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PET Recommendation Report 3

PET Imaging in Melanoma

T Petrella and C Walker-Dilks

Report Date: January 19, 2009

PET Recommendation Report 3 is comprised of 2 sections and is available on the CCO Web site (https://www.cancercare.on.ca)
PEBC PET Recommendation Reports page at:
https://www.cancercare.on.ca/toolbox/qualityguidelines/other-reports/petrecs/

Section 1: Recommendations
Section 2: Evidentiary Base

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PET Recommendation Report 3: Section 1

PET Imaging in Melanoma: Recommendations

T Petrella and C Walker-Dilks

Report Date: January 19, 2009

QUESTIONS

- 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 melanoma?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for melanoma?
- What benefit to clinical management does PET or PET/CT contribute when recurrence of melanoma 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 melanoma?
- 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 melanoma.

INTENDED PURPOSE

- This recommendation report is primarily 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 and an update of that systematic review undertaken to retrieve the same level of evidence for the period from August 2005 to June 2008.

Diagnosis/Staging

PET is recommended for staging of high-risk patients with potentially resectable disease.
One study (Brady et al [2]) evaluated the additive benefit of PET to CT as a preoperative imaging technique. The combination of PET and CT had higher sensitivity than either technique alone. Information from the preoperative imaging results of PET plus CT led to treatment change in 35% of patients. Another study (Strobel et al [3]) showed a sensitivity, specificity, and accuracy of 85%, 96%, and 91%, respectively, for the depiction of metastases in high-risk melanoma.

Qualifying Statement

- Criteria for high risk include lymph node metastases, deep head and neck melanoma, and evidence of satellitosis or in-transit metastases. These include patients with American Joint Committee on Cancer (AJCC) stage IIC and III disease.

PET is not recommended for the diagnosis of sentinel lymph node micrometastatic disease or for staging of I, IIa, or IIb melanoma.
Nine primary studies in the HTA review (1) and three primary studies from the 2005-2008 update (Kell et al [4], Maubec et al [5], Cordova et al [6]) evaluated PET or PET/CT as a useful adjunct to lymphatic staging in patients with primary melanoma. The sensitivity of PET was too low to detect sentinel node metastases in early-stage melanoma (sensitivity range 0% to 22%).

Qualifying Statement

None.

The routine use of PET or PET/CT is not recommended for the diagnosis of brain metastases.
A limitation of PET is the normal uptake of fleurodeoxyglucose (FDG) into the brain, leading to uncertainty in the detection of cerebral metastases. Several small studies have confirmed this, showing low sensitivity of PET for the detection of brain metastases. One study (Pfannenberg et al [7]) showed that MRI was superior to PET in detecting brain metastases.

Qualifying Statement

None.

The routine use of PET is not recommended for the detection of primary uveal malignant melanoma.
One primary study (Kato et al [8]) showed that single photon emission computed tomography (SPECT) was superior to PET for detection of uveal melanoma. The sensitivity of PET was 11%.

Qualifying Statement

None.

Assessment of Treatment Response

A recommendation cannot be made for or against the use of PET for the assessment of treatment response in malignant melanoma due to insufficient evidence.
No prospective studies exist that examine PET or PET/CT in the assessment of treatment response for melanoma.

Qualifying Statement

None.

Recurrence/Restaging

A recommendation cannot be made for or against the use of PET for routine surveillance due to insufficient evidence.
No prospective studies exist that examine PET in the assessment of recurrence.

Qualifying Statement

None.

Solitary Metastasis Identified at Time of Recurrence

PET is recommended for isolated metastases at time of recurrence or when contemplating metastectomy.
There is some evidence showing change in patient management with the use of PET or PET/CT prior to metastectomy (HTA review [1], Koskivuo et al [9]). However, prospective studies assessing isolated metastases alone have not been conducted.

Qualifying Statement

None.

