Functional Imaging FDG

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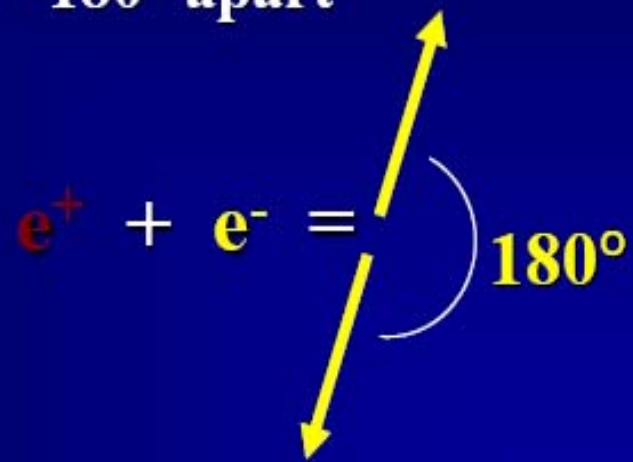
COINCIDENCE IMAGING

Positron Decay

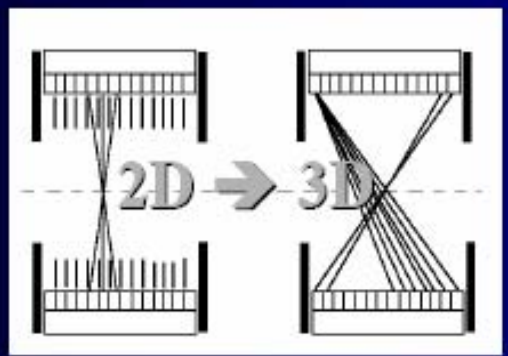
Positron Annihilation

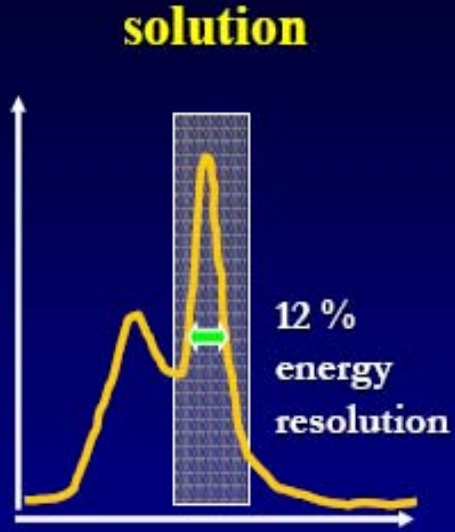
- Two 511 keV photons
- Emitted simultaneously
- 180° apart



PET

PET tracers annihilate with emission of two 511 Kev gamma rays emitted at 180 degree apart.



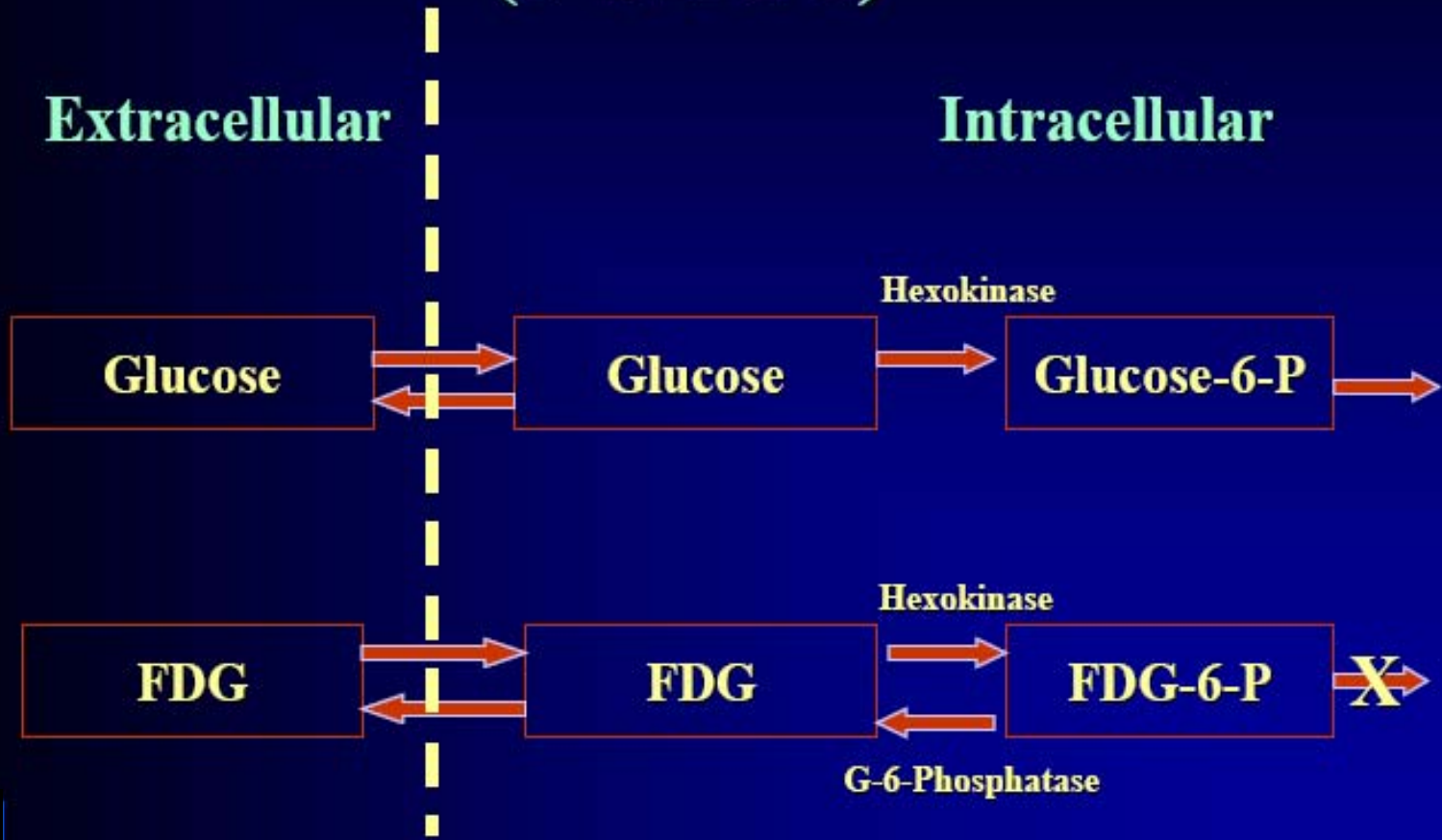


PET RADIOPHARMACEUTICALS

PET tracers in Oncology.

Fluodeoxyglucose F-18
Water O-15
Sodium acetate C-11
Carbon monoxide C-11
Fluoride F-18
Methionine C-11
Thymidine C-11
Ammonia N13

FLUORINE-18 FLUORODEOXYGLUCOSE (F-18 FDG)



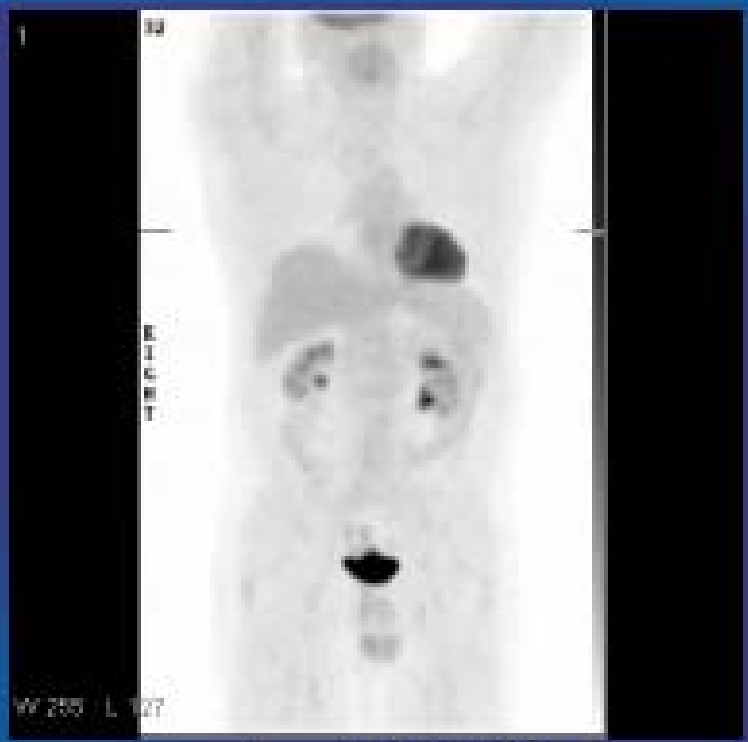
Metabolic pathway of glucose and ^{18}F FDG

Oncological PET

HCFA / CMS Approved

- Lung
- Malignant Lymphoma
- Colorectal
- Malignant Melanoma
- Esophagus
- Head & Neck Cancer
- Breast
- Brain
- Melanoma
- Pancreas
- Bone & Soft Tissue
- Ovarian Cancer.
- Thyroid Ca.

