Canadian Agency for Drugs and Technologies in Health

Issue 8 January 2008

HTA

HEALTH TECHNOLOGY UPDATE

A newsletter on new and emerging health care technologies in Canada

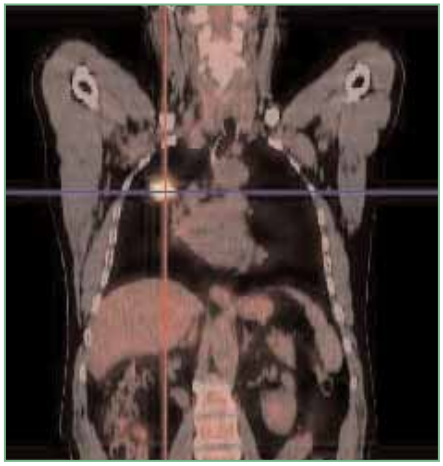
Scanning the horizon

Informing decision makers about emerging medical technologies

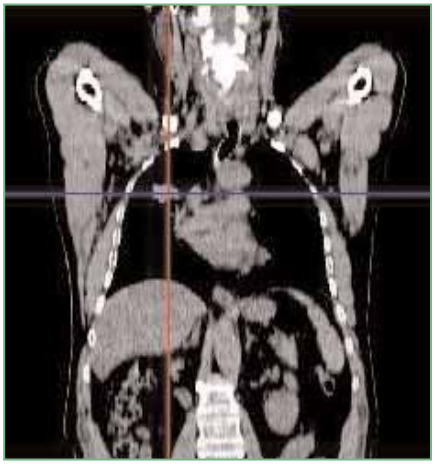
Our inaugural issue of *Health Technology Update*, in 2005, provided an update on positron emission tomography (PET) in Canada. Two years later, PET is still a hot topic here, partly because the technology is expensive to buy and operate and also because of the shortage of trained technologists and the complexities involved in licensing and producing the cyclotron-generated radiopharmaceuticals.

This issue of the *Health Technology Update* provides an update on the expanding distribution and funding of PET in Canada as well as information on the regulatory approval of several radiopharmaceutical products used in the scan.

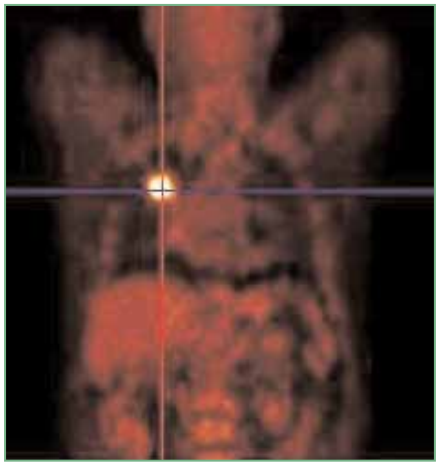
We also want to tell you about a new gender-based knee implant and emerging treatments for congestive heart failure and bone cancer pain. As always, we hope you will find this issue informative and useful.



PET scan of the lung and abdomen.



CT scan of the same area.



Fused PET/CT image of the lung and abdomen confirms the precise location of a lung cancer lesion that displays increased FDG uptake.

Image courtesy of the Great-West Life PET/CT Centre at the Health Sciences Centre, Winnipeg.

In this issue

Your feedback on the newsletter is always welcome, as are suggestions for new technologies to review in future issues. Please send comments to: Catherine Allison, Editor.

E-mail: catherinea@cadth.ca

Positron Emission Tomography in Canada: An Update

Positron emission tomography (PET) is a non-invasive nuclear medicine imaging technology that produces images of metabolic processes in the body. PET can be used to visualize abnormalities of metabolism caused by cancer, heart disease, and neurological disorders.

Photo courtesy of the Great-West Life PET/CT Centre at the Health Sciences Centre, Winnipeg.

Siemens Biograph™ 16 HR PET/CT scanner

Hybrid PET/CT Scanners

Hybrid scanners that have both PET and computed tomography (CT) components became commercially available in 2001.[1] These are quickly replacing stand-alone PET scanners.

