA	NA
Sun et al, 2015 [5]	Meta-analysis	6 studies (609 patients with breast cancer)	FDG PET or PET/CT	NA	Histopathology, clinical and imaging follow-up	**Distant metastasis** Pooled Sens: 99% Pooled Spec: 95% Pooled +LR: 21.1 Pooled –LR: 0.02 Pooled DOR: 1407 AUC: 0.99	**Distant metastasis** Pooled Sens: 57% Pooled Spec: 88% Pooled +LR: 4.8 Pooled –LR: 0.49 Pooled DOR: 8.8 AUC: 0.83	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
Caglar et al, 2016 [6]	Retrospective	150 patients (breast cancer suspected of having bone metastases)	FDG PET/CT	Bone scintigraphy, SPECT/CT	Histopathology, imaging and clinical follow-up	**Bone metastasis** Sens: 97.6%* Spec: 100% PPV: 100% NPV: 96.9% Accuracy: 98%	**Bone metastasis** ***Bone scintigraphy*** Sens: 86.9%* Spec: 100% PPV: 100% NPV: 85% Accuracy: 92% ***SPECT/CT*** Sens: 89.5% Spec: 96.7% PPV: 97.4% NPV: 86.7% Accuracy: 92%	NA
Hildebrandt et al, 2016 [7]	Prospective	100 patients (suspected breast cancer recurrence or verified local recurrence and potential distant disease)	FDG PET/CT	CeCT, bone scintigraphy	Biopsy, clinical follow-up	**Distant recurrence** Sens: 100% Spec: 91% **Bone recurrence** Sens: 100% Spec: 98% **Local recurrence** Sens: 74% Spec: 100%	**Distant recurrence** ***CeCT*** Sens: 77% Spec: 83% ***CeCT+bone scintigraphy*** Sens: 91% Spec: 72% **Bone recurrence** ***CeCT*** Sens: 61% Spec: 99% ***Bone scintigraphy*** Sens: 78% Spec: 87% ***CeCT+bone scintigraphy*** Sens: 83% Spec: 85% **Local recurrence** ***CeCT*** Sens: 37% Spec: 90%	NA
Liu et al, 2016 [8]	Meta-analysis	6 studies (382 patients with breast cancer)	FDG PET/CT	MRI	Pathology	**pCR assessment to NAC** Pooled Sens: 86%* Pooled Spec: 72%* Pooled +LR: 3.1 Pooled -LR: 0.19 Pooled DOR: 16 AUC: 0.88	**pCR assessment to NAC** Pooled Sens: 65%* Pooled Spec: 88%* Pooled +LR: 5.6 Pooled -LR: 0.40 Pooled DOR: 14 AUC: 0.84	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET) Q test: 0.82*	Diagnostic Accuracy (Conventional) Q test: 0.77*	Change in Patient Management
Hulikal et al, 2015 [9]	Prospective	38 patients receiving NAC (biopsy-proven, unilateral, newly diagnosed, locally advanced breast cancer)	FDG PET/CT	^{99m}Tc MDP bone scan, CeCT of the chest and abdomen	Histopathology	**Prediction of response** Sens: 88% Spec: 50% PPV: 88% NPV: 50% Accuracy: 82%	NA	In initial staging, PET/CT upstaged the disease in 33% of patients. Response assessment with PET/CT resulted in change of treatment regimen in 14% of patients.
Magometschnigg et al, 2015 [10]	Prospective	172 patients (suspicious breast lesions found on mammography or breast ultrasonography)	FDG PET/CT	Ce-MRI	Histopathology	**Differentiating between benign and malignant lesions** Sens: 97% Spec: 80% PPV: 94.1% NPV: 88.9% Accuracy: 93% AUC: 0.89	**Differentiating between benign and malignant lesions** Sens: 100% Spec: 70% PPV: 91.7% NPV: 100% Accuracy: 93% AUC: 0.85	NA
Jalaguier-Coudray et al, 2016 [11]	Retrospective	80 patients who needed NAC (biopsy-confirmed breast cancer)	FDG PET/CT	MRI	Histology, imaging follow-up	**Additional lesions** Sens: 78.3% Spec: 87.5% Accuracy: 81.9%	NA	NA
Hogan et al, 2015 [12]	Retrospective	235 patients (146 stage I-III ILC; 89 stage III IDC)	FDG PET/CT	Physical examination, mammography, breast US, breast MRI, surgical findings	Pathology	NA	NA	PET/CT revealed unsuspected distant metastases in 8% (12/146) of ILC patients. In stage III IDC patients, 22% (20/89) were upstaged to IV by PET/CT.
Taghipour et al, 2016 [13]	Retrospective	92 patients; 426 fourth and subsequent follow-up PET/CT scans after completion of primary treatment (biopsy-proven breast cancers)	FDG PET/CT	NA	Pathology, clinical follow-up	**Recurrence or metastasis** Sens: 97.7% Spec: 98.1% PPV: 98.8% NPV: 96.3% Accuracy: 97.9%	NA	21.1% (90/426) of PET/CT scans led to a change in patient management (24—initiation of new treatment, 64—change in previous treatment regimen, 2—stopped treatment). Overall survival was significantly better in patients with all negative follow-up scans in comparison to those with at least one positive follow-up scan (HR=4.65; 95% CI: 1.3-16.8; p<0.001).

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
Epilepsy								
Lascano et al, 2016 [14]	Prospective	58 patients (underwent surgery for medically intractable epilepsy)	FDG PET	MRI, SPECT, HD-ESI	Clinical follow-up (Engel Class I)	**Predicting seizure-free outcome** Sens: 65.9% Spec: 58.8% PPV: 79.4% NPV: 41.7% OR: 2.8	**Predicting seizure-free outcome** ***MRI*** Sens: 70.7% Spec: 70.6% PPV: 85.3% NPV: 50.0% OR: 5.8 ***SPECT*** Sens: 53.7% Spec: 70.6% PPV: 81.5% NPV: 38.7% OR: 2.8 ***HD-ESI*** Sens: 87.8% Spec: 47.1% PPV: 80.0% NPV: 61.5% OR: 6.4	NA
Menon et al, 2015 [15]	Retrospective	117 patients (drug-resistant epilepsy)	FDG PET/CT	MRI	Comprehensive patient management conference	NA	NA	PET/CT findings directed 31.6% (37/117) of patients for surgery and 10.3% (12/117) of patients for intracranial monitoring.
Esophageal Cancer								
Liu et al, 2016 [16]	RCT	157 patients (operable squamous cell cancer of the esophagus)	FDG PET/CT (n=83)	CT (n=74)	Pathology, follow-up	**Nodal metastasis (station-based)** Sens: 86.5%* Spec: 94.0% Accuracy: 92.2%*	**Nodal metastasis (station-based)** Sens: 76.3%* Spec: 90.8% Accuracy: 87.2%*	PET/CT-directed operation allowed the removal of significantly more involved lymph nodes (2.83 vs. 1.76; p=0.039) and their stations (1.65 vs. 1.08; p=0.042). There was no significant difference in the mean OS between the PET/CT group and the CT group (28.4 months vs. 25.7 months; p=0.38). However, the mean DFS for the PET/CT group was significantly higher than that for the CT group (27.1 months vs. 18.9 months; p=0.019). The 1-, 2-, and 3-year DFS rates were 78.3%, 49.2%, and