Imaging Function with [^{18}F]-FDG



Normal FDG-PET Scan

BBWH Nuclear Medicine

What is an FDG-PET scan?

- It is not a cancer scan
  - Wide range of potential false positive and false negatives

An FDG-PET scan is:

- A map of glucose metabolism in the body
  - In 3D space (spatial domain)
  - At a particular time (temporal domain)
    - Dual time point imaging (DDx cancer vs infection)

BIDMC Nuclear Medicine

Role of FDG-PET in oncology

- Shown to be more accurate than conventional staging and restaging in a range of malignancies
  - Upstage cancer – reduces futile and toxic therapies (also cost savings)
  - Downstage cancer – allows more therapeutic options
  - More accurately restage and assess treatment response of cancer

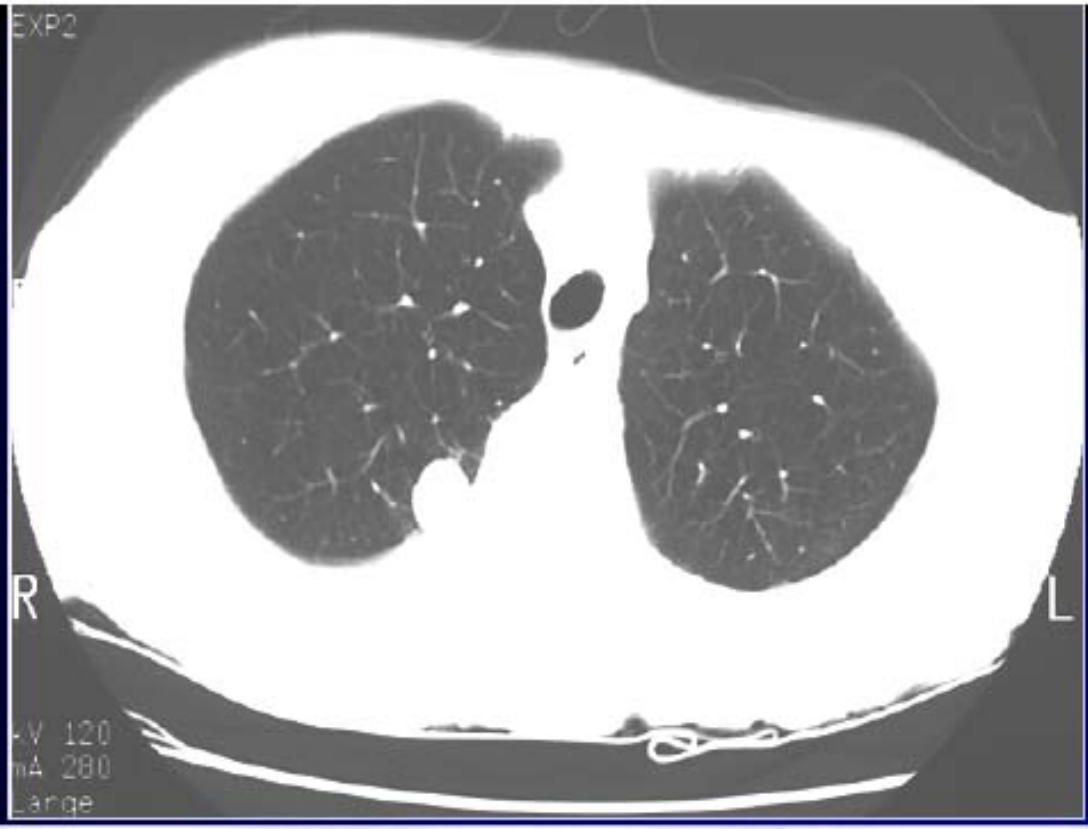
RBWH Nuclear Medicine

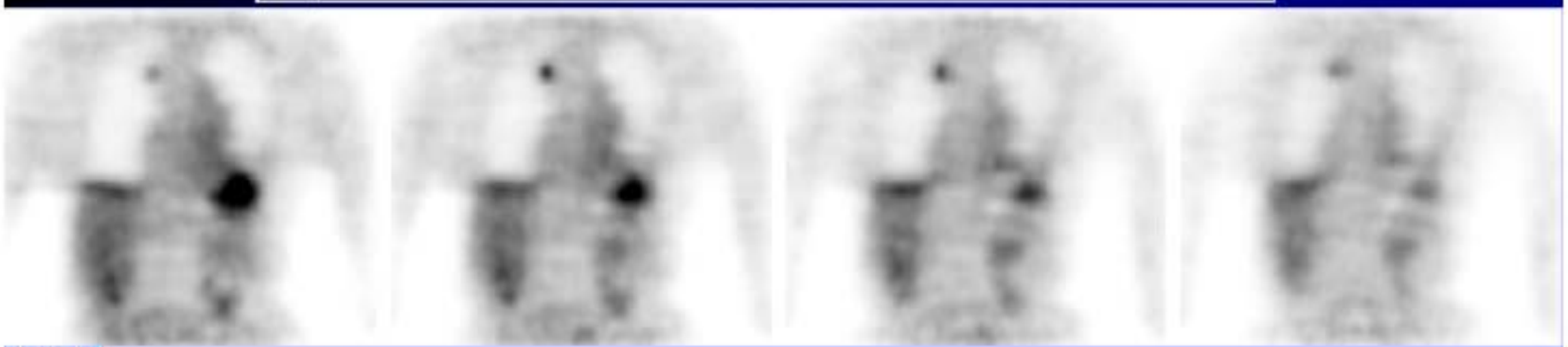
Tumours with low FDG uptake or otherwise difficult to visualise on PET scans

- BAC lung
- Mucinous adenocarcinomas
- Carcinoid
- Low grade sarcoma
- Some low grade lymphomas esp MALT, SLL
- Hepatocellular carcinoma
- Cerebral metastases
- Prostate
- Renal

RBWH Nuclear Medicine

NSCLC





SUMMARY OF EVIDENCE FOR FDG PET IN LUNG CANCER

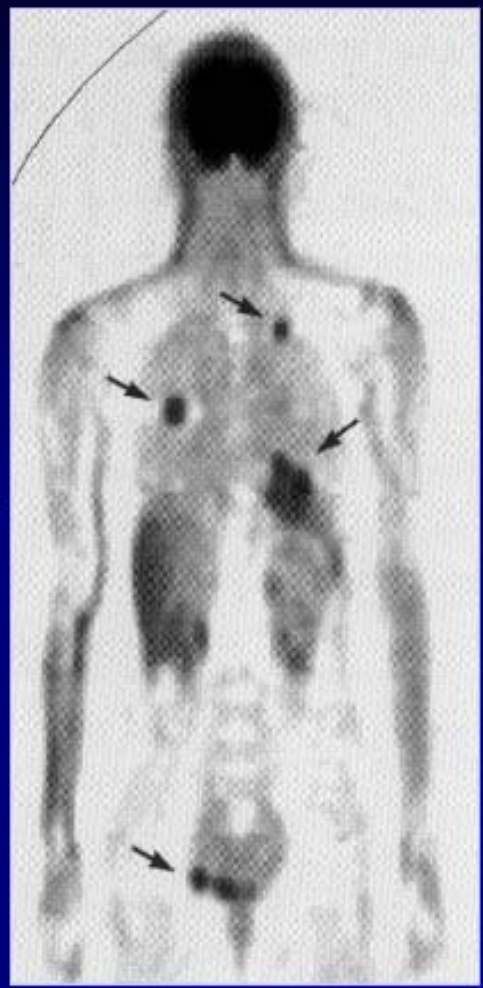
For Staging:

