

## Positron Emission Tomography (PET)

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### A New Era in Cancer Imaging in Nova Scotia

**June 2008 marked the beginning of a new era in cancer imaging in Nova Scotia, with the opening of the QEII Positron Emission Tomography (PET) Centre. Since that time more than 2,500 cancer patients have been assessed with this novel imaging modality. These assessments have provided a more accurate and confident evaluation of disease status, and have resulted in changes in cancer management for a significant number of patients.**

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### What is PET?

PET imaging is predicated on the injection of a radioactive tracer, a “radiopharmaceutical”, into patients, with the subsequent imaging of the distribution of the radiopharmaceutical throughout the body, including within active malignancy. This approach to imaging, known as *molecular imaging*, differs from more familiar modalities such as computed tomography (CT) scanning, which are considered *anatomic imaging*. This approach is not specific to PET, and indeed is the premise of Nuclear Medicine, which has played an important role in medical imaging for decades. However, PET utilizes unique radiopharmaceuticals, and offers technological advantages with respect to imaging quality, which have established it as the state-of-the-art in cancer imaging.

PET radiopharmaceuticals are composed of two components, a radioisotope and a pharmaceutical. The pharmaceutical governs the distribution of the radiopharmaceutical throughout the body, including uptake into cancer cells. The decay of the radioisotope results in emission of a positron (a positively-charged electron) and ultimately gamma rays which are detected by the PET scanner, delineating the distribution of the radiopharmaceutical throughout the body. Currently the vast majority of PET scans, including all scans at the QEII, use the radiopharmaceutical 2-deoxy-2-[<sup>18</sup>F]fluoro-D-glucose (<sup>18</sup>F-FDG), a glucose analog labelled with radioactive <sup>18</sup>F, which has a half-life of 109 minutes. <sup>18</sup>F-FDG is incorporated to a high degree into neoplasms, because of increased metabolic activity and alterations in enzymatic activity.

State-of-the-art PET scanners, such as that at the QEII, incorporate a CT scanner into the PET unit, resulting in “hybrid imaging” of both molecular (PET) and anatomic (CT) parameters, synergistically enhancing evaluation of tumours. The CT performed as part of a PET-CT is however a low-dose CT, with the result that patients receive less radiation from a PET-CT than from a dedicated CT scan of the comparable portion of the body.

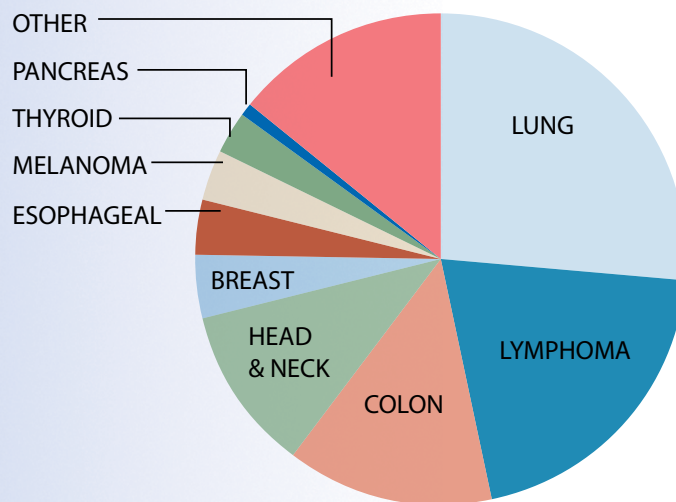
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## Nova Scotia Experience

There are currently nine cancers approved for funding in Nova Scotia, including lung, colorectal, gastro-esophageal, breast, head and neck, thyroid, and pancreatic cancers, and, lymphoma and melanoma. However, many other cancers can benefit from evaluation with PET. In Nova Scotia these are approved on an individual case basis. PET scanning has also proven valuable in evaluation of cardiac disease, neurologic disorders, and inflammatory diseases, but these applications are not currently publicly funded in Nova Scotia. A summary of the indications for the 2,440 scans performed as of 23 August 2010 is provided below. The “Other” category includes a wide variety of other malignancies. In addition to adult Nova Scotians, the studies have included pediatric patients from the IWK Health Centre, as well as patients from Newfoundland, PEI, and New Brunswick.

