Beaune 2002

NUCLEAR MEDICINE: PET CAMERA for routine diagnostic use

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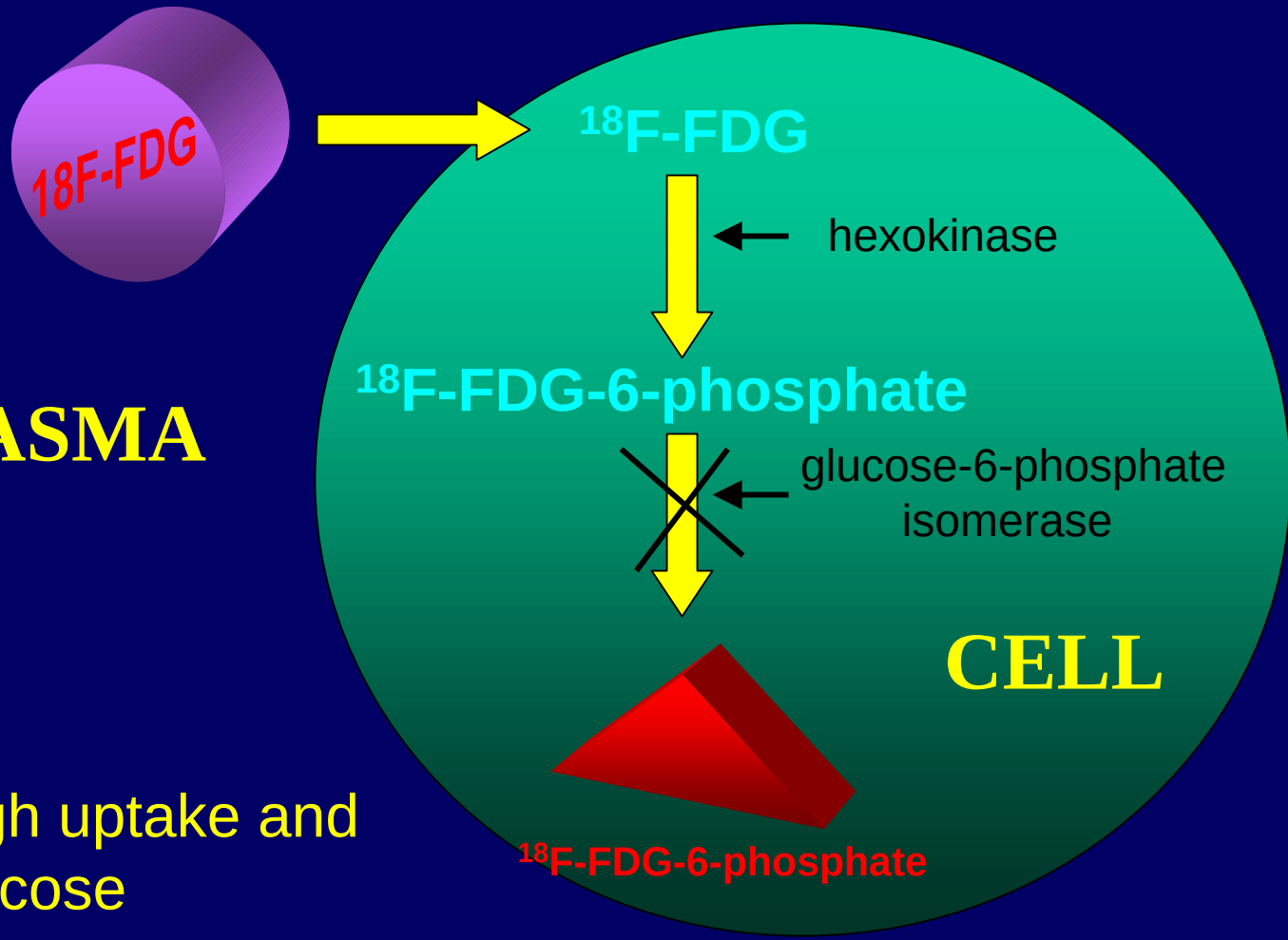
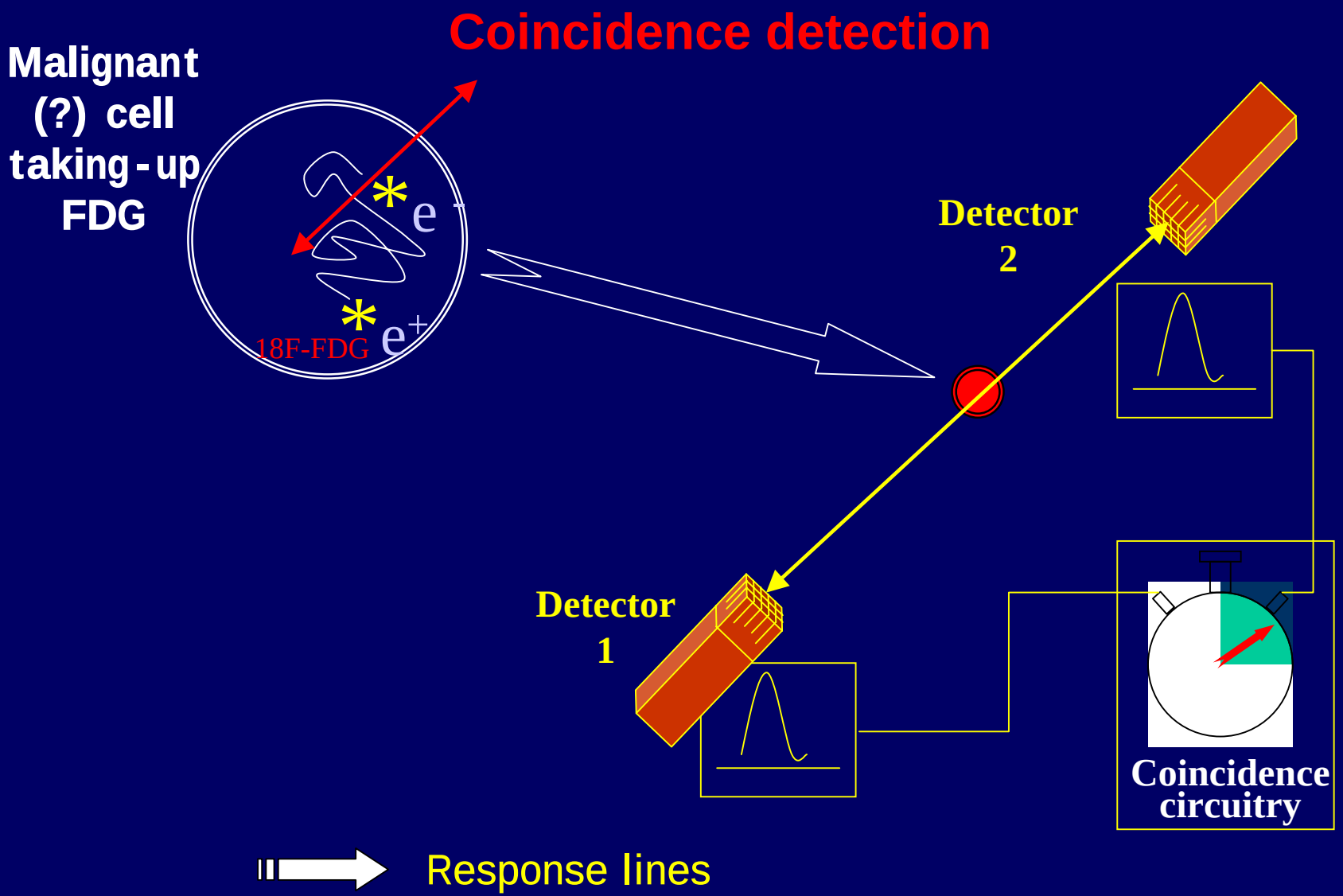
[^{18}F]-FDG, radiolabled analogous of glucose the physiological sugar



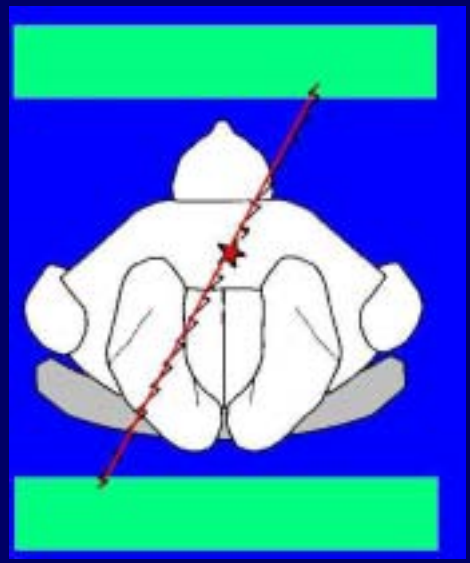
Cancer ➡ high uptake and utilisation of glucose

PRINCIPLE OF PET

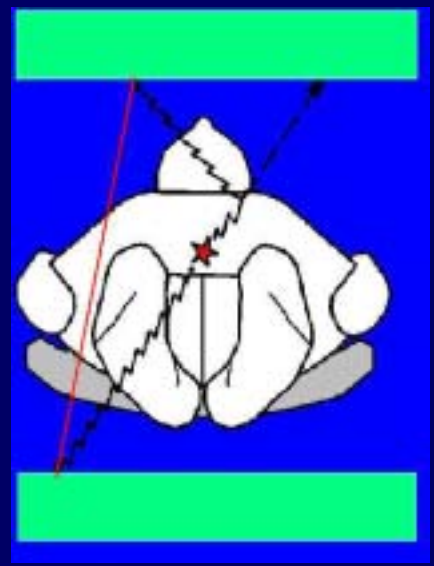


PET DATA ACQUISITION

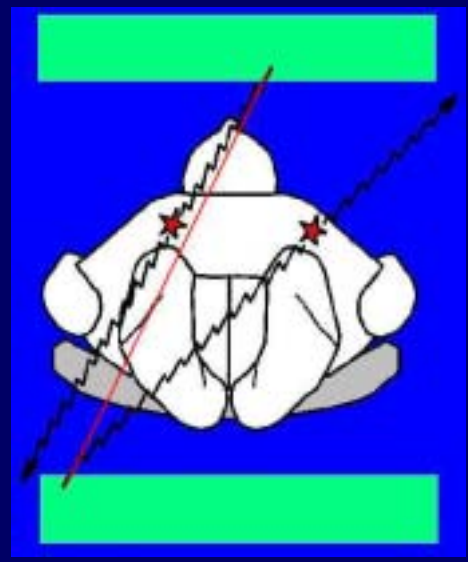
3 types of events may occur



TRUE coincidences



Scattered coincidences



Random coincidences

⇒ SIGNAL / NOISE RATIO

Dual or triple head gamma-camera in 2D coincidence mode (CDET)

- Axis or Irix (Marconi)
- 19 mm Na I (Tl) thick crystals
- axial filters (septa) for 2D mode acquisition
- no attenuation correction by means of an external source

Triple-head gamma-camera (Irix)

ADAC-CPET : dedicated PET machine in 3D mode

- Full ring 25 mm Na I (Tl) thick crystals
- Attenuation correction by an external source
- 2 MBq/kg [18F]-FDG
- 6 min emission + 2 min transmission per bed position
- 6-7 bed positions for imaging the head and the torso (ca 60 min)
- Iterative reconstruction

Why and how to enhance PET imaging performance FOR clinical utility ?

What do clinicians/researchers want?[1]

What can physicists deliver? [2]

answers at bottom of slide

Slide inspired by Joel Karp (physicist)

