cancer care ontario | action cancer ontario
program in evidence-based care | programme de soins fondé sur des preuves

PET Recommendation Report 2 Version 2

PET Imaging in Head and Neck Cancer

J. Yoo, C. Walker-Dilks, and S. Henderson

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

Report Date: January 19, 2009
Report Update: February 9, 2012

The full PET Recommendation Report 2 Version 2 consists of 2 sections and is available on the CCO website (http://www.cancercare.on.ca)
PEBC PET Recommendations Reports page at:
http://www.cancercare.on.ca/toolbox/qualityguidelines/other-reports/petrecs/

Section 1: Recommendations
Section 2: Evidentiary Base and Consensus Process

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

Journal Citation (Vancouver Style): Yoo J, Henderson S, Walker-Dilks C. Evidence-based guideline recommendations on the use of positron emission tomography imaging in head and neck cancer. Clin Oncol. 2012 Sep 25. doi: 10.1016/j.clon.2012.08.007. Epub: 2012 Sep 26.

Report Citation (Vancouver Style): Yoo J, Walker-Dilks C, Henderson S. PET imaging in head and neck cancer. Toronto (ON): Cancer Care Ontario; 2009 [updated 2012 Feb 9]. Program in Evidence-based Care PET Recommendation Report No.: 2 Version 2.

cancer care ontario | action cancer ontario
program in evidence-based care | programme de soins fondé sur des preuves

PET Recommendation Report 2 Version 2: Section 1

PET Imaging in Head and Neck Cancer: Recommendations

J. Yoo, C. Walker-Dilks, and S. Henderson

Report Date: January 19, 2009
Report Update: February 9, 2012

QUESTIONS

Diagnosis/Staging

- What benefit to clinical management does positron emission tomography (PET) or positron emission tomography/computed tomography (PET/CT) contribute to the diagnosis or staging of head and neck cancer?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for head and neck cancer?

Recurrence/Restaging

- What benefit to clinical management does PET or PET/CT contribute when recurrence of head and neck cancer is suspected but not proven?
- What benefit to clinical management does PET or PET/CT contribute to restaging at the time of documented recurrence for head and neck cancer?
- What is the role of PET when a solitary metastasis is identified at the time of recurrence and a metastectomy is being contemplated?

TARGET POPULATION

Patients with head and neck cancer are the target population for this recommendation report.

INTENDED PURPOSE

- This recommendation report is intended to guide the Ontario PET Steering Committee in their decision making concerning indications for the use of PET imaging.
- This recommendation report may also be useful in informing clinical decision making regarding the appropriate role of PET imaging and in guiding priorities for future PET imaging research.

RECOMMENDATIONS AND KEY EVIDENCE

These recommendations are based on an evidentiary foundation consisting of one recent high-quality U.K. Health Technology Assessment (HTA) systematic review (1) that included systematic review and primary study literature for the period from 2000 to August

2005, an update of this systematic review undertaken to retrieve the same level of evidence for the period from August 2005 to June 2008, and a subsequent literature search was conducted to retrieve literature from June 2008 to July 2011.

Diagnosis/Staging

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.
HTA review 2007 (1): One systematic review of four primary studies and one additional primary study showed PET was sensitive and specific and useful where doubt exists (CT/MRI gave different and less optimal results). PET changed stage and treatment planning. **2005-2008 update:** Chang et al (2), Liu et al (3), Kim et al (4), Liu et al (5), Minovi et al (6), Brouwer et al (7), Yen et al (8), Connell et al (9). **2008-2011 update:** Kim et al (22), Law et al (23), Lonneux et al (24), Ng et al (25), Martin et al (26), Senft et al (27), Yamazaki et al (28) and Wang et al (29) all identified that PET was superior to conventional imaging for the detection and staging of head and neck squamous cell carcinoma. Additionally, Deantonio et al (30), Dietl et al (31), Gardner et al (32) and Guido et al (33) indicated that the addition of PET improved primary tumour delineation and nodal staging and subsequently changed the clinical management of several patients in each study.

PET is recommended in all patients after conventional imaging and in addition to, or prior to, diagnostic panendoscopy where the primary site is unknown.
HTA review 2007 (1): Two systematic reviews (each with eight primary studies) and two additional primary studies showed that PET can detect primary unknown tumours in patients with cervical lymph node metastases. PET detects 30% of primary tumours, including those missed by conventional imaging. **2005-2008 update:** One primary study showed that PET is better than conventional imaging in detecting site of primary tumour (Chen et al [10]). **2008 2011 update:** One primary study indicated that patients with cervical metastasis and an unknown primary site after undergoing conventional imaging or clinical examination benefit from PET/CT prior to panendoscopy (Rudmik et al [34])

PET is recommended for staging and assessment of recurrence of patients with nasopharyngeal carcinoma if conventional imaging is equivocal.
HTA review 2007 (1): This topic was not addressed in the HTA review. **2005-2008 update:** Seven primary studies showed that PET scanning was more accurate than conventional imaging in identifying metastatic disease (Chang et al [2], Liu et al [3], Kim et al [4], Liu et al [5], Minovi et al [6], Brouwer et al [7], Yen et al [8]). **2008 - 2011 update:** Law et al (23) identified PET as being a valuable staging tool for the detection of nasopharyngeal carcinoma and changed patient management in 16 of 48 patients.

Qualifying Statements

- This report makes no distinction between studies examining PET and those examining PET/CT.
- Conventional imaging refers to CT and/or magnetic resonance imaging (MRI) unless otherwise specified.

- Retrospective design studies were excluded from this review, but several exist favouring the use of PET for head and neck cancer.
- With respect to primary site (T):
  - PET appears to be more accurate for the diagnosis of primary tumours, especially in cases where CT/MRI results are equivocal (2008-2011 update: Guido et al [33], Wang et al.[29])
  - PET can identify the primary site in 30% of cases when undetected by clinical assessment and conventional imaging.
  - PET can detect some synchronous primaries that may be missed by other modalities.
- With respect to regional nodes (N):
  - In the clinically N-0 neck, PET does not appear to be better than conventional imaging, because of an unacceptably high false-negative rate. There is little evidence that PET leads to change in patient management (2005-2008 update: Hafidh et al [16], Ng et al [17], Schoder et al [18], Wensing et al [19], Kim et al [20]; 2008-2011 update: Moeller et al [35]and Kyzas et al [36], Liao et al [37]).
- There was moderate evidence that PET scanning changed nodal staging status and/or radiation treatment planning. However, in many cases there was no pathologic confirmation of PET versus conventional imaging discrepancy. Exceptions were cases where distant metastatic disease was identified by PET and changed treatment (2005-2008 update: Connell et al [9]).
- With respect to distant disease (M):
  - There is strong evidence that PET imaging is valuable in detecting distant metastatic disease and is better than conventional imaging. The advantage of PET is overwhelming for patients at high risk for distant disease, which includes locally advanced disease and nasopharyngeal carcinoma. The substantial incidence of false-positive rates of PET may mitigate the advantages for low-risk patients (2008-2011 update: Kim et al [22], Law et al [23], Lonneux et al [24], Martin et al [26], Ng et al [25], Senft et al [27], Yamazaki et al [28], Wang et al [29]).

Recurrence/Restaging

PET is recommended for restaging patients who are being considered for major salvage treatment, including neck dissection.
HTA review 2007 (1): This topic was not addressed in the HTA review. **2005-2008 update**: Patients being evaluated for locoregional recurrence and considered for salvage should have PET in order to help tailor further therapy. Examples include larynx, skull base and nasopharynx, salivary gland, and neck disease (Chen et al [10], Gordin et al [11], Brouwer et al [12], Chan et al [13], Gil et al [14], Roh et al [15]). **2008-2011 update:** Abgral et al (38) and Isles et al (39) confirmed the effectiveness of PET in assessing for recurrence of head and neck squamous cell carcinomas in patients. Contrary to this, Inohara et al (40) found PET to be of no additional value to determine the persistence of nodal disease after chemoradiotherapy. Additionally, Porceddu et al (41) supports the use of PET-directed management of the neck after chemoradiotherapy in that it spares unnecessary neck dissections.

Qualifying Statements

- With respect to recurrence and tumour surveillance after treatment, the evidence suggests that sites of disease that are clinically accessible for assessment did not benefit from PET imaging. However, for disease sites that were either not clinically accessible or difficult to examine, PET imaging showed significant advantages over conventional evaluation.

  - Larynx: moderate evidence that PET is beneficial/better than conventional imaging in detecting recurrent disease. PET also reduced the need for debilitating laryngeal biopsies (2005-2008 update: Gordin et al [11], Brouwer et al [12]).
  - Skull base and nasopharynx: moderate evidence that PET is beneficial/better than conventional imaging in detecting recurrent disease (2005-2008 update: Chan et al [21], Gil et al [14]).
  - Salivary gland: moderate evidence suggesting an advantage with PET (2005-2008 update: Roh et al [15]).
  - Nodal disease: For N+ patients, moderate evidence exists that PET is better than conventional imaging in detecting the status of residual disease following radiotherapy or chemoradiotherapy. The use of PET reduced both false-positive and false-negative rates compared to the gold standard (2005-2008 update: Chen et al [10]). It is of relevance to note that clinical trials are currently being conducted in Ontario on this matter. Once published, they will be evaluated for inclusion and incorporated into the recommendation report in subsequent updates.
  - There is evidence that PET detects distant relapse. There is strong evidence that the detection of distant disease leads to major changes in patient management in the salvage setting (2005-2008 update: Brouwer et al [7], Chang et al [2], Kim et al [4], Liu et al [3], Liu et al [5], Minovi et al [6], Yen et al [8]; 2008-2011 update: Senft et al [27]).
- With respect to the role of PET in assessing status of neck lymphadenopathy following radiation or chemoradiation, moderate evidence suggests that PET-directed management of the neck after therapy, appropriately spares neck dissections in patients with PET-negative residual CT abnormalities (2008-2011 update: Porceddu et al [41]).

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

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

REFERENCES

1. Facey K, Bradbury I, Laking G, Payne E. Overview of the clinical effectiveness of positron emission tomography imaging in selected cancers. Health Technol Assess. 2007 Oct;11(44):iii-iv, xi-267.
2. Chang JT, Chan SC, Yen TC, Liao CT, Lin CY, Lin KJ, et al. Nasopharyngeal carcinoma staging by (18)F-fluorodeoxyglucose positron emission tomography. Int J Radiat Oncol Biol Phys. 2005 Jun 1;62(2):501-7.
3. Liu FY, Chang JT, Wang HM, Liao CT, Kang CJ, Ng SH, et al. [18F]fluorodeoxyglucose positron emission tomography is more sensitive than skeletal scintigraphy for detecting bone metastasis in endemic nasopharyngeal carcinoma at initial staging. J Clin Oncol. 2006 Feb 1;24(4):599-604. Erratum in: J Clin Oncol. 2006 Jul 20;24(21):3515. Ng, Shu-Kung [corrected to Ng, Shu-Hang].
4. Kim SY, Roh JL, Yeo NK, Kim JS, Lee JH, Choi SH, et al. Combined 18F-fluorodeoxyglucose-positron emission tomography and computed tomography as a primary screening method for detecting second primary cancers and distant metastases in patients with head and neck cancer. Ann Oncol. 2007 Oct;18(10):1698-703. Epub 2007 Aug 22.
5. Liu FY, Lin CY, Chang JT, Ng SH, Chin SC, Wang HM, et al. 18F-FDG PET can replace conventional work-up in primary M staging of nonkeratinizing nasopharyngeal carcinoma. J Nucl Med. 2007 Oct;48(10):1614-9. Epub 2007 Sep 14.
6. Minovi A, Hertel A, Ural A, Hofmann E, Draf W, Bockmuehl U. Is PET superior to MRI in the pretherapeutic evaluation of head and neck squamous cell carcinoma? Kulak Burun Bogaz Ihtis Derg. 2007;17(6):324-8.
7. Brouwer J, Senft A, de Bree R, Comans EF, Golding RP, Castelijns JA, et al. Screening for distant metastases in patients with head and neck cancer: is there a role for (18)FDG-PET? Oral Oncol. 2006 Mar;42(3):275-80. Epub 2005 Nov 2.
8. Yen TC, Chang JT, Ng SH, Chang YC, Chan SC, Lin KJ, et al. The value of 18F-FDG PET in the detection of stage M0 carcinoma of the nasopharynx. J Nucl Med. 2005 Mar;46(3):405-10.
9. Connell CA, Corry J, Milner AD, Hogg A, Hicks RJ, Rischin D, et al. Clinical impact of, and prognostic stratification by, F-18 FDG PET/CT in head and neck mucosal squamous cell carcinoma. Head Neck. 2007 Nov;29(11):986-95.
10. Chen AY, Vilaseca I, Hudgins PA, Schuster D, Halkar R. PET-CT vs contrast-enhanced CT: what is the role for each after chemoradiation for advanced oropharyngeal cancer? Head Neck. 2006 Jun;28(6):487-95.
11. Gordin A, Daitzchman M, Doweck I, Yefremov N, Golz A, Keidar Z et al. Fluorodeoxyglucose-positron emission tomography/computed tomography imaging in patients with carcinoma of the larynx: diagnostic accuracy and impact on clinical management. Laryngoscope. 2006 Feb;116(2):273-8.
12. Brouwer J, de Bree R, Comans EF, Akarriou M, Langendijk JA, Castelijns JA, et al. Improved detection of recurrent laryngeal tumor after radiotherapy using (18)FDG-PET as initial method. Radiother Oncol. 2008 May;87(2):217-20. Epub 2008 Mar 7.
13. Chan SC, Yen TC, Ng SH, Lin CY, Wang HM, Liao CT, et al. Differential roles of 18F-FDG PET in patients with locoregional advanced nasopharyngeal carcinoma after primary curative therapy: response evaluation and impact on management. J Nucl Med. 2006 Sep;47(9):1447-54.
14. Gil Z, Even-Sapir E, Margalit N, Fliss DM. Integrated PET/CT system for staging and surveillance of skull base tumors. Head Neck. 2007 Jun;29(6):537-45.

15. Roh JL, Ryu CH, Choi SH, Kim JS, Lee JH, Cho KJ, et al. Clinical utility of 18F-FDG PET for patients with salivary gland malignancies. J Nucl Med. 2007 Feb;48(2):240-6.
16. Hafidh MA, Lacy PD, Hughes JP, Duffy G, Timon CV. Evaluation of the impact of addition of PET to CT and MR scanning in the staging of patients with head and neck carcinomas. Eur Arch Otorhinolaryngol. 2006 Sep;263(9):853-9. Epub 2006 May 25.
17. Ng SH, Yen TC, Chang JT, Chan SC, Ko SF, Wang HM, et al. Prospective study of [18F]fluorodeoxyglucose positron emission tomography and computed tomography and magnetic resonance imaging in oral cavity squamous cell carcinoma with palpably negative neck. J Clin Oncol. 2006 Sep 20;24(27):4371-6.
18. Schöder H, Carlson DL, Kraus DH, Stambuk HE, Gönen M, Erdi YE, et al. 18F-FDG PET/CT for detecting nodal metastases in patients with oral cancer staged N0 by clinical examination and CT/MRI. J Nucl Med. 2006 May;47(5):755-62.
19. Wensing BM, Vogel WV, Marres HA, Merkx MA, Postema EJ, Oyen WJ, et al. FDG-PET in the clinically negative neck in oral squamous cell carcinoma. Laryngoscope. 2006 May;116(5):809-13. Erratum in: Laryngoscope. 2006 Jul;116(7 Pt1):1302.
20. Kim MR, Roh JL, Kim JS, Lee JH, Cho KJ, Choi SH, et al. Utility of 18F-fluorodeoxyglucose positron emission tomography in the preoperative staging of squamous cell carcinoma of the oropharynx. Eur J Surg Oncol. 2007 Jun;33(5):633-8. Epub 2007 Mar 27.
21. Chan SC, Ng SH, Chang JT, Lin CY, Chen YC, Chang YC, et al. Advantages and pitfalls of 18F-fluoro-2-deoxy-D-glucose positron emission tomography in detecting locally residual or recurrent nasopharyngeal carcinoma: comparison with magnetic resonance imaging. Eur J Nucl Med Mol Imaging. 2006 Sep;33(9):1032-40. Epub 2006 Apr 19.
22. Kim SY, Kim JS, Doo H, Lee H, Lee JH, Cho KJ, et al. Combined [18F]fluorodeoxyglucose positron emission tomography and computed tomography for detecting contralateral neck metastases in patients with head and neck squamous cell carcinoma. Oral Oncol. 2011;47(5):376-80.
23. Law A, Peters LJ, Dutu G, Rischin D, Lau E, Drummond E, et al. The utility of PET/CT in staging and assessment of treatment response of nasopharyngeal cancer. J Med Imag Radiat Oncol. 2011;55(2):199-205.
24. Lonneux M, Hamoir M, Reychler H, Maingon P, Duvillard C, Calais G, et al. Positron emission tomography with [18F]fluorodeoxyglucose improves staging and patient management in patients with head and neck squamous cell carcinoma: a multicenter prospective study. J Clin Oncol. 2010;28(7):1190-5.
25. Ng SH, Chan SC, Yen TC, Liao CT, Lin CY, Tung-Chieh Chang J, et al. PET/CT and 3-T whole-body MRI in the detection of malignancy in treated oropharyngeal and hypopharyngeal carcinoma. Eur J Nucl Med Mol Imag. 2011;38(6):996-1008.
26. Martin RCW, Fulham M, Shannon KF, Hughes C, Gao K, Milross C, et al. Accuracy of positron emission tomography in the evaluation of patients treated with chemoradiotherapy for mucosal head and neck cancer. Head Neck. 2009;31(2):244-50.
27. Senft A, de Bree R, Hoekstra OS, Kuik DJ, Golding RP, Oyen WJG, et al. Screening for distant metastases in head and neck cancer patients by chest CT or whole body FDG-PET: A prospective multicenter trial. Radiother Oncol. 2008;87(2):221-9.
28. Yamazaki Y, Saitoh M, Notani K-i, Tei K, Totsuka Y, Takinami S-i, et al. Assessment of cervical lymph node metastases using FDG-PET in patients with head and neck cancer. Ann Nucl Med. 2008;22(3):177-84.
29. Wang Y-F, Liu R-S, Chu P-Y, Chang F-C, Tai S-K, Tsai T-L, et al. Positron emission tomography in surveillance of head and neck squamous cell carcinoma after definitive chemoradiotherapy. Head Neck. 2009;31(4):442-51.

