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PET Six-Month Monitoring Report 2010-1

Evidence from Primary Studies and Systematic Reviews and Recommendations from Clinical Practice Guidelines January to June 2010

A. Raifu and the Program in Evidence-based Care Disease Site Group Reviewers

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

Report Date: April 15, 2011

The complete PET Six-Month Monitoring Report consists of a Summary and a Full Report

For further information about this report, please contact:

Sarah Henderson, Program in Evidence-Based Care
Phone: 905-527-4322 ext. 42822 Fax: 905 526-6775 E-mail: ccopgi@mcmaster.ca

For information about the PEBC and the most current version of all reports, please visit the CCO Web site at http://www.cancercare.on.ca/ or contact the PEBC office at:
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SUMMARY

Question

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

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

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

Target Population

The target population for this report is adult patients with suspected or diagnosed cancer(s) (The cancer is not limited to those cancers with approved or Ontario Health Insurance (OHIP)-insured services).

Methods

Full articles and abstracts published between January 1, 2010 and June 31, 2010 were systematically searched through MEDLINE and EMBASE for evidence from primary studies and systematic reviews (see Appendix 1 and 2, respectively). The search strategies used are available on request from the PEBC. In addition, clinical practice guidelines published in 2010 were also searched for with the search terms "PET" and "positron emission tomography" through the National Guidelines Clearinghouse (http://www.guideline.gov/) and the SAGE Inventory of Cancer Guidelines (http://www.cancerguidelines.ca/Guidelines/inventory/index.php) databases.

Results

Thirty-two primary studies and five systematic reviews were extracted from the search. Two of the primary studies are randomized clinical trials (RCT). There were also two non-randomized controlled trials (NRCT), 16 prospective cohort studies, one case-control study, and 14 retrospective studies. Ten clinical practice guidelines were extracted from the two databases.

Funding

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FULL REPORT

QUESTION

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The 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 the Committee with regular updates of recently published literature reporting on the use of PET in cancer patients. 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 report is the first of what will be a series of 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 and abstracts published between January and June 2010 were systematically searched through MEDLINE and EMBASE for evidence from primary studies and systematic reviews (see Appendix 1 and 2, respectively). The search strategies used are available on request to the PEBC. In addition, clinical practice guidelines published in 2010 were also searched for in the National Guidelines Clearinghouse (NGC) (http://www.guideline.gov/) and the SAGE Inventory of Cancer Guidelines (http://www.cancerguidelines.ca/Guidelines/inventory/index.php) databases.

Inclusion Criteria for Clinical Practice Guidelines

Any clinical practice guideline that contained recommendations with respect to PET was included.

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 Fludeoxy-glucose (FDG) PET in cancer in humans
2. Published as a full article in a peer review journal
3. Reported evidence related to change in patient clinical management, or clinical outcomes
4. Used a suitable reference standard (i.e., pathological and clinical follow-up) when appropriate
5. Were one of the following (1):
   - Randomized controlled trial (RCT)
   - Quasi-randomized controlled trial (Q-RCT)
   - Non-randomized controlled trial (NRCT)

- Historically controlled trial (HCT)
- Controlled before and after study (CBA)
- Prospective cohort study (PCS)
- Nested case-control study (NCC)
- Case-control study (CC)
- Retrospective study (RCS)

6. Included 12 or more patients for the prospective study or 50 or more patients for the retrospective study of the cancer of interest

Inclusion Criteria for systematic reviews

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

Exclusion Criteria

1. Pediatric studies
2. Letters and editorials.
3. Studies of non-FDG PET

RESULTS

Literature Search Results

Primary Studies and Systematic Reviews

Thirty-two primary studies met the inclusion criteria. Of the 32 primary studies, there are two RCTs, two NRCTs, one case-control, 16 prospective cohort, and 14 retrospective studies. Appendix 3 contains a summary of the evidence from the 32 studies. Five systematic reviews (1-5) met the inclusion criteria. Each of these five systematic reviews conducted a meta-analysis to pool the results from their selected studies.

Lymphoma

The Poulou et al (1) systematic review contains 16 studies that measured the overall prognostic value of a pretransplant PET scan in patients with lymphoma. Progression-free (PFS) and overall survival (OS) were the outcomes of interest. The summary hazard ratio (HR) was 3.23 (95% confidence interval (CI), 2.14 to 4.87) for seven studies and 4.53 (95% CI, 2.50 to 8.22) for another six studies included in the 16 studies. The summary HR of greater than 1 suggests a worse PFS and OS (i.e., greater probability of the event) for patients with positive PET scans compared to patients with negative PET scans.

Esophageal Cancer

The remaining four systematic studies (2-5) evaluated the diagnostic value of PET. The Kwee et al (2) systematic review includes 20 studies. The purpose of the review (2) was to evaluate the diagnostic performance of PET in the prediction of tumour response to neoadjuvant therapy in patients with esophageal cancer. The sensitivity and specificity of FDG PET in the included 20 studies ranged from 33% to 100% and 30% to 100%, respectively. The summary estimate sensitivity and specificity were 67% (95% CI, 62% to 72%) and 68% (95% CI, 64% to 73%), respectively.

Cutaneous Melanoma

Twenty-four studies were included in the Jimenez-Requena et al (3) systematic review that evaluated the performance of PET in the staging and restaging of cutaneous melanoma. Fifteen of the 24 studies reported the sensitivity and specificity of PET in the regional staging of melanoma, which ranged from 0% to 100% and 17% to 100%, respectively. For the detection of melanoma metastases, 15 studies reported the sensitivity and specificity of PET as ranging from 4% to 100% and 44% to 98%, respectively.

Non-Small Cell Lung Cancer

The systematic review by Rebollo-Aguirre et al (4) was aimed at induction therapy response assessment with PET in patients with non-small cell lung cancer (NSCLC). The review identified nine PET studies with a sensitivity and specificity ranging from 80% to 100% and 0% to 100%, respectively. The overall summary estimated the sensitivity and specificity at 63.8% (95% CI, 53.3% to 73.7%) and 85.3% (95% CI, 80.4% to 89.4%). The pooled estimated positive likelihood ratio for the detection of distant metastases in three studies was 5.86 (95% CI, 3.64 to 9.43), and the diagnostic odds ratio for the detection of regional metastases in the same three studies was 37.89 (95% CI, 15.80 to 90.86). The overall summary estimated the negative likelihood of the detection of distant metastases in six studies to be 0.15 (95% CI, 0.10 to 0.21).

Cervical Cancer

The purpose of the Kang et al (5) systematic review was to assess the diagnostic performance of PET in detecting paraaortic lymph node (PALN) metastases in patients with cervical cancer. The summary estimated sensitivity and specificity of PET in the 10 studies included the review was 34% (95% CI, 10% to 72%) and 97% (95% CI, 93% to 99%), respectively. The low estimated sensitivity was attributed to heterogeneity, with suspected partial verification bias in studies with low prevalence. The pooled estimated positive and negative likelihood ratio were 12.49 (95% CI, 4.64 to 33.62) and 0.68 (95% CI, 0.40 to 1.15), respectively, with a diagnostic odds ratio of 18.49 (95% CI, 4.72 to 72.43).

Clinical Practice Guidelines

Ten clinical practice guidelines were retrieved from the NGC and SAGE databases. None were dedicated PET guidelines, but each contains at least one recommendation on the use of PET imaging in cancer. The identified clinical practice guidelines with their respective recommendations on PET are presented in Table 1.

Table 1. Identified guidelines and their corresponding recommendation on PET.

