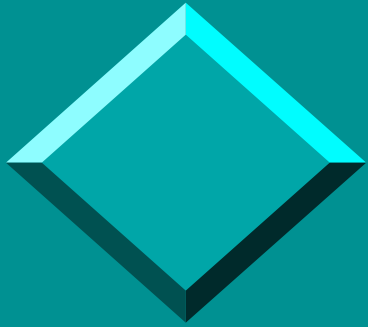




18F-FDG PET CT and liver metastases from colo- rectal cancer

Eric ZERBIB

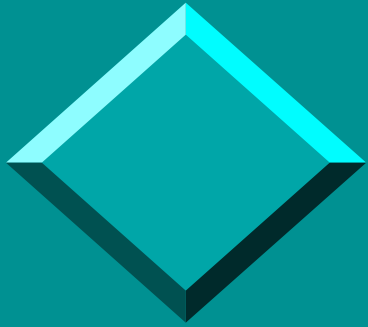
CIMEN (www.cimen.fr)

Centre Chirurgical Val d 'Or

14 rue Pasteur

92210 Saint-Cloud

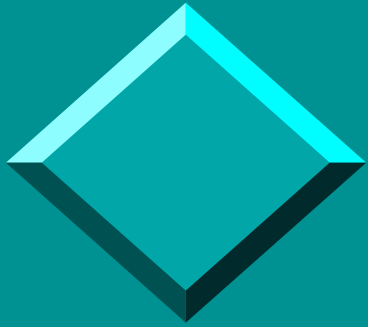
eric.zerbib@cimen.fr



18F-FDG PET CT and liver metastases from colo- rectal cancer

Preliminary comments :

- ✓ FDG PET is not a specific investigation for liver studies. It makes the scanning of the whole body (excepted brain) and is efficient in the diagnosis of liver metastases including liver metastases from colo-rectal cancer.
- ✓ FDG PET is not anatomopathology ! It investigates glucosis metabolism which is special IN MOST OF cancerous cells. This have important consequences for interpretation.

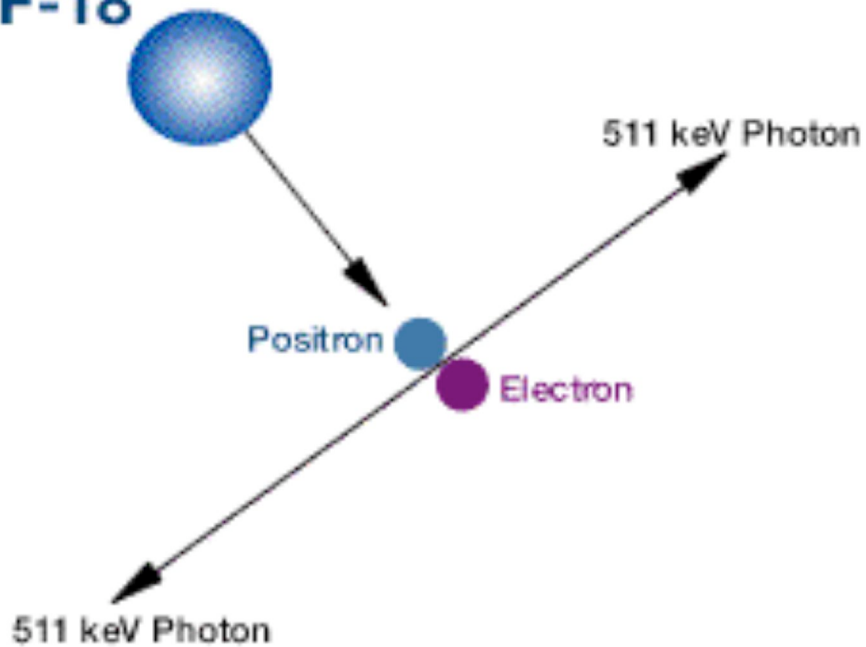


PET and PET-CT and isotopes

Background :

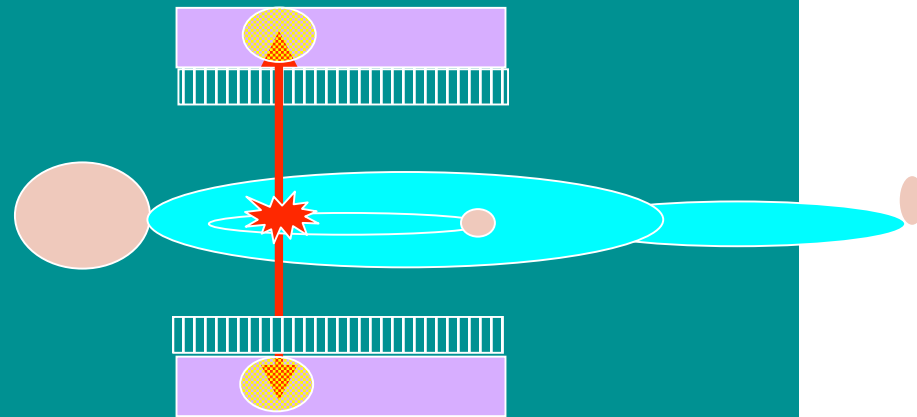
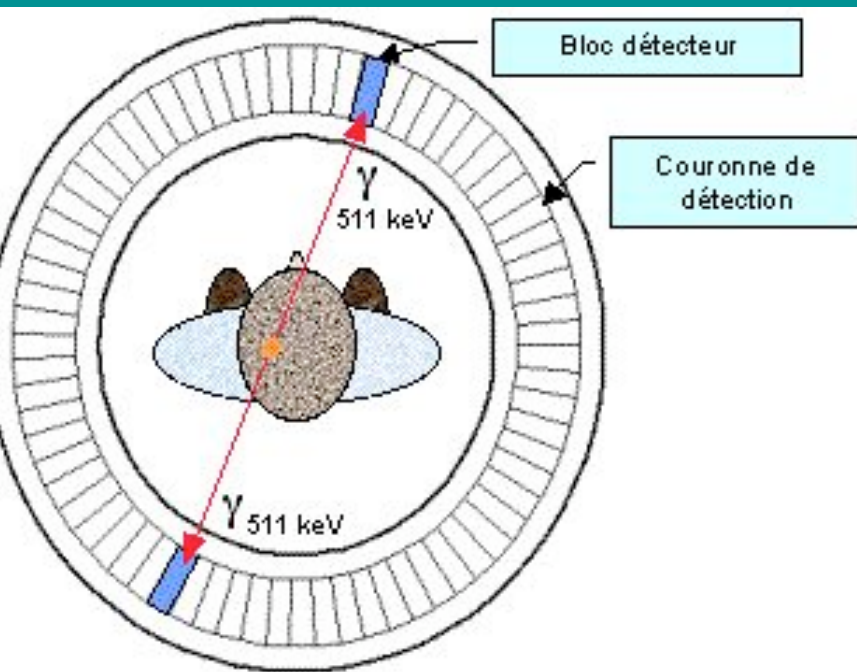
- ✓ PET : detection of a couple of photons coming from the disintegration of one positron
- ✓ CT : computed tomography
- ✓ PET-CT : makes the fusion of the two acquisitions : but makes attenuation correction very important to see the deep organs and helps us to see the anatomy which cannot be appreciate by PET pictures only
- ✓ Radiopharmaceutical : is specific of an organ or a system : FDG, Choline, F-DOPA, FLT, Rubidium

F-18



Background

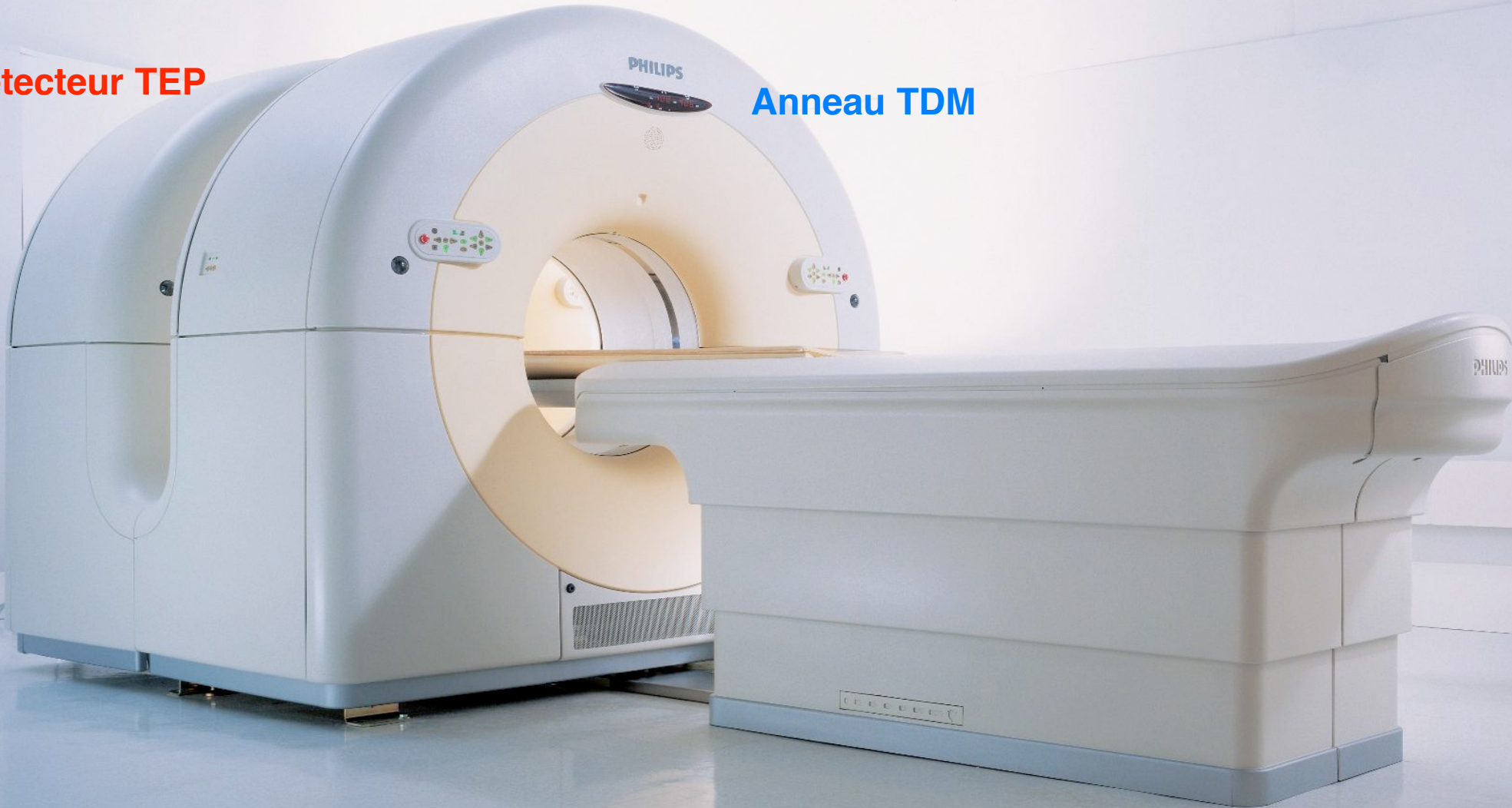
- ^{18}F : radioactive isotope
Half live : 110 min
- positron annihilation
with an électron and
emission of 2 x 511 keV
photons