30. Deantonio L, Beldi D, Gambaro G, Loi G, Brambilla M, Inglese E, et al. FDG-PET/CT imaging for staging and radiotherapy treatment planning of head and neck carcinoma. Radiat. Oncol. 2008;3:29.
31. Dietl B, Marienhagen J, Kuhnel T, Schreyer A, Kolbl O. The impact of FDG-PET/CT on the management of head and neck tumours: The radiotherapist's perspective. Oral Oncol. 2008;44(5):504-8.
32. Gardner M, Halimi P, Valinta D, Plantet MM, Alberini JL, Wartski M, et al. Use of single MRI and 18F-FDG PET-CT scans in both diagnosis and radiotherapy treatment planning in patients with head and neck cancer: Advantage on target volume and critical organ delineation. Head Neck. 2009;31(4):461-7.
33. Guido A, Fuccio L, Rombi B, Castellucci P, Cecconi A, Bunkheila F, et al. Combined 18F-FDG-PET/CT imaging in radiotherapy target delineation for head-and-neck cancer. Int J Radiation Oncology Biology Physics. 2009;73(3):759-63.
34. Rudmik L, Lau HY, Matthews TW, Bosch JD, Kloiber R, Molnar CP, et al. Clinical utility of PET/CT in the evaluation of head and neck squamous cell carcinoma with an unknown primary: A prospective clinical trial. Head Neck. 2011;33(7):935-40.
35. Moeller BJ, Rana V, Cannon BA, Williams MD, Sturgis EM, Ginsberg LE, et al. Prospective risk-adjusted [18F]fluorodeoxyglucose positron emission tomography and computed tomography assessment of radiation response in head and neck cancer. J Clin Oncol. 2009;27(15):2509-15.
36. Kyzas PA, Evangelou E, Denaxa-Kyza D, Ioannidis JPA. 18F-fluorodeoxyglucose positron emission tomography to evaluate cervical node metastases in patients with head and neck squamous cell carcinoma: A meta-analysis. J Nat Cancer Inst. 2008;100(10):712-20.
37. Liao CT, Wang HM, Huang SF, Chen IH, Kang CJ, Lin CY, et al. PET and PET/CT of the neck lymph nodes improves risk prediction in patients with squamous cell carcinoma of the oral cavity. J Nucl Med. 2011;52(2):180-7.
38. Abgral R, Querellou S, Potard G, Le Roux P-Y, Le Duc-Pennec A, Marianovski R, et al. Does 18F-FDG PET/CT improve the detection of posttreatment recurrence of head and neck squamous cell carcinoma in patients negative for disease on clinical follow-up? J Nucl Med.. 2009;50(1):24-9.
39. Isles MG, McConkey C, Mehanna HM. A systematic review and meta-analysis of the role of positron emission tomography in the follow up of head and neck squamous cell carcinoma following radiotherapy or chemoradiotherapy. Cl Otolaryngol. 2008;33(3):210-22.
40. Inohara H, Enomoto K, Tomiyama Y, Yoshii T, Osaki Y, Higuchi I, et al. The role of CT and 18F-FDG PET in managing the neck in node-positive head and neck cancer after chemoradiotherapy. Acta OtoLaryngol. 2009;129(8):893-9.
41. Porceddu SV, Pryor DI, Burmeister E, Burmeister BH, Poulsen MG, C. FM, et al. Results of a prospective study of positron emission tomography-directed management of residual nodal abnormalities in node-positive head and neck cancer after definitive radiotherapy with or without systemic therapy. Head Neck. 2011. Epub 2011Jan 14.

cancer care ontario | action cancer ontario
program in evidence-based care | programme de soins fondé sur des preuves

PET Recommendation Report 2 Version 2: Section 2

PET Imaging in Head and Neck Cancer: Evidentiary Base and Consensus Process

J. Yoo, C. Walker-Dilks, and S. Henderson

Report Date: January 19, 2009
Report Update: February 9, 2012

QUESTIONS

Diagnosis/Staging

- What benefit to clinical management does PET or PET/CT contribute to the diagnosis or staging of head and neck cancer?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for head and neck cancer?

Recurrence/Restaging

- What benefit to clinical management does PET or PET/CT contribute when recurrence of head and neck cancer is suspected but not proven?
- What benefit to clinical management does PET or PET/CT contribute to restaging at the time of documented recurrence for head and neck cancer?
- What is the role of PET when a solitary metastasis is identified at the time of recurrence and a metastectomy is being contemplated?

INTRODUCTION

The Ontario PET Steering Committee made a special request to the Clinical Council of Cancer Care Ontario to co-lead the development of guidance regarding the clinical uses of PET imaging. The Program in Evidence-based Care (PEBC), working with the PEBC Disease Site Groups (DSGs), synthesized the clinical research and drafted recommendations for 10 disease sites. Recommendations for the use of PET in colorectal cancer, esophageal cancer, head and neck cancer, and melanoma were reviewed at a consensus meeting on 19 September 2008, and recommendations for the use of PET in brain, ovarian, cervical, testicular, small-cell lung, and pancreatic cancer were reviewed at a consensus meeting on 25 November 2008. In order to provide the Ontario PET Steering Committee with the most current evidence and recommendations, a supplemental update of the current literature encompassing the years 2008 to July 2011 was conducted.

METHODS

Overview

In order to develop the recommendations and achieve consensus, a three-step methodology was undertaken.

Step 1 – Systematic review. A systematic review of the published literature was undertaken (see details below). This was conducted by one clinical lead author, nominated by the PEBC Head and Neck DSG and a PEBC methodologist. The systematic review served as the evidentiary foundation for a set of draft recommendations developed by this team.

Step 2 – Consensus by the PEBC Head and Neck DSG. The draft recommendations were refined during a DSG teleconference. The Head and Neck DSG is comprised of medical and radiation oncologists and surgeons and supported by a PEBC research methodologist. This step was not conducted for the report updates.

Step 3 – Provincial PET imaging consensus meeting. The draft recommendations were vetted at a larger provincial PET imaging consensus meeting co-hosted by Cancer Care Ontario and the Provincial PET Steering Committee. The meeting was facilitated and supported by members of the PEBC team. Participants included representatives of the PEBC DSGs, other clinical experts in the areas of nuclear and diagnostic medicine, members of the Cancer Care Ontario clinical leadership team, and representatives from the Ontario PET Steering Committee and the Ontario Health Technology Assessment Committee. As with step 2, this was not conducted for the report updates.

Step 4 - On-going evidence review and updating. A biannual review of the literature will be conducted to ensure the relevance of the current recommendations. The systematic literature review will be conducted by the PEBC research coordinator and the lead clinical expert(s) selected from the Head and Neck DSG. A consensus committee will only be convened if the updated literature profoundly changes existing recommendations or provides sufficient evidence for a new recommendation. If no changes or minor changes result from the update, at a minimum the updated recommendation report will be reviewed by the director of the PEBC and approved by the Ontario PET Steering Committee.

The systematic review and companion recommendations are intended to promote evidence-based decisions in Ontario, Canada. The PEBC is supported by the Ontario Ministry of Health and Long-Term Care through Cancer Care Ontario. All work produced by the PEBC is editorially independent from its funding source.

SYSTEMATIC REVIEW

Literature Search

A scoping review undertaken by the PEBC methodologist to identify any existing systematic reviews on PET imaging in the cancers of interest yielded such a review. The U.K. HTA systematic review (1) (referred to as the HTA review from this point forward) evaluated the effectiveness of fluorodeoxyglucose (FDG) imaging in several selected cancers, including head and neck. The document included systematic reviews and individual primary studies dating from 2000 to August 2005. Because the HTA review sufficiently covered the questions and methodologies of interest to this recommendation report, its results were used for the evidence base from 2000 to August 2005, and its search strategies were performed in MEDLINE and EMBASE to update the literature to July 2011. The update strategies for MEDLINE and EMBASE are in Appendix 1 and Appendix 2 respectively.

Study Selection Criteria

All systematic reviews and primary studies in the HTA review that addressed the questions of interest in this recommendation report (diagnosis, staging, treatment response,

recurrence, and restaging) were included. The inclusion criteria of the HTA review were employed to select systematic reviews and primary studies identified in the update search.

The inclusion criteria for systematic reviews included in the HTA review and used in the update were:

- dedicated to FDG PET in the selected cancers in humans;
- contained evidence related to diagnostic accuracy, change in patient management, clinical outcomes, or treatment response.

The inclusion criteria for primary studies included in the HTA review and used in the update were:

- prospective clinical study of dedicated FDG PET in a single cancer of interest;
- study published after the search date of a robust systematic review covering that cancer management decision;
- study published as a full article in a peer-reviewed journal;
- study reported evidence related to diagnostic accuracy, change in patient management, or clinical outcomes;
- study included ≥ 12 patients with the cancer of interest;
- study used a suitable reference standard (pathological confirmation and clinical follow-up) when appropriate.

The citations and abstracts from the update searches were reviewed by the PEBC research coordinator and marked as relevant or not relevant, according to the inclusion criteria from the HTA review, and were classified by disease site. The research coordinator and the clinical lead for each DSG reviewed the relevant citations and full text of the articles for final decision on inclusion.

Synthesizing the Evidence

The HTA review did not pool individual studies. Data were extracted into separate tables for systematic reviews and primary studies for each type of management decision. The same approach was used for data extraction for the evidence from August 2005 to June 2008 and subsequently from July 2008 to July 2011. Full text and data extractions of the studies from the update search were provided to the clinical lead author to aid in the formulation of the recommendations. Telephone conferences and email correspondence between the clinical lead and the PEBC methodologist took place to clarify details and answer questions.

CONSENSUS

DSG Consensus Process

The clinical lead author wrote summaries of the key evidence, draft recommendations, and qualifying statements for the questions pertaining to diagnosis/staging, assessment of treatment response, and recurrence/restaging. The ensuing documents were circulated to all members of the GI DSG and discussed during a teleconference. The recommendations that were generated during this process are referred to below as the DRAFT DSG recommendations. The intent of these recommendations was to guide discussion at the consensus meeting. This step was not considered necessary for the 2011 update because evidence was consistent with the existing evidence base and no global changes were made to the existing recommendations.

Provincial Consensus Process

The consensus meeting on 19 September 2008 was conducted as follows:

- Consensus meeting participants sat at tables specifically set up to discuss a particular disease site (colorectal, esophageal, head and neck, and melanoma). The Head and

Neck table held the clinical lead and any other Head and Neck DSG members attending, in addition to other invited health professionals.

- The recommendations and summary of key evidence drafted by the clinical lead and refined and confirmed by the Head and Neck DSG were presented by the clinical lead to the group at the Head and Neck table.
- During small-group discussion at the Head and Neck table in the morning and discussion among the entire consensus meeting participants in the afternoon, the recommendations underwent further refinement and modification. The attendees voted on the revised recommendations to indicate their extent of agreement on a scale from 1 to 9 (1 indicating strong agreement, 5 indicating no agreement or disagreement, and 9 indicating strong disagreement).

After the consensus meeting, the exact wording of the recommendations was slightly modified for consistency with the recommendations resulting from the other disease discussions. These modifications included using emphatic, unambiguous language (i.e., *PET is recommended*...) and removing the need to distinguish between PET and PET/CT. It was made clear at the consensus meetings that PET imaging alone is being phased out and PET/CT imaging is the current standard. Thus, the term PET is used to cover PET and PET/CT imaging. These recommendations are referred to below as the FINAL RECOMMENDATIONS and were the foundation for any new or updated recommendations identified in the literature updates. Any updates to the recommendations arising from subsequent literature updates proceed the original recommendation.

The committee has not been reconvened for the 2011 update because the evidence base is consistent with the existing recommendations.

RESULTS

Literature Search Results

The HTA review (1) results for head and neck cancer included five systematic reviews and 31 primary studies. The 2005 to 2008 update included two systematic reviews and 35 primary studies. The 2008 to 2011 update included 18 primary studies and two systematic reviews. One study, (Porceddu et al [37]) was identified by the lead author and was not identified via the systematic search. At the time of this recommendation report this article was an electronic publication only and was not indexed in the MEDLINE or EMBASE databases. As it met the inclusion criteria of the systematic literature review, it was included in the 2008-2011 literature update.

Data extracted from the systematic reviews and primary studies in the HTA review (1) are available on the HTA website (pages 131-159). Data extracted from the primary studies from the updated 2008 and 2011 searches are in Appendix 3 and 4 respectively. The key evidence identified by the search is described below in an abbreviated fashion.

Key Evidence

Diagnosis/Staging

Diagnosis and Patient Management

- HTA review 2007 (1): One systematic review of four primary studies and one additional primary study showed PET was sensitive and specific and useful where doubt exists (CT/MRI give different results). PET changed stage and treatment planning.
- 2005-2008 update: Chang et al (2), Liu et al (3), Kim et al (4), Liu et al (5), Minovi et al (6), Brouwer et al (7), Yen et al (8), Connell et al (9).
- 2008 – 2011 update: Kim et al (38), Law et al (39), Lonneux et al (40), Martin et al (41), Ng et al (42), Senft et al (43), Yamazaki et al (44) all indicated that PET was superior to conventional imaging for the diagnosis and staging of head and neck squamous cell

carcinoma and provided additional information that heightened staging accuracy. Deantonio et al (45), Dietl et al (46), Gardner et al (47) and Guido et al (48) indicated that the addition of PET improved primary tumour delineation and nodal staging and subsequently changed the clinical management of several patients in each study.

Diagnosis of an Unknown Primary Tumour

- HTA review 2007 (1): Two systematic reviews (each with eight primary studies) and two additional primary studies showed that PET can detect primary unknown tumours in patients with cervical lymph node metastases. PET detects 30% of primary tumours, including those missed by conventional imaging.
- 2005-2008 update: One primary study showed that PET is better than conventional imaging in detecting site of primary tumour (Chen et al [10]).
- 2008-2011 update: One primary study indicated that patients with cervical metastasis and an unknown primary site benefitted from PET/CT prior to panendoscopy (Rudmik et al [49]).

Detection of Metastatic Disease

- 2005-2008 update: Seven primary studies showed that PET scanning was more accurate than conventional imaging in identifying metastatic disease (Chang et al [2], Liu et al [3], Kim et al [4], Liu et al [5], Minovi et al [6], Brouwer et al [7], Yen et al [8]).
- 2008-2011 update: Eight primary studies indicated that PET was effective in detecting distant metastatic disease (Kim et al [38], Law et al [39], Lonneux et al [40], Martin et al [41], Ng et al [42], Senft et al [43], Yamazaki et al [44], Wang et al [50]).

Recurrence/Restaging

- HTA review 2007 (1): This topic was not addressed in the HTA review
- 2005-2008 update: Patients being evaluated for locoregional recurrence and considered for salvage should have PET in order to help tailor further therapy. Examples include larynx, skull base and nasopharynx, salivary gland, and neck disease (Chen et al [10], Gordin et al [11], Brouwer et al [12], Chan et al [13], Gil et al [14], Roh et al [15]).
- 2008 – 2011 update: Abgral et al (52) and Isles et al (53) confirmed the effectiveness of PET in assessing for recurrence of head and neck squamous cell carcinomas in patients. Contrary to this, Inohara et al (54) found PET to be of no additional value to determine the persistence of nodal disease after chemoradiotherapy.
- 2008 – 2011 update: With respect to the role of PET in assessing the status of neck lymphadenopathy following radiation or chemoradiation, the evidence suggests that PET-directed management of the neck after therapy appropriately spares neck dissections in patients with PET-negative residual CT abnormalities (Porceddu et al [37]).

RECOMMENDATIONS

DIAGNOSIS/STAGING

Clinical Question

What benefit to clinical management does PET or PET/CT contribute to the diagnosis or staging of head and neck cancer?

DRAFT DSG Recommendation 2008

PET should be used in the diagnosis and staging of patients with advanced stage head and neck squamous cell carcinoma (Stage III, IV).

Provincial Consensus Meeting Deliberations

There was general agreement among the large group with this recommendation, and some changes were suggested with respect to specific components. It was recommended that "diagnosis" be omitted and "M" and "bilateral nodal staging" be added. It was also requested that doubt about conventional imaging be made clearer by using the term "equivocal".

Recommendation Put to Vote

PET should be used in the M and bilateral nodal staging of patients with advanced stage head and neck squamous cell carcinoma (Stage III, IV) where conventional imaging is equivocal.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree	N/A
	1	2	3	4	5	6	7	8	9	
Total	**3**	**8**	**3**	**3**	**2**					

Votes = 19

Issues raised on voting questionnaire:

-I worry that the quality of evidence is fairly poor.

