Update on PET Imaging in Breast Cancer

Surgical Oncology Network
Breast Cancer Conference

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Don Wilson, BSc, MD, FRCPC (Nuc Med), FRCPC (Rad Onc)
Medical Director, BCCA Centre of Excellence for
Functional Cancer Imaging

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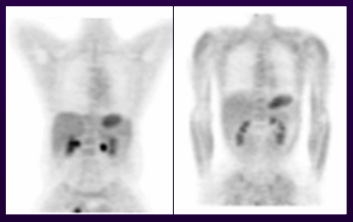
Why PET?

- Isotopes of naturally occurring elements
- High sensitivity
- Accurate quantification
- Whole body scan capability
- High clinical sensitivity & specificity



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Advantages of PET over Anatomical Imaging

- Functional change often precedes anatomical change
- Benign vs malignant
- Post-treatment change vs recurrence
- Ideally suited for pre-clinical and clinical imaging of cancer biology

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Potential Role for PET

- Characterization of breast lesions
- Axillary lymph node staging
- *Restaging/detection of recurrent disease
- *Evaluation of response to treatment

**Medicare approved for reimbursement in USA*

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Normal Variants and Biologic Correlates

- ^{18}F-FDG uptake in breast cancer correlates with:
  - Microvasculature
  - Glucose transporter expression
  - Tumor volume
  - Proliferation rate
- FDG localization higher in:
  - Ductal vs lobular carcinoma
  - Grade 3 vs grade 1-2 carcinomas

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Normal Variants and Biologic Correlates

- Increased FDG uptake may be seen in:
  - Dense breasts/young patients
  - Lactating breasts
  - Mastitis
  - Recent incisions/hematomas
  - Some fibroadenomas
  - Muscle and brown fat

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Characterization of Primary Breast Cancer

- No role in detection/diagnosis of non-invasive breast cancer
- Invasive disease sensitivity 83 – 93%
- Results of FDG-PET vary as a result of the heterogeneity of breast cancers
  - False negatives: <1cm, well differentiated (tubular, lobular histologies)

Samson et al., Acad Radiol 2002; 9: 773-83.

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Characterization of Primary Breast Cancer

Size	Patients	Sensitivity
In situ	12	42%
< 2 cm	44	68%
2 – 5 cm	62	92%
>5 cm	14	100%
Invas. Ductal	97	76%
Invas. Lobular	23	35%

Avril. J Clin Onc. 2000; 18: 3495-3502.

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Characterization of Primary Breast Cancer

- Recent metaanalysis* showed a NPV of 88% (diagnosis missed in 12%)
- FDG-PET not suitable for breast cancer screening
- Development of dedicated PET instrumentation may increase role of PET in diagnosis of breast cancer

**Samson et al., Acad Radiol 2002; 9: 773-83.*

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Initial Staging of the Axilla

Effectiveness for occult axillary disease

Centers for Medicare and Medicaid services (CMS)

- Metaanalysis 203 pts (4 studies) 2002
  - confirmed breast cancer
  - no palpable axillary nodes
  - no distant mets
  - PET before node dissection

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Initial Staging of the Axilla

- Pooled sensitivity 81% (40-93%)
- Specificity 95% (87-100%)

Conclusions:

False negative rate for PET too high (19%)

- Axillary node sampling should remain the standard of care.

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Initial Staging of the Axilla

Wahl. J Clinical Onc. 2004; 22: 277-285

Prospective, multicenter trial 360 pts with newly diagnosed invasive breast cancer

- Mean sensitivity 61% (54-67%)
- Mean specificity 80% (79-81%)
- Nodal SUV >1.8 PPV 90% but sensitivity of 32%

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Initial Staging of the Axilla

Wahl. J Clinical Onc 2004; 22: 277-285

Conclusion:

- FDG-PET often fails to detect axillae with few and small nodal mets.
- Not routinely recommended for axillary staging in newly diagnosed breast cancer pts

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Internal Mammary/Mediastinal Lymph Node Metastases