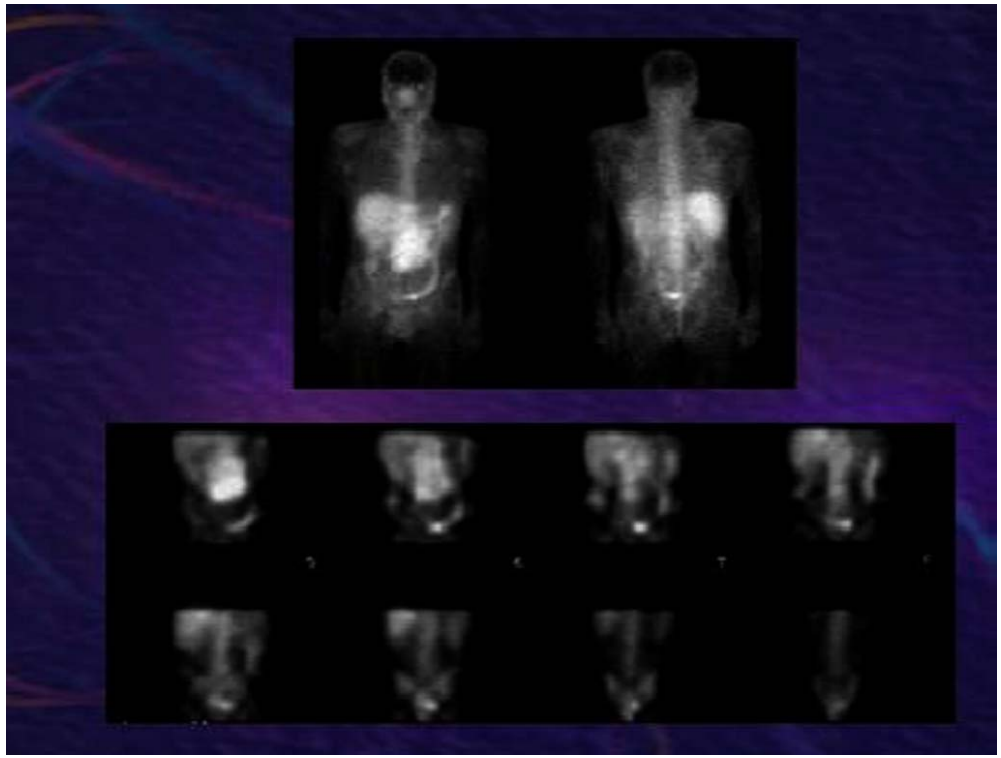
- An estimated 37% change was noted in management effect, based on 1,565 patient studies

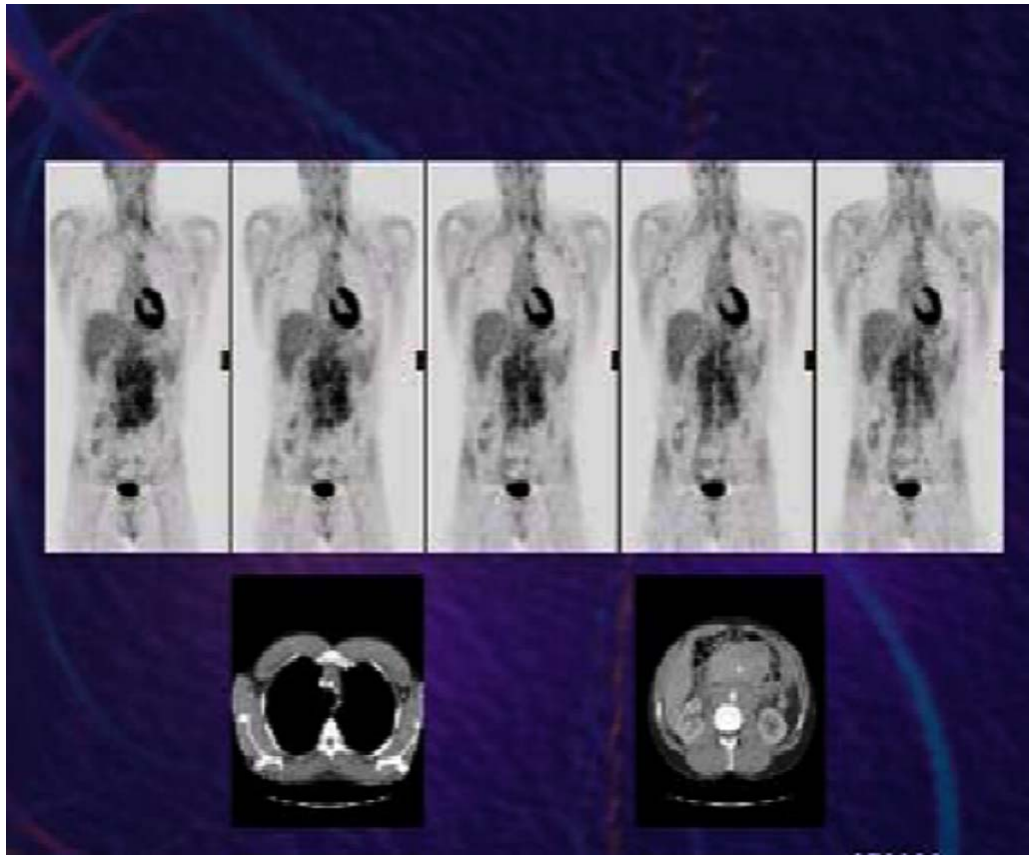
Gambhir S.S., et al. "A Tabulated Summary of the FDG PET Literature" J Nucl Med; Vol. 42(5):1S-93S, 2001

COLON CANCER

Metastatic Colon Cancer







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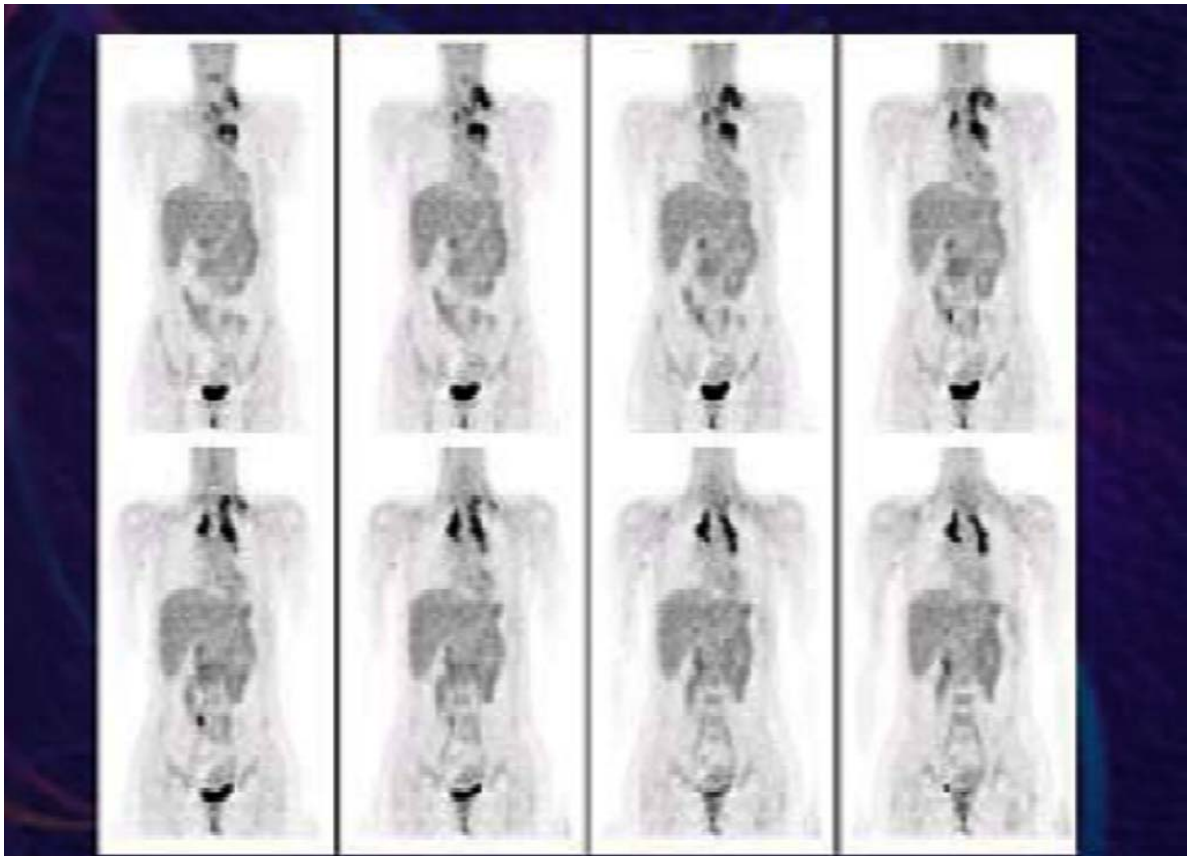