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*The distribution of PET scans performed in Nova Scotia, June 2008-August 2010*



As the half life of  $^{18}\text{F}$ -FDG is just 109 minutes, it must be produced and delivered daily. For the first two years of operation it was flown in from Montreal each morning. However, a medical cyclotron and radiopharmaceutical production facility has been installed at the QEII, the only such facility east of Quebec. As of July 2010 we have been using our locally-produced  $^{18}\text{F}$ -FDG in clinical practice.

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*The QEII PET-CT Scanner at the VG Site*



## Impact of PET in the management of cancer

### Cancer Diagnosis

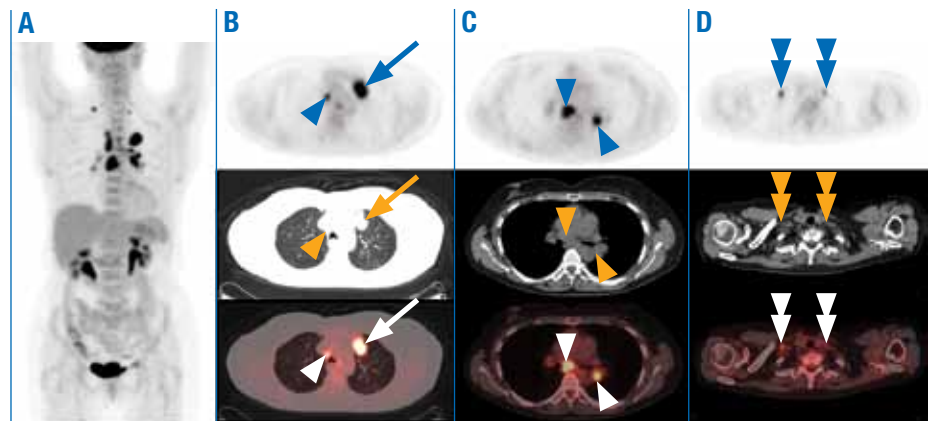
PET is used to evaluate cancer status at several time points in the course of the disease. There is a limited but very useful role of PET before cancer is diagnosed, mainly in the evaluation of the solitary pulmonary nodule (SPN). This is a common finding on CT, and a PET scan may be requested to help establish the likelihood of malignancy. Increased uptake on PET is very suggestive of malignancy, and further work-up is indicated, while absence of uptake is highly suggestive of a benign etiology. The spatial resolution of PET limits its utility to evaluation of nodules at least 8-10mm in size. PET is also very useful in the evaluation of the unknown primary malignancy when conventional evaluation has failed to locate the primary: the  $^{18}\text{F}$ -FDG-avidity of many tumour types, combined with the (near) whole body extent of the PET scan, renders PET very useful in this scenario.

### Cancer Staging

A more common application of PET is in the initial staging of a wide variety of malignancies. In comparison with anatomic imaging such as CT, PET offers much greater tumour-to-background contrast, and can identify the presence of a tumour in lesions not called on CT, or absence of tumour in lesions which were suspicious on CT. Changes in stage are more commonly in the direction of upstaging, with PET identifying previously unsuspected sites of disease, although occasionally PET downstages patients. In both scenarios more appropriate patient management can be instituted.