Eubank et al., J Clin Onc 2001; 19: 3519 – 3523

73 consecutive pts with recurrent or metastatic dx

	CT	PET
Sensitivity	54%	85%
Specificity	85%	90%
Accuracy	73%	88%

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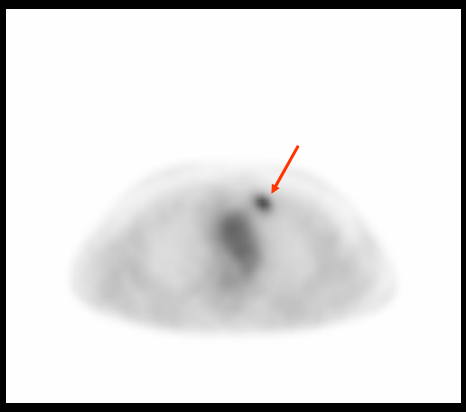
Left breast cancer with internal mammary lymph node metastasis



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Delineating Recurrent and Metastatic Disease

Hubner et al., Clin Posit Imag. 2000; 3: 197-205

	CT	PET
Sensitivity	71%	85%
Specificity	54%	73%

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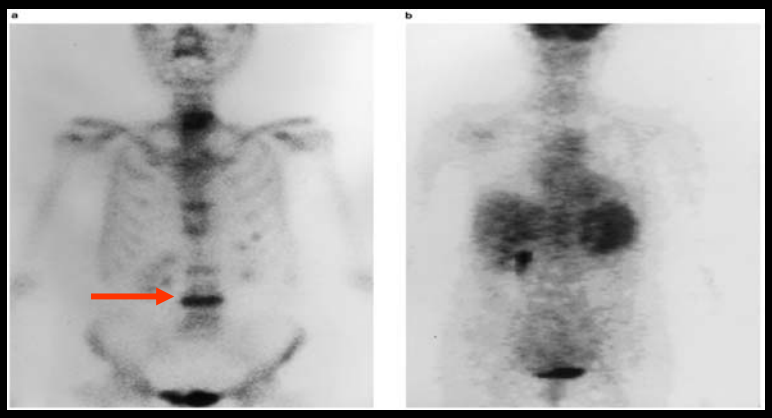

Bone scan FDG-PET

76 yo woman. Tc-99 MDP bone scan shows increased uptake in lumbar spine due to degenerative change (false positive) whereas FDG-PET is normal (true neg finding).

Ohta, Nuc Med Commun 2001; 22(8): 875-879

Delineating Recurrent and Metastatic Disease

Moon et al., J Nuc Med., 1998; 39: 431-435

- 57 pts suspected disease recurrence
- Sensitivity 93%
- Specificity 79%

- Nonosseous mets only – Sensitivity 96%

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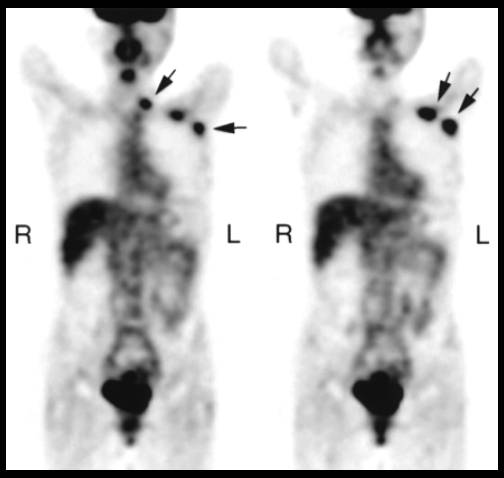

Recurrent Breast cancer involving left axillary and supraclavicular lymph nodes. MRI interpreted as post-radiotherapy fibrosis

UCLA School of Medicine

Delineating Recurrent and Metastatic Disease

Limitations of PET:

- Lower sensitivity than bone scan for osseous mets
  - PET better than bone scan for osteolytic lesions
- Not sensitive for detecting brain mets
- Resolution

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Delineating Recurrent and Metastatic Disease

Vranjesevic et al., J Nuc Med., 2002, 43; 325-329

Prediction of Outcome by PET

61 women — Reason of PET Evaluation:
- 69% evaluation for residual/recurrent dx
- 16% evaluation of increasing tumor markers
- 15% suspicious findings on CT

PET done within 3 mos of CI and correlated with clinical outcome

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Delineating Recurrent and Metastatic Disease

Vranjesevic et al., J Nuc Med., 2002, 43; 325-329

	CI*	PET
Sensitivity	79%	93%
Specificity	68%	84%
NPV	59%	80%

*Conventional imaging (X-ray, bone scan, CT, MRI, US)