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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. Brady MS, Akhurst T, Spanknebel K, Hilton S, Gonen M, Patel A, et al. Utility of preoperative [(18)]f fluorodeoxyglucose-positron emission tomography scanning in high-risk melanoma patients. Ann Surg Oncol. 2006 Apr;13(4):525-32. Epub 2006 Feb 15.
3. Strobel K, Dummer R, Husarik DB, Pérez Lago M, Hany TF, Steinert HC. High-risk melanoma: accuracy of FDG PET/CT with added CT morphologic information for detection of metastases. Radiology. 2007 Aug;244(2):566-74.
4. Kell MR, Ridge JA, Joseph N, Sigurdson ER. PET CT imaging in patients undergoing sentinel node biopsy for melanoma. Eur J Surg Oncol. 2007 Sep;33(7):911-3. Epub 2007 Jan 4.
5. Maubec E, Lumbroso J, Masson F, Suciu V, Kolb F, Mamelle G, et al. F-18 fluorodeoxy-D-glucose positron emission tomography scan in the initial evaluation of patients with a primary melanoma thicker than 4 mm. Melanoma Res. 2007 Jun;17(3):147-54.
6. Cordova A, Napoli P, Costa R, Giambona C, Tripoli N, Moschella F. 18Fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET) imaging versus sentinel lymph node biopsy (SLNB) in the staging of cutaneous melanoma in AJCC stage I and II. Chirurgia 19(3)()(pp 189-191), 2006 Date of Publication: Jun 2006 2006;(3):189-91.
7. Pfannenberg C, Aschoff P, Schanz S, Eschmann SM, Plathow C, Eigentler TK, et al. Prospective comparison of 18F-fluorodeoxyglucose positron emissiontomography/computed tomography and whole-body magnetic resonance imaging in staging of advanced malignant melanoma. Eur J Cancer. 2007 Feb;43(3):557-64. Epub 2007 Jan 16.
8. Kato K, Kubota T, Ikeda M, Tadokoro M, Abe S, Nakano S, et al. Low efficacy of 18F-FDG PET for detection of uveal malignant melanoma compared with 123I-IMP SPECT. J Nucl Med. 2006 Mar;47(3):404-9.
9. Koskivuo IO, Seppänen MP, Suominen EA, Minn HR. Whole body positron emission tomography in follow-up of high risk melanoma. Acta Oncol. 2007;46(5):685-90.

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PET Recommendation Report 3: Section 2

PET Imaging in Melanoma: Evidentiary Base and Consensus Process

T Petrella and C Walker-Dilks

Report Date: January 19, 2009

QUESTIONS

- 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 melanoma?
- What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for melanoma?
- What benefit to clinical management does PET or PET/CT contribute when recurrence of melanoma 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 melanoma?
- 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 together 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.

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 Melanoma 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 Provincial Melanoma DSG. The draft recommendations were refined during a DSG teleconference. The Melanoma DSG is comprised of medical oncologists, surgeons, and pathologists and is supported by a PEBC research methodologist.

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.

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) PET imaging in several selected cancers, including melanoma. 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 June 2008. The update strategies for MEDLINE and EMBASE are in Appendices 1 and 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 the 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. Full text and data extractions of the studies from the update search were provided to the clinical lead authors to aid in the formulation of the recommendations. Telephone conferences and email correspondence between the clinical leads 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 Melanoma DSG and were discussed during a teleconference. The recommendations 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.

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 & neck, and melanoma). The melanoma table held the clinical lead and any other Melanoma 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 Melanoma DSG were presented by the clinical lead to the group at the colorectal table.
- During the small-group discussion at the Melanoma 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 are provided in Section 1 of this report.

RESULTS

Literature Search Results

The HTA review results for melanoma included two systematic reviews and 17 primary studies. The 2005 to 2008 update included nine primary studies. Data extracted from the systematic reviews and primary studies in the HTA review (1) are available on the HTA website (pages 208-222). Data extracted from the primary studies from the updated search are in Appendix 3. The key evidence identified by the search is described below in an abbreviated fashion.

Key Evidence

Diagnosis/Staging

- One study (Brady et al [2]) evaluated the additive benefit of PET to CT as a preoperative imaging technique. The combination of PET and CT had higher sensitivity than either technique alone. Information from the preoperative imaging results of PET plus CT led to treatment change in 35% of patients. Another study (Strobel et al [3]) showed a sensitivity, specificity, and accuracy of 85%, 96%, and 91%, respectively, for the depiction of metastases in high-risk melanoma.
- Nine primary studies in the HTA review (1) and three primary studies from the 2005-2008 update (Kell et al [4], Maubec et al [5], Cordova et al [6]) evaluated PET or PET/CT as a useful adjunct to lymphatic staging in patients with primary melanoma. The sensitivity of PET was too low to detect sentinel node metastases in early-stage melanoma (sensitivity range 0% to 22%).
- A limitation of PET is the normal uptake of FDG into the brain, leading to uncertainty in the detection of cerebral metastases. Several small studies have confirmed this, showing low sensitivity of PET for the detection of brain metastases. One study (Pfannenberg et al [7]) showed that MRI was superior to PET in detecting brain metastases.
- One primary study (Kato et al [8]) showed that SPECT was superior to PET for detection of uveal melanoma. The sensitivity of PET was 11%.

Assessment of Treatment Response

- No prospective studies exist that examine PET or PET/CT in the assessment of treatment response for melanoma.