The hybrid machine allows CT and PET images to be collected sequentially on the same device. The x-ray CT image shows a detailed view of the anatomy, while the PET component maps both normal and abnormal tissue function. The resulting fused image allows functional abnormalities to be pinpointed within the body with greater accuracy.[1–3]

The hybrid machine also reduces the overall scanning time by 30% to 40% compared with a stand-alone PET scan. This allows higher patient throughput and a more comfortable exam for the patient,[2] which can be completed during a single session.

How It Works

Prior to the PET/CT scan, patients receive an intravenous injection of 18-fluoro-2-deoxyglucose (FDG), a glucose molecule that is attached to a radioactive tracer (fluorine-18). Fast-growing tumour cells absorb glucose more quickly than healthy tissue; and when the radiolabelled glucose accumulates in malignant tissues, it shows up as "hot spots" on the PET scan image. In heart disease and neurological disorders, the PET image can reveal the location of malfunctions, such as the locus of seizures in epilepsy or areas of poor blood flow in heart disease.

FDG Production

FDG is produced in a laboratory from radioisotopes generated by a cyclotron (particle accelerator). FDG has a short shelf life and must be delivered to the PET scanning facility within five hours of production.[4] Therefore, PET scanners must be located relatively close to a cyclotron, which may limit the use of this technology in some parts of Canada. The locations of publicly funded cyclotrons are shown in a chart on page 4.

Recent Report Assessing PET

A review of the clinical and cost-effectiveness of PET is beyond the scope of this newsletter, but a recent report from the UK may be of interest:

Overview of the clinical effectiveness of positron emission tomography imaging in selected cancers. UK National Institute for Health Research, Health Technology Assessment Programme.
Available: http://www.hta.ac.uk/fullmono/mon1144.pdf

FDG Regulations

In Canada, FDG is regulated as a radiopharmaceutical drug. Four manufacturers have obtained Health Canada approval to use FDG for specific indications (see the table below).

However, most FDG used for clinical PET scanning in Canada is currently regulated as an investigational drug and accessed using a Clinical Trial Application. Centres that provide PET scans must serve as a clinical trial sponsor and gather clinical efficacy and safety data for all patients who receive FDG.

FDG products that have received Health Canada approval

FDG Trade Name	Manufacturer	Diagnostic Indication(s) for Use
CanTrace™	IPET Pharmaceuticals Inc.,* Vancouver, BC	Breast, lung, and colorectal cancer
Glucovision	Hamilton Health Sciences Corporation, Hamilton, ON	Lung cancer
FluGlucoScan injection	Alberta Cancer Board, Edmonton, AB	Lung and colorectal cancer
Gludef®	Bristol-Myers Squibb Medical Imaging,* Saint-Laurent, QC	Lung cancer

*private company

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PET Scan Funding in Canada

The clinical use of positron emission tomography (PET) in Canada continues to expand, primarily for the evaluation and management of several types of cancer.

As of November 2007, there were 22 centres performing publicly funded PET scans in seven Canadian provinces. See page 4 for the location of the scanners as well as the cyclotron and FDG manufacturing sites. Privately owned PET centres in Canada are shown in the table on page 8.

The largest expansion of PET services has occurred in Quebec, with a 14-fold increase in operational funding since 2005. It is anticipated that by early 2009 there will be a total of 12 PET/CT scanners performing clinical scans in Quebec following the installation of five new scanners at hospitals in Trois-Rivières, Gatineau, Rimouski, Chicoutimi, and Quebec City.