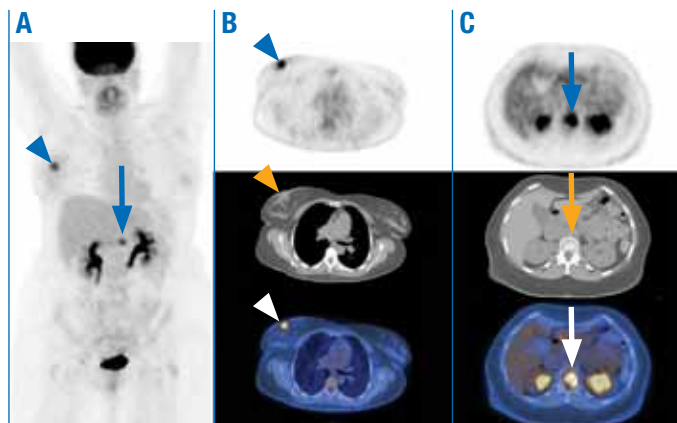
### PET Scan in Staging: Lung Cancer

A patient with a newly-discovered left lung cancer underwent traditional staging with CT, which revealed abnormal lymph nodes in the left side of the thorax only. However, a PET-CT scan was obtained, which revealed a different story. **(A)** 3D image from the PET scan demonstrates abnormal intense uptake in both sides of the thorax, as well as the supraclavicular space bilaterally. Other areas of uptake, including base of brain, kidneys, bladder, and bowel are physiologic. Axial images through the upper thorax **(B)**, mid thorax **(C)**, and supraclavicular level **(D)** (top image: PET, middle image: CT at same level, bottom image: fused PET-CT) confirms intense uptake in the primary lung malignancy (arrows), as well as within bilateral mediastinal nodes (arrowheads) and small supraclavicular nodes (double arrowheads).



### PET Scan in Staging: Breast Cancer

A patient with right breast cancer was staged as local disease only by conventional techniques, with no loco-regional or distal metastases. A PET-CT was obtained, revealing intense uptake in the breast lesion (arrowhead), but also in a structure (arrow) projecting between the kidneys on the 3D PET Image **(A)**. Axial slices through the level of the breast **(B)** confirm intense uptake in the primary breast cancer (arrowhead). Slices at the level of the kidneys **(C)** reveal intense uptake throughout much of the T12 vertebral body (arrows), extending into the pedicle on the left, in keeping with a solitary osseous metastasis. This correctly identifies the patient as Stage 4, and the intent of her therapy is changed from curative to palliative, with the addition of systemic therapy. Even in retrospect there were no convincing anatomic changes at T12 on the CT scan.



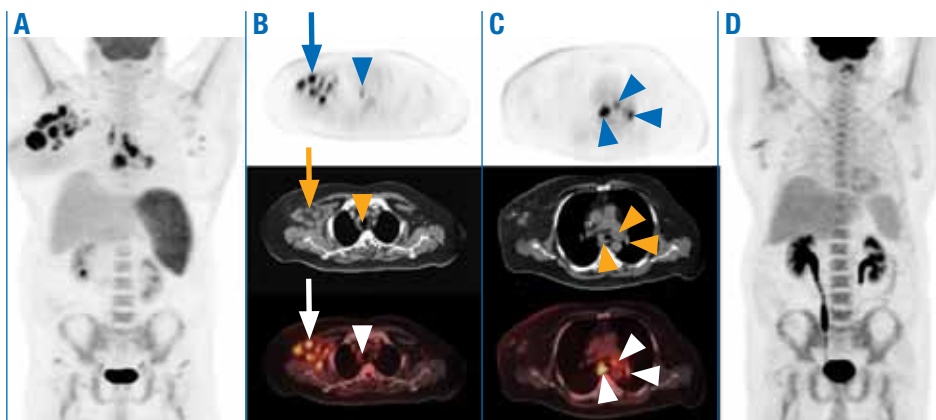
### ***Assessing Response to Therapy***

PET is also widely used in assessment of tumour response to therapy, most commonly at the end of therapy, but occasionally mid-way through. Reduction in tumour size on CT does not necessarily mean the tumour has been entirely irradiated, while conversely a residual mass on CT does not necessarily indicate residual viable tumour. In many applications molecular imaging with PET is more accurate in determining true tumour status. Because recent chemotherapy and radiation therapy can alter  $^{18}\text{F}$ -FDG uptake, PET scans must be appropriately timed post-therapy. While recommendations vary with cancer type, typically 2-3 weeks are recommended post chemotherapy and 6-8 weeks post radiation therapy. When a mid-therapy assessment is required and the interval between cycles is shorter than these recommendations, scans should be performed as close as possible to the next chemotherapy cycle.

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#### *PET Scan to Assess Cancer Therapy: Lymphoma*

A patient with lymphoma underwent a PET-CT scan for staging purposes (**A-C**). The 3D PET image (**A**) demonstrated intense abnormal uptake within multiple bilateral axillary lymph nodes (right much greater than left) and numerous mediastinal nodes, as well as milder, but still pathologic, uptake within neck, retroperitoneal, and inguinal lymph nodes. The spleen is also seen to be enlarged, with diffuse increased uptake throughout it, in keeping with splenic lymphomatous involvement. Axial slices through the upper thorax (**B**) and mid thorax (**C**) confirm uptake within numerous right axillary nodes (arrows) as well as mediastinal nodes (arrowheads). Follow-up PET-CT after chemotherapy (**D**) reveals complete normalization of the nodal and splenic uptake, indicating successful therapy, and a low likelihood of recurrence. (Mild linear uptake in the right axilla is due to inflammation associated with drainage of a seroma.)