Recurrence/Restaging

- No prospective studies exist that examine PET in the assessment of recurrence.

Solitary Metastasis at Time of Recurrence

- There is some evidence showing a change in patient management with the use of PET or PET/CT prior to metastectomy (HTA review (1), Koskivuo et al [9]). However, prospective studies assessing isolated metastases alone have not been conducted.

RECOMMENDATIONS
DIAGNOSIS/STAGING
Clinical Question
What benefit to clinical management does PET or PET/CT contribute to the diagnosis or staging of melanoma?

DRAFT DSG Recommendations
a) The use of PET is recommended for the staging of high-risk patients with potentially resectable metastatic disease.
b) PET or PET/CT is not recommended for the diagnosis of sentinel lymph node micrometastatic disease.
c) The routine use of PET or PET/CT is not recommended for the diagnosis of brain metastases.
d) The routine use of PET or PET/CT is not recommended for the detection of primary uveal malignant melanoma.

Provincial Consensus Meeting Deliberations
No major issues were raised during morning or afternoon discussions pertaining to the use of PET imaging in melanoma. Only slight changes in wording were made from the draft stage to the final recommendations.

Recommendations Put to Vote
a) The use of PET is recommended for the staging of high-risk patients with potentially resectable disease.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	11	7	2							

Votes = 21

b) PET is not recommended for the diagnosis of sentinel lymph node micrometastatic disease nor for staging of I, IIa, or IIb melanoma.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	15	5	1							

Votes = 21

c) The routine use of PET is not recommended for the diagnosis of brain metastases.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	15	6								

Votes = 21

d) The routine use of PET is not recommended for the detection of primary uveal malignant melanoma.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	14	5	2							

Votes = 21

FINAL RECOMMENDATIONS

a) PET is recommended for the staging of high-risk patients with potentially resectable disease.
b) PET is not recommended for the diagnosis of sentinel lymph node micrometastatic disease nor for staging of I, IIa, or IIb melanoma.
c) The routine use of PET or PET/CT is not recommended for the diagnosis of brain metastases.
d) The routine use of PET is not recommended for the detection of primary uveal malignant melanoma.

Qualifying Statement

- Criteria for high risk include lymph node metastases, deep head and neck melanoma, and evidence of satellitosis or in-transit metastases. These include patients with AJCC stage IIc, and III disease.

ASSESSMENT OF TREATMENT RESPONSE

Clinical Question

What benefit to clinical management does PET or PET/CT contribute to the assessment of treatment response for melanoma?

DRAFT DSG Recommendation

There is no evidence to recommend PET or PET/CT for the assessment of treatment response in malignant melanoma.

Provincial Consensus Meeting Deliberations

The melanoma recommendations were the first to be presented to the large group. There was discussion about whether an absence of evidence translated into a recommendation against the use of PET or whether a recommendation could not be made. After discussion among small and large groups, the precedent was set that an absence of evidence does not translate to a recommendation against the use of PET. It was agreed that the wording should be changed to state that a recommendation cannot be made for or against the use of PET due to insufficient evidence.

Recommendation Put to Vote:

A recommendation cannot be made for or against the use of PET for the assessment of treatment response in malignant melanoma due to insufficient evidence.

	1 – Strongly Agree			5 – Neither Agree nor Disagree				9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	12	8	1							

Votes = 21

FINAL RECOMMENDATION

A recommendation cannot be made for or against the use of PET for the assessment of treatment response in malignant melanoma due to insufficient evidence.

Qualifying Statement

None.

RECURRENCE/RESTAGING

Clinical Question

What benefit to clinical management does PET or PET/CT contribute when recurrence of melanoma 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 melanoma?

DRAFT DSG Recommendation

There is insufficient evidence to recommend use of PT or PET/CT for routine surveillance for melanoma recurrence.

Provincial Consensus Meeting Deliberations

Because of an absence of evidence on this topic, it was decided to change from a negative recommendation to a recommendation cannot be made.

Recommendations Put to Vote:

A recommendation cannot be made for or against the use of PET for the assessment of treatment response in malignant melanoma due to insufficient evidence.

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

Votes = 21

FINAL RECOMMENDATION

A recommendation cannot be made for or against the use of PET for the assessment of treatment response in malignant melanoma due to insufficient evidence.

Qualifying Statement

None.

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 a metastectomy is being contemplated?

DRAFT DSG Recommendation

PET or PET/CT should be considered for isolated metastases at time of recurrence or when contemplating metastectomy.

Provincial Consensus Meeting Deliberations

No major issues were raised during morning or afternoon discussions on this question.