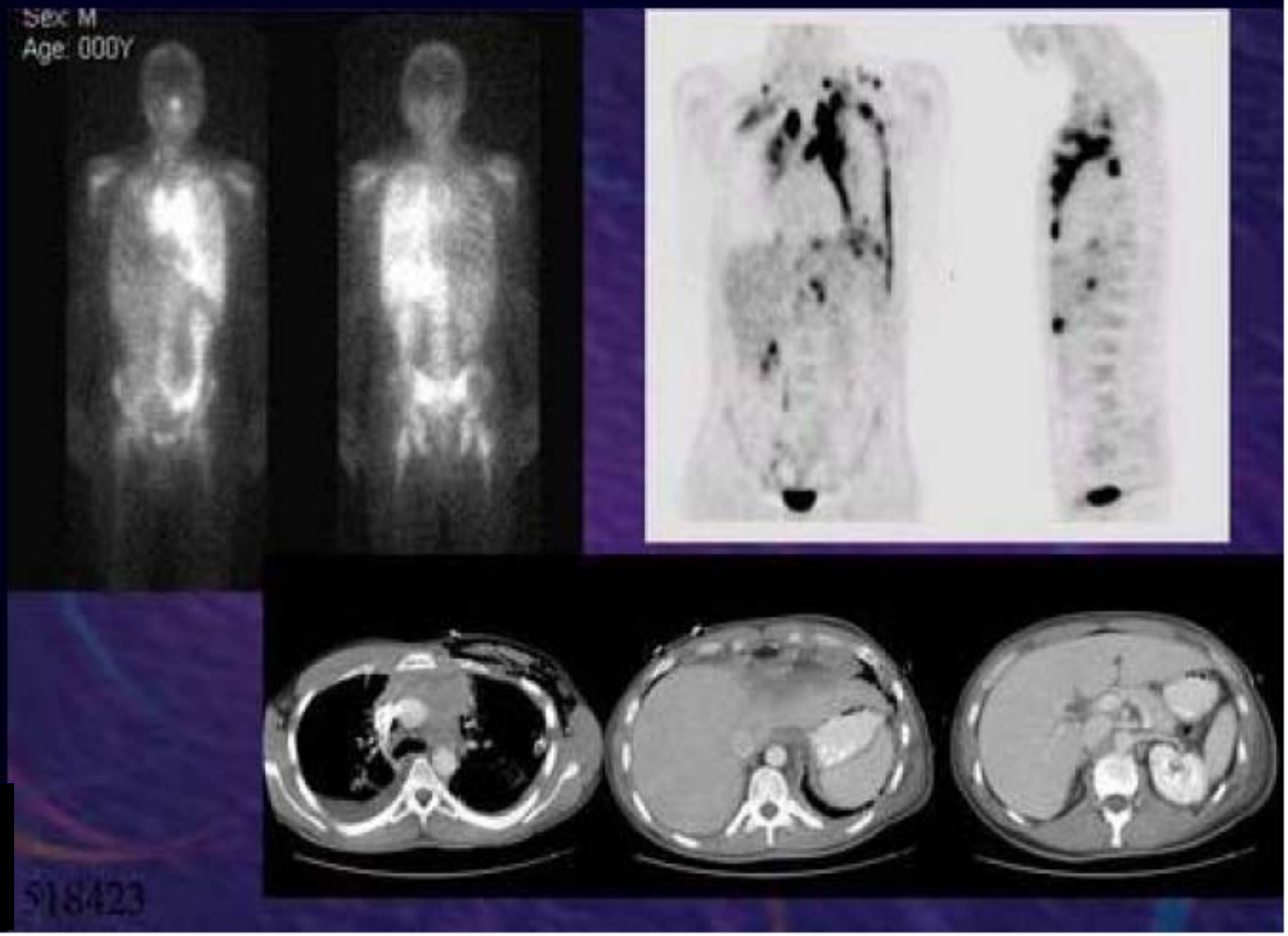
Advantages of Nuclear Medicine?

- Metabolic imaging
- Quantitation is possible especially with PET
- PET provides ideal solution to quantitate tumor biological parameters such as metabolism, receptor quantity, cell proliferation and uptake of therapeutic agents.

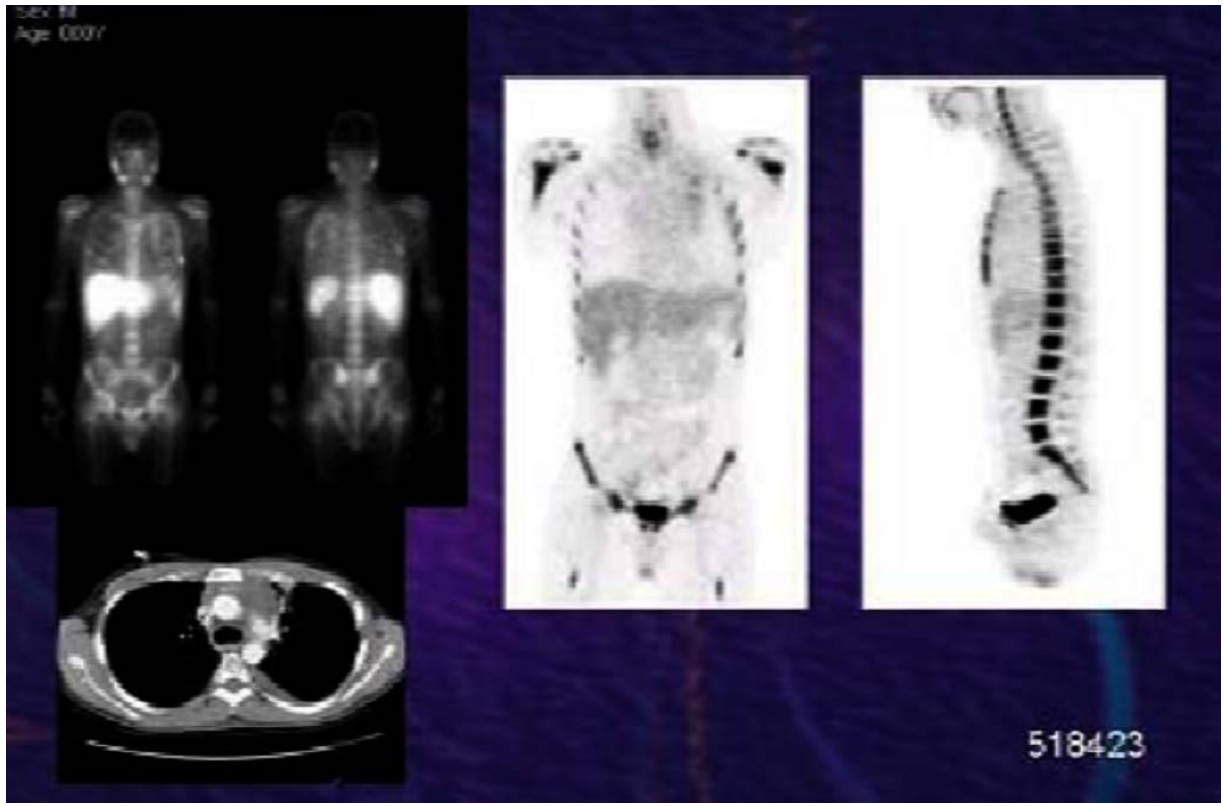
EVALUATING TREATMENT RESPONSE

- Tumor response to chemotherapy:
  - Biologic and metabolic decrease in metabolic function and trapping of radiopharmaceuticals occurs:
    - Very early after initiation of treatment
    - Precedes clinical decrease in tumor size
    - Precedes decrease in size detected by X-ray, CT or MRI.
- Important to be evaluated early in the course of treatment in order to either continue on same chemotherapy or change to a different regimen before bone marrow depression.