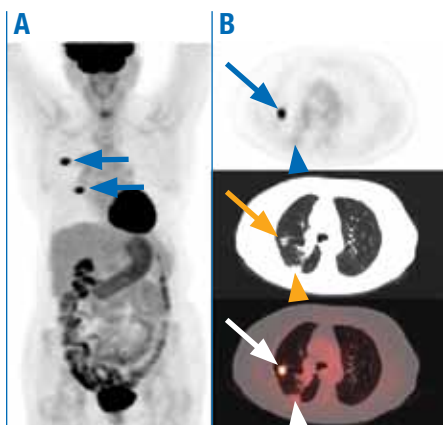
## Impact of PET in the management of cancer (continued)

### Longer Term Follow-up

PET may be used in the longer term assessment of cancer, for example in determining whether a tumour has recurred when conventional imaging is equivocal.

### *PET Scan to Assess for Cancer Recurrence: Lung Cancer*

A patient with previous lung cancer was suspected of having recurrence based on CT. A PET-CT was obtained to confirm the recurrence, and to establish its extent. 3D image from the PET scan (**A**) reveals 2 small foci of intense uptake in the right lung (arrows), in keeping with cancer recurrence. There are no findings suspicious for malignancy beyond the thorax: intense uptake in the heart and right colon are normal variants, while diffuse uptake throughout the stomach is typical of gastritis. Axial slices (**B**) at the level of the upper lesion confirm the intense uptake is in a small lung nodule (arrow). The second focus of uptake was in a similar nodule, not shown. Note that there is an additional abnormality on CT at this level (arrowhead). However, there is just minimal uptake within it on PET, establishing this as a benign entity (likely atelectasis).



## Where does PET fit relative to conventional imaging modalities in cancer management?

It is clear that PET is an important tool in the investigation of cancer. Needless to say other imaging modalities continue to play a critical role in oncology, and the question is “where does PET fit?” A full discussion of which imaging modalities are indicated in all scenarios is clearly beyond the scope of this article. However, a few illustrative examples are provided.

First of all, it has been established that PET is not indicated in the setting of screening for cancer, as the yield is relatively low. As an example, the superior spatial resolution of mammography, along with its lower cost, confirm it as the imaging modality of choice in breast cancer screening.

The workhorse of cancer imaging is, and will continue to be, CT. CT provides excellent in-vivo assessment of anatomy and structural changes. It is less expensive than PET, and is widely available throughout the province. However, as discussed earlier, PET provides superior tumour-to-background contrast in many cancers, and as such may find cancer within structures considered normal on CT, and better characterizes whether there is residual viable tumour following therapy in many scenarios. Many cancer site teams at the QEII have incorporated PET into their routine evaluation of cancer in defined situations. Of course, as with any test, a PET should only be ordered if there is a reasonable likelihood that the outcome will change management. For example, patients at very low risk for metastases, and conversely those who clearly have wide-spread metastatic disease on conventional imaging, may not benefit from PET scanning.

MRI and Ultrasound are widely used diagnostic imaging modalities, but each has only limited utility in oncology. Uses of ultrasound in oncology include evaluation of the female pelvic organs, and in trouble-shooting situations such as establishing whether a lesion identified on CT is a simple cyst, but really ultrasound does not routinely compete with PET. MRI is primarily of benefit in malignancies of the central nervous system, and is superior to PET in this regard. The high physiologic glucose utilization by the brain results in high  $^{18}\text{F}$ -FDG uptake, potentially masking pathologic uptake in brain lesions. Indeed, you will note from the previous examples that the majority of the brain is not even included on the routine PET scan. MRI is also used in oncology in musculoskeletal tumours and occasionally in abdominal malignancies: the relative advantage of PET versus MRI in these scenarios is under development.

