

Positron Emission Tomography Clinical Applications

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CANCER CENTER
Making Cancer History™



Major research advances in cancer treatment, prevention, and screening

- 1.4 million Americans will be diagnosed
- 570,000 will die of the disease
- Survival rates for cancer are increasing from 50% to 64% over the last 30 years
- New chemotherapy regimens
- Targeted Therapies
- Prevention

J Clin Oncol. 2006 Jan 1;24(1):190-205.

WHO Tobacco Free Initiative

- Tobacco is the second major cause of death in the world.
- 5 million deaths each year
- If current smoking patterns continue, it will cause 10 million deaths/year by 2020.
- Half the people that smoke today –
- 650 million people- will eventually be killed by tobacco.

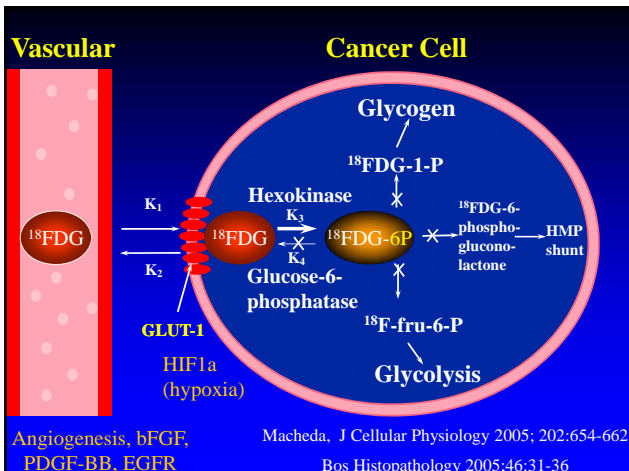
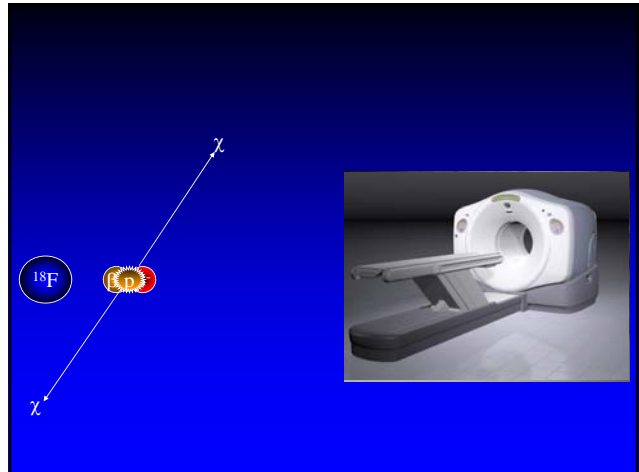
http://www.who.int/tobacco/health_priority/en/index.html

Role of FDG PET in Oncology Synergy of Anatomy & Function

- FDG PET - excellent tumor detection
 - distinguish benign from malignant
 - identify nodal and distant metastases
- CT - excellent resolution
 - T stage and localization
- PET AND CT Improve accuracy of staging
 - extent of disease

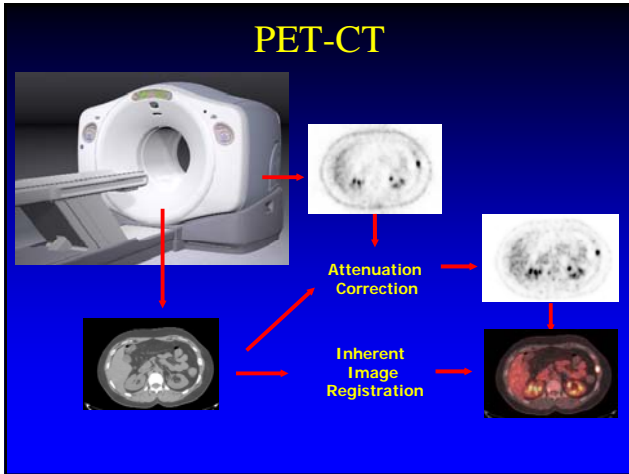
Positron Emitters (Cyclotron)

- F-18 (108 min)
 - FDG (glycolysis/ cardiac viability), ion (bone)
- C-11 (20 Min)
 - methionine (amino acid metabolism)
- N-13 (10 min)
 - ammonia (myocardial perfusion)
- O-15 (2 min)
 - water (cerebral perfusion)
- Cu, Zn, K, Br, I, P, Fe, Ga



FDG PET Patient Preparation

- Fasting - 6 hours/overnight (“south beach prep”)
 - Encourage water intake
 - Last meal – high protein low carbohydrate
 - Medications - o.k.
- Head Neck, Breast Ca, Thyroid Ca
 - Xanax 0.5 mg p.o. 5-10 min pre-inj
- Diabetic patients
 - Well controlled



- ### PET/CT Scanning Technique
- FDG 15-20 mCi IV bolus
 - 60-90 minute uptake phase
 - Arms up except - melanoma, head neck
 - CT - 120Kvp 120 mA (can go lower)
 - Breath hold with CT over chest (8 slices)
 - Free breathing with CT (16 of > slices)
 - Soft tissue, lung/bone CT recon
 - PET – 1.5-3.0 min 2D emission scan/FOV