Author	Guideline	Title	Location	Recommendation
Lung Cancer				
Crino et al, 2010 (38)	ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up	Early stage and locally advanced (non-metastatic) non-small cell lung cancer	Page 104	Lung cancer screen and staging: Patients amenable for radical surgery with curative intent are recommended for PET scanning. When there are abnormal results on PET scan with mediastinal lymph node enlargement, a biopsy of mediastinal lymph node is recommended, through different invasive techniques for confirmation of the N2–N3 node status such as mediastinoscopy BNA, EBUS-NA.
Breast Cancer				
Carlson et al, 2011	NCCN Guidelines Version 2	NCCN Clinical Practice Guidelines in Oncology:	Page 72 (MS-9)	The panel did not recommend the use of PET for stage I, stage II or T3N1M0 due to high

Author	Guideline	Title	Location	Recommendation
(39)		Breast Cancer		false-negative rate detection of small lesion.
Cervical Cancer				
Greer et al, 2011 (40)	NCCN Guidelines Version 1	NCCN Clinical Practice Guidelines in Oncology: Cervical Cancer	Page 33 (MS-11)	CT, MRI or combined PET-CT is recommended for optimum staging of patients with stage IB2, IIA2 or advanced-stage tumours.
Colon Cancer				
Engstrom et al, 2011 (41)	NCCN Guidelines Version 2	NCCN Clinical Practice Guidelines in Oncology: Colon Cancer	Page 42 (MS-5)	Invasive nonmetastatic colon cancer: The panel consensus was that PET-CT scan should not be done routinely and should not be done as a matter of general surveillance. PET-CT scan does not obviate the need for a contrast-enhanced diagnostic CT scan. PET-CT scan is not recommended for assessment of sub-centimetre lesions since they are routinely below the level of PET detection. Synchronous metastatic disease: PET-CT scan is not recommended for routine scanning, baseline imaging, or follow-up but preoperative PET-CT scan at baseline is recommended only if prior anatomic imaging indicates the presence of potentially surgically curable M1 disease. Metachronous metastatic disease: PET-CT is not recommended for routine monitoring of disease recurrence. PET-CT scans are not recommended to be used for routine monitoring of the progression of metastatic disease. Post-treatment surveillance: PET-CT scans are not recommended and should not be used routinely as pre-operative baseline study or surveillance. PET-CT is not recommended for post-treatment surveillance of patients with resected early-stage colorectal cancer. PET-CT is not recommended to be routinely used to detect metastatic disease in the absence of other evidence of such disease.
Hodgkin Lymphoma				
Hoppe et al, 2010 (42)	NCCN Guidelines Version 2	NCCN Clinical Practice Guidelines in Oncology: Hodgkin Lymphoma	Page 29 (MS-4) Page 40 (MS-15) Page 43 (MS-18)	PET scans are recommended for initial staging of patients with lymphoma and Hodgkin lymphoma, and for evaluating residual masses at the end of treatment. PET scans are also recommended to define the extent of disease if CT scan is equivocal. PET scans are not recommended for routine surveillance due to the risk of false-positives. PET scans are recommended for evaluating initial staging and treatment response assessment at restaging.
Melanoma				
Coit et al, 2011 (43)	NCCN Guidelines Version 1	NCCN Clinical Practice Guidelines in Oncology: Melanoma	Page 29 (MS-5)	Routine cross-sectional imaging (CT, PET, MRI) is not recommended for patients with localized melanoma.

Author	Guideline	Title	Location	Recommendation
			Page 38 (MS-14)	Chest X-ray, CT, MRI, and/or PET/CT can be considered to screen for recurrent or metastatic disease at the discretion of the physician
			Page 39 (MS-15)	Chest X-ray, CT, and/or PET/CT or MRI should be considered for staging and to evaluate specific signs or symptoms for a local recurrence after adequate prior wide excision
Non-Small Cell Lung Cancer				
Ettinger et al, 2011 (44)	NCCN Guidelines Version 3	NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer	Page 32 (NSCL -C - 3 of 7)	PET-CT is highly recommended for the treatment plan especially in cases with significant atelectasis and when IV contrast is contraindicated.
			Page 68 (MS-2)	Surveillance and treatment of recurrences and metastases: PET or brain MRI is not indicated for routine follow-up
Occult Primary (Cancer of Unknown Primary)				
Ettinger et al, 2011 (45)	NCCN Guidelines Version 2	NCCN Clinical Practice Guidelines in Oncology: Occult Primary (Cancer of Unknown Primary)	Page 38 (MS-8)	Initial evaluation: PET is not recommended for routine screening except in some cases where local or regional therapy is considered (category 2B recommendation).
Rectal Cancer				
Engstrom et al, 2011 (46)	NCCN Guidelines Version 3	NCCN Clinical Practice Guidelines in Oncology: Rectal Cancer	Page 43 (MS-6)	Clinical evaluation/Staging: PET is not routinely indicated at baseline.
			Page 54 (MS-17)	Treatment of Metachronous metastases: PET-CT scanning is not recommended for routine monitoring of disease recurrence.
			Page 55 (MS-18)	PET-CT scans are not recommended for routine monitoring of metastatic disease progression. PET-CT is not recommended and should not be obtained either as a routine pre-operative baseline study or for routine surveillance.
			Page 56 (MS-19)	PET-CT is not recommended for post-treatment surveillance of patients with resected early-stage colorectal cancer. PET-CT is not recommended to be routinely detecting metastatic disease in the absence of other evidence of such disease.
Penile Cancer				
Pizzocaro et al, 2010 (47)	EAU Guidelines	EAU Guidelines on Penile Cancer		Regional metastases: A pelvic PET/CT scan is indicated in patients with metastatic inguinal nodes (Grade of recommendation: C). Distant metastases: PET-CT scan also allows evidence of distant metastasis (Grade of recommendation: C). If PET-CT is not available, abdominal CT scan and chest X-ray are advisable, and in symptomatic M1 patients, a bone scan is also advisable (Grade of recommendation: C).

NCCN: National Comprehensive Cancer Network; ESMO: European Society for Medical Oncology; EAU: European Association of Urology

Disease Site Group Reviews
Note: for 2010, all the DSG reviews can be found in the *Six-Month Monitoring Report 2010-2*.

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Appendix 1. MEDLINE search strategy.