FINAL RECOMMENDATION

Original Recommendation 2008: PET is recommended in the M and bilateral nodal staging of patients with advanced stage head and neck squamous cell carcinoma (Stage III, IV) where conventional imaging is equivocal.

Updated Recommendation 2011: 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.

DRAFT DSG Recommendation

PET should be used in all patients where the primary site is unknown.

Provincial Consensus Meeting Deliberations

Some additions were suggested to this recommendation in both the morning and afternoon discussions. "Unknown" was clarified as meaning "after conventional imaging", and it was agreed that this be included in the recommendation. It was also suggested that the recommendation not exclude what is usually done (i.e., panendoscopy). During the large group discussion, issues were raised about when PET would be done, for instance, after panendoscopy? The response was to do PET first because then a targeted panendoscopy can be done.

Recommendation Put to Vote

PET should be used in all patients after conventional imaging and in addition to diagnostic panendoscopy where the primary site is unknown.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree	N/A
	1	2	3	4	5	6	7	8	9	
Total	**4**	**7**	**5**	**3**						

Votes = 19

Issues raised on voting questionnaire:

-I would prefer panendoscopy first, then PET scan if required.

-Neck nodes, biopsy-proven squamous cell carcinoma.
-Neck nodes with squamous cell histology only?
-Useful for follow-up/prognosis.
-Squamous cell carcinoma LN neck – otherwise nonmetastatic.

FINAL RECOMMENDATION

Original Recommendation: PET is recommended in all patients after conventional imaging and in addition to diagnostic panendoscopy where the primary site is unknown.

Updated Recommendation: PET is recommended in all patients after conventional imaging and prior to, or in addition to, diagnostic panendoscopy where the primary site is unknown.

DRAFT DSG Recommendation 2008

PET should be used for staging patients at moderate or high risk of distant metastatic disease (e.g., nasopharyngeal carcinoma, unexplained symptoms in early stage patients, stage III-IV).

Provincial Consensus Meeting Deliberations

There was debate during the small group discussion about the coverage of this recommendation. The suggestion was made that the most important aspect was nasopharyngeal carcinoma, and the decision was made to change the recommendation to emphasize nasopharyngeal carcinoma. There was general agreement among the large group with this recommendation, with the additional indication of the lack of clinical evidence of distant disease.

Recommendation Put to Vote

PET should be used for staging patients with nasopharyngeal carcinoma without clinical evidence of distant disease.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree	N/A
	1	2	3	4	5	6	7	8	9	
Total	**3**	**8**	**6**	**2**						

Votes = 19

FINAL RECOMMENDATION

Original Recommendation 2008: PET is recommended for staging patients with nasopharyngeal carcinoma without clinical evidence of distant disease.

Updated Recommendation 2011: PET is recommended for the staging and assessment of recurrence in patients with nasopharyngeal carcinoma if conventional imaging is equivocal.

Qualifying Statements

- This report makes no distinction between studies examining PET and those examining PET/CT.
- Conventional imaging refers to CT and/or MRI unless otherwise specified.
- Retrospective design studies were excluded from this review, but several exist favouring the use of PET for head and neck cancer.
- With respect to primary site (T):
  - PET appears to be more accurate for the diagnosis of primary tumours, especially in cases where CT/MRI results are equivocal.

  - PET can identify the primary site in 30% of cases when undetected by clinical assessment and conventional imaging.
  - PET can detect some synchronous primaries that may be missed by other modalities.
- With respect to regional nodes (N):
  - In the clinically N-0 neck, PET does not appear to be better than conventional imaging, because of an unacceptably high false-negative rate. There is little evidence that PET leads to a change in patient management (2005-2008 update: Hafidh et al [16], Ng et al [17], Schoder et al [18], Wensing et al [19], Kim et al [20]; 2008-2011 update: Moeller et al [51] and Kyzas et al [55], Liao et al [56]). There was some evidence that PET scanning changed nodal staging status and/or radiation treatment planning. However, in many cases there was no pathologic confirmation of PET versus conventional imaging discrepancy. Exceptions were cases where distant metastatic disease was identified by PET, which changed treatment (2005-2008 update: Connell et al [9]).
- With respect to distant disease (M):
  - There is strong evidence that PET imaging is valuable in detecting distant metastatic disease and is better than conventional imaging. The advantage of PET is overwhelming for patients at high risk for distant disease, which include locally advanced disease and nasopharyngeal carcinoma (2008-2011 update: Kim et al [38], Law et al [39], Lonneux et al [40], Martin et al [41], Ng et al [42], Senft et al [43], Yamazaki et al [44], Wang et al [50]). The substantial incidence of false-positive rates of PET may mitigate the advantages for low-risk patients.

ASSESSMENT OF TREATMENT RESPONSE

Clinical Question

What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for head and neck cancer?

This question was not formally addressed in the head and neck evidence review, but a lack of compelling evidence was noted during the review process and subsequent updates.

RECURRENCE/RESTAGING

Clinical Question

What benefit to clinical management does PET or PET/CT contribute when recurrence of head and neck cancer is suspected but not proven? What benefit to clinical management does PET or PET/CT contribute to restaging at the time of documented recurrence for head and neck cancer?

DRAFT DSG Recommendation 2008

PET should be used for restaging patients being considered for major salvage treatment (surgery or other).

Provincial Consensus Meeting Deliberations

No major issues were raised during discussion of this recommendation.

Recommendation Put to Vote

PET should be used for restaging patients being considered for major salvage treatment (surgery or other).

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree	N/A
	1	2	3	4	5	6	7	8	9	
Total	**8**	**8**	**2**	**1**						

Votes = 19

FINAL RECOMMENDATION

Original Recommendation 2008: PET is recommended for restaging patients who are being considered for major salvage treatment (surgery or other).

Updated Recommendation 2011: PET is recommended for restaging patients who are being considered for major salvage treatment, including neck dissection.

Qualifying Statements

- With respect to recurrence and tumour surveillance after treatment, the evidence suggests that sites of disease that are clinically accessible for assessment did not benefit from PET imaging. However, for disease sites that were either not clinically accessible or difficult to examine, PET imaging showed significant advantages over conventional evaluation.
  - Oral cavity and oropharynx: insufficient evidence that PET is beneficial.
  - Larynx: moderate evidence that PET is beneficial/better than conventional imaging in detecting recurrent disease. PET also reduced the need for debilitating laryngeal biopsies (2005-2008 update: Gordin et al [11], Brouwer et al [12]).
  - Skull base and nasopharynx: moderate evidence that PET is beneficial/better than conventional imaging in detecting recurrent disease (2005-2008 update: Chan et al [21], Gil et al [14]).
  - Salivary gland: some evidence suggesting an advantage with PET (2005-2008 update: Roh et al [15]).
  - Nodal disease: For N+ patients, some evidence exists that PET is better than conventional imaging in detecting the status of residual disease following radiotherapy or chemoradiotherapy. The use of PET reduced both false-positive and false-negative rates compared to the gold standard (2005-2008 update: Chen et al [10]). 2008-2011 update: clinical trials are currently being conducted in Ontario on this matter. Once published, they will be evaluated for inclusion and incorporated into the recommendation report in subsequent updates.
  - There is evidence that PET detects distant relapse. There is strong evidence that the detection of distant disease leads to major changes in patient management in the salvage setting (2005-2008 update: Brouwer et al [7], Chang et al [2], Kim et al [4], Liu et al [3], Liu et al [5], Minovi et al [6], Yen et al [8] 2008-2011 update: Senft et al [43]).
- With respect to the role of PET in assessing status of neck lymphadenopathy following radiation or chemoradiation, the evidence suggests that PET-directed management of the neck after therapy appropriately spares neck dissections in patients with PET-negative residual CT abnormalities (2008-2011 update: Porceddu et al [37]).

SOLITARY METASTASIS IDENTIFIED AT TIME OF RECURRENCE

Clinical Question

What is the role of PET when a solitary metastasis is identified at the time of recurrence and the metastectomy is being contemplated?

This question was not addressed in the head and neck evidence review.

FUTURE RESEARCH

Practical treatment considerations and some retrospective data would suggest a benefit for selected patients with unusual pathologic tumour types that arise in the head and neck (e.g., neuroendocrine tumours). A tumour registry that includes the results of PET imaging would be of value.

JOURNAL REFERENCE

The following guideline recommendations have been published in *Clinical Oncology* (©2012 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved; www.clinicaloncologyonline.net):

- Yoo J, Henderson S, Walker-Dilks C. Evidence-based guideline recommendations on the use of positron emission tomography imaging in head and neck cancer. Clin Oncol. 2012 Sep 25. doi: 10.1016/j.clon.2012.08.007. Epub: 2012 Sep 26.

ACKNOWLEDGEMENTS

The Head and Neck DSG would like to thank Dr. John Yoo for taking the lead in drafting this systematic review.

For a complete list of the Head and Neck DSG members, please visit the CCO website at http://www.cancercare.on.ca/

Funding

The PEBC is a provincial initiative of Cancer Care Ontario supported by the Ontario Ministry of Health and Long-Term Care. All work produced by the PEBC is editorially independent from the Ontario Ministry of Health and Long-Term Care.

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

REFERENCES

1. Facey K, Bradbury I, Laking G, Payne E. Overview of the clinical effectiveness of positron emission tomography imaging in selected cancers. Health Technol Assess. 2007 Oct;11(44):iii-iv, xi-267.
2. Chang JT, Chan SC, Yen TC, Liao CT, Lin CY, Lin KJ, et al. Nasopharyngeal carcinoma staging by (18)F-fluorodeoxyglucose positron emissiontomography. Int J Radiat Oncol Biol Phys. 2005 Jun 1;62(2):501-7.
3. Liu FY, Chang JT, Wang HM, Liao CT, Kang CJ, Ng SH, et al. [18F]fluorodeoxyglucose positron emission tomography is more sensitive than skeletal scintigraphy for detecting bone metastasis in endemic nasopharyngeal carcinoma at initial staging. J Clin Oncol. 2006 Feb 1;24(4):599-604. Erratum in: J Clin Oncol. 2006 Jul 20;24(21):3515. Ng, Shu-Kung [corrected to Ng, Shu-Hang].
4. Kim SY, Roh JL, Yeo NK, Kim JS, Lee JH, Choi SH, et al. Combined 18F-fluorodeoxyglucose-positron emission tomography and computed tomography as a primary screening method for detecting second primary cancers and distant metastases in patients with head and neck cancer. Ann Oncol. 2007 Oct;18(10):1698-703. Epub 2007 Aug 22.
5. Liu FY, Lin CY, Chang JT, Ng SH, Chin SC, Wang HM, et al. 18F-FDG PET can replace conventional work-up in primary M staging of nonkeratinizing nasopharyngeal carcinoma. J Nucl Med. 2007 Oct;48(10):1614-9. Epub 2007 Sep 14.
6. Minovi A, Hertel A, Ural A, Hofmann E, Draf W, Bockmuehl U. Is PET superior to MRI in the pretherapeutic evaluation of head and neck squamous cell carcinoma? Kulak Burun Bogaz Ihtis Derg. 2007;17(6):324-8.
7. Brouwer J, Senft A, de Bree R, Comans EF, Golding RP, Castelijns JA, et al. Screening for distant metastases in patients with head and neck cancer: is there a role for (18)FDG-PET? Oral Oncol. 2006 Mar;42(3):275-80. Epub 2005 Nov 2.
8. Yen TC, Chang JT, Ng SH, Chang YC, Chan SC, Lin KJ, et al. The value of 18F-FDG PET in the detection of stage M0 carcinoma of the nasopharynx. J Nucl Med. 2005 Mar;46(3):405-10.
9. Connell CA, Corry J, Milner AD, Hogg A, Hicks RJ, Rischin D, et al. Clinical impact of, and prognostic stratification by, F-18 FDG PET/CT in head and neck mucosal squamous cell carcinoma. Head Neck. 2007 Nov;29(11):986-95.
10. Chen AY, Vilaseca I, Hudgins PA, Schuster D, Halkar R. PET-CT vs contrast-enhanced CT: what is the role for each after chemoradiation for advanced oropharyngeal cancer? Head Neck. 2006 Jun;28(6):487-95.
11. Gordin A, Daitzchman M, Doweck I, Yefremov N, Golz A, Keidar Z, et al. Fluorodeoxyglucose-positron emission tomography/computed tomography imaging in patients with carcinoma of the larynx: diagnostic accuracy and impact on clinical management. Laryngoscope. 2006 Feb;116(2):273-8.
12. Brouwer J, de Bree R, Comans EF, Akarriou M, Langendijk JA, Castelijns JA, et al. Improved detection of recurrent laryngeal tumor after radiotherapy using (18)FDG-PET as initial method. Radiother Oncol. 2008 May;87(2):217-20. Epub 2008 Mar 7.
13. Chan SC, Yen TC, Ng SH, Lin CY, Wang HM, Liao CT, et al. Differential roles of 18F-FDG PET in patients with locoregional advanced nasopharyngeal carcinoma after primary curative therapy: response evaluation and impact on management. J Nucl Med. 2006 Sep;47(9):1447-54.
14. Gil Z, Even-Sapir E, Margalit N, Fliss DM. Integrated PET/CT system for staging and surveillance of skull base tumors. Head Neck. 2007 Jun;29(6):537-45.
15. Roh JL, Ryu CH, Choi SH, Kim JS, Lee JH, Cho KJ, et al. Clinical utility of 18F-FDG PET for patients with salivary gland malignancies. J Nucl Med. 2007 Feb;48(2):240-6.

16. Hafidh MA, Lacy PD, Hughes JP, Duffy G, Timon CV. Evaluation of the impact of addition of PET to CT and MR scanning in the staging of patients with head and neck carcinomas. Eur Arch Otorhinolaryngol. 2006 Sep;263(9):853-9. Epub 2006 May 25.
17. Ng SH, Yen TC, Chang JT, Chan SC, Ko SF, Wang HM, et al. Prospective study of [18F]fluorodeoxyglucose positron emission tomography and computed tomography and magnetic resonance imaging in oral cavity squamous cell carcinoma with palpably negative neck. J Clin Oncol. 2006 Sep 20;24(27):4371-6.
18. Schöder H, Carlson DL, Kraus DH, Stambuk HE, Gönen M, Erdi YE, et al. 18F-FDG PET/CT for detecting nodal metastases in patients with oral cancer staged N0 by clinical examination and CT/MRI. J Nucl Med. 2006 May;47(5):755-62.
19. Wensing BM, Vogel WV, Marres HA, Merkx MA, Postema EJ, Oyen WJ, et al. FDG-PET in the clinically negative neck in oral squamous cell carcinoma. Laryngoscope. 2006 May;116(5):809-13. Erratum in: Laryngoscope. 2006 Jul;116(7 Pt1):1302.
20. Kim MR, Roh JL, Kim JS, Lee JH, Cho KJ, Choi SH, et al. Utility of 18F-fluorodeoxyglucose positron emission tomography in the preoperative staging of squamous cell carcinoma of the oropharynx. Eur J Surg Oncol. 2007 Jun;33(5):633-8. Epub 2007 Mar 27.
21. Chan SC, Ng SH, Chang JT, Lin CY, Chen YC, Chang YC, et al. Advantages and pitfalls of 18F-fluoro-2-deoxy-D-glucose positron emission tomography in detecting locally residual or recurrent nasopharyngeal carcinoma: comparison with magnetic resonance imaging. Eur J Nucl Med Mol Imaging. 2006 Sep;33(9):1032-40. Epub 2006 Apr 19.
22. Vogel WV, Wensing BM, van Dalen JA, Krabbe PF, van den Hoogen FJ, Oyen WJ. Optimised PET reconstruction of the head and neck area: improved diagnostic accuracy. Eur J Nucl Med Mol Imaging. 2005 Nov;32(11):1276-82. Epub 2005 Jul 16.
23. Yen TC, Chang YC, Chan SC, Chang JT, Hsu CH, Lin KJ, et al. Are dual-phase 18F-FDG PET scans necessary in nasopharyngeal carcinoma to assess the primary tumour and loco-regional nodes? Eur J Nucl Med Mol Imaging. 2005 May;32(5):541-8. Epub 2004 Dec 30.
24. Meller B, Sommer K, Gerl J, von Hof K, Surowiec A, Richter E, et al. High energy probe for detecting lymph node metastases with 18F-FDG in patients with head and neck cancer. Nuklearmedizin. 2006;45(4):153-9.
25. Pauleit D, Zimmermann A, Stoffels G, Bauer D, Risse J, Flüss MO, et al. 18F-FET PET compared with 18F-FDG PET and CT in patients with head and neck cancer. J Nucl Med. 2006 Feb;47(2):256-61.
26. Gordin A, Golz A, Keidar Z, Daitzchman M, Bar-Shalom R, Israel O. The role of FDG-PET/CT imaging in head and neck malignant conditions: impact on diagnostic accuracy and patient care. Otolaryngol Head Neck Surg. 2007 Jul;137(1):130-7.
27. Jeong HS, Baek CH, Son YI, Ki Chung M, Kyung Lee D, Young Choi J, et al. Use of integrated 18F-FDG PET/CT to improve the accuracy of initial cervical nodal evaluation in patients with head and neck squamous cell carcinoma. Head Neck. 2007 Mar;29(3):203-10.
28. Miyakubo M, Oriuchi N, Tsushima Y, Higuchi T, Koyama K, Arai K, et al. Diagnosis of maxillofacial tumor with L-3-[18f]-fluoro-alpha-methyltyrosine (FMT)PET: a comparative study with FDG-PET. Ann Nucl Med. 2007 Feb;21(2):129-35.
29. Nahmias C, Carlson ER, Duncan LD, Blodgett TM, Kennedy J, Long MJ, et al. Positron emission tomography/computerized tomography (PET/CT) scanning for preoperative staging of patients with oral/head and neck cancer. J Oral Maxillofac Surg. 2007 Dec;65(12):2524-35.
30. Roh JL, Yeo NK, Kim JS, Lee JH, Cho KJ, Choi SH, et al. Utility of 2-[18F] fluoro-2-deoxy-D-glucose positron emission tomography and positron emission tomography/computed tomography imaging in the preoperative staging of head and neck squamous cell carcinoma. Oral Oncol. 2007 Oct;43(9):887-93. Epub 2007 Jan 4.