- ### CMS Coverage for PET in Oncology
- Diagnosis, Staging, Restaging of Cancer
 - Lung (NSCLC), Esophageal Ca, Lymphoma, Melanoma, Colorectal, Head/Neck, **Cervical Ca**
 - Breast Ca
 - Re-staging - locoregional recurrence /metastasis
 - Monitoring tumor response
 - Thyroid CA (-) I-131, > TGB
 - National Oncologic PET Registry



Staging

International System for Staging Lung Cancer

TNM Descriptors:

T - primary tumor

N - lymph nodes

M - metastases

Mountain. Chest 1997; 111:1710-1717

Lung Cancer Staging

- Treatment based on stage
- Survival correlates with stage

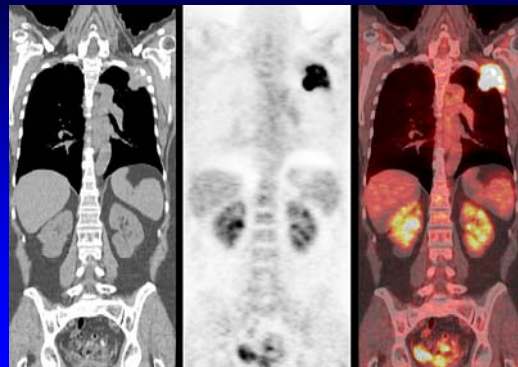
Stage	5-Year Survival
I	60-80%
II	5-50%
IIIa	10-40%
IIIb, IV	<5%

Computed Tomography (CT)

- Excellent for Extent of Disease Evaluation
- Limited in distinguishing benign from malignant lesions
- Limited for Chest Wall and Mediastinal invasion
- Sensitivity/Specificity: 50-70%

Veselle J Thor Cardiovasc Surg 124:511-519, 2002
Vansteenkiste Lancet Oncology Vol 5; 531-540, 2004

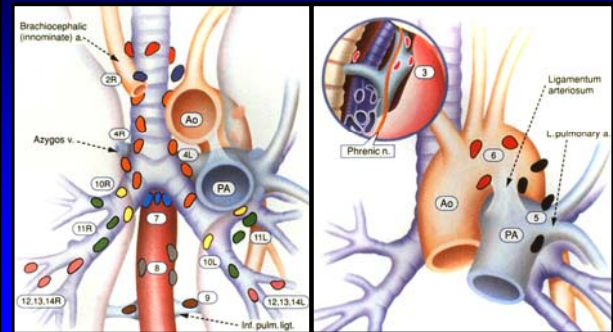
T3



Staging the Mediastinum

- CT- 1 cm short-axis diameter has the best trade-off between sensitivity and specificity
 - Glazer GM. Normal mediastinal lymph nodes: number and size according to American Thoracic Society mapping. Am J Roentgenol 1985;144:261—5.
- Malignant lymph nodes may be < 1 cm and this explains the limited sensitivity of CT, estimated to be 57%, specificity of 82%
 - Toloza EM. Noninvasive staging of non-small cell lung

PET/CT The “N” Factor



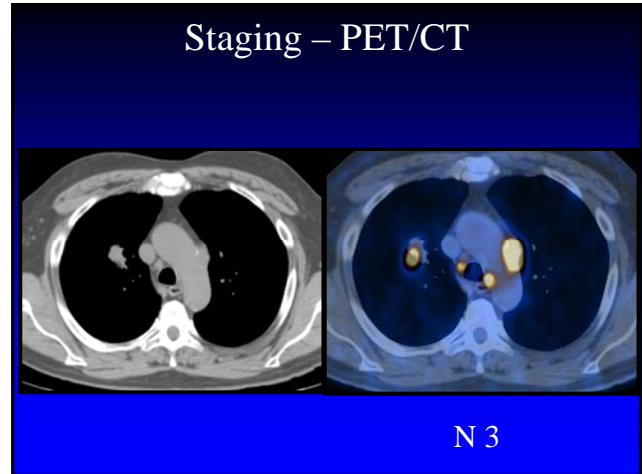
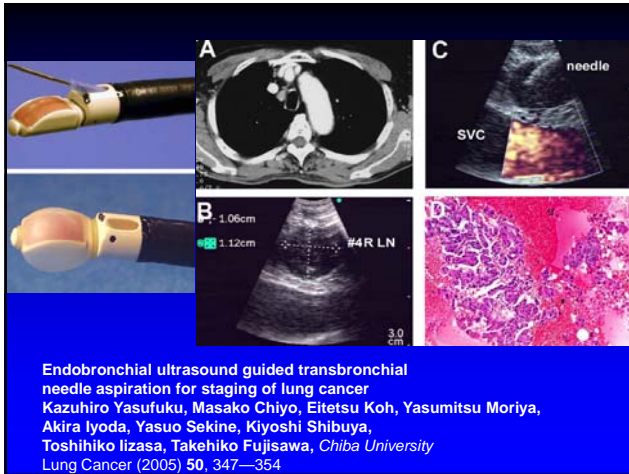
FDG PET Improves Staging

- PET potentially avoided unnecessary thoracotomy in 1 out of 5 patients
 - Reed J et.al. Thorac Cardiovasc Surg. 2003;126(6):1943-51
 - Van Tinteren et.al. Lancet 2002; 359: 1388–92
- Nodal Stage:Sensitivity/Specificity 85/91%
 - High NPV
- M1 detection – mean 13%
 - Stage I -7.5%, Stage II - 18%, Stage III – 24%
 - McManus, et.al. I J R O B P 2001;50:287293