1. Tomography, Emission-Computed/ or (positron adj emission adj tomography).ti,ab. or PET.ti,ab. or PET-FDG.ti,ab. or Fluorodeoxyglucose F18/ or 18f fluorodeoxyglucose.ti,ab. or 18f fluorodeoxyglucose.ti,ab. or 18fdg.ti,ab. or 2-fluoro-2-deoxy-d-glucose.ti,ab. or 2-fluoro-2-deoxyglucose.ti,ab. or 18f-fdg.ti,ab. or fluorine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or flourine-18-fluorodeoxyglucose.ti,ab. or flourine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluordeoxyglucose.ti,ab. or positron emission tomography/ or PET-CT.ti,ab. or PET$CT.ti,ab.
2. deoxyglucose/ or deoxyglucose.ti,ab. or desoxyglucose.ti,ab. or desoxy-glucose.ti,ab. or desoxy-d-glucose.ti,ab. or deoxy-d-glucose.ti,ab. or 2deoxyglucose.ti,ab. or 2deoxy-d-glucose.ti,ab. or fluorodeoxyglucose.ti,ab. or fluorodesoxyglucose.ti,ab. or fludeoxyglucose.ti,ab. or fluordeoxyglucose.ti,ab. or fluodeoxyglucose.ti,ab. or fluordesoxyglucose.ti,ab. or 18fluorodeoxyglucose.ti,ab. or 18fluorodesoxyglucose.ti,ab. or fdg$.ti,ab. or 18fdg$.ti,ab. or 18f-dg$.ti,ab.
3. (fluor or 2fluor$ or fluoro or flouro or fluorodeoxy or fludeoxy or flourodeoxy or fluorine or 18f or 18flu$ or 18fluo$).ti,ab.
4. glucose.ti,ab.
5. (pet or petscan$ or pet ct).ti,ab.
6. Tomography, Emission-Computed/
7. emission.ti,ab.
8. (tomograph or tomographs or tomographic$ or tomogrpahy or tomographies).ti,ab.
9. 7 and 8
10. 5 or 6 or 9
11. 3 and 4
12. 2 or 11
13. 10 and 12
14. exp neoplasm/ or neoplasm staging/ or cancer$.ti,ab. or tumor$.ti,ab. or tumour$.ti,ab. or carcinoma$.ti,ab. or neoplasm$.ti,ab. or staging.ti,ab. or metastas$.ti,ab. or metastatic.ti,ab. or exp neoplasm metastasis/ or exp neoplastic processes/ or neoplastic process$.ti,ab. or adenocarcinoma$.ti,ab.
15. 1 and 14
16. 13 and 14
17. 15 or 16
18. limit 17 to (human and english language and yr="2010")
19. (comment or editorial or letter or case reports).pt.
20. 18 not 19
21. (integrative research review$ or research integration or (methodologic$ adj10 review$) or (methodologic$ adj10 overview$) or (quantitativ$ adj10 review$) or (quantitativ$ adj10 overview$) or (quantitativ$ adj10 synthes$) or (systematic adj10 review$) or (systematic adj10 overview$) or (metaanal or meta anal$)).ti,ab. or meta-analysis/
22. (review-tutorial or review-academic or review).pt. or (pooling or pooled analys$ or mantel heanszel$).ti,ab.
23. (peto$ or der simonian or dersimonian or fixed effect$).ti,ab.
24. 21 or 22
25. 20 and 24
26. 20 not 24
27. (conference or conference proceeding or conference proceeding$ or conference paper or conference paper$ or discussion or discussion$ or in brief or invited comment or invited comment$).ti,ab.
28. 25 not 27
29. 26 not 27
30. (201001: or 201002: or 201003: or 201004: or 201005: or "201006").ed.
31. 28 and 30
32. 29 and 30

Appendix 2. EMBASE search strategy.

1. Tomography, Emission-Computed/ or (positron adj emission adj tomography).ti,ab. or PET.ti,ab. or PET-FDG.ti,ab. or Fluorodeoxyglucose F18/ or 18f fluorodeoxyglucose.ti,ab. or 18f fluorodeoxyglucose.ti,ab. or 18fdg.ti,ab. or 2-fluoro-2-deoxy-d-glucose.ti,ab. or 2-fluoro-2-deoxyglucose.ti,ab. or 18f-fdg.ti,ab. or fluorine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluorodeoxyglucose.ti,ab. or flourine-18-fluorodeoxyglucose.ti,ab. or flourine-18-flourodeoxyglucose.ti,ab. or fluorine-18-fluordeoxyglucose.ti,ab. or positron emission tomography/ or PET-CT.ti,ab. or PET$CT.ti,ab.
2. deoxyglucose/ or deoxyglucose.ti,ab. or desoxyglucose.ti,ab. or desoxy-glucose.ti,ab. or desoxy-d-glucose.ti,ab. or deoxy-d-glucose.ti,ab. or 2deoxyglucose.ti,ab. or 2deoxy-d-glucose.ti,ab. or fluorodeoxyglucose.ti,ab. or fluorodesoxyglucose.ti,ab. or fludeoxyglucose.ti,ab. or fluordeoxyglucose.ti,ab. or fluodeoxyglucose.ti,ab. or fluordesoxyglucose.ti,ab. or 18fluorodeoxyglucose.ti,ab. or 18fluorodesoxyglucose.ti,ab. or fdg$.ti,ab. or 18fdg$.ti,ab. or 18f-dg$.ti,ab.
3. (fluor or 2fluor$ or fluoro or flouro or fluorodeoxy or fludeoxy or flourodeoxy or fluorine or 18f or 18flu$ or 18fluo$).ti,ab.
4. glucose.ti,ab.
5. (pet or petscan$ or pet ct).ti,ab.
6. Tomography, Emission-Computed/
7. emission.ti,ab.
8. (tomograph or tomographs or tomographic$ or tomogrpahy or tomographies).ti,ab.
9. 7 and 8
10. 5 or 6 or 9
11. 3 and 4
12. 2 or 11
13. 10 and 12
14. exp neoplasm/ or neoplasm staging/ or cancer$.ti,ab. or tumor$.ti,ab. or tumour$.ti,ab. or carcinoma$.ti,ab. or neoplasm$.ti,ab. or staging.ti,ab. or metastas$.ti,ab. or metastatic.ti,ab. or exp neoplasm metastasis/ or exp neoplastic processes/ or neoplastic process$.ti,ab. or adenocarcinoma$.ti,ab.
15. 1 and 14
16. 13 and 14
17. 15 or 16
18. limit 17 to (human and english language and yr="2010" and em=201001-201026)
19. (comment or editorial or letter or case reports).pt.
20. 18 not 19
21. (integrative research review$ or research integration or (methodologic$ adj10 review$) or (methodologic$ adj10 overview$) or (quantitativ$ adj10 review$) or (quantitativ$ adj10 overview$) or (quantitativ$ adj10 synthes$) or (systematic adj10 review$) or (systematic adj10 overview$) or (metaanal or meta anal$)).ti,ab. or meta-analysis/
22. (review-tutorial or review-academic or review).pt. or (pooling or pooled analys$ or mantel heanszel$).ti,ab.
23. (peto$ or der simonian or dersimonian or fixed effect$).ti,ab.
24. 21 or 22
25. 20 and 24
26. 20 not 24
27. (conference or conference proceeding or conference proceeding$ or conference paper or conference paper$ or discussion or discussion$ or in brief or invited comment or invited comment$).ti,ab.
28. 25 not 27
29. 29. 26 not 27

Appendix 3. Summary of primary studies evidence for PET 6-month monitoring between January to June 2010.