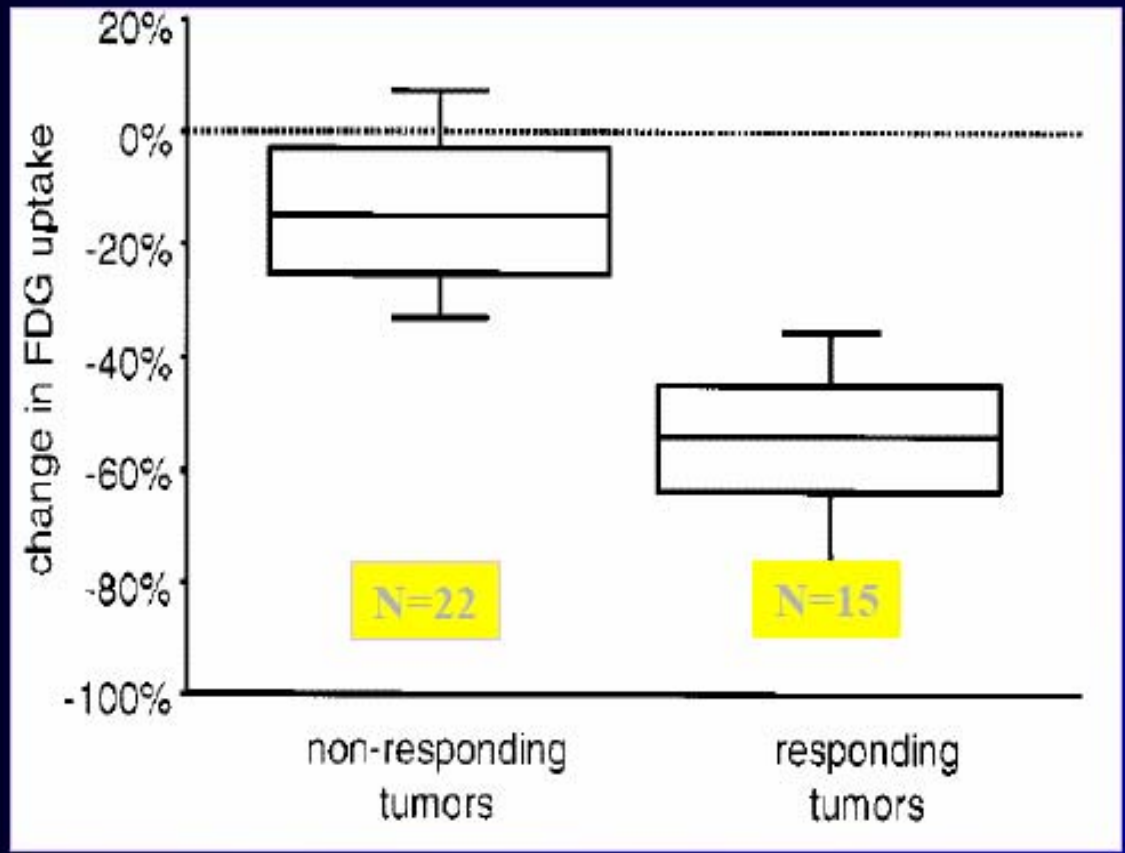
NHL Pre-chemotheray



NHL Post-chemotheray



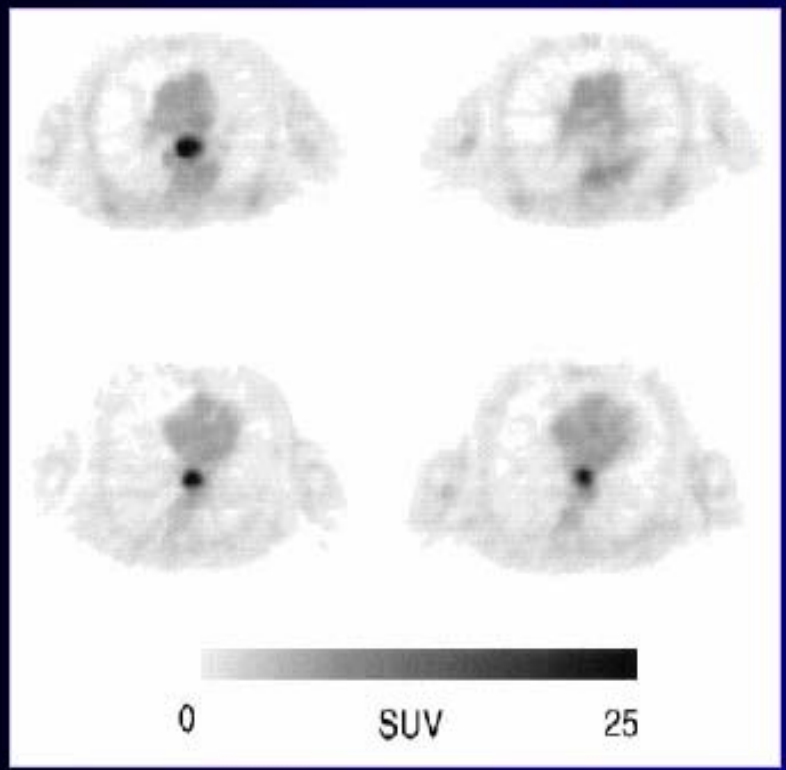
FDG-PET PREDICTION OF RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN CARCINOMA OF THE GE JUNCTION