Lymph Nodes - PET/CT

	<u>CT</u>	<u>PET</u>	<u>PET/CT</u>
<u>Sens</u>	70	89	89
<u>Spec</u>	59	89	94
<u>Accu</u>	63	89	93

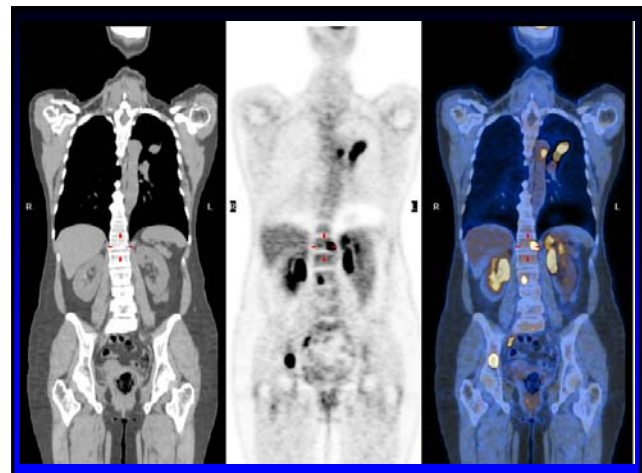
Antoch. Radiology, 2003



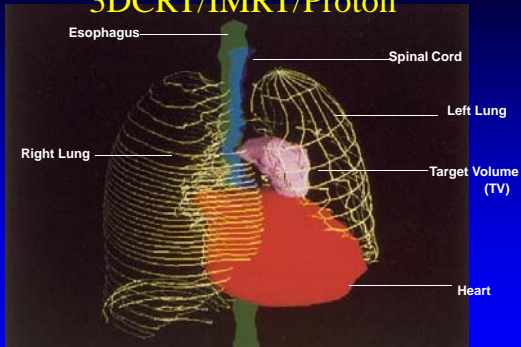
ASCO NSCLC Dx Guideline 2003 Staging Distant Metastases

- General – FDG PET recommended when there is no evidence of distant metastatic disease on CT scan chest
- Bone – bone scan optional, Bx/MR/CT
- Brain – CT/MRI
- Adrenal – FDG PET/US/CT - Bx
- Liver - FDG PET/US/CT - Bx

Pfister J Clin Oncol:2004;22:333-353



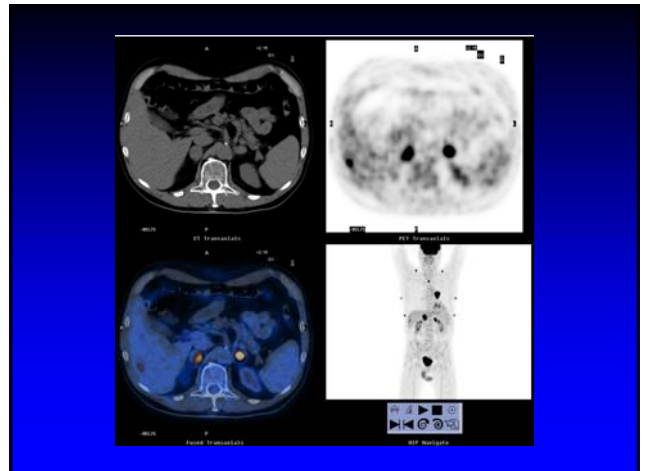
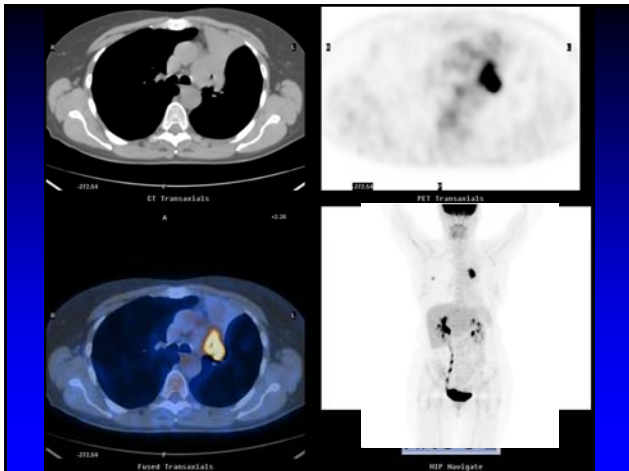
How to reduce NTCP? 3DCRT/IMRT/Proton



Delineation of GTV & Normal Organs in the Thorax

Effect of FDG-PET on Radiation Treatment Volumes in NSCLC

Study	Year	Patients w/ change in RTP
Hiffer	(1998)	7/15 (46%)
Nestle	(1999)	12/34 (35%)
Munley	(1999)	12/35 (34%)
Vanuytsel	(2000)	45/73 (62%)
Giraud	(2001)	5/12 (42%)
McManus	(2001)	38/102 (37%)
Erdi	(2002)	7/11 (64%)
Ciernik	(2003)	18/39 (56%)*
Brianzoni	(2005)	11/25 (44%)*PET/CT



MELANOMA PET Imaging Summary

- Thin melanomas ($T1 \leq 1.0$ mm) radiologic, FDG-PET imaging not cost-effective
- Stage II (T2-4, N0 clinically), Sentinel Node Biopsy, CXR and LDH
- Stage III (N1-3) and IV (M1), CT/MR/PET to detect occult metastases if resection a therapeutic consideration