Author, year	Objective	# of pts	PET study type	Reference Test	Compari-son Test	Results	Conclusions
Anal cancer							
Kidd et al 2010 (6)	To evaluate anal cancer uptake of FDG measured as the maximum SUVmax by PET and its correlation with prognostic factors.	77	PCS	Histology and clinical follow-up	Not Reported	Median follow-up was 24.2 mos (range: 4.9 to 59.3 mos). At last follow-up, 59 pts were alive with no disease, 7 alive with disease, 8 died of the disease, 2 died of other causes, and 1 died of toxicity treatment. There was no statistically significant relationship between clinical tumour size and SUVmax. Disease-free survival was significantly worse for pts with SUVmax ≥ 5.6 (p=0.05) and higher SUVmax was not associated with worse cause-specific survival (p not significant)	SUVmax is a valuable biomarker of anal cancer prognosis, predicting increased risk of lymph node metastasis and worse disease-free survival.
Breast cancer							
Aukema et al 2010 (7)	To evaluate the impact of FDG PET/CT on clinical management in patients with locoregional breast cancer recurrence amenable for locoregional treatment and to compare the PET/CT results with the conventional imaging data.	56	RCS	Histopath	MRI, CT, Liver ultrasound, and bone scint	The median time to recurrence was 4.0 years (range: 0.4 to 17.8 years). FDG PET/CT findings changed the management of 27 pts (48%) out of 56 clinically eligible pts for curative surgery of the local recurrence. 21 of the 27 pts received all conventional imaging modalities while 6 had partial conventional imaging. Palliative chemotherapy was started in 20 pts, these pts were not treated with surgery of the local recurrence. Radiotherapy only was given to 3 pts. Three pts underwent neo-adjuvant chemotherapy prior to surgery, and in 1 pt a contralateral axillary lymph node dissection was performed. In 5 pts, new lesions detected by PET/CT did not affect clinical management.	FDG PET/CT, which adjusted clinical management in almost half of the pts in these series, plays an important role in the staging of pts with confirmed locoregional breast cancer recurrence. FDG PET/CT could potentially replace conventional staging imaging in patients with a locoregional breast cancer recurrence, and thus spare a significant proportion extensive but futile local treatment.
Jung et al, 2010 (8)	To evaluate the usefulness of serial FDG PET in potentially operable breast cancer with neoadjuvant chemotherapy	66	RCT	Histopath and clinical follow-up	PET assessed among pts randomized into 2 treatment arms (AC vs. TX)	Median follow-up was 61.5 (range: 13.5 to 71.8) mos. The pCR rate of the TX group was higher than that of AC but no statistically significance. The reduction of the primary tumour SUVp was more significant in those whose disease showed clinical response than those whose disease did not respond to therapy (78.0% ± 21.0% vs. 21.0% ± 22.7%, P<.001) as well as in the pCR group than the non-pCR group (89.2% ± 11.1% vs. 66.9% ± 29.6%, P<.001). The 5-year DFS rate was higher in patients who achieved primary tumour and axillary lymph node pCR than those who did not, although the difference did not reach statistical significance (100% vs. 82.1% in primary tumour; p=0.18; and 94.7% vs. 80.9% in axillary lymph node; p=0.15).	The SUVp reduction rate (RR) in FDG-PET is correlated with clinical and pathological responses. Moreover, it may serve as a prognostic factor in breast cancer patients who receive neoadjuvant chemotherapy when FDG-PET scans are taken both at baseline and at the completion of four cycles of chemotherapy.
Martoni et al, 2010 (9)	To investigate the value of FDG PET scan monitoring to predict	34	PCS	Histology and clinical follow-up	MRI and CT	PET at baseline: Baseline SUVmax in all patients was abnormal with median SUVmax of 9.6 (range: 2.5 to 23). Baseline PET study changed the clinical stage in	The current study confirmed that the early evaluation of metabolic response by FDG-PET monitoring during PCT for breast cancer correlates

Author, year	Objective	# of pts	PET study type	Reference Test	Compari-son Test	Results	Conclusions
	the pathologic response after PCT with particular attention to the optimal timing of early evaluation and its correlation with the standard biopathologic tumour profile.					6 pts. No statistically significant difference between the baseline SUVmax of pathologic responders (pR) pNR with p=0.41. Metabolic response: The mean percentage change in SUVmax was greater in patients who had a pR than those with pNR throughout the period of PET monitoring but with no statistically significant difference. PET predicted that 6 of 16 individual pts who had estrogen receptor (ER)-positive/human epidermal growth factor2 receptor (HER2)-negative tumour would obtain a pNR.	with the pathologic response documented at the time of surgery. However, such evaluation does not appear to be useful in selectively identifying those patients who will achieve an optimal pathologic response (pCR or pathologic minimal residual disease pMRD) because of the high number of false-positive results. Conversely, FDG-PET individually was able to identify 30% of patients who would not have an optimal pathologic response. It is noteworthy that this predictive power is limited only to ER-positive tumours, an observation that warrants further study in a larger patient series. If these findings are confirmed, then FDG-PET performed at baseline and after 2 cycles of PCT could supply important information to be used in the decision-making process.
Cervical cancer							
Chou et al, 2010 (10)	To assess the value of PET in the management of cervical adenocarcinoma/adenosquamous carcinoma (AC/ASC).	83	RCS	Histopath	MRI	The 5-year overall survival was 85.5% in our series (IB/IIA 89.8%, IIB 62.9%). FIGO stage IIB, Pelvic lymph node (PLN) metastasis, deep cervical stromal invasion, tumour size measured on MRI ≥40 mm and SUVmax of primary tumour >5.3 were associated with poor 5-year overall survival. The SUVmax cut-off value of primary tumour as determined by ROC curve was 5.3. The 5-year overall survival of cervical cancer patients with tumour SUVmax ≤5.3 was 100% and of those with SUVmax >5.3 was 77.2% (p=0.020).	PET or PET/CT provided significantly better diagnostic efficacy than MRI in detecting PALN metastasis. SUVmax of primary cervical tumour >5.3, stage IIB, deep cervical stromal invasion, tumour size measured on MRI ≥40 mm and PLN metastasis were significant poor prognostic factors.
Kidd et al, 2010 (11)	To evaluate the prognostic significance of the maximum standardized uptake value (SUVmax) FDG as measured by PET in pelvic lymph nodes in patients with cervical cancer.	83	PCS	Histopath	CT	The SUVmax of pelvic lymph node (SUV_{PLN}) was found to be correlated with response on the 3-mo post-treatment FDG-PET scan. The SUV_{PLN} was correlated with the risk of having persistent disease (p=0.0025) and specifically with the risk of having persistent disease in pelvic lymph nodes (p= 0.0003). Eighty-two percent of patients with evidence of persistent disease in the pelvic lymph nodes on their post-treatment FDG-PET scan eventually demonstrated evidence of a pelvic disease recurrence. The SUV_{PLN} was predictive of an increased risk of ever developing a pelvic disease recurrence (p=0.0035). The actuarial risk of pelvic disease recurrence was significantly higher for patients with an elevated SUV_{PLN} (p=0.0092. For this group of patients, the risk of pelvic disease recurrence was not found to be significantly correlated with the SUVmax of cervical tumour (SUV_{cervix}) with p=0.1774.	The findings of the current study have important implications for the management of patients with cervical cancer; in particular, these results suggest that patients with highly FDG-avid pelvic lymph nodes should be closely monitored after treatment with concurrent chemoradiation. Moreover, the finding of persistent pelvic lymph node disease after standard therapy in such patients may warrant additional intervention given the high risk of pelvic disease recurrence. The results of the current study, together with the other FDG-PET–based prognostic factors, could have significant implications in translational research.
Kidd et al, 2010 (12)	To evaluate the frequency, pattern of	560	PCS	Histopath and clinical	CT	At the time of last follow-up, the disease status for the outcome group included 317 patients with no	In this study, it is shown that the frequency and pattern of cervical cancer lymph node metastasis