Recommendation Put to Vote

PET is recommended for isolated metastases or when contemplating matestectomy.

	1 – Strongly Agree			5 – Neither Agree nor Disagree			9 – Strongly Disagree		N/A
	1	2	3	4	5	6	7	8	9	
Total	11	6	3					1		

Votes = 21

FINAL RECOMMENDATION

PET is recommended for isolated metastases or when contemplating matestectomy.

Qualifying statement
None

FUTURE RESEARCH

Areas for future research were not discussed in the process of drafting these recommendations.

ACKNOWLEDGEMENTS

The Melanoma DSG would like to thank Dr. Teresa Petrella for taking the lead in drafting this systematic review.

For a complete list of the Melanoma DSG members, please visit the CCO Web site at http://www.cancercare.on.ca/

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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. [cited 2009 Jan 19]. Available from: http://www.ncchta.org/fullmono/mon1144.pdf
2. Brady MS, Akhurst T, Spanknebel K, Hilton S, Gonen M, Patel A, et al. Utility of preoperative [(18)]f fluorodeoxyglucose-positron emission tomography scanning in high-risk melanoma patients. Ann Surg Oncol. 2006 Apr;13(4):525-32. Epub 2006 Feb 15.
3. Strobel K, Dummer R, Husarik DB, Pérez Lago M, Hany TF, Steinert HC. High-risk melanoma: accuracy of FDG PET/CT with added CT morphologic information for detection of metastases. Radiology. 2007 Aug;244(2):566-74.
4. Kell MR, Ridge JA, Joseph N, Sigurdson ER. PET CT imaging in patients undergoing sentinel node biopsy for melanoma. Eur J Surg Oncol. 2007 Sep;33(7):911-3. Epub 2007 Jan 4.
5. Maubec E, Lumbroso J, Masson F, Suciu V, Kolb F, Mamelle G, et al. F-18 fluorodeoxy-D-glucose positron emission tomography scan in the initial evaluation of patients with a primary melanoma thicker than 4 mm. Melanoma Res. 2007 Jun;17(3):147-54.
6. Cordova A, Napoli P, Costa R, Giambona C, Tripoli N, Moschella F. 18Fluoro-2-deoxy-D-glucose-positron emission tomography (FDG-PET) imaging versus sentinel lymph node biopsy (SLNB) in the staging of cutaneous melanoma in AJCC stage I and II. Chirurgia 19(3)()(pp 189-191), 2006 Date of Publication: Jun 2006 2006;(3):189-91.
7. Pfannenberg C, Aschoff P, Schanz S, Eschmann SM, Plathow C, Eigentler TK, et al. Prospective comparison of 18F-fluorodeoxyglucose positron emissiontomography/computed tomography and whole-body magnetic resonance imaging in staging of advanced malignant melanoma. Eur J Cancer. 2007 Feb;43(3):557-64. Epub 2007 Jan 16.
8. Kato K, Kubota T, Ikeda M, Tadokoro M, Abe S, Nakano S, et al. Low efficacy of 18F-FDG PET for detection of uveal malignant melanoma compared with 123I-IMP SPECT. J Nucl Med. 2006 Mar;47(3):404-9.
9. Koskivuo IO, Seppänen MP, Suominen EA, Minn HR. Whole body positron emission tomography in follow-up of high risk melanoma. Acta Oncol. 2007;46(5):685-90.
10. Strobel K, Skalsky J, Kalff V, Baumann K, Seifert B, Joller-Jemelka H, et al. Tumour assessment in advanced melanoma: value of FDG-PET/CT in patients with elevated serum S-100B. Eur J Nucl Med Mol Imaging. 2007 Sep;34(9):1366-75. Epub 2007 Mar 28.

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

Search run 24 June 2008

Combines basic FDG PET strategy with Mijnhout FDG PET strategy and 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 2. EMBASE search strategy update U.K. Health Technology Assessment systematic review on PET imaging in selected cancers.

Search run 2 July 2008

Combines basic FDG PE strategy with Mijnhout FDG PET strategy and 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 3. PET for melanoma: summary of the primary study evidence from 2005 to 2008.