Sentinel Lymph Node Biopsy

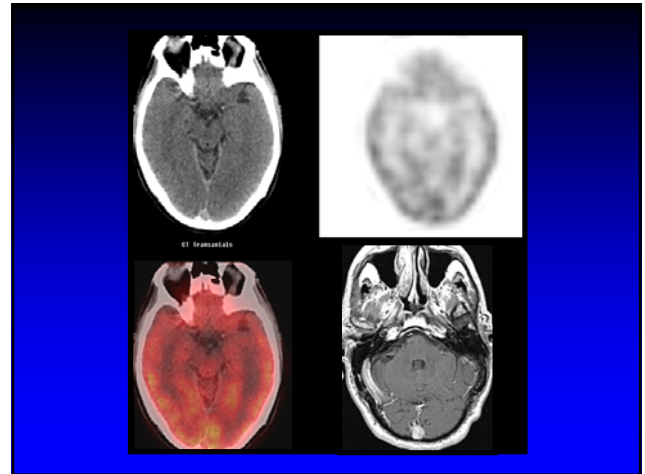
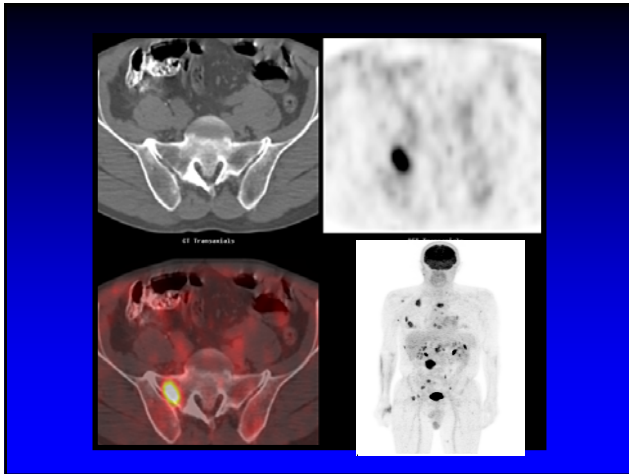


FDG PET High risk Melanoma

- Prospective 100 pts (>1.5 mm)
- Accuracy -
 - FDG PET -92%, Conventional - 77%
- CT - better in lung (87% vs 69%)
 - PET - better in abdomen (100% vs 27%)
 - Cervical metastasis (100% vs 66%)
- FDG PET sensitive and specific for staging

Rinne et al. Cancer; 82(9):1664-71 1998

- 67 year old patient, melanoma right foot Clark level IV, Breslow thickness 4.5 mm.
- Right groin lymph node dissection, 2 of 4 nodes containing microscopic metastases.
- Referred for assessment of extent of systemic metastases.

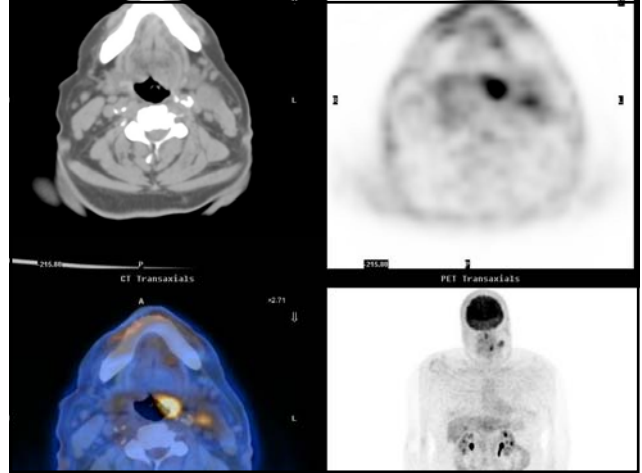
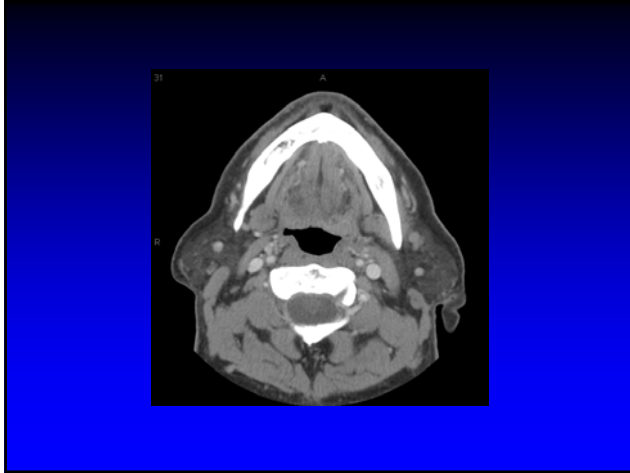


Role of FDG PET Head and Neck Ca

- T staging
 - unknown primary
- N Staging
- Post treatment setting
- Monitoring of Response to Therapy