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
								32.5%, respectively, in the PET/CT group and 62.6%, 26.3%, and 14.4%, respectively, in the CT group.
Gastrointestinal Cancer								
Gade et al, 2015 [17]	Retrospective	73 patients (suspicion of recurrent CRC due to at least one rising CEA or CEA above upper limit of normal)	FDG PET/CT	CT, MRI	Histopathology, clinical and imaging follow-up	**Recurrence** Sens: 85.7% Spec: 94.7% PPV: 93.8% NPV: 87.8%	NA	NA
Huang et al, 2015 [18]	Retrospective	112 patients (suspicious recurrent CRC related to elevated serum CEA level)	FDG PET/CT	NA	Histology, cytology, imaging follow-up	**Recurrence** Sens: 96.6% Spec: 91.3% PPV: 97.7% NPV: 87.5% Accuracy: 95.5%	NA	NA
Hussein and Nassef, 2016 [19]	Prospective	96 patients (CRC with suspected recurrence)	FDG PET/CT	CeCT	Pathophysiology, clinical or imaging follow-up	**Recurrence (patient-based)** Sens: 92% Spec: 72.7%* Accuracy: 88.5% **(lesion-based)** Sens: 88.3% Spec: 67.4% Accuracy: 64.1%	**Recurrence (patient-based)** Sens: 87.8% Spec: 13.6%* Accuracy: 70.8% **(lesion-based)** Sens: 77.3% Spec: 30% Accuracy: 80.9%	NA
Yu et al, 2015 [20]	Meta-analysis	26 studies (1794 patients with CRC)	FDG PET/CT	NA	Histopathology, clinical and imaging follow-up	**Local recurrence** Pooled Sens: 94% Pooled Spec: 94% Pooled +LR: 14.39 Pooled –LR: 0.08 Pooled DOR: 208.67 Q test: 0.933 AUC: 0.978	NA	NA
Ye et al, 2015 [21]	Meta-analysis	28 studies (2283 patients with primary CRC without surgery or any other treatment)	FDG PET or PET/CT	CT	Histology	**T staging** Pooled Sens: 73% Pooled Spec: 99% Pooled +LR: 9.26 Pooled -LR: 0.15 Pooled DOR: 75.02 AUC: 0.96 **N staging** Pooled Sens: 62%	**N staging** Pooled Sens: 79% Pooled Spec: 46% Pooled +LR: 1.42 Pooled -LR: 0.58 Pooled DOR: 3.71 AUC: 0.69 **M staging** Pooled Sens: 91%	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						Pooled Spec: 70% Pooled +LR: 2.83 Pooled -LR: 0.60 Pooled DOR: 6.14 AUC: 0.76 **M staging** Pooled Sens: 91% Pooled Spec: 95% Pooled +LR: 25.40 Pooled -LR: 0.14 Pooled DOR: 186.4 AUC: 0.97	Pooled Spec: 16% Pooled +LR: 1.09 Pooled -LR: 0.29 Pooled DOR: 4.34 AUC: 0.87	
Schneider et al, 2016 [22]	Retrospective	199 patients (adenocarcinoma of the rectum who received neoadjuvant long-course chemoradiation)	FDG PET/CT	CT, MRI	Histology, consensus from a multidisciplinary team	NA	NA	PET/CT was responsible for a change in stage in 27% (53/199) of patients and a change in management in 11% (22/199) of patients. MRI and CT were responsible for a change in stage in 41% (81/199) and 10% (19/199) of patients, respectively. MRI and CT both impacted patient management in 4% (8/199) of cases.
Xia et al, 2015 [23]	Meta-analysis	15 studies (867 CRC patients with liver metastases)	FDG PET/CT	NA	Follow-up	NA	NA	Patients with a metabolic response to treatment have significantly better EFS (HR=0.45; p=0.005) and OS (HR=0.36; p=0.004) than nonresponding patients. High pre-treatment SUV was significantly associated with poor OS (HR=1.24; p=0.008). However, there was no significant effect of post-treatment SUV for predicting OS (HR=1.68; p=0.30).
Salem et al, 2015 [24]	Prospective	35 patients; 98 lesions (indeterminate hepatic focal lesions)	FDG PET/CeCT	CeCT, DW-MRI	Histopathology, follow-up	**Malignant lesions (patient-based)** Sens: 100% Spec: 67% PPV: 94% NPV: 100% Accuracy: 94% **(lesion-based)**	**Malignant lesions (patient-based)** ***CeCT*** Sens: 79% Spec: 67% PPV: 92% NPV: 40% Accuracy: 77%	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						Sens: 94% Spec: 75% PPV: 94% NPV: 75% Accuracy: 90%	***DW-MRI*** Sens: 97% Spec: 83% PPV: 97% NPV: 83% Accuracy: 94% **(lesion-based)** ***CeCT*** Sens: 78% Spec: 80% PPV: 94% NPV: 48% Accuracy: 79% ***DW-MRI*** Sens: 94% Spec: 95% PPV: 99% NPV: 79% Accuracy: 94%	
Shao et al, 2015 [25]	Retrospective	58 patients (suspected malignant liver lesions)	FDG PET/CT	US	Pathology	**Diagnosis** Sens: 92.9% Spec: 100%	**Diagnosis** Sens: 95.5% Spec: 100%	NA
Polat et al, 2015 [26]	Retrospective	113 patients (GI cancer and showing suspected metastasis on CT)	FDG PET/CT	CT	Histopathology, clinical follow-up, consensus from a multidisciplinary council	**Hepatic metastasis** Sens: 78.9%* Spec: 98.7%* Accuracy: 92.0% **Extrahepatic metastasis** Sens: 87.5% Spec: 87.7%* Accuracy: 88%	**Hepatic metastasis** Sens: 94.7%* Spec: 48.0%* Accuracy: 64.0% **Extrahepatic metastasis** Sens: 75.0% Spec: 70.4%* Accuracy: 72%	Management was changed after PET/CT evaluation in 39.8% (45/113) of patients whose prior CT examination had suggested suspected metastasis (26—medical treatment to surgery, 10—surgery to medical treatment, 2—initiated chemotherapy treatment, 7—chemotherapy treatment not started).
Lee et al, 2016 [27]	Retrospective	190 patients (asymptomatic gastric cancer after curative surgical resection)	FDG PET/CT	Serum tumour marker, contrast-enhanced abdominopelvic CT, gastroduodenoscopy	Histopathology, clinical and imaging follow-up	**Recurrence** Sens: 84.2% Spec: 87.7% PPV: 43.2% NPV: 98.0%	NA	NA
Li et al, 2016 [28]	Meta-analysis	14 studies (828 patients with gastric cancer who underwent surgical	FDG PET or PET/CT	NA	Histopathology, clinical and imaging follow-up	**Recurrence (patient-based)** Pooled Sens: 85% Pooled Spec: 78% Pooled +LR: 3.9	NA	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		resection)				Pooled –LR: 0.19 Pooled DOR: 21 AUC: 0.86 **(lesion-based)** Pooled Sens: 75%		
Santhosh et al, 2015 [29]	Retrospective	50 patients (resection for periampullary carcinoma)	FDG PET/CeCT	CeCT	Biopsy, clinical and imaging follow-up	**Recurrence** Sens: 96.1% Spec: 91.6% PPV: 92.6% NPV: 95.6% Accuracy: 94.0% AUC: 0.94*	**Recurrence** Sens: 76.9% Spec: 75.0% PPV: 76.9% NPV: 75.0% Accuracy: 76.0% AUC: 0.76*	NA
Genitourinary Cancer								
Aljabery et al, 2015 [30]	Prospective	54 patients who were candidates for cystectomy (locally advanced bladder cancer)	FDG PET/CT	CT	Histopathology	**Lymph node metastasis (patient-based)** Sens: 41% Spec: 86% PPV: 58% NPV: 76% **(region-based)** Sens: 25% Spec: 92% PPV: 37% NPV: 87% **(side-based)** Sens: 38% Spec: 82% PPV: 44% NPV: 78%	**Lymph node metastasis (patient-based)** Sens: 41% Spec: 89% PPV: 64% NPV: 77% **(region-based)** Sens: 13% Spec: 97% PPV: 41% NPV: 85% **(side-based)** Sens: 31% Spec: 94% PPV: 64% NPV: 79%	NA
Jeong et al, 2015 [31]	Prospective	61 patients scheduled to undergo radical cystectomy and extended pelvic LND with curative intent (muscle-invasive bladder cancer or high-grade T1 disease)	FDG PET/CT	CT	Histopathology	**Lymph node metastasis (patient-based)** Sens: 47.1% Spec: 93.2% PPV: 72.7% NPV: 82.0% +LR: 6.9 -LR: 0.6 **(nodal packet-based)** Sens: 14.8% Spec: 97.8% PPV: 23.5% NPV: 96.2% +LR: 6.8 -LR: 0.9	**Lymph node metastasis (patient-based)** Sens: 29.4% Spec: 97.7% PPV: 83.3% NPV: 78.2% +LR: 12.9 -LR: 0.7 **(nodal packet-based)** Sens: 11.1% Spec: 98.7% PPV: 27.3% NPV: 96.1% +LR: 8.3 -LR: 0.9	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
Uttam et al, 2016 [32]	Prospective	15 patients undergoing radical cystectomy (muscle invasive transitional cell carcinomas of the bladder)	FDG PET/CT	CT	Histopathology	**Pelvic lymph node metastasis** Sens: 100% Spec: 58.3% PPV: 37.5% NPV: 100%	**Pelvic lymph node metastasis** Sens: 100% Spec: 50.0% PPV: 33.3% NPV: 100%	NA
Alongi et al, 2016 [33]	Retrospective	104 patients (certain diagnosis of renal cell carcinoma after definitive surgery)	FDG PET/CT	CT	Histology, other imaging modalities (CeCT, MRI, bone scan), clinical and imaging follow-up	**Recurrence** Sens: 74% Spec: 80% PPV: 83% NPV: 70% Accuracy: 84%	**Recurrence** Sens: 88.8% Spec: 70.2% PPV: 85.3% NPV: 76.4% Accuracy: 82.5%	PET/CT findings influenced therapeutic management in 43.3% (45/104) of patients (16—palliative to curative, 24—new chemotherapy or immunotherapy initiated, 5—observational approach adopted)
Ozturk, 2016 [34]	Retrospective	132 patients (operated renal cell carcinoma)	FDG PET/CT	NA	Histopathology, clinical follow-up	**Restaging** Sens: 93.8% Spec: 88.2% PPV: 92.6% NPV: 88.2% Accuracy: 91.6%	NA	NA
Kitajima et al, 2016 [35]	Retrospective	83 patients (suspected recurrence of urothelial transitional cell carcinoma)	FDG PET/CT	CeCT	Histopathology, clinical and imaging follow-up	**Recurrence and/or metastasis (patient-based)** Sens: 97.4% Spec: 93.3% PPV: 92.5% NPV: 97.7% Accuracy: 95.2% **(lesion site-based)** ***Intrapelvic local recurrence*** Sens: 100% Spec: 100% ***Abdominal/ pelvic/inguinal lymph node*** Sens: 100% Spec: 98.4% ***Neck/chest lymph node*** Sens: 100% Spec: 98.7% ***Bone***	**Recurrence and/or metastasis (patient-based)** Sens: 86.8% Spec: 93.3% PPV: 91.7% NPV: 89.4% Accuracy: 90.4% **(lesion site-based)** ***Intrapelvic local recurrence*** Sens: 87.5% Spec: 98.7% ***Abdominal/ pelvic/inguinal lymph node*** Sens: 81.8% Spec: 96.7% ***Neck/chest lymph node*** Sens: 37.5% Spec: 98.7% ***Bone***	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						Sens: 93.8%* Spec: 98.5% ***Lung*** Sens: 86.7% Spec: 98.5% ***Liver or adrenal gland*** Sens: 100% Spec: 100% ***Muscle or skin*** Sens: 100% Spec: 100%	Sens: 25.0%* Spec: 100% ***Lung*** Sens: 93.3% Spec: 98.5% ***Liver or adrenal gland*** Sens: 100% Spec: 100% ***Muscle or skin*** Sens: 50% Spec: 100%	
Tanaka et al, 2016 [36]	Prospective	56 patients (primary or recurrent upper urinary tract cancer)	FDG PET/CT	CT	Histopathology, imaging follow-up	**Metastasis (patient-based)** Sens: 95% Spec: 91% Accuracy: 93% **(lesion-based)** Sens: 85%*	**Metastasis (patient-based)** Sens: 82% Spec: 85% Accuracy: 84% **(lesion-based)** Sens: 50%*	PET/CT findings changed the assessment of disease extent in 32.1% (18/56) of patients. Management plan was changed based on PET/CT findings in 19.6% (11/56) of patients (3—RNU with regional LND to RNU with extended LND, 1—regional LND added to RNU, 1—NAC added to RNU, 2—cancellation of NAC prior to RNU, 1—cancellation of treatment because of denial of recurrence, 2—RNU to palliative treatment, 1—palliative treatment to RNU).
Ardito et al, 2015 [37]	Retrospective	57 patients (presumed adrenocortical carcinoma recurrence at CT scan)	FDG PET/CT	CT	Histopathology, imaging follow-up	**Recurrence** ***Liver*** Sens: 50%* Spec: 99% PPV: 95% NPV: 78% +LR: 38.0 -LR: 0.51 ***Peri-renal space*** Sens: 79% Spec: 94% PPV: 91% NPV: 86% +LR: 13.06 -LR: 0.22 ***Abdomen*** Sens: 70%	**Recurrence** ***Liver*** Sens: 80%* Spec: 89% PPV: 80% NPV: 89% +LR: 7.40 -LR: 0.22 ***Peri-renal space*** Sens: 87% Spec: 94% PPV: 91% NPV: 91% +LR: 14.44 -LR: 0.13 ***Abdomen*** Sens: 76%	The management strategy was changed based on PET/CT findings in 21.1% (12/57) of patients (8—surgery to follow-up, 1—surgery to chemotherapy, 1—lung surgery to thoraco-abdominal surgery, 1—liver surgery to extended abdominal surgery, 1—abdominal surgery to thoraco-abdominal surgery).