Weber, et al., J Clin Oncol 19:3058, 2001

FDG-PET PREDICTION OF RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN CARCINOMA OF THE GE JUNCTION

Baseline Day 14



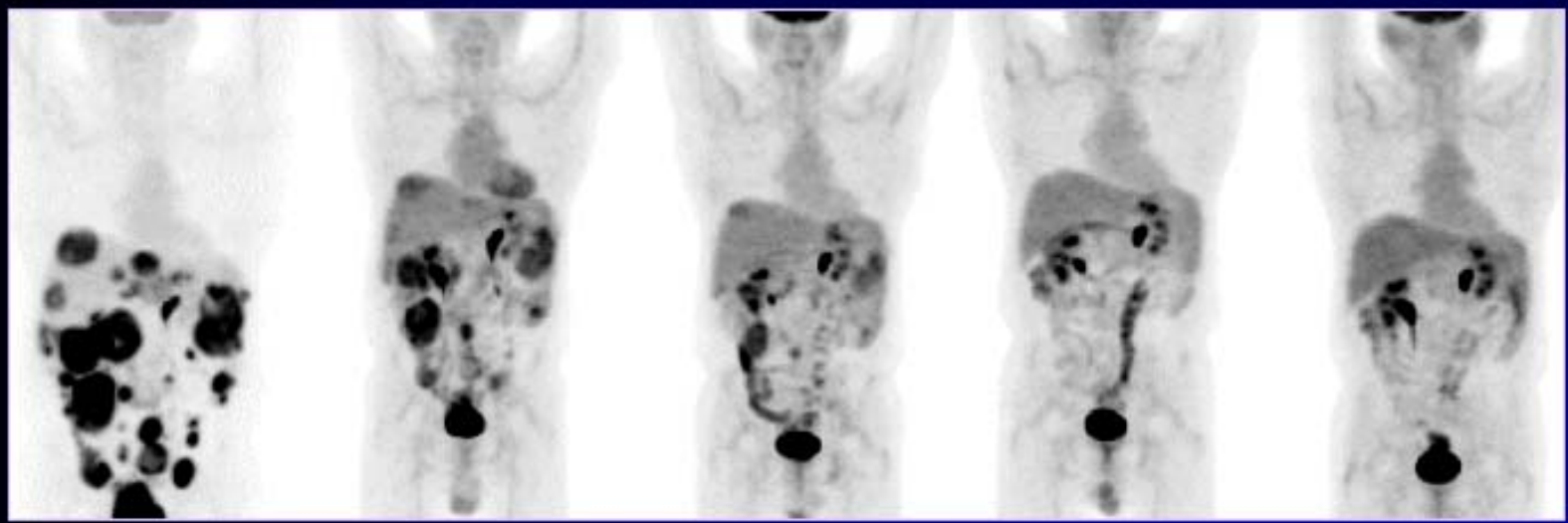
Responder

Non-responder

Weber, et al., J Clin Oncol 19:3058, 2001

METABOLIC RESPONSE TO GLEEVEC IN GIST

DANA-FARBER CANCER INSTITUTE



Baseline 24 hours 7 days 2 months 5.5 months

OTHER PET APPROACHES FOR ASSESSING RESPONSE TO THERAPY

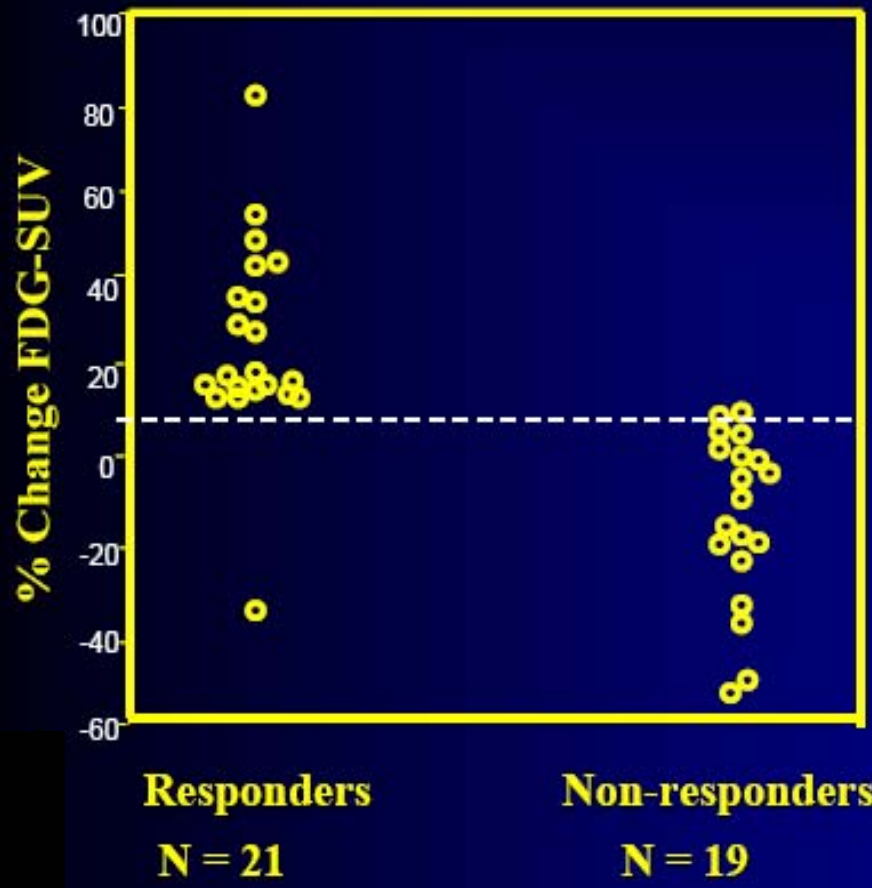
- Monitoring
  - Blood flow
  - Amino acid metabolism
  - DNA synthesis (proliferation)
  - Apoptosis
- Predicting
  - Chemotherapeutic agents
  - MDR substrates
  - Hypoxia tracers
  - Receptor ligands

PREDICTING RESPONSE OF ADVANCED BREAST CANCER TO HORMONAL THERAPY

- Hormonal therapy
  - Low morbidity alternative to chemotherapy
  - Only 50-60% of patients with ER+ breast cancer respond to hormonal therapy
  - Suggests that receptors not always functional
- Hypothesis: FDG-PET can be used to define functional estrogen receptors by detecting metabolic response to receptor agonist

PREDICTING RESPONSE TO HORMONAL THERAPY

"Metabolic Flare"



- FDG-PET before and after 7-10 days tamoxifen in 40 pts. with advanced ER+ cancers
- With change ≥ 10%:

  PPV 91%

  NPV 94%

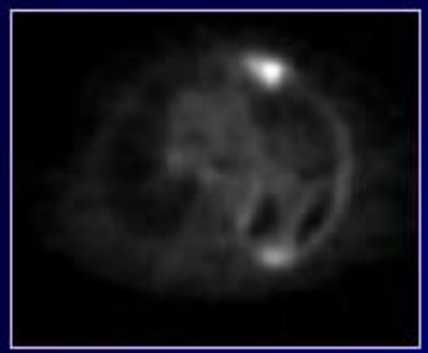
  for predicting response

Mortimer, et al. JCO 2001; 19:2797

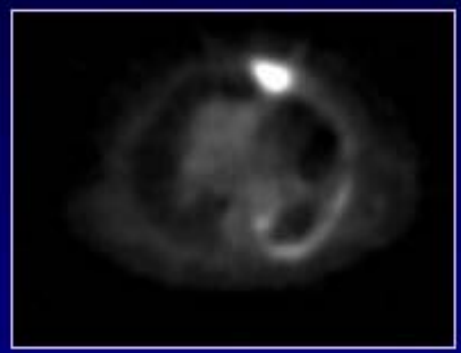
BREAST CARCINOMA: THERAPY FDG-PET PREDICTING OF RESPONSE TO HORMONAL

Before Hormonal Therapy | After Hormonal Therapy

Responder



SUV=4.7



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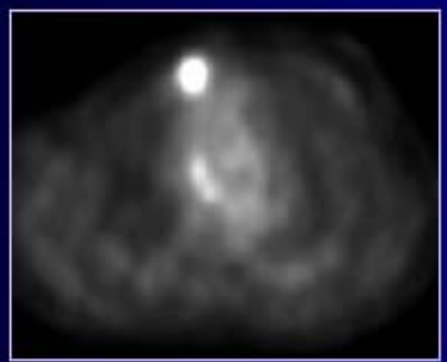
Non-responder



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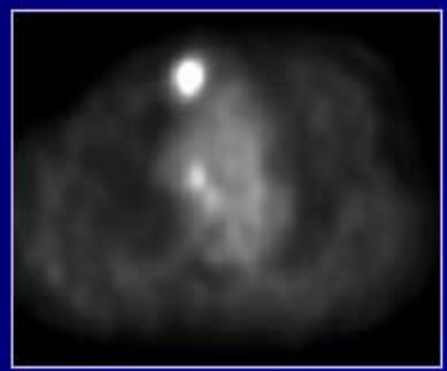


SUV=5.5

Clinical Trials (11)	Imaging Modality
Lymphoma (2)	FDG PET-CT DCE MRI
Head and Neck (2)	FDG, FLT, F18-FMISO PET
Brain (2)	FDG, FLT, PET MRS, DCE MRI
Ovarian (1)	FLT, FDG PET
Lung (1)	FDG PET
GU (1)	C-11 Acetate PET
Radiation Oncology (2)	FDG, FLT, F18-FMISO PET

Monitor the response of tumors to antiproliferative treatment

3'-Deoxy-3'-[18F]fluorothymidine ([18F]FLT)

FLT is a substrate for thymidine kinase (first step in DNA synthesis)

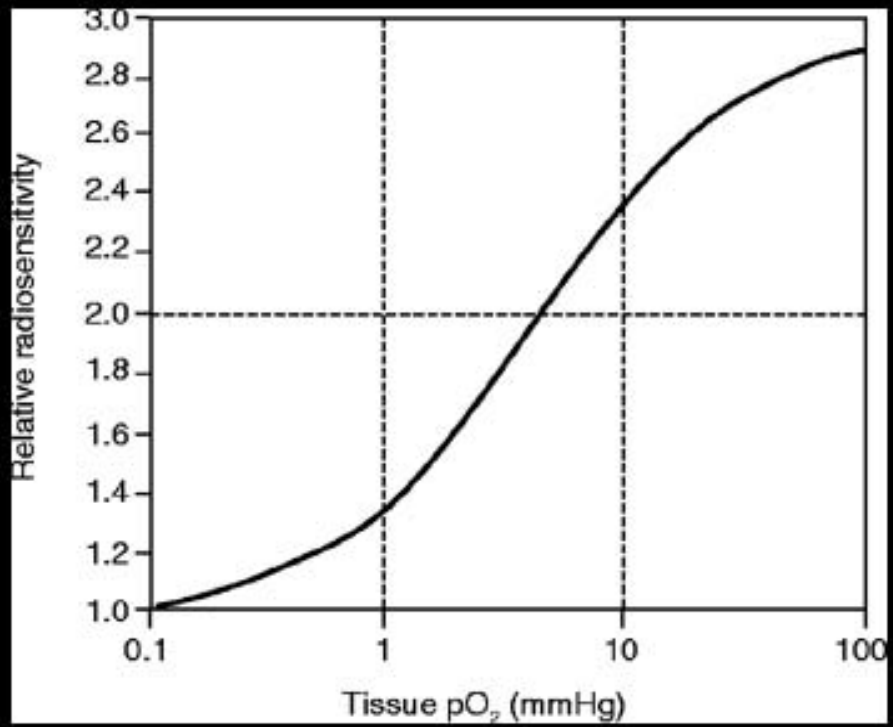
F-18 FLT shows regions of cell proliferation