PET significantly better in predicting DFS

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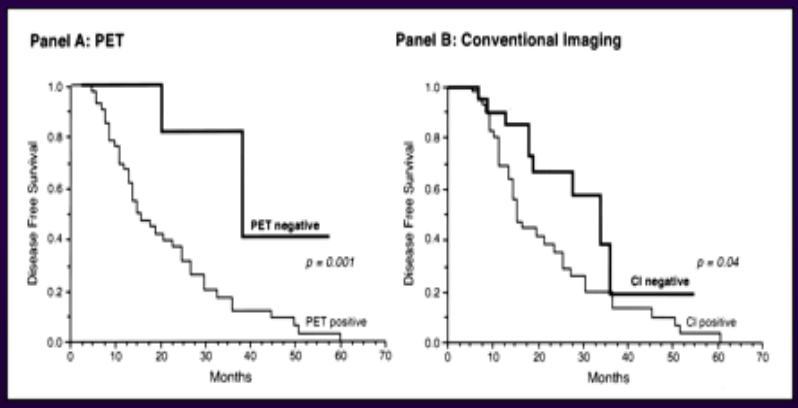
Delineating Recurrent and Metastatic Disease

Vranjesevic et al., J Nuc Med., 2002, 43; 325-329



Kaplan-Meier estimates of disease free survival

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Delineating Recurrent and Metastatic Disease

Impact on Patient Management

Yap et al., J Nuc Med, 2001; 42: 1334-1337

- Prospective survey 160 breast cancer patients
- PET changed the clinical stage in 36%
  - 28% upstaged
  - 8% downstaged
- Resulted in:
  - intermodality changes in 28%
  - intramodality changes in 30%

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Evaluating Treatment Response

- Earlier recognition of ineffective therapy
  - allow change to an alternative, more effective regimen
  - avoid morbidity and costs
- Potential roles:
  - neoadjuvant (locally advanced)
  - distant metastatic disease

Metabolic change precedes anatomic change

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Evaluating Treatment Response

- Rapid decrease in glucose metabolism in responders can be detected as early as after the first cycle of CTX
- Serial measurements of SUV

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Financial Considerations

FDG-PET is expensive

- PET scanner ~2–5 million $CAD
- Cost per scan ~$2000
- FDG-PET can be cost-effective
  - Demonstrated in lung, colon, melanoma etc
  - PET potentially reduces ineffective/unnecessary treatment and morbidity

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Conclusions

- Role of FDG-PET in characterizing breast cancers remains to be defined.
- PET cannot detect micrometastases and should not replace surgical staging of axillary nodes.
- PET is not indicated in the routine assessment of primary breast cancer.

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Conclusions

- PET can detect metastatic disease missed by CI and may be considered when staging or restaging patients with known or suspected distant mets.
  - CI is equivocal or confusing
    - eg. liver lesions, brachial plexopathy, equivocal bone scan
  - Restaging prior to aggressive local therapy
  - Rising tumor markers

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Conclusions

- PET may be useful for early therapy evaluation in pts with locally advanced and/or metastatic disease.

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Future Prospects

- New technologies will increase the role of PET in breast cancer:
  - Higher resolution scanners
  - PET/CT
  - PET/stereotactic mammography units
  - Gamma probes for PET isotopes

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Molecular Imaging with PET in Breast Cancer

	PET Tracer
Glucose metabolism	^{18}F-FDG
Cell proliferation	^{18}F-thymidine
Hypoxia	^{18}F-FMISO
Protein synthesis	^{11}C-methionine
Receptors	^{18}F-estradiol, HER2/*neu* minibody
Gene expression	^{18}F-antisense oligonucleotides

