Policy Forum

Health Technology Policy Information

Positron Emission Tomography in Oncology

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The Policy Forum

The Policy Forum is a pan-Canadian committee of senior health care decision-makers tasked with the development of evidence-based joint policy initiatives related to the implementation, management, and decommissioning of health technologies. The Policy Forum was created in response to Health Technology Strategy 1.0, and its subsequent Implementation Strategy, approved by the Conference of Deputy Ministers in May 2004 and April 2005 respectively. Members of the Policy Forum include senior officials involved in health policy from each of the 14 federal, provincial, and territorial health ministries, as appointed by the Deputy Ministers of Health. Also included are two non-voting members: one from Industry Canada and the other from the Interprovincial and Territorial Medical Directors group. The Canadian Agency for Drugs and Technologies in Health (CADTH) serves as the secretariat for the Forum.

This is the first information paper produced by the Policy Forum. The evidence summary is based on a report produced by the Health Technology Inquiry Service at CADTH.[1] This research was conducted at the request of the Policy Forum to provide a common evidence base that can be used to inform decisions about the use of positron emission tomography (PET) in oncology in Canada.

The intended audience for this information paper includes decision-makers at provincial and territorial ministries of health, cancer agencies, health regions, cancer centres, and clinicians in the field of oncology. The purpose of the document is to assist these individuals in making evidence-based decisions about the use of PET to support the diagnosis, staging/re-staging, response to treatment, and detection of recurrence in various cancers. This document is not intended to serve as a clinical guideline.

Policy Interest

As the incidence of many cancers continues to rise, the Canadian health care system faces increasing pressure to provide technologies and therapeutics for diagnosis and treatment. Although PET is not a new technology, variations in its use and availability remain due, in part, to uncertainty about appropriate use. In an effort to support optimal use of this technology, the Policy Forum has sought evidence on the clinical effectiveness of PET in oncology compared with other commonly used imaging technologies (such as computed tomography [CT] and magnetic resonance imaging [MRI]) as well as the indications for the use of PET in oncology. It is important to determine the effectiveness of this technology in oncology, because accurate information about the nature of the cancer is vital to determining the most appropriate treatment strategy and making changes to the treatment plan in cases where the response is poor.

[1]Unless otherwise stated, evidence presented in this document was obtained from the following source:
Mujoomdar M, Moulton K, Nkansah E. *Positron emission tomography (PET) in oncology: a review of the clinical effectiveness and indications for use.* Ottawa: Canadian Agency for Drugs and Technologies in Health — Health Technology Inquiry Service; 2009.

Key Research Findings

- Varying levels of evidence suggest that PET is equally or more effective than other imaging modalities (CT or MRI) for a number of oncologic indications.
- Generally, studies that evaluated both imaging modalities found that the effectiveness of PET combined with CT (PET/CT) was either equal to or greater than PET alone.
- PET may be effective in the disease management of a number of different cancers and may be more effective when compared with other imaging modalities currently used as standards of care.

The Technology

Positron Emission Tomography (PET)

- creates a three-dimensional image of physiological and biochemical processes in the body by tracking the deposition of radioactive molecules (positron-emitting radiopharmaceuticals) to various sites
- the most common radioactive tracer is 2-[18F]fluoro-2-deoxyglucose (FDG), a glucose analogue
- tracers accumulate in tissues with high metabolic activity, including tumours, but also sites of inflammation, trauma, and infection
- precise anatomical information can rule out areas of non-specific uptake of tracer and false positives
- PET/CT hybrid scanners combine functional information from PET with precise structural and anatomical information from CT

Implementation Status (current as of August 17, 2009)

Health Canada regulates the use of FDG and other positron-emitting radiopharmaceuticals, which means that a New Drug Submission must be filed in order to manufacture these substances and that PET scans can be provided only under a Clinical Trials Application for indications that have not been approved. PET is available in most Canadian jurisdictions. Descriptions of the approach of the provinces and territories to managing this technology are included in the table below.