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						Spec: 99% PPV: 97% NPV: 85% +LR: 52.14 -LR: 0.30 ***Thorax*** Sens: 53% Spec: 95% PPV: 80% NPV: 85% +LR: 11.2 -LR: 0.49 ***Bone and other sites*** Sens: 86% Spec: 98% PPV: 86% NPV: 98% +LR: 42.86 -LR: 0.15	Spec: 94% PPV: 89% NPV: 87% +LR: 13.71 -LR: 0.25 ***Thorax*** Sens: 86% Spec: 90% PPV: 76% NPV: 95% +LR: 9.10 -LR: 0.15 ***Bone and other sites*** Sens: 86% Spec: 98% PPV: 86% NPV: 98% +LR: 42.86 -LR: 0.15	
Kassem, 2016 [38]	Prospective	34 patients (testicular tumours)	FDG PET/CT	CT	Histopathology, serum tumour markers levels	**Staging** Sens: 88.9% Spec: 87.5% PPV: 88.9% NPV: 87.5%	NA	NA
Gynecological Cancer								
Kim et al, 2016 [39]	Retrospective	287 patients (endometrial cancer)	FDG PET/CT	MRI	Histology	**Primary tumour** Sens: 91.6% Spec: 64.3% PPV: 96.6% NPV: 40.9% Accuracy: 89.3% **Lymph node metastasis (patient-based)** Sens: 70.0%* Spec: 95.4% PPV: 74.4%* NPV: 94.3%* Accuracy: 91.3%* **(lesion-based)** Sens: 79.4% Spec: 96.7% PPV: 75.5% NPV: 97.4% Accuracy: 94.8% **Distant**	**Primary tumour** Sens: 86.4% Spec: 57.1% PPV: 95.7% NPV: 27.6% Accuracy: 83.9% **Lymph node metastasis (patient-based)** Sens: 34.0%* Spec: 95.0% PPV: 58.6%* NPV: 87.2%* Accuracy: 84.3%* **(lesion-based)** Sens: 51.6% Spec: 97.6% PPV: 73.5% NPV: 94.1% Accuracy: 92.5%	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						metastasis Sens: 92.9% Spec: 98.9% PPV: 81.3% NPV: 99.6% Accuracy: 98.6%		
Signorelli et al, 2015 [40]	Prospective	71 patients (high-risk early-stage endometrial cancer)	FDG PET/CT	NA	Histopathology	**Pelvic lymph node metastasis (patient-based)** Sens: 84.6% Spec: 98.3% PPV: 91.7% NPV: 96.6% Accuracy: 95.8% **(pelvic nodal chains-based)** Sens: 70.0% Spec: 98.2% PPV: 70.0% NPV: 98.2% Accuracy: 96.7%	NA	NA
Bollineni et al, 2016 [41]	Meta-analysis	21 studies (1239 patients with endometrial cancer)	FDG PET/CT	NA	Histopathology, clinical and imaging follow-up	**Lymph node metastasis (patient-based)** Pooled Sens: 72% Pooled Spec: 94% Pooled +LR: 10.9 Pooled –LR: 0.36 Pooled DOR: 39.7 AUC: 0.94 Q test: 0.88 **Recurrence** Pooled Sens: 95% Pooled Spec: 91% Pooled +LR: 8.8 Pooled –LR: 0.08 Pooled DOR: 171.7 AUC: 0.97 Q test: 0.93	NA	NA
Simcock et al, 2015 [42]	Prospective	73 patients with endometrial cancer (48 high-risk or intermediate-risk disease after primary	FDG PET/CT	CT	Histology, sequential imaging with or without biopsy, clinical follow-up	NA	NA	Among the patients referred for adjuvant radiation, PET/CT findings had a medium impact in 20.8% (10/48) of patients (3—additional radiotherapy boost, 4—radiotherapy field change, 3—entered into a

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		surgery, 25 recurrent disease)						trial involving chemoradiotherapy) and a high impact in 14.6% (7/48) of patients (2—planned radiotherapy to extended field with chemotherapy, 1—planned radiotherapy to whole abdominal radiotherapy, 2—planned radiotherapy to further surgery, 2—planned radiotherapy to palliation). Among patients with known recurrent disease, PET/CT findings had a medium impact in 12.0% (3/25) of patients (1—Provera added to radiotherapy, 2—radiotherapy field change) and a high impact in 28.0% (7/25) of patients (5—curative adjuvant treatment to palliation, 2—observation to radiation).
Yang et al, 2016 [43]	Retrospective	113 patients (newly diagnosed cervical cancer staged IB1-IIA2)	FDG PET/CT	Clinical examination	Pathology	**Staging** Accuracy: 94.7% **Lymph node metastasis** Sens: 53.8% Spec: 95.0% PPV: 58.3% NPV: 94.1% AUC: 0.744 **Deep cervical stromal invasion** Sens: 98.4% Spec: 59.2% PPV: 75.9% NPV: 96.7% AUC: 0.788	**Staging** Accuracy: 83.2%	NA
Chen et al, 2016 [44]	Prospective	25 patients; 43 PET scans (newly diagnosed, histologically confirmed	FDG PET/CT	Chest plain radiography, abdominal and pelvic MRI or CT, chest or neck CT	Histology or cytology, clinical and imaging follow-up	NA	NA	PET/CT had a positive impact on clinical management in 18.6% (8/43) of scans (3—additional regions of distal lymph node

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		primary small-cell cervical cancer)						metastasis, 3—bone metastasis, 2—exclusion of false-positive MRI lesions).
Alessi et al, 2016 [45]	Prospective	29 patients scheduled for surgery (elevated value of serum CA125 and transvaginal ultrasound detection of suspected ovarian malignancies)	FDG PET/CT	US	Histopathology	**Differentiating between malignant and benign tumours (SUV_{max} of 3.5)** Sens: 91.3% Spec: 67% Accuracy: 83%	NA	PET/CT findings identified limiting factors for optimal cytoreductive surgery in 28.6% (6/21) of patients with epithelial ovarian cancer. These patients were deemed not amenable to cytoreducibility and NAC was initiated.
Tawakol et al, 2016 [46]	Prospective	111 patients (clinical suspicion of ovarian tumour recurrence)	FDG PET/CeCT	CeCT	Histopathology, tumour markers, clinical and imaging follow-up	**Recurrence or residual disease (study-based)** Sens: 96%* Spec: 92%* PPV: 97% NPV: 90% Accuracy: 95%* **(site-based)** ***Peritoneum*** Sens: 96%* Spec: 100%* Accuracy: 98%* ***Primary tumour site*** Sens: 100% Spec: 98% Accuracy: 99%* ***Pelvi-abdominal lymph nodes*** Sens: 100%* Spec: 100% Accuracy: 100%* ***Other distant sites*** Sens: 92%* Spec: 100%* Accuracy: 98%*	**Recurrence or residual disease (study-based)** Sens: 84%* Spec: 59%* PPV: 84% NPV: 59% Accuracy: 76%* **(site-based)** ***Peritoneum*** Sens: 69%* Spec: 85%* Accuracy: 76%* ***Primary tumour site*** Sens: 79% Spec: 94% Accuracy: 90%* ***Pelvi-abdominal lymph nodes*** Sens: 58%* Spec: 99% Accuracy: 85%* ***Other distant sites*** Sens: 67%* Spec: 87%* Accuracy: 81%*	NA
Robertson et al, 2016 [47]	Prospective and retrospective	50 patients; 83 imaging studies (suspected or known primary	FDG PET/CT	CT, MRI	Electronic patient records	NA	NA	Following PET/CT, a change in patient management was planned in 36.1% (30/83) of imaging studies