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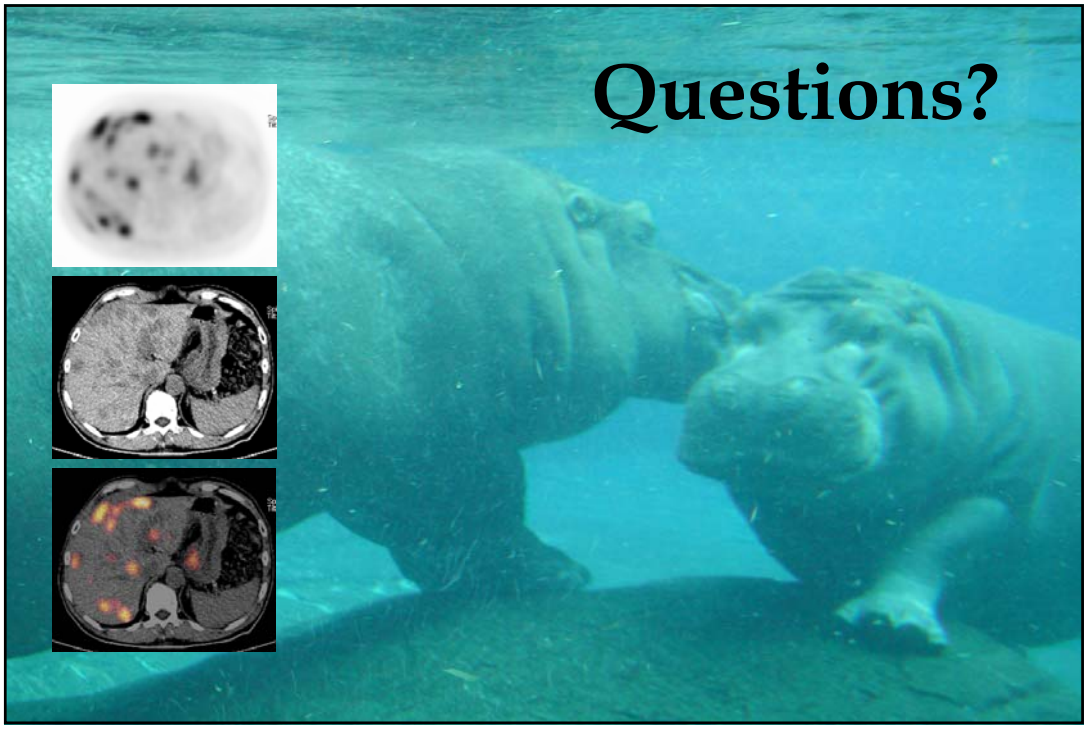
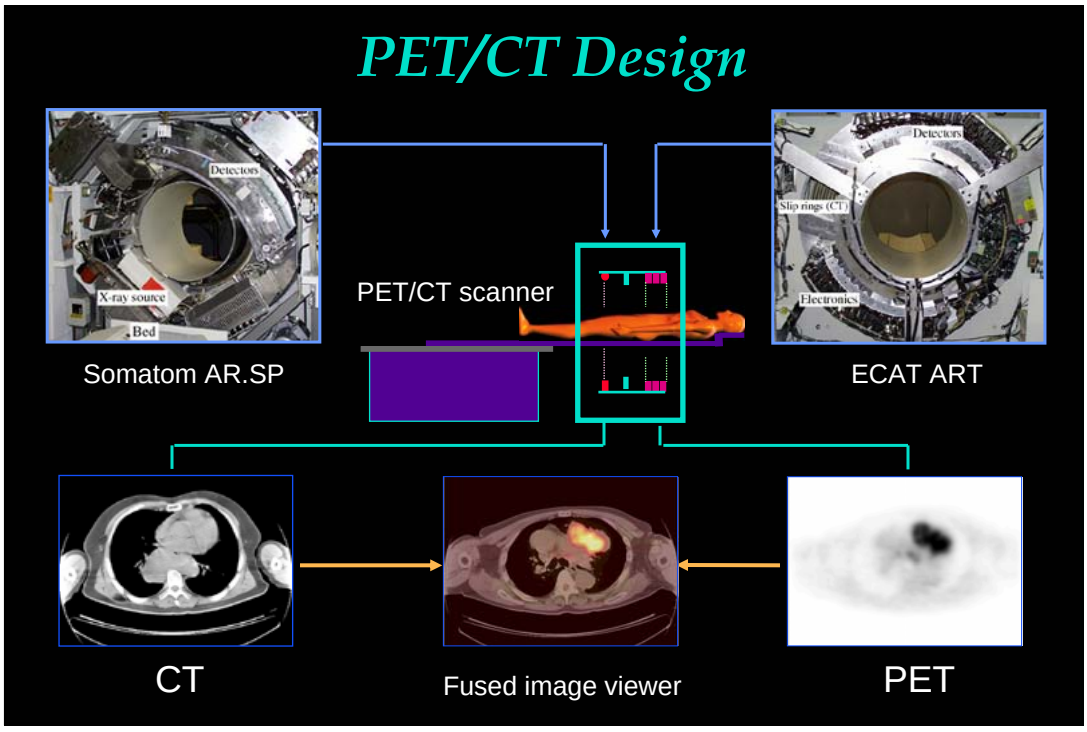
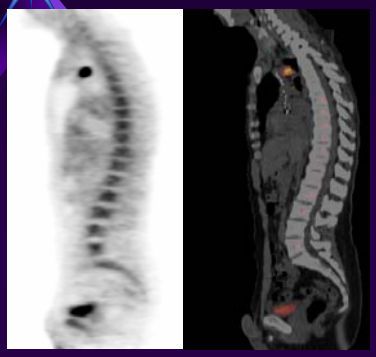
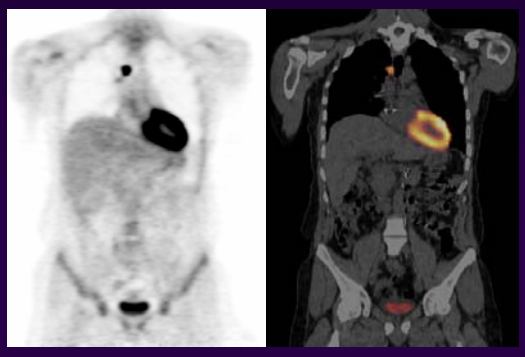