Positron Emission Tomography in Canada		
Jurisdiction	PET Availability	Current Status
British Columbia	In province	The BC Cancer Agency operates the only PET/CT scanner in the province at its Vancouver Centre. Since beginning clinical operations on June 28, 2005, more than 9,200 adult and 500 pediatric oncology patients from across BC have undergone publicly funded PET/CT scans at this facility. Indications are based on provincial tumour group approved, evidence-based guidelines for the use of PET/CT in oncology. Scans are currently performed under clinical trials agreements with Health Canada for adult and pediatric oncology populations. The PET/CT program is funded for 3,100 scans per year and is currently at maximum clinical capacity. Construction of a cyclotron and FDG production facility is currently underway at the agency's Vancouver centre with an anticipated completion date in September 2009.
Yukon	Out-of-territory	Yukon does not have a PET scanner. PET scans for Yukon residents are largely performed in British Columbia with a few in Alberta. Requests for PET scans are forwarded to the hospital claims assessor. If the request is unusual, it is also examined by the medical advisor. Requests for PET scans are generally forwarded from the treating oncologist, and to date none has been declined.
Northwest Territories	Out-of-territory	The Northwest Territories does not have a PET scanner and accepts responsibility for PET scanning of residents required to have this investigation through a cancer treatment institution or hospital as part of a cancer related work-up. This is done on a prior-approval basis.
Alberta	In province	In Alberta, PET/CT has been available for clinical use in the public system since April 2005 and is currently provided at three facilities (Foothills Hospital, Cross Cancer Institute, and University of Alberta Hospital). During the 2007-2008 fiscal year, 3,318 PET/CT scans were provided, with the majority being for indications in oncology. PET clinical trials using FDG have closed because the notice of compliance has been received. The PET Advisory Committee is considering a registry for PET indications related to infections and is in favour of a national oncology PET registry. Alberta Health and Wellness has produced a document entitled “Approach to Maintaining the Provincial List of Indications for the Use of PET,” which has been reviewed by the PET Advisory Committee.
Saskatchewan	Out-of-province	Saskatchewan does not currently have a PET or PET/CT scanner. Patients who require a scan (approximately 300 per year) receive the service in either Alberta or Manitoba.
Manitoba	In province	PET became operational in Manitoba in 2005. In Manitoba, the vast majority of PET scans are for cases of adult oncology patients. There are also cases of select pediatric oncology patients as well as a small number of non-oncology patients (e.g., brain scans for hard-to-medically-manage seizure disorders). The Manitoba program has recently received ethics approval to participate in a clinical trial using a PET bone scanning agent (NA F-18). This is part of the contingency planning related to nuclear reactor-based medical isotopes (for example, in response to the Chalk River nuclear reactor going offline), because the radiopharmaceuticals for PET are produced by a different technology (medical cyclotron). The medical cyclotron is in the process of being

Positron Emission Tomography in Canada		
Jurisdiction	PET Availability	Current Status
		commissioned in Winnipeg. Manitoba's current PET/CT unit was delivered in 2004. The cyclotron will be commissioned soon, which will significantly increase capacity and ability to meet demand (expanding indications and increased utilization for existing indications). It would be ideal for clinical needs, and a requirement for research, for a PET/CT unit to be located in the same building as the cyclotron (i.e., to facilitate short-lived isotopes, which are delivered to the PET/CT suite by a pneumatic tube system).
Ontario[2]	In province	In Ontario, PET scans are publicly funded for listed cardiac and oncologic indications (see the OHIP Bulletin at http://www.health.gov.on.ca/english/providers/program/ohip/bulletins/4000/bul4498.pdf for detailed information). The Ontario Ministry of Health and Long-Term Care, on the advice of Cancer Care Ontario, continues to collect evidence of effectiveness on the use of PET scans for other indications in the following three ways: 1. Registries. PET scans are available through ministry-funded registries for several non-insured indications where evidence of effectiveness is being collected. 2. Trials. Clinical trials are being conducted to determine if PET improves diagnosis and treatment strategies for colorectal adenocarcinoma metastases, recurrent cancer, cervical cancer, and stage III non-small cell lung cancer. Additional studies may be launched in future. 3. PET Access Program. Patients who may benefit from a PET scan, but who are not eligible for an insured scan, registry or clinical trial, may be referred to the PET Access Program by their physicians. An expert panel, comprising oncologists, radiologists, and nuclear medicine specialists, adjudicates all requests made to the program. Between October 2006 and March 31, 2008, 170 applications were made; 68 were approved.
Quebec[3]	In province	In 2001, the Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS) issued a report with findings in favour of the clinical utility of PET for a number of indications, including those for oncology. The report also included recommendations regarding the deployment of the technology. The plan would ensure that the provision of PET scans would be linked to research and would take place in collaboration with university hospital centres and university institutes. Data collection would inform future decisions about the use of PET in Quebec. Quebec has been funding PET scans since 2003.
Nova Scotia	In province	A publicly funded PET/CT scanner began operation in Halifax in June 2008. During this first year of operation, 806 PET/CT scans were conducted for oncologic indications in residents of Nova Scotia. Some additional scans were

