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)

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

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PET Recommendation Report 2 Version 2: Section 1

PET Imaging in Head and Neck Cancer: Recommendations

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

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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]).

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