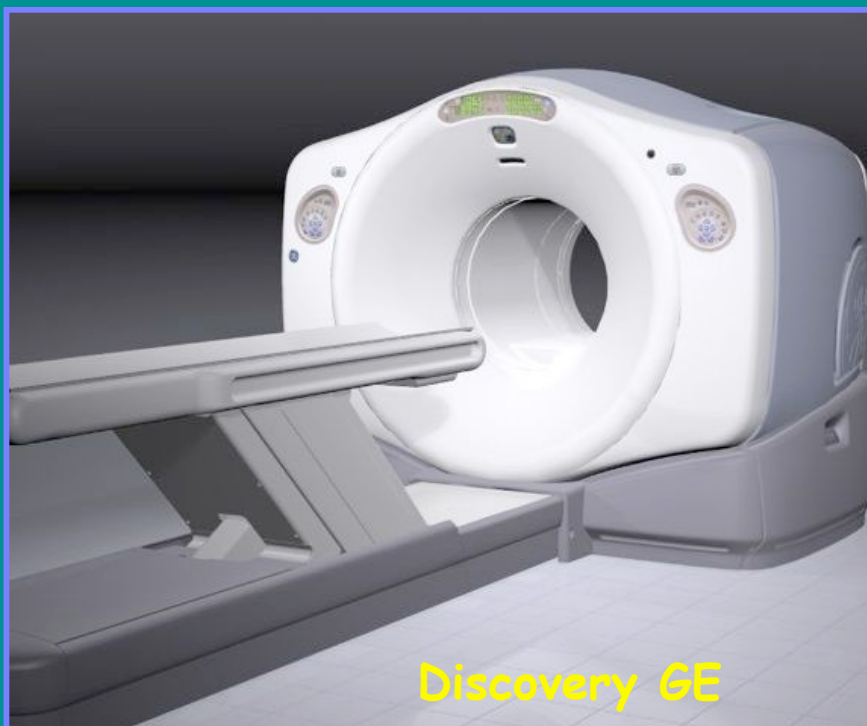
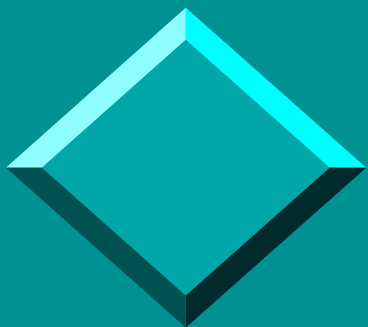


Caméra hybride TEP-TDM

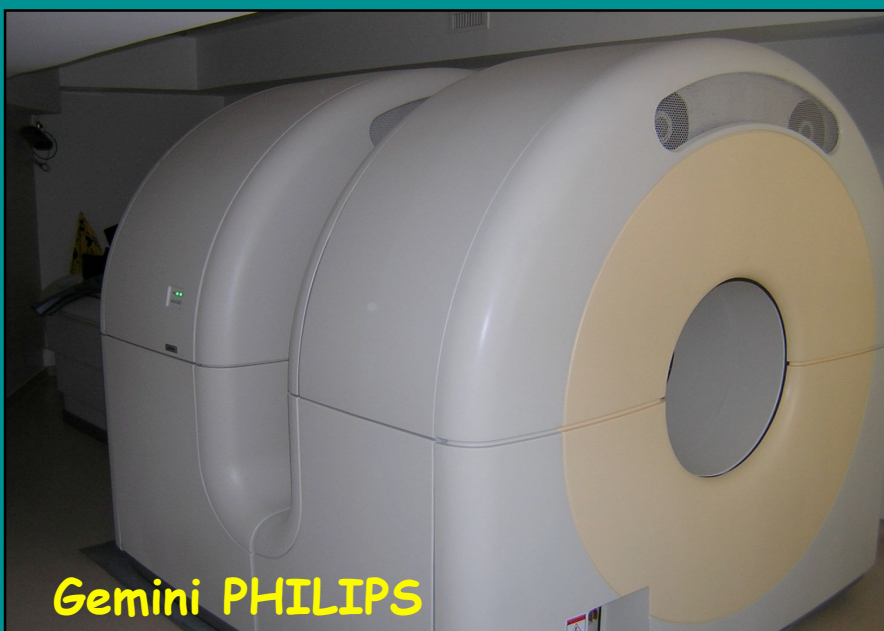
Détecteur TEP

Anneau TDM





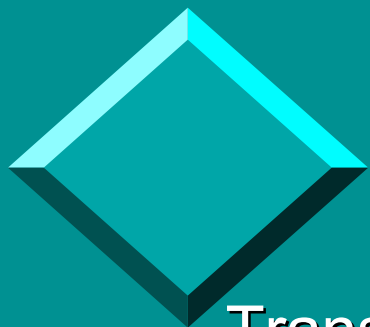
Discovery GE



Gemini PHILIPS

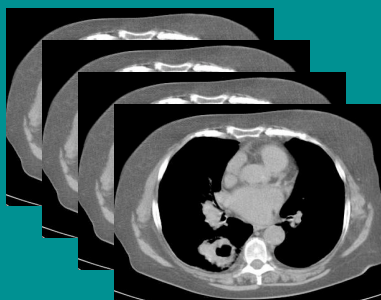
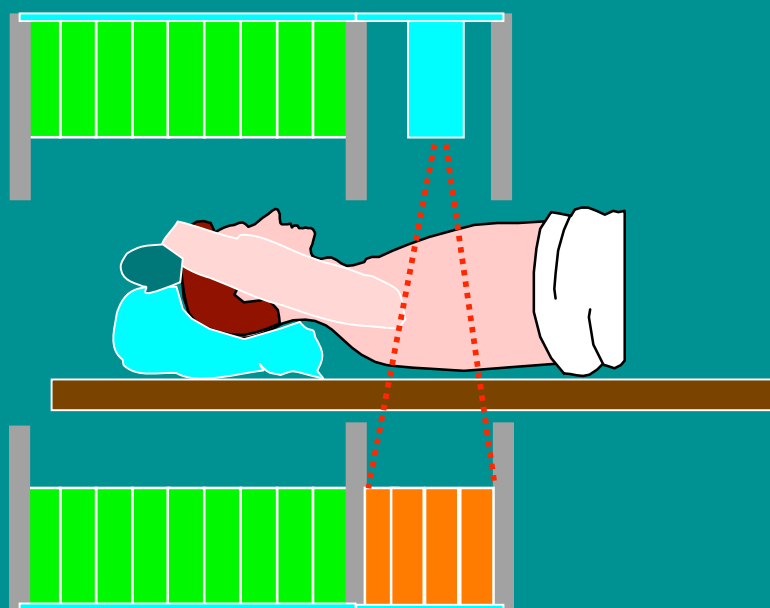


Biograph SIEMENS

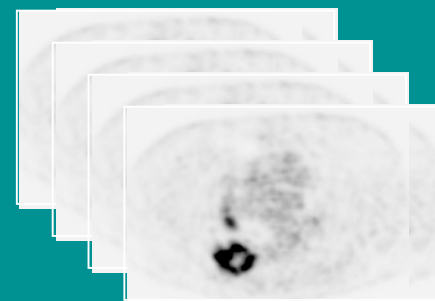
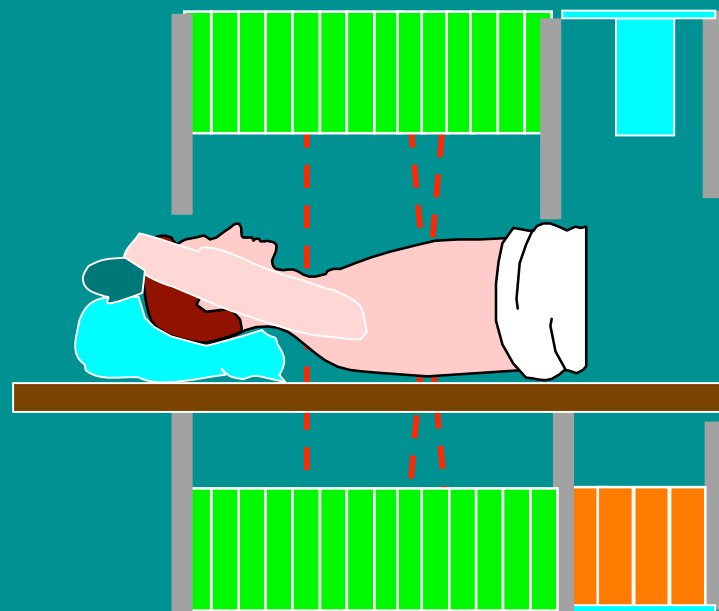