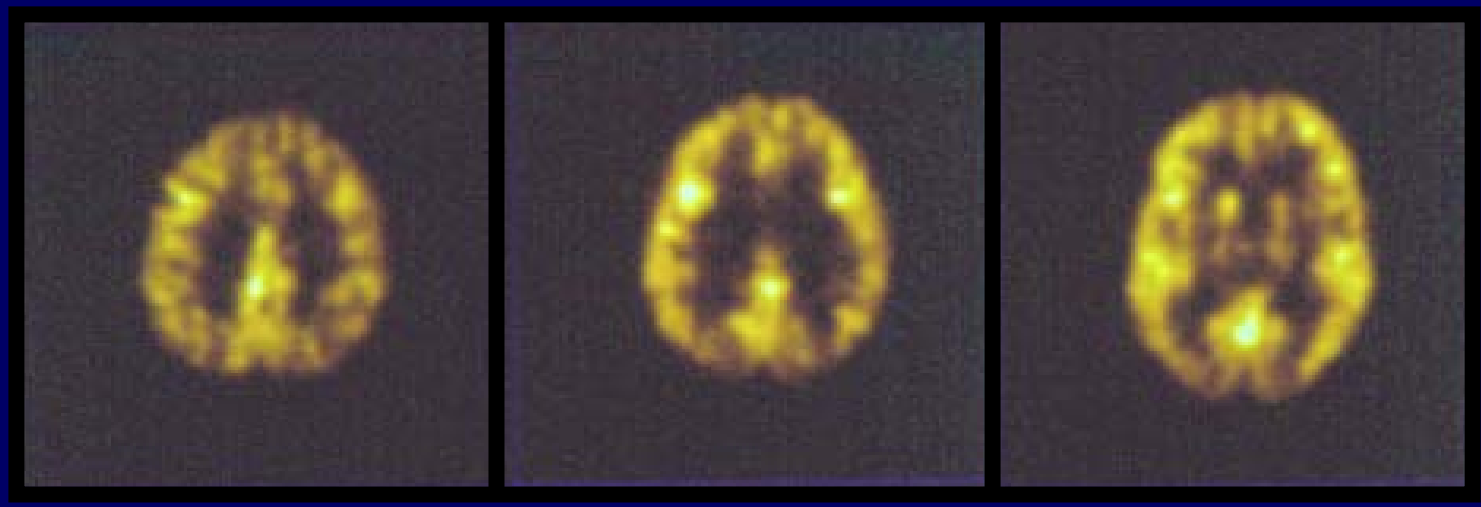
University of Pennsylvania

[1] they want it all

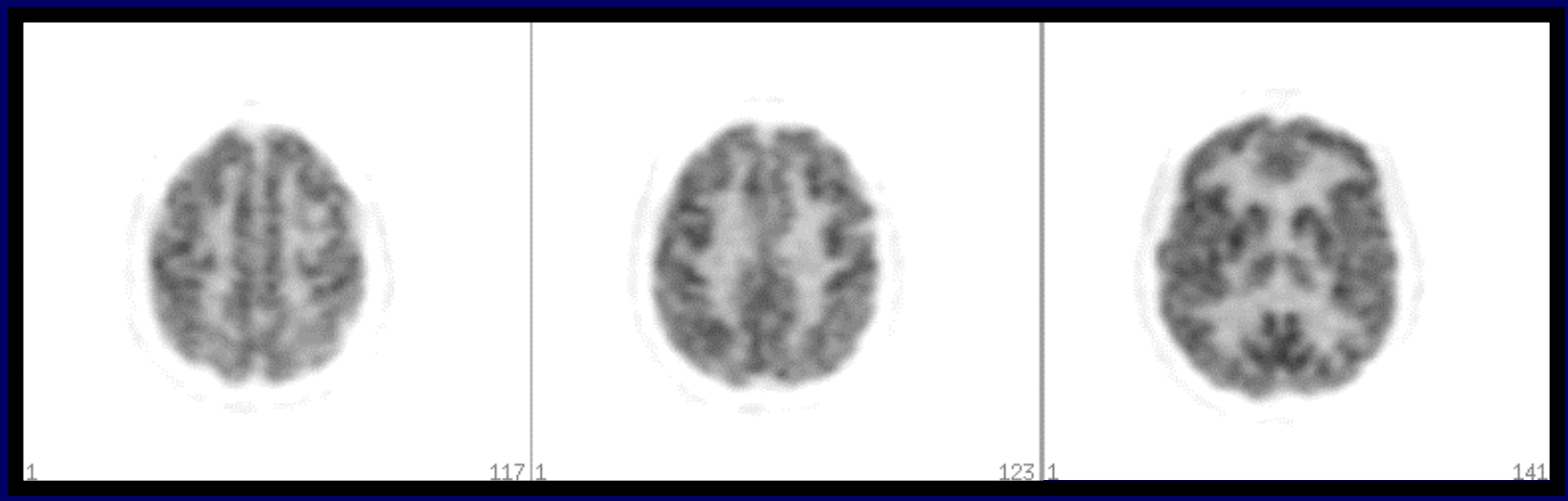
[2] never enough

Image quality in PET continues to improve

Mid 1980's



2001

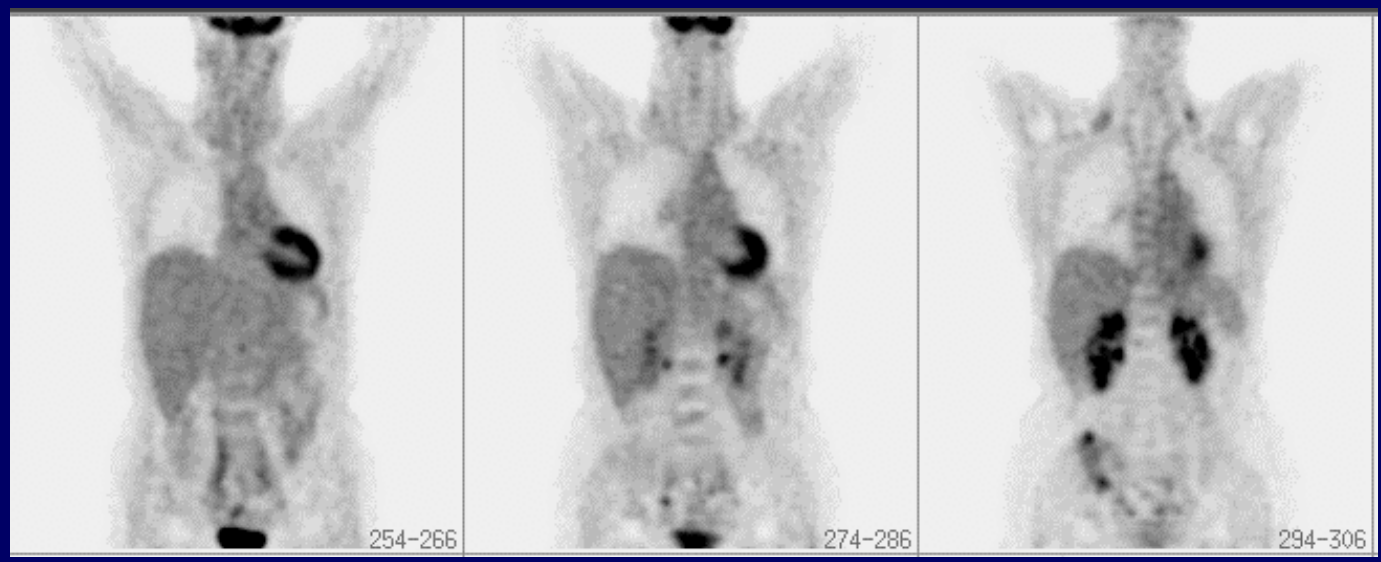


University of Pennsylvania PET Center

Image quality in PET continues to improve

Mid 1980's

2001



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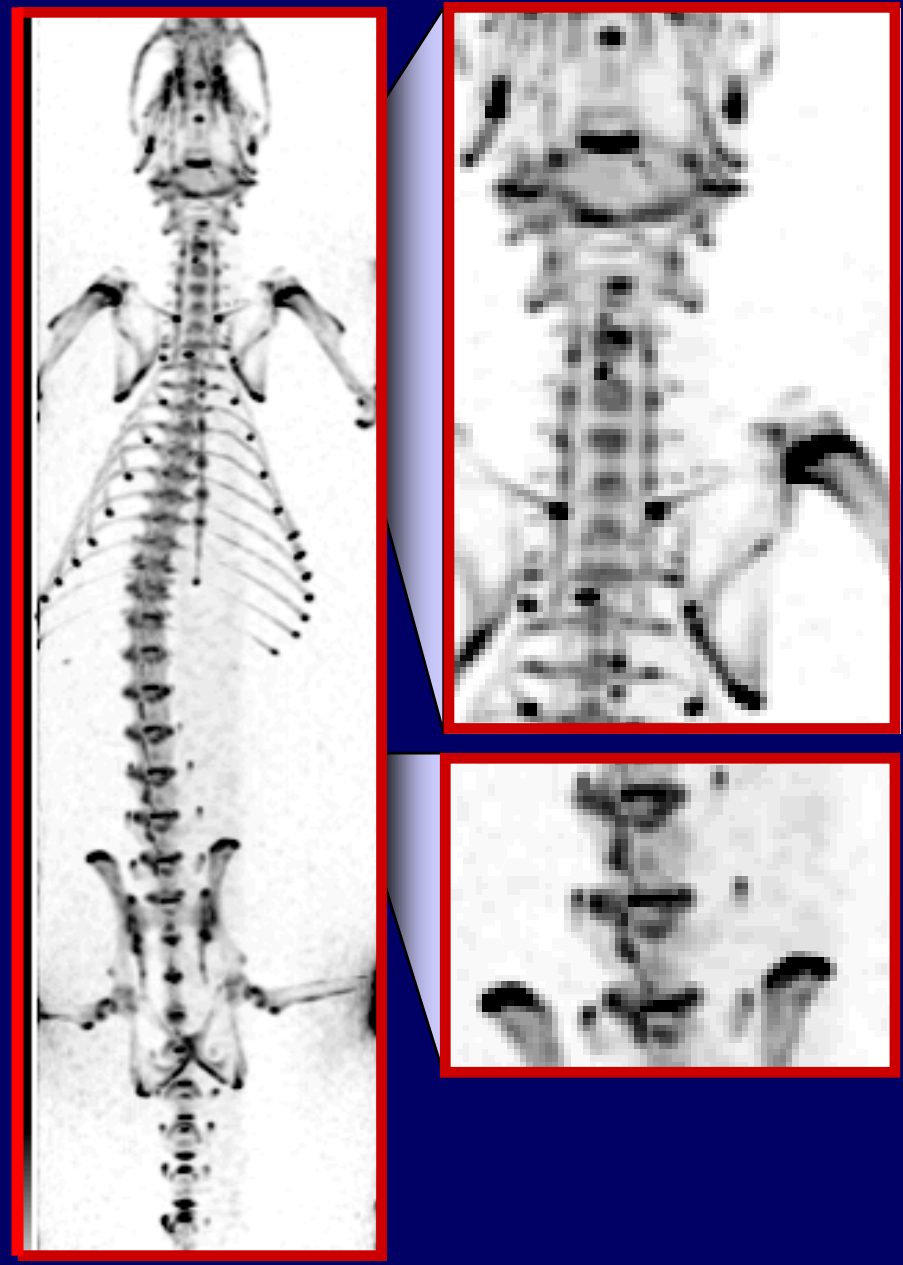
HIDAC Rat ^{18}F Bone Image

17 MBq 18-Fluoride

List mode recon (FAIR)

- 0.5mm voxels
- 1 pass EM
- resolution recovery



Reader AJ et al - UMIST (DIAS), Paterson Institute, & Christie Hospital

Jeavons AP et al - Oxford Positron Systems

Missimer J et al - Paul Scherrer Institute

What are critical design/performance parameters for small animal imaging?

- Transverse FOV : 11 to 30 cm
- Axial FOV : < 2 to 28 cm
- Sensitivity : < 1 to 4% (point source)
- Energy resolution : < 15% to > 25%
- Spatial Resolution : < 1 mm to 3 mm

- Data corrections : scatter and attenuation
- Reconstruction : FBP vs. iterative (modeling)
- Cost : $100k to $800k ??

Can technology developed for animal scanners be applied to human PET scanners - research or clinical purposes?

Clinician's wish list

- Image quality, Image quality, Image quality
  spatial resolution, contrast, low noise
- Short scan time
  patient comfort, patient throughput
- Low cost
  facilitate purchase of new equipment
- Reliability in an hospital environment
  minimise down-time, uniform QC
- PET/CT for anatomical localisation of foci and accurate attenuation correction
  increase confidence of lesion detectability

Researcher's wish list

- Everything the clinician wants
  (see previous slide)
- Accurate quantification
  dynamic imaging capability

Physicist's to-do list

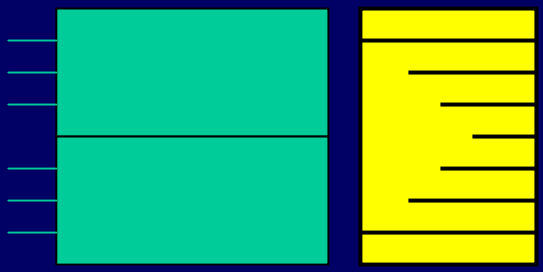
- Crystal size/PMT configuration
  1-to-1 crystal:PMT -> encoding schemes
- Better (faster) scintillators
  BGO, NaI(Tl) -> LSO, GSO
- Scanner design/geometry
  2D -> 3D (no septa)
- Data corrections/image reconstruction
  scatter and randoms correction
  attenuation corr. w/ post-injection transmission scan
  filtered backprojection -> iterative reconstruction

Decreasing crystal size/PMT size

1:1 crystal:PMT coupling

Wash. U. PET III (1976)
50 x 50 x 75 mm^3 NaI(Tl)
50 mm PMT

LBL Donner 600 (1985)
3 x 10 x 30 mm^3 BGO -1 ring
14 mm PMT



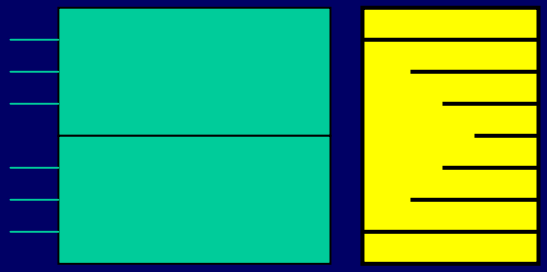
Block Detector *1985 Casey, Nutt*

CTI EXACT / Accel
8 x 8 array BGO/LSO
6.4 x 6.4 x 20 mm^3
25 mm PMTs (4)

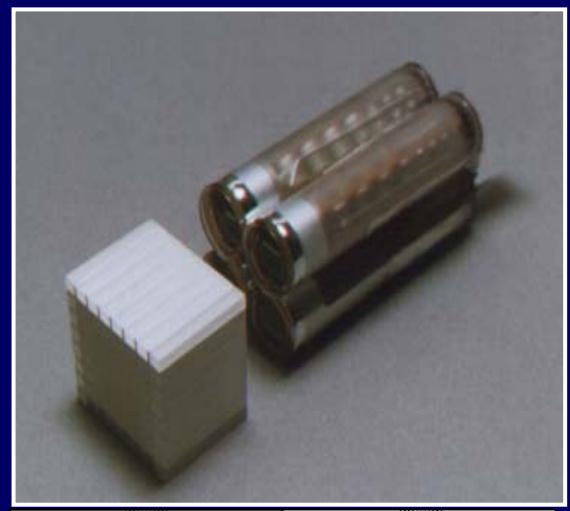
CTI HR+
8 x 8 array BGO
4 x 4 x 30 mm^3
19 mm PMTs (4)

MDAnderson - Quad Share
7 x 7 array BGO
2.7 x 2.8 x 30 mm^3
19 mm PMTs (4)

DETECTOR BLOCKS



[Casey *et al.*, 1985]



CTI HR+

8 x 8 array BGO

4 x 4 x 30 mm^3

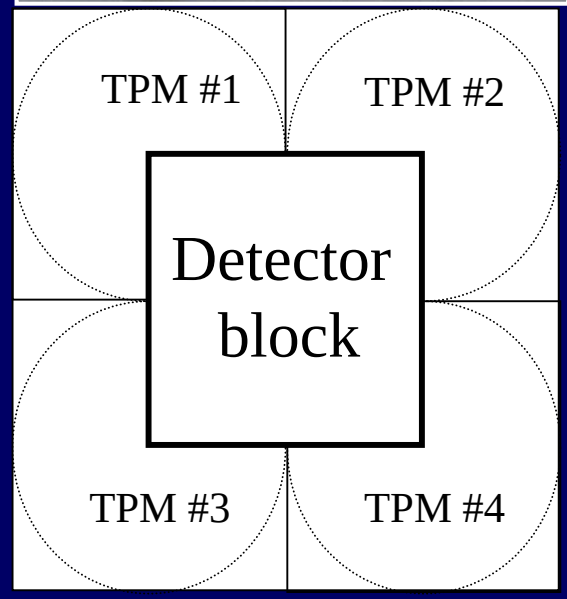
TPM 19 mm (4)

CTI Accel

8 x 8 array LSO

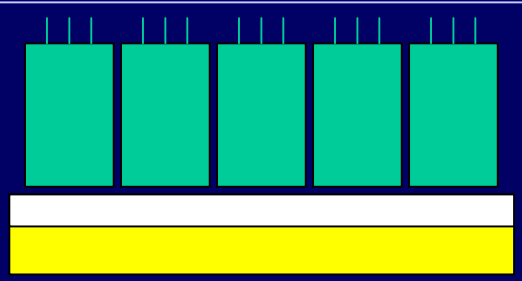
6,4 x 6,4 x 20 mm^3

TPM 25 mm (4)



Partage quadratique

Position encoding with larger PMTs



Continuous detector - Anger camera

U. Chicago / Searle (1976)

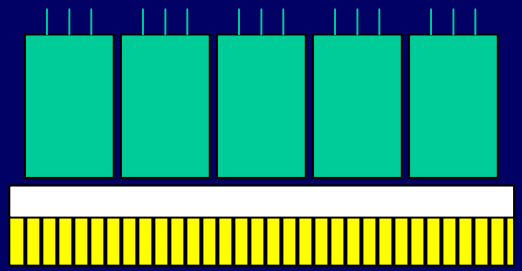
25 mm-thick NaI(Tl) camera

75 mm PMT

Penn-PET / C-PET (1983-present)

500 x 300 x 25 mm^3 NaI(Tl)

50-62 mm PMT



Discrete crystals/optical coupling

MGH PCR I-II (1983 - 1988)

I: 4 x 20 x 30 mm^3 BGO

II: 3 x 5.6 x 30 mm^3 BGO

14-20 mm PMT

Penn G-PET / ADAC Allegro (2001)

4 x 4 x 10 mm^3 GSO

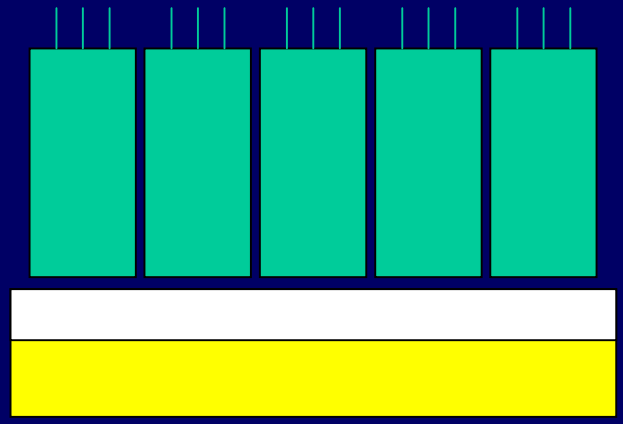
4 x 6 x 20 mm^3 GSO

39 mm PMT

CONTINUOUS DETECTORS

CDET

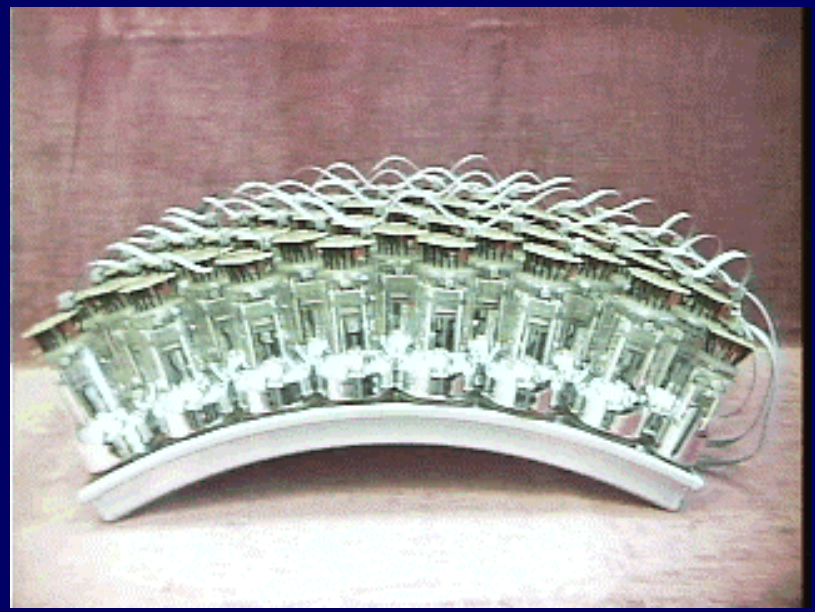
NaI(Tl) 16- 25 mm thick



C-PET ADAC-UGM

NaI(Tl) 500 x 300 x 25 mm³

TPM: 50-62 mm



Comparison of scintillators for PET

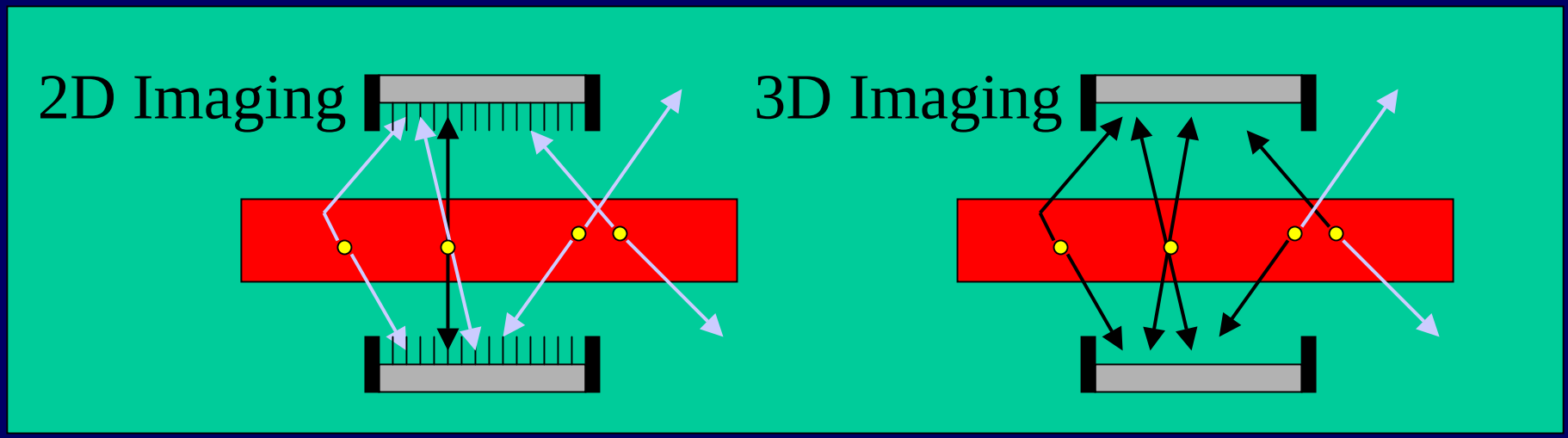
	NaI(Tl)	BGO	LSO	GSO
• Cost	$	$$	$$$	$$$
• Stop power (1/cm)	0.34	0.91	0.81	0.67
• Decay time (ns)	240	300	40	60
• Light output	100%	15%	75%	30%
• Energy Resol.*	7%	14%	12%	9%

* assumes full light collection

Measured energy resolution at 511 keV

Depends on light output ***and*** intrinsic scintillator resolution

2D (septa) vs. 3D (no septa)