Questions?


PET/CT Design
Detectors
X-ray source
Bed
Somatom AR.SP
PET/CT scanner
Detectors
Slip rings (CT)
Electronics
ECAT ART
CT
Fused image viewer
PET

PET/CT scanners:

University of Pittsburgh





Renal Cancer

46 year old male with renal cancer, status post nephrectomy and chemotherapy. biograph identified mediastinal lymph node metastasis.

Scan protocol: CT 100 mAs, 130 kV, pitch 1.5, 5 mm slice width
PET 555 MBq FDG, 180 min p.i., 5 min/bed, 6 beds, 30 min scan time

Data Courtesy of Indiana University PET Imaging Center

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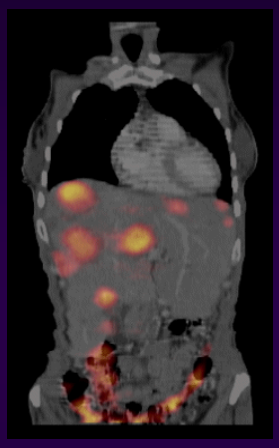

Hepatocellular Cancer

42 year old female referred with stomach pain. Ultrasound showed multiple liver lesions. PET/CT to evaluate partial liver resection and partial living donor transplantation. biograph identified no distant metastases; liver tumor penetration of diaphragm. Transplantation cancelled.

Scan protocol: CT 125 mAs, 130 kV, pitch 1.5, 5 mm slice width
PET 388 MBq FDG, 60 min p.i., 5 min/bed, 6 beds

Data Courtesy of University Hospital Essen

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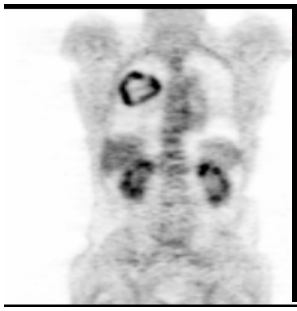

Lung Cancer
Case: 63 year old male with a mass in the right lung.
biograph LSO identified peripheral lesion activity.
Scan protocol: CT i.v. and oral contrast, 100 mAs, 130 kVp, 5 mm slices
PET 500 MBq FDG, 60 min p.i, 2 min/bed, 6 beds, 12 min scan time

Data Courtesy of Hong Kong Baptist Hospital

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Commercial PET/CT Scanners

Siemens/CTI

Phillips/ADAC

GE Medical Systems

Monitoring Response to Treatment

In NSCLC, a single, early post-treatment PET scan is a better predictor of response than:

- CT response
- stage
- pre-treatment performance status

Mac Manus: J Clin Oncol, Volume 21(7).April 1, 2003.1285-1292

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Limitations of FDG-PET

- Resolution
- Sensitivity may be less for low grade tumors
- Patient may move during scan
- Brown fat, sarcoidosis, benign inflammation – false positives

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Breast Cancer

	Patient Studies	Sensitivity PET	Sensitivity CT	Specificity PET	Specificity CT	Accuracy PET	Accuracy CT
Diagnosis	318	91		93		95	
Staging	2034	91	63	88	96	90	0
Dx/Staging	65	75		83		83	
Recurrence	977	80	90	85	96	82	89
Monitoring Response	269	81		96		92	

A tabulated Summary of the FDG PET Literature. J of Nucl Med. 2001 May; 42 (5 Suppl)

Trends in FDG-PET Oncology

- Identify functional change
- Diagnose disease
- Stage disease
- Plan patient specific treatment
- Monitor disease response

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Why PET?