[2]Ontario PET Steering Committee. *PET Scan Primer: A Guide to the Implementation of Positron Emission Tomography Imaging in Ontario*. Toronto: Queen's Printer of Ontario; 2008. Available: http://www.cancercare.on.ca/common/pages/UserFile.aspx?fileId=13624.

[3]Agence d'évaluation des technologies et des modes d'intervention en santé (AETMIS). *Positron emission tomography in Québec*. Report prepared by François Pierre Dussault, Van H. Nguyen, and Fatiha Rachet. (AETMIS 01-3 RE). Montréal: AETMIS, 2001, xviii-270.

Positron Emission Tomography in Canada		
Jurisdiction	PET Availability	Current Status
		provided for the other maritime provinces. The FDG used with this machine is purchased from a private company in Montreal and flown in as needed. No research protocols are required under this arrangement. It is anticipated that once a cyclotron is built in Halifax, the volume of services will increase to around 1,440 scans per year. Nova Scotia insures the use of PET/CT only for specific oncologic indications. As new evidence emerges, other indications will be considered and reviewed as required.
New Brunswick	In province	In New Brunswick, PET/CT scanning is provided as a provincial service at one site (Saint John). Service at a second site in Moncton is planned but is few years from becoming operational. The PET/CT service was established and offered as a clinical trial study and is still operating under those terms. The isotope is flown to Saint John from Quebec, and the service is available two to three days a week. Guidelines have been developed by a provincial PET/CT advisory committee, and requisitions are reviewed and approved according to these guidelines by the nuclear medicine physicians overseeing the service. Only oncology cases are eligible for publicly funded PET/CT scans in the province. Six hundred scans per year have been approved for funding.
Prince Edward Island	Out-of-province	P.E.I. does not have a PET scanner. PET scans for P.E.I. residents are largely performed in Nova Scotia with a few others in Quebec. Requests for PET scans are forwarded to the Out of Province Hospital Claims Assessor. If the request is unusual it is also examined by the Medical Consultant. Requests for PET scans are generally forwarded from the treating oncologist or respirologist. Currently P.E.I. only insures the use of PET/CT for specific oncologic indications. As new evidence emerges other indications will be considered and reviewed as required.
Newfoundland and Labrador	Out-of-province	Newfoundland and Labrador does not have a publicly owned PET scanner within the province. Patients requiring a PET scan are sent out of province, typically to Halifax. The province insures the procedure on a pre-approval basis for oncologic indications. Most of the scans performed are for colorectal cancer, lung cancer, or lymphoma.

CT = computed tomography; FDG = 2-[$_{18}$F]fluoro-2-deoxyglucose; MRI = magnetic resonance imaging; PET = positron emission tomography; PET/CT = a diagnostic tool using both PET and CT imaging techniques.

Clinical Evidence Summary

PET may be effective in the disease management of a number of different cancers, and it may be more effective when compared with other imaging modalities currently used as standards of care. The findings of a review performed by CADTH[4] suggest that PET may be equally or more effective than other imaging modalities (CT or MRI) for a number of oncologic indications. The effectiveness of PET/CT has repeatedly been demonstrated to be either equal to or greater than PET alone.

There is evidence of moderate quality to support a number of uses of PET scans for a variety of cancers. The highest quality evidence is for the use of PET to monitor treatment response in breast cancer and lymphoma and for diagnosis of non–small-cell lung cancer.

A literature search identified 14 existing evidence-based guidelines, although none of these was issued by national bodies. The strength of the evidence supporting the recommendations varies from weak to strong. The majority of the recommendations were related to the use of PET in the treatment of lung cancer.