Case of Unknown Primary

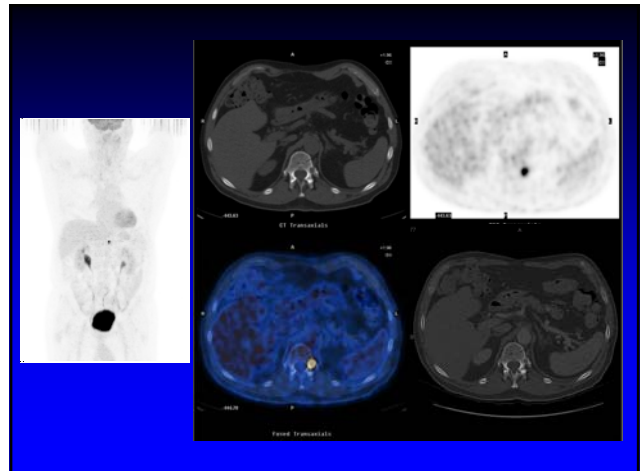
- 68 year old man
- Presents with left neck mass
- Biopsy – keratinizing squamous cell ca
- MDACC physical exam – no mucosal lesions, fiber optic exam of the upper aerodigestive tract negative.
- Workup – PET/CT and Diagnostic CT



FDG PET in Thyroid CA

- Negative whole body I-131 scans
 - 37 pts post thyroidectomy and I-131 Rx
- Elevated thyroglobulin
 - PET localized disease in 71%
 - 1FP, 5 FN (small cervical nodes)
 - PPV - 92%
- Low thyroglobulin - NPV - 93%
- 19/37 - PET changed clinical management

J Clin Endocrinol Metab; 84(7):2291-302 1999



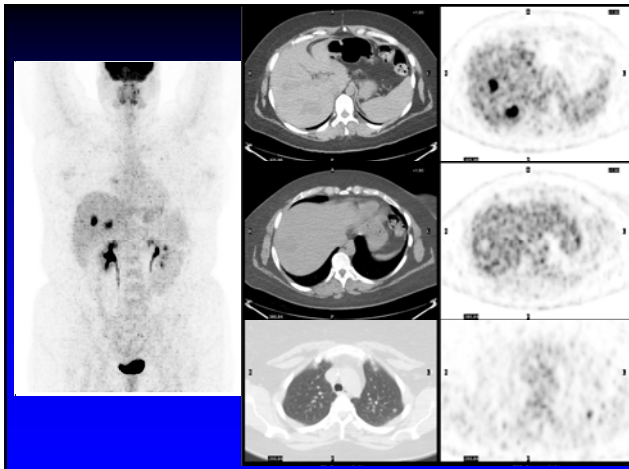
COLORECTAL CANCER Role of PET

- Rectal CA pre-op: nodal and distant mets
- Liver resection - R/O extra-hepatic mets
- Rising CEA, negative CT
- Pelvic abnormalities post surgery or RT
- Monitoring of Response

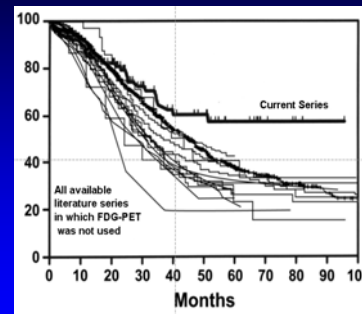
Utility of FDG PET prior to resection of liver metastases

- 40 pts evaluated prior to resection
- PET influenced clinical management in 40% and directly altered management in 23%
 - 6 patients spared laparotomy
 - 3 patients had extrahepatic mets
 - *PET missed peritoneal mets in 3 pts
 - *PET missed sub-centimeter liver lesions

Am J Surg; 178(4):282-7 1999



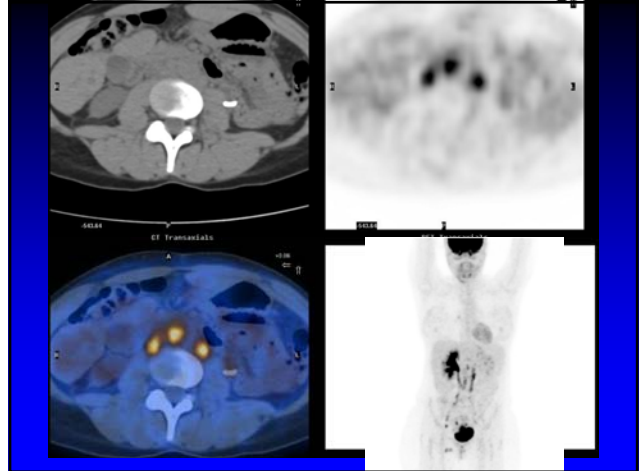
Overall Survival of Patients Undergoing Hepatic Resection for Metastatic Colorectal Ca



Ann Surg. 2001 Mar;233(3):293-9.

FDG PET in Cervical Ca

- Nodal Staging – FDG PET is better
 - PET>CT sensitivity 86-100% >25-67%
 - (Rose 1999, Grigsby 1999, Sugawara 1999)
 - PET>MRI sensitivity 83-91% > 50-73%
 - (Vogelsang 1999, Reinhardt/Narayan 2001)
- Prognosis – Miller, Int J Rad Onc Biol Phys 2002 53:353-9
- IMRT – Esthappann, Int J Radiat Oncol Biol Phys. 2004 58(4):1289-97
- Response – Grigsby J Clin Oncol. 2004 Jun 1;22(11):2167-71.