31. Babin E, Desmonts C, Hamon M, Bénateau H, Hitier M. PET/CT for assessing mandibular invasion by intraoral squamous cell carcinomas. Clin Otolaryngol. 2008 Feb;33(1):47-51.
32. Brkovich VS, Miller FR, Karnad AB, Hussey DH, McGuff HS, Otto RA. The role of positron emission tomography scans in the management of the N-positive neck in head and neck squamous cell carcinoma after chemoradiotherapy. Laryngoscope. 2006 Jun;116(6):855-8.
33. Yen TC, Lin CY, Wang HM, Huang SF, Liao CT, Kang CJ, et al. 18F-FDG-PET for evaluation of the response to concurrent chemoradiation therapy with intensity-modulated radiation technique for Stage T4 nasopharyngeal carcinoma. Int J Radiat Oncol Biol Phys. 2006 Aug 1;65(5):1307-14.
34. Kim SY, Lee SW, Nam SY, Im KC, Kim JS, Oh SJ, et al. The Feasibility of 18F-FDG PET scans 1 month after completing radiotherapy of squamous cell carcinoma of the head and neck. J Nucl Med. 2007 Mar;48(3):373-8.
35. Goerres GW, Schmid DT, Schuknecht B, Eyrich GK. Bone invasion in patients with oral cavity cancer: comparison of conventional CT with PET/CT and SPECT/CT. Radiology. 2005 Oct;237(1):281-7. Epub 2005 Aug 18. Erratum in: Radiology. 2006 Apr;239(1):303.
36. Kunkel M, Helisch A, Reichert TE, Jeong JH, Buchholz HG, Benz P, et al. Clinical and prognostic value of [(18)F]FDG-PET for surveillance of oral squamous cell carcinoma after surgical salvage therapy. Oral Oncol. 2006 Mar;42(3):297-305. Epub 2005 Nov 28.
37. Porceddu SV, Pryor DI, Burmeister E, Burmeister BH, Poulsen MG, C. FM, et al. Results of a prospective study of positron emission tomography-directed management of residual nodal abnormalities in node-positive head and neck cancer after definitive radiotherapy with or without systemic therapy. Head Neck. 2011.
38. Kim SY, Kim JS, Doo H, Lee H, Lee JH, Cho KJ, et al. Combined [18F]fluorodeoxyglucose positron emission tomography and computed tomography for detecting contralateral neck metastases in patients with head and neck squamous cell carcinoma. Oral Oncol. 2011;47(5):376-80.
39. Law A, Peters LJ, Dutu G, Rischin D, Lau E, Drummond E, et al. The utility of PET/CT in staging and assessment of treatment response of nasopharyngeal cancer. J Med Imag Radiat Oncol. 2011;55(2):199-205.
40. Lonneux M, Hamoir M, Reychler H, Maingon P, Duvillard C, Calais G, et al. Positron emission tomography with [18F]fluorodeoxyglucose improves staging and patient management in patients with head and neck squamous cell carcinoma: a multicenter prospective study. J Clin Oncol. 2010;28(7):1190-5.
41. Martin RCW, Fulham M, Shannon KF, Hughes C, Gao K, Milross C, et al. Accuracy of positron emission tomography in the evaluation of patients treated with chemoradiotherapy for mucosal head and neck cancer. Head and Neck. 2009;31(2):244-50.
42. Ng SH, Chan SC, Yen TC, Liao CT, Lin CY, Tung-Chieh Chang J, et al. PET/CT and 3-T whole-body MRI in the detection of malignancy in treated oropharyngeal and hypopharyngeal carcinoma. Eur J Nucl Med Mol Imagi. 2011;38(6):996-1008.
43. Senft A, de Bree R, Hoekstra OS, Kuik DJ, Golding RP, Oyen WJG, et al. Screening for distant metastases in head and neck cancer patients by chest CT or whole body FDG-PET: A prospective multicenter trial. Radiat Oncol. 2008;87(2):221-9.
44. Yamazaki Y, Saitoh M, Notani K-i, Tei K, Totsuka Y, Takinami S-i, et al. Assessment of cervical lymph node metastases using FDG-PET in patients with head and neck cancer. Ann Nucl Med. 2008;22(3):177-84.
45. Deantonio L, Beldi D, Gambaro G, Loi G, Brambilla M, Inglese E, et al. FDG-PET/CT imaging for staging and radiotherapy treatment planning of head and neck carcinoma. Radiat Oncol. 2008;3:29.

46. Dietl B, Marienhagen J, Kuhnel T, Schreyer A, Kolbl O. The impact of FDG-PET/CT on the management of head and neck tumours: The radiotherapist's perspective. Oral Oncol. 2008;44(5):504-8.
47. Gardner M, Halimi P, Valinta D, Plantet MM, Alberini JL, Wartski M, et al. Use of single MRI and 18F-FDG PET-CT scans in both diagnosis and radiotherapy treatment planning in patients with head and neck cancer: Advantage on target volume and critical organ delineation. Head Neck. 2009;31(4):461-7.
48. Guido A, Fuccio L, Rombi B, Castellucci P, Cecconi A, Bunkheila F, et al. Combined 18F-FDG-PET/CT Imaging in radiotherapy target delineation for head-and-neck cancer. Int J Radiat Oncol Biol Phys. 2009;73(3):759-63.
49. Rudmik L, Lau HY, Matthews TW, Bosch JD, Kloiber R, Molnar CP, et al. Clinical utility of PET/CT in the evaluation of head and neck squamous cell carcinoma with an unknown primary: A prospective clinical trial. Head Neck. 2011;33(7):935-40.
50. Wang Y-F, Liu R-S, Chu P-Y, Chang F-C, Tai S-K, Tsai T-L, et al. Positron emission tomography in surveillance of head and neck squamous cell carcinoma after definitive chemoradiotherapy. Head Neck. 2009;31(4):442-51.
51. Moeller BJ, Rana V, Cannon BA, Williams MD, Sturgis EM, Ginsberg LE, et al. Prospective risk-adjusted [18F]fluorodeoxyglucose positron emission tomography and computed tomography assessment of radiation response in head and neck cancer. J Clin Oncol. 2009;27(15):2509-15.
52. Abgral R, Querellou S, Potard G, Le Roux P-Y, Le Duc-Pennec A, Marianovski R, et al. Does 18F-FDG PET/CT improve the detection of posttreatment recurrence of head and neck squamous cell carcinoma in patients negative for disease on clinical follow-up? J Nucl Med. 2009;50(1):24-9.
53. Isles MG, McConkey C, Mehanna HM. A systematic review and meta-analysis of the role of positron emission tomography in the follow up of head and neck squamous cell carcinoma following radiotherapy or chemoradiotherapy. Clin Otolaryngol. 2008;33(3):210-22.
54. Inohara H, Enomoto K, Tomiyama Y, Yoshii T, Osaki Y, Higuchi I, et al. The role of CT and 18F-FDG PET in managing the neck in node-positive head and neck cancer after chemoradiotherapy. Acta Oto-Laryngol. 2009;129(8):893-9.
55. Kyzas PA, Evangelou E, Denaxa-Kyza D, Ioannidis JPA. 18F-fluorodeoxyglucose positron emission tomography to evaluate cervical node metastases in patients with head and neck squamous cell carcinoma: A meta-analysis. J Nat Cancer Inst. 2008;100(10):712-20.
56. Liao CT, Wang HM, Huang SF, Chen IH, Kang CJ, Lin CY, et al. PET and PET/CT of the neck lymph nodes improves risk prediction in patients with squamous cell carcinoma of the oral cavity. J Nucl Med2011;52(2):180-7.

Appendix 1a. MEDLINE search strategy update U.K. Health Technology Assessment systematic review on PET imaging in selected cancers.

Search run 24 June 2008
Includes primary studies (n=2060) and systematic reviews (n=856)
Retrieval period from August 2005 to June 2008

Ovid MEDLINE(R) 1996 to June Week 2 2008

#	Searches	Results
1	Tomography, Emission-Computed/	14196
2	(positron adj emission adj tomography).ti,ab.	14193
3	PET.ti,ab.	21371
4	PET-FDG.ti,ab.	155
5	Fluorodeoxyglucose F18/	7990
6	18f fluorodeoxyglucose.ti,ab.	1118
7	18fdg.ti,ab.	330
8	2-fluoro-2-deoxy-d-glucose.ti,ab.	250
9	2-fluoro-2-deoxyglucose.ti,ab.	59
10	18f-fdg.ti,ab.	1351
11	fluorine-18-fluorodeoxyglucose.ti,ab.	524
12	positron-emission tomography/	8899
13	PET-CT.ti,ab.	1772
14	PET$CT.ti,ab.	2
15	or/1-14	31518
16	deoxyglucose/	2869
17	deoxyglucose.ti,ab.	2574
18	desoxyglucose.ti,ab.	16
19	desoxy-glucose.ti,ab.	11
20	deoxy-d-glucose.ti,ab.	1977
21	desoxy-d-glucose.ti,ab.	12
22	2deoxyglucose.ti,ab.	2
23	2deoxy-d-glucose.ti,ab.	6
24	fluorodeoxyglucose.ti,ab.	3420
25	fluorodesoxyglucose.ti,ab.	16
26	fludeoxyglucose.ti,ab.	42
27	fluordeoxyglucose.ti,ab.	23
28	fluordesoxyglucose.ti,ab.	3
29	18fluorodeoxyglucose.ti,ab.	49
30	18fluorodesoxyglucose.ti,ab.	1
31	18fluordeoxyglucose.ti,ab.	0
32	fdg$.ti,ab.	6977
33	18fdg$.ti,ab.	331
34	18f-dg$.ti,ab.	5
35	or/16-34	12309
36	fluor.ti,ab.	472
37	2fluor$.ti,ab.	12
38	fluoro.ti,ab.	6187

39	fluorodeoxy.ti,ab.	67
40	fludeoxy.ti,ab.	3
41	fluorine.ti,ab.	2680
42	18f.ti,ab.	4596
43	18flu$.ti,ab.	98
44	or/36-43	11911
45	glucose.ti,ab.	103645
46	pet.ti,ab.	21371
47	petscan$.ti,ab.	5
48	Tomography, Emission-Computed/	14196
49	pet ct.ti,ab.	1772
50	emission.ti,ab.	37628
51	tomograph.ti,ab.	751
52	tomographs.ti,ab.	165
53	tomographic$.ti,ab.	11313
54	tomography.ti,ab.	76598
55	tomographies.ti,ab.	116
56	or/51-55	85792
57	50 and 56	20590
58	46 or 47 or 48 or 49 or 57	35054
59	44 and 45	2573
60	35 or 59	12507
61	58 and 60	8366
62	exp neoplasms/	806680
63	neoplasm staging/	49856
64	cancer$.ti,ab.	389251
65	tumor$.ti,ab.	349790
66	tumour$.ti,ab.	75060
67	carcinoma$.ti,ab.	165074
68	neoplasm$.ti,ab.	32308
69	lymphoma.ti,ab.	41481
70	melanoma.ti,ab.	27108
71	staging.ti,ab.	20085
72	metastas$.ti,ab.	81288
73	metastatic.ti,ab.	53184
74	exp neoplasm metastasis/	46034
75	exp neoplastic processes/	109110
76	neoplastic process$.ti,ab.	884
77	non small cell.ti,ab.	13022
78	adenocarcinoma$.ti,ab.	35985
79	squamous cell.ti,ab.	25718
80	nsclc.ti,ab.	7274
81	osteosarcoma$.ti,ab.	5515
82	phyllodes.ti,ab.	477
83	cytosarcoma$.ti,ab.	0
84	fibroadenoma$.ti,ab.	1061

85	(non adj small adj cell).ti,ab.	13022
86	(non adj2 small adj2 cell).ti,ab.	13100
87	(nonsmall adj2 cell).ti,ab.	853
88	plasmacytoma$.ti,ab.	1308
89	myeloma.ti,ab.	11218
90	multiple myeloma.ti,ab.	8668
91	lymphomblastoma$.ti,ab.	0
92	lymphocytoma$.ti,ab.	72
93	lymphosarcoma$.ti,ab.	344
94	immunocytoma.ti,ab.	110
95	sarcoma$.ti,ab.	20984
96	hodgkin$.ti,ab.	18282
97	(nonhodgkin$ or non hodgkin$).ti,ab.	12659
98	or/62-97	972317
99	15 and 98	11146
100	61 and 98	5465
101	99 or 100	11152
102	limit 101 to (english language and humans and yr="2005 - 2008")	4528
103	(comment or editorial or letter or case reports).pt.	978402
104	102 not 103	3145
105	(integrative research review$ or research integration).ti,ab.	37
106	(methodologic$ adj10 review$).ti,ab.	2371
107	(methodologic$ adj10 overview$).ti,ab.	130
108	(quantitativ$ adj10 review$).ti,ab.	1548
109	(quantitativ$ adj10 overview$).ti,ab.	124
110	(quantitativ$ adj10 synthes$).ti,ab.	875
111	(systematic adj10 review$).ti,ab.	15200
112	(systematic adj10 overview$).ti,ab.	404
113	(metaanal$ or meta anal$).ti,ab.	18450
114	meta-analysis/	15791
115	meta analysis.pt.	15791
116	or/105-115	38409
117	(review-tutorial or review-academic or review).pt.	835243
118	(pooling or pooled analys$ or mantel haenszel$).ti,ab.	5302
119	(peto$ or der simonian or dersimonian or fixed effect$).ti,ab.	2655
120	116 or 117 or 118 or 119	857219
121	104 and 120	920
122	104 not 120	2225
123	(200508: or 200509: or 20051: or 2006: or 2007: or 2008:).ed.	1865975
124	121 and 123	856
125	122 and 123	2060
126	from 124 keep 1-856	856
127	from 125 keep 1-1000	1000
128	from 125 keep 1001-2000	1000
129	from 125 keep 2001-2060	60

Appendix 1b. MEDLINE search strategy update U.K. Health Technology Assessment systematic review on PET imaging in selected cancers.

Retrieval period from August 2005 to July 2011

Ovid MEDLINE(R) without revisions 1996 to July Week 3 2011

#	Searches
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$.ti,ab. or lymphoma.ti,ab. or melanoma.ti,ab. or staging.ti,ab. or metastas$.ti,ab. or metastatic.ti,ab. or exp neoplasm metastasis/ or exp neoplastic processes/ or neoplastic process$.ti,ab. or non small cell.ti,ab. or adenocarcinoma$.ti,ab. or squamous cell.ti,ab. or nsclc.ti,ab. or osteosarcoma$.ti,ab. or thymoma.ti,ab. or phyllodes.ti,ab. or cytosarcoma$.ti,ab. or fibroadenoma$.ti,ab. or (non adj small adj cell).ti,ab. or (non adj2 small adj2 cell).ti,ab. or (nonsmall adj2 cell).ti,ab. or myeloma.ti,ab. or multiple myeloma.ti,ab. or lymphoblastoma$.ti,ab. or lymphocytoma$.ti,ab. or lymphosarcoma$.ti,ab. or immunocytoma.ti,ab. or sarcoma$.ti,ab. or hodgkin$.ti,ab. or (nonhodgkin$ or non hodgkin$).ti,ab.
15	1 and 14
16	13 and 14
17	15 or 16
18	limit 17 to (human and english language and yr="2008 - 2011")

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	(200806: or 200807: or 200808: or 200809: or 20081: or 2009: or "2010").ed.
31	28 and 30
32	29 and 30

Appendix 2a. EMBASE search strategy update U.K. Health Technology Assessment systematic review on PET imaging in selected cancers.