Author, year	Objective	# of pts	PET study type	Reference Test	Compari-son Test	Results	Conclusions
	spread, and prognostic significance of lymph node metastasis for pts with cervical cancer.			follow-up		evidence of disease, 38 alive with disease, 32 dead of intercurrent disease, seven dead from treatment-related toxicity, and 119 dead of disease. There was significant association between lymph node metastasis on PET and worse disease-specific survival. The risk of disease recurrence increased incrementally based on the most distant level of FDG-PET lymph node involvement, with a hazard ratio of 2.40 (95% CI, 1.63 to 3.52) for pelvic, 5.88 (95% CI, 3.80 to 9.09) for para-aortic, and 30.27 (95% CI, 16.56 to 55.34) for supraclavicular involvement. Disease-specific survival for cervical cancer also showed a progressive worsening based on the most distant level of lymph node involvement.	on FDG PET is influenced by FIGO stage and parallel historical surgical data. PET reliably and efficiently determines cervical cancer lymph node involvement noninvasively in the pretreatment setting. FDG-PET lymph node staging stratifies patient outcome within their stage groupings. Independent of clinical stage, FDG-PET lymph node staging divides patients into distinct disease-specific survival groups. Additionally, PET lymph node staging quantifies the relative risk of recurrence and death from cervical cancer. These results will likely have important implications for management of cervical cancer patients with lymph node metastasis on FDG PET.
Kidd et al, 2010 (13)	To evaluate the toxicity and clinical outcomes for cervical cancer patients treated definitively with intensity-modulated radiation therapy (IMRT) compared with non-IMRT treatment.	452	PCS	Histopath	CT	Any persistent or new disease found on FDG PET correlated with overall recurrence risk ($P < 0.0001$) and cause-specific survival (p=0.0001) in all patients. There was no significant difference in post-therapy FDG PET findings between IMRT and non-IMRT patients (p=0.9774). The difference in recurrence-free survival between the two groups is not statistically significant (p=0.0738). The overall cause-specific survival and overall survival are better in IMRT. There is significant difference in the cumulative hazard function rates for the development of bowel or bladder complications for the IMRT and non-IMRT groups (p=0.0351).	This study shows the feasibility of cervical cancer IMRT with the incorporation of FDG-PET information for treatment planning, and demonstrates that PET-guided IMRT significantly decreases toxicity while maintaining disease control. These valuable findings could encourage the next transition in treating cervical cancer, expanding the use of FDG-PET-guided IMRT and thereby decreasing treatment-related toxicity.
Small et al, 2010 (14)	To evaluate the use of lymphangiogram, CT, MRI, and PET imaging of lymph node metastasis in patients receiving definitive chemoradiotherapy for cervical cancer.	20	PCS NRCT	Histopath	lymphangio gram, CT, MRI	Agreement between imaging was most consistent in the common iliacs ($P = 0.001$) and least in the para-aortic region (p=0.41). Disease-free survival (DFS) at 1 year was statistically associated with positive PET imaging (25%) compared with negative PET imaging (86%) p=0.033) in the common iliac lymph node region. No other single lymph node region in any modality was significantly associated with survival. One-year DFS in patients with any positive areas on PET imaging was 50% compared with 90% in patients with negative PET imaging (p=0.02). Seven patients were noted to have no metastasis in any region by all 3 of the imaging modalities; the 1-year DFS in these 7 patients was 100% compared with 59% in the 13 patients with any positive nodal area (p=0.05).	The presence of lymphadenopathy on PET imaging was associated with poorer outcome and reduced DFS. PET imaging is a critical component of the nonsurgical evaluation of cervical cancer patients undergoing definitive radiotherapy.

Author, year	Objective	# of pts	PET study type	Reference Test	Compari-son Test	Results	Conclusions
Tsai et al, 2010 (15)	To determine the possible impact of FDG PET on extrapelvic metastasis detection, radiation field design, and survival outcome for cervical cancer pts with enlarged pelvic nodes on MRI image.	129	RCT	NR	MRI	The 4-year overall survival rates were 79% and 85% (p=0.65) for the PET and the control groups, respectively. The corresponding figures for disease-free survival were 75% and 77% (p=0.64), and for distant metastasis-free survival they were 82% and 78% (p=0.83), respectively. If the 7 patients with extrapelvic metastasis were excluded, there was still no significant difference in overall survival between patients with negative extrapelvic metastasis on PET (59 patients) and those in the control group.	Pretreatment FDG-PET can improve the detection of extrapelvic metastasis, mainly PALN, and help select patients for extended-field concurrent chemoradiation therapy. The addition of FDG-PET did not translate into a survival benefit, as we had expected, although the relatively low detection rate of extrapelvic lesions in this trial (11% vs. 26% in our pilot study) and the insufficient number of cases might be the culprit.+
Colorectal cancer							
Glazer et al, 2010 (16)	To determine the accuracy of PET scans to detect residual viable colorectal cancer liver metastases after a significant response to systemic chemotherapy.	224	Case control	Histopath	CT, MRI, Ultrason	Over 85% of the pts had a reduction of greater than 25% in hepatic tumour burden after chemotherapy according to multimodality imaging results. The following group of pts had greater than 50% reduction in their metastasis according to pathologically confirmed radiologic response. Complete (>90%): 3 pts (3.4%) Major (>50 to 90%): 35 pts (40.2%) Minor (25 to 50%): 37 pts (42.5%) None (< 25%): 12 pts (13.8%). Based on these selected group of pts, there was 93.5% survival rate with median follow-up of 15 mos (range: 1 week to 6 years)., median time to death after the first 90 days (n =7) was 9.4 mos (range: 6.5 to 48.3 mos). There was a single perioperative death (at 1 week) and another death during the first 90 days for a total 90-day mortality rate of 1.4%.	Positron emission tomography within 4 weeks of chemotherapy is not a useful test for evaluation of colorectal hepatic metastases. The high rate of false-negative results is likely due to metabolic inhibition caused by chemotherapeutic drugs. We recommend that physicians not use PET in patients recently completing chemotherapy; they should undergo the appropriate oncologic hepatic operation based on the high probability of viable malignant disease.
Esophageal cancer							
Jingu et al, 2010 (17)	To reveal the utility of FDG PET within 7 days after chemoradiotherapy to predict prognosis in patients with postoperative recurrent esophageal cancer.	20	PCS	Histopath	Upper GI endoscopy, Ultrason, CT	The 1-year and 3-year cause-specific survival rates in the 20 pts were 80.0% (95% CI, 62.5–97.5%) and 48.0% (95% CI, 25.6–70.4%), respectively with a median cause-specific survival period of 24.0 mos (95% CI, 3.0–45.0). The 1-year and 3-year local control rates in the 20 patients were 69.1% (95% CI, 48.4–9.7%) and 51.8% (95% CI, 28.9–74.7%), respectively. There was a significant difference between cause-specific survival rates in pts with SUVmax > 2.4 and pts with SUVmax ≤ 2.4 after CRT (3 years, 20% vs. 77.8%; p=0.033). There was also a significant difference between local control rates in pts with SUVmax > 2.4 and pts with SUVmax ≤ 2.4 after CRT (3 years, 23.3% vs. 78.8%; p=0.01). The 1- and 3-year overall survival rates in the 20 pts were 75.0% (95% CI, 56.0–94.0%) and 40.0% (95% CI, 18.5–61.5%), respectively, with a median overall survival period of 23.5 mos (95% CI, 21.3–25.7).	This prospective study showed that FDG-PET after CRT predicts survival prognosis in patients with locoregional postoperative recurrent esophageal cancer. We particularly emphasize that FDG-PET performed even < 7 days after CRT enables prognosis prediction. FDG-PET could be the earliest diagnostic modality for local control and survival prognosis in patients with locoregional postoperative recurrent esophageal cancer.