Finally, other Nuclear Medicine modalities, such as the bone scan, are widely used in oncology. Again the details of when PET is indicated versus conventional imaging is beyond the scope of this article; clearly, if the primary intent is to rule out osseous metastases only, a bone scan is likely appropriate. A few cancers, such as most thyroid and neuroendocrine tumours, are better imaged with traditional nuclear medicine techniques (radioiodine, radiolabelled Octreotide or MIBG) than with PET.

*Cancer Care Nova Scotia* is a program of the Department of Health. Its mandate is to evaluate, coordinate and strengthen the cancer system in Nova Scotia.

*Cancer Care Nova Scotia* works with and supports professionals and stakeholders in the health care system to bring about patient-centred change. Its ultimate goal is to reduce the burden of cancer on individuals, families, communities and the health care system.

*In Practice* is a supplement to *Cancer Care Nova Scotia's* newsletter. It is written specifically for primary care practitioners with information that we hope will make a difference in your cancer practice.

Please contact Christine Smith, Communications Manager, *Cancer Care Nova Scotia*, by phone at 902-473-2932 or by email at [christine.smith@ccns.nshealth.ca](mailto:christine.smith@ccns.nshealth.ca) with comments or suggestions for future topics.



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## Where does PET fit relative to conventional imaging modalities in cancer management? *(continued)*

There has been much discussion in the medical and lay press in the past couple of years about the medical isotope shortage, and the question arises as to the implications of the new medical cyclotron at the QEII. In short, the production of PET radioisotopes, such as  $^{18}\text{F}$ , is different than the production of traditional Nuclear Medicine radioisotopes, such as  $^{99\text{m}}\text{Tc}$  Technetium which is used in bone scanning and many other Nuclear Medicine procedures.  $^{18}\text{F}$  can be produced in a small medical cyclotron, such as the one recently installed at the QEII, whereas conventional Nuclear Medicine isotopes such as  $^{99\text{m}}\text{Tc}$  are produced in large specialized reactors, such as that at Chalk River, Ontario. Thus, PET cyclotrons do not solve our medical radioisotope shortage. However, there is a trend toward converting some traditional Nuclear Medicine studies to PET-based studies, and in the future our cyclotron may somewhat mitigate the effects of the isotope shortage.

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## What is the process of ordering a PET scan, and what should your patient expect?

PET scans are ordered by oncologists or other specialists dealing with oncology. Patients are contacted by PET Centre staff in advance of their scan to ensure they are appropriately prepared for the study. Because  $^{18}\text{F}$ -FDG is a glucose analog, blood glucose levels must be controlled to maximize tumour uptake. As such, patients may be instructed to be NPO or have a light breakfast, depending on the time of their appointment. Diabetic patients will typically be booked early in the day, with food and medication preparation being similar to that for surgery.

Following injection of the radiopharmaceutical, patients sit quietly for 45 minutes to allow distribution of the tracer. They then enter the scanner, which is similar to a CT scanner, and undergo imaging which takes about 30 minutes. The CT component of the PET-CT is currently performed without intravenous contrast, so there are no issues with respect to renal insufficiency or contrast reactions. As  $^{18}\text{F}$ -FDG is a glucose analog administered in minute quantities, patients do not experience any reaction to the radiopharmaceutical. Claustrophobia is rare, and indeed is much less than in MRI scanners. PET-CT scans are performed by Nuclear Medicine technologists, and are interpreted by Nuclear Medicine physicians.

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## Conclusions

PET imaging has recently been introduced in Nova Scotia, and has played an important role in the management of cancer patients. PET is useful in a wide range of cancers, and at several time points in the disease, including diagnosis (eg the SPN), staging, therapy monitoring, and subsequent follow-up. However, it is not indicated in all cancer scenarios. For further information, contact Dr. Steven Burrell at [sburrell@dal.ca](mailto:sburrell@dal.ca) or 902-473-6161, or Dr. Andrew Ross, PET Director, at [aross@dal.ca](mailto:aross@dal.ca) or 902-473-2825.

For information on patient preparation for a PET scan, contact the PET Department staff at 902-473-5936. Further information on PET Scanning can be found in the guidelines of the Society of Nuclear Medicine ([http://interactive.snm.org/docs/jnm30551\\_online.pdf](http://interactive.snm.org/docs/jnm30551_online.pdf)).