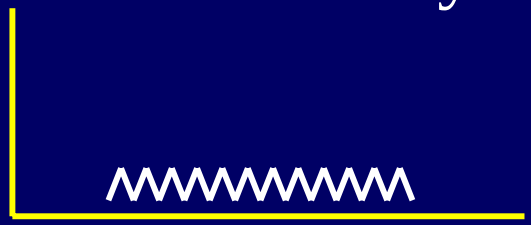


Low Scatter fraction ~ 10%
with poor ΔE/E ~ 25%

High Scatter fraction ~ 30%
with good ΔE/E ~ 10%

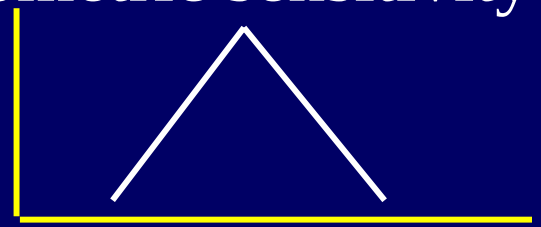
Low geometric sensitivity

2D

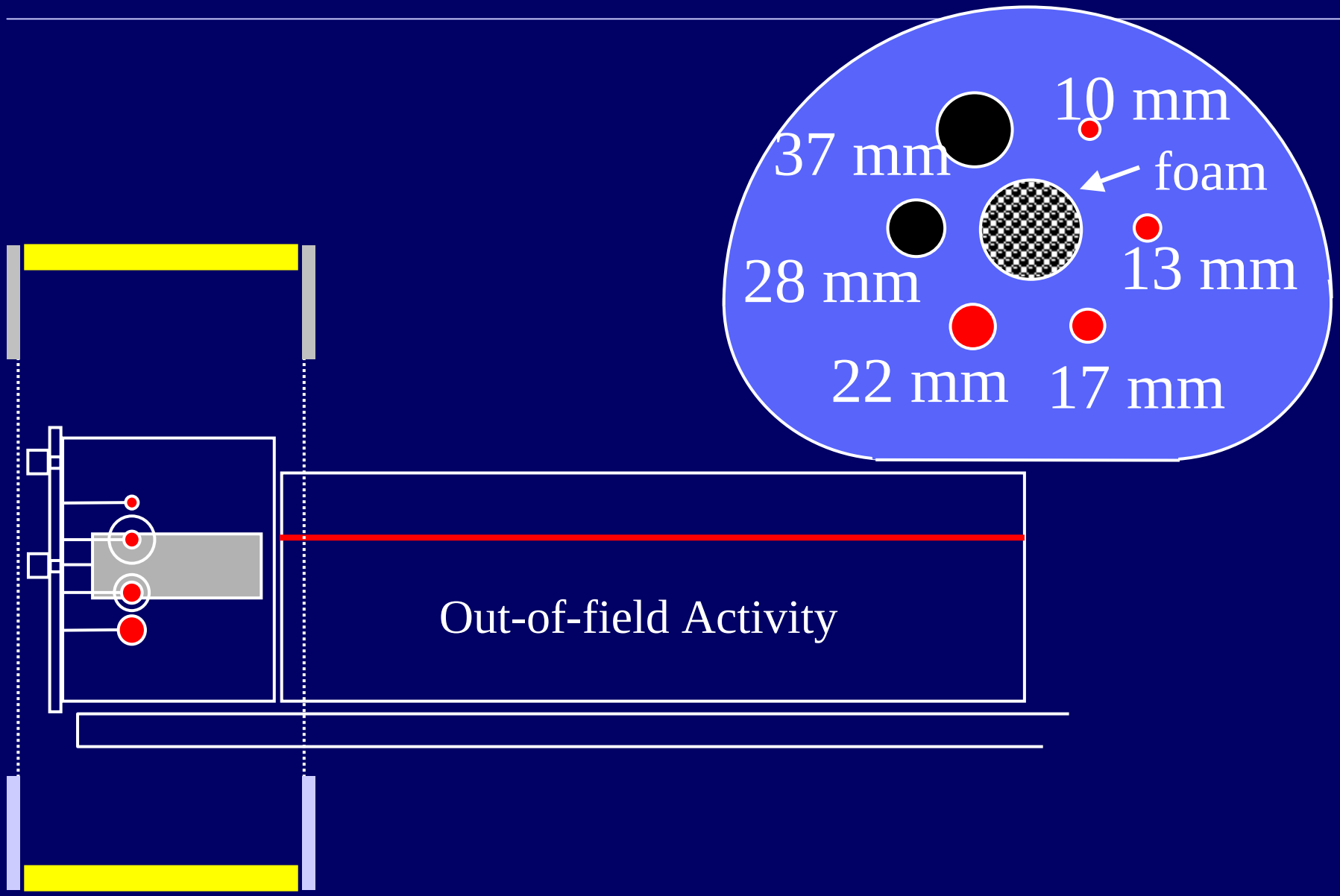


High geometric sensitivity

3D



NEMA NU2-2001 Image Quality Phantom



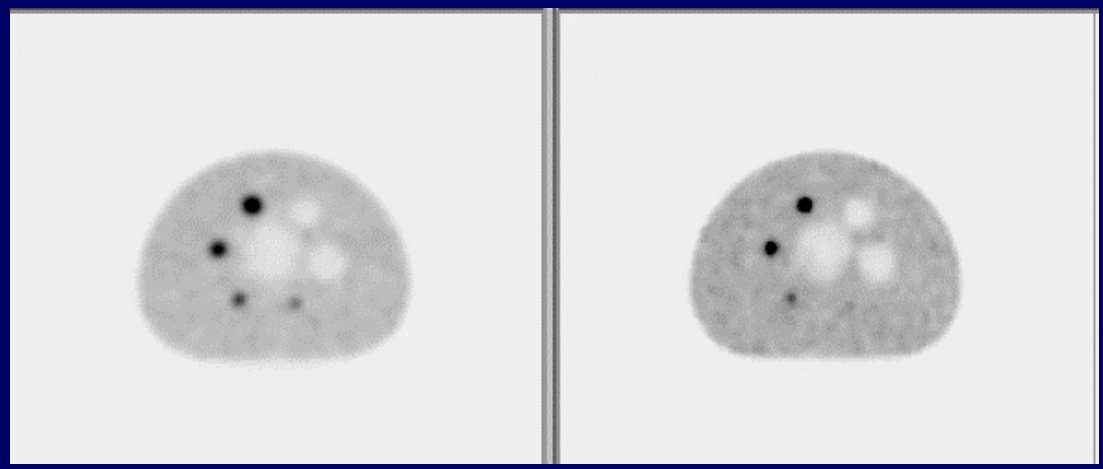
Can we qualitatively assess image quality - lesion detectability?

NEMA NU2-2001 Image quality phantom (IEC)

hot spheres : 1.0-cm, 1.3-cm, 1.7-cm. 2.2-cm
cold spheres : 2.8-cm, 3.7-cm

Em: 4 min

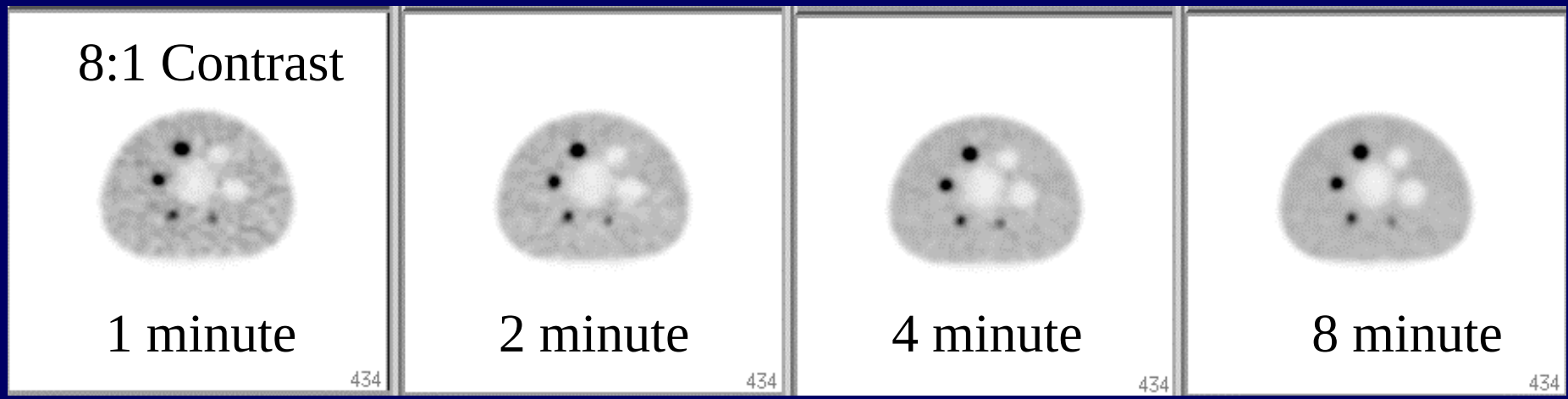
Tx: 40 sec

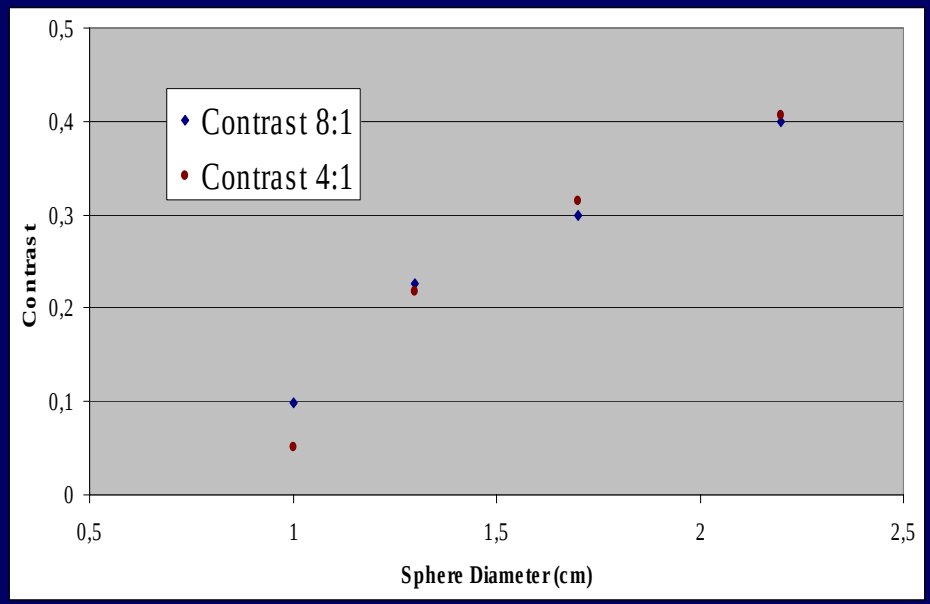


8:1 contrast 4:1 contrast

Background 4 kBq/mL

Can we quantify lesion uptake?





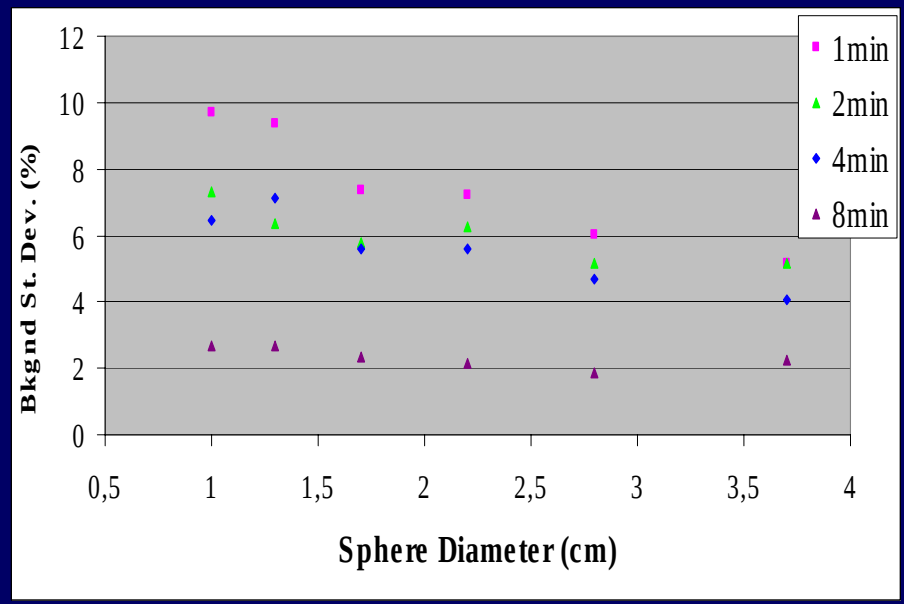
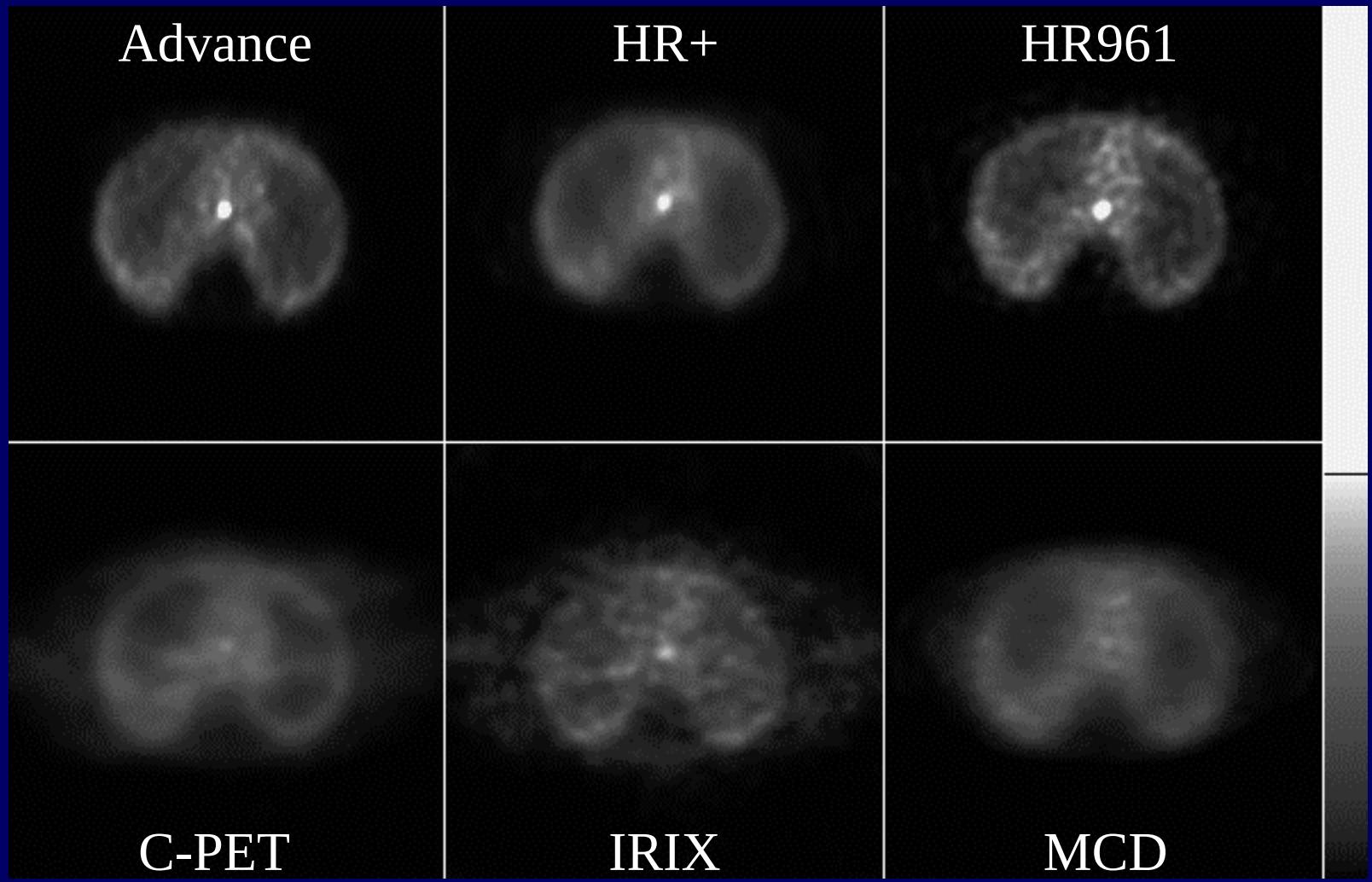


IMAGE QUALITY of various PET machines. Phantom study

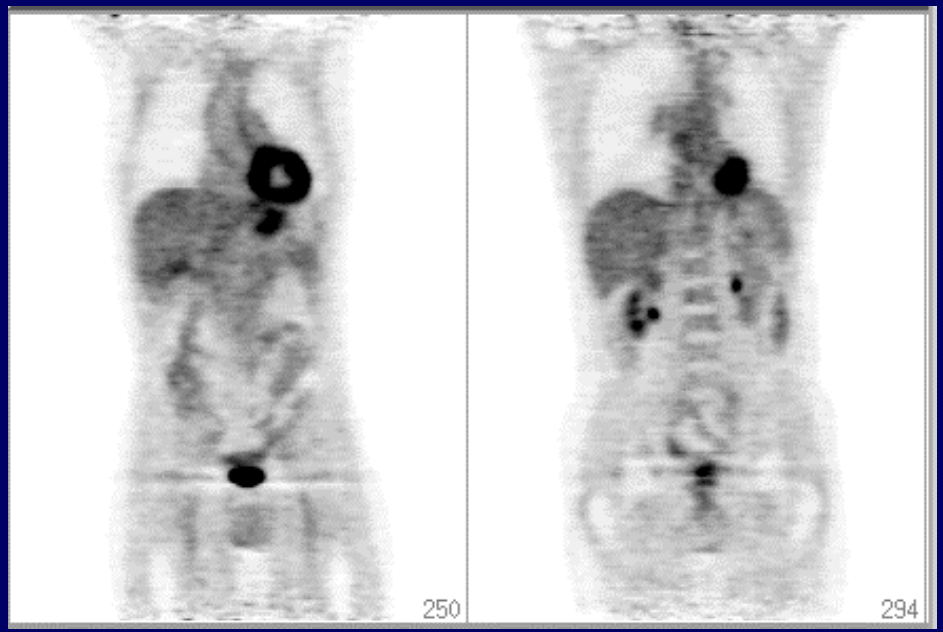


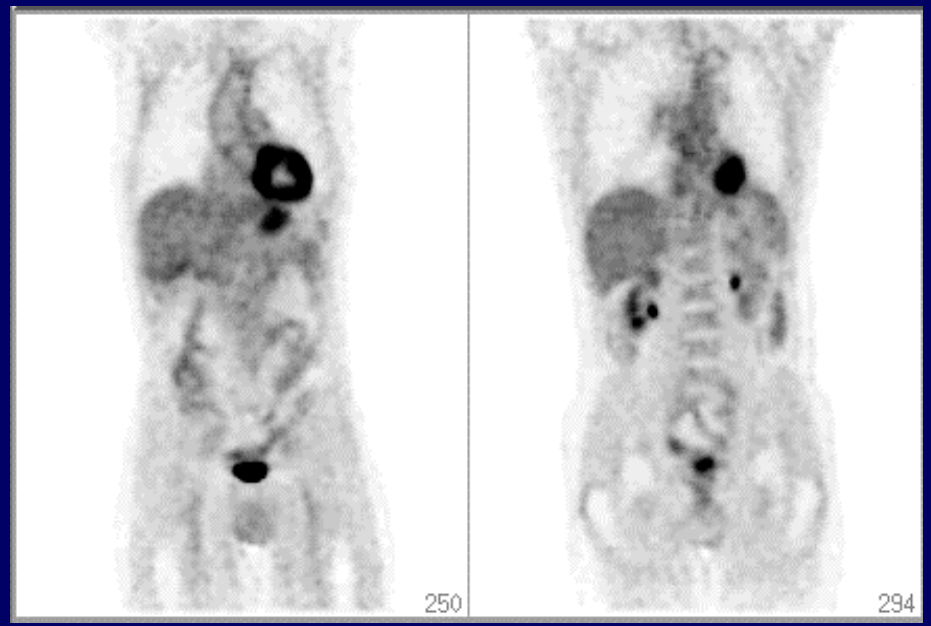
[Kadmas *et al.*, 2001]

Fully 3D Iterative Reconstruction improves image quality

FORE +
2.5D RAMLA

3D RAMLA





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ADAC Allegro scanner

Data Corrections

- Scatter correction : *10% (2D) to 30-60% (3D)*
  model-based, convolution, energy window, tail-fit
- Randoms correction : *limits injected activity in 3D*
  delayed coincidence, singles calculation, tail-fit
- Attenuation correction : *5x (brain) to 30x (body)*
  coincidence rod source, singles point source, CT
  post-injection Tx scan protocol (~1 hour FDG uptake)
  image segmentation to reduce scan duration

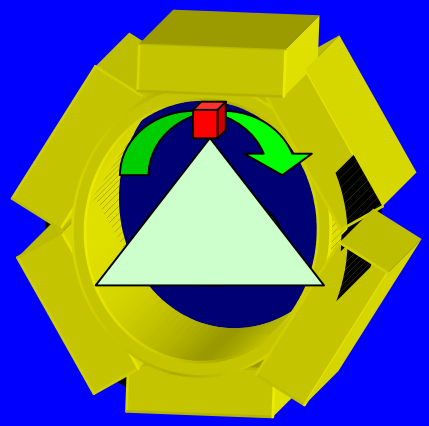
Why do we need attenuation correction?