Author, year	Objective	# of pts	PET study type	Reference Test	Compari-son Test	Results	Conclusions
						SUVmax before and after CRT and SUVD% had no significant correlation with overall survival (p=0.236, 0.11, and 0.858, respectively).	
Gastric lymphoma							
Yi et al, 2010 (18)	To studied the clinical relevance of FDG PET uptake in patients with primary gastric lymphoma who underwent PET/CT	42	PCS	Histopath	CT	35/39 (89.7%) achieved a complete response, 2 pts died due to disease progression and one patient with diffuse large B-cell lymphoma (DLBCL) died due to lymphoma. The estimated two-year overall survival rate for high SUVmax group was 62.3% while 100.0% for low SUVmax in pts with gastric DLBCL.	PET/CT scan can be used in staging patients with primary gastric lymphoma as it has a well-established role in the management of nodal lymphoma in general; however, the residual 18F-FDG uptake observed during follow-up should be interpreted cautiously and should be combined with endoscopy and multiple biopsies of the stomach.
Head and Neck cancer							
Farrag et al, 2010 (19)	To determine if FDG PET uptake assessment during the treatment can be used as a predictive factor for the outcome in a group of head and neck cancer pts treated with radical radiotherapy by tomotherapy ± chemotherapy.	43	PCS	Histopath	NR	Median follow-up (fu) time was 12.7 mos (range: 3 to 34.5 mos). At last fu, 72% of the pts were living and 58% were free from disease. Two-year OS and disease-free survival (DFS) were 66 and 52% respectively. PET1 study: Median SUVmax was 8.11 (range: 2.41 to 15.13). SUVmax was significantly correlated with OS. Two-year OS was 81% for low SUVmax group versus 50% for high SUVmax group (p=0.027). PET 2 study: Median SUVmax was 4.03 (range: 1.94 to 7.58). SUVmax was also significantly correlated with outcome. Two-year OS was significantly better in low SUVmax 82% versus 50% (p=0.026).	Although the number of patients included in this study was relatively small we conclude that 18F-FDG-PET evaluation during treatment is promising and in the future it may help in defining response categories and modifying treatment for non-responders. Our study adds to the very few studies which examined the issue of PET scan during radiotherapy. SUVmax value is more reliable than visual assessment in predicting the treatment outcome.
Inohara et al, 2010 (20)	To evaluate prognostic value of pretreatment and posttreatment FDG Pet in advanced hypoparyngeal carcinoma treated by chemotherapy.	31	PCS	Histopath	CT	Patients showing local partial response (PR) presented significantly higher pretreatment SUVmax than those showing local complete response (CR) (p=0.046). There was no significant difference in pretreatment SUVmax between patients with and without local persistent or recurrent disease (p=0.61). Local control and cause-specific survival were not associated with conventional prognostic factors (T and N categories, and TNM stage). However, there were significant association of posttreatment SUVmax with both local control and cause-specific survival. Pts with high posttreatment SUVmax had significantly poorer local control (HR: 6.96; 95% CI: 2.03 to 23.83; p=0.002) compared with low posttreatment SUVmax. Also, high posttreatment SUVmax pts had poorer cause-specific survival (HR: 9.72; 95% CI: 1.83 to 51.50; p=0.0075).	We conclude that in patients with hypopharyngeal squamous cel carcinoma (SCC) treated by concurrent chemoradiotherapy, retreatment FDG-PET does not serve to predict the response to chemoradiotherapy, whereas posttreatment FDG-PET serves to identify a subset of patients at risk of treatment failure and to predict local control, as well as survival. Patients with high posttreatment FDG uptake may benefit from adjuvant chemotherapy to improve organ preservation and survival. A multi-institutional prospective study is needed to establish the usefulness of FDG-PET in this regard.

Author, year	Objective	# of pts	PET study type	Reference Test	Compari-son Test	Results	Conclusions
Liao et al, 2010 (21)	To investigate whether the combination of clinical information, pathologic results, and preoperative maximal standardized uptake value (SUVmax) at the primary tumour and regional lymph nodes might improve the prognostic stratification in this patient group.	347	PCS	Histopath	CT, MRI	In multivariate analysis, a cutoff SUVtumour-max of 8.6, a cutoff SUVnodal-max of 5.7, and the presence of pathologic lymph node metastases were found to be significant prognosticators for the 5-year DFS. A scoring system using these three prognostic factors was formulated to define distinct prognostic groups. The 5-year rates for patients with a score between 0 and 3 were as follows: neck control, 94%, 86%, 77%, 59% ($p<0.0001$); distant metastases, 1%, 7%, 22%, 47% ($p<0.0001$); disease-specific survival, 93%, 85%, 61%, 36%, respectively ($p<0.0001$).	The combined evaluation of pathologic node status and SUVmax at the primary tumour and regional lymph nodes may improve prognostic stratification in oral cavity squamous cell carcinoma (OSCC) patients, potentially leading to tailor-made, more effective treatments. We are currently planning to conduct a prospective multi-arm clinical trial aiming to assess whether adjuvant therapy would improve survival rates in OSCC patients with p-Stage III to IV disease and a score of 0 or 1. A further randomized trial investigating whether a more intensively therapeutic regimen may improve survival in OSCC patients with p-Stage III to IV disease and a score of 4 is also warranted. Finally, OSCC patients with p-Stage III to IV disease and a score of 2 may be treated following the recommendations of the current guidelines.
Lonneux et al, 2010 (22)	To address the impact of FDG PET on the initial staging and management of pts with head and neck squamous cell carcinoma (HNSCC).	233	Prospec NRCT	Histopath	CT or MRI	PET yielded an accurate stage change in 20% of patients (47 of 233 patients). However, the error rate in TNM staging was 5.6% (13 of 233 patients). No metastatic (M1) disease or second primary tumour was missed by PET. PET results had a low impact in the management of 80.7% (188/233). There was a change in TNM stage in 57 pts where PET was correct in 14 pts, wrong in 11 pts, and unconfirmed in 32 pts. PET impact in management of 12 pts (5.2%) was classified as medium. A change in N classification resulted in modified radiation fields in 8 pts and modified surgical resection in 3 pts. A PET result in change in management was classified as high in 20 pts (8.6%). Distant metastases were detected in 6 pts by PET and confirmed by biopsy in all but one patient. This shift the therapeutic plan from curative to palliative. PET excluded metastases disease in 9 pts. In summary, a significant change in patient management was observed in 32 patients (13.7% of the patient population; in 5.2% of patients because of a change in the N stage and in 8.6% because of a change in the M stage).	This large multicentric prospective study demonstrated that adding PET-FDG imaging significantly improved the pretherapeutic TNM classification of HNSCC. This higher staging accuracy resulted in altering patient management in 13.7% of patients, with the greater impact being a result of the detection of metastatic or additional disease. Our results support the implementation of PET-FDG imaging in the routine imaging work-up of HNSCC.
Razfar et al, 2010 (23)	To determine efficacy of combined PET/CT in identifying recurrent thyroid cancer and to elucidate its role in the clinical management of thyroid carcinoma.	121	RCS	Histopath	US, WBI, CT, MRI	Changes in clinical management were compared between pts with elevated thyroglobulin (≥ 10.0 ng/mL) and pts with low thyroglobulin (< 10.0 ng/mL). Additional PET/CT information was more likely to change the clinical management among patients having elevated thyroglobulin levels ($p=0.001$).	Additional information from PET-CT frequently guides the clinical management of recurrent thyroid carcinoma and aids in the selection of appropriate salvage or palliative therapies.

