

PET Recommendation Report 6

PET Imaging in Cervical Cancer

A Fyles and C Walker-Dilks

Report Date: January 19, 2009

PET Recommendation Report 6 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

For further information about this report, please contact:

Dr. Anthony Fyles, Princess Margaret Hospital, 610 University Avenue, Toronto, Ontario, Canada M5G 2M9 Telephone (416) 946-6522; Fax (416) 946-2111; Email <u>anthony.fyles@rmp.uhn.on.ca</u>

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

Citation (Vancouver Style): Fyles A, Walker-Dilks C. PET Imaging in cervical cancer. Toronto (ON): Cancer Care Ontario; 2009 Jan 19. Program in Evidence-based Care PET Recommendation Report No.: 6.



Recommendation Report - PET #6: Section 1

PET Imaging in Cervical Cancer: Recommendations

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

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 systematic review from the U.S. Agency for Health Research and Quality (AHRQ) (1) that included primary study literature for the period from 2003 to March 2008.

Diagnosis/Staging

PET is not recommended for diagnosis of cervical cancer.

PET is not recommended for staging early stage cervical cancer.

A recommendation cannot be made for or against the use of PET for staging advanced stage cervical cancer due to insufficient evidence. However, ongoing studies will clarify the role of PET in advanced disease.

Multiple prospective and retrospective clinical trials have evaluated the diagnostic accuracy of PET or PET/CT for determining involvement of pelvic and para-aortic nodes compared to surgical staging or CT/magnetic resonance imaging (MRI). A 2008 meta-analysis by Selman et al (2) on diagnostic tests for lymph node status in cervical cancer included seven studies on PET. Of the seven studies, two were included in the Alberta 2008 AHRQ review (1), and five were included in the Duke University AHRQ review (3). In pooled estimates of test prediction of lymph node status, PET was inferior to sentinel node biopsy, but superior to MRI and CT. Selman et al (2) also compared post-test probabilities of PET in early versus (vs.) advanced disease and showed PET to perform well in advanced disease compared with early disease.

For the staging workup of patients with cervical cancer who are potential candidates for curative therapy, there is insufficient evidence to indicate that PET benefits clinical management by improving the accuracy of staging for nodal and metastatic disease, particularly in women with early disease treated surgically. One trial (Bjurberg et al [4]) demonstrated a change in management (i.e., change in radiation fields or conversion from curative to palliative intent) in four of 17 (24%) women with locally advanced disease, due to the identification of new metastases on PET/CT. The impact on treatment outcome is not clear, and for women with advanced disease treated with chemoradiation, further (ideally randomized) trials evaluating clinical impact are needed.

Qualifying Statements

- Most cervix cancers take up fluorodeoxyglucose (FDG) and are easily visualized on PET scan; however, as biopsy is needed for the diagnosis, there is little benefit to clinical management in using PET for assessment of the primary tumour.
- The impact of the detection of otherwise occult metastases of uncertain biology is unknown. In addition, although detection of metastases may render treatment palliative in intent, patients should not be deprived of aggressive chemoradiation to achieve pelvic control and optimal palliation.

Assessment of Treatment Response

PET is not recommended (following or early during therapy) for the purpose of predicting response to chemoradiation therapy.

Studies have demonstrated that chemo-radiation responders (defined at various times after treatment) have a better outcome than those with partial response or new development of metastases (Schwarz et al [5]). This is not surprising, and since salvage treatment of poor responders is unlikely to be effective, the clinical impact of using PET for response assessment remains to be determined.

Qualifying Statement

None.

Recurrence/Restaging

A recommendation cannot be made for or against the use of PET for evaluation of suspected recurrence, due to insufficient evidence.

Several trials have evaluated PET in women without clinical evidence of recurrence but with elevated serum SCC antigen. Chang et al (6) included 27 patients with elevated SCC-Ag levels but no evidence of recurrent disease. PET results were positive in 19 patients, only two of whom had local recurrence alone. Two patients had false-positive PET studies on further investigation and follow up.

For women with clinical or imaging suspicion of recurrence, PET will only be of use in those with salvageable disease in the pelvis or regional nodes, and the clinical impact of PET in this situation is unknown.

Qualifying Statement

None.