Provincial Funding for PET Scans

ALBERTA will fund approximately 3,500 clinical PET scans in 2008 from global regional health budgets.
Source: *Dr. Sandy McEwan, Cross Cancer Institute, Edmonton.*

BRITISH COLUMBIA funds 3,000 PET scans annually at the BC Cancer Agency's Vancouver Centre.
Source: *Dr. Don Wilson, BC Cancer Agency, Vancouver.*

MANITOBA is funding up to 1,000 PET scans annually from global regional health budgets. This will double to 2,000 scans annually when a new cyclotron becomes operational in Winnipeg in early 2008.
Source: *Shirley Dzogan, Manitoba Health, Winnipeg.*

NEW BRUNSWICK's operational funding is set at $1.335 million to perform 600 PET scans annually with one PET/CT scanner in Saint John. This funding is expected to double when a second PET/CT scanner opens in Moncton in 2008 or 2009.
Source: *François Varin, Department of Health, Hospital Services, Fredericton.*

NOVA SCOTIA will fund 1,500 PET scans annually when a new PET/CT scanner opens in February 2008. Operational funding is set at $1.9 million per year while FDG is supplied from Sherbrooke, Quebec. Funding will decrease to approximately $800,000 annually when a new cyclotron and FDG manufacturing site open in Halifax in 2009.
Source: *Abe Almeda, Nova Scotia Department of Health, Halifax.*

"**ONTARIO** provides funding for PET scans through clinical trials, two registry studies, and the Ontario PET Access Program. Three active clinical trials evaluate the role of PET in the diagnosis and staging of head and neck cancer, metastatic lung cancer, and colorectal cancer with liver metastases. Two clinical trials (on potentially resectable non-small cell lung cancer and breast cancer) have completed patient accrual and the results are being analyzed. The Ontario PET Steering Committee is considering indications for new clinical trials. The Ontario Cancer PET registry study coordinated by Hamilton Health Sciences Centre provides PET scans for patients with a solitary pulmonary nodule, potentially resectable non-small cell lung cancer, or suspected recurrent cancers (thyroid, germ cell, and colorectal) with elevated tumour marker but negative anatomical findings in traditional imaging tests. The Ontario Cardiac PET Registry Study led by the University of Ottawa Heart Institute provides FDG PET myocardial viability assessments to patients with severe ventricular dysfunction being considered for revascularization or a heart transplant. Patients who are not candidates for the clinical trials or registry studies may apply for a PET scan through the Ontario PET Access Program. A panel of an oncologist, a nuclear medicine physician, and a radiologist reviews each application on a case-by-case basis, and determines whether a PET scan would be appropriate. The number of PET scans being provided in Ontario is not limited by funding, but depends on patient need. Based on current indications recommended by the Ontario PET Steering Committee, approximately 2,000 PET scans are currently anticipated in fiscal year 2007/2008."
Submitted by: *Shirley Lee, Ontario Ministry of Health and Long-Term Care, Medical Advisory Secretariat, Toronto.*

QUEBEC will fund 21,000 PET scans at 12 scanning facilities during 2008. Operational funding for the scans is approximately $14 million.
Source: *Serge Péloquin, Ministère de la Santé et des Services sociaux du Québec, Quebec City.*