Acquisition des images

Transmission

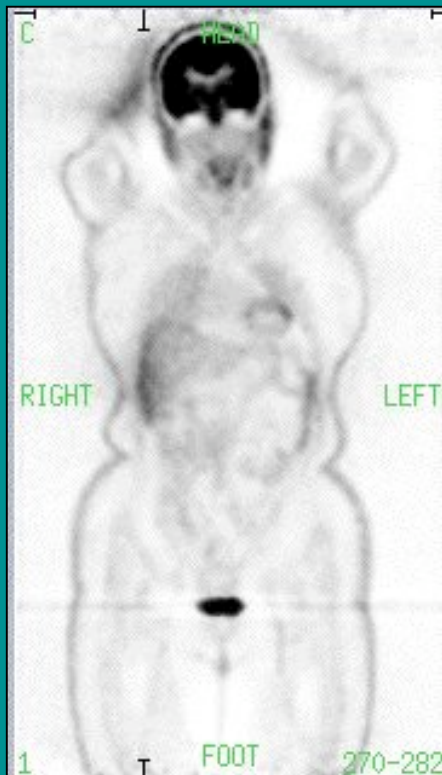


Emission

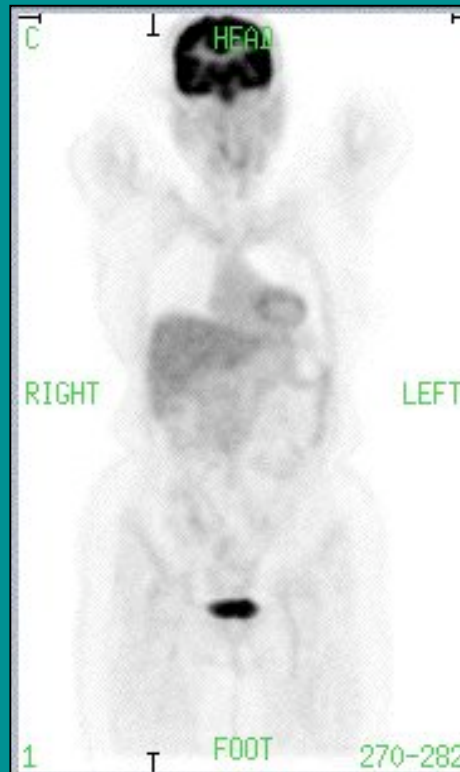


Images TEP - ^{18}F -FDG

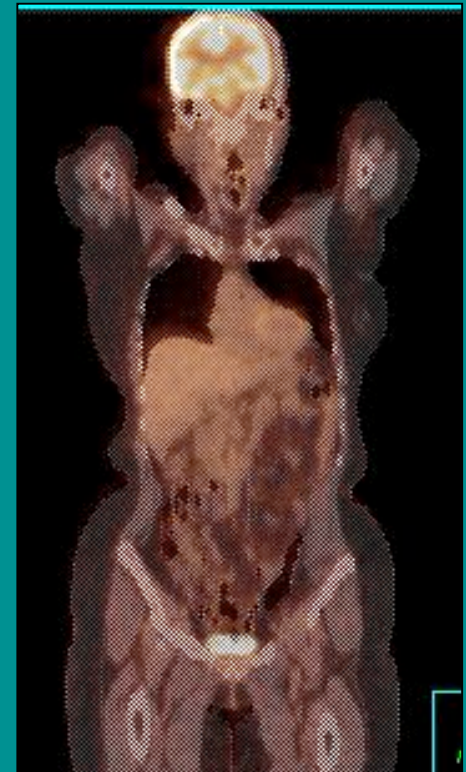
without attenuation correction



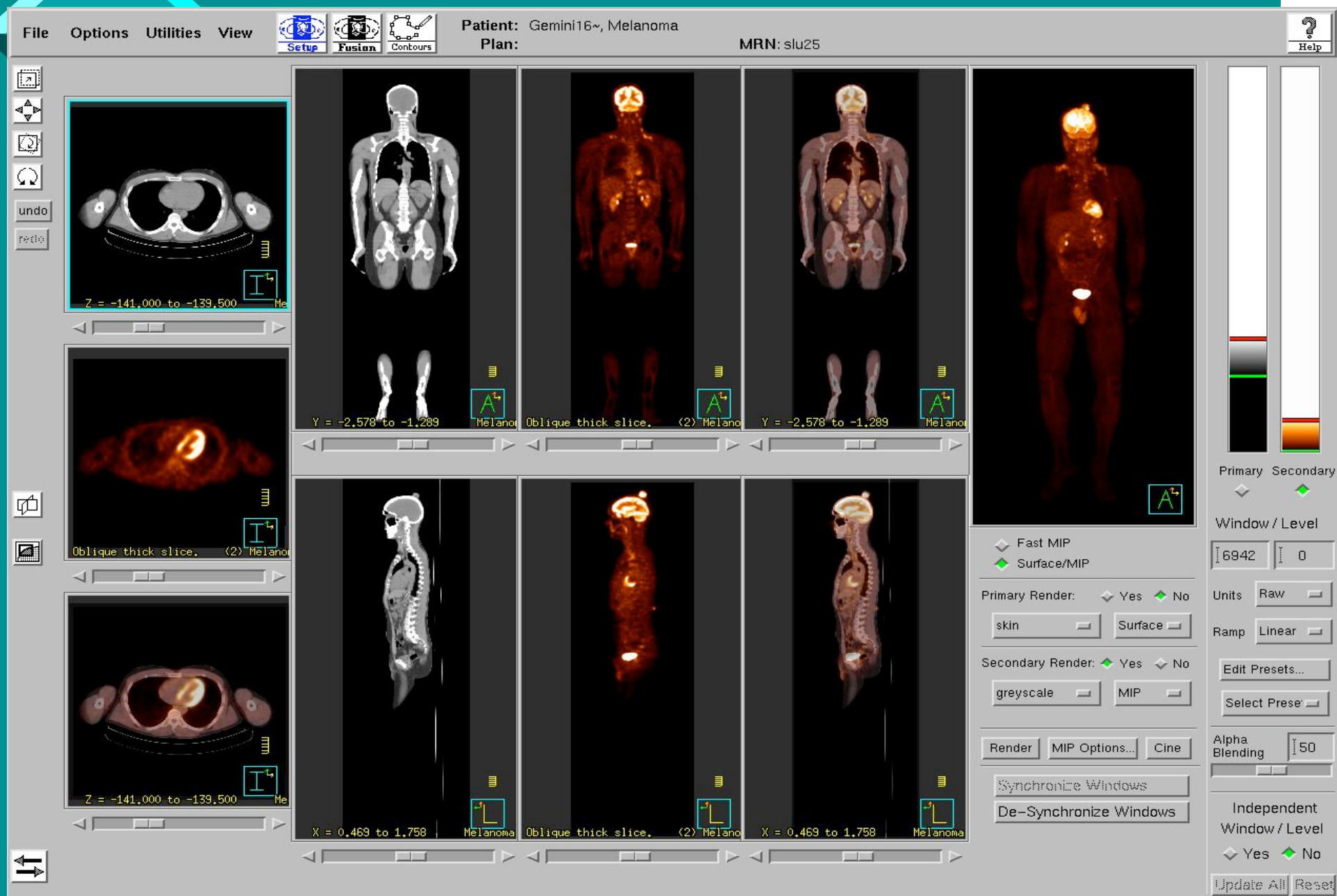
with attenuation correction



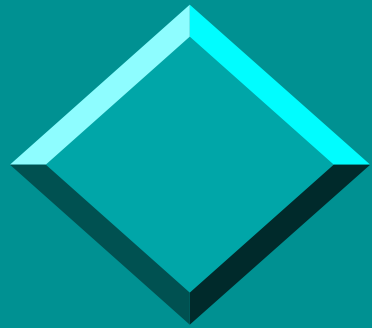
Fusion PET-CT



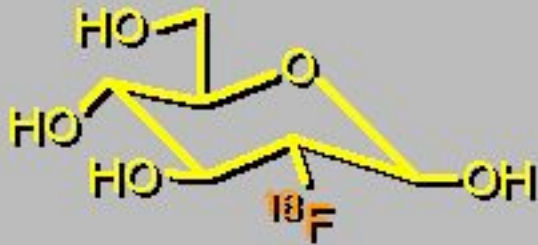
PET-CT Fusion



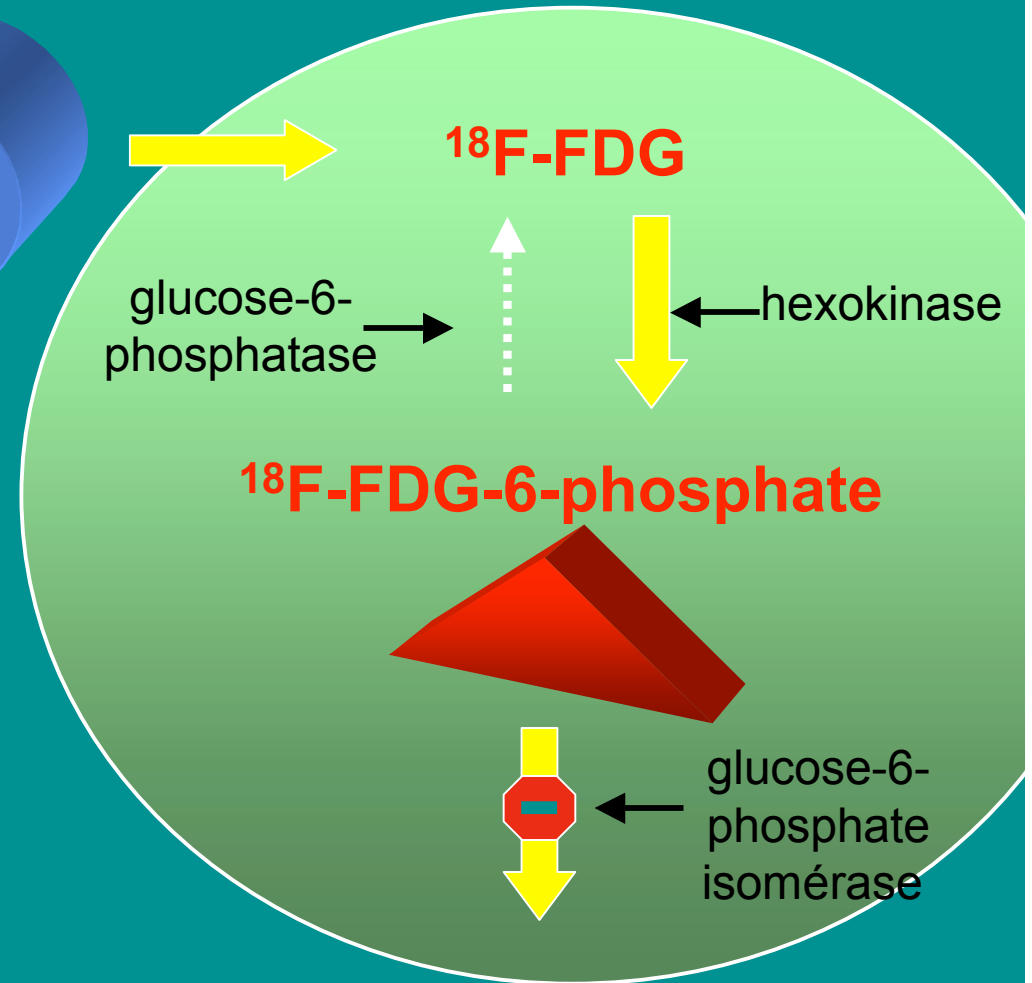
Les traceurs TEP



Le FDG-(18F)