Search run 2 July 2008
Includes primary studies (n=4285) and systematic reviews (n=1497)
Retrieval period from 2005 to July 2008

EMBASE 1996 to 2008 Week 26

#	Searches	Results
1	deoxyglucose/	2417
2	deoxyglucose.ti,ab.	2570
3	desoxyglucose.ti,ab.	13
4	desoxy-glucose.ti,ab.	15
5	deoxy-d-glucose.ti,ab.	1947
6	desoxy-d-glucose.ti,ab.	10
7	2deoxyglucose.ti,ab.	3
8	2-deoxy-d-glucose.ti,ab.	1815
9	fluorodeoxyglucose.ti,ab.	3629
10	fluorodesoxyglucose.ti,ab.	20
11	fludeoxyglucose.ti,ab.	46
12	fluordeoxyglucose.ti,ab.	27
13	fluordesoxyglucose.ti,ab.	5
14	18fluorodeoxyglucose.ti,ab.	63
15	18fluorodesoxyglucose.ti,ab.	3
16	18fluordeoxyglucose.ti,ab.	0
17	fdg$.ti,ab.	7410
18	18fdg$.ti,ab.	472
19	18f-dg$.ti,ab.	9
20	or/1-19	12333
21	fluor.ti,ab.	440
22	2fluor$.ti,ab.	10
23	fluoro.ti,ab.	7009
24	fluorodeoxy.ti,ab.	90
25	fludeoxy.ti,ab.	1
26	fluorine.ti,ab.	3221
27	18f.ti,ab.	6816
28	18flu$.ti,ab.	143
29	or/21-28	14709
30	glucose.ti,ab.	104283
31	pet.ti,ab.	22197
32	petscan$.ti,ab.	9
33	computer assisted emission tomography/	1421
34	pet ct.ti,ab.	2023
35	emission.ti,ab.	42287
36	tomograph.ti,ab.	755
37	tomographs.ti,ab.	141
38	tomographic$.ti,ab.	10759

39	tomography.ti,ab.	75334
40	tomographies.ti,ab.	108
41	or/36-40	84118
42	35 and 41	21289
43	31 or 32 or 33 or 34 or 42	33404
44	29 and 30	2956
45	20 or 44	12557
46	43 and 45	8790
47	cancer$.ti,ab.	385221
48	tumor$.ti,ab.	340943
49	tumour$.ti,ab.	76396
50	carcinoma$.ti,ab.	162315
51	neoplasm$.ti,ab.	30388
52	lymphoma.ti,ab.	40473
53	melanoma.ti,ab.	27301
54	staging.ti,ab.	20100
55	metastas$.ti,ab.	79569
56	metastatic.ti,ab.	52902
57	neoplastic process$.ti,ab.	827
58	neoplas$.ti,ab.	66122
59	exp neoplasm/	874595
60	cancer staging/	62622
61	exp metastasis/	110090
62	exp "oncogenesis and malignant transformation"/	74028
63	or/47-62	1009399
64	46 and 63	5802
65	(editorial or letter or review).pt.	1107915
66	64 not 65	4890
67	limit 66 to (human and english language and yr="2005 - 2008")	1987
68	(integrative research review$ or research integration).ti,ab.	20
69	(methodologic$ adj10 review$).ti,ab.	1824
70	(methodologic$ adj10 overview$).ti,ab.	138
71	(quantitativ$ adj10 review$).ti,ab.	1467
72	(quantitativ$ adj10 overview$).ti,ab.	124
73	(quantitativ$ adj10 synthes$).ti,ab.	915
74	(systematic adj10 review$).ti,ab.	14736
75	(systematic adj10 overview$).ti,ab.	402
76	(metaanal$ or meta anal$).ti,ab.	18093
77	meta-analysis/	30401
78	(pooling or pooled analys$ or mantel haenszel$).ti,ab.	4802
79	(peto$ or der simonian or dersimonian or fixed effect$).ti,ab.	1566
80	or/68-79	55380
81	46 and 63 and 80	107
82	(editorial or letter).pt.	441971
83	81 not 82	107
84	limit 83 to (human and english language and yr="2005 - 2008")	38

85	(positron adj emission adj tomography).ti,ab.	14828
86	PET.ti,ab.	22197
87	PET-FDG.ti,ab.	163
88	FDG-PET.ti,ab.	5206
89	fludeoxyglucose F 18/	10204
90	18f fluorodeoxyglucose.ti,ab.	1594
91	18fdg.ti,ab.	471
92	2-fluoro-2-deoxy-d-glucose.ti,ab.	252
93	2-fluoro-2-deoxyglucose.ti,ab.	56
94	18f-fdg.ti,ab.	2013
95	fluorine-18-fluorodeoxyglucose.ti,ab.	539
96	positron emission tomography/	30927
97	or/85-96	37717
98	cancer$.ti,ab.	385221
99	tumor$.ti,ab.	340943
100	tumour$.ti,ab.	76396
101	carcinoma$.ti,ab.	162315
102	neoplasm$.ti,ab.	30388
103	lymphoma.ti,ab.	40473
104	melanoma.ti,ab.	27301
105	staging.ti,ab.	20100
106	metastas$.ti,ab.	79569
107	metastatic.ti,ab.	52902
108	neoplastic process$.ti,ab.	827
109	neoplas$.ti,ab.	66122
110	exp neoplasm/	874595
111	cancer staging/	62622
112	exp metastasis/	110090
113	exp "oncogenesis and malignant transformation"/	74028
114	or/98-113	1009399
115	97 and 114	14319
116	115 not 65	10146
117	limit 116 to (human and english language and yr="2005 - 2008")	4284
118	80 or review.pt.	696716
119	115 and 118	3275
120	119 not 82	3269
121	limit 120 to (human and english language and yr="2005 - 2008")	1497
122	67 or 117	4285
123	84 or 121	1497

Appendix 2b. EMBASE search strategy update U.K. Health Technology Assessment systematic review on PET imaging in selected cancers.

Retrieval period from 2008 to July 2011

Embase 1996 to 2011 Week 29

#	Searches
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$.ti,ab. or lymphoma.ti,ab. or thymoma.ti,ab. or melanoma.ti,ab. or staging.ti,ab. or metastas$.ti,ab. or metastatic.ti,ab. or exp neoplasm metastasis/ or exp neoplastic processes/ or neoplastic process$.ti,ab. or non small cell.ti,ab. or adenocarcinoma$.ti,ab. or squamous cell.ti,ab. or nsclc.ti,ab. or osteosarcoma$.ti,ab. or phyllodes.ti,ab. or cytosarcoma$.ti,ab. or fibroadenoma$.ti,ab. or (non adj2 small adj2 cell).ti,ab. or (nonsmall adj2 cell).ti,ab. or plasmacytoma$.ti,ab. or myeloma.ti,ab. or multiple myeloma.ti,ab. or lymphoblastoma$.ti,ab. or lymphocytoma$.ti,ab. or lymphosarcoma$.ti,ab. or immunocytoma.ti,ab. or sarcoma$.ti,ab. or hodgkin$.ti,ab. or (nonhodgkin$ or non hodgkin$).ti,ab.
15	1 and 14
16	13 and 14
17	15 or 16
18	limit 17 to (human and english language and yr="2008 - 2010")

19	(comment or comment$ or discussion or discussion$ or editorial comment$ or in brief or letter or case reports or invited commentary).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$).ti,ab.
24	21 or 22
25	20 and 24
26	20 not 24
27	limit 26 to (editorial or letter or note)
28	26 not 27
29	(conference or conference proceeding or conference proceeding$ or conference paper or conference paper$).ti,ab.
30	28 not 29
31	(session summary or conference paper or discussion or in brief or invited comment or invited comment$).ti.
32	30 not 31

Appendix 3. PET for head and neck cancer: summary of the evidence from 2005 to 2008.

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
Diagnosis/Staging								
Chang, 2005 (2)	Evaluate the role of dual-phase FDG-PET in the staging of NPC.	95	Imaged from head to upper thigh	Biopsy if feasible. Follow-up if biopsy not feasible	None	Nuclear medicine physicians blinded to other imaging results and clinical data	Overall distant metastasis: FDG-PET: sens – 100%, spec – 90.1%, PPV – 63.6%, NPV – 100%, accuracy – 91.6% By metastatic site: Lung: sens – 100%, spec – 97.8%, accuracy – 97.9%, PPV – 60%, NPV – 100% Mediastinum: sens – 100%, spec – 96.6%, accuracy – 96.8%, PPV – 66.7%, NPV – 100% Liver: sens – 100%, spec – 98.9%, accuracy – 98.9%, PPV – 75%, NPV – 100% Bone: sens – 100%, spec – 96.7%, accuracy – 96.8%, PPV – 57.1%, NPV – 100% Infraclavicular LN: sens – 100%, spec – 97.8%, accuracy – 97.9%, PPV – 50%, NPV – 100%	FDG-PET stages N and M disease of NPC more accurately and sensitively than does the conventional workup. Patients with advanced node disease, particularly N3 disease, would benefit the most from FDG-PET.
Vogel, 2005 (22)	Assess the impact of better image quality from optimized head and neck reconstruction (OHR) images on diagnostic yield in the staging of malignancies in the head and neck area.	28	FDG-PET	Histology	Std whole body reconstructions (SWR) vs. OHR based images	Nuclear medicine physicians blinded to the final pathological diagnosis	Primary tumour: FDG-PET SWR images: sens – 92% FDG-PET OHR images: sens – 100% Lymph node metastases: FDG-PET SWR images: sens – 11%, spec – 89%, PPV – 33%, NPV – 68% FDG-PET OHR images: sens – 44%, spec – 74%, PPV – 44%, NPV – 74%	Routine whole-body PET reconstruction parameters may prove inadequate for the head and neck area. Image reconstruction adapted to low photon attenuation in the head and neck area may improve image quality and the diagnostic value of FDG-PET, despite higher false positive rate attributable to the fact that visualization of FGD accumulation in benign reactive lymph nodes is also enhanced.
Yen, 2005 (Eur J Nucl Med Mol Imag) (23)	Determine the usefulness of dual-phase FDG-PET in assessing primary NPC and its regional nodal metastases.	84	Images from the head and neck to upper thigh and then three hours later from the head and neck to upper chest	Histology, clinical and imaging follow-up	MRI	Nuclear medicine physicians blinded to relevant clinical information, except for primary diagnosis	PET @ 40 min and @ 40 min + 3 h and MRI all had 100% sensitivity and 100% accuracy to detect the main tumour. Total lesions: PET @ 40 min: sens – 97.7%, spec – 94.9%, accuracy – 96.7% PET @ 40 min + 3 h: sens – 98.9%, spec – 95.5%, accuracy – 97.6% MRI: sens – 93.5%, spec – 91.1%, accuracy – 92.6% Metastatic LN's PET @ 40 min: sens – 96.6%, spec – 94.9%, accuracy – 95.8% PET @ 40 min + 3h: sens – 98.3%, spec – 95.5%, accuracy – 97% MRI: sens – 90.5%, spec – 91.1%, accuracy – 90.8%	FDG-PET is superior to MRI in identifying lower neck nodal metastasis of NPC. Additional 3h FDG-PET contributes no further information in the detection of primary tumours or loco-regional metastatic nodes in untreated patients with NPC. MRI and FDG-PET have an equal ability to identify primary tumours and retropharyngeal, upper neck, and supraclavicular lymph nodes.

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
Gordin, 2006 (11)	Assess the role of PET/CT compared to PET and CT in laryngeal carcinoma; also evaluated the impact of PET/CT results on patient care	42	Whole body PET with noncontrast enhanced CT	Histology	Contrast-enhanced CT and PET	Nuclear medicine physicians not blinded to patient data	Diagnosis by PET/CT examination: PET-CT: sens – 92%, spec – 96%, PPV –96%, NPV – 92%, accuracy – 94% PET: sens – 92%, spec – 73%, PPV – 76%, NPV – 90%, accuracy – 86% CT: sens – 88%, spec – 8%, PPV – 52%, NPV – 40%, accuracy – 51% Diagnosis by lesion: PET-CT: sens – 96%, spec – 96%, PPV – 96%, NPV – 96%, accuracy – 96% PET: sens – 96%, spec – 61%, PPV – 71%, NPV – 95%, accuracy – 79% CT: sens – 83%, spec – 38%, PPV – 56%, NPV – 70%, accuracy – 61% Impact on patient care: PET/CT altered care for 25/42 patients Previously planned diagnostic procedures eliminated in 13 patients Planned therapy changed in 9 patients (8 patients down-staged, 1 patient up-staged).	The performance of PET-CT is better than standalone PET or CT in patients with cancer of the larynx. PET-CT had a major impact on management of 59% of patients. When a PET-CT study is negative, additional clinical and radiologic follow up can be postponed, at least temporarily. A positive PET-CT scan should encourage the head and neck surgeon to obtain a biopsy from the larynx and guide it to a metabolically active area.
Hafidh, 2006 (16)	Assess the impact of the addition of whole body PET scanning to their institution's standard investigation protocol for new patients with head and neck SCC (CT and MRI)	48	Multi-ring PET, scan from mid-thigh to crown of skull	Histology	CT and MRI	NR	Identify primary tumour: PET: 41/45 correctly identified CT: 40/45 correctly identified MRI: 41/45 correctly identified Cervical node dissection: PET: sens – 70%, spec – 75%, PPV – 82.3%, NPV – 60%, accuracy – 71.9% CT: sens – 40%, spec – 83.3%, PPV – 80%, NPV – 45.5%, accuracy – 56.2% MRI: sens – 55%, spec – 83.3%, PPV – 84.6%, NPV – 52.6%, accuracy – 65.6% ** the sensitivity, PPV and accuracy for each test reported in the publication are not correct. The numbers above are based on calculated 2x2 tables, for which the numbers contained within were obtained from the text and tables of the publication.	Pet is comparable to current conventional imaging modalities in detecting primary tumours. The high rate of false positive results of PET in nodal metastasis highlights the higher sensitivity of PET in detecting nodal disease. PET only slightly improved the classification of N+ necks PET has no considerable role to play in N0 neck imaging protocols PET is less sensitive than both CT and MRI in detecting occult nodal disease. PET proved to be disappointingly similar to CT and MRI in an attempted identification of a small number of unknown primaries. PET was not reliable in detecting distant metastasis, as the rate of false positive findings was high. However, interpretation of results is limited by the small number of study patients with distant metastases. These findings cast doubt on the merit of the routine addition of PET to the current investigative radiology protocols for presenting HNSCC patients.

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
								Maximum SUV is a reasonable index of malignancy in HNSCC primary and metastatic tumour. This study established a maximum SUV of 3.2 for nodal tumour.
Liu, 2006 (3)	Evaluate FDG-PET and skeletal scintigraphy (SS) for detecting bone metastasis in endemic NPC patients at initial staging	30 of 202 eligible pts were found to have bone metastasis	PET scans from vertex to upper thighs	Clinical and/or radiological follow-up (histology, SS, PET, MRI)	Whole-body SS	Nuclear physicians blinded to individual patient data	Detection of bone metastasis (patient based): PET: Sens – 70%, Spec – 98.8%, accuracy – 94.6% SS: Sens – 36.7%, Spec – 97.7%, accuracy – 88.6%	FDG-PET is more sensitive and accurate than SS to detect bone metastasis, especially for lesions in the vertebral spine.
Meller, 2006 (24)	To develop and test a new gamma-sensitive probe with electronic collimation capable to detect 511 keV positron annihilation quanta	36	FDG-PET	Histology	Ultrasound (US), positron emission probe (PEP)	NR	Detection of lymph node involvement: PET: sens – 86%, spec – 80%, PPV – 85%, NPV – 80%, accuracy – 83% PEP: sens – 95%, spec – 60%, PPV – 77%, NPV – 90%, accuracy – 81% US: Sens – 95%, spec – 40%, PPV – 69%, NPV – 86%, accuracy – 72%	PET has the highest specificity as compared with PEP and US, but lower sensitivity. PET and PEP had similar accuracies
Ng, 2006 (17)	Assess the clinical usefulness of FDG-PET, CT/MRI and their visual correlation in oral SCC patients with palpably negative neck	134	Images from the vertex to the upper thighs	Histology	CT/MRI	Nuclear medicine physicians blinded to CT/MRI findings	Patient basis: FDG-PET: sens – 51.4%, spec – 91.9%, accuracy – 81.3%, PPV – 69.2%, NPV – 84.3% CT/MRI: sens – 31.4%, spec – 91.9%, accuracy – 76.1%, PPV – 57.9%, NPV – 79.1% FDG-PET + CT/MRI: sens – 57.1%, spec – 96%, accuracy – 85.8%, PPV – 83.3%, NPV – 86.4% For results from different levels see study summary	FDG-PET is superior to CT/MRI for detecting palpably occult neck metastasis of oral SCC. Because FDG-PET could reduce the probability of occult neck metastasis to less than 15% in T1 to T3 tumours, it should be indicated for evaluation of these subpopulations.
Pauleit, 2006 (25)	Investigate the diagnostic potential of FET-PET in patients with HNSCC by comparing FET to FDG and conventional imaging using CT	21	FET-PET and FDG-PET	Histology	CT	Nuclear medicine physicians blinded to clinical information	FDG-PET: Sens 93%, Spec 79%, Accuracy 83% FET-PET: Sens 75%, Spec 95%, Accuracy 86% CT: Sens 64%, Spec 86%, Accuracy 80%	FET may not replace FDG in the PET diagnostics of H and N cancer but may be a helpful additional tool in selected patients by allowing better differentiation of tumour tissue from inflammatory tissue. The sensitivity of FET PET in SCC is inferior to that of FDG-PET b/c of lower SUVs..
Schoder, 2006 (18)	Determine the diagnostic accuracy of FDG-PET/CT in patients with HNSCC and N0 neck who were scheduled to undergo elective neck dissection as part of their routine surgical treatment.	31	Scans of the head and neck from the midskull to the thoracic inlet	Histology	None	Nuclear medicine physicians not blinded to clinical or CT/MRI data	Primary tumour: PET/CT: sens – 87.1 Nodal levels: PET/CT: sens – 67%, spec – 95%, PPV – 50%, NPV – 98%, accuracy - 94% Neck sides: PET/CT: sens – 67%, spec – 85%, PPV – 60%, NPV – 88%, accuracy – 80%	FDG-PET can identify lymph node metastases in a segment of patients with oral cancer and N0 neck. A negative test can exclude metastatic deposits with high specificity. Despite reasonably high overall accuracy, the clinical application of PET/CT in the N0 neck may be