Publicly Funded PET Scanners and Cyclotrons in Canada

Province	Hospital or Centre, and Province	Type (number of scanners)	Number of Cyclotrons	Additional Information
British Columbia	BC Cancer Agency, Vancouver	PET/CT (1)	1	TRIUMF cyclotron operates principally for research
			1 (anticipated)	New on-site cyclotron and radiopharmaceutical lab expected to be operational in fall 2008
Alberta	Cross Cancer Institute, Edmonton	PET (1) (used for research only) PET/CT (1)	1	
	University of Alberta Hospital, Edmonton	PET/CT (1)		FDG obtained from Cross Cancer Institute
	Foothills Hospital, Calgary	PET/CT (1)		FDG obtained from Cross Cancer Institute
Manitoba	Health Sciences Centre, Winnipeg	PET/CT (1)	1 (anticipated)	New on-site cyclotron expected to be operational in 2008
Ontario	Hamilton Health Sciences, Hamilton	PET (1)	1	
	St. Joseph's Healthcare, Hamilton	PET/CT (1)		
	Ottawa Hospital, Ottawa	PET/CT (1)		
	Ottawa Heart Institute, Ottawa	PET/CT (1) PET (1)	1	The PET scanner will be decommissioned in 2008
	Centre for Addiction and Mental Health, Toronto	PET (1) PET/CT (1) (both scanners used for brain research only)	1	
	Princess Margaret Hospital, Toronto	PET/CT (2)	1 (anticipated)	New on-site cyclotron expected to be operational in late 2009
	Sunnybrook Health Sciences Centre, Toronto	PET/CT (1)		
	St. Joseph's Health Care, London	PET/CT (1)	1 (anticipated)	New on-site cyclotron expected to be operational in 2009
	Hospital for Sick Children, Toronto	PET/CT (1)		
Quebec*	McGill University Health Centre (Montreal General Hospital), Montreal	PET/CT (1)		FDG obtained from Montreal Neurological Institute and Sherbrooke cyclotrons
	Hôtel-Dieu Hospital (Centre hospitalier de l'Université de Montréal), Montreal	PET/CT (1)		FDG obtained from privately owned cyclotron (Pharmalogic, Montreal)
	Hôtel-Dieu Hospital (Centre hospitalier universitaire de Québec), Quebec City	PET/CT (1)		
	University of Sherbrooke Hospital, Sherbrooke	PET/CT (1)	1	Second on-site cyclotron planned for 2010
	Jewish General Hospital, Montreal	PET/CT (1)		FDG obtained from Pharmalogic
	Maisonneuve-Rosemont Hospital, Montreal	PET/CT (1) expected to be operational in January 2008		
	Sainte-Justine Hospital, Montreal	PET/CT (1) expected to be operational in January 2008		
New Brunswick	Saint John Regional Hospital, Saint John	PET/CT (1)	FDG supplied by Sherbrooke cyclotron	Another PET/CT scanner anticipated to be operating at the Dr. Georges-L. Dumont Regional Hospital in Moncton by late 2008 or early 2009
Nova Scotia	Queen Elizabeth Health Sciences Centre, Halifax	PET/CT (1) expected to be operational by February 2008	1 (anticipated)	New on-site cyclotron and radiopharmacy anticipated to be operational in late 2009

* Quebec also funds PET scanners used for research purposes at the following centres: Montreal Neurological Institute (two PET scanners), Montreal's Notre-Dame Hospital (one PET/CT scanner), and University of Sherbrooke Hospital (one PET/CT scanner).

Gender Solutions™: Knee Replacement Implants for Women

Knee replacement implants designed for women acknowledge anatomical differences and attempt to overcome perceived limitations of existing unisex implants.

Total knee replacement (TKR) is a type of surgery used for patients with advanced arthritis or other conditions who have exhausted all other forms of more conservative care. TKR involves replacing part of the femur (thigh bone) and tibia (shin bone) with two metallic implants that will together function as a new knee. Many implants are currently available for TKR, the majority of which are unisex; smaller sizes are usually used in women.

How It Works

The Gender Solutions™ High-Flex Knee (Zimmer, Inc.) femoral implant was developed following extensive clinical experience with Zimmer's NexGen™ unisex TKR implant as well as radiographic research comparing the knees of men and women.[1] Differences were noted in the shape, size, and movement of the femur. Based on these anatomic and biomechanical differences, a TKR femoral implant was designed specifically for women by modifying the unisex NexGen TKR implant.

The main differences between the Gender Solutions TKR implant and the unisex NexGen TKR implant are:

- The Gender Solutions implant is slightly thinner from side to side.
- The rear portion of the Gender Solutions implant is slightly thinner from front to back.
- The shape of the Gender Solutions implant is modified slightly to accommodate a woman's wider pelvis, which affects how the femur moves in relation to the patella (knee cap).

The Gender Solutions implant may improve clinical outcomes following TKR in women and increase patients' satisfaction with their surgery by providing an implant that feels more natural to them. However, there is no published evidence to confirm such improvements.