Fletcher et al. (2008) performed a systematic review of the role of PET in oncology to develop recommendations on the use of PET in cancer. The recommendations, presented in the following table, were made based on the evidence of the clinical effectiveness of PET for various indications.

Recommendations for Use of Positron Emission Tomography for Diagnosis, Staging, and Detecting Recurrence of Cancer[5]			
Cancer Type	Purpose		
	Diagnosis	Staging/Re-staging	Detecting Metastases or Recurrence
Breast	Not useful for routine diagnosis, but may be useful in high-risk patients with lesions greater than 2 cm and elevation in serum tumour markers	Not useful for routine axillary staging	Not useful for routine detection of metastases or recurrence
Colorectal	Not useful for the routine detection of primary colorectal cancer	Useful for the evaluation of resectable liver metastases	May be a useful addition to the clinical work-up if carcinoembryonic antigen marker is elevated
Esophageal	Not reported	Useful for preoperative staging (some effectiveness at detecting local nodal metastases)	Useful for detecting distant metastases
Head and Neck	Not useful as an addition to CT or MRI	PET in combination with CT or MRI improves nodal	May be useful addition to the conventional work-up

[4]Mujoomdar M, Moulton M, Nkansah E. *Positron emission tomography (PET) in oncology: a review of the clinical effectiveness and indications for use.* Ottawa: Canadian Agency for Drugs and Technologies in Health — Health Technology Inquiry Service; 2009.
[5]Fletcher JW, Djulbegovic B, Soares HP, Siegel BA, Lowe VJ, Lyman GH, et al. Recommendations on the use of 18F-FDG PET in oncology. *J Nucl Med* 2008;49(3):480-508.

Recommendations for Use of Positron Emission Tomography for Diagnosis, Staging, and Detecting Recurrence of Cancer[5]			
Cancer Type	Purpose		
	Diagnosis	Staging/Re-staging	Detecting Metastases or Recurrence
		or distant disease staging	strategies to detect recurrences
Non–small-cell lung cancer	Useful in the differentiation between benign and malignant lesions in patients with solitary pulmonary nodules	Useful	Useful in the diagnostic work-up for detecting distant metastases
Small-cell lung cancer	No conclusions — insufficient evidence	No conclusions — insufficient evidence	No conclusions — insufficient evidence
Lymphoma	Not reported	Useful in pretreatment staging of lymphoma. Also evidence of effectiveness in staging/re-staging lymphoma following treatment (both Hodgkin disease and non-Hodgkin lymphoma)	Useful
Melanoma	Not reported	Useful	Useful
Pancreatic	Useful when conventional imaging results are inconclusive	Not reported	Not reported
Sarcomas	No conclusions — insufficient evidence	No conclusions — insufficient evidence	No conclusions — insufficient evidence
Thyroid	Not reported	Not reported	Useful for detecting recurrence in patients treated for well-differentiated thyroid cancer when the findings of ^{131}I scintigraphy are negative, but the thyroglobulin serum marker is elevated
Unknown primary	Useful in the detection of primary tumours not detected by conventional clinical work-up means	Not reported	Not reported

CT = computed tomography; MRI = magnetic resonance imaging; PET = positron emission tomography.

Next Steps

As PET trials currently underway in the jurisdictions progress, the Policy Forum will update this document to reflect any new information so it can be considered when making decisions about the use of PET in other parts of the country. In the future, depending on the nature and quality of the evidence, the Policy Forum may provide policy advice for consideration by the jurisdictions.

Disclaimer

This report is prepared by the Canadian Agency for Drugs and Technologies in Health (CADTH) for the Health Technology Strategy Policy Forum (herein referred to as the Policy Forum). The Policy Forum is a federal, provincial and territorial coalition of interests for health technology policy, seeking to achieve common purpose and economies through identifying areas of common policy interest, sharing health technology information and collaborating where beneficial to the members.

This Policy Information Document is intended to provide a summary of evidence and other considerations for decision makers within the Canadian health care system. The document is based on a review of the existing published and unpublished material available to CADTH at the time of preparation, and was guided by expert input and advice throughout its preparation.

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