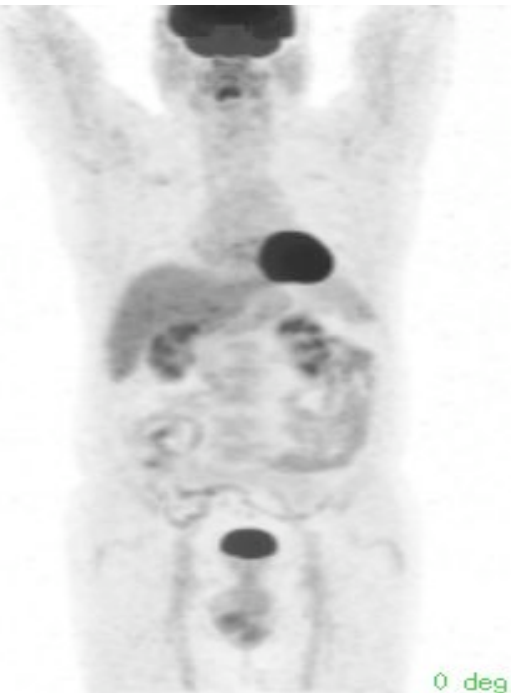
^{18}F -fluorodésoxyglucose
= analogue radioactif du glucose



Cellule cancéreuse



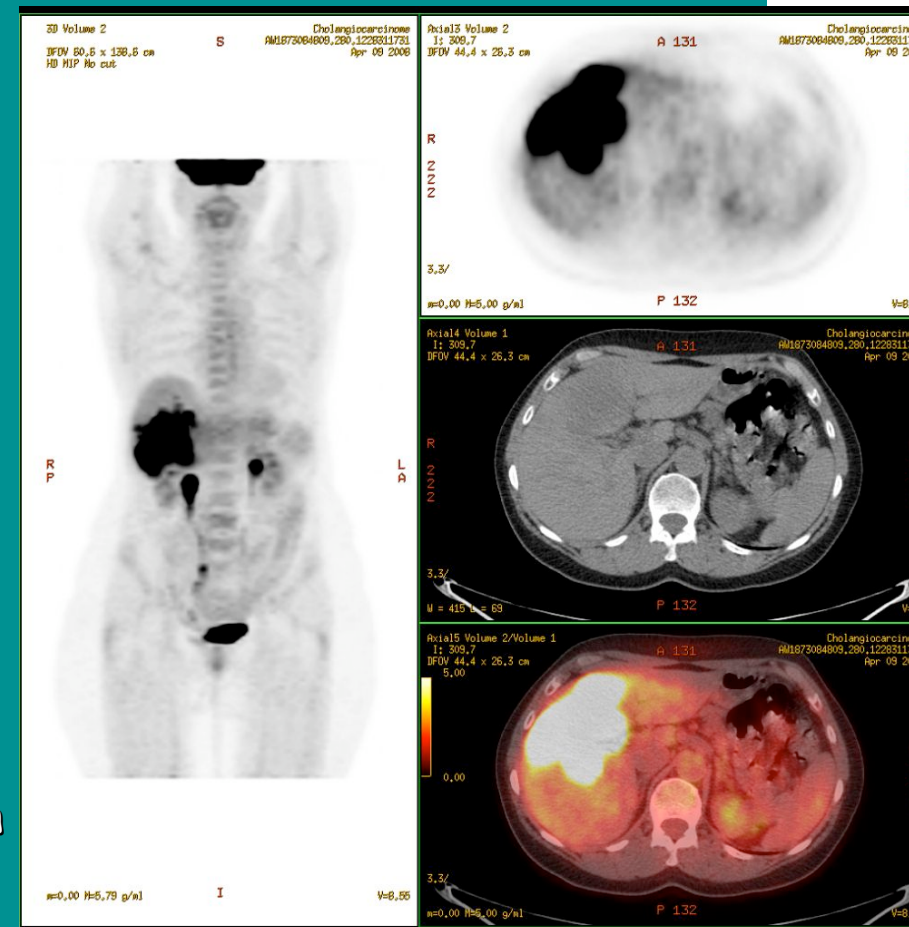
consommation de glucose $\nearrow$ (transporteur
activité enzymatique)

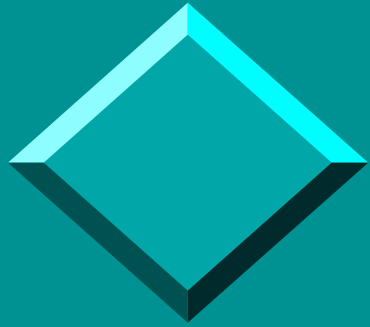


FDG PET and the liver

Hepatocyte cells have strong glucose-6 phosphatase activity :

- ✓ No uptake in the normal hepatocyte cell
- ✓ This allows detection of liver metastases
- ✓ This explains there is no uptake in hepatocellular carcinoma (if well differentiated)
- ✓ This explains the intense uptake in cholangiocarcinoma

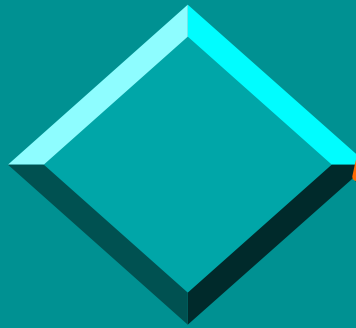




PET and colorectal cancer

Main indications

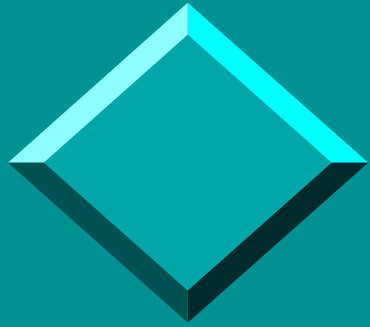
- ✓ For initial diagnosis and initial staging : NO INDICATION
- ✓ Recurrence of colorectal cancer : exploration of non identified lesion or unexplained rising CEA level
- ✓ Recurrence versus fibrosis
- ✓ New staging before surgery in case of isolated secondary localization (hepatic most of time)



PET and liver metastases from colorectal cancer

Main indications : No specific indication for hepatic metastases but :

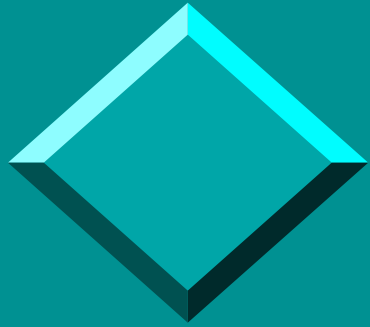
- ✓ Characterization of a liver lesion : metastases versus hepatic angioma
- ✓ Residual abnormalities after radiofrequency
- ✓ Before surgery of a single liver metastases
- ✓ Evaluation of therapies



PET and liver metastases from colorectal cancer

In fact, discussion is :

- ✓ What's happening when we see hot spot in the liver ?
- ✓ Is FDG PET-CT more or less sensitive and specific than the other imaging modalities : CT and MRI
- ✓ Pitfalls and artifacts must be known by every one for not inducing false positive or false negative results



PET and liver metastases from colorectal cancer

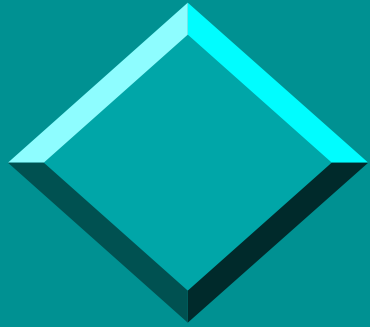
PET-CT versus CT alone or MRI for liver metastases from colorectal cancer:

- ✓ Same Sensitivity (91-95 %) et accuracy (90 %) between PET-CT and CT alone.
- ✓ But PET is more specific for lesions > 1 cm and PET > CT (Sp = 100 % VS 50 %) in prior hepatectomy

Selzner M et al, Ann Surg 2004, 240, 1027-36

- ✓ MRI > PET for small lesion

Kong g, Eur J Nucl Med Mol IM, 2008, 1323-9



PET and liver metastases from colorectal cancer

Important Message:

- ✓ Hepatic angioma and Focal Nodular Hyperplasia : NEVER UPTAKE OF FDG
- ✓ Red Blood cell scintigraphy seems to be replaced today by FDG PET-CT for characterization of giant hemangiomas



Detection of recurrence

New staging before surgery of a single lesion +++++

✓ Single liver metastase :

- Research other localizations (lungs, nodes, peritoneal carcinomatosis, suprarenal glands, etc...)

TEP : Se = 91,5 % Sp = 95,4 %

TDM : Se = 60,9 % Sp = 91,1 %

- New staging the liver itself :

TEP : Se = 88,0 % Sp = 96,1 %

TDM : Se = 82,7 % Sp = 84,1 %

*Méta analyse de Wiering B et al ,Cancer 2005, 104, 2658-70 et al,
(Langhenhoff et Lonneux 2002,*



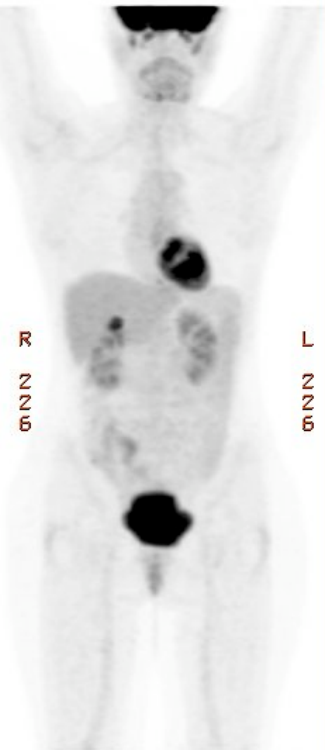
Recurrence detection

Evaluation of a single localization before surgery

Unexpected lesions revealed by FDG PET with modification of management in :

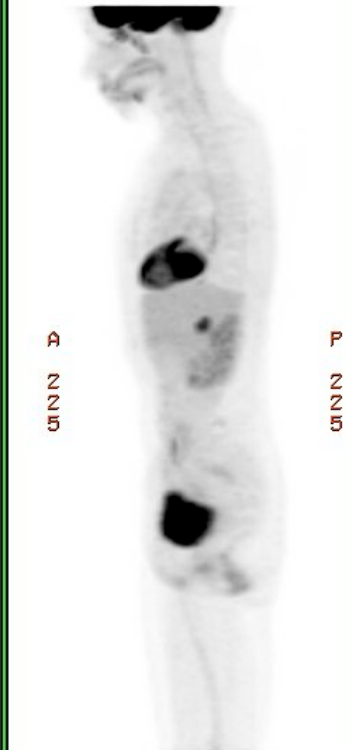
- ✓ 42 % of cases (Beets, 1994)
- ✓ 32 % of cases (Lai, 1996)
- ✓ 32 % of cases (Valk 1999)
- ✓ 28 % of cases (Delbeke 1999)
- ✓ 20 % of cases (Ruers 2002)
- ✓ 21 % of cases (Selzner 2004)
- ✓ 20 % of cases (Kuker 2007)

6VERSE0040REHEM001 Dan preop meta hep unique
 AM1265908205.897.1207138885
 DFOV 45.1 x 180.5 cm Apr 02 2008
 HD HIP No cut