Author, year	Objective	# of pts	PET study type	Reference Test	Compari-son Test	Results	Conclusions
Razfar et al, 2010 (24)	To evaluate the efficacy of combined positron emission tomography-computed tomography (PET-CT) in identifying salivary gland malignancies and to examine the role of PET-CT in the management of these patients.	55	RCS	Histopath	CT	The result of PET after 5 mos of diagnosis played a major role in imaging modality in formulating a treatment plan in 8 pts (14.5%). PET portion of the exam confirmed CT findings with intravenous contrast and thus added to management in 18 pts.	PET-CT is effective in the evaluation of salivary cancers and is particularly useful in initial staging and for surgical and radiation therapy planning. Although the combined PET-CT is a valuable adjuvant, there appears to be less added benefit in long-term surveillance and detecting distant metastasis where CT alone with contrast is likely sufficient for this group of patients. Added information from PET-CT can help guide management, especially when determining whether a patient is a candidate for definitive or palliative treatment.
Xie et al, 2010 (25)	To evaluate the prognostic value of maximal standard uptake values (SUVsmax) from serial FDG PET/CT in patients with locally advanced nasopharyngeal carcinoma (NPC).	62	RCS	Histopath	US, WBI, CT, MRI	5-year overall survival (OS) and disease-free survival (DFS) were 62.9% and 51.6% respectively. There is a significant better OS and DFS for pts with lower SUV than pts with higher SUV (p=0.018 and 0.0163, respectively). Pts with metabolic partial response (MPR) had significantly lower 5-year OS and DFS than pts with metabolic complete response (MCR) (p=0.0237 and 0.0186, respectively). There was a weak correlation between SUVmax at the primary site and neck nodes (r=0.399). Poor prognosis was associated with an SUVmax of neck nodes larger than that at the primary tumour site (p=0.0440).	FDG PET/CT uptake before and after treatment, as determined by SUVmax, maybe a valuable tool to evaluate prognosis in locally advanced NPC patients. Patients with a high FDG uptake of pre or post-treatment may be considered at increased risk of failure and may benefit from more effective approaches, for instance, higher radiation dose or combined more aggressive chemotherapy, and consequently improve treatment efficiency.
Hepatocellular carcinoma (HCC)							
Higashi et al, 2010 (26)	To investigate retrospectively the efficacy of FDG PET as an in vivo marker for tumour viability of HCC after non-operative therapy and as a prognostic predictor for post-treatment overall survival in patients with unresectable HCC.	67	RCS	Histopath	CT, MRI	Of 18 patients diagnosed as negative by post-therapeutic PET, 17 survived more than 12 mos (negative predictive value, 94.4%). All 37 patients diagnosed as positive by post-therapeutic PET died within 24 mos (positive predictive value: 100%). Survival prediction in 24 mos by FDG PET was quite accurate with the value of 93.6% (44/47 cases). Low FDG group (pts diagnosed as negative at the post-therapeutic PET) showed higher survival (average survival 607.9 ± 29.7 days) than the high FDG group (average survival: 327.5 ± 40.1 days). There is also statistically significant difference in survival between the two groups.	The present study suggests the following: (1) post-therapeutic PET performed within 1 mo after non-operative therapy can be a good predictor of survival in unresectable HCC patients, (2) patients with unresectable HCC diagnosed as positive by post-therapeutic FDG PET study are highly supposed to die within 24 mos, while patients diagnosed as negative are highly supposed to survive more than 12 mos and (3) a negative result of post-therapeutic FDG PET study may not always mean tumour cell death, and further treatment or further clinical follow-up would be needed.
Lung cancer							
Houseni et al, 2010 (27)	To determine whether dual-phase 18F-FDG PET can predict the outcome in patients with primary lung adenocarcinoma.	100	RCS	Histopath	CT	All prognostic factors with significance in the univariate analysis were included in the multivariate model to evaluate their interaction and joint effect on the overall survival. The adjusted Cox proportional hazards regression model revealed 4 factors to be independently correlated with the	Percentage SUVmax change over time in a pre-therapy FDG PET scan is a strong predictor of mortality in patients with lung adenocarcinoma. This predictor proved to be powerful on univariate analysis and independent on the Cox regression model.

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						overall survival including platelet count (relative risk=1.15, p=0.05), staging (relative risk=2.15, p=0.04), metastatic state (relative risk = 1.32, p= 0.02), and percentage SUVmax change over time (relative risk = 1.52, p=0.01).	Therefore, we anticipate that dual-phase FDG PET with measurement of the percentage SUVmax change may significantly affect the management of patients with lung adenocarcinoma and could be complementary to other well-known factors. These results remain to be confirmed in a larger prospective study.
Veit-Haiback, et al, 2010 (28)	To evaluate the value of several FDG-PET/CT-parameters in therapy response evaluation concerning prediction of survival at baseline and after three cycles of therapy.	41	PCS	Histopath	CT	There was no relation of the sum of baseline CT-measurements and the initial PET-parameters (SUVmax, SUVmean, TLG, PETvol) with survival. PET-measurement based on international guidelines (EORTC criteria with SUVmax) identified 14 responders after three cycles of therapy (mean decrease: −49.2% vs. baseline), 23 patients with stable disease (mean deviation:−5.1% vs. baseline) and 4 patients with progressive disease (mean increase: +43.1% vs. baseline). Because of a lack of established criteria, response data were not calculated for TLG and PETvol.	Response evaluation based on modified RECIST by CT as well as response evaluation by TLG and PETvol in FDG-PET, but not SUVmax-measurements are predictive for survival in malignant pleural mesothelioma (MPM).
Non small cell lung cancer							
Agarwal et al, 2010 (29)	To determine if the maximum standardized uptake value (SUVmax) of the primary tumour as determined by preoperative 18F-fluoro-2-deoxyglucose (18F-FDG) positron emission tomography (PET) is an independent predictor of overall survival and to assess its prognostic value after stratification according to pathological staging.	363	RCS	Histopath	NR	The median SUVmax was 5.9 for all subjects, 4.5 for stage IA, 8.4 for stage IB, and 10.9 for stage IIB. There was significant difference in overall survival when stratified by median SUVmax and optimal cutoff SUVmax in the whole group of cases (logrank test, p=0.018 and p=0.004, respectively). Multivariate Cox hazard model showed that SUVmax was not an independent predictor of overall survival (p>0.05)	The results demonstrate that each doubling of SUVmax as determined by preoperative PET is associated with a 1.28-fold increase in hazard of death in early-stage (I & II) NSCLC. Preoperative SUVmax is not an independent predictor of overall survival in that it loses its prognostic value in multivariate analyses and also after stratification according to pathological staging.
Nair et al, 2010 (30)	To examine the association between FDG PET scan and prognosis in patients with surgically treated, clinical stage A non-small cell lung cancer (NSCLC).	**75**	RCS	Histopath	CT	Survivors were more likely to have adenocarcinoma than nonsurvivors (p=0.044). SUVmax for survivors was 4.9 ± 2.5 compared with 7.1 ± 3.9 for nonsurvivors (p=0.045), and SUVmean for survivors was 3.6 ± 2.2 compared with 4.9 ± 3.6 for nonsurvivors, which was not significant (*p*=0.18). Visual score was similar in survivors and nonsurvivors, and it correlated poorly with SUV max (r^2=0.11). Bivariate analysis:	We found that higher tumour FDG uptake, as measured by SUVmax, is independently associated with worse survival in patients with resected clinical stage IA NSCLC, both before and after adjustment for age, prior history of cancer, tumour size, histology and type of resection. This information could be used to improve prognostication and to identify high-risk patients for inclusion in future trials of adjuvant therapy following surgical resection.