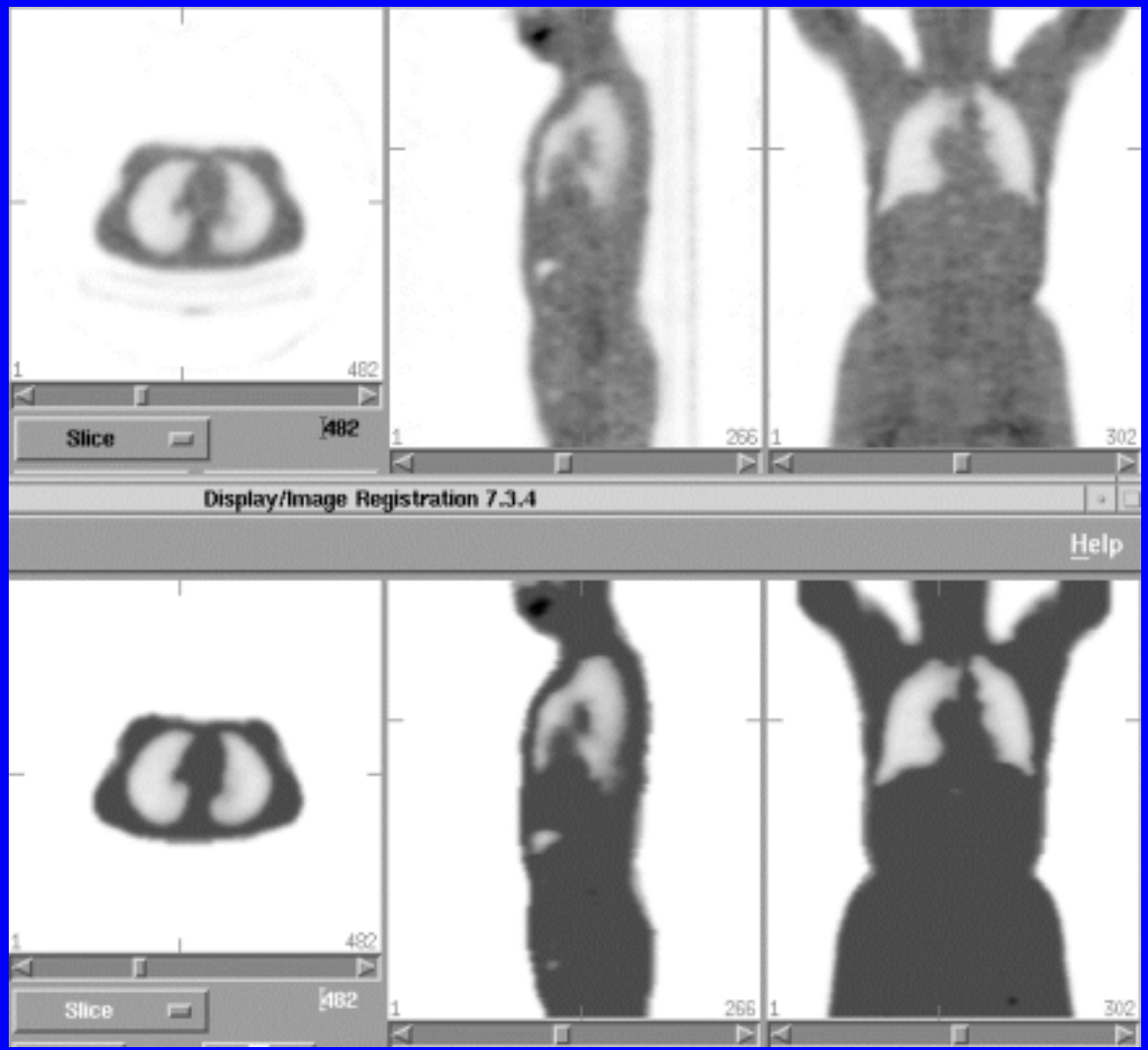
- More accurate activity distribution
  uniform liver, 'cold lungs'
- Improved lesion detectability
  deep lesions
- Reduce image artifacts and streaking
  reconstruct using consistent data
- Improved image quality with iterative reconstruction
  include attenuation into model

But…attenuation correction must be

FAST - compared to emission scan
ACCURATE - e.g. near lung boundary
LOW NOISE - minimize noise propagation

ATTENUATION CORRECTION





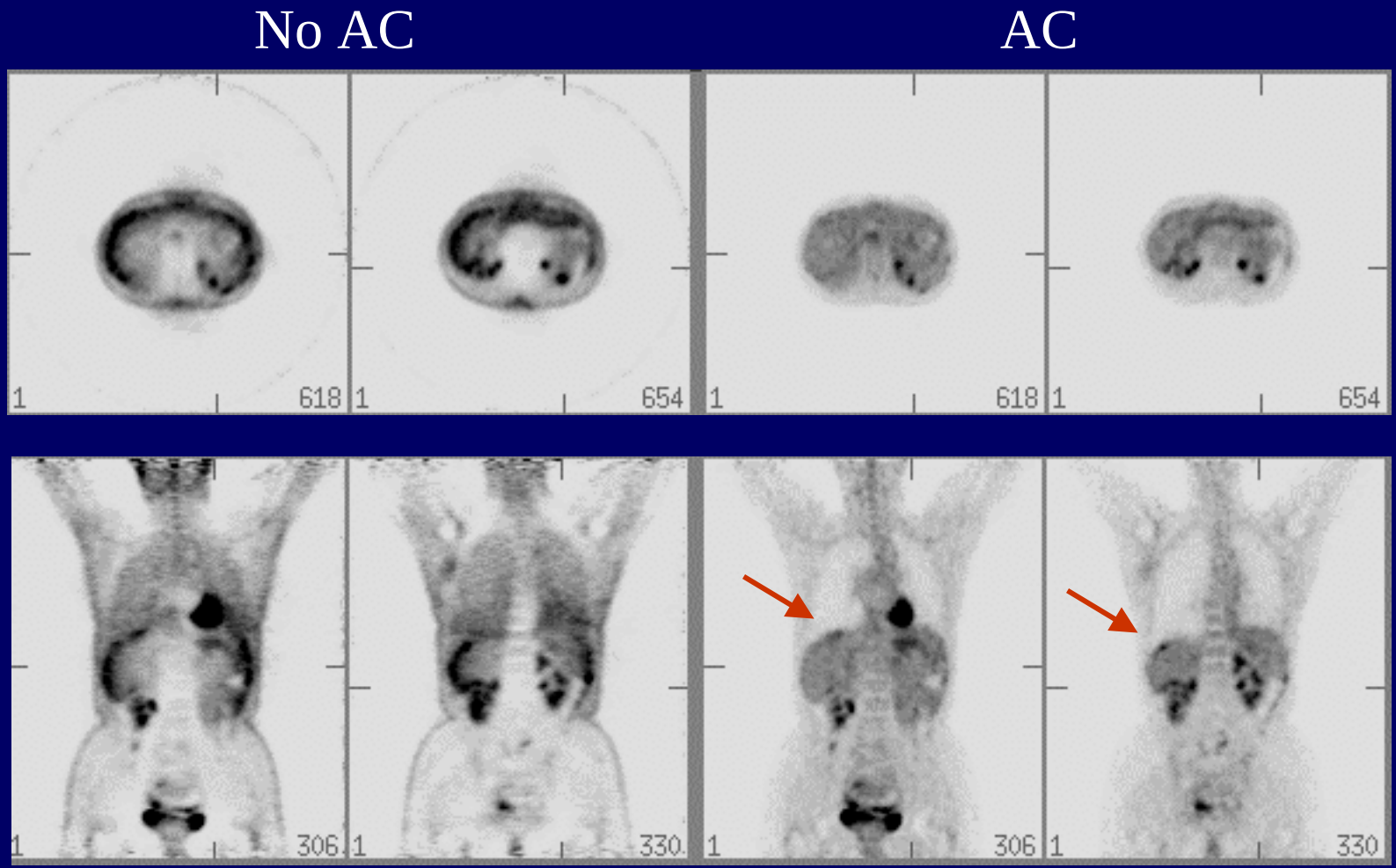
ADAC Allegro

750 MBq ^{137}Cs

Tx:

40 s acquisition/bed position

Attenuation correction - increased confidence of liver lesion



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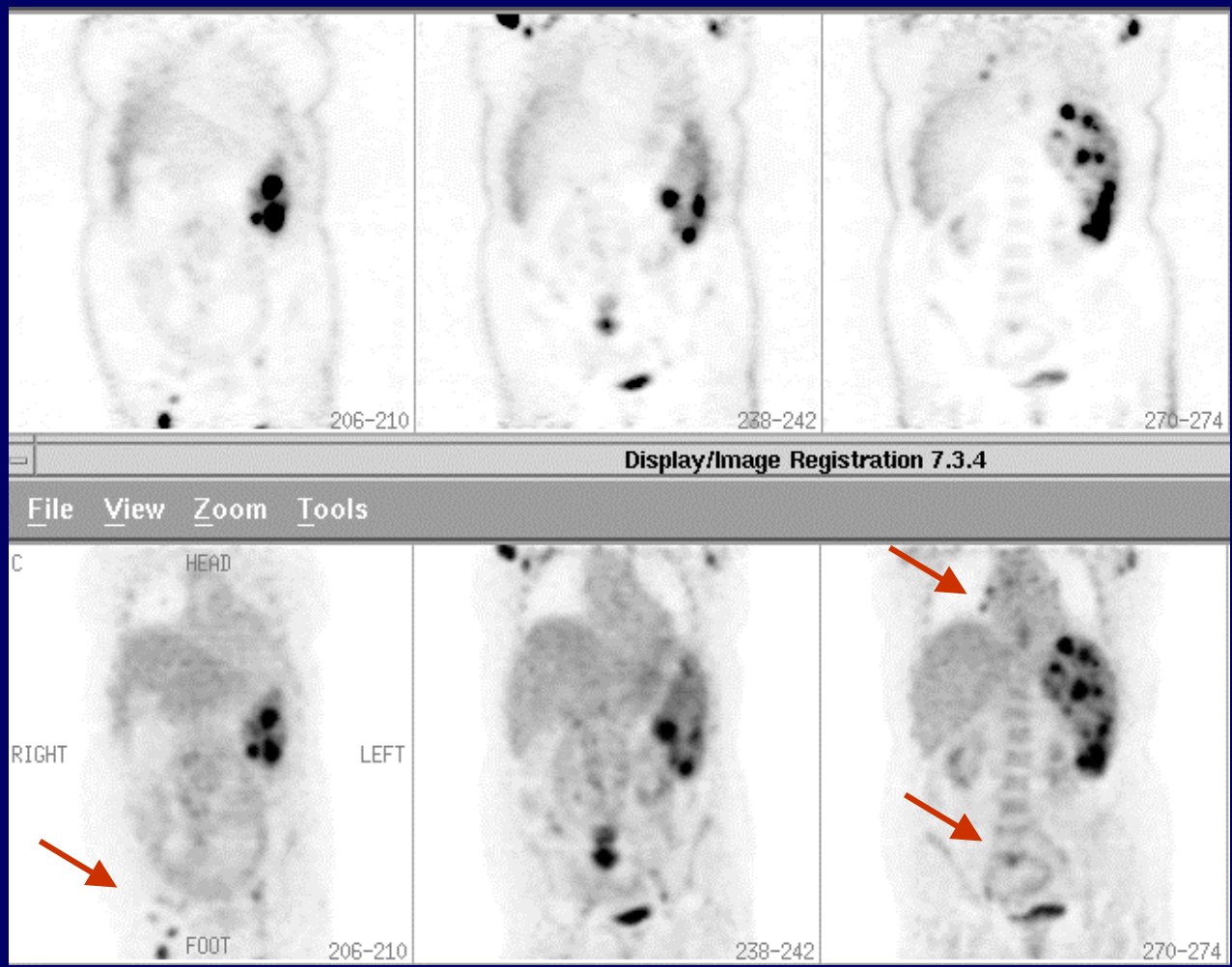
ADAC Allegro

Attenuation correction - improved overall lesion detectability : *lung, groin, spine*

No AC

AC



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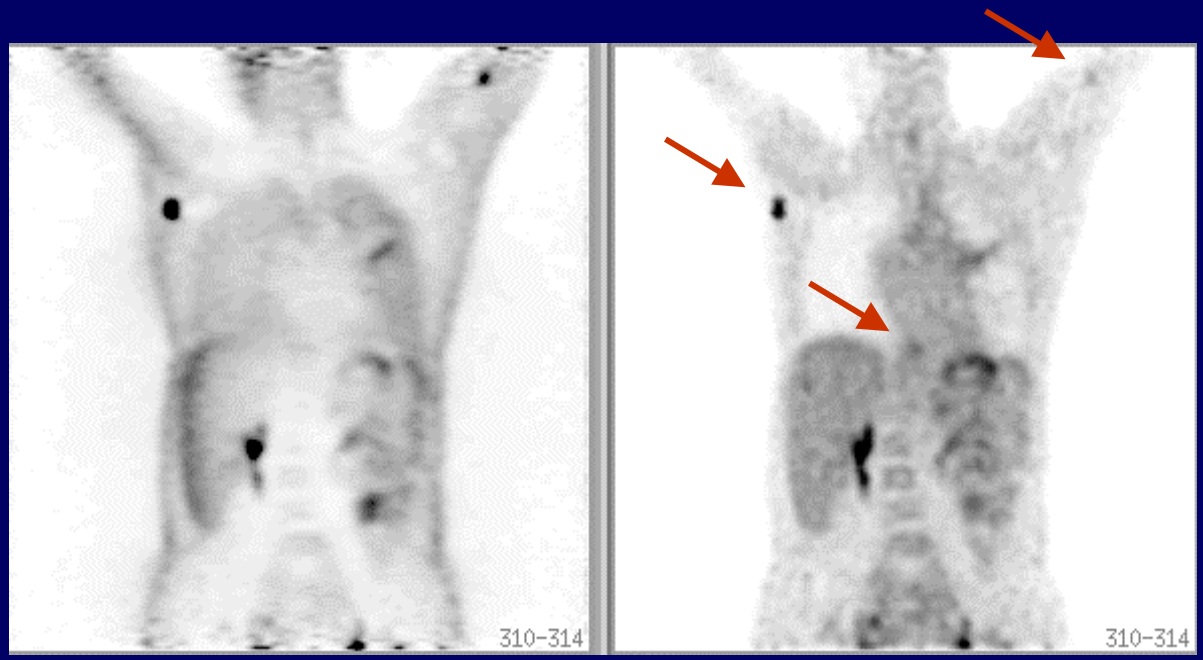
ADAC Allegro

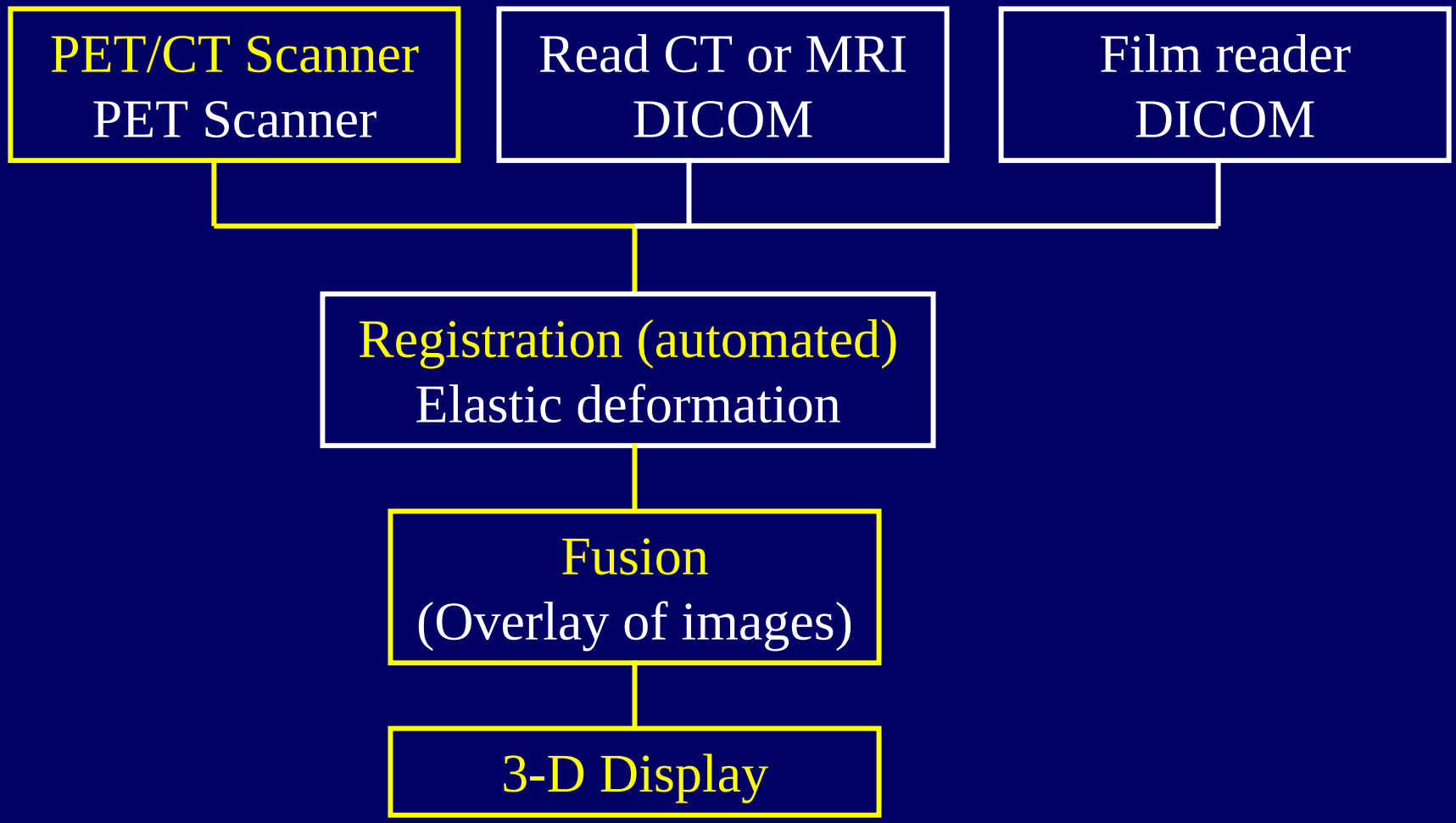
Attenuation correction - better comparison of relative activity of deep (mediastinum) vs. superficial (axilla) lesions

No AC

AC



Multimodality Imaging - PET/CT



Is the PET/CT instrument needed for all PET studies, or only specific applications (e.g. radiation treatment planning)?

PET/CT Scanner or Import Images?

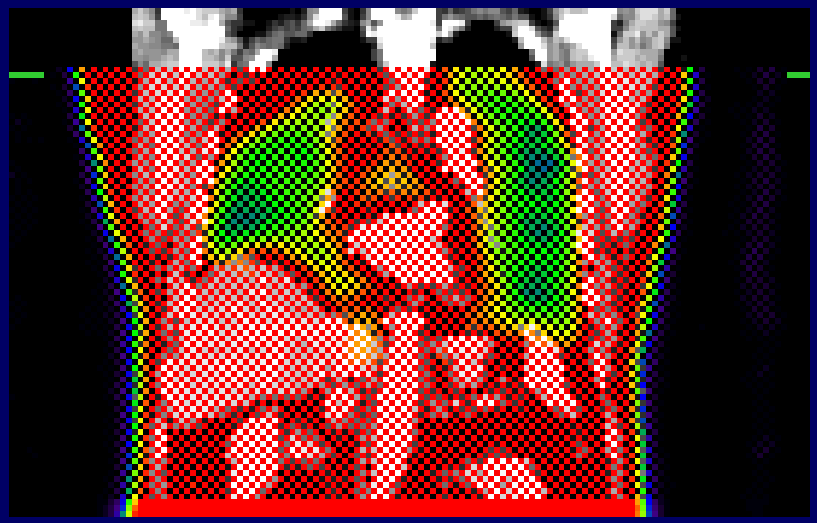
- Technical Issues - Import Images:
  - Fetch and display of 2 images is non-trivial
  - Requires more sophisticated registration - *non-rigid*

- Technical Issues - PET/CT
  - Can't overlay MRI
  - CT - breath-hold? arms up?
  - CT - diagnostic quality? or only for registration?
  - PET - design trade-offs, e.g. shielding, patient port
  - PET Tx - replaced by CT for attenuation correction?
  - Is non-rigid (elastic) registration still required?