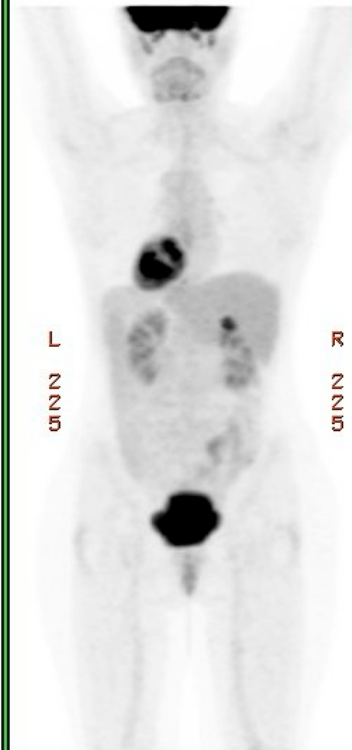
R 2 2 6 L 2 2 6
 m=0.00 H=7.64 g 1483 V=1.17

6VERSE0040REHEM001 Dan preop meta hep unique
 AM1265908205.897.1207138885
 DFOV 45.1 x 180.4 cm Apr 02 2008
 HD HIP No cut



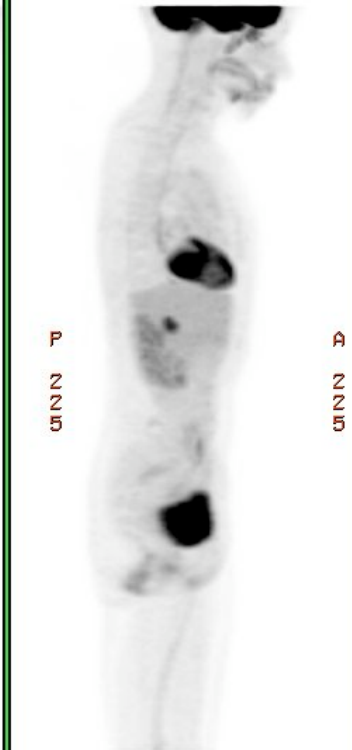
A 2 2 5 P 2 2 5
 m=0.00 H=7.64 g 1483 V=1.53

6VERSE0040REHEM001 Dan preop meta hep unique
 AM1265908205.897.1207138885
 DFOV 45.1 x 180.4 cm Apr 02 2008
 HD HIP No cut



L 2 2 5 R 2 2 5
 m=0.00 H=7.64 g 1483 V=1.53

6VERSE0040REHEM001 Dan preop meta hep unique
 AM1265908205.897.1207138885
 DFOV 45.1 x 180.4 cm Apr 02 2008
 HD HIP No cut



P 2 2 5 A 2 2 5
 m=0.00 H=7.64 g 1483 V=1.53

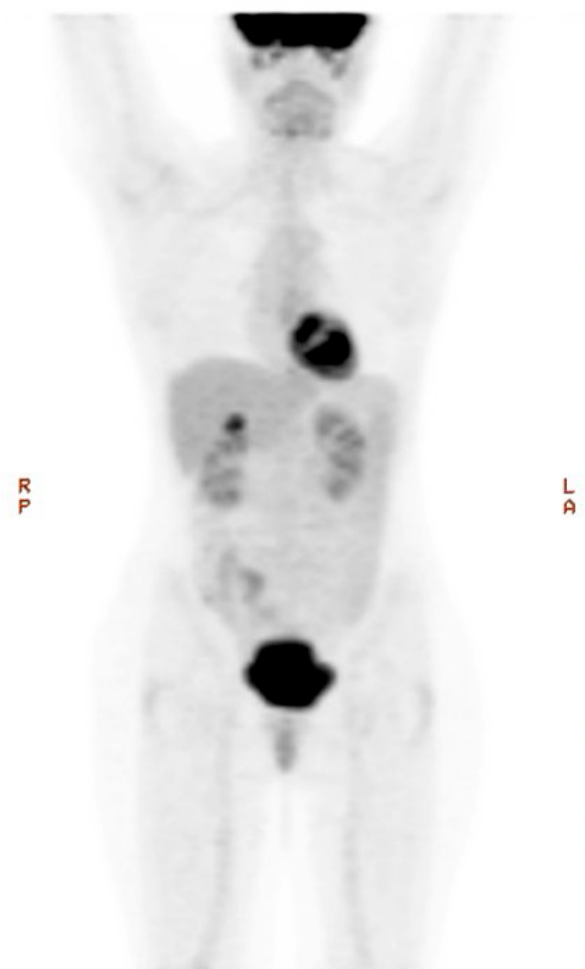
Lésion du colon
 transverse
 opérée le 14
 décembre 2006
 suite
 l'ablation d'un
 « kyste »
 ovarien
 correspondant à
 une extension
 de la lésion
 de la colique

Découverte en
 décembre 2007
 d'une méta
 hépatique
 unique

Evaluation après
 CT et
 éventuelle
 exérèse

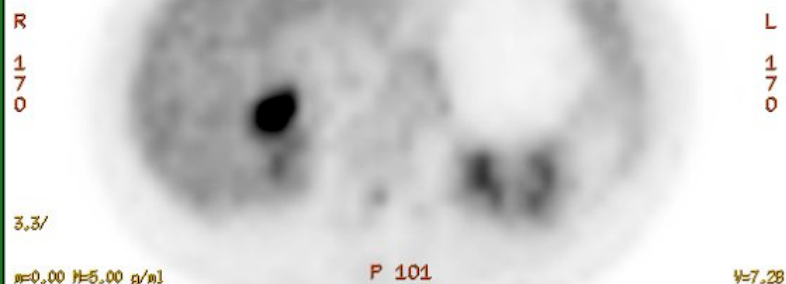
1 méta unique

3D Volume 2 COLON TRANSVERSE OPERE Bilan preop meta hep unique
S AM1203946505,897,1207138985
DFOV 60,6 x 138,6 cm
HD HIP No cut
Apr 02 2008



m=0,00 H=7,60 g/ml I V=7,28

Axial3 Volume 2 COLON TRANSVERSE OPERE Bilan preop meta hep unique
I: 214,2 A 100 AM1203946505,897,1207138985
DFOV 33,9 x 20,1 cm
Apr 02 2008



Axial4 Volume 1 COLON TRANSVERSE OPERE Bilan preop meta hep unique
I: 214,2 A 100 AM1203946505,897,1207138985
DFOV 33,9 x 20,1 cm
Apr 02 2008



Axial5 Volume 2/Volume 1 COLON TRANSVERSE OPERE Bilan preop meta hep unique
I: 214,2 A 100 AM1203946505,897,1207138985
DFOV 33,9 x 20,1 cm
5,00
Apr 02 2008



m=0,00 H=5,00 g/ml P 101 V=7,28

Lésion du colon transverse opérée le 14 décembre 2006 suite à l'ablation d'un « kyste » ovarien correspondant à une extension de la lésion colique

Découverte en décembre 2007 d'une métastase hépatique unique

Evaluation après CT et éventuelle exérèse

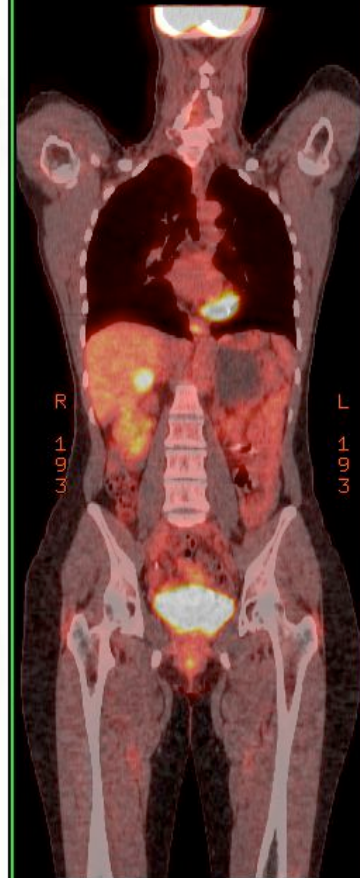
1 méta unique

ERSEROPERE Phlamepdeop meta hep unique
P: 19.1 AM1263943506.897.1207138985
DFOV 38.7 x 154.8 cm Apr 02 2008



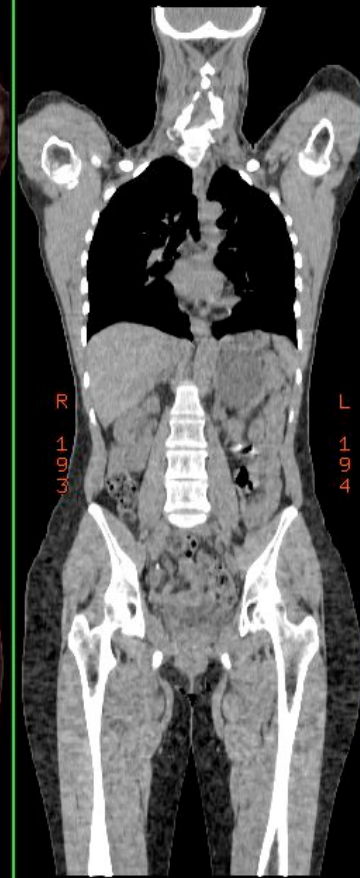
5.5/
M=0.00 H=7.64 g 1055 V=7.28

ISVERSEROPERE Phlamepdeop meta hep unique
P: 19.1 AM1263943506.897.1207138985
DFOV 38.7 x 154.8 cm Apr 02 2008



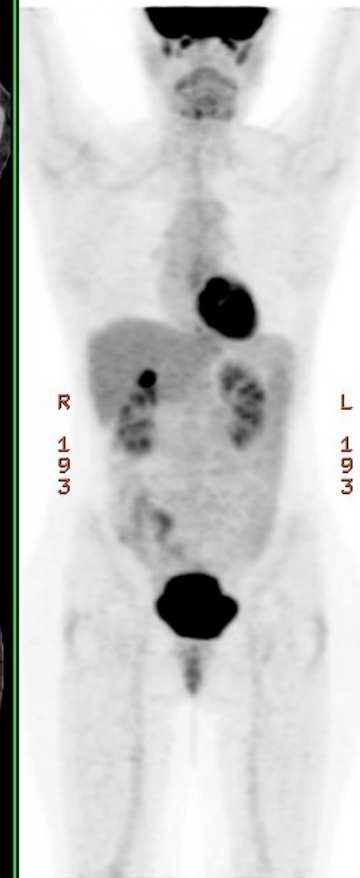
5.5/
M=0.00 H=5.04 g 1055 V=7.28

ISVERSEROPERE Phlamepdeop meta hep unique
P: 19.0 AM1263943506.897.1207138985
DFOV 38.7 x 154.8 cm Apr 02 2008