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		or recurrent vulvar/vaginal cancer)						(19—observation or additional imaging to biopsy or treatment, 11—biopsy or treatment to observation or additional imaging).
Head and Neck Cancer								
Buyukdereli et al, 2016 [48]	Prospective	46 patients scheduled for thyroidectomy (thyroid nodules of indeterminate cytology)	FDG PET/CT	FNAB	Histopathology	**Malignant lesions** Sens: 94% Spec: 62% PPV: 59% NPV: 95%	NA	NA
Piccardo et al, 2016 [49]	Prospective	87 patients scheduled to undergo thyroidectomy (thyroid nodules with undetermined cytology)	FDG PET/CT	MPUS, ^{99m}Tc MIBI scintigraphy	Histopathology	**Malignancy** Sens: 94%* Spec: 58% PPV: 37% NPV: 98%* Accuracy: 66%*	**Malignancy** ***MPUS*** Sens: 50%* Spec: 52% PPV: 21% NPV: 80%* Accuracy: 52%* ***^{99m}Tc MIBI scintigraphy*** Sens: 56%* Spec: 52% PPV: 23% NPV: 82%* Accuracy: 53%*	NA
Trivino Ibanez et al, 2016 [50]	Prospective	81 patients (high/intermediate risk for recurrent differentiated thyroid carcinoma after radioactive iodine ablation therapy)	FDG PET/CT	^{131}I WBS-SPECT/CT	Pathology, other diagnostic imaging techniques (CT, US, or MRI), follow-up	**Recurrent or metastatic lesions** Sens: 92.5%* Spec: 90.2%* PPV: 90.2% NPV: 92.5% Accuracy: 91.4%*	**Recurrent or metastatic lesions** Sens: 22.5%* Spec: 100%* Accuracy: 61.7%*	PET/CT findings led to a change in the initial staging in 25.9% (21/81) of patients and had a high therapeutic impact in 38.3% (31/81) of patients by establishing the need for treatment (20—surgery, 6—radioactive iodine empiric therapy, 1—thermal ablation, 1—radiofrequency ablation, 3—treatment with tyrosine kinase-inhibiting drugs).
Caetano et al, 2016 [51]	Meta-analysis	7 studies (260 patients with suspected recurrence of differentiated thyroid carcinoma and	FDG PET/CT	^{131}I scintigraphy	Histopathology, clinical and imaging follow-up	**Recurrence** Pooled Sens: 93% Pooled Spec: 81% Pooled +LR: 5.0 Pooled –LR: 0.09 Pooled DOR: 58 AUC: 0.93	NA	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		negative ^{131}I whole-body scintigraphy)				Q test: 0.3 I^2: 95		
Taghipour et al, 2015 [52]	Retrospective	96 patients; 246 follow-up scans (biopsy-proven HPV-related oropharyngeal squamous cell carcinoma after completion of primary treatment)	FDG PET/CT	Clinical assessment	Histopathology, clinical follow-up	**Recurrence or metastasis** Sens: 97.0% Spec: 92.5% PPV: 67.0% NPV: 99.5% Accuracy: 93.1%	NA	There was a change in management from no treatment to new treatment (surgery, chemotherapy or radiation therapy alone or in combination) after 12.6% (32/254) of scans.
Bird et al, 2016 [53]	Retrospective	146 patients radically treated with primary definitive radiotherapy (stage III/IV histologically confirmed oropharyngeal squamous cell carcinoma)	FDG PET/CT	Clinical examination	Histology, clinical and imaging follow-up	**Predicting residual disease** Sens: 92.0% Spec: 85.1% PPV: 56.1% NPV: 98.1%	NA	NA
Chun et al, 2016 [54]	Retrospective	89 patients (laryngeal squamous cell carcinoma)	FDG PET/CT	CT, MRI	Histopathology	**Cervical nodal metastasis** Sens: 74.2% Spec: 93.0% PPV: 58.9% NPV: 96.4% Accuracy: 90.8%	NA	NA
Chaukar et al, 2016 [55]	Prospective	70 patients (oral squamous cell carcinoma and clinically node-negative neck)	FDG PET/CT	US, CeCT	Histopathology	**Cervical nodal metastasis** Sens: 82% Spec: 54% PPV: 57% NPV: 79% Accuracy: 66% AUC: 0.676	**Cervical nodal metastasis** ***US*** Sens: 79% Spec: 69% PPV: 66% NPV: 80% Accuracy: 73% AUC: 0.736 ***CeCT*** Sens: 74% Spec: 85% PPV: 80%	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
							NPV: 82% Accuracy: 80% AUC: 0.805	
Zhou et al, 2016 [56]	Meta-analysis	23 studies (1253 patients with suspected residual or recurrent nasopharyngeal carcinoma)	FDG PET or PET/CT	NA	Histopathology, clinical and imaging follow-up	**Residual or recurrent lesions** Pooled Sens: 93% Pooled Spec: 87% Pooled +LR: 5.52 Pooled –LR: 0.12 Pooled DOR: 55.31 AUC: 0.947 Q test: 0.887	NA	NA
Mehanna et al, 2016 [57]	RCT	564 patients; 1:1 allocation (squamous-cell carcinoma of the oropharynx, hypopharynx, larynx, oral cavity, or an unknown primary site in the head or neck with clinical and radiologic stage N2 or N3 nodal metastases)	FDG PET/CT (performed 12 weeks after the end of chemoradiotherapy)	Planned neck dissection	Pathology, clinical and imaging follow-up	NA	NA	PET/CT surveillance resulted in fewer neck dissections than did planned dissection surgery (54 vs. 221). The rates of surgical complications were similar between the two groups (42% vs. 38%, respectively). The 2-year OS rate was 84.9% in the surveillance group and 81.5% in the planned-surgery group (HR=0.92; 95% CI: 0.65-1.32; p=0.004 for noninferiority). The 2-year rate of locoregional control was 91.9% (95% CI: 88.5%-95.3%) in the surveillance group and 91.4% (95% CI: 87.8%-95.0%) in the planned-surgery group.
Park et al, 2016 [58]	Prospective	160 patients (previously untreated head and neck squamous cell carcinoma)	FDG PET/CT	CeCT/MRI	Histopathology	**Cervical lymph node metastasis (patient-based)** Sens: 91.5%* Spec: 83.3% PPV: 88.7% NPV: 87.3% Accuracy: 88.1%* **(neck side-based)** Sens: 91.1%* Spec: 88.2% PPV: 87.9% NPV: 91.3%	**Cervical lymph node metastasis (patient-based)** Sens: 73.4%* Spec: 85.1% PPV: 88.5% NPV: 69.5% Accuracy: 78.8%* **(neck side-based)** Sens: 69.6%* Spec: 91.6% PPV: 88.6% NPV: 76.2%	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						Accuracy: 89.6%* **(neck level-based)** Sens: 78.9%* Spec: 91.8%* PPV: 69.2% NPV: 94.9% Accuracy: 89.3%*	Accuracy: 81.0%* **(neck level-based)** Sens: 53.0%* Spec: 94.2%* PPV: 68.1% NPV: 89.5% Accuracy: 86.3%*	
Qualliotine et al, 2015 [59]	Retrospective	85 patients who underwent pre-operative PET/CT and primary surgery (head and neck squamous cell carcinoma)	FDG PET/CeCT	CT, MRI	Pathology	**Regional cervical metastasis** Sens: 87.5% Spec: 44.8% PPV: 75.4% NPV: 65.0% Accuracy: 72.9%	NA	NA
Cacicedo et al, 2015 [60]	Prospective	84 patients (stage III-IV head and neck squamous cell carcinoma)	FDG PET/CT	Physical examination, neck and chest CeCT, neck MRI	Histology, clinical and imaging follow-up, multidisciplinary tumour board	NA	NA	PET/CT findings changed the staging of 15.5% (13/84) of patients (10—upstaged, 3—downstaged). Patient management was altered in 26.2% (22/84) of patients (6—curative to palliative, 3—palliative to curative, 3—surgery, 2—surgery ± radiotherapy to radical chemoradiotherapy, 6—change in radiotherapy field and dose, 2—change in type of neck dissection).
Su et al, 2016 [61]	Meta-analysis	15 studies (1155 patients with head and neck cancer)	FDG PET/CT	MRI, CT, US	Pathology	**Predicting extracapsular spread (neck/node-based)** Pooled Sens: 86% Pooled Spec: 86%	**Predicting extracapsular spread *MRI* (neck/node-based)** Pooled Sens: 85% Pooled Spec: 84% Pooled +LR: 4.62 Pooled –LR: 0.19 Pooled DOR: 60.27 AUC: 0.945 Q test: 0.884 **(patient-based)** Sens: 8% Spec: 100% ***CT***	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
							(neck/node-based) Pooled Sens: 77% Pooled Spec: 85% Pooled +LR: 4.84 Pooled –LR: 0.29 Pooled DOR: 19.24 AUC: 0.862 Q test: 0.792 **(patient-based)** Pooled Sens: 55% Pooled Spec: 87% ***US*** **(neck/node-based)** Pooled Sens: 87% Pooled Spec: 75%	
Sjovall et al, 2016 [62]	Prospective	105 patients who underwent radical radiotherapy ± chemotherapy (locally advanced, neck node-positive, biopsy-proven head and neck squamous cell carcinoma)	FDG PET/CT	NA	Pathology, clinical follow-up	**Persistent tumour (6 weeks post-treatment)** Sens: 62.5% Spec: 92% PPV: 56% NPV: 94% Accuracy: 88%	NA	NA
Kim et al, 2016 [63]	Retrospective	78 patients (received radical chemoradiotherapy for locally advanced head and neck squamous cell carcinoma)	FDG PET/CT	CT, MRI	Histology, clinical and imaging follow-up	**Immediate locoregional and/or systemic failure (postSUV_{max} of 4.4)** Sens: 90.0% Spec: 83.8% PPV: 45.0% NPV: 98.3%	**Immediate locoregional and/or systemic failure** Sens: 44.4% Spec: 89.4% PPV: 36.4% NPV: 92.2%	NA
Taghipour et al, 2016 [64]	Retrospective	98 patients who underwent surgical resection as primary treatment (biopsy-proven head and neck	FDG PET/CT	Clinical assessment	Histopathology, clinical follow-up	**Post-treatment assessment for residual disease** Sens: 80.0% Spec: 89.5% PPV: 66.7% NPV: 94.4% Accuracy: 87.5%	NA	Post-treatment PET/CT prompted a change in subsequent management in 20.4% (20/98) of patients (20—new treatment started). There was a significant benefit in overall survival for patients with a