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- High sensitivity
- Accurate quantification
- Whole body scan capability
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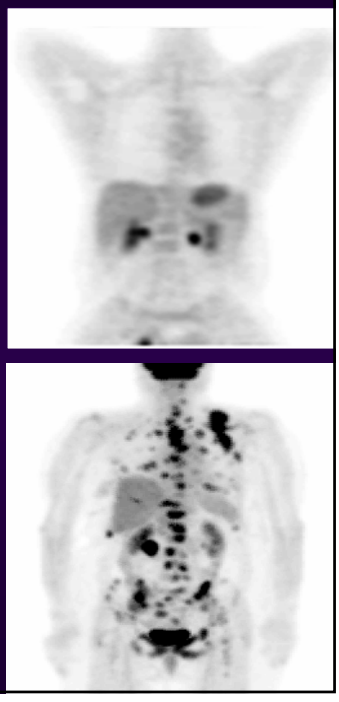

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The Role of FDG-PET in Breast Cancer

- Indications for FDG-PET Imaging
  - Staging after tissue diagnosis if suspicion of distant metastases is high
  - Restaging after treatment or recurrence
  - Evaluation of response to therapy

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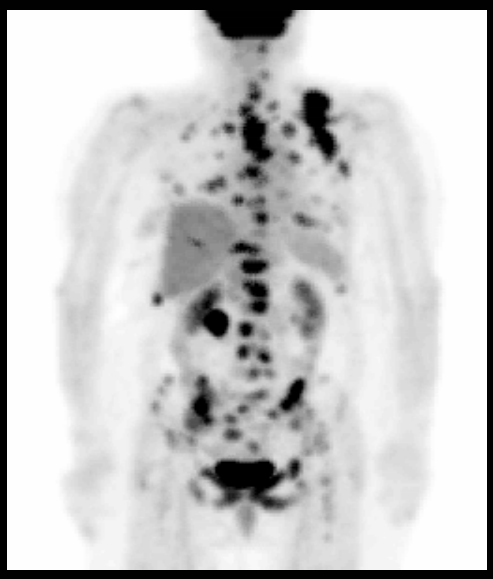
- 68 yo patient with breast cancer and chest wall pain



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Limitations of Conventional Imaging in Oncology

- Functional change often precedes anatomical change
  - Diagnosis and staging
  - Residual mass
  - Anatomical regression takes time
- Treatment related new findings

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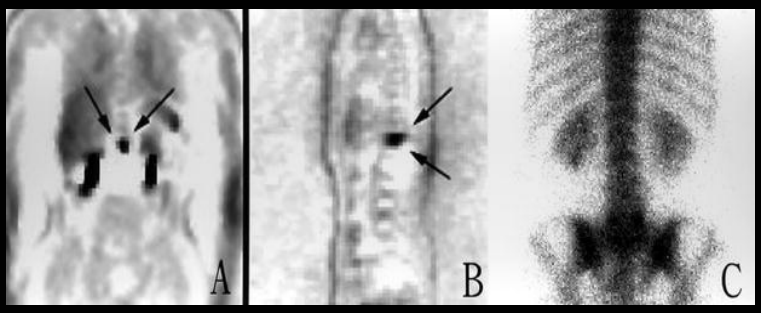

50 yo woman. FDG-PET (A,B) shows met in spine which is not seen in Tc-99m MDP bone scan (C) (false neg).

Yang, J Cancer Res Clin Onc 2002; 128(6): 325-328

Internal Mammary/Mediastinal Lymph Node Metastases

Multicentre Study to Assess the Positive Predictive Value of PET in the Preoperative Evaluation on Internal Mammary Lymph Nodes in Breast Cancer Subjects

Status: ongoing

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Anatomical versus Functional Imaging