Author, year	Objective	# of pts	PET	Reference Test	Compa-rison Test	Blinding	Key Results (see full data extractions for additional details)	Conclusions
Diagnosis/Staging								
Strobel, 2007a (10)	To assess value of FDG PET/CT in melanoma with elevated S-100B tumour marker levels	47	PET/CT	Histopathology, cytopathology, clinical-radiological follow up	None	PET interpretation blinded to results of other imaging & level of S-100B	Detection of metastases: Sens=97%, Spec=100%, Accuracy=98%	In melanoma patients with elevated S-100B tumour marker levels, FDG PET/CT reliably identified lymph node or distant metastases and reliably excluded metastases.
Kell, 2007 (4)	To assess the value of PET/CT in patients having SLNB for early stage melanoma	83	PET/CT skull base to feet	Histology of SLNB specimens	None	NR	Detection of occult lymphatic metastasis: Sens=22%, Spec=90%, PPV=40%, NPV=78%	The results do not support the use of PET/CT as a useful adjuvant to lymphatic staging in patients with primary melanoma.
Strobel, 2007 (3)	To determine the accuracy of PET/CT in the depiction of metastases in high risk melanoma	124	PET/CT from head to lower legs	Histology, other imaging modalities, and clinical follow up	PET/CT + dedicated CT interpreta tion	PET/CT was interpreted blinded to other imaging	Detection of metastases: PET/CT: Sens=85%, Spec=96%, PPV=94%, NPV=89%, Accuracy=91% PET/CT+dedicated CT readout: Sens=98%, Spec=94%, PPV=93%, NPV=99%, Accuracy=96%	Dedicated analysis of coregistered CT images significantly improved the accuracy of PET/CT for depiction of metastases.
Maubec, 2007 (5)	To determine value of FDG PET for detection of regional and/or distant metastasis in primary melanoma thicker > 4 mm	25	PET/CT from head to midthigh	Pathology & clinical - radiological follow up	Sentinel node biopsy	NR	Detection of primary tumour: Sens=17%, Spec=74% Microscopic lymph node disease in basins: Sens=0%, Spec=92% Distant sites: 3 false +ve	PET scan was not useful in the initial workup of patients with a primary melanoma.
Pfannenberg, 2007 (7)	To compare the diagnostic accuracy of PET/CT and wbMRI for staging	64	PET/CT from skull base to lower legs	Histology from metatastectomy, imaging & clinical follow up	PET, CT, wbMRI	PET, CT, & MRI scans individually were blinded to each other; histology blinded to imaging	N&M staging: PET/CT Sens=91%, Spec=77%, PPV=91%, NPV=77%, Accuracy=87% PET Sens=70%, Spec = 84%, PPV=91%, NPV=54%, Accuracy=74% CT Sens=77%, Spec=70%, PPV=86%, NPV=56%, Accuracy=75% MRI Sens=80%, Spec=76%, PPV=89%, NPV=61%, Accuracy=79%	PET/CT was more accurate than MRI in overall detection of malignant lesions, but more detailed analysis of sites indicates the imaging modalities notably differ between sites.
Brady, 2006 (2)	To determine additive benefit of FDG PET to CT as pre-operative imaging modality in stage IIc, III, and IV melanoma	103	FDG PET	Pathology and clinical and radiological follow up	CT	NR	Detection of occult disease PET Sens=68%, Spec=92% CT Sens=48%, Spec=95% Combination Sens=77%, Spec=92%	PET imaging in addition to CT scanning should be considered before operation in patients high risk for occult metastatic disease
Kato, 2006 (8)	To compare usefulness of FDG PET and ^{123}I-IMP SPECT in detection of uveal melanoma	19	FDG PET	Histopathology and follow up monitoring	^{123}I-IMP SPECT	NR	Detection of uveal melanoma: PET Sens=11%, Spec=100% SPECT Sens=100%, Spec=100%	SPECT was superior to PET in detection of uveal melanoma.
Cordova, 2006 (6)	To determine value of FDG PET in predicting regional lymph node involvement in primary melanoma stage I & II	25	FDG PET	Postoperative histology	SLNB	NR	Detection of sentinel node metastases: PET Sens=20%, Spec=87% SLNB Sens=100%	FDG PET was not accurate for the detection of regional lymph node metastases.
Recurrence/restaging								
Koskivuo, 2007 (9)	To evaluate FDG PET in detecting clinically silent metastases in follow up of high risk melanoma	30	FDG PET	Sentinel node biopsy and clinical follow up	None	NR	Melanoma recurrence: PET Sens=86%, Spec=96%, PPV=86%, NPV=96%	FDG PET is a valuable follow up tool in high risk melanoma to diagnose recurrences.

Abbreviations: CT, computed tomography; FDG PET, fluorodeoxyglucose positron emission tomography; IMP SPECT, iodoamphetamine single photon emission computed tomography; NPV, negative predictive value; NR, not reported; PPV, positive predictive value; Sens, sensitivity; SLNB, sentinel lymph node biopsy; Spec, specificity; wbMRI, whole body magnetic resonance imaging.