1.0/
M = 400 L = 10 1054 V=38

ISVERSEROPERE Phlamepdeop meta hep unique
P: 19.0 AM1263943506.897.1207138985
DFOV 38.7 x 154.8 cm Apr 02 2008
HD HIP No cut



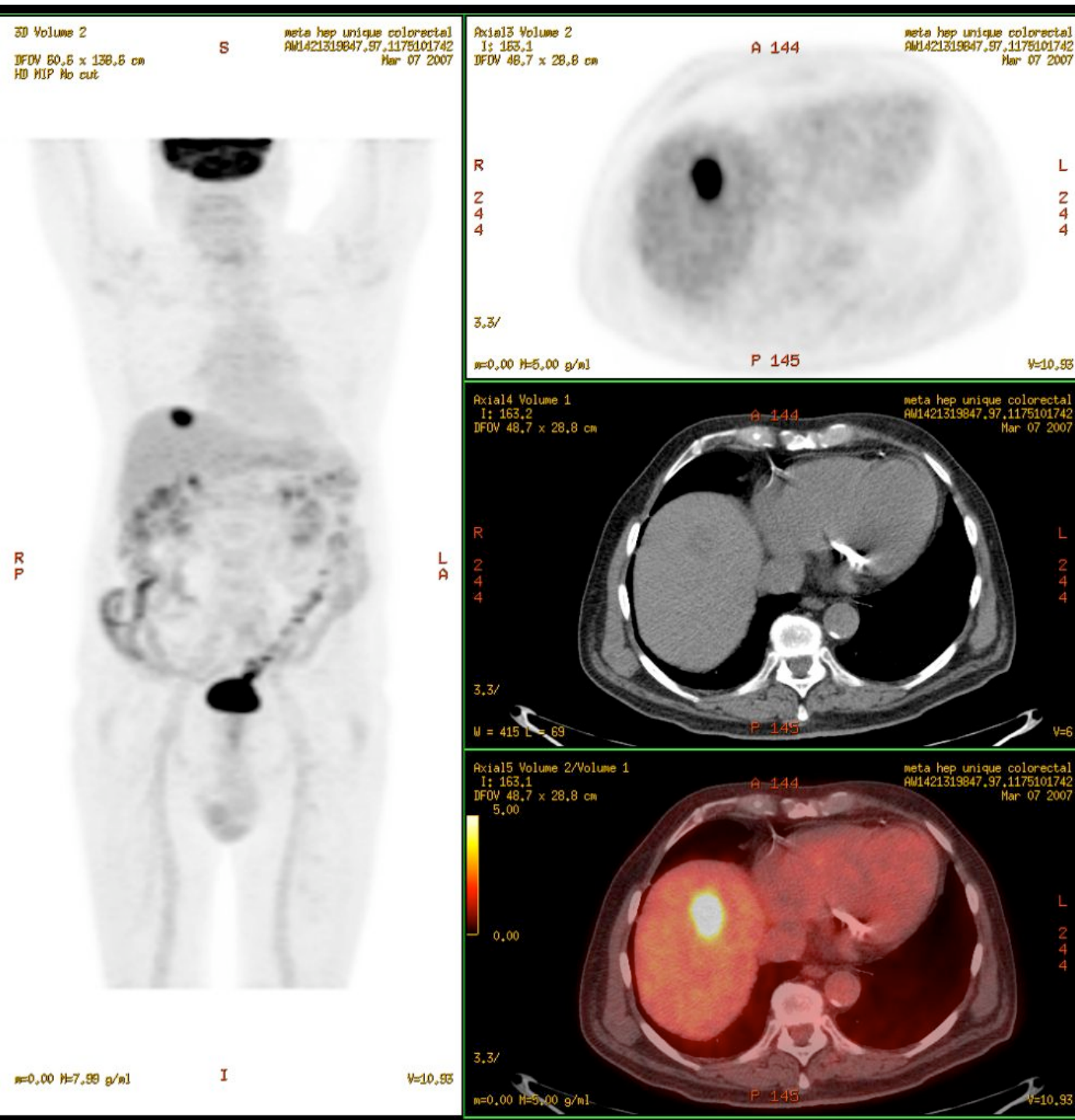
5.5/
M=0.00 H=5.04 g 1054 V=7.28

Lésion du
transverse
opérée le 14
décembre 2006
suite
l'ablation d'un
« kyste »
ovarien
correspondant à
une extension
de la lésion
colique

Découverte
décembre 2007
d'une
hépatique
unique

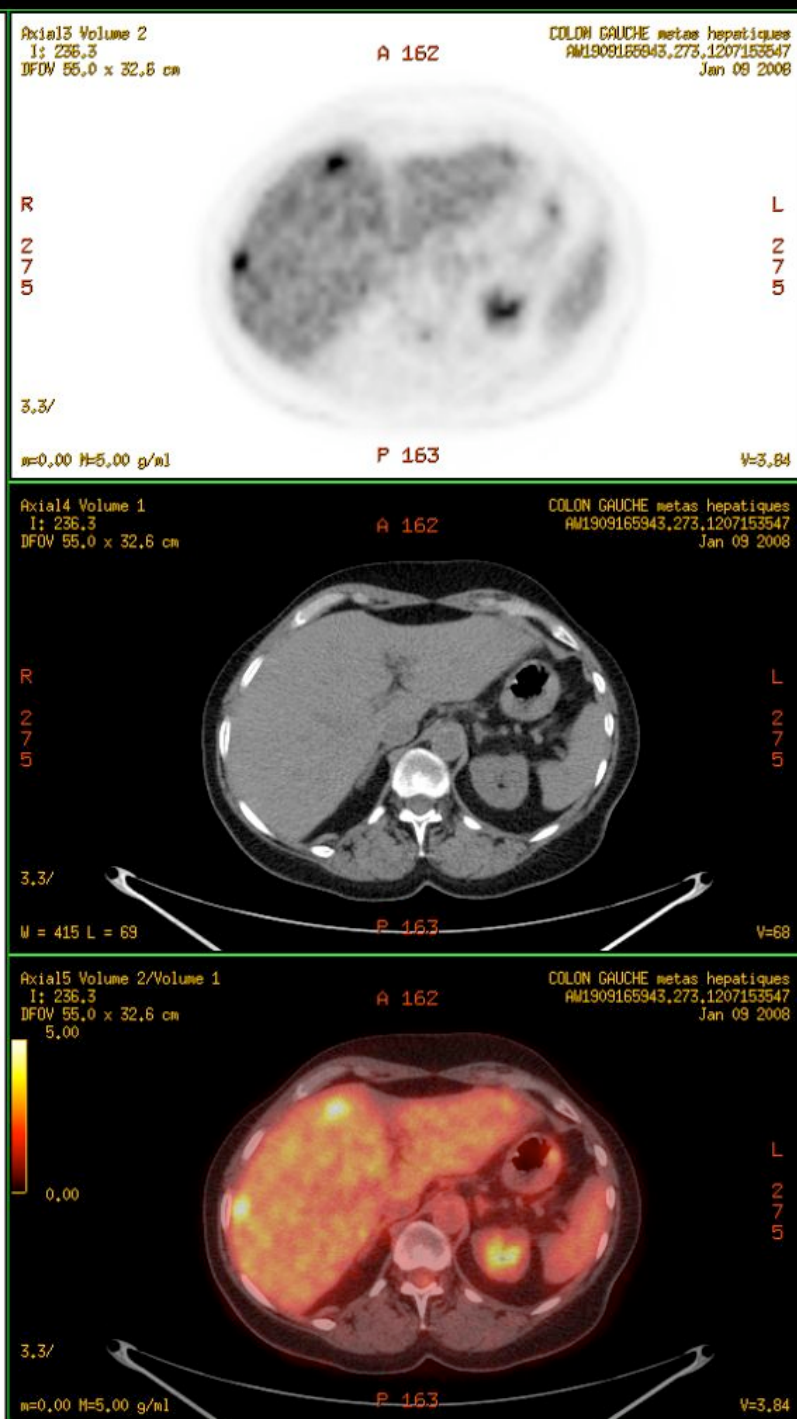
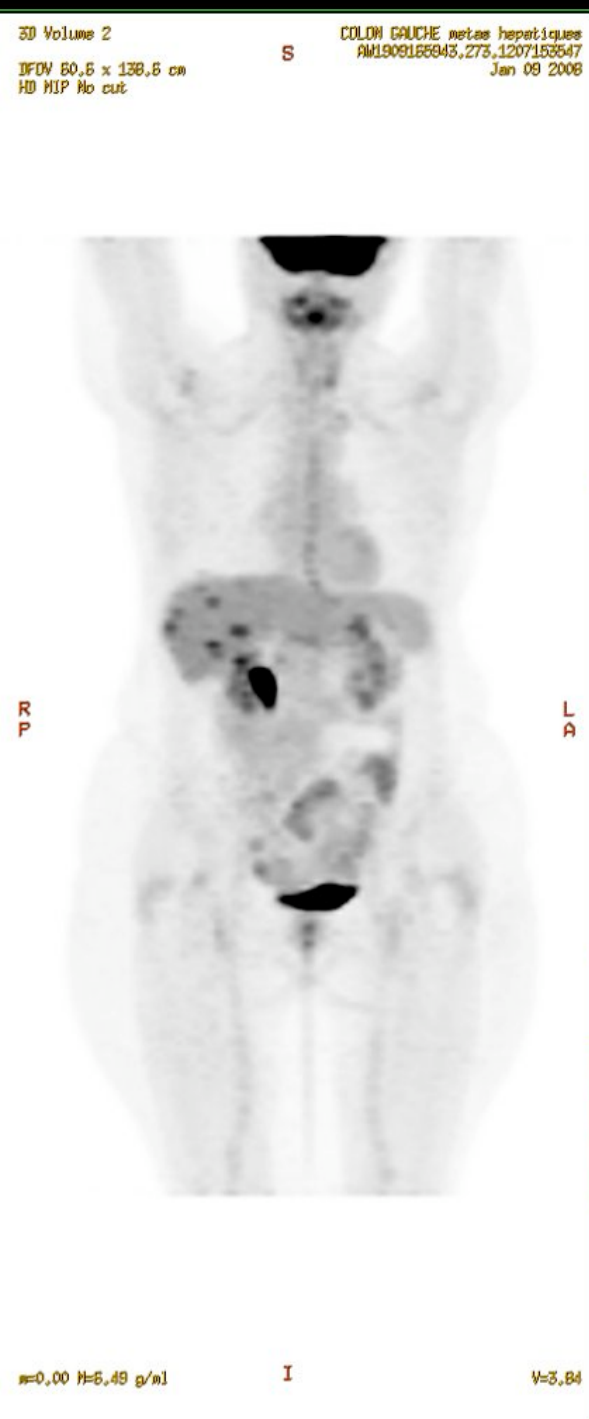
Evaluation
CT et
éventuelle
exérèse