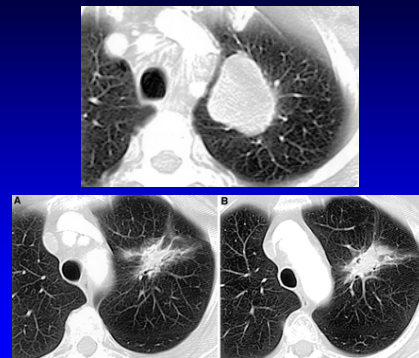


Monitoring Anti-Cancer Rx

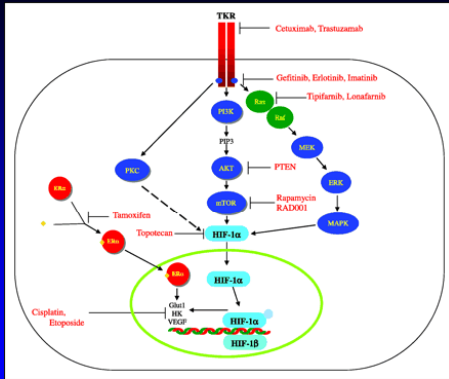
- Moertel, Hanley Cancer 1976: 38:388-394 – solid wood spheres covered with foam, 16 oncologists used calipers/rulers “palpate”
 - False (+) rate acceptable if 50% decrease in size
- WHO – 2 perpendicular diameters
 - 50% or > Reduction product – partial response
- RECIST – Response Evaluation Criteria in Solid Tumors – 30% decrease in longest dia

Weber WA J Nucl Med 2005;46:983-995

Interobserver and intraobserver variability in measurement of NSCLC lesions



J Clin Oncol. 2003 Jul 1;21(13):2574-82.



Clin Cancer Res. 2005 Apr 15;11(8):2785-808.

Oncology Biomarker Qualification Initiative FDA, NCI, part of the NIH and CMS

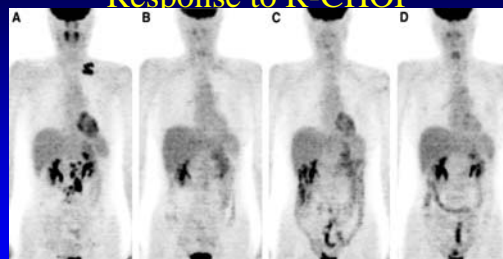
- First project to be implemented will serve to validate and standardize the use of FDG-PET
- Trials of patients being treated for non-Hodgkin's lymphoma, to determine if FDG-PET is a predictor of tumor response.
- Data resulting from this type of evidence-based study will help both FDA and CMS work with drug developers based on a common understanding of the roles of these types of assessments.

<http://www.cancer.gov/newscenter/pressreleases/OBQI>

Response	Definition	Nodal Masses
CR	Disappearance of all evidence of disease	FDG-avid or PET (+) prior to therapy; mass of any size permitted if PET negative
PR	Regression of measurable disease and no new sites	FDG-avid or PET (+) prior to therapy; one or more PET positive at previously involved site
SD	Failure to attain CR/PR or PD	FDG-avid or PET (+) prior to therapy; PET (+) at prior sites of disease and no new sites on CT or PET
PD	Any new lesion or increase by 50% of previously involved sites from nadir	Appearance of a new lesion(s) > 1.5 cm in any axis, 50% increase in SPD of more than one node, or 50% increase in longest diameter of a previously identified node > 1 cm in short axis
		Lesions PET (+) if FDG-avid lymphoma or PET (+) prior to therapy

Revised response criteria for malignant lymphoma. Cheson et al, JCO 2007; 25(5):579-86

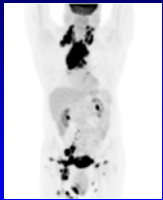
Large B-cell Diffuse Lymphoma Response to R-CHOP



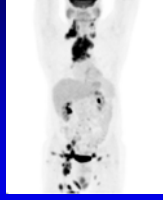
Baseline	1 Day	20 Days	End
SUV _{cor} = 7.7	SUV _{cor} = 1.2	SUV _{cor} = 0.0	SUV _{cor} = 0.0