Compare with Ki-67 (MiB-1) immunoperoxidase stain

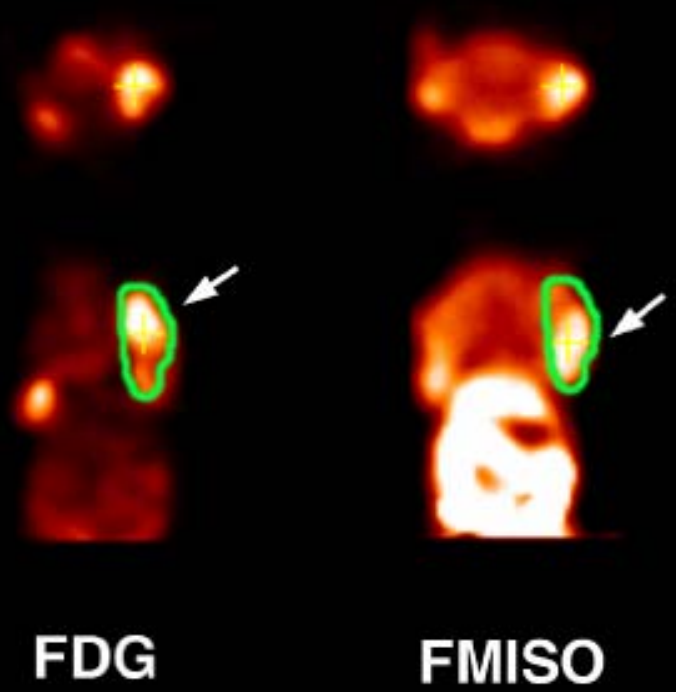
The Role of Hypoxia in Clinical Response to Stereotactic Radiosurgery in Head and Neck Cancer (Drs. Lai, Grandis)

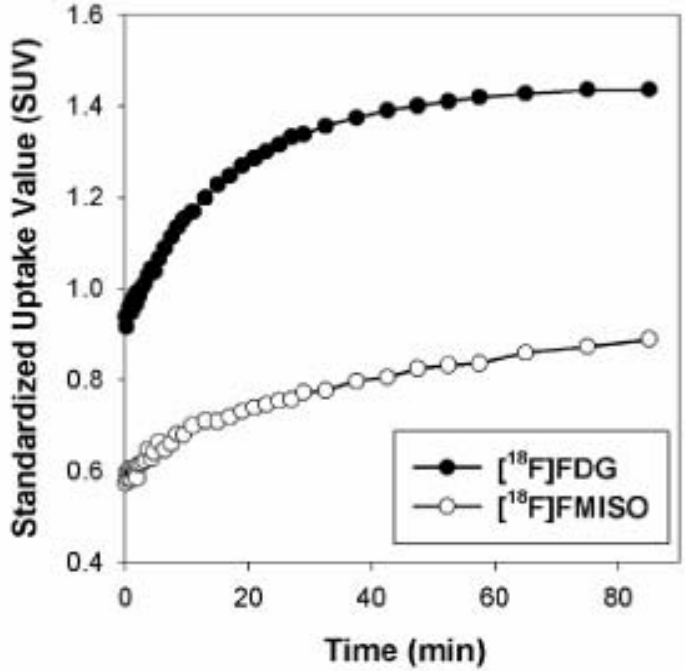
Hypoxia Tracer Development
F-18 Fluoromisonidazole (F-18 FMISO)

Hypoxia reduces tumor sensitivity to radiation therapy and chemotherapy



PET Imaging of SCC Murine Tumors ([^{18}F]-FDG vs. [^{18}F]-FMISO)

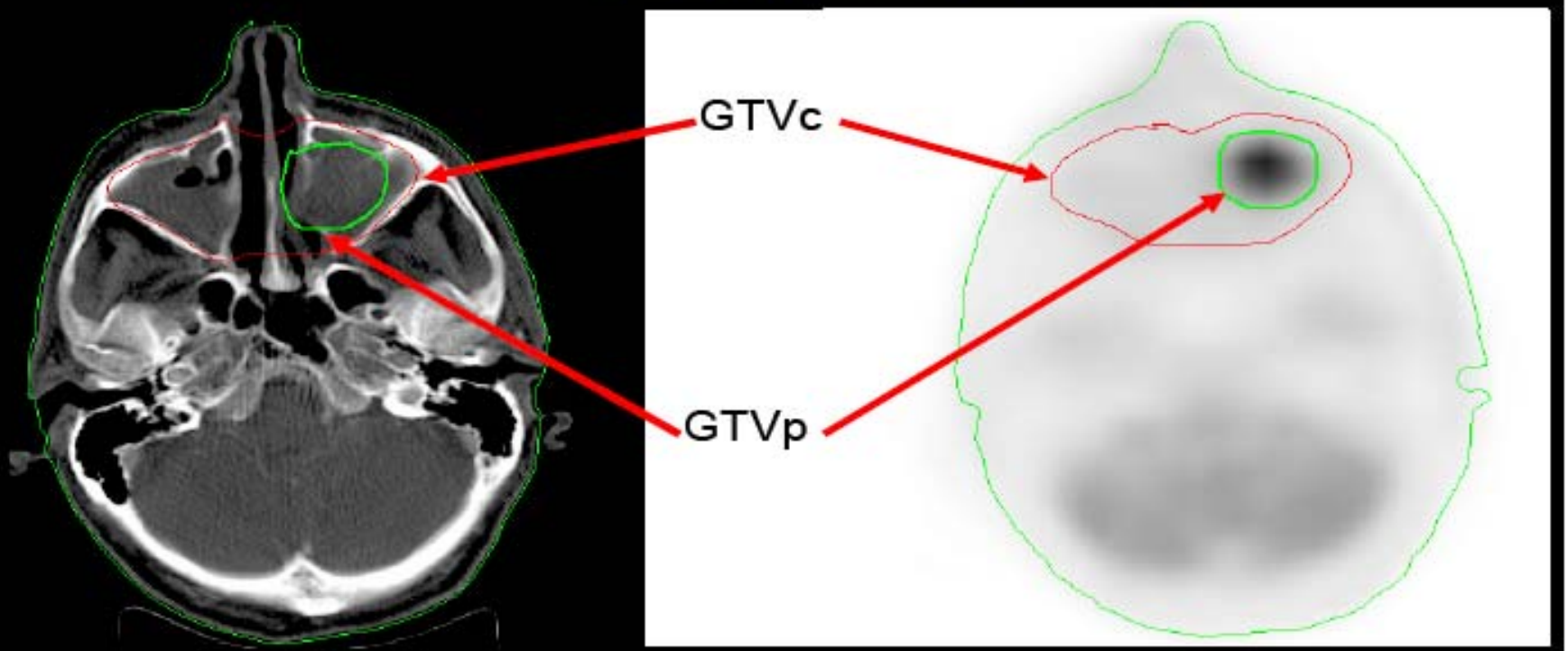




Left. MicroPET images show increased FDG uptake in the anterior metabolic portion of the tumor, while FMISO uptake was increased in the posterior hypoxic portion of the tumor