1 méta unique



Bilan d'une lésion
du segment
VIII chez un
patient opéré
d'un adéno-
carcinome
rectal

1 volumineuse
métastase
hépatique
unique



Patiente opérée le
28/12/2006
d'une
colectomie
gauche

Adressée le
09/01/2008
Suspicion de
métastases
hépatiques et
de carcinose
péritonéale

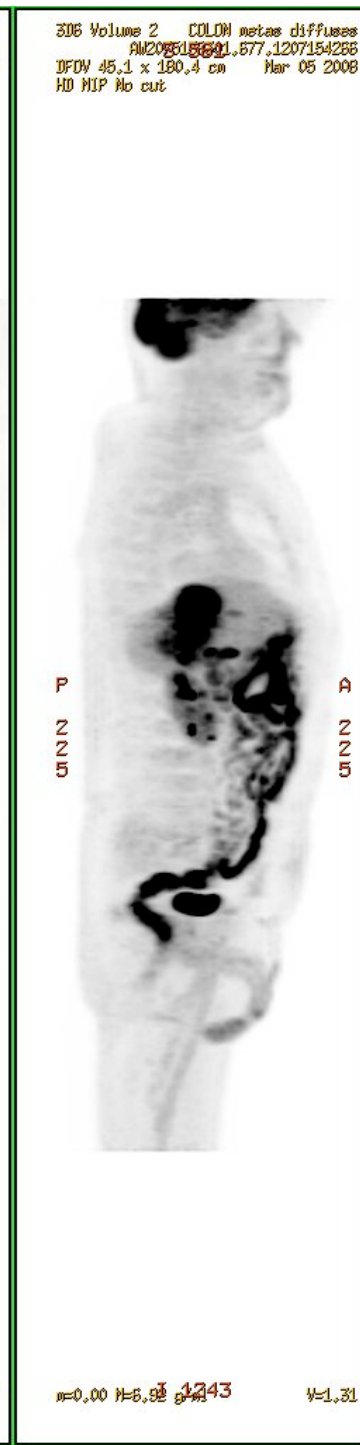
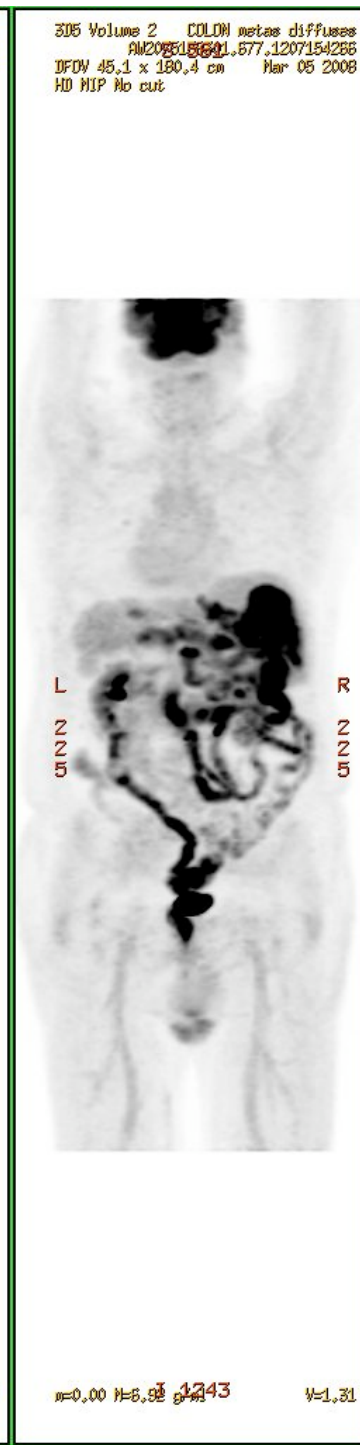
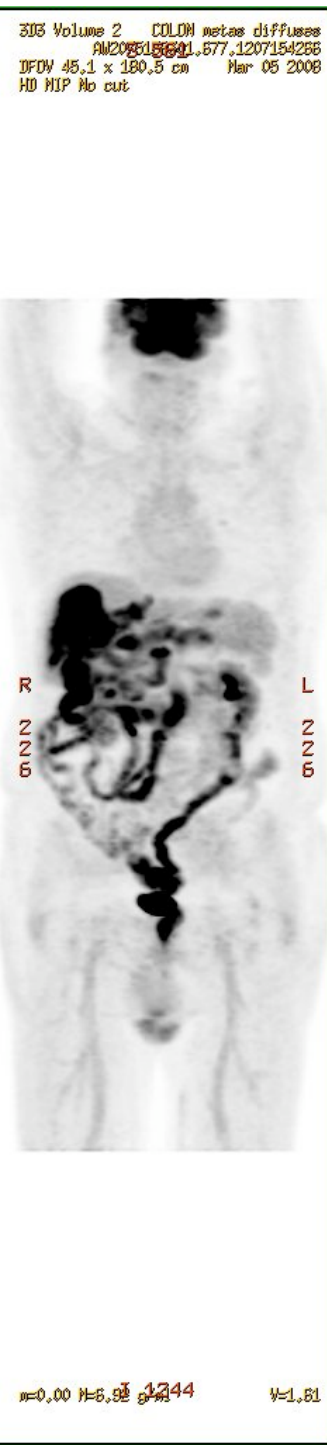
Nombreux foyers
hépatiques
droits mais
aussi gauche

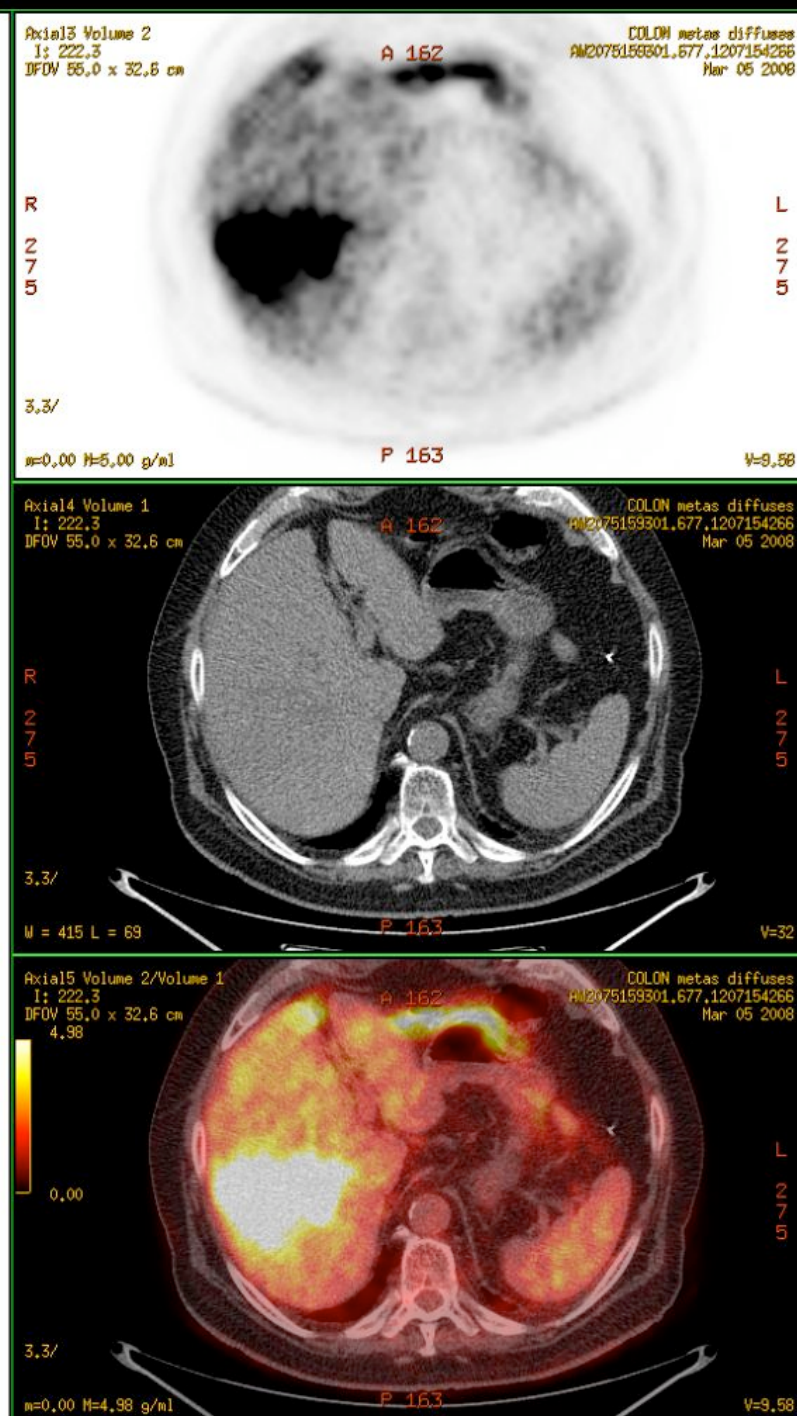
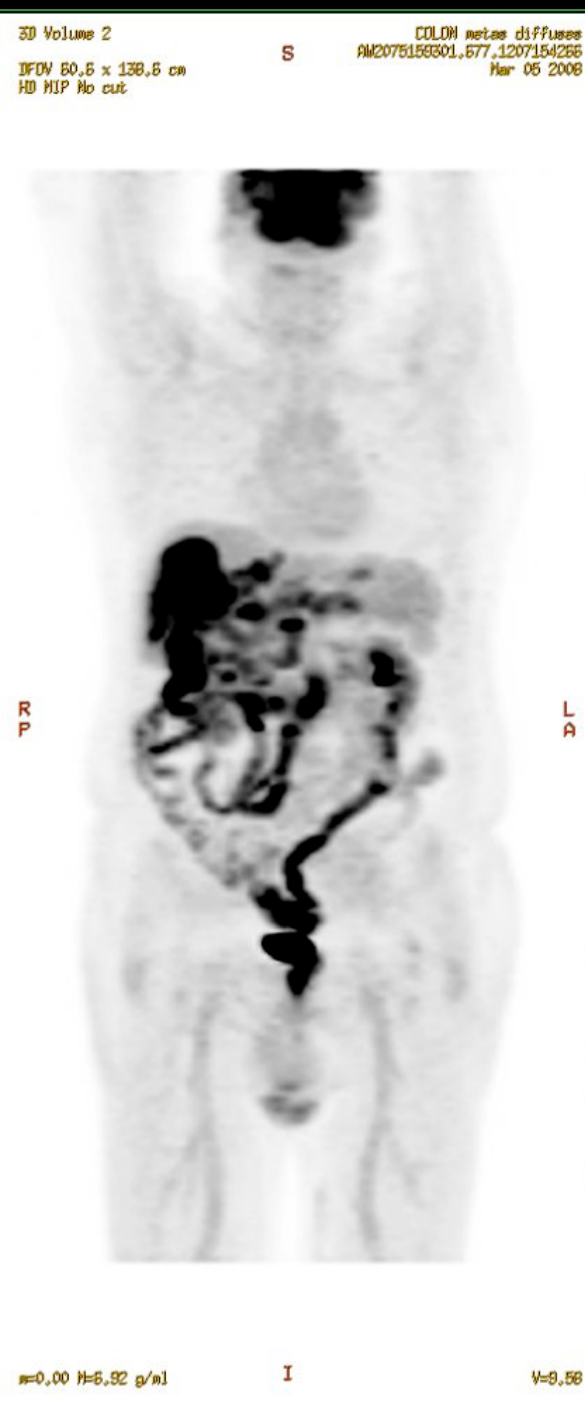
Pas d'activité sur
les images
tissulaires

d'une

Bilan
probable
rechute
métastatique
hépatique d'un
cancer du colon
traité en 2000