Yamane et al. J Nucl Med 2004; 45:1838

Follicular Lymphoma



4 cycles R-CHOP



2 cycles R-ESHAP



2 cycles R-hyperCVAD

FDG PET Breast Cancer

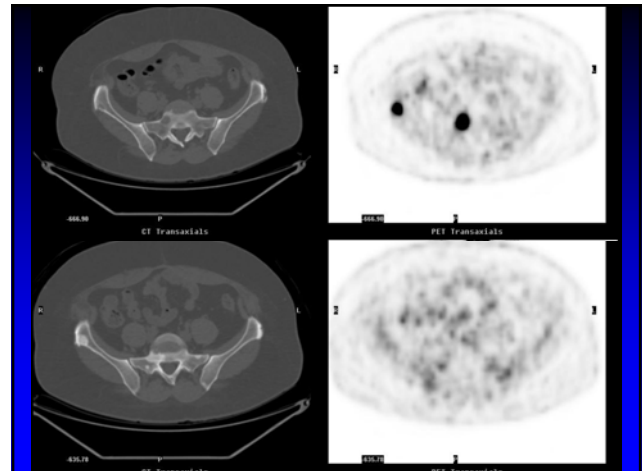
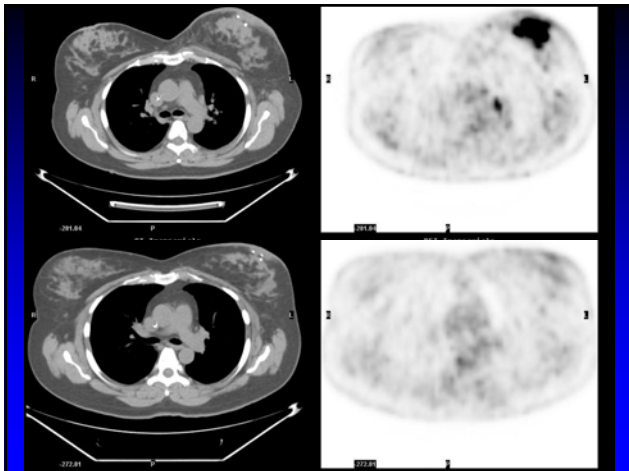
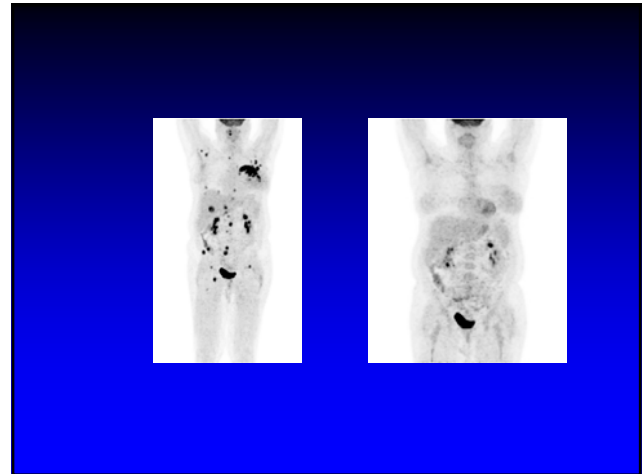
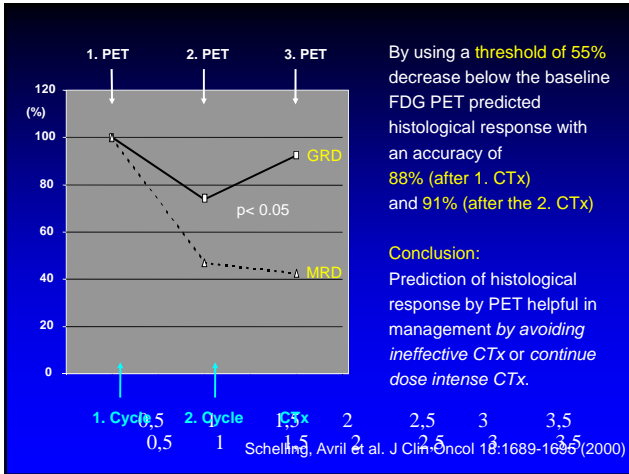
- Diagnosis – limitations, size/type
- Axillary Staging – limitations, SLN
- Evaluation of Recurrent disease
- Evaluation of Locally Advanced Cancer
- Evaluation of Response
 - Define criteria for different types
 - Improvement of outcomes

Inflammatory Breast Cancer

- Rare, aggressive, young, poor prognosis
- MRI was the most accurate imaging technique in detecting a primary breast parenchymal lesion
- Sonography can be useful in diagnosing regional nodal disease.
- PET/CT provides additional information on distant metastasis, and it should be considered in the initial staging of IBC.

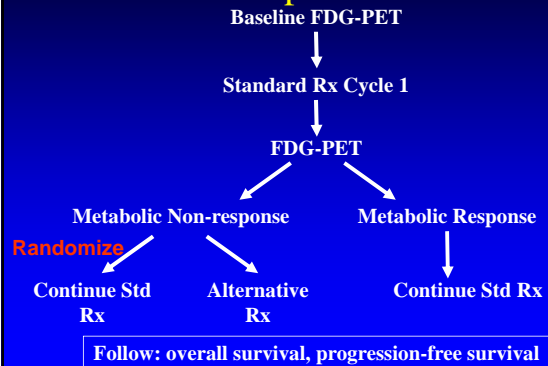
Yang WT et.al. Breast Cancer Res Treat. 2007 Jul 26;





FDG PET-Guided Chemotherapy:

Sample Trial



CMS Coverage for PET

- Epilepsy - Localize the seizure foci in patients with intractable seizures that are being worked up for surgery (FDG)
- Alzheimer's Disease (FDG)
- Myocardial Perfusion Imaging
 - Rb82 (Generator)
 - N-13 Ammonia (NH3)
- Myocardial Viability
 - F-18 FDG

Dementia

- Affects 8% of persons > 65 years
- Affects 47% of persons > 85 years
- Alzheimer's disease accounts for 70%