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		squamous cell carcinoma)						negative post-treatment PET/CT scan compared with those with a positive scan (HR=5.65; 95% CI: 2.48-12.83; p<0.001).
Suenaga et al, 2016 [65]	Retrospective	170 patients (suspected recurrent head and neck squamous cell carcinoma)	FDG PET/CeCT, FDG PET/ncCT	CeCT	Surgery, biopsy, imaging and clinical follow-up	**Local recurrence** ***PET/CeCT*** Sens: 94.1%* Spec: 94.1% PPV: 64.0% NPV: 99.3% Accuracy: 94.1%* AUC: 0.980* ***PET/ncCT*** Sens: 82.3%* Spec: 92.8%* PPV: 56.0% NPV: 97.9% Accuracy: 91.2% AUC: 0.958* **Regional recurrence** ***PET/CeCT*** Sens: 72.7%* Spec: 96.6% PPV: 76.2% NPV: 96.0% Accuracy: 93.5%* AUC: 0.856* ***PET/ncCT*** Sens: 68.2%* Spec: 95.9% PPV: 71.4% NPV: 95.3% Accuracy: 92.4%* AUC: 0.857* **Distant metastasis** ***PET/CeCT*** Sens: 60.0% Spec: 99.4% PPV: 90.0% NPV: 96.4% Accuracy: 95.9% AUC: 0.918 ***PET/ncCT*** Sens: 53.3%	**Local recurrence** Sens: 29.4%* Spec: 97.4%* PPV: 55.6% NPV: 92.5% Accuracy: 90.6%* AUC: 0.824* **Regional recurrence** Sens: 40.9%* Spec: 95.9% PPV: 60.0% NPV: 91.6% Accuracy: 88.8%* AUC: 0.732* **Distant metastasis** Sens: 33.3% Spec: 99.4% PPV: 83.3% NPV: 93.9% Accuracy: 93.5% AUC: 0.856 **Metachronous second primary cancer** Sens: 37.5% Spec: 98.7% PPV: 75.0% NPV: 93.8% Accuracy: 92.9% AUC: 0.861	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						Spec: 99.4% PPV: 88.9% NPV: 95.7% Accuracy: 95.9% AUC: 0.912 **Metachronous second primary cancer** ***PET/CeCT*** Sens: 73.3% Spec: 98.1% PPV: 78.6% NPV: 96.8% Accuracy: 95.3% AUC: 0.905 ***PET/ncCT*** Sens: 56.3% Spec: 98.1% PPV: 75.0% NPV: 95.6% Accuracy: 94.1% AUC: 0.888		
Mani et al, 2016 [66]	Retrospective	52 patients (head and neck squamous cell carcinoma of unknown primary)	FDG PET/CT	Panendoscopy	Histopathology	**Primary site** Sens: 82.8% Spec: 87.0% PPV: 88.9% NPV: 80.0%	NA	NA
Hematologic Cancer								
Press et al, 2016 [67]	Prospective	331 patients (stage III or IV classic HL)	FDG PET/CT (interim-PET performed after 2 cycles of ABVD. Patients with negative findings continued ABVD. Those with positive findings	NA	Biopsy, clinical and imaging follow-up	NA	NA	The 2-year PFS for patients with negative interim-PET was 82%. The 2-year PFS for patients with positive interim-PET was 64%. Escalated BEACOPP was significantly more toxic than ABVD (85.7% vs. 36.7% grade 4/5 toxicities; p<0.001).

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
			received escalated BEACOPP)					
Ganesan et al, 2015 [68]	Phase II	50 patients (newly diagnosed advanced HL, stages IIB-IVB)	FDG PET/CT (interim-PET performed after 2 cycles of ABVD)	NA	Biopsy, clinical and imaging follow-up	NA	NA	Patients with a negative interim PET scan continued four more cycles of ABVD. Patients with a positive interim PET scan received four cycles of escalated BEACOPP. PET-positive patients had an inferior 2-year EFS when compared with PET-negative patients despite escalation of therapy (50% vs. 82%; p=0.013).
Johnson et al, 2016 [69]	RCT	1119 patients (previously untreated advanced classic HL)	FDG PET/CT (interim-PET performed after 2 cycles of ABVD. Patients with negative findings were randomized to continue ABVD or receive AVD. Those with positive findings received BEACOPP)	NA	Follow-up	NA	NA	The 3-year PFS was 85.7% in the ABVD group and 84.4% in the AVD group. The 3-year OS was 97.2% with ABVD and 97.6% with AVD. The 3-year PFS and OS for patients with positive PET findings were 67.5% and 87.8%, respectively.
Barrington et al, 2016 [70]	Retrospective	1211 patients (advanced HL, stages IIB to IV and stage IIA)	FDG PET/CT	Clinical assessment, CeCT	Biopsy, follow-up	NA	NA	PET/CT findings upstaged 13.6% (159/1171) of patients and downstaged 6.3% (74/1171) of patients.
Basit et al, 2016 [71]	Retrospective	119 patients treated with	FDG PET/CT	NA	Biopsy, clinical and imaging	**Prediction of relapse**	NA	Compared to patients with positive interim-PET,

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		CHOP or R-CHOP (newly diagnosed DLBCL)	(interim-PET performed after 2-4 cycles)		follow-up	Sens: 79% Spec: 55% PPV: 35% NPV: 89%		patients with negative interim scans had better PFS (92% vs. 72%; p=0.002) and OS (88% vs. 66%; p=0.005) at 2 years. Patients with negative end-of-treatment-PET also fared significantly better than those with positive end-of-treatment scans with respect to PFS (94% vs. 35%; p<0.001) and OS (96% vs. 44%; p<0.001) at 2 years.
Taghipour et al, 2016 [72]	Retrospective	77 patients; 208 fourth and subsequent follow-up PET/CT scans (biopsy-proven NHL)	FDG PET/CT	NA	Histopathology, clinical and imaging follow-up	NA	NA	36.4% (12/33) of PET/CT scans led to a change in the management of patients with clinical suspicion of recurrence (6—new treatment initiated, 5—change in treatment modality, 1—discontinuation of treatment). For patients without previous clinical suspicion of recurrence, 9.2% (16/175) of PET/CT scans led to a change in management (14—new treatment initiated, 1—change in treatment regimen, 1—treatment stopped).
Perry et al, 2016 [73]	Retrospective	64 patients; 68 scans (follicular lymphoma)	FDG PET/CT	NA	Histology	**Bone marrow involvement** PPV: 48.5% NPV: 100%	NA	NA
Melanoma								
Schule et al, 2016 [74]	Retrospective	64 patients (stage III/IV melanoma)	FDG PET/CT	CT	Pathology, follow-up	**Distant metastasis (lesion-based)** Sens: 90.6% Spec: 77.2%	**Distant metastasis (lesion-based)** Sens: 77.1% Spec: 69.9%	PET/CT findings led to a change in the primary CT-based treatment decisions in 54.7% (35/64) of patients (13—surgery to follow-up, 3—surgery to chemoradiotherapy, 4—change in the extent of metastasectomy, 8—surgical treatment,