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
								limited by the combination of limited sensitivity for small metastatic deposits and a relatively high number of false-positive findings. The surgical management of the N0 neck should therefore not be based on PET/CT findings alone.
Wensing, 2006 (19)	Evaluate whether further reduction of occult metastatic disease in oral carcinoma can be achieved by adding FDG-PET scanning to the preoperative workup	30 (2 patients excluded), left with 28 patients	Scans of head and neck area	Surgery, histology	Ultrasound-guided fine needle aspiration	NR	Lymph node metastases: FDG-PET: sens – 33%, spec – 76%, accuracy – 63%	In patients with cN0 SCC of the oral cavity, FDG-PET does not contribute to the preoperative workup. FDG-PET does not replace SOHND as a staging procedure.
Connell, 2007 (9)	Determine the incremental value of PET/CT over conventional assessment for staging, posttreatment assessment of response and ongoing follow-up in HNSCC	76	Images of neck, thorax, abdomen, and pelvis	Cytology, histology and/or clinical and radiologic follow-up	Conventional assessment	Not blinded	Staging: 35 patients had staging PET/CT scan. PET/CT change TNM classification in 12 (34%) patients: 2 patients were down-staged and 10 were up-staged. Clinical impact: high 4/35, medium 10/35 Accuracy assessment not possible b/c most patients did not receive histopathologic confirmation.	PET/CR has a major incremental impact in the staging of patients with HNSCC.
Gordin, 2007 (26)	Assess the role of PET/CT compared with PET and CT separately in head and neck cancer. The impact of PET/CT results on patient treatment also investigated.	90	Whole body PET and non-contrast enhanced CT	Histology (n=56) and clinical and radiologic follow up (n=28)	Contrast enhanced CT and/or MRI (CI) of head and neck	Images analyzed independently of each other	Diagnosis for malignancy: PET/CT: sens – 88.5%, spec – 94.5%, PPV – 93.9%, NPV – 89.7%, accuracy – 91.6% PET: sens – 88.5%, spec – 70.9%, PPV – 74.2%, NPV – 86.7%, accuracy – 79.4% CI: sens – 92.3%, spec 18.2%, PPV – 51.6%, NPV – 71.4%, accuracy – 54.2% PET/CT altered further clinical management in 51 (56%) of patients. PET/CT eliminated the need for previously planned diagnostic procedures in 24 patients. PET/CT results led to changes in planned therapy in 21 patients. Staging: PET/CT: sens – 100%, spec – 100%, PPV – 100%, NPV – 100%, accuracy – 100% PET: sens – 100%, spec – 67%, PPV – 92%, NPV – 100%, accuracy 93% CI: sens – 100%, spec – 33%, PPV – 85%, NPV – 100%, accuracy – 86%	PET/CT has high diagnostic performance in the assessment of head and neck cancer and induced a change in further clinical management in more than half of the study population. When a PET/CT study is negative, additional clinical and radiological follow-up can be postponed, at least temporarily. A positive study should encourage and guide the surgeon to obtain tissue diagnosis.
Jeong, 2007 (27)	Evaluate the accuracy of evaluating cervical lymph nodes using PET/CT fusion	47	Scans from the thigh to the head	Histology	Contrast-enhanced CT (CECT)	Nuclear medicine physicians	Detection of cervical lymph node disease PET/CT: sens – 91.8%, spec – 98.9%,	Combined PET/CT images are more accurate than the PET or CECT images alone for conducting

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
	images for SCC of the head and neck compared to using PET or contrast-enhanced CT.					blinded to information about primary tumour site and clinical information	PPV – 96.6%, NPV – 97.3%, accuracy – 97.1% PET: sens – 80.3%, Spec – 92.8%, PPV – 79%, NPV – 93.3%, accuracy – 89.7% CECT: sens – 90.2%, spec – 93.9%, PPV – 83.3%, NPV – 96.6%, accuracy – 93%	cervical node evaluation in patients with HNSCC.
Kim, 2007 (Eur J Surg Oncol) (20)	Compared FDG-PET with CT/MRI for preoperative staging of patients with SCC of the oropharynx	32	Scans from head to mid-thigh	Histology	CT/MRI	Nuclear medicine physicians blinded to CT/MRI and pathology results	CT/MRI correctly identified tumours in 25/32 patients FDG-PET correctly identified tumours in 30/32 patients By presence of positive neck side: FDG-PET: sens – 96.5%, spec – 90%, PPV – 96.5%, NPV – 90%, accuracy – 94.9% CT/MRI: sens – 75.9%, spec – 90%, PPV – 95.6%, NPV – 56.2%, accuracy – 79.5% By presence of positive cervical levels FDG-PET: sens – 95.7%, spec – 86.2%, PPV – 73.8%, NPV – 98%, accuracy – 89% CT/MRI: sens – 78.7%, spec – 87.1%, PPV – 71.2%, NPV – 91%, accuracy – 84.7%	FDG-PET is superior to CT/MRI in detection of primary tumours and metastatic neck disease of oropharyngeal SCC. The improved preoperative staging of FDG PET may help in planning treatment, but its accuracy is insufficient to replace pathologic staging based on neck dissection.
Kim, 2007b (Ann Oncol) (4)	Evaluate the ability of combined FDG-PET/CT to detect second primary cancers and distant metastases in head and neck cancer	349 eligible patients (of 425 recruited)	PET and CT scans from skull base to upper thighs	Histology	Further conventional imaging work ups	Nuclear medicine physicians not blinded to patient information	Detection of second primary of distant metastases Sens: 97.5%, Spec 92.6%, PPV 62.9%, NPV 99.7%, accuracy 93.1%	Combined FDG-PET/CT is useful as a primary screening method for detecting second primary cancers and distant metastases in patients with primary HNC. FDG-PET/CT had high sens, spec and NPV but low PPV, suggesting that additional diagnostic methods are essential to rule out false positives and to avoid false upstaging to M1 for appropriate therapeutic planning.
Liu, 2007 (5)	To compare the diagnostic efficacies of FDG-PET, clinical work up and their combination for primary staging in patients with NPC.	300	Images form vertex to upper thigh.	Histology and clinical follow-up	Clinical work up (CWU, incl: MRI, radiography, ultrasound, whole-body scintigraphy)	Nuclear medicine physician blinded to patient clinical findings	Patient based: PET – Sens 82%, Spec 97.1%, accuracy 94% CWU – Sens 32.8%, Spec 96.7%, Accuracy 83.7% PET + CWU – Sens 83.6%, Spec 93.7%, Accuracy 91.7%	FDG-PET is superior to CWU in primary M staging of nonkeratinizing NPC. The diagnostic efficacy did not improve by combining PET with CWU. Therefore, PET can replace CWU in primary M staging of nonkeratinizing NPC.
Minovi, 2007 (6)	Compare the effectiveness of FDG-PET with MRI in determining the pretherapeutic tumour staging of patients with HNSCC	34	Whole body PET scans	Histology	MRI	NR	Primary tumour detection: Sens 97% Lymph node metastases: PET – Sens. 100%, Spec 87.5%, PPV 77.8%, NPV 100%; MRI – Sens 85.7%, Spec 87.5%, PPV 75%, NPV 93.3%	PET is not superior to MRI in the pretherapeutic evaluation of H&N cancers. PET seems to be useful to detect distant metastases.

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
Miyakubo, 2007 (28)	Compare the diagnostic ability of FMT-PET and FDG-PET for the diagnosis of maxillofacial tumours	43 total - 36 with malignant tumour, 10 with benign tumour	Both FMT and FDG-PET Scans from head to thigh	Histology	FMT vs. FDG	NR	FMT-Pet had better contrast than FDG-PET in 27/36 patients with malignant lesions. ROC analysis primary lesion: FMT-PET: Sens – 83%, Spec – 80%, PPratio – 93%, NPratio – 57%, accuracy – 83% FDG-PET: Sens – 81%, Spec – 80%, PPratio – 94%, NPratio – 53%, accuracy – 80% Diagnosis of lymph node metastasis FMT-PET: Sens – 70%, spec – 96%, PPratio – 88%, NPratio – 89%, accuracy – 89% FDG-PET: Sens – 90%, Spec – 81%, PPratio – 64%, NPratio – 96%, accuracy – 83%	FMT and FDG uptakes in malignant tumours were significantly higher than those in benign tumours. Both FMT- and FDG-PET could differentiate b/w malignant and benign lesions, and they were almost equally effective in detecting maxillofacial tumours. FMT-PET had better contrast b/w malignant lesions and normal structures than FDG-PET, b/c FMT uptake in the normal organs was significantly lower than FDG uptake.
Nahmias, 2007 (29)	Investigate the role of FDG-PET/CT in the preoperative prediction of the presence and extent of neck disease in patients with N0 and N+ neck designations in oral/head and neck cancer.	70	Whole body CT and PET scans from base of the brain to upper thigh followed by scans from the orbits to the top of the aorta	Histology	None	Radiologist blinded to pathology findings	Identification of neck disease: Overall: Sens – 48%, Spec – 99% N0 neck: Sens – 79%, spec – 82% N+ neck: Sens – 95%, spec – 25% Identification of nodal disease: Overall: Sens – 88%, spec – 76% N0 neck: Sens – 26%, Spec – 99% ** NB: a single patient contributed 32 of 53 false-negative nodes N+ neck: Sens – 62%, Spec – 99% **NB: a single patient contributed 15 of 46 false-negative nodes	The oral/head and neck oncologic surgeon should not base the need for neck surgery in clinically negative or positive necks based on the result of the PET/CT scan. Time-honoured principles of surgical management of the cervical lymph nodes should continue to form the basis for decision making in this discipline.
Roh, 2007 (J Nucl Med) (15)	Determine the use of FDG PET in preoperative staging of salivary gland cancer	34	Whole-body FDG-PET	Histology of primary tumours and lymph nodes	CT	PET image interpretation was done blinded to CT and pathology results	FDG PET more sensitive than CT in detecting primary tumours and metastatic neck disease Primary tumours: PET sens 91%, CT sens 79% +ve neck findings: PET: sens – 93%, Spec – 85%, PPV – 88%, NPV – 92%, accuracy – 89% CT: sens – 80%, spec – 77%, PPV – 80%, NPV – 77%, accuracy - 79% Cervical levels with metastases PET: sens – 81%, spec – 90%, PPV – 81%, NPV – 90%, accuracy – 86% CT: sens – 56%, spec – 92%, PPV – 79%, NPV – 80%, accuracy – 80%	In patients with salivary gland malignancies, FDG-PET is clinically useful in initial staging, histologic grading, and monitoring after treatment but not in predicting patient survival.

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
Roh, 2007b (Oral Oncol) (30)	Assess the value of combined PET/CT over PET for initial staging in patients with newly diagnosed HNSCC	167	Scans from skull base to upper thighs	Histology	PET + CT/MRI vs. PET/CT + CT/MRI	NR	Primary tumour: PET: sens – 98%, CT/MRI: sens – 86% PET/CT: sens 97%, CT/MRI: sens – 88% Cervical metastases: PET: sens – 90%, spec – 88%, PPV – 92%, NPV – 86%, accuracy – 89%; CT/MRI: sens – 77%, spec – 81%, PPV – 86%, NPV – 71%, accuracy – 79% PET/CT: sens – 91%, spec – 87%, PPV – 88%, NPV – 90%, accuracy – 89%; CT/MRI: sens – 76%, spec – 83%, PPV – 83%, NPV – 76%, accuracy – 79%	Compared with PET alone, preoperative FDG PET/CT may not yield significantly improved diagnostic accuracy in patients with HNSCC. Despite their high accuracy, PET and PET/CT may not abrogate the need for conventional imaging and pathologic staging based on primary resection and neck dissection.
Babin, 2008 (31)	Evaluate PET/CT in detecting mandibular tumour involvement in cancer of the oral cavity and oropharynx	17	FDG-PET	Histology	CT	Nuclear medicine physician blinded to radiologist's findings	PET/CT: sens – 100%, spec – 85%, PPV – 60%, NPV – 100% CT: sens – 33%, spec – 100%, PPV – 100%, NPV – 87%	These results encourage the use of PET/CT when assessing mandibular invasion.
Gil, 2007 (14)	To determine the utility of pre-and postoperative PET/CT scans in staging and follow-up of skull base tumours.	47	PET/CT	Histopathology	None	No blinding.	PET/CT: sens=77%, spec=81%, PPV=83%, NPV=76% Clinical management was changed in 11 patients: Upstaging occurred in 1 patient preoperatively and 10 patients postoperatively.	PET/CT imaging offers accurate anatomical data and tumour staging in the skull base.
Treatment Response								
Brkovich, 2006 (32)	Identify the value of PET scanning in determining which patients with N+ necks who have undergone curative chemo for SCC of the upper-aerodigestive tract have viable residual cervical metastases and therefore would benefit from posttreatment neck dissection.	19 patients, 2 with bilateral neck dissection, therefore, 21 neck specimens	Whole body PET	Histology or clinical follow-up	None	NR	To detect residual metastases: sens – 75%, spec – 64.7%, PPV – 33%, NPV – 91.7% 7 patients met all inclusion criteria but did not complete salvage neck dissection. Posttreatment PET scans were done at 14.6 weeks and all were –ve for residual disease. Clinical follow-up of this cohort has demonstrated only one neck recurrence in the 8 necks with a mean follow-up of 11.5 months, which is in agreement with the study group that completed posttreatment neck dissection.	PET imaging may be a useful tool to guide the surgeon. PPV low (33%), but a negative PET scan may allow the surgeon to avoid unnecessary neck dissection (NPV 91.7%).
Chan, 2006 (Eur J Nucl Med) (21)	Determine the role of PET in detecting locally residual/recurrent NPC in comparison with MRI	112	PET scans from head to upper thigh	Histology if possible, if not possible, clinical and imaging follow-up	MRI	Nuclear imaging physicians blinded to MRI results	Treatment response (residual tumour): PET – Sens 75%, Spec 94.4%, PPV 33.3%, NPV 99%, accuracy 93.8% MRI – Sens 75%, Spec 89.8%, PPV 21.4%, NPV 99%, accuracy 89.3% SUV: tumour 6.5 $\pm$ 1.8; non tumour 2.8 $\pm$ 0.8, p,0.001 Retrospective ROC analysis led to decision to use SUV cut-off value of 4.2	FDG-PET demonstrates superior specificity in assessing treatment response for NPC patients with initial T4 disease, as compared with MRI. FDG-PET results should be interpreted with caution in patients with initial T1-2 disease b/c ICBT may induce false +ve findings. Gold standard to determine residual NPC should consist of

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
								both nasopharyngeal biopsy and clinical/imaging follow-up
Chan, 2006b (J Nucl Med) (13)	Compare the efficacies of whole-body PET and conventional work up (CWU) in evaluating the treatment response for patients with locoregional advanced NPC after primary curative treatment and investigates the impact of PET on patient management	131	Scanned from head to upper thigh	Image-guided biopsy on suspected malignant lesions, if possible. If not possible, close clinical or imaging follow up for at least 6 months	CWU	Nuclear medicine physicians blinded to CWU results	Treatment response: Overall: In stage II disease FDG-PET: Sens 100%, spec 95.7%, accuracy 95.8% CWU: Sens 25%, spec 96.7%, accuracy 95.3% In stage Iva-b disease FDG-PET: sens 91.7%, spec 97.6%, accuracy 97.2% CWU: sens 58.3%, spec 91.7%, accuracy 89.4% For local, regional lymph node and distant results see study summary page Clinical impact of FDG-PET on management of 131 patients with NPC after curative treatment Stage III disease: negative: 11%, no change: 85%, positive: 4% Stage IVa-b disease: negative: 5%, no change: 57%, positive: 38%	The sens and spec of PET in revaluating the treatment response for patients with stage Iva-b NPC were higher than those of CWU. The sens of PET was higher but the spec of PET and CWU were similar in patients with stage III NPC. PET resulted in positive impacts on the management of 1/3 of patients with stage Iva-b NPC> The main +ve impacts were reducing unnecessary imaging follow-up in patients with T4 disease and disclosing unexpected residual second primary tumours. The impact on patients with stage III NPC was less prominent.
Chen, 2006 (10)	Assess the utility of PET-CT compared with contrast-enhanced CT in predicting persistent cancer either at the primary site or cervical lymphatics in patients with advanced oropharyngeal cancer treated with concurrent chemoRT	30	PET-CT scans from skull vertex to midabdomen	Biopsy (primary tumour) or neck dissection (neck)	Contrast enhanced CT (CECT)	Nuclear radiologist blinded to contrast enhanced CT results	Primary site: PET-CT: sens – 50%, spec – 84.6%, PPV – 20%, NPV – 95.7%, accuracy – 82.1% CECT: sens – 50%, spec – 88.5%, PPV – 25%, NPV – 95.8%, accuracy – 85.7% Lymph nodes (neck): PET-CT: sens – 100%, spec – 69.5%, PPV – 36.3%, NPV – 100%, accuracy – 74.1% CECT: sens – 100%, spec – 52.2%, PPV – 26.7%, NPV – 100%, accuracy – 59.3%	PET-CT seems to be superior to CECT in predicting persistent disease in the neck after chemoRT for oropharyngeal or unknown primary cancer, but not at the primary site. The possibility of a false-positive result in the neck remains high, and thus overtreatment may result. Even more concerning are the false negative results.
Yen, 2006 (33)	Understand if SUV is a significant predictor for local response, either before or 3 months after concurrent chemoRT (CCRT) and to determine if the changes in SUV, between the two measurements, were a reliable predictor for local response vs.. nonresponse to CCRT	39 (42 recruited but 3 excluded)	PET from head to upper thigh	Clinical follow-up with biopsies done when there were +ve, concordant, equivocal or discordant lesions on MRI and PET scans	MRI	Nuclear medicine physicians blinded to knowledge of MRI findings when analyzing PET scans	3 of 4 non responders were detected by the 3 month posttherapy PET scan and the other from the 6 month posttherapy PET scan which was done b/c of equivocal PET and MRI findings at 3 months. Non responders: Before CCRT SUV: 15.6; after CCRT SUV: 5.5 Responders: Before CCRT SUV: 10.9; after CCRT SUV 2.1 3 months after CCRT SUV was lower in responders vs. non responders All responders had SUV < 4.0 and all non responders had SUV > 4.0	The SUV for stage T4 NPC, 3 months after completion of CCRT was a significant predictor for local tumour response. The cutoff SUV of 4.0 at 3 months after CCRT was useful to predict the outcomes of local treatment that can be offered as a diagnostic reference for recurrent or residual tumour for NPC treatment. Both the baseline SUV and change in SUV b/w baseline and 3 months after CCRT were only marginally