Who Might Benefit

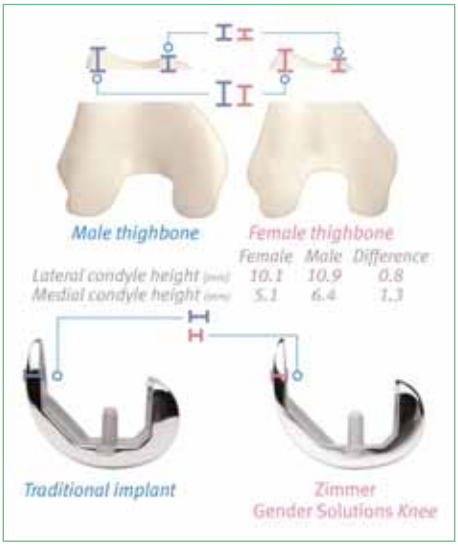
There were about 33,600 knee replacement procedures in Canada in 2004–2005; of these, approximately 60% were in women.[2] The Gender Solutions implant is indicated for all female patients requiring TKR, unless they have anatomical deformities in the knee joint. The implant may also be used in some men if warranted by their anatomy.

Regulatory Status

The Gender Solutions implant was licensed by Health Canada in late 2006 under Zimmer's NexGen licensing. It also received US Food and Drug Administration licensing in 2006. Several other companies have announced plans to market gender-specific TKR implants in the near future.[3]

Evidence

Currently, there are no published trials of the Gender Solutions implant. The evidence to support its claimed superiority over the existing NexGen unisex implant is based on unpublished cadaveric and radiographic studies. Results from recently launched clinical trials of the Gender Solutions knee implant are expected to be available in the next two to five years.



Differences between the Gender Solutions™ High-Flex Knee implant and a traditional implant.

Cost

The Canadian cost for the implant is currently unavailable.

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CorCap™: A Support Device for the Failing Heart

CorCap™ is a supportive device that is sewn around the heart to help normalize its shape and function. It may improve quality of life for some patients with heart failure.

Heart Failure

In heart failure, the heart becomes progressively enlarged and less efficient at pumping blood. Patients become tired and short of breath with everyday activities. Heart failure is common with aging, can be hard to treat, and is a leading cause of hospital admission.[1]

How It Works

The CorCap™ Cardiac Support Device (CSD) is a pliable mesh-like structure that is sutured into place around the heart during open heart surgery.

Who Might Benefit

More than 400,000 Canadians have heart failure, and about 50,000 new cases are diagnosed each year.[1] The prevalence of heart failure is increasing as the population ages and the management of other heart diseases improves. New drugs and technologies have helped, although survival rates have improved little over recent decades.[1] The CorCap device is intended for patients with moderate to severe heart failure that is worsening despite drug therapy.[2]

Regulatory Status

CorCap CSD (Acorn Cardiovascular) is not licensed in Canada and is approved only for investigational use in the US. In 2005, the US Food and Drug Administration did not approve the device due to lack of clear evidence of effectiveness, possible increased surgical risk, and concerns about the difficulty of subsequent heart surgery.[2] According to Acorn Cardiovascular, an additional study has been initiated to assess the device's safety and efficacy in 50 to 75 patients undergoing concomitant mitral valve repair; results are anticipated in 2008. The CorCap CSD is available in Europe.

Evidence

The Acorn CSD study included 300 patients in North America (almost equally men and women; average age of 52 years); 193 of the patients (64%) also required mitral valve surgery. By 2003, all patients had entered the study and half were randomly assigned to receive CorCap. After three years of follow-up, patients with CorCap devices showed statistically significant improvements in some (but not all) aspects of cardiac function, had better quality of life, and needed fewer additional heart operations; however, survival and the rate of repeat hospitalizations were no better.[3–5]

Cost

No device cost information is available. As open heart surgery is required, device insertion would be costly, although the procedure takes less than 30 minutes and in some patients could be done along with other necessary heart surgery.[5] Costs may be offset if further heart procedures are avoided — particularly heart transplantation, which is expensive, has poor outcomes, and is limited by the lack of available organs.[6]