Rigid-body registration can’t compensate for body shape deformation

Elastic Deformation - why we need it:

- CT performed with breath holding
- CT usually performed with arms up
- Bladder will fill between PET and CT



The arms were raised higher in the CT scan compared to the PET scan

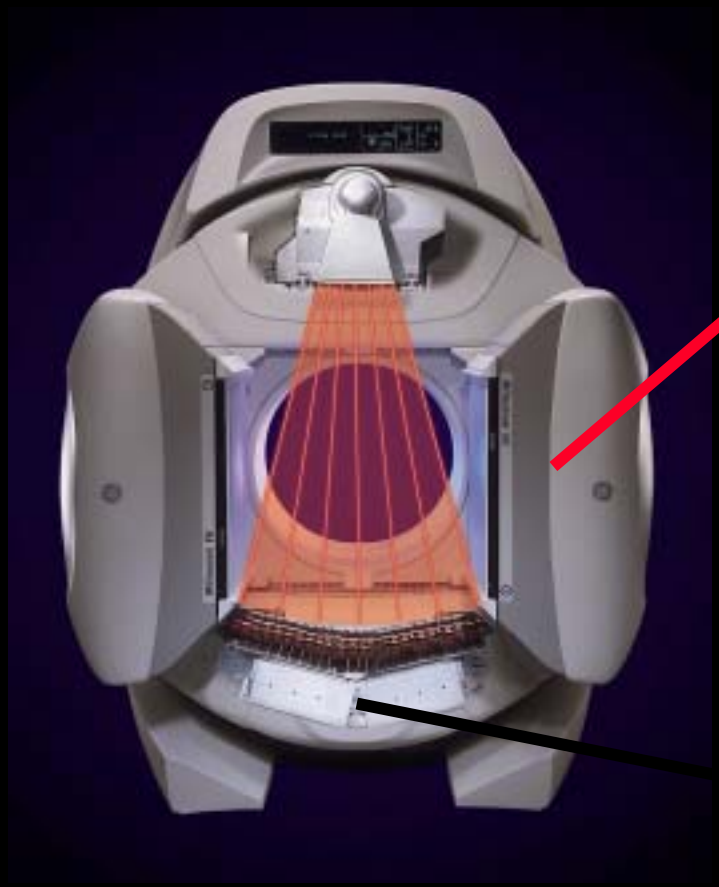
Near-term directions for PET imaging

- Short emission acquisition times (~20 min)
  - Step-and-shoot (7-8 positions)
  - Continuous bed motion
- Very short transmission scan (< 2 min)
  - Continuous, spiral acquisition - PET Tx or CT
- Better visualization of small tumors
  - Smaller crystals
  - More counts
  - Better energy resolution - reduction of scatter, randoms

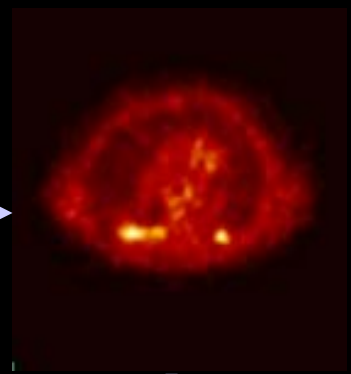
Near-term directions for PET imaging

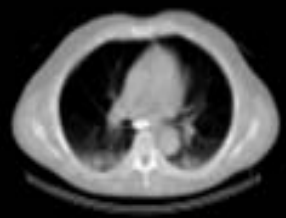
- Faster, fully 3D image reconstruction
  - Iterative algorithms with system modeling, priors
  - Increasing number of LORs -> list-mode reconstruction
- Combined instruments for multi-modality imaging
  - PET/CT; human *and* animal
  - Non-rigid, elastic matching algorithms
- Improved accuracy of quantification (research)

HYBRID CDET/CT MACHINES

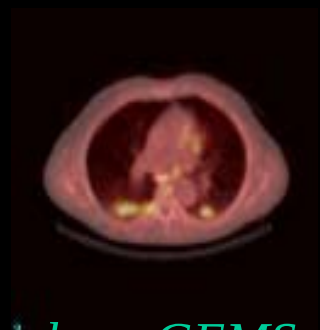


Attenuation Correction



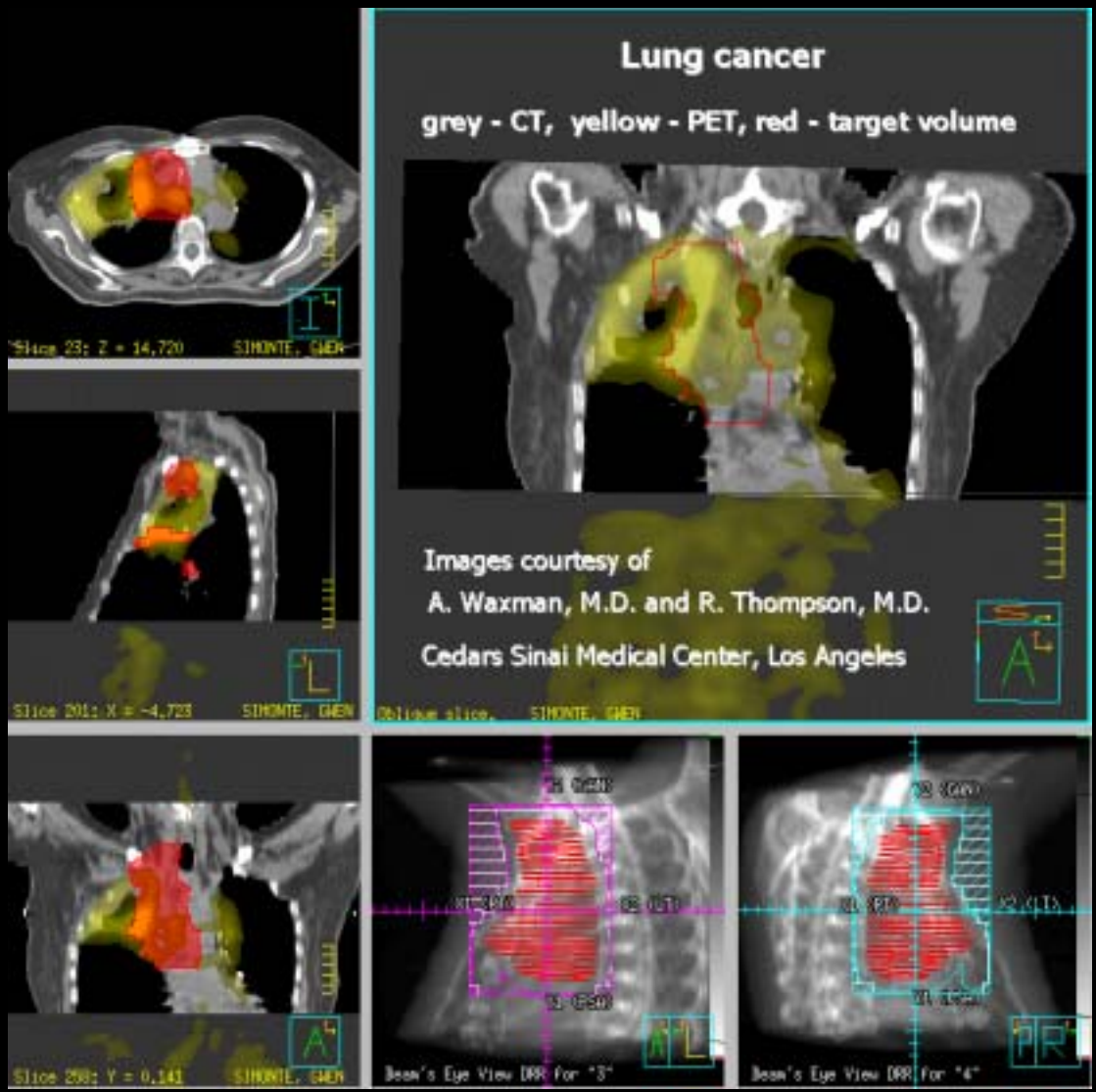


Inherent Image Registration



Hawkeye,GEMS

HYBRID PET/CT MACHINES:
Radiation therapy treatment planning



compare:

red area:
CT-based target volume

yellow:
metabolically active tissue determined by FDG-PET (cancer)

Without the metabolic information from PET therapy planning is not optimal.

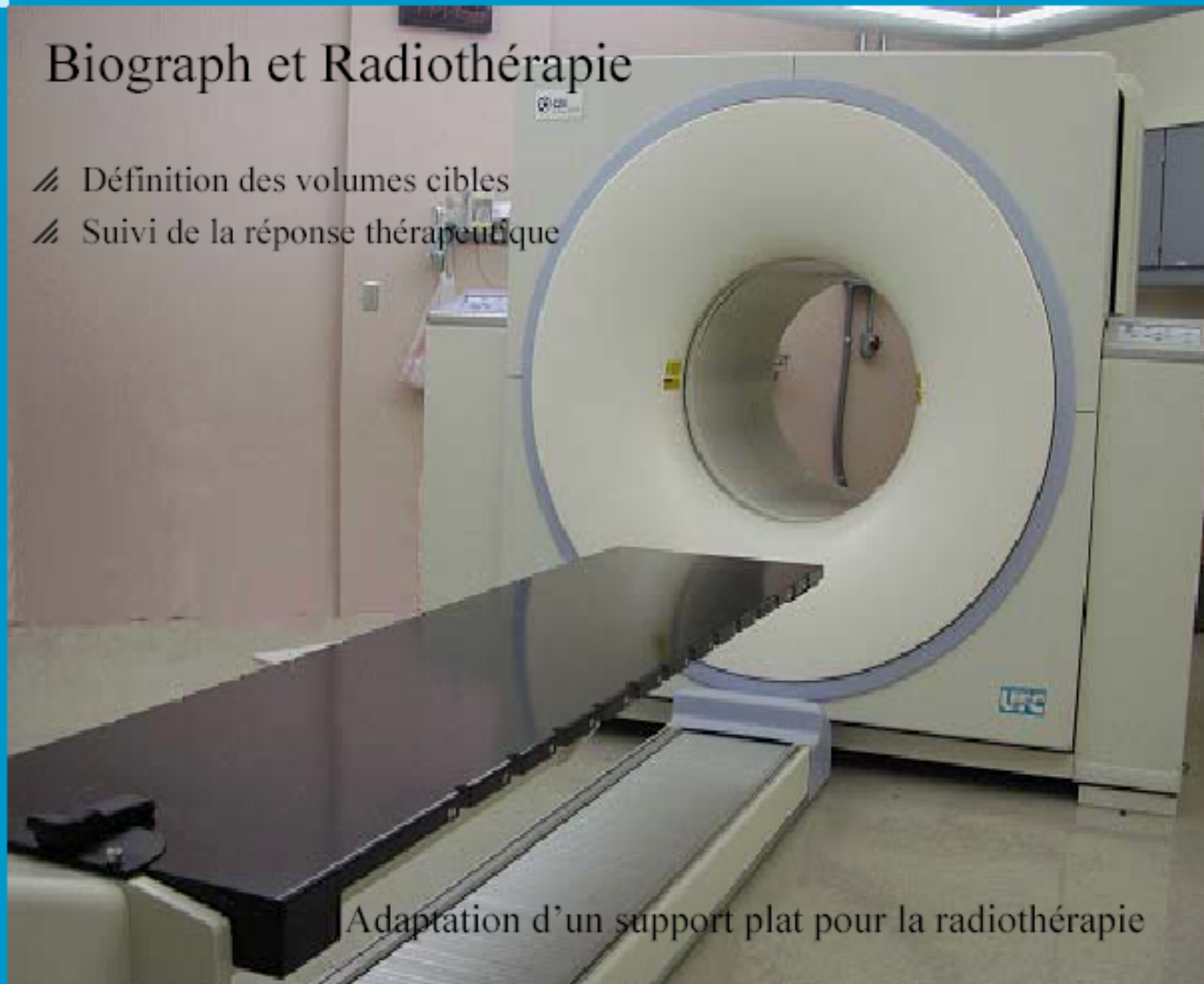
Direct connectivity between ADAC Pinnacle RTP system and ADAC PET systems.

Gemini,PMS

SIEMENS

Biograph et Radiothérapie

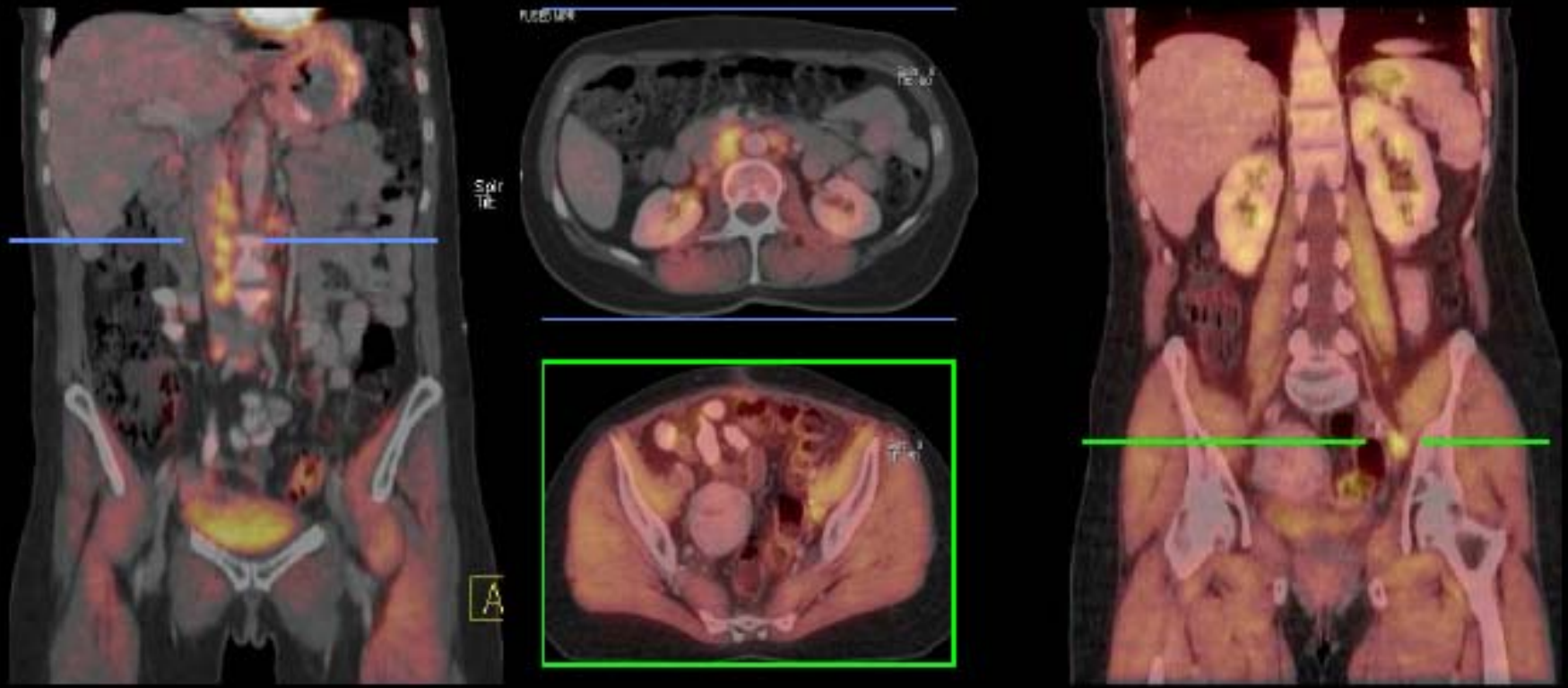
- Définition des volumes cibles
- Suivi de la réponse thérapeutique



Adaptation d'un support plat pour la radiothérapie

PET/CT Staging and IMRT of Cervical Cancer

Résultats: Fixation de plusieurs nodules para-aortique et d'un nodules distant sur le bassin.

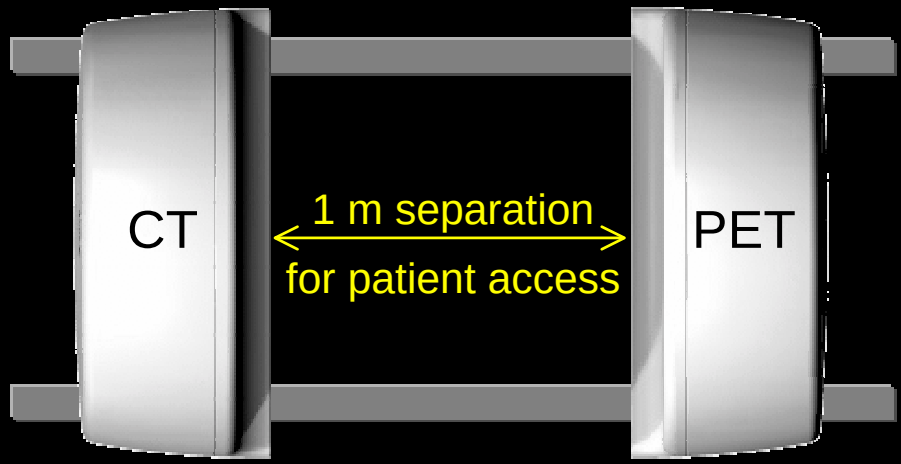


HYBRID PET/CT MACHINES: Interventional imaging

Example: Identify active lymph node using PET – biopsy using CT.

Integrated Operation
(CT/PET Imaging)

Separated Operation
(Independent CT imaging)



Gemini,PMS

Clinician's criteria for clinical utility when comparing to other modalities

- Longer patient survival or disease free survival
  almost impossible to assess for a diagnostic procedure
- Impact on staging or modification of therapeutic attitude
  assessed by the referring clinician
- Better detection of actual lesions
  Sensitivity : True positive / malignant
- More secure affirmation of the absence of disease
  Specificity : True negative / non malignant

Clinician's criteria for clinical utility when comparing to other modalities

In a large number of cancer clinical settings

- FDG-PET has been demonstrated to have a better sensitivity (delineation of actual malignant foci) than "conventional" imaging
- FDG-PET has also been demonstrated to have a better specificity than conventional imaging
- But few studies have been published to evaluate the clinical impact of FDG-PET on staging the patient and on his clinical management (therapeutic decision making).