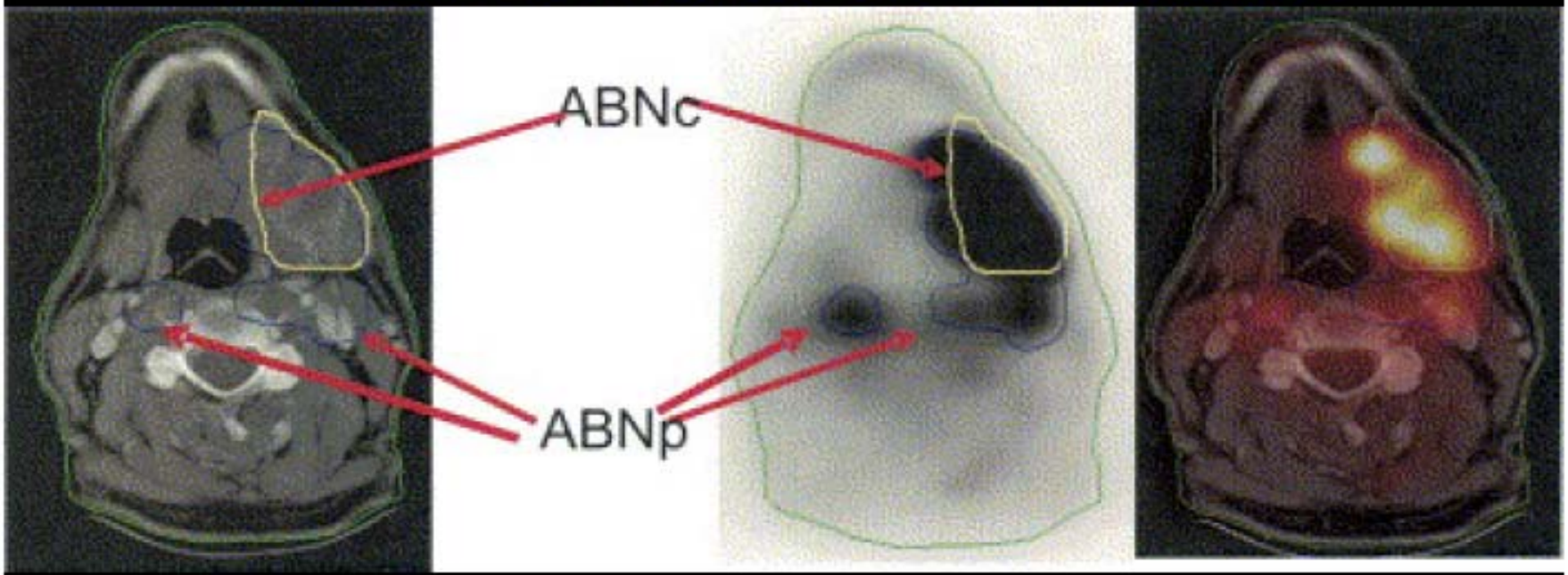
Right. Time-activity curves of tumor uptake

Ethmoid Sinus Carcinoma – CT and PET contours for tumor areas depicting anatomic and functional abnormalities



GTVc = gross tumor volume on CT
GTVp = gross tumor volume on PET

CT and PET contours for nodal areas depicting anatomic and functional abnormalities



ABNc = abnormal nodal region on CT; ABNp = abnormal nodal region on PET.

Additional areas of FDG avidity on PET, not discernable as abnormal on CT.

21 patients were simulated for treatment on PET-CT for IMRT in Varian Eclipse planning system

Volumes for the primaries were larger anatomically (CT) compared with PET

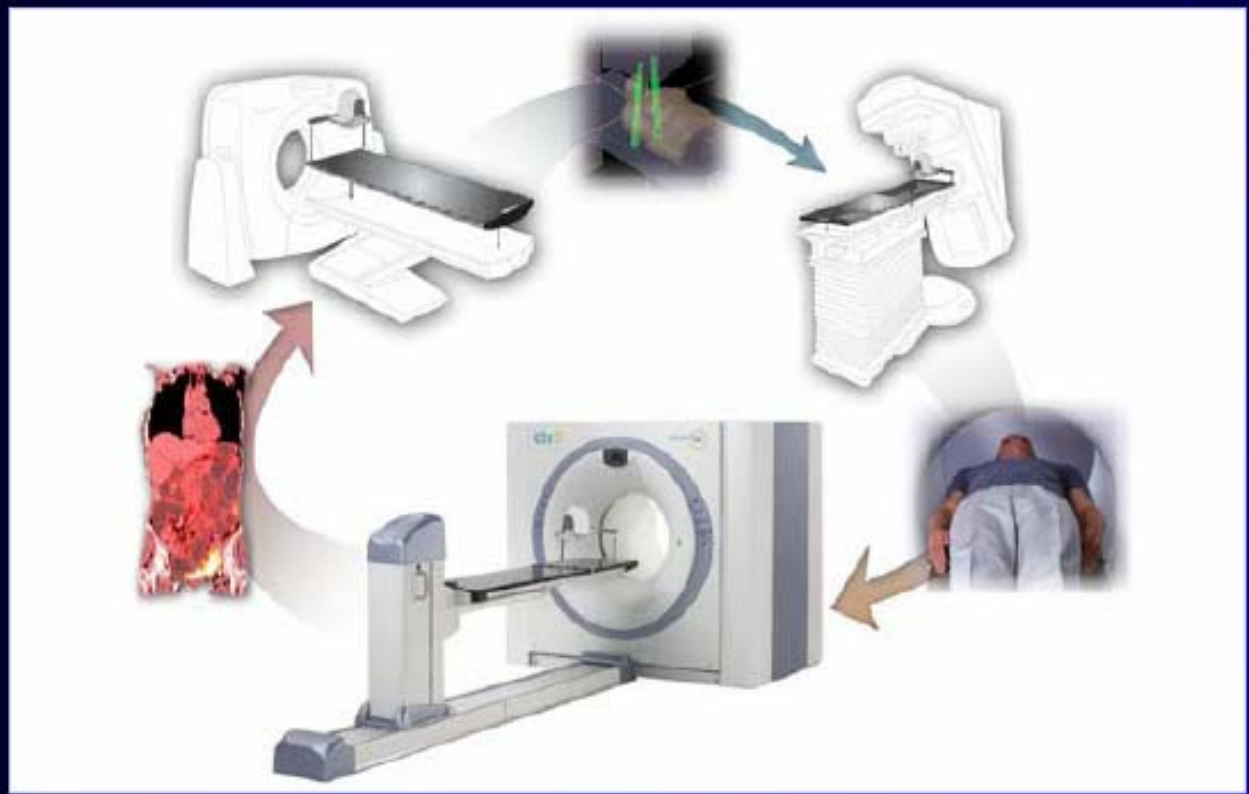
In 8/21 patients, additional areas of disease were seen on PET compared to CT

CT/PET Image Fusion

- Guide surgery or biopsy
- Oncology
  - fibrosis vs. active tumor
  - evaluation of therapy response
  - uptake of FDG vs. size on CT
- Radiotherapy Applications
  - Tailor field size to viable tumor
  - Assessment of residual mass on CT post therapy

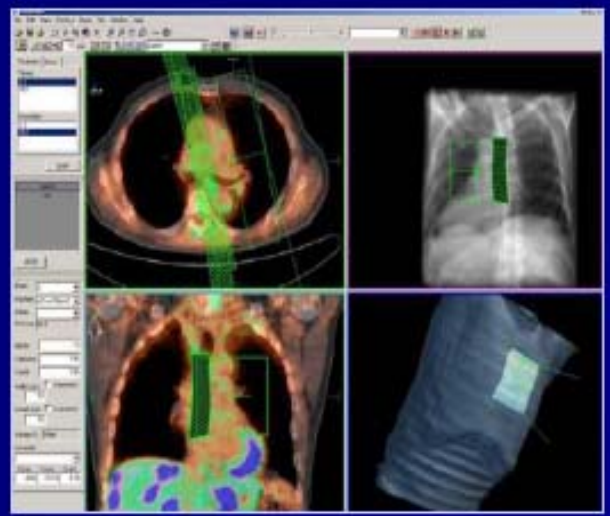
Clinical Integration

From Imaging to Planning to Therapy



Therapy Connectivity

- Therapy Connectivity
  - PET and CT DICOM
  - Established connectivity with:
    - Varian, Nomos, Nucletron…etc



Limitations of PET

General Limitations:

- High cost.
- Require large space.
- High training for the operating staff is a must.

Specific Limitations:

- FDG-is a non-specific agent.
- False positive uptake in granulomas.
- Difficult to interpret in areas of normal uptake.
- Depend on glucose transport, that's why not sensitive in mucine & mucinous secreting tumors.