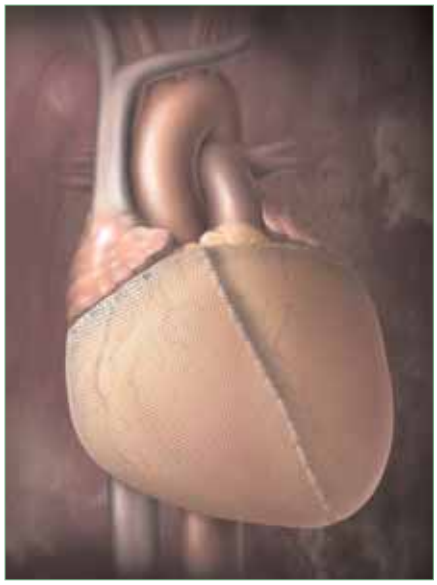

Photo courtesy of Acorn Cardiovascular, Inc.

The CorCap™ Cardiac Support Device

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The Treatment of Cancer Pain from Bone Metastases Using ExAblate® (Magnetic Resonance-Guided Focused Ultrasound)

Pain from bone metastases is often severe and can seriously decrease quality of life.

ExAblate® 2000 is a thermal heating device that delivers high intensity focused ultrasound waves to kill cells at a precise focal point without damaging adjacent healthy tissue. Currently used to treat uterine fibroids, this non-invasive procedure is being investigated for the palliation of painful bone metastases in patients who do not respond to other treatments.

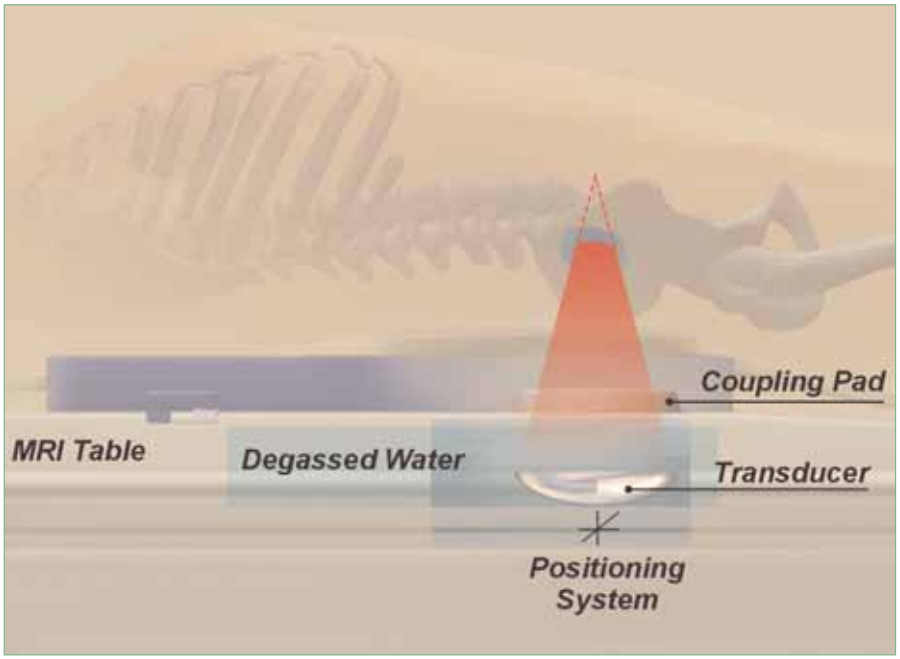

Photo courtesy of InSightec Ltd.

Once the MRI scanner has provided a three-dimensional image of the target, the ExAblate® transducer delivers high intensity focused ultrasound to the site.