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						The hazard of death was significantly associated with both SUVmax (HR per 1 unit increment, 1.27; 95% CI, 1.09-1.48) and SUVmean (HR per 1 unit increment, 1.20; 95% CI, 1.01-1.43). Two Multivariate analysis after adjusting for potential confounders: 1. Both squamous histology (HR, 4.54; 95% CI, 1.09-18.9) and SUVmax (HR, 1.21; 95% CI, 1.01-1.45) remained significant predictors of worse survival. 2. Only SUVmax was significantly associated with worse survival (HR, 1.24; 95% CI, 1.06-1.44).	
Wauters et al, 2010 (31)	To study the influence of FDG-PET on long-term outcome.	139	RCS	Histopath	CT, US, MRI, bone scintigraphy	The median survival time was 35.6 mos with 5-year survival rate of 39.8% for all pts. There was a significantly better long-term prognosis ($p<0.0001$) for pts with early stage on conventional staging (CS) plus PET (CS+PET) who received a radical treatment.	This long-term follow-up analysis confirms that addition of PET to CS results in better stage designation and prognosis. Additionally, discordant findings between CS and CS+PET should be considered relevant, with need for cytological/histological examination.
Neuroendocrine tumour							
Binderup et al, 2010 (32)	To investigate the prognostic value of FDG-PET in patients with neuron endocrine (NE) tumours.	98	PCS	Histopath	CT	The overall risk of death was significantly higher in the FDG-positive group than the FDG-negative group with a hazard ratio (HR) of 10.3 [95% CI: 1.3-78.7]. Pts in the FDG-PET–positive group had a significantly lower progress-free survival (PFS) compared with the FDG-PET–negative group with a HR of 9.4 (95% CI, 2.9-30.8; log rank: $P < 0.001$)	This study for the first time shows a strong prognostic value of FDG-PET for NE tumours, which exceeds the prognostic value of traditional markers such as Ki67, CgA, and liver metastases. Despite the convincing results, further studies are needed with longer follow-up for validation of these findings. If confirmatory, we suggest that FDG-PET may become an important routine-imaging modality for NE tumours.
Ovarian cancer							
Risum et al, 2010 (33)	To investigate if the use of diagnostic FDG-PET/CT leads to stage migration in patients with advanced ovarian cancer and to evaluate the prognostic significance of FDG-PET/CT.	66	PCS	Histopath	CT	The median overall survival (OS) was significantly longer for pts with PET/CT stage II than for pts with PET/CT stage IV ($p=0.03$). The influence on survival of the prognostic variables PET/CT stage IV, complete debulking, and performance status ≤2 was analyzed. Median OS rates were 29.9 mos for the 27 patients with PET/CT stage IV, 36.5 mos for the 25 patients undergoing complete debulking, and 30.2 mos for the 64 patients with GOG performance status ≤2 (Table 4). Using univariate analysis, the PET/CT stage IV, complete debulking after primary surgery, and performance status were statistically significant prognostic variables. However, using multivariate Cox regression analysis, complete debulking after primary surgery was found to be the only statistically significant independent prognostic	In primary advanced ovarian cancer the use of diagnostic FDG-PET/CT leads to stage migration. Adequate staging is the foundation for ovarian cancer treatment and advanced imaging for optimal evaluation of metastases should be promoted in clinical trials. The strongest determinant of patient outcome is residual abdominal tumour after primary surgery.

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						variable.	
Pancreatic cancer							
Sperti et al, 2010 (34)	To assess the impact of FDG-PET in detecting recurrences, and influencing their management, of patients with previously resected pancreatic cancer (PC).	72	PCS	Histopath	CT	Overall survival was longer for group 2 (CT non-diagnostic) than for group 1 (CT positive for tumour relapse) but not significantly so (p=0.09). Disease-free survival was similar in groups 1 and 2, while residual life survival was significantly longer (p<0.01) for group 2 than for group 1. Three group 1 and three group 2 patients are still alive 22, 31, and 56 and 27, 46, and 104 mos, respectively, after primary surgery. PET on treatment of relapsed pts: PET negative results supported the decision to perform resection of tumour relapses. PET on treatment of non-relapsed pts: PET findings changed the clinical management for 32 of the 72 (44.4%) pts.	Tumour relapse is detected earlier by FDG PET than by CT in a significant percentage of patients after a potentially curative resection for PC. FDG PET can help select the best candidates for surgical exploration, although its actual usefulness is still to be defined. It influences treatment strategies in a significant percentage of patients (44.4%). Finally, FDG-PET is useless for patients with multiple recurrences or metastases already demonstrated by CT.
Pleural mesothelioma							
Nowak et al, 2010 (35)	To determine how quantitative FDG PET imaging adds prognostic information to conventional clinical variables at diagnosis and to construct a prognostic nomogram.	93	PCS	Histopath	CT	Univariate analysis showed that sarcomatoid histology (p<0.0005), weight loss (p=0.031), and EORTC good prognosis category (p=0.049) were significantly associated with survival analysis. Multivariate analysis showed that in patients with sarcomatoid histology, the addition of other prognostic factors was not contributory.	Sarcomatoid histology remains the strongest prognostic factor. In patients with non sarcomatoid disease, volumetric FDG PET parameters are more predictive of survival than tumour-node-metastasis staging, suggesting that tumour volume and glycolytic activity may be more important determinants of prognosis in malignant pleural mesothelioma than anatomic extent of disease.
Renal cell carcinoma							
Rodriguez et al, 2010 (36)	To evaluate the accuracy, diagnostic, validity, and clinical impact of FDG PET in the management of recurrent metastatic disease in pts with RCC	58	RCS	Histopath	CT, MRI, bone scintigraphy	Impact information of PET in management of pts with RCC was obtained in all the analyzed studies, independent of whether the result was positive or negative. PET had high impact in 25 cases (43.10%). In 8 of the pts, treatment was changed from immunotherapy to chemotherapy. In 5 pts, treatment was changed from immunotherapy/chemotherapy to clinical follow-up. In 3 pts, treatment was changed from immunotherapy to radiotherapy. In 2 pts treatment was changed from different diagnostic procedure to clinical follow-up.	The clinical impact was high in 25 cases (43%) and we found no impact in only 10 studies (17.2%). We concluded that 18F-FDG PET was useful and had a high clinical impact in the management of recurrent and metastatic RCC. From our data, it seemed that a positive PET study was more helpful to the physician than a negative study.
Thymoma							
Cardillo et al, 2010 (37)	To evaluate factors influencing long-term survival of patients with locally advanced thymoma/thymic	61	PCS	Histopath	CT, MRI	Median follow-up time was 77 mos for all pts. The overall 10-year survival rate was 50.6%. Univariate analysis with 10-year survival rate: 57.9% in group A and 38.1% in group B (p=0.03); 59.8% in stage III and 28.2% in stage IVa (p=0.02);	Complete resection, Masaoka stage, induction chemotherapy and histological WHO classification showed to be independent predictors of survival in locally advanced thymoma/thymic carcinoma. Preoperative staging of a thymoma is a difficult

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	carcinoma (Masaoka stages III and IVa) treated by immediate surgery or induction therapy plus surgery.					48.8% in R0 resection and 36.5% in R1 resection (p=0.04). According to histological classification, the 10-year overall survival for subtypes AB, B1, B2, B3 and thymic carcinoma was 63.8%, 100%, 0%, 85.7% and 54.1%, respectively (p=0.3). Multivariate analysis showed that complete resection (p=0.02), Masaoka stage (stage III vs. stage IV; p=0.02), induction chemotherapy (group A vs. group B; p=0.003) and histological WHO subtype AB (AB vs. B1 plus B2 plus B3; p=0.01) are statistically independent predictors of survival. Pts who did not receive radiotherapy had 61.6% 10-year survival rate in comparison to 42.5% of pts who received radiotherapy.	task and such problem represents the bias of the present study. Furthermore, because of the rarity of the neoplasm, multicentric prospective randomized trials with larger number of patients are needed for conclusive assessment of predictors of survival in locally invasive thymomas/thymic carcinoma.

Notes: 18F-FDG PET = F-fluorodeoxy glucose positron emission tomography-computed tomography; AC = 11C-acetate; CI = confidence interval; CT = computerized tomography; DFS = Disease free survival Histopath = Histopathology; HR = hazard ratio; mo(s) = month(s); MRI = magnetic resonance imaging; NR = Not Reported; NRCT = Nonrandomized controlled trial; OS = Overall survival; PCS = Prospective cohort study; PCT = preoperative chemotherapy; pNR = pathologic nonresponders; pt(s) = patient(s); RCC – renal cell carcinoma RCS = Retrospective study; RCT = Randomized controlled trial; SUV_{max} = Standard Uptake Value (maximum); ultrason = ultrasonography; TX = Docetaxel; US = ultrasound; vs. = versus; WBI = whole body imaging.