PET is recommended for women with recurrence who are candidates for pelvic exenteration or chemoradiation with curative intent.

Several studies have demonstrated significant changes in management in women with documented recurrent disease. In 12 patients with histologically confirmed relapsed disease (Bjurberg et al [4]), the treatment strategy was changed in three patients (25%).

Lai et al (7) included 40 patients with documented recurrent or persistent cervical carcinoma after definitive radiotherapy or surgery and potentially curable disease. Fifteen of 40 women (37.5%) were spared futile curative treatment, and in seven, curative treatment was continued but the treatment field or modality was changed following the demonstration of metastases on PET scan. Maximizing risk benefit ratios and avoiding the morbidity of major surgery is a meaningful endpoint in this admittedly small group of women.

Schwarz et al (5) (cited in the AHRQ report but not in data tables) showed that three-month posttherapy PET results provided an indication of response to treatment and were predictive of survival.

Qualifying Statement

None.

Funding

The PEBC is a provincial initiative of Cancer Care Ontario 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.

Copyright

This report is copyrighted by Cancer Care Ontario; the report and the illustrations herein may not be reproduced without the express written permission of Cancer Care Ontario. Cancer Care Ontario reserves the right at any time, and at its sole discretion, to change or revoke this authorization.

Disclaimer

Care has been taken in the preparation of the information contained in this report. Nonetheless, any person seeking to apply or consult the report is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or guarantees of any kind whatsoever regarding the report content or use or application and disclaims any responsibility for its application or use in any way.

PET REPORT 6 IN REVIEW

Contact Information For further information about this report, please contact:

Dr. Anthony Fyles, Princess Margaret Hospital, 610 University Avenue, Toronto, Ontario Canada M5G 2M9, telephone (416) 946-6522, fax (416) 946-2111, email <u>anthony.fyles@rmp.uhn.on.ca</u>

For information about the PEBC and the most current version of all reports, please visit the CCO Web site at http://www.cancercare.on.ca/ or contact the PEBC office at: Phone: 905-525-9140, ext. 22055 Fax: 905-522-7681

PET REPORT 6 IN REVIEW

REFERENCES

- 1. McEwan AJ, Gulenchyn K, Ospina M, Horton J, Seida J, Vandermeer B, et al. Positron emission tomography for nine cancers (bladder, brain, cervical, kidney, ovarian, pancreatic, prostate, small cell lung, testicular). Rockville, Maryland: Agency for Healthcare Research and Quality; August 2008. Draft.
- 2. Selman TJ, Mann C, Zamora J, Appleyard TL, Khan K. Diagnostic accuracy of tests for lymph node status in primary cervical cancer: a systematic review and meta-analysis. CMAJ. 2008 Mar 25;178(7):855-62.
- Matchar DB, Kulasingam SL, Havrilesky L, Mann LO, Myers ER, McCrory DC, et al. Positron emission tomography for six cancers (brain, cervical, small cell lung, ovarian, pancreatic, and testicular). Rockville, Maryland: Agency for Healthcare Research and Quality; 2004 Feb [cited 2009 Jan 19]. Available from:

http://www.cms.hhs.gov/mcd/viewtechassess.asp?where=search&tid=21

- 4. Bjurberg M, Kjellén E, Ohlsson T, Ridderheim M, Brun E. FDG-PET in cervical cancer: staging, re-staging and follow-up. Acta Obstet Gynecol Scand. 2007;86(11):1385-91. Epub 2007 Sep 4.
- 5. Schwarz JK, Siegel BA, Dehdashti F, Grigsby PW. Association of posttherapy positron emission tomography with tumor response and survival in cervical carcinoma. JAMA. 2007 Nov 21;298(19):2289-95.
- 6. Chang TC, Law KS, Hong JH, Lai CH, Ng KK, Hsueh S, et al. Positron emission tomography for unexplained elevation of serum squamous cell carcinoma antigen levels during followup for patients with cervical malignancies: a phase II study. Cancer. 2004 Jul 1;101(1):164-71.
- 7. Lai CH, Huang KG, See LC, Yen TC, Tsai CS, Chang TC, et al. Restaging of recurrent cervical carcinoma with dual-phase [18F]fluoro-2-deoxy-D-glucose positron emission tomography. Cancer. 2004 Feb 1;100(3):544-52.