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management 2—chemotherapy to follow-up, 3—follow-up of equivocal lesions to exclusion of metastases, 2—first line to second line chemotherapy).
van Wissen et al, 2016 [75]	Retrospective	70 patients (stage IIIB or IIIC melanoma)	FDG PET/CT	NA	Pathology	**Inguinal lymph node metastasis** Sens: 97% Spec: 50% PPV: 90% NPV: 71% **Iliac lymph node metastasis** Sens: 67% Spec: 91% PPV: 73% NPV: 81%	NA	NA
Singnurkar et al, 2016 [76]	Prospective	319 patients (potentially resectable localized high-risk melanoma or recurrent disease under consideration for metastasectomy)	FDG PET/CT	NA	Confirmatory imaging, histological proof, and ultimate patient management was at the discretion of the treating oncologist	NA	NA	There was significant upstaging after PET/CT in 17.6% (56/319) of patients ($p<0.0001$). There was a significant relationship between upstaging with PET/CT and the frequency of patients undergoing surgical resection of metastases distant to the primary melanoma site ($p=0.034$).
Neuro-oncology								
Wang et al, 2015 [77]	Meta-analysis	23 studies (685 patients with glioma treated with surgery or radiotherapy or chemotherapy)	FDG PET or PET/CT	MRS	Histopathology, imaging follow-up	**Recurrence** Pooled Sens: 70% Pooled Spec: 88% Pooled +LR: 3.98 Pooled –LR: 0.38 AUC: 0.866 Q test: 0.797	**Recurrence** Pooled Sens: 87% Pooled Spec: 86% Pooled +LR: 5.57 Pooled –LR: 0.17 AUC: 0.933 Q test: 0.869	NA
Non-FDG Tracers $^{11}C/^{18}F$-Choline								
Hernandez-Arguello et al, 2016 [78]	Prospective	21 patients (untreated primary prostate carcinoma and candidates for radical	^{11}C-Choline PET/CT	MRI	Histopathology	**Tumour detection** Sens: 100% Spec: 70% PPV: 83% NPV: 100%	**Tumour detection** Sens: 46% Spec: 100% PPV: 100% NPV: 54%	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		prostatectomy)						
Ouyang et al, 2016 [79]	Meta-analysis	77 studies (patients with prostate cancer)	^{11}C/^{18}F-Choline PET/CT	FDG PET/CT, TRTE, SWE	Histopathology	**Diagnosis** ***^{11}C-Choline PET/CT*** Pooled Sens:78.3% Pooled Spec: 79.2% AUC: 0.853 ***^{18}F-Choline PET/CT*** Pooled Sens: 73.5% Pooled Spec: 90.1% AUC: 0.909	**Diagnosis** ***FDG PET/CT*** Pooled Sens: 76.3% Pooled Spec: 78.3% AUC: 0.84 ***TRTE*** Pooled Sens: 69.7% Pooled Spec: 75.7% AUC: 0.791 ***SWE*** Pooled Sens: 94.4% Pooled Spec: 91.9% AUC: 0.954	NA
Lopci et al, 2015 [80]	Prospective	45 patients; 50 PET/CT scans (primary or relapsing hepatocellular carcinoma)	^{11}C-Choline PET/CT	CeCT/MRI	Histopathology, multidisciplinary consensus	**Diagnosis (scan-based)** Sens: 88% Spec: 90% **(lesion-based)** Sens: 78%* Spec: 86%* Accuracy: 79%*	**Diagnosis (scan-based)** Sens: 90% Spec: 73% **(lesion-based)** Sens: 65%* Spec: 55%* Accuracy: 64%*	PET/CT provided information that modified the therapeutic strategy in 24.4% (11/45) of patients (3—radiation therapy to no further treatment/follow-up, 3—surgery to systemic therapy, 2—radiation therapy to systemic therapy, 1—surgery to local treatment, 1—local treatment to radiation therapy, 1—inappropriate liver resection).
Castilla-Lievre et al, 2016 [81]	Prospective	33 patients (suspicion of hepatocellular carcinoma based on CT and/or MRI imaging)	^{11}C-Choline PET/CT	FDG PET/CT	Histopathology, imaging follow-up	**Diagnosis (patient-based)** Sens: 75% **(lesion-based)** Sens: 67%	**Diagnosis (patient-based)** Sens: 36% **(lesion-based)** Sens: 30%	NA
^{68}Ga-DOTATATE/DOTATOC								
Albanus et al, 2015 [82]	Retrospective	54 patients (histologically confirmed NET)	^{68}Ga-DOTATATE PET/CeCT	CeCT	Clinical and imaging follow-up	**Bone metastasis** Sens: 100%* Spec: 89%* PPV: 81%* NPV: 100%*	**Bone metastasis** Sens: 47%* Spec: 49%* PPV: 30%* NPV: 67%*	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						Lymph node metastasis Sens: 92%* Spec: 83%* PPV: 82%* NPV: 92%* **Lung metastasis** Sens: 100% Spec: 95%* PPV: 83%* NPV: 100%	**Lymph node metastasis** Sens: 64%* Spec: 59%* PPV: 57%* NPV: 65%* **Lung metastasis** Sens: 100% Spec: 82%* PPV: 56%* NPV: 100%	
Skoura et al, 2016 [83]	Retrospective	728 patients; 1258 scans (confirmed or suspected NETs)	^{68}Ga-DOTATATE PET/CT	NA	Histopathology, imaging follow-up, consensus from a multidisciplinary team	**Primary, recurrent, or metastatic lesions** Sens: 97.0% Spec: 95.1% PPV: 98.5% NPV: 90.4% Accuracy: 96.6%	NA	The treatment plan was changed after 40.9% (515/1258) of ^{68}Ga-DOTATATE PET/CT scans due to new and unexpected findings (362—initiated chemotherapy or PRRT, 52—resection, 71—another chemotherapy regimen started, 5—excluded a suspected NET, 2—cessation of previous treatment, 2—rejection of PRRT, 2—revealed candidates for liver transplant, 19—precise management change unclear from records).
Sadowski et al, 2016 [84]	Prospective	131 patients (biochemical or radiologic suspicion and/or known diagnosis of GEP NET)	^{68}Ga-DOTATATE PET/CT	^{111}In-pentetreotide SPECT/CT, CT/MRI	Histopathology, consensus from a multidisciplinary team	**Primary tumours and/or metastasis (lesion-based)** Sens: 63.7%	**Primary tumours and/or metastasis (lesion-based)** ***^{111}In-pentetreotide SPECT/CT*** Sens: 22.1% ***CT/MRI*** Sens: 38.9%	On the basis of ^{68}Ga-DOTATATE PET/CT findings, 32.8% (43/131) of patients had a change in management recommendation.
Deppen et al, 2016 [85]	Prospective	78 patients (known or suspected pulmonary or GEP NETs)	^{68}Ga-DOTATATE PET/CT	^{111}In-pentetreotide SPECT or SPECT/CT	Pathology, CT, MRI, consensus from a multidisciplinary team	**Diagnosis (patient-based)** Sens: 96% Spec: 93% PPV: 96% NPV: 93% Accuracy: 94%*	**Diagnosis (patient-based)** Sens: 72% Spec: 93% PPV: 95% NPV: 65% Accuracy: 82%*	The addition of ^{68}Ga-DOTATATE PET/CT changed treatment plans in 35.9% (28/78) of patients (9—intramodality changes, 8—surgery cancelled or radical change in type of surgery, 12—referred for PRRT).