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
								significant predictors for local tumour response.
Connell, 2007 (9)	Determine the incremental value of PET/CT over conventional assessment for staging, posttreatment assessment of response and ongoing follow-up in HNSCC	76	Images of neck, thorax, abdomen, and pelvis	Cytology, histology and/or clinical and radiologic follow-up	Conventional assessment	Not blinded	Treatment response: 30 patients had PET/CT to assess treatment response. PET/CT altered the assessment of locoregional response in 13 (43%) patients. Primary site: 8/30 had altered response assessment on PET/CT vs. conventional assessment: 6 showing partial response on conventional assessment and complete metabolic response on PET/CT were true negative. 2 were false positive Nodal site: 10/30 had altered response assessment on PET/CT vs. conventional assessment: 8 showing partial response on conventional assessment and complete metabolic response on PET/CT were true negative, 1 was true positive, and 1 patient died without knowledge of true neck node status. Clinical impact: high 11/30 (37%) Accuracy: primary site – 4 false positives, nodal sites 3 false positives, distant sites – 1 false positive Follow-up 30 patients had 35 follow-up PET/CT scans, 28 for suspected recurrence and 7 for routine surveillance. Clinical impact: high 12/35 (34%) Accuracy: primary site – 3 false positive, nodal site – 1 false positive, distant site – 7 false negative.	PET/CR has a major incremental impact in the posttreatment management of patients with HNSCC. PET/CT has a very high NPV for residual/recurrent locoregional disease in posttreatment evaluation, determining those patients in whom ongoing observation rather than surgical intervention is appropriate and safe management. The addition of posttreatment PET/CT scan into the patient's posttreatment management paradigm now constitutes optimal posttreatment care.
Gordin, 2007 (11)	Assess the role of PET/CT compared with PET and CT separately in head and neck cancer. The impact of PET/CT results on patient treatment also investigated.	90	Whole body PET and non-contrast enhanced CT	Histology (n=56) and clinical and radiologic follow up (n=28)	Contrast enhanced CT and/or MRI (CI) of head and neck	Images analyzed independently of each other	Performance for treatment response PET/CT: sens – 87%, spec – 100%, PPV – 100%, NPV – 75%, accuracy – 91% PET: sens – 87%, spec – 100%, PPV – 100%, NPV – 75%, accuracy – 91% Conv Imaging: sens – 87%, spec – 33%, PPV – 77%, NPV – 50%, accuracy – 72%	When a PET/CT study is negative, additional clinical and radiological follow-up can be postponed, at least temporarily. A positive study should encourage and guide the surgeon to obtain tissue diagnosis.

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
Kim, 2007c (J Nucl Med) (34)	Evaluate the clinical efficacy of FDG-PET performed 1 month after the completion of RT for determining the response to RT in patients with HNSCC	97	PET /CT from skull base to pelvis	Histology and clinical follow-up	None	NR	Sens. 88.2%, Spec 95.5%, PPV 65.2%, NPV 98.8% and accuracy 94.9% to detect residual disease (total) Sens 83.3%, Spec 91.8%, PPV 58.8%, NPV 97.5%, accuracy 90.7% to detect primary tumour Sens 100%, Spec 98.9%, PPV 83.3%, NPV 100%, Accuracy 99% to detect nodal disease SUV response to treatment: Primary tumour: before treatment – median 6.5 [range 2.3-23.0]; after treatment – median 1.8 [range: basal status value–9.7]. Lymph node: before treatment – median 5.6 [range: 1.2-16.8]; after treatment – median 1.8 [range: basal status value-8.6]	FDG-PET performed 1 month after the end of RT is a valuable diagnostic method for evaluating the response to RT in patients with HNSCC. If patients have negative FDG-PET findings, we recommend only 1 month of follow-up; however, when positive FDG-PET findings are observed, further evaluation is needed. FDG-PET results should be interpreted with caution in patients with initial T1-2 disease b/c ICBT may induce false +ve findings. Gold standard to determine recurrent NPC should consist of both nasopharyngeal biopsy and clinical/imaging follow-up
Recurrence/Restaging								
Brouwer, 2006 (7)	Evaluate the value of FDG-PET for distant metastases in at-risk HNSCC patients	34	Images from mid-femur to cranial vault	Chest CT, biopsy or clinical follow-up	None	Nuclear medicine physicians blinded to results of the other examinations and final clinical diagnosis	FDG-Pet correctly identified 1 patient with distant metastases and 3 patients with second primary tumours. Increased FDG uptake in 5 patients were not confirmed during follow-up During revised reading of 9 suspicious PET scans, 1 was true positive for distant metastases and 2 were true positive for second primary tumours. PET was equivocal in 4, of which 1 was positive for second primary tumour.	Whole body FDG-PET may have additional value in screening for distant metastases and second primary tumours, if applied to the subset of patients who are at substantial risk. Whether this application of FDG-PET will indeed be (cost)-effective, is now studied in a larger cohort of patients in a multicenter study. Finally, these initial data suggest that in this patient population, the use of PET-CT scanners might be productive since apparent discrepancies can be solved readily while preserving the yield of whole body FDG-PET.
Yen, 2005b (J Nucl Med) (8)	Assess the efficacy of PETin detecting distant metastases in NPC patients with MO staging based on conventional imaging	140 total (118 newly diagnosed, 22 disease recurrent)	FDG-PET	CT-guided or sonography-guided biopsy, if possible. If not possible, clinical follow-up (MRI/CT/PET) performed at 3-6	None	Nuclear imaging physicians blinded to other imaging results	To detect distant metastases: Sens: 100%, Spec: 86.9%	PET has made a major impact on the detection of distant metastases in NPC patients with primary lesions and stage M0 disease, especially those who also have stage N2-3 disease. Because of the higher incidence of distant metastases in patients with recurrent NPC than in those with primary tumours, FDG-PET is also recommended for assessing recurrent NPC before embarking on salvage therapy. Cost of FDG-PET and occurrence

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
				months				and rate of false-positive uptake are still problematic. The most important contribution of FDG-PET for patients with NPC is the ability to reveal occult distant metastases on chest radiography, liver sonography, and conventional bone scanning.
Chan, 2006 (Eur J Nucl Med) (21)	Determine the role of PET in detecting locally residual/recurrent NPC in comparison with MRI	34	PET scans from head to upper thigh	Histology if possible, if not possible, clinical and imaging follow-up	MRI	Nuclear imaging physicians blinded to MRI results	Local recurrence: PET – Sens 95.5%, Spec 83.3%, PPV 91.3%, NPV, 90.9%, accuracy 91.2% MRI – Sens 95.5%, Spec 75%, PPV 87.5%, NPV 90%, accuracy 88.2% SUV tumour: 8.5 $\pm$ 3.8, non tumour 2.6 $\pm$ 1.0, $p<0.001$ Retrospective ROC analysis led to decision to use SUV cut-off value of 4.2	FDG-PET has equal sensitivity but higher specificity to detect recurrent NPC as compared with MRI
Goerres, 2005 (35)	Compare the accuracy of helical contrast material-enhance CT alone with that of coregistered PET/CT and coregistered SPECT/CT for detecting bone invasion in patients scheduled to undergo surgery because oral cavity carcinoma with possible bone invasion was suspected on the basis of clinical evaluation.	34	PET-CT	Bone resection and soft tissue adjacent to bone was also obtained to rule out bone involvemen t	SPECT/CT, contrast-enhanced CT	Nuclear medicine physicians were blinded to the results of SPECT/CT and contrast-enhanced CT, but knew the clinical information	Detection of bone invasion PET/CT: sens – 100%, spec – 91%, accuracy – 94%, PPV – 86%, NPV – 100% SPECT/CT: sens – 92%, spec – 86%, accuracy – 88%, PPV – 79%, NPV – 95% Contrast-enhanced CT: sens – 92%, spec – 100%, accuracy – 97%, PPV – 100%, NPV – 96% Whole body examination for distant bone metastasis: Skeletal scintigraphy did not depict distant bone metastases in 34 patients PET/CT depicted distant metastases in 1 patient (lung, thoracic wall and mediastinum) and verified by US guided biopsy of the thoracic wall at autopsy	The identification of bone involvement in patients with oral cavity carcinomas is reliably performed with helical CT and thin sections. In patients who undergo PET/CT for whole-body staging or repeat staging, the CT information from PET/CT is reliable, whereas FDG uptake does not help better identify bone invasion.
Kunkel, 2006 (36)	Determine if FDG-PET provides clinically relevant diagnostic and prognostic information for the management of oral SCC patients after salvage surgery	41	PET scans of viscerocraniu m, neck, thorax and epigastric region	Clinical &/or radiological follow-up (pathology, CT, obvious clinical evidence of tumour progression IDd in follow-up)	None	Nuclear imaging physicians who were not blinded	Identification of tumour sites (overall): Sens 85% FDG-PET for re-staging after recurrent oral cavity SCC: 1) Local recurrence: sens – 92%, spec – 75%, PPV – 63%, NPV – 95% 2) Lymph node metastases: Sens – 88%, Spec – 98%, PPV – 93%, NPV – 97% 3) Distant metastases: Sens – 73%, Spec – 97%, PPV – 89%, NPV – 91%	FDG-PET can facilitate re-staging and clinical management in "high-risk" patients with oral cavity SCC SUV $\leq$ 4 suggests promising outcome, which SUV > 4 indicated a fatal disease course.
Gordin, 2007 (26)	Assess the role of PET/CT compared with PET and CT	90	Whole body PET and non-	Histology (n=56) and	Contrast enhanced CT	Images analyzed	Performance for distant metastases: PET/CT: sens – 93%, spec – 100%,	In assessment of locoregional disease, PET/CT provides better

Author, year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Conclusions
	separately in head and neck cancer. The impact of PET/CT results on patient treatment also investigated.		contrast enhanced CT	clinical and radiologic follow up (n=28)	and/or MRI (CI) of head and neck	independently of each other	PPV – 100%, NPV – 88%, accuracy – 95% PET: sens – 92%, spec – 71%, PPV – 87%, NPV – 83%, accuracy – 86% CI: sens – 100%, spec – 29%, PPV – 74%, NPV – 100%, accuracy – 71% Performance for locoregional disease: PET/CT: sens – 78%, spec – 93%, PPV – 82%, NPV – 91%, accuracy – 88% PET: sens – 78%, spec – 69%, PPV – 52%, NPV – 88%, accuracy – 72% CI: sens – 83%, spec – 14%, PPV – 29%, NPV – 67%, accuracy – 35%	anatomic localization of foci with abnormal FDG uptake and significantly reduces the number of FP or equivocal PET and CI results. When a PET/CT study is negative, additional clinical and radiological follow-up can be postponed, at least temporarily. A positive study should encourage and guide the surgeon to obtain tissue diagnosis.
Brouwer, 2008 (12)	Evaluate the value of FDG-PET in detecting recurrent laryngeal carcinoma after radiotherapy	30	Scans from base of skull to clavicle	Biopsy	None	Nuclear medicine physicians not blinded to clinical information	To detect recurrence: FDG-PET: sens – 88%, spec – 82%, PPV – 64%, NPV – 95%, accuracy – 83%	FDG-PET promising to detect recurrent laryngeal carcinoma after radiotherapy, and selecting patients for direct laryngoscopy. FDG-PET may help avoid futile invasive procedures. Disparities among observers remain, thus training is necessary to improve consistency of reporting in clinical practice and trials.

Abbreviations: CT, computed tomography; FDG PET, fluorodeoxyglucose positron emission tomography; FET, fluoroethyltyrosine; FMT, flurometh**y**l-d-tyrosine; FP, false positive; LN, lymph node; MRI, magnetic resonance imaging; ROC, receiver operating characteristic; NPC, nasopharyngeal carcinoma; NPV, negative predictive value; NR, not reported; PPV, positive predictive value; SCC, squamous cell carcinoma; Sens, sensitivity; Spec, specificity; SPECT, single photon emission computed tomography; SUV, standardized uptake value; vs., versus.

.

Appendix 4. PET for head and neck cancer: summary of the evidence from 2008 to 2011.

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
Diagnosis/Staging								
Deantonio et al (45)	Investigate the potential impact of using PET/CT image fusion for the management of patients with head and neck carcinoma. Specifically, we analyzed how PET/CT may change the clinical stage and the delineation of gross tumour volume (GTV) for radiation treatment planning.	22	Whole-body PET	Histopathology. The clinical stage was defined according to the 2002 American Joint Committee on Cancer-International Union Against Cancer (AJCC-UICC) classification	CT	Not specified	PET/CT imaging lead to a change in the TNM categories and in the clinical stage in 5/22 (22%) cases compared to CT alone	The study showed that FDG-PET/CT images for primary head and neck carcinoma had a potential impact on both tumour staging and treatment planning. A clinical stage variation was observed in 22% of cases. Based on the data as well as the other literature results, the future scenario of imaging for radiotherapy of head and neck tumours may include the use of functional imaging such as FDG-PET/CT with the aim to characterize the biological features of the tumour and optimize the use of highly conformal and biologically effective radiation treatment.
Dietl et al (46)	What was impact of FDG-PET/CT on general therapy management and radiotherapy planning in patients with stage IV head and neck tumours.	35	Whole-body PET	Histopathology	Pan-endoscopy and local tumour spread has been mapped by CT in 26 patients and by MRI in 9 patients.	3 specialist physicians from the fields of radiotherapy, nuclear medicine and radiology jointly performed a visual and semi-quantitative interpretation of the whole-body PET/CT scans.	FDG-PET/CT detected distant metastases for the first time in six patients (17.1%). A second primary tumour was visualised in five patients (14.3%), in two patients as a solitary pulmonary focus. Compared with the morphometric definition, nodal status based on metabolic activity was upstaged in 12 patients (34.3%) – with four patients (11.4%) showing pathological glucose utilisation in the retropharyngeal LNs – and downstaged in eight patients (22.9%). Overall, FDG-PET/CT yielded additional diagnostic information in 23 patients (65.7%). On the basis of the information yielded by FDG-PET/CT, treatment strategies were modified from curative to palliative in six patients (17.1%). Because of the diagnosis of a second primary tumour, two patients (5.7%) received additional curative therapy as part of an interdisciplinary treatment strategy. In the light of FDG-PET/CT, the changes in nodal status based on metabolic activity (i.e., upstaging or downstaging) resulted in modification of RT volume and dose in 20 patients (57.1%). Overall, FDG-PET/CT resulted in a treatment change or RT modification in 23 patients (65.7%)	FDG-PET/CT in AJCC stage IV head and neck cancer yielded additional diagnostic information in 65.7% of patients, with subsequent modification of treatment strategy in 17.1% and implementation of further curative therapy in 5.7%. Based on the findings of FDG-PET/CT, modification of RT was performed in 57.1% of patents in the study. From the radiotherapist's perspective, therefore, the implementation of FDG-PET/CT to refine and optimise the baseline staging of stage IV head and neck cancer is indubitably useful and justifiable.