Clinician's criteria for clinical utility when comparing to other modalities

That is why our team undertook a survey of the clinical impact of FDG-PET in oncology

- By means of a questionnaire that has been validated in California
- filled by the referring clinician of our cancer patients referred for FDG-PET during year 2000
- to evaluate the rate of changes in patient's staging and/or in clinical management induced by FDG-PET

Questionnaire

INFLUENCE DE LA TEP AU FDG SUR LA DECISION THERAPEUTIQUE EN CANCEROLOGIE

Identification du patient : Nom : _____ Prénom : _____ Date de naissance : _____
Cancer primitif : _____ Date de découverte (ou de premier traitement) : _____

ETAT AVANT L'EXAMEN TEP

Répondre à chacune des trois premières questions et éventuellement la 4ème, en entourant la réponse correspondant au cas du patient pour les questions 2) 3) et éventuellement 4) :

1) Stadification TNM (ou classification selon Dukes ou grade). Si non évalué mettre « ? » :

2) Sans le résultat de la TEP, comment traiteriez-vous le patient ?
a) Traitement médical
b) Chirurgie
c) Radiothérapie
d) Pas de traitement

3) Pourquoi souhaitez-vous disposer de la TEP ?
a) Stadification plus précise
b) Caractérisation d'une tumeur (bénigne ou bien maligne)
c) Surveillance d'un traitement
d) Suivi de la maladie

4) Si et seulement si vous avez répondu d) à la question 3, préciser :
a) Recherche systématique de récidive sans symptôme clinique ou biologique
b) Apparition d'une image anormale ou douteuse sur les examens d'imagerie conventionnelle
c) Persistance d'une masse résiduelle à distance de la fin du traitement
d) Elévation isolée d'un marqueur tumoral. Lequel ? _____
e) Bilan préopératoire d'une récidive avérée en apparence opérable
f) Autre. Préciser : _____

Nom en majuscules et signature du médecin prescripteur qui a rempli le formulaire :

ETAT APRES L'EXAMEN TEP

Répondre à chacune des trois questions, en entourant la réponse correspondant au cas du patient pour les questions 5) et 7) :

1) L'examen TEP a-t-il modifié le stade ?
a) Augmentation
b) Diminution
c) Sans changement

6) Stadification TNM retenue (ou classification selon Dukes ou grade définitif). Si non évalué mettre « ? »
T
N
M

7) L'examen TEP a-t-il modifié l'attitude thérapeutique ou la prise en charge du patient ?
a) Non
b) Chirurgie remplacée par traitement médical
c) Chirurgie remplacée par radiothérapie
d) Chirurgie remplacée par abstention thérapeutique
e) Traitement médical remplacé par chirurgie
f) Traitement médical remplacé par radiothérapie
g) Traitement médical remplacé par abstention thérapeutique
h) Radiothérapie remplacée par traitement médical
i) Radiothérapie remplacée par chirurgie
j) Radiothérapie remplacée par abstention thérapeutique
k) Abstention thérapeutique remplacée par traitement médical
l) Abstention thérapeutique remplacée par chirurgie
m) Abstention thérapeutique remplacée par radiothérapie
n) Modification du traitement médical
o) Modification du geste chirurgical
p) Modification du protocole de radiothérapie

Nom en majuscules et signature du médecin prescripteur qui a rempli le formulaire :

Nom **Signature**

[18F]-FDG IMPACT IN NON-SMALL CELL LUNG CANCER

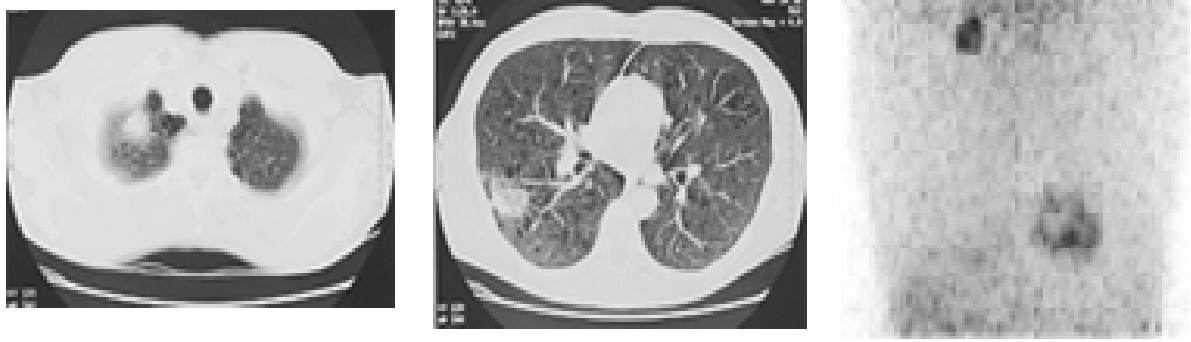
Lung cancer & ^{18}F-FDG

Tumour characterisation

Staging

Recurrences

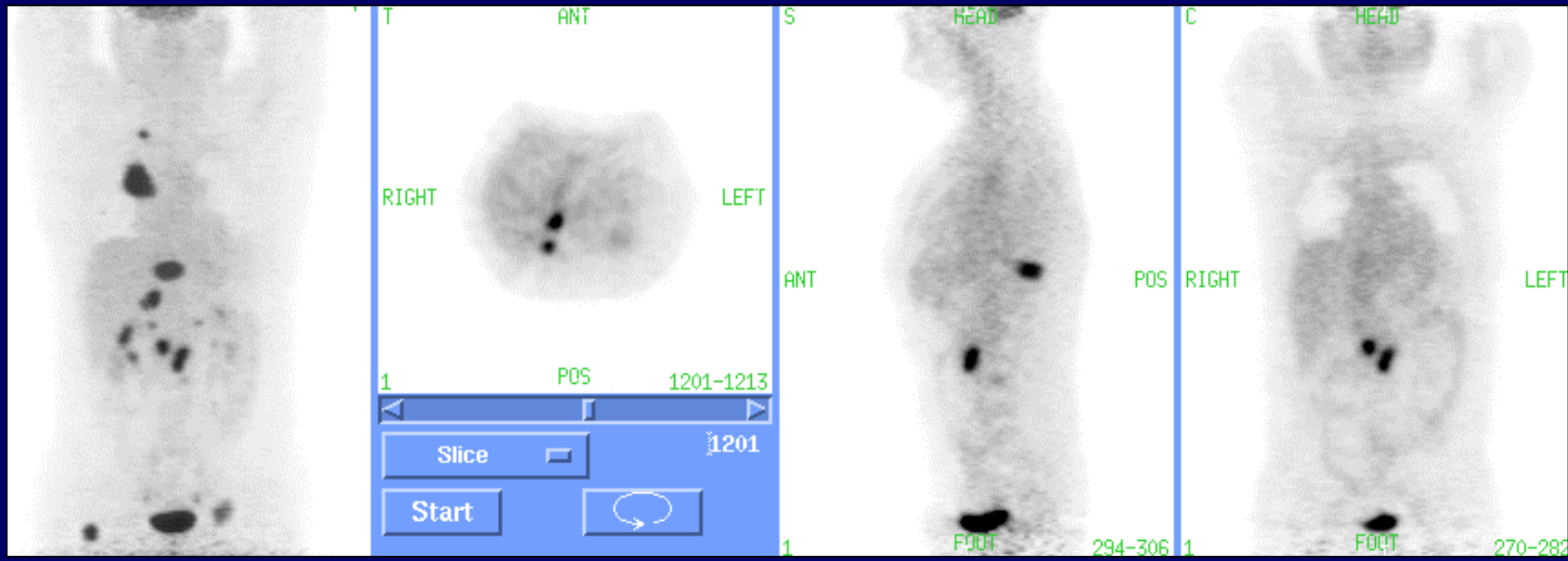
Treatment follow-up



Two lung nodules at CT, one at FDG C-PET :

the one that was malignant.

Thoracic mass : characterisation and staging with 18F-FDG



45 mm mass in the right lung and equivocal 15 mm image of the right adrenal gland at CT . C-PET-FDG: stage N3M1 (right subclavicular LN, spine metastases,
right adrenal gland, abdominal LN)
Histology after both mediastinoscopy and cervicotomy was negative.
Transbronchial biopsy of the mass confirmed an indifferenciated carcinoma with a sarcomatous component.
Two weeks after FDG-PET tumour progession objectivated the cervical metastasis => chemotherapy

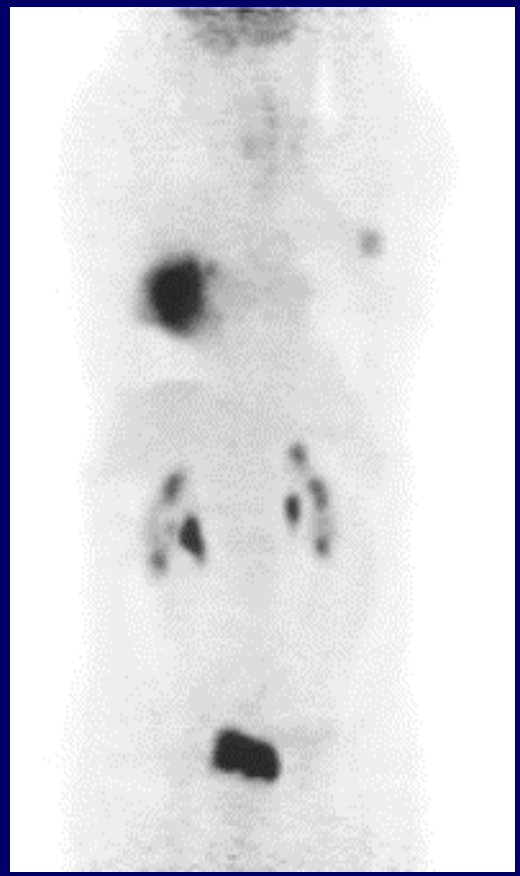
Lung cancer & ^{18}F-FDG

Tumour characterisation

Staging

Recurrences

Treatment follow-up



Staging of a right lung cancer, initial stage T2N1M0

C-PET FDG staging T2N1M1 : left axillary lymph node metastasis confirmed by histology.

=> from surgery to chemotherapy

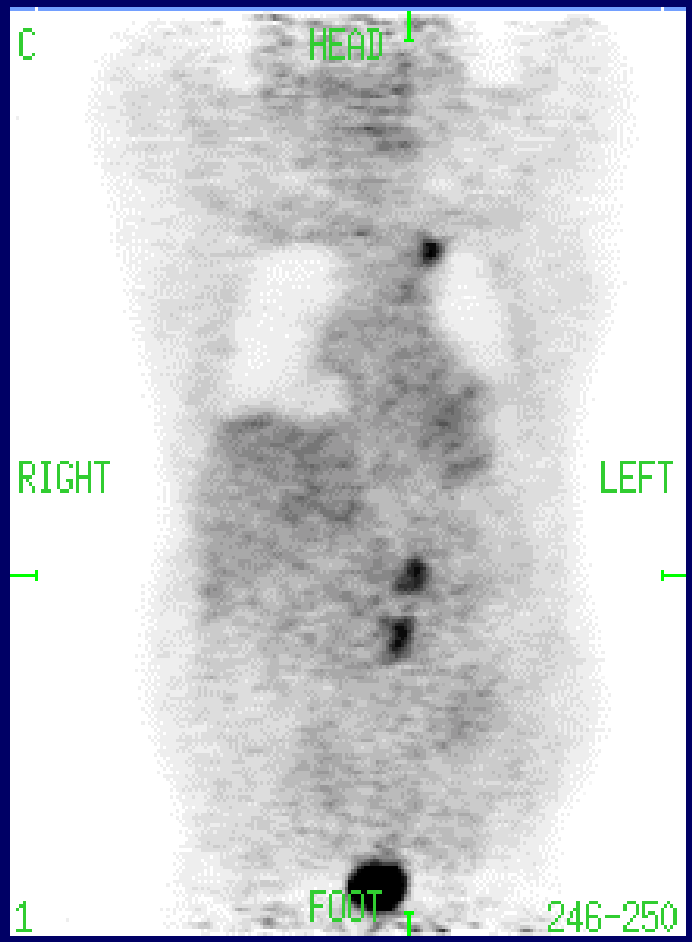
Lung cancer & ^{18}F-FDG

Tumour characterisation

Staging

Recurrences

Treatment follow-up



Suspicion of recurrence of a lung cancer treated by surgery and chemotherapy. Rising CEA levels. Normal CT 3 months before. C-PET-FDG: Foci of left pleura, left mediastinal LN, left adrenal gland, abdominal LN => Chemotherapy

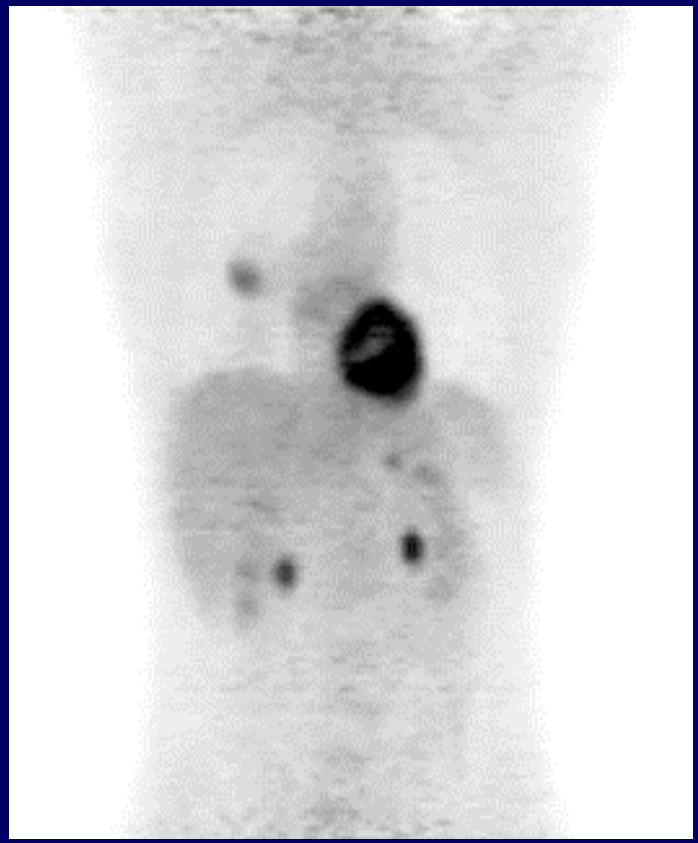
Lung cancer & ^{18}F-FDG

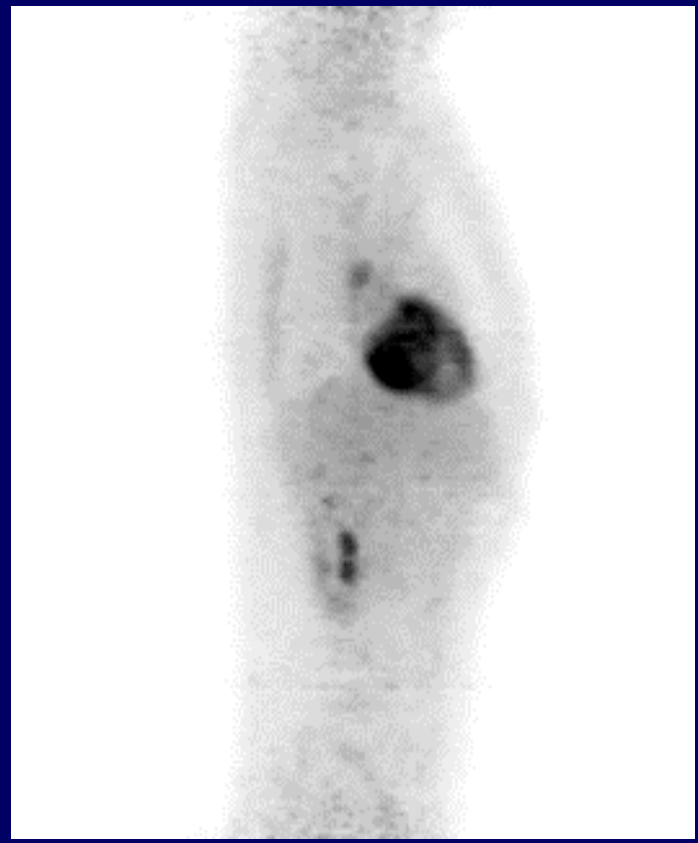
Tumour characterisation

Staging

Recurrences

Treatment follow-up





Radiation therapy for a right parahilar malignant mass of the lung. Viable tumour ? Adrenal mass at CT. C-PET : cancer tissue in the lung but not in the adrenals. The persistence of viable malignant tissue in a 20 mm nodule of the right lung was confirmed at surgery. One year later, no evolution occurred at the adrenal level, confirming the absence of metastasis.

Lung cancer : impact of FDG on staging

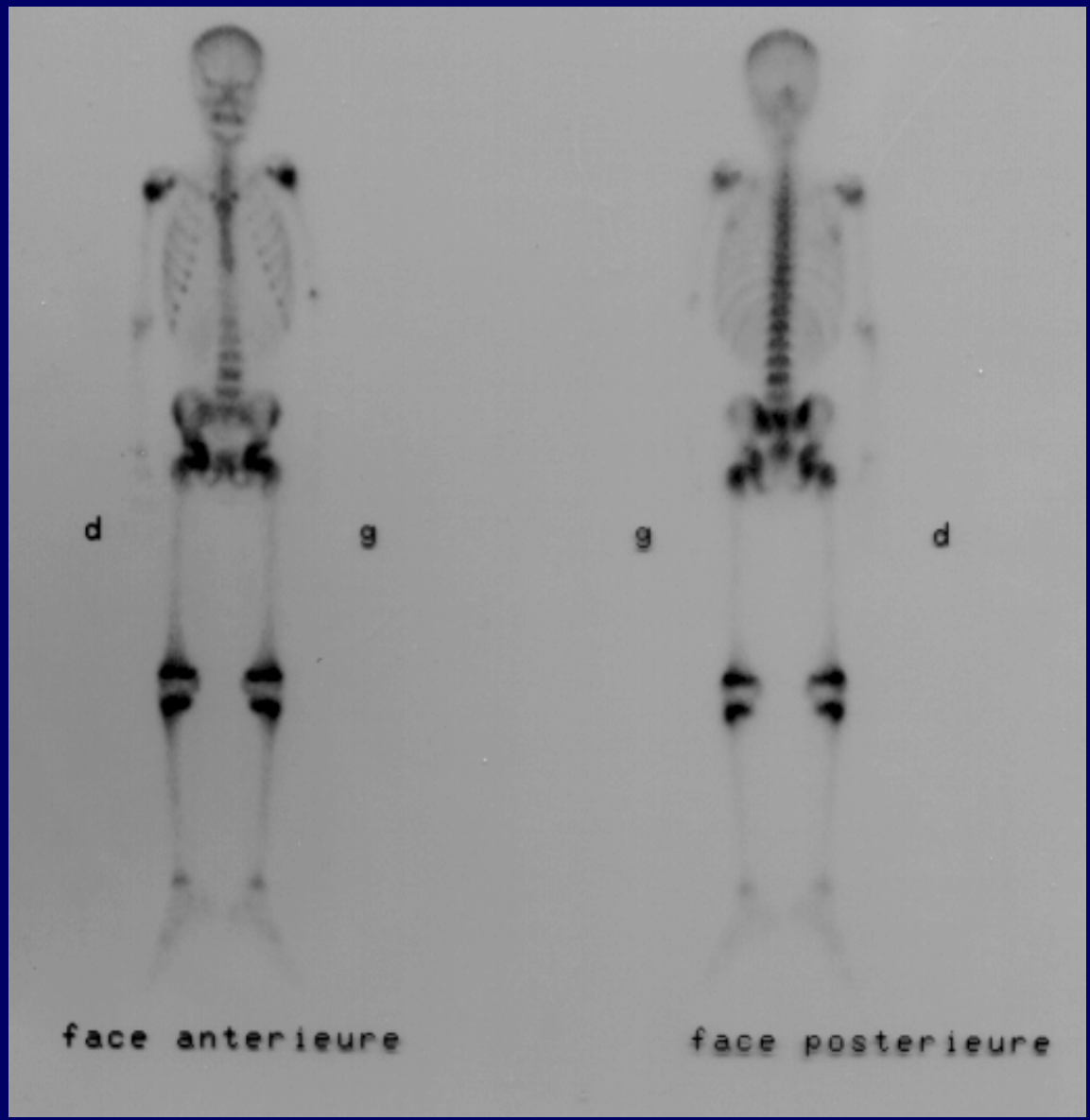
Reference	n =	Changing N stage	Changing M stage	Changing global stage
Valk 1995	99	16%	30%	
Bury 1997	106		14%	
Steinert 1997	47	17%		
Weder 1998	94		14%	20%
Gupta 1999	103	37%	11%	
Saunders 1999	97	13%	20%	
Pieterman 2000	102		11%	61%
Kalff 2001	59		24%	48%
AP-HP 2000 PET	122			40%