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
Deppen et al, 2016 [86]	Meta-analysis	10 studies (465 patients with pulmonary or GEP NETs)	^{68}Ga-DOTATATE PET/CT	^{111}In-DTPA-octreotide scintigraphy, other not specified	Pathology, imaging follow-up	**Diagnosis or staging (patient-based)** Pooled Sens: 90.9% Pooled Spec: 90.6%	NA	NA
Van Binnebeek et al, 2016 [87]	Prospective	53 patients (metastatic NET)	^{68}Ga-DOTATOC PET/CT	^{111}In-pentetreotide SPECT	Histopathology (when available), imaging follow-up	**Metastatic lesions (lesion-based)** Sens: 99.9%*	**Metastatic lesions (lesion-based)** Sens: 60.1%*	NA
^{68}Ga-PSMA								
van Leeuwen et al, 2016 [88]	Prospective	70 patients who had undergone radical prostatectomy and were being considered for salvage radiation therapy (biochemical recurrence of prostate cancer)	^{68}Ga-PSMA PET/CT	CeCT	Histopathology (when available)	NA	NA	PET/CT findings led to a major management change in 28.6% (20/70) of patients (5—increase in salvage radiation therapy volume and addition of adjuvant androgen deprivation therapy, 1—salvage LND, 6—salvage radiation therapy plus adjuvant androgen deprivation therapy, 4—stereotactic radiotherapy of a pelvic lymph node, 3—stereotactic radiotherapy for a lesion outside the pelvis with or without androgen deprivation therapy, 1—salvage radiation therapy to the prostatic fossa plus stereotactic radiotherapy for an extrapelvic lesion).
^{18}F-FLT								
Wang et al, 2015 [89]	Meta-analysis	17 studies (548 patients with pulmonary lesions)	^{18}F-FLT PET or PET/CT	FDG PET or PET/CT	Pathology, follow-up	**Malignancy** Pooled Sens: 80%* Pooled Spec: 82%* AUC: 0.87	**Malignancy** Pooled Sens: 89%* Pooled Spec: 66%* AUC: 0.90	NA
Vineeth Kumar et al, 2016 [90]	Prospective	23 patients (suspected pancreatobiliary tumours on CeCT)	^{18}F-FLT PET/CT	CeCT, FDG PET/CT	Histopathology, FNAC	**Differentiating between benign and malignant tumours** Sens: 88.2% Spec: 100%* PPV: 100%	**Differentiating between benign and malignant tumours** ***CeCT*** Sens: 100% Spec: 12.5%	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						NPV: 80% Accuracy: 92% AUC: 0.684	PPV: 70.8% NPV: 100% Accuracy: 72% ***FDG PET/CT*** Sens: 94.1% Spec: 12.5%* PPV: 69.6% NPV: 50% Accuracy: 68% AUC: 0.437	
Nakajo et al, 2015 [91]	Prospective	40 patients (adrenal tumours)	^{18}F-FLT PET/CT	FDG PET/CT	Pathology, clinical and imaging follow-up	**Diagnosis** ***Visual*** Sens: 100% Spec: 97%* Accuracy: 98%* AUC: 0.97* ***SUV_{max} of >1.9*** Sens: 100% Spec: 97%* Accuracy: 98%* AUC: 0.98* ***SUV_{max} ratio of >1.9*** Sens: 100% Spec: 97%* Accuracy: 98%* AUC: 0.98*	**Diagnosis** ***Visual*** Sens: 91% Spec: 63%* Accuracy: 71%* AUC: 0.81* ***SUV_{max} of >3.0*** Sens: 91% Spec: 67%* Accuracy: 73%* AUC: 0.82* ***SUV_{max} ratio of >1.08*** Sens: 100% Spec: 70%* Accuracy: 78%* AUC: 0.86*	NA
Minamimoto et al, 2016 [92]	Prospective	46 patients (newly diagnosed DLBCL)	^{18}F-FLT PET/CT (interim-PET performed after 2 cycles of R-CHOP or R-EPOCH)	FDG PET/CT	Clinical and imaging follow-up	**Predicting residual disease** Sens: 83% Spec: 97% PPV: 91%* NPV: 94%* Accuracy: 94%	**Predicting residual disease** ***Using IHP*** Sens: 92% Spec: 56% PPV: 42%* NPV: 95% Accuracy: 65% ***Using EORTC*** Sens: 92% Spec: 56% PPV: 42%* NPV: 95% Accuracy: 65% ***Using PERCIST 1.0*** Sens: 50% Spec: 79% PPV: 46%* NPV: 82%*	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
							Accuracy: 72% ***Using Deauville*** Sens: 92% Spec: 59% PPV: 44%* NPV: 95% Accuracy: 67%	
Staniuk et al, 2016 [93]	Prospective	29 patients undergoing resective operation (gastric cancer)	^{18}F-FLT PET/CT	CeCT	Histopathology	**Regional lymph node metastasis (SUV_{max} of 1.5)** Sens: 90%* Spec: 88.9%* PPV: 94.7% NPV: 80% Accuracy: 89.7% AUC: 0.958*	**Regional lymph node metastasis (Short-axis diameter of 8 mm)** Sens: 55.6%* Spec: 75%* PPV: 78.9% NPV: 45.4% Accuracy: 69% AUC: 0.708*	NA
NSCLC								
Pak et al, 2015 [94]	Meta-analysis	28 studies (3255 patients with NSCLC)	FDG PET/CT	NA	Histology	**Nodal staging (node-based)** Pooled Sens: 62% Pooled Spec: 92% Pooled +LR: 7.82 Pooled –LR: 0.41 Pooled DOR: 19.12 **(patient-based)** Pooled Sens: 67% Pooled Spec: 87% Pooled +LR: 5.20 Pooled –LR: 0.37 Pooled DOR: 13.91	NA	NA
Wang et al, 2015 [95]	Meta-analysis	4 studies (1330 patients with pulmonary space-occupying lesions)	FDG PET/CT	NA	Histology, cytology	**Diagnosis** Pooled Sens: 98.7% Pooled Spec: 58.2%	NA	NA
Nam et al, 2016 [96]	Retrospective	111 patients (resected lung adenocarcinoma manifesting as ground-glass opacity)	FDG PET/CT	CT	Histology, serial imaging follow-up	**Recurrence (postoperative surveillance)** Sens: 72.2% Spec: 93.5% PPV: 68.4% NPV: 94.6% Accuracy: 90.1%*	**Recurrence (postoperative surveillance)** Sens: 94.4% Spec: 98.9% PPV: 94.4% NPV: 98.9% Accuracy: 98.2%*	NA
Sheikhbahaei	Retrospective	201 patients	FDG	NA	Histopathology,	**Residual tumour**	NA	PET/CT findings led to

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
et al, 2016 [97]		who underwent therapy assessment (34 SCLC, 167 NSCLC)	PET/CT		clinical or imaging follow-up	**(Hopkins Criteria)** Sens: 89% Spec: 80% PPV: 92.8% NPV: 71.4% Accuracy: 86.7%		initiation of new treatment plan in 70.8% (102/144) of patients with positive residual disease on post-treatment PET/CT (26—surgery, 44—palliative or new chemotherapeutic regimen, 24—radiation therapy, 8—combined chemoradiation therapy).
Noda et al, 2016 [98]	Retrospective	84 patients; 91 tumours (lung adenocarcinoma)	FDG PET/CT	NA	Histopathology	**Lymphovascular invasion (SUV_{max} of 2.32)** Sens: 89% Spec: 78% AUC: 0.88 **Lymphatic invasion (SUV_{max} of 3.26)** Sens: 86% Spec: 89% AUC: 0.91	NA	NA
Pancreatic Cancer								
Burge et al, 2015 [99]	Prospective	53 patients (resectable pancreas, ampullary or distal bile duct adenocarcinoma)	FDG PET/CT	ERCP, biliary stenting, primovist enhanced MRI, EUS, laparoscopy, CeCT scan of the chest, abdomen and pelvis	Histology, follow-up	NA	NA	The planned surgical treatment was abandoned in 16.1% (9/56) of patients as a result of PET/CT identifying unexpected metastases. However, metastases were missed by PET/CT in 7.5% (4/53) of patients.
Kim et al, 2015 [100]	Retrospective	285 patients (resectable or borderline resectable pancreatic cancer)	FDG PET/CT	CT, CA19-9, EUS	Pathology, clinical and imaging follow-up	NA	NA	PET/CT findings changed the management of 10.9% (31/285) of patients due to detection of metastatic disease.
Jung et al, 2016 [101]	Retrospective	110 patients (curatively resected pancreatic cancer)	FDG PET/CT	CT, CA19-9	Pathology, clinical and imaging follow-up	**Recurrence** Sens: 84.5%* Spec: 84.6% PPV: 94.7% NPV: 62.8% Accuracy: 84.5%*	**Recurrence** ***CT*** Sens: 75.0% Spec: 73.1% PPV: 90.0% NPV: 47.5% Accuracy: 74.5% ***CA19-9*** Sens: 67.9%*	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
							Spec: 88.5% PPV: 95.0% NPV: 46.0% Accuracy: 72.7%*	
Pediatric Cancer								
Hurley et al, 2016 [102]	Retrospective	39 patients (high-grade osteosarcoma)	FDG PET/CT	Bone scintigraphy	Histopathology, clinical and imaging follow-up	**Osseous metastasis (lesion-based)** Sens: 93.2%* Spec: 89.1% PPV: 91.7% NPV: 91.1% Accuracy: 91.4% **(examination-based)** Sens: 100% Spec: 91.4% PPV: 62.5% NPV: 100% Accuracy: 92.5%	**Osseous metastasis (lesion-based)** Sens: 74.6%* Spec: 95.7% PPV: 95.7% NPV: 74.6% Accuracy: 83.8% **(examination-based)** Sens: 60% Spec: 100% PPV: 100% NPV: 94.6% Accuracy: 95%	NA
Sarcoma								
Jesus-Garcia et al, 2016 [103]	Prospective	36 patients (cartilage lesions)	FDG PET/CT	X-rays, CT, scintigraphy, MRI	Pathology, imaging follow-up	**Differentiating between chondroma and chondrosarcoma (SUV_{max} of 2.2)** Sens: 94.7% Spec: 94.1% PPV: 94.7% NPV: 94.1% Accuracy: 94.4%	NA	NA
Lee et al, 2016 [104]	Retrospective	56 patients (newly diagnosed uterine carcinosarcoma)	FDG PET/CT	MRI	Pathology	**Primary lesions (patient-based)** Sens: 98.1% Spec: 33.3% PPV: 96.3% NPV: 50.0% Accuracy: 94.6% **Paraaortic lymph node metastasis (region-based)** Sens: 77.8%* Spec: 90.2%* PPV: 80.8% NPV: 88.5% Accuracy: 85.9% **Pelvic lymph**	**Primary lesions (patient-based)** Sens: 98.1% Spec: 100% PPV: 100% NPV: 75.0% Accuracy: 98.2% **Paraaortic lymph node metastasis (region-based)** Sens: 51.9%* Spec: 100%* PPV: 100% NPV: 79.7% Accuracy: 83.3% **Pelvic lymph**	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						node metastasis (region-based) Sens: 61.1% Spec: 86.8% PPV: 68.8% NPV: 82.5% Accuracy: 78.6% **Total lymph node metastasis (patient-based)** Sens: 66.7% Spec: 78.1% PPV: 69.6% NPV: 75.8% Accuracy: 73.2% **Extrauterine metastasis (patient-based)** Sens: 100% Spec: 78.9% PPV: 69.2% NPV: 100% Accuracy: 85.7%	**node metastasis (region-based)** Sens: 50.0% Spec: 89.5% PPV: 69.2% NPV: 79.1% Accuracy: 76.8% **Total lymph node metastasis (patient-based)** Sens: 54.2% Spec: 84.4% PPV: 72.2% NPV: 71.1% Accuracy: 71.4%	
Unknown Primary								
Yaylali et al, 2016 [105]	Retrospective	50 patients (unknown primary malignancy whose conventional intervention test results were negative)	FDG PET/CT	CT, MRI, mammography, endoscopy	Histopathology	**Malignant lesions** Sens: 87.5% Spec: 33.3% PPV: 70.0% NPV: 60.0% Accuracy: 68.0%	NA	NA
Tamam et al, 2016 [106]	Retrospective	87 patients (bone metastases of unknown primary whose conventional intervention test results were negative)	FDG PET/CT	Not specified	Histopathology, clinical and imaging follow-up	**Primary site** Sens: 82% Spec: 44% PPV: 93% NPV: 28% Accuracy: 73%	NA	NA
Various Sites								
Lange et al, 2016 [107]	Retrospective	395 patients; 409 bone biopsies	FDG PET/CT	X-ray, CT, MRI, ^{99m}Tc bone scintigraphy	Pathology	**Skeletal malignancies** Sens: 92.3%* Spec: 63.2%*	**Skeletal malignancies** ***X-ray*** Sens: 33.0%*	NA