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
Gardner et al (47)	Compared parotid glands, chiasma, and GTV as determined on CT and MRI by 2 different operators, and evaluated whether the use of 18F-FDG PET-CT has changed the treatment planning volumes	35	Whole-body PET	Histopathology	CT and MRI	Volumes were delineated by a head and neck–specialized radiotherapist and reviewed by a head and neck–specialized radiologist	The use of 18F-FDG PET-CT changed the treatment design in 6 of 21 patients. In 2 patients, 18F-FDG PET-CT indicated intrathoracic metastasis, subsequently proved histologically, and they were switched to palliative treatment. In another patient, 18FFDG PET-CT showed extension to the skull base which was not initially detected by other image modalities but was confirmed by bone CT. In further 3 patients, bilateral rather than unilateral lymph node extension was detected by 18F-FDG PET-CT and confirmed by fine-needle biopsy.	The 18FDG PET-CT proved to be helpful for metastasis detection and detection of lymph node extension, and is therefore useful for more accurate treatment design
Guido et al (48)	To evaluate the effect of the use of 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET)/ computed tomography (CT) in radiotherapy target delineation for head-and-neck cancer compared with CT alone.	38	Skull to the upper abdomen	Histopathology	CT	A nuclear medicine physician (P.C.), with expertise in PET imaging, visually interpreted the 18F-FDG PET studies and defined the 18F-FDG-PET–positive regions interpreted as malignant on the emission images.	Combined 18F-FDG PET/CT determined a change in the tumour stage in 6 of 38 cases. All changes were related to additional nodal information.	The implementation of combined PET/CT imaging has the potential to improve primary tumour delineation and nodal staging for imaging experts and nonexperts, such as trainees in radiation oncology or radiation oncologists without experience in head-and neck cancer, thus reducing equivocal image interpretations and improving evaluator confidence.
Kim et al (38)	Evaluate the clinical utility of FDG PET/CT as well as CT and MRI in the identification of nodal metastasis in the contralateral neck in patients with head and neck SCC.	114	Not stated	Histopathology	CT, MRI	PET/CT images were interpreted by and experienced nuclear medicine physician. CT and MRI results were interpreted by an experienced radiologist. No specific information on blinding was reported.	PET/CT detected the presence or absence of cervical metastasis in the ipsilateral and contralateral neck in 105 (92%) and 95 (83%) patients, respectively. CT/MRI accurately detected the presence of cervical nodal metastases in the ipsilateral and contralateral neck in 99 (87%) and 95 (83%) patients, respectively. The sensitivity and accuracy of PET/ CT was significantly superior to that of CT/MRI on contralateral neck ($P < 0.05$ each). It was not on the ipsilateral neck ($P = 0.063$). The sensitivity and accuracy of PET/CT were significantly higher than that of CT/MRI on both sides of the neck ($P < 0.01$ each). The	Combined PET/CT is superior to CT/MRI in detecting metastatic cervical nodes in patients with HNSCC who underwent bilateral neck dissection. PET/CT and CT/MRI had low sensitivity in identifying contralateral cervical metastases, due to the limitations of these imaging modalities in assessing small lymph nodes. Findings indicate that preoperative imaging modalities may not nullify the need for contralateral neck surgery or radiation therapy indicated in patients with HNSCC.

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
							sensitivity of PET/CT for detecting contralateral metastatic nodes was significantly higher than that of CT/MRI, both on a per-patient (58% vs.. 25%,P = 0.031) and a per-level (52% vs.. 36%, P = 0.008) basis, but the sensitivities of both methods were low.	
Law et al (39)	Evaluate the impact of FDG PET/CT as an adjunct to conventional imaging in the management of nasopharyngeal cancer for both the initial staging and assessment of post-treatment response.	48	PET/CT scan incorporating the neck thorax, abdomen and pelvis	Histopathology	Conventional imaging (CT or MRI)	PET/CT images were interpreted by and experienced nuclear medicine physician. CT and MRI results were interpreted by an experienced radiologist. No specific information on blinding was reported.	The clinical impact of PET/Ct was high (I.e. changed treatment modality or intent) in 4 (8%) patients; medium (treatment modality was unchanged but RT planning technique or dose was altered) in 12 (25%) patients, and low (no change in treatment modality or intent) in 32 (66%) patents. Twenty-one patients were scanned for post-treatment response. PET/CT was less frequently equivocal than MRI (3 vs. 8/21). A complete metabolic response on PET/CT was associated with a 93% negative predictive value for subsequent recurrence.	PET/CT is a valuable staging tool for the detection of occult metastatic disease and defining the extent of neck nodal disease. Posttreatment, a complete metabolic response on PET/CT has a very high negative predictive value with fewer equivocal results than MRI.
Liao et al (56)	Prospectively assess the sensitivity and specificity of FDG PET/CT for detecting neck lymph node metastases in patients with oral cavity SCC, with pathologic results as the reference standard. Investigate whether pretreatment visual scores in the neck lymph nodes may improve risk stratification	473	Head to mid-thigh	Histopathology	CT or ultrasound biopsy	Two experienced nuclear medicine physicians and 1 radiologist interpreted FDG PET (PET/CT) images. Interpretation was based on visual evaluation, and decisions were reached by consensus	FDG PET correctly diagnosed 164 of 211 patients with neck metastases and 152 of 262 subjects without pathologic neck metastases, resulting in a patient-based sensitivity and specificity of 77.7% and 58.0%, respectively.	PET findings at the neck lymph nodes have limited sensitivity and specificity for primary staging of OSCC.
Lonneux et al (40)	The study was designed to address the impact of whole-body 18F-FDG PET imaging used in conjunction with the usual staging work-up on the initial staging and therapeutic management with HNSCC	233	Whole-body PET imaging (from head to mid-thighs)	Histology	Conventional staging (physical examination, neck palpation, fibroscopic and direct endoscopic examination	After conventional staging was performed a multidisciplinary meeting was held, and the TNM stage and therapeutic	Staging: PET stage and conventional stage were discordant in 100 patients (43%), for whom a gold standard was available in 60 patients. PET was accurate in 47 patients and inaccurate in 13 patients. For these 100 patients with discordant results, the sensitivity of PET staging was 91% (95^{th} CI), specificity was 63% (95^{th} CI), PPV was 75% (95^{th} CI), NPV 85% (95^{th}	Study demonstrated that adding 18F-FDG PET imaging significantly improved the pre-therapeutic 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. The results

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
					with biopsy, CT or MRI)	decision were set in Envelope 1. PET images were read by experienced nuclear medicine physicians who were blinded to the results of the conventional staging process. Results of the PET scan were sent to the referring clinician who reported to the multi-disciplinary team which then integrated PET results with the conventional staging into envelope 2.	CI), accuracy was 22% and positive likelihood ratio was 0.14. PET staging was found to be statistically significantly more accurate than conventional staging (p<0.0001) Impact on patient management: 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 N stage and in 8.6% because of a change in the M stage).	support the implementation of 18FDG PET imaging in the routine imaging work-up of HNSCC.
Ng et al (42)	Prospective comparison of the diagnostic capability of FDG PET/CT and whole body MRI and their combination in detecting malignancy in treated oropheryngeal or hypopharngeal SCC	79	Whole body FDG PET/CT	Pathology or follow-up imaging	Whole body MRI	Two radiologists and two nuclear medicine physicians independently analysed the WB-MRI and PET/CT findings, respectively. The readers were blinded to the other imaging findings but were aware of the study protocol.	The patient-based sensitivity of PET/ CT was higher than that of MRI (72.4 vs. 55.2%, p=0.13). Combined interpretation of PET/CT and MRI raised the sensitivity up to 75.9%. The false positive rate of PET/CT (12.5%) was lower than that of MRI (23.8 %), but there were no significant differences in terms of specificity (94.4 vs. 90.0%, p=0.5). Combined interpretation of PET/CT and MRI did not improve specificity.	PET/CT showed a trend towards higher diagnostic capability than MRI in detecting residual/recurrent tumours or second primary tumours in oropharyngeal or hypopharyngeal SCC, although the results were not statistically significant. The combined use of PET/CT and MRI provided more added value to MRI alone than to PET/CT alone. Additional PET/CT can be useful in patients with questionable MRI findings for the presence of malignancy. Therefore, PET/CT should be the procedure of choice in the evaluation of oropheryngeal or hypopharngeal SCC patients treated by definitive concurrent chemoradiotherapy considered at high risk for residual disease or in the presence of suspected recurrence.

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
Senft et al (43)	Define the added value of whole-body FDG-PET in screening for distant metastases in patients with head and neck squamous cell carcinoma and risk factors.	92	Whole-body PET	Histopathology	Chest CT	The interpreters were blinded to the alternative modality and clinical outcome.	Accuracy of PET and PET/CT in the detection of distant metastases- *PET*: Sensitivity: 53%; Specificity: 93%; PPV: 80%; NPV: 80%; Accuracy: 80% *PET/CT:* Sensitivity: 63%; Specificity: 95%; PPV: 86%; NPV: 84%; Accuracy: 84% Accuracy of PET and PET/CT in the detection of distant metastases and synchronous primary tumours – *PET*: Sensitivity: 58%; Specificity: 93%; PPV: 85%; NPV: 76%; Accuracy: 78% *PET/CT:* Sensitivity: 66% Specificity: 94%; PPV: 89%; NPV: 80%; Accuracy: 83% Accuracy of PET and PET/CT in the detection of distant metastases patients with locoregional control – *PET*: Sensitivity: 68%; Specificity: 93%; PPV: 79%; NPV: 89%; Accuracy: 86% *PET/CT:* Sensitivity: 82% Specificity: 95%; PPV: 86%; NPV: 93%; Accuracy: 91%	FDG-PET in a valuable took in screening for distant metastases in HNSCC patients with high risk factors. Screening with a combination of CT-scan of the thorax and whole-body FGD-PET decreases over-treatment. It results in a reduction of futile mostly extensive treatments in these patients.
Yamazaki et al (44)	Establish the diagnostic accuracy of FDG-PET for lymph node metastases in HNSCC, and to ascertain the factors that affect this accuracy, determining the smallest detectable size of disease by means of analyzing tumour involvement of each metastatic node histological sections.	26	Whole-body PET	Histopathology	CT	All PET images were visually interpreted by at least two experienced nuclear medicine physicians by consensus. The lesions were considered to be positive if a definite, localized area with higher uptake than the surrounding normal tissue was present, excluding physiologic uptake.	The sensitivity, specificity, accuracy, PPV and NPV per neck side for FDG-PET were 74% (17/23), 92% (11/12), 80% (28/35), 94% (17/18) and 65% (11/17) respectively.	FDG-PET is a useful tool for preoperative evaluation of the neck because it accurately detects metastatic lymph nodes ≥10mm in diameter and had fewer false-positive results than CT. The high specificity of FDG-PET for lymph node metastases may play an important role in avoiding unnecessary neck dissection.

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
Treatment Response								
Martin et al (41)	The primary aim of the study was to analyse the accuracy and benefit of PET in staging and assessing treatment response in patients treated with primary chemoradiotherapy for mucosal carcinomas of the head and neck. The secondary aim was to compare PET results with clinical examination and conventional imaging.	78	PET scans extended from the mid-cerebrum to the anterior superior iliac spine.	Histopathology	Standard clinical evaluation (endoscopic evaluation with biopsy), CT and MRI	No information on blinding outlined in the study.	The sensitivity and specificity of PET were 82% and 95% respectively. PPV and NV were also 82% and 95% with an overall accuracy of 92%. The likelihood ratio of a positive test was 0.19. When the researchers compared the accuracy of PET , conventional imaging and clinical outcomes they found that PET had a better accuracy in predicting a complete response (CR) (PET vs.. clinical p<0.002; PET vs. conventional imaging p<0.001)	The researchers showed that a complete response (CR) on posttreatment PET is accurate (NPV, 95%) in predicting clinical outcome in mucosal head and neck cancer treated with chemoradiotherapy. PET resulted in important management changes when patients were identified as having distant metastatic disease. Patients who have CR on repeat PET have a significant survival advantage over those who do not. The researchers believe that PET should be considered the standard of care in the evaluation of mucosal head and neck cancer treated with chemoradiotherapy.
Moeller et al (51)	Compare the accuracy of radiation response assessment by FDG-PET/CT and contrast-enhanced CT and define patient subsets likely to derive maximal benefits from the addition of FDG-PET/CT imaging to conventional response assessment.	98	Not Stated	Histopathology	Contrast-enhanced CT	Interpreter blinded to results of other modality	Accuracy of FDG-PET for the prediction of treatment response for primary tumours: Sensitivity: 70%; Specificity: 93.7%; NPV: 96.1%; PPV 58.3% Accuracy of FDG-PET for the prediction of treatment response for nodal tumours: Sensitivity: 75%; Specificity: 76.1%; NPV: 96.2%; PPV: 27.3%	The results of this study do not support the broad application of FDG-PET/CT for radiation response assessment in unselected head and neck cancer patients. However, FDG-PET/CT may be in imaging modality of choice for patients with highest risk disease, particularly those with HPV-negative tumours.
Recurrence/Restaging								
Abgral (52)	Determine the benefits of hybrid 18F-FDG PET/CT in detecting subclinical locoregional recurrence of HNSCC and distant metastases	91	Whole-body 18F-FDG PET/CT	Histology	Histopathology for locoregional findings and radiotherapy , CT or MRI for distant metastasis	All images were interpreted qualitatively by two nuclear medicine physicians without prior knowledge of the follow-up status of the patients.	The sensitivity and specificity or 18F-FDG PET/CT in the study for the diagnosis of HNSCC recurrence were 100% (30/30) and 85% (52/61), respectively. The positive predictive value was 77% (30/39). The overall negative predictive value was 100% (52/52). The overall accuracy was 90% (82/91).	The results of the study confirmed the high-effectiveness of 18F-FDG PET/CT in assessing for recurrence of HNSCC in patients who have been considered cured of the disease. The findings suggest that 18F-FDG PET/CT is more accurate than conventional follow-up physical examinations alone in such patients. The systematic use of PET/CT at 12 months of the usual follow-up could be proposed, but cost-effectiveness and survival impact remain to be evaluated.

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
Inohara et al (54)	The study was designed to address whether CT or 18F-FDG PET is superior in its ability to detect persistent nodal disease after definitive chemoradiotherapy in patients with node-positive HNSCC	48	Whole-body PET scanning	Histology	CT scans	Each image was reviewed by two experienced nuclear radiologists and interpretation was made by consensus.	The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value of CT or 18F-FDG PET in detecting the pathology of persistent or recurrent nodal disease. Statistical analysis revealed no significant difference between the two imaging modalities in terms of specificity, accuracy, PPV and negative predictive value while CT was superior to F-FDG PET in sensitivity (p=0.046)	Post-treatment 18F-FDG PET is of no additional value to determine the indication of a planned neck dissection in this setting. It seems that patients with a complete regional response on CT at 7 weeks after chemoradiotherapy can be spared from planned neck dissection, regardless of initial node stage.
Porceddu et al (37)	Determine the proportion of patients that were appropriately spared a neck dissection as defined by the absence of subsequent nodal failure.	112	Skull vertex to mid-thigh	Pathology and follow-up	CT	2 nuclear medicine physicians independently reviewed all the datasets on dedicated display systems.	The NPVs for PET and CT nodal response assessment were 98.1% and 96.8%, respectively. False-positive findings occurred in 1.8% of cases for PET and 38% for CT with corresponding PPVs of 77.8, and 14% respectively. Outcomes based on N classification and p16 status:. For the p16-positive group, the NPVs and PPVs were 98.2% and 66.7 respectively, for PET compared to 96.7% and 6.9%, respectively, for CT.	PET provided additional valuable information over contrast enhanced CT alone is a appropriately selected population allowing the avoidance of unnecessary neck dissections. Study demonstrates that PET directed management of the neck after definitive chemoradiotherapy in N+ head and neck squamous cell carcinoma appropriately spares neck dissections in patients with PET-negative residual nodal abnormalities without compromising isolated nodal control.
Wang et al (50)	Evaluate the roll of FDG-PET in in post-CRT surveillance of HNSCC. Compare the diagnostic utility of PET and CT.	54	Whole-body PET	Histopathology	Chest CT	2 nuclear medicine physicians visually interpreted PET images and an experienced specialist reviewed all reports with the knowledge of clinical information.	PET demonstrated better performance than CT in post-CRT surveillance. Considering all 54 post-CRT PET scans, sensitivity for detecting primary tumours was 100%, specificity was 93%, PPV was 80% and NPV was 100%. For cervical diseases, sensitivity was 100%, specificity 98%, PPV 92% and NPV 100%. For distant metastases, sensitivity was 100%, specificity was 98%, PPV was 86% and NPV was 100%. PET had a high impact on the clinical management on 16/44 patients (36%)	FDG-PET in an effective non-invasive tool in the post-CRT surveillance of HNSCC with both excellent sensitivity and PPV. Results showed that it provided early information concerning distant metastases, smaller tumours and second primary cancers in the upper aerodigestive tract for some selected patients.
Unknown Primary								
Rudmik et al (49)	Clinical utility of PET/CT in the work-up of head and neck SCC with an unknown primary in a cohort of patients subjected to a standardized diagnostic protocol. Primary objective was to determine whether	20	PET/CT of the thoracic inlet to the upper thighs and a dedicated	Histopathology	High resolution CT or chest x-ray	Images were interpreted by a radiologist with subspecialty training in nuclear medicine.	PET/CT was positive in 14 of 20 patients (70%) with the base of tongue the most common site (8, 40%) followed by the tonsil (4, 20%). Traditional imaging identified the primary site in 5 patients (25%) whereas PET/CCT directed biopsy identified the primary site in 11	Patients with cervical metastasis and an unknown primary site after undergoing clinical examination benefit from PET/CT prior to panendoscopy. Until more evidence is available the authors believe that bilateral tonsillectomy should remain part of the standard

Author, Year	Objective	# of pts	PET	Reference Test	Comparison Test	Blinding	Results	Authors Conclusions
	the addition of a preoperative PET/CT improves the detection rate of the primary site compared with the traditional approach of expert clinical examination with endoscopy, preoperative CT/MRI and panendoscopy with biopsies of high-risk regions.		FDG PET/CT of the neck				patients (55%). The approaches were found to be statistically significant (p=0.03) in favour of PET/CT directed approach. The sensitivity and specificity of PET/CT were 92% and 63% respectively. The PPV and NPV were 79% and 83% respectively.	panendoscopy in this patient population.

Abbreviations: CT, computed tomography; FDG PET, fluorodeoxyglucose positron emission tomography; FP, false positive; LN, lymph node; MRI, magnetic resonance imaging; ROC, receiver operating characteristic; NPC, nasopharyngeal carcinoma; NPV, negative predictive value; NR, not reported; PPV, positive predictive value; SCC, squamous cell carcinoma; Sens, sensitivity; Spec, specificity; SPECT, single photon emission computed tomography; SUV, standardized uptake value; vs., versus.