Impact of FDG-PET on clinical management of patients with lung cancer

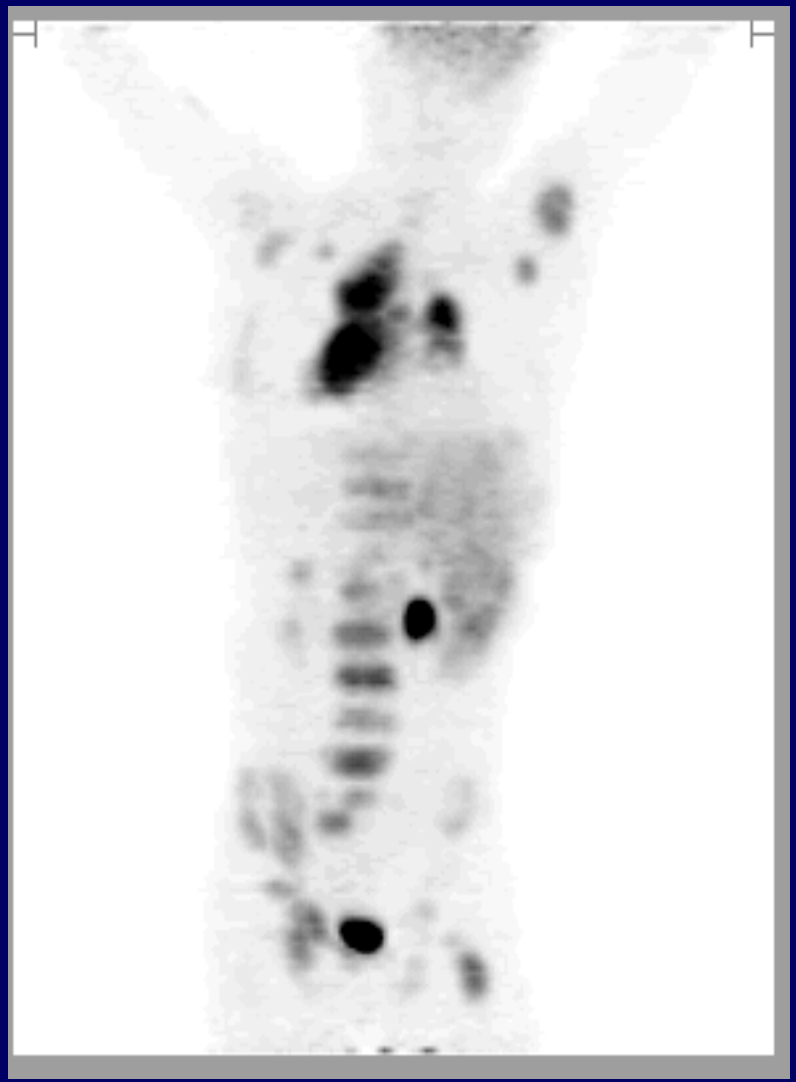
Reference	n =	Modification rate
Lewis 1994	34	41%
Valk 1996	72	48%
Bury 1997	106	26%
Ferlin 1997	22	18%
Saunders 1999	97	37%
Kalff 2001	105	67%
TOTAL	*436*	*51%*
AP-HP 2000 PET	118	53%

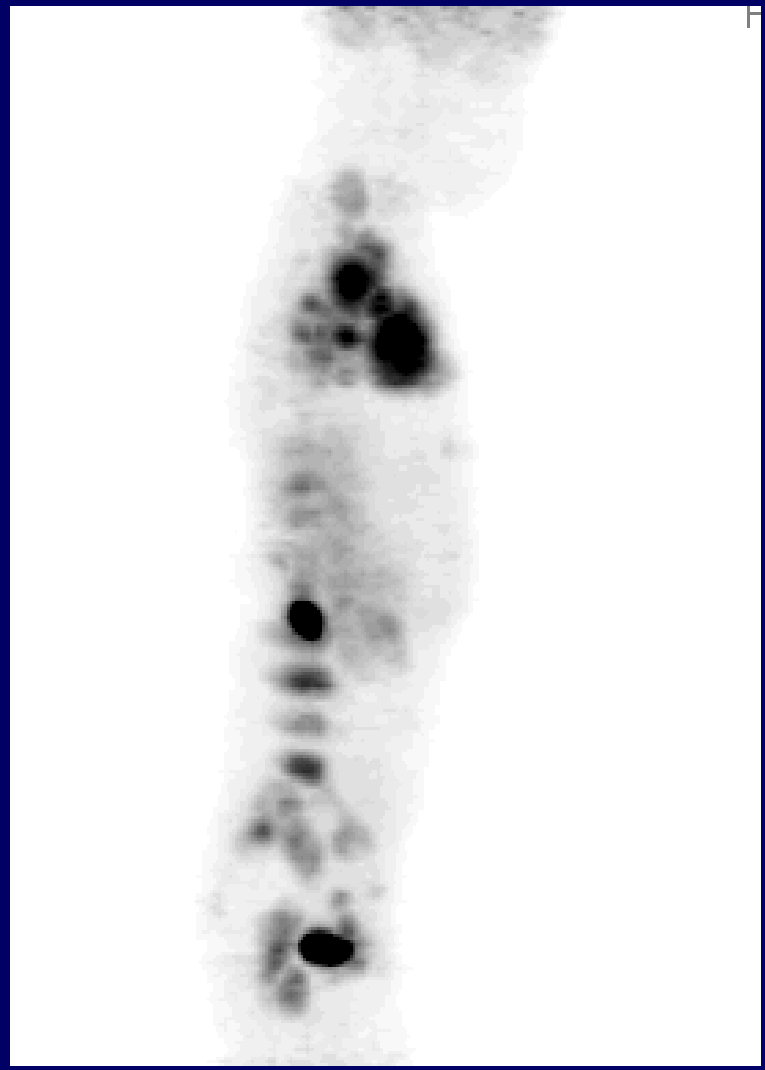
[18F]-FDG IMPACT

IN LYMPHOMA

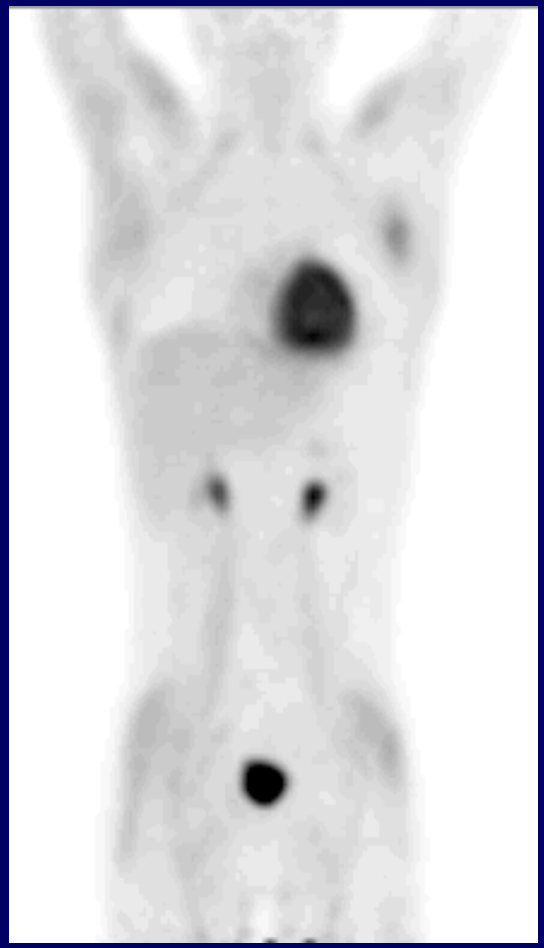


Bone scintigraphy of a child at the initial staging of Hodgkin ’s lymphoma

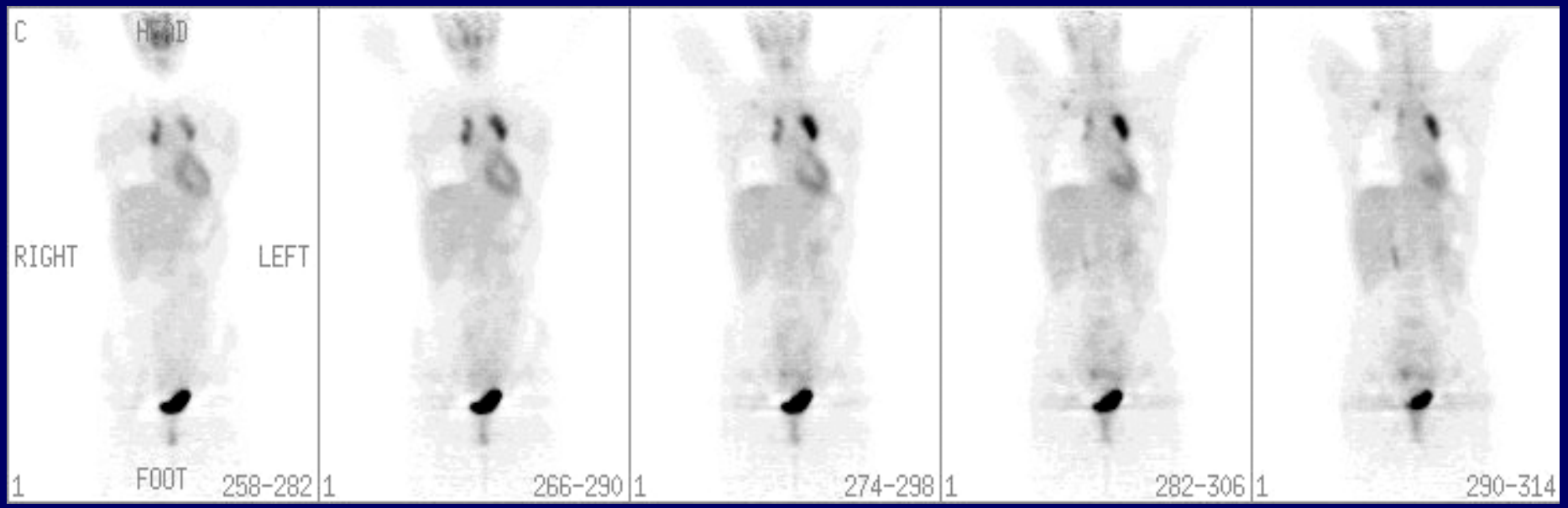




3D display : FDG-PET examination of the same child before treatment



3D display : FDG-PET examination of the same child after chemotherapy



FDG-PET (coronal slices with attenuation correction) showed an active focus in the region of the thymus and right intrathoracic lymph nodes.

A biopsy of the thymus itself was therefore performed and proved to be metastatic. FDG-PET was judged by the clinician as "very contributive to patient's management".

Impact on staging and re-staging : comparison of AP-HP and Californian studies

LYMPHOMA	AP-HP	Shöder et al.
None	30 (70%)	27 (54%)
Upstaging	10 (23%)	11 (22%)
Downstaging	3 (7%)	12 (24%)
Total	**43**	**50**
Modification rate	**30%**	**46%**

Schöder H *J Nucl Med* 2001 (8) ; 42 : 1139-1143.

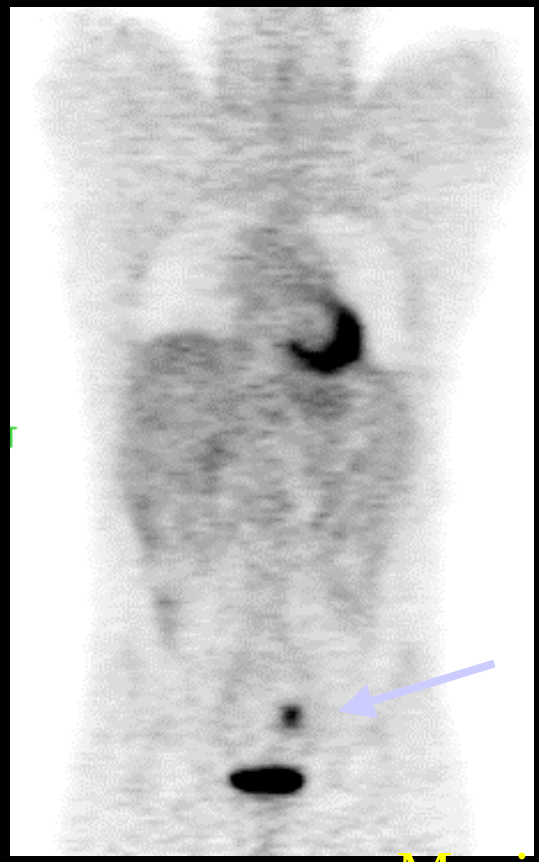
CHANGE IN PATIENTS MANAGEMENT

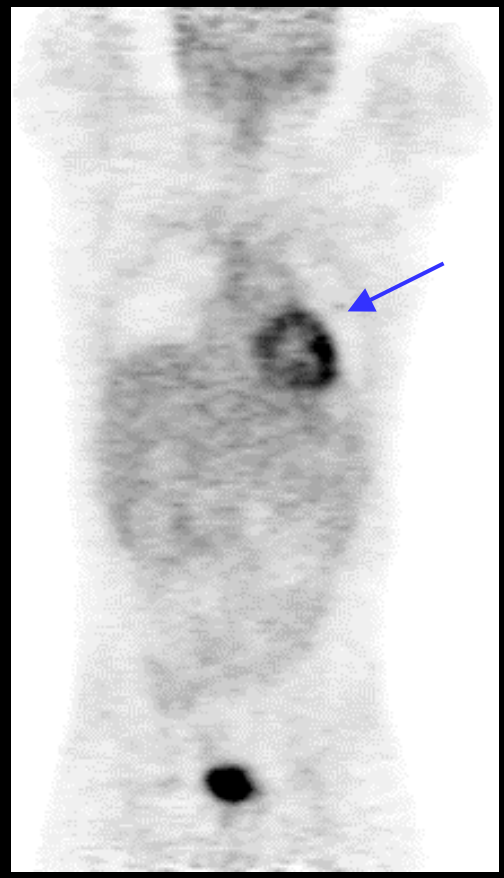
LYMPHOMA	AP-HP	Schöder et al
None	26 *(60 %)*	17 *(32 %)*
Inter-modality changes	7 *(17 %)*	22 *(42 %)*
Intra-modality changes	10 *(23 %)*	5 *(10 %)*
Combination and other changes	-	8 *(16 %)*
Total	**43**	**52**
Modification rate	***40 %***	***68 %***

Schöder H *J Nucl Med* 2001 (8) ; 42 : 1139-1143.

[18F]-FDG IMPACT IN RECURRENT COLORECTAL CANCER

Coronal slices





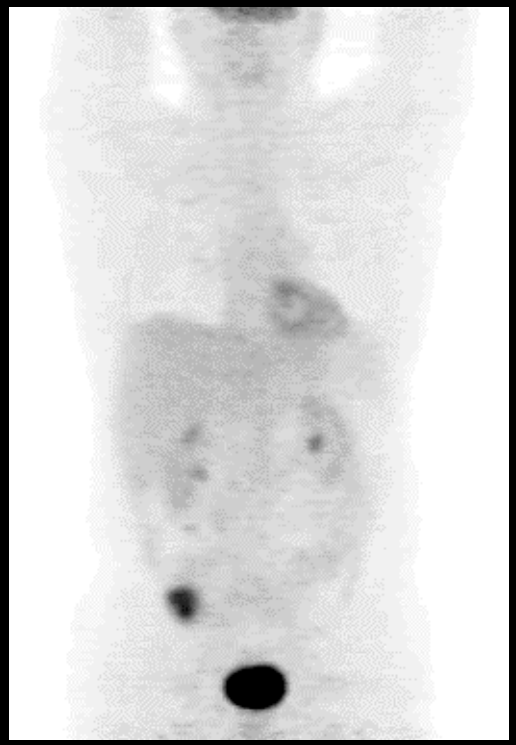
Mucinous colorectal cancer

Preoperative evaluation of lung metastases (→)

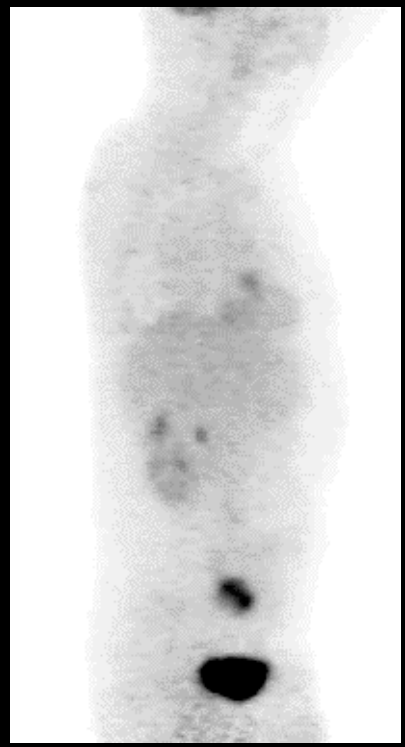
Intense uptake of FDG in the pelvis (→)

Management : inter-modality change from thoracic surgery to chemotherapy (after explorative laparotomy: extensive peritoneal carcinomatosis)