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
						PPV: 83.7% NPV: 80.0% Accuracy: 82.7%	Spec: 96.1%* PPV: 86.1% NPV: 66.3% Accuracy: 69.5% ***CT*** Sens: 75.6%* Spec: 89.2%* PPV: 91.4% NPV: 70.9% Accuracy: 81.1% ***MRI*** Sens: 90.5% Spec: 81.1% PPV: 86.8% NPV: 87.5% Accuracy: 87.1% ***Bone scintigraphy*** Sens: 74.1% Spec: 62.5% PPV: 87.0% NPV: 41.7% Accuracy: 71.4%	
Redondo-Cerezo et al, 2015 [108]	Retrospective	54 patients (suspicious lymphadenopathy of unknown origin on CT)	FDG PET/CT	EUS-FNA	Pathology, clinical and imaging follow-up	**Malignancy** Sens: 75% Spec: 25% PPV: 50% NPV: 50% Accuracy: 50%	**Malignancy** Sens: 91.3% Spec: 100% PPV: 100% NPV: 92.5% Accuracy: 95.8%	NA
Barabasch et al, 2015 [109]	Prospective	35 patients who underwent Y90-radioembolization for secondary-progressive liver metastases from solid tumours (20 colorectal, 13 breast, 1 pharyngeal, 1 unknown)	FDG PET/CT	DW-MRI	Serological data, clinical and imaging follow-up	**Early response assessment** Sens: 65%* PPV: 88% NPV: 56%	**Early response assessment** Sens: 96%* PPV: 96% NPV: 92%	NA
Kubota et al, 2015 [110]	Prospective	560 patients (208 lung cancer, 126	FDG PET or PET/CT	No FDG PET or PET/CT	Parameters for management strategy	NA	NA	Modifications of the management strategy based on PET or PET/CT findings

Citation	Study Type	Population	PET Type	Conventional Intervention	Reference Standard	Diagnostic Accuracy (PET)	Diagnostic Accuracy (Conventional)	Change in Patient Management
		breast cancer, 82 CRC, 23 head and neck cancer, 50 malignant lymphoma, 3 brain tumour, 20 pancreas cancer, 7 malignant melanoma, 41 cancer of unknown origin)			evaluation			were made in 71.6% (149/208) of lung cancer patients, 44.4% (56/126) of breast cancer patients, 75.6% (62/82) of CRC patients, 65.2% (15/23) of head and neck cancer patients, 70.0% (35/50) of malignant lymphoma patients, 85.0% (17/20) of pancreas cancer patients, and 78.0% (32/41) of patients with cancer of unknown origin.
Ali et al, 2016 [111]	Retrospective	53 patients (20 breast cancer, 12 prostatic carcinoma, 7 bronchogenic carcinoma, 9 lymphoma, 5 colonic carcinoma)	FDG PET/CT	CT	Histopathology, clinical and imaging follow-up	**Osseous metastasis (lesion-based)** Sens: 100% Spec: 80.8% PPV: 98.6% NPV: 100% Accuracy: 98.7%	**Osseous metastasis (lesion-based)** Sens: 93.9% Spec: 34.6% PPV: 95.2% NPV: 29.0% Accuracy: 89.9%	NA
Ali et al, 2016 [112]	Retrospective	82 patients (27 breast cancer, 23 bronchogenic carcinoma, 12 colon cancer, 8 pancreatic carcinoma, 7 ovarian carcinoma, 5 malignant mesothelioma)	FDG PET/CT	CT	Histopathology, clinical and imaging follow-up	**Hepatic metastasis (lesion-based)** Sens: 98% Spec: 100% PPV: 100% NPV: 84% Accuracy: 98% **(patient-based)** Sens: 99% Spec: 100% PPV: 100% NPV: 90% Accuracy: 99%	**Hepatic metastasis (lesion-based)** Sens: 95% Spec: 81% PPV: 98% NPV: 63% Accuracy: 94% **(patient-based)** Sens: 100% Spec: 56% PPV: 95% NPV: 100% Accuracy: 95%	NA

Abbreviations: +LR: positive likelihood ratio; -LR: negative likelihood ratio; ^{11}C-choline: carbon-11 choline; ^{18}F-choline: fluorine-18 choline; ^{18}F-FLT: fluorine-18 2',3'-dideoxy-3'-fluoro-2-thiothymidine; ^{68}Ga-DOTATATE: gallium-68 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid D-phenyl-1-tyrosine-3-octreotate; ^{68}Ga-DOTATOC: gallium-68 1,4,7,10-tetraazacyclododecane-N,N',N'',N'''-tetraacetic acid D-phenyl-1-tyrosine-3-octreotide; ^{68}Ga-PSMA: gallium-68-labeled prostate-specific membrane antigen ligand with chelator HBED-CC; ^{99m}Tc: technetium-99m; ^{111}In-DTPA-octreotide: indium-111 diethylenetriaminepentaacetic acid octreotide; ^{111}In-pentetreotide: indium-111 pentetreotide; ^{131}I: iodine-131; ABVD: doxorubicin, bleomycin, vinblastine, and dacarbazine combination chemotherapy; AUC: area under the curve; AVD: doxorubicin, vinblastine, and dacarbazine combination chemotherapy; BEACOPP: bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisolone combination chemotherapy; CA125: cancer antigen 125; CA19-9: cancer antigen 19-9; CEA: carcinoembryonic antigen; CeCT: contrast-enhanced computed tomography; Ce-MRI: contrast-enhanced magnetic resonance imaging; CHOP: cyclophosphamide-hydroxydoxorubicin-oncovin-prednisone; CI: confidence interval; CRC: colorectal cancer; CT: computed tomography; Deauville: Deauville

response criteria; DFS: disease-free survival; DLBCL: diffuse large B-cell lymphoma; DOR: diagnostic odds ratio; DW-MRI: diffusion-weighted magnetic resonance imaging; EFS: event-free survival; EORTC: European Organization for Research and Treatment of Cancer response criteria; ERCP: endoscopic retrograde cholangiopancreatography; EUS: endoscopic ultrasonography; EUS-FNA: endoscopic ultrasonography-guided fine-needle aspiration; FDG: fluorodeoxyglucose; FNAB: fine-needle aspiration biopsy; FNAC: fine-needle aspiration cytology; GEP: gastroenteropancreatic; GI: gastrointestinal; HD-ESI: high-density electric source imaging; HL: Hodgkin lymphoma; HPV: human papillomavirus; HR: hazard ratio; I^2: inconsistency index; IDC: infiltrating ductal carcinoma; IHP: International Harmonization Project response criteria; ILC: infiltrating lobular carcinoma; LND: lymph node dissection; MDP: methylene diphosphonate; MIBI: methoxyisobutylisonitrile; MPUS: multiparametric ultrasonography; MRI: magnetic resonance imaging; MRS: magnetic resonance spectroscopy; NA: not applicable/not available; NAC: neoadjuvant chemotherapy; ncCT: non-contrast-enhanced computed tomography; NET: neuroendocrine tumour; NHL: non-Hodgkin lymphoma; NPV: negative predictive value; NSCLC: non-small cell lung cancer; OR: odds ratio; OS: overall survival; pCR: pathological complete response; PERCIST 1.0: Positron-Emission tomography Response Criteria in Solid Tumours, version 1.0; PET: positron emission tomography; PFS: progression-free survival; PPV: positive predictive value; PRRT: peptide receptor radionuclide treatment; Q test: Cochran Q statistic; R-CHOP: rituximab-cyclophosphamide-hydroxydoxorubicin-oncovin-prednisone; RCT: randomized controlled trial; R-EPOCH: rituximab-etoposide-prednisone-vincristine-cyclophosphamide-doxorubicin; RNU: radical nephroureterectomy; SCLC: small cell lung cancer; Sens: sensitivity; SLN: sentinel lymph node; Spec: specificity; SPECT: single photon emission computed tomography; SUV: standardized uptake value; SWE: shear-wave elastography; TRTE: transrectal real-time elastosonography; US: ultrasound; WBS-SPECT: whole-body scan single photon emission computed tomography; Y90: yttrium-90

*$p<0.05$