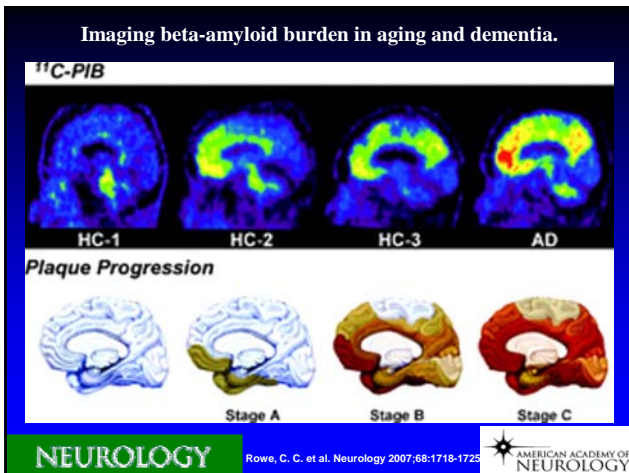
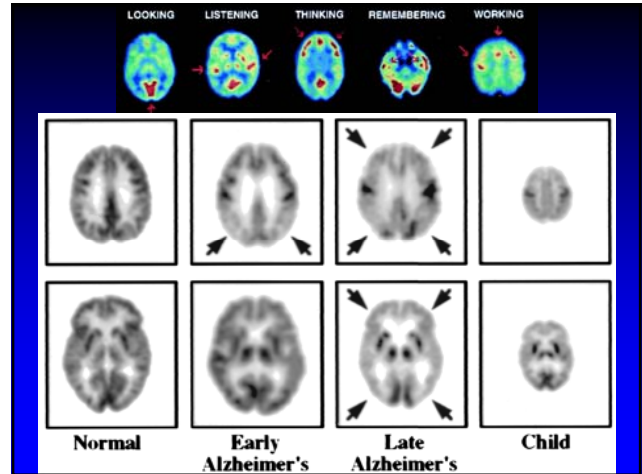
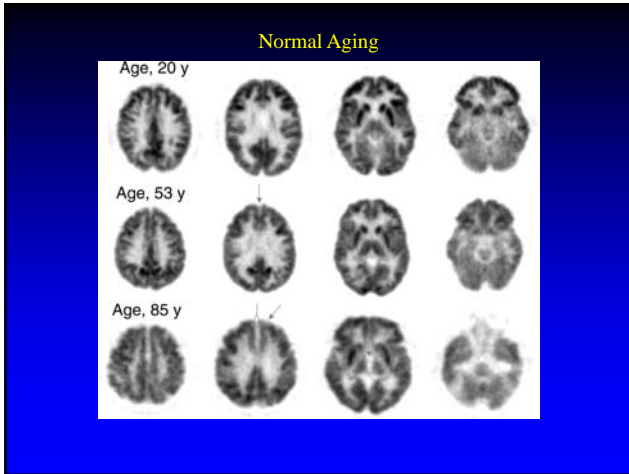
I have a photographic memory, but once in a while I forget to take off the lens cap

-Milton Berle

Proposed criteria for the diagnosis of Alzheimer's disease

- Early and significant episodic memory impairment
- One or more abnormal biomarkers :
- MRI – atrophy: medial temporal lobe, hippocampi, entorhinal cortex, amygdala
- PET - FDG, FDDNP, PiB (Pittsburgh cpd)
- CSF analysis of amyloid beta or tau proteins

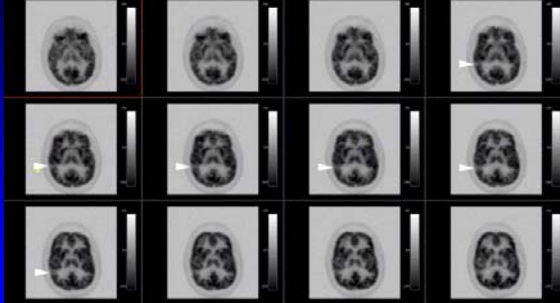
Dubois, B. et.al. Lancet Neurol. 2007 Aug;6(8):734-46.



Conclusions

- Memory loss is part of aging process
- Alzheimer's disease is most common cause of dementia
- FDG-PET is accurate in the early diagnosis of Alzheimer's disease
- Molecular imaging agents are being developed that will be more accurate than FDG

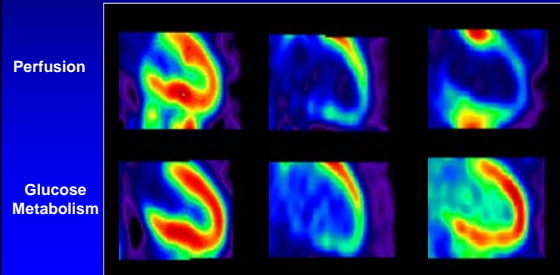
FDG-PET in a 17-year-old patient with intractable partial epilepsy not localized by EEG or MRI (normal).



Epilepsy Behav. 2006 Feb;8(1):91-101.

Perfusion and Metabolism Patterns

Normal Irreversible Dysfunction Reversible Dysfunction



Diagnostic accuracy of Rb-82 myocardial perfusion PET: comparison with Tc-99m MIBI SPECT.

- 112 SPECT Tc-99m sestamibi and 112 PET rubidium-82 MPI—in patient populations matched by sex, BMI, and presence/extent CAD.
- Diagnostic accuracy was higher for PET for both stenosis severity thresholds of 70% (89% vs 79%, $p = .03$) and 50% (87% vs 71%, $p = .003$) and was higher in men and women, in obese and nonobese patients, and multivessel CAD
- Myocardial perfusion PET was superior to SPECT in image quality, interpretive certainty, and diagnostic accuracy.

Bateman, TM J Nucl Cardiol. 2006 Jan-Feb;13(1):24-33.

PET demonstrates small perfusion defect of severe intensity in the mid and basal lateral walls with significant but not complete reversibility. On CTA, severe luminal narrowing of the proximal (LAD) and (LCx). The integrated PET-CT results suggest only the LCx stenosis is hemodynamically significant.