How It Works

ExAblate is used in combination with magnetic resonance imaging (MRI) to identify and monitor the precise location of the painful bone lesions. Once the lesion is identified, ExAblate delivers a beam of high intensity focused ultrasound to the target, raising the temperature sufficiently to cause tissue destruction. The precise mechanism of analgesia is unknown, but immediate pain relief may be due to the destruction of nerve tissue, while continued analgesia may result from a decrease in tumour mass and subsequent pressure on the bone.[1]

The treatment takes approximately 80 minutes and is performed in an out-patient clinic.[1] Patients are given intravenous sedation and analgesia to prevent movement during the procedure. Potential complications of ExAblate treatment include superficial skin burns and thermal damage to adjacent heat-sensitive organs.[2]

Who Might Benefit

Bone metastases are common in cancer patients. Almost all patients with metastatic prostate cancer have tumours that have spread to the bone.[3] In breast cancer, bone is the second most common site of metastases, affecting 90% of patients with progressive breast cancer.[1]

Early Evidence

The first feasibility study included 13 patients.[1] Ten patients reported reductions in pain intensity (as measured by a Visual Analog Scale) and medication use during a mean follow-up period of two months. In most cases, pain reduction was noted as early as three days following ExAblate treatment. Some patients reported a small increase in pain in the immediate post-procedural period, but this pain subsided shortly after. One patient was unable to tolerate the ultrasound-induced pain and treatment was stopped. Two patients died (due to disease progression) within the first month after treatment.[1]

A second feasibility study of ExAblate for pain palliation is underway at Toronto's Mount Sinai Hospital.

Future Developments

MRI-guided high intensity focused ultrasound is also being evaluated for its ability to destroy malignant cells in cancers of the breast, bone, liver, kidney, pancreas, uterus, and prostate.[4]

Regulatory Status

The ExAblate 2000 system (InSightec Ltd., Israel) was licensed by Health Canada in 2007 for the treatment of uterine fibroids.

Cost

According to InSightec, the ExAblate 2000 system costs approximately US$1 million. This does not include the cost of the MRI scanner used during the procedure.

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Recent *Issues in Emerging Health Technologies* bulletins from CADTH

These reports are available without cost on the CADTH web site.

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📖 **Capsule colonoscopy: PillCam® Colon**
Available: http://www.cadth.ca/media/pdf/E0034_PillCam-Colon_cetap_e.pdf

📖 **Subcutaneous open-loop insulin delivery for type 1 diabetes: Paradigm® Real-Time System**
Available: http://www.cadth.ca/media/pdf/E0045_Type-1-Diabetes-Paradigm-Real-Time-System_cetap_e.pdf

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Available: http://www.cadth.ca/media/pdf/E0032_pharmacogenomics-warfarin-therapy_cetap_e.pdf

📖 **Yttrium-90 microspheres (TheraSphere® and SIR-Spheres®) for the treatment of unresectable hepatocellular carcinoma**
Available: http://www.cadth.ca/media/pdf/E0038_TheraSphere_cetap_e.pdf

Private PET Scan Clinics in Canada

Clinic Name	Location	Type of Scanner	Cost per Scan
Ville Marie PET/CT Centre	Montreal	PET/CT	$2,500
Clinique Radiologique de la Capitale	Quebec City	PET/CT	$2,500
Care Imaging LP	Mississauga	PET	$2,358
The Vancouver PETSCAN Centre (scheduled to close in Dec. 2007)	Vancouver	PET	$2,850 (with reduced rates if additional scans are required)
Premier Diagnostic Health Services (will begin operations in BC in early 2008)	Richmond	PET/CT	$2,850 (anticipated price, with reduced rates if additional scans are required)

Canadian Agency for Drugs and Technologies in Health

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600–865 Carling Ave.
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Tel.: (613) 226–2553
Fax: (613) 226–5392
Web site: www.cadth.ca

Editor/Writer: Catherine Allison
Contributing Writers: Simon Dagenais, Vicki Foerster, Andra Morrison, James Murtagh
Information Specialist: Andra Morrison
Copy Editor: Barbara Greenwood Dufour
Layout and Design: Nathalie Charron, Matt Kulka
Web Designer: Martha Oram

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