3D anterior



3D right lateral

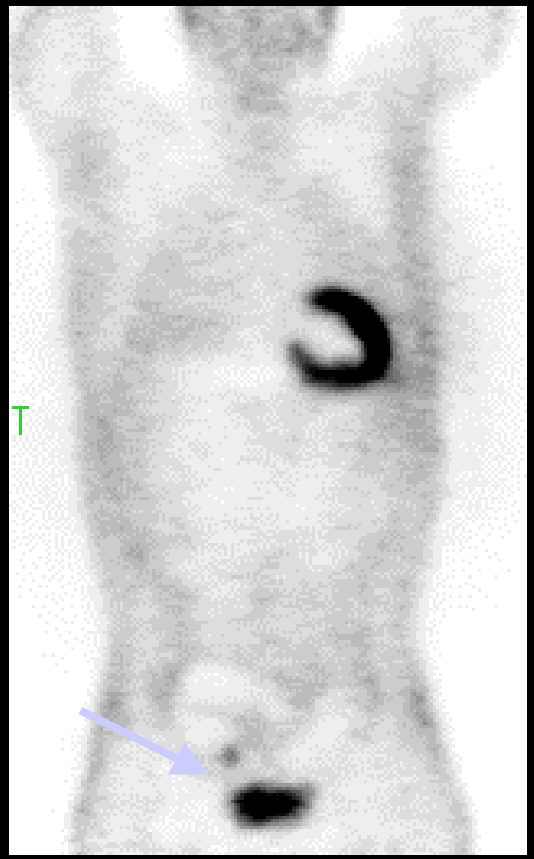


Isolated rising CEA levels

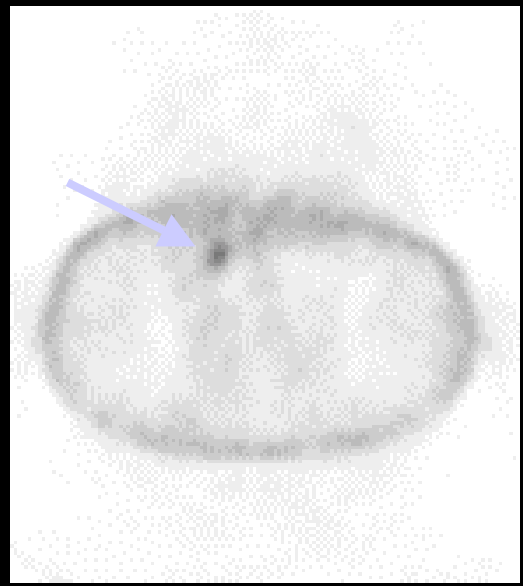
FDG : One single focus in the right abdomen

Management : inter-modality change from no treatment to surgery (isolated local recurrence)

Coronal slice



Transverse slice



Suspicion of anastomotic anorectal recurrence

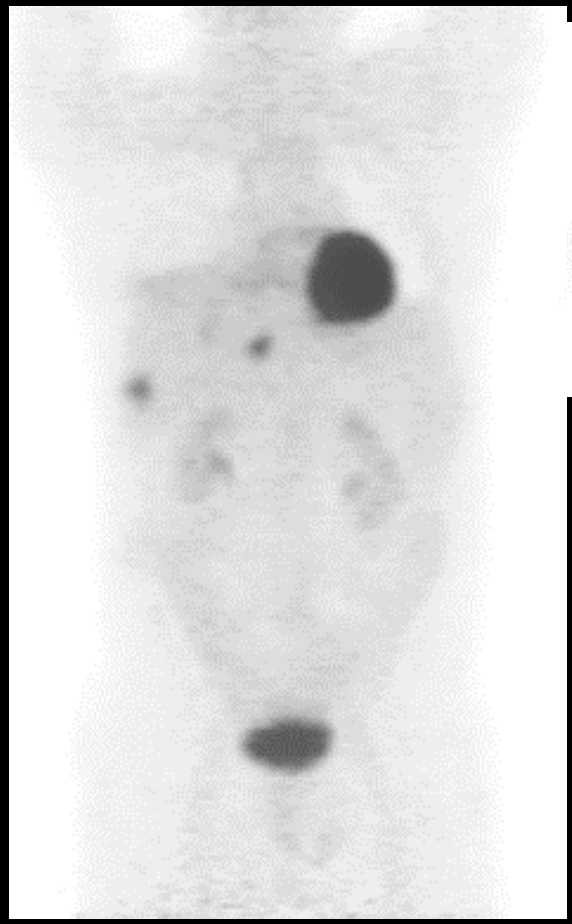
FDG negative in the site of anastomosis but positive in the right anterior pelvis

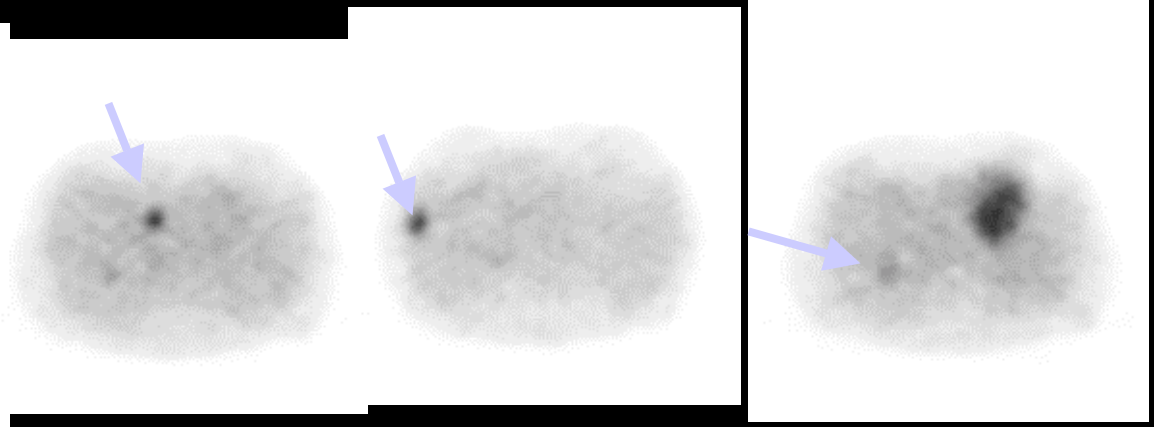
Management :

intramodality-change in surgical procedure. The anastomosis was TN and the pelvic uptake corresponded to an abcess (FP)

Coronal slice

Transverse slices





Sigmoid cancer

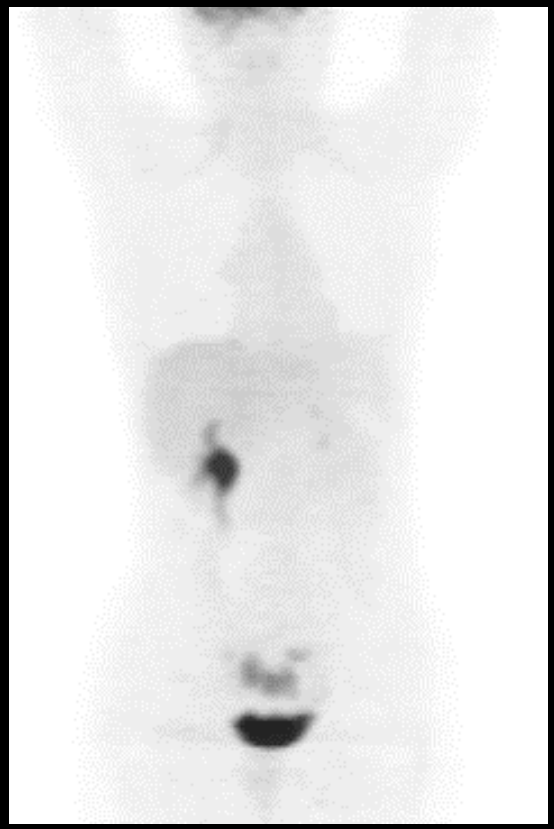
Evaluation of liver metastases after chemotherapy

FDG : 3 hepatic foci

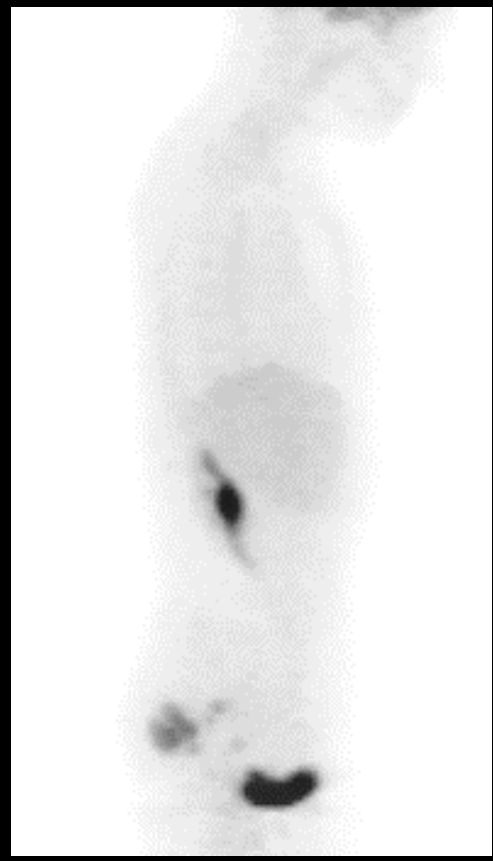
Management :

intra-modality change in chemotherapy regimen

3D anterior

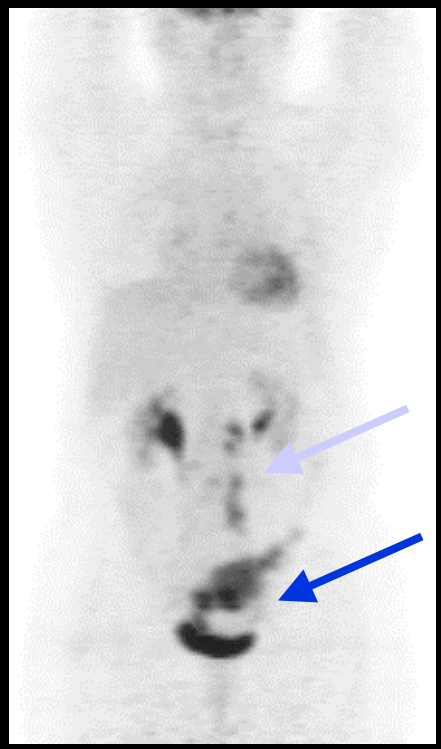


3D Right profile

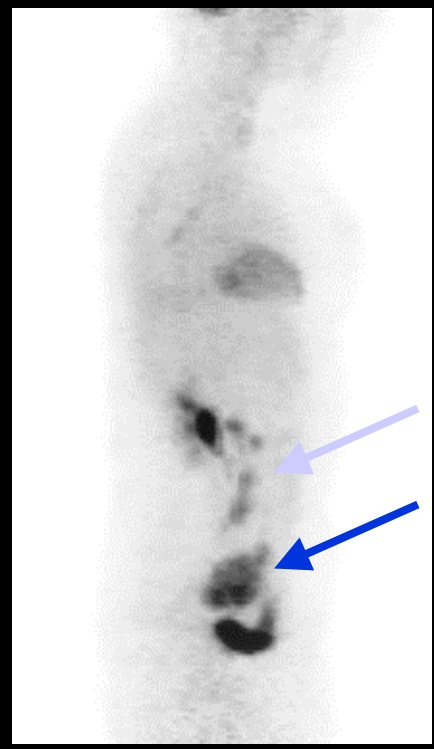


Evaluation of liver metastases after chemotherapy FDG : pelvic foci. **Management** : management change by combination of modalities from chemotherapy to chemotherapy + radiotherapy (after biopsy assessment of the pelvic recurrence)

3D anterior



Right profile

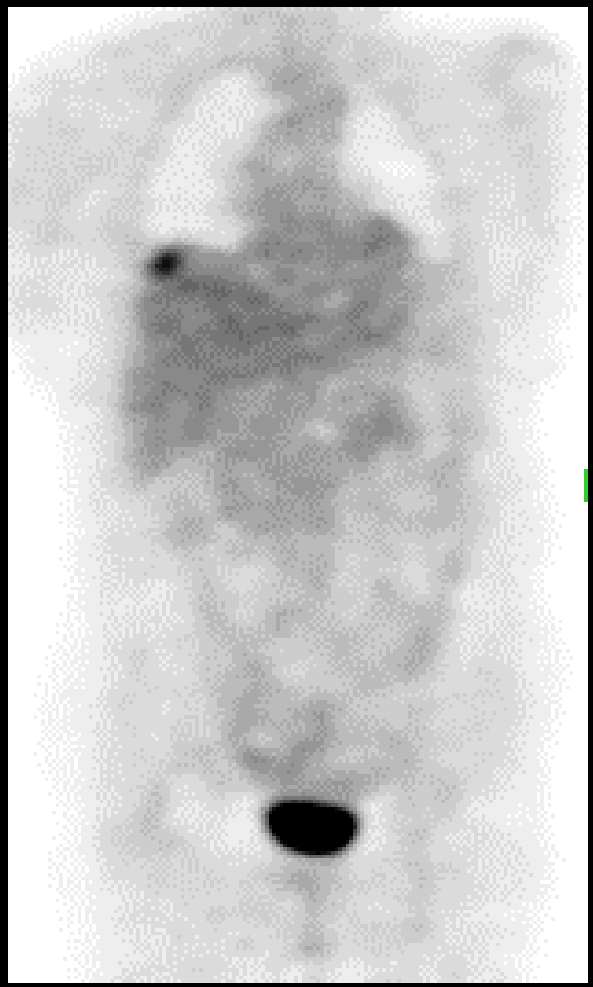


Sigmoid cancer

Evaluation before radiotherapy of lomboaortic lymph nodes

FDG : lomboaortic foci (→) + extensive pelvic focus (→)

Management : inter-modality change from radiotherapy to chemotherapy



Coronal slice

Chemotherapy for isolated rising CEA levels

FDG : isolated uptake in the liver

Management : inter-modality change from chemotherapy to surgery

IMPACT ON RE-STAGING

COLORECTAL	AP-HP	Meta et al
None	100 *(65 %)*	32 *(56 %)*
Upstaging	45 *(30 %)*	20 *(35 %)*
Downstaging	8 *(5 %)*	5 *(9 %)*
Total	**153**	**57**
Modification rate	***35 %***	***44 %***

Meta J *J Nucl Med* 2001 ; 42 (4) : 586-90.

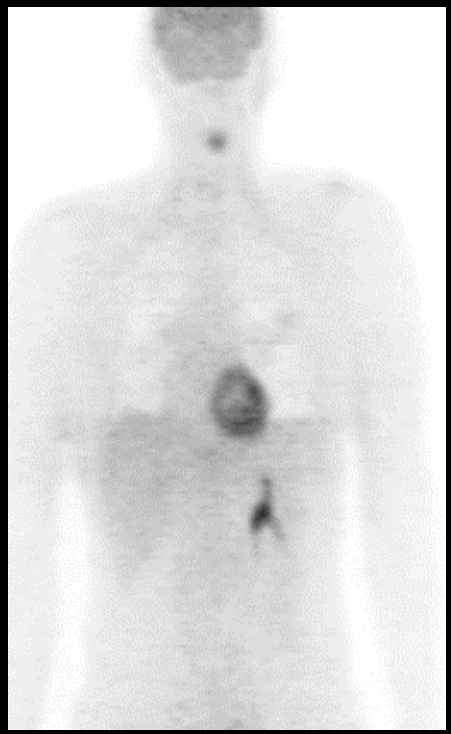
CHANGE IN PATIENTS MANAGEMENT

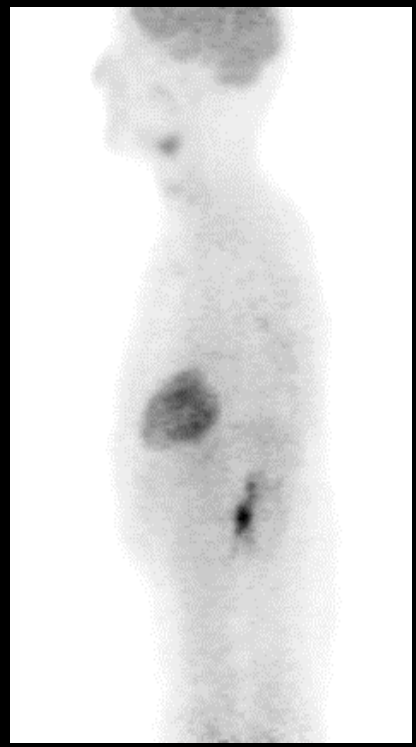
COLORECTAL	AP-HP	Meta et al
None	87 *(57 %)*	19 *(33 %)*
Replacement of surgery	20 *(14 %)*	10 *(17 %)*
Indication of surgery	20 *(13 %)*	7 *(12 %)*
Other inter-modality changes	18 *(3 %)*	5 *(9 %)*
Intra-modality changes	21 *(14 %)*	11 *(19 %)*
Combination and other changes	-	6 *(10%)*
Total	**152**	**58**
Modification rate	***44 %***	***67 %***

Meta J *J Nucl Med* 2001 ; 42 (4) : 586-90.

[18F]-FDG IMPACT IN RECURRENT HEAD AND NECK CANCER :

31% change in patient management

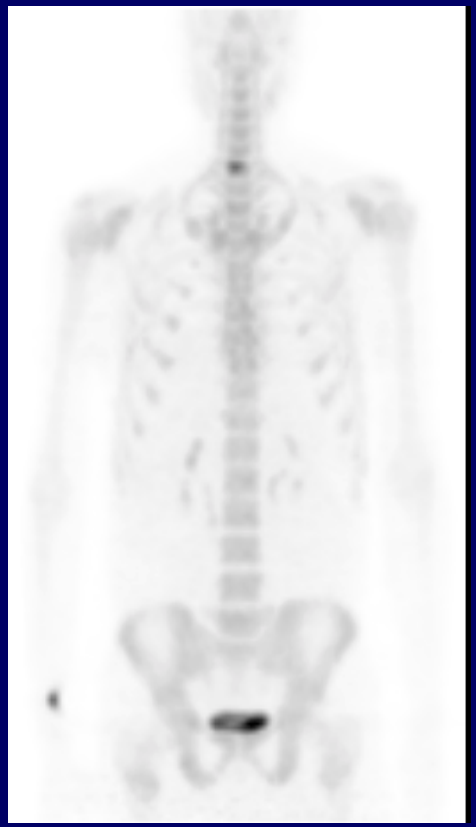




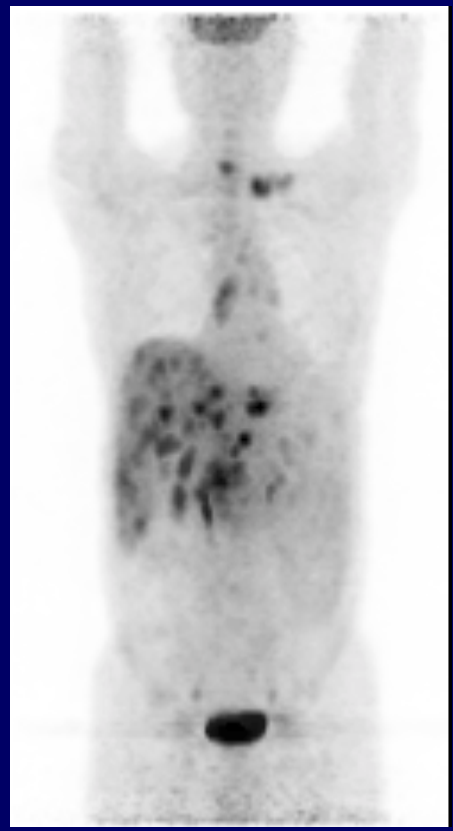
Suspicion of recurrence of an epidermoid carcinoma of the tongue due to a doubtful MRI image. Normal clinical aspect.
Intense FDG uptake by the doubtful part of the tongue.
Decision of biopsy that confirmed the recurrence.

MANY OTHER CLINICAL INDICATIONS OF [18F]-FDG

Staging of a pancreas cancer



[F-18] - F Na



[F-18] - FDG

CONCLUSIONS

Major impact of FDG-PET in many cancer indications, evaluated by the referring physician, using a PET machine of average performances.

• This major impact, already observed in California, was confirmed in France, with a greater response rate to the survey (73% in the present study versus 35% on average in the Californian studies).

• The rate of management changes seems to increase as time passes probably because the experience of the referring physician improves and he has a larger confidence in FDG-PET.