Volumineuse lésion
du
VIII segment



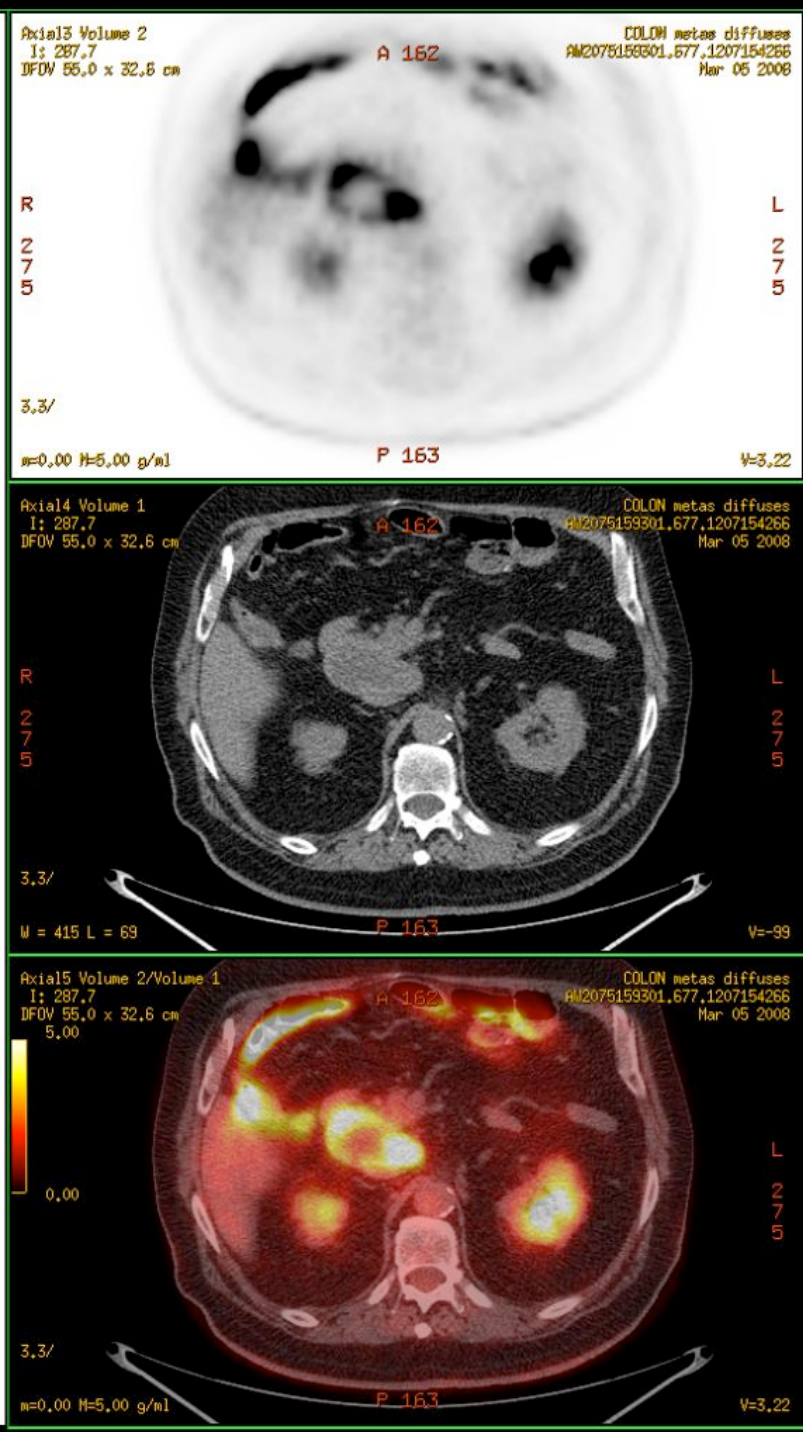
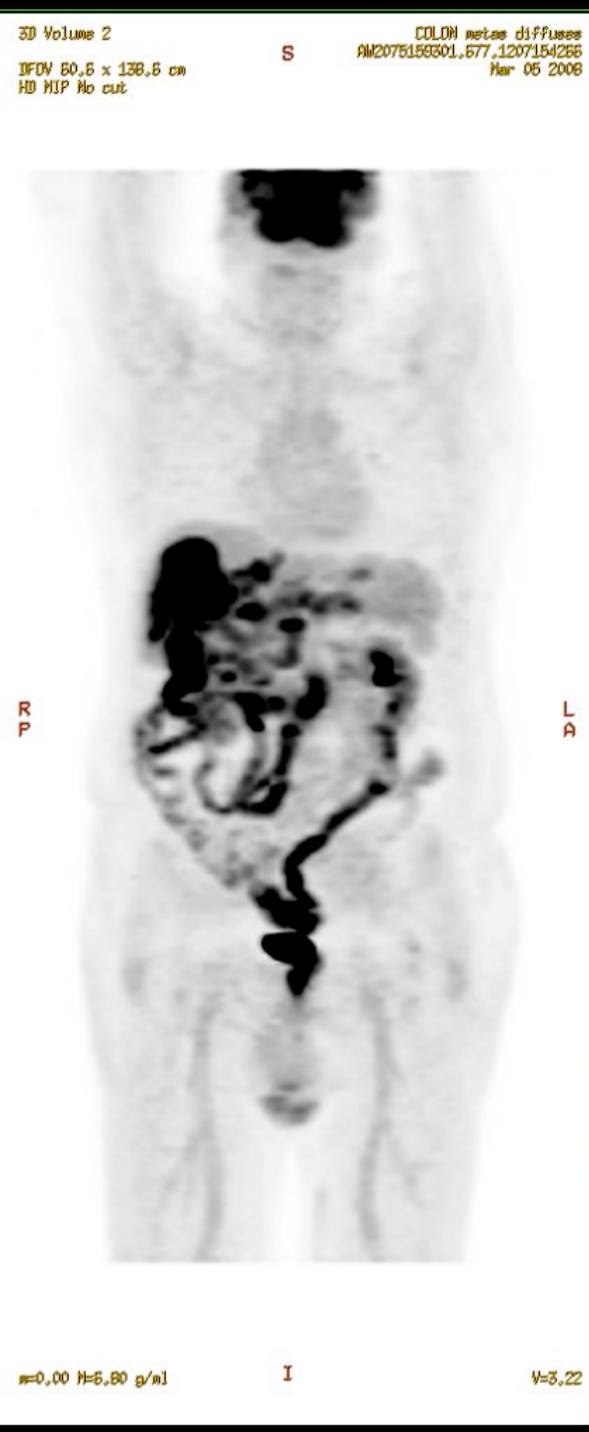


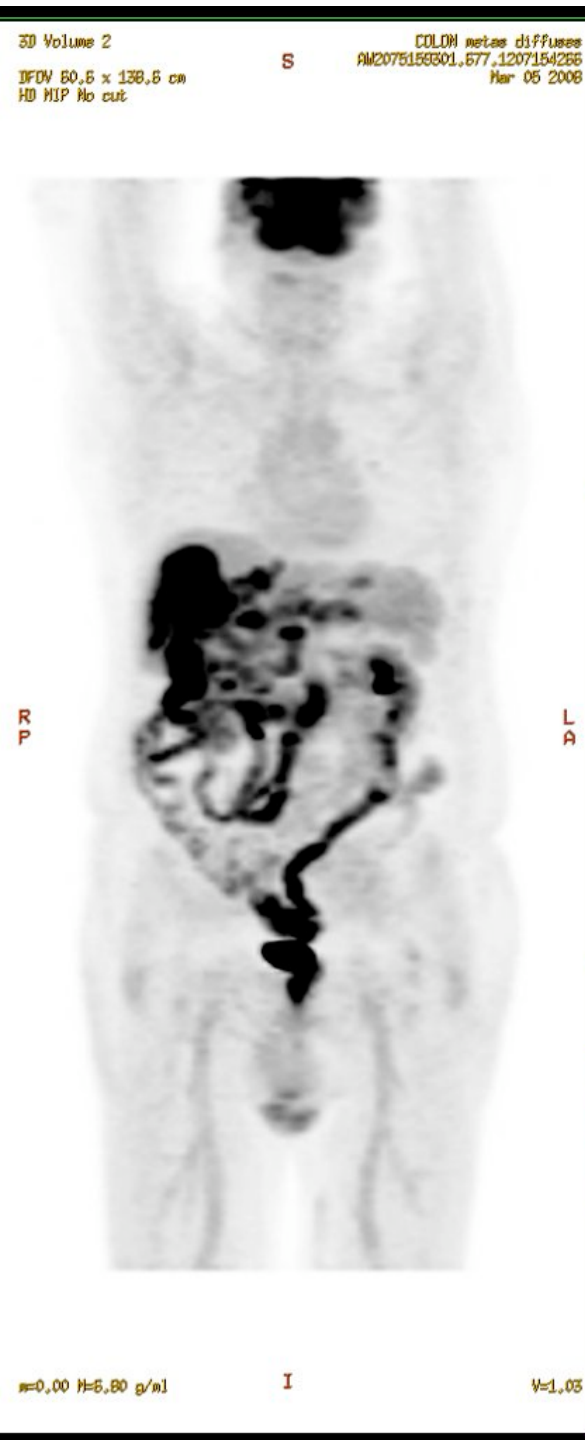
Bilan

probable
rechute
métastatique
hépatique
cancer du colon
traité en 2000

Volumineuse
des
VIII et I

Masse
correspondant à
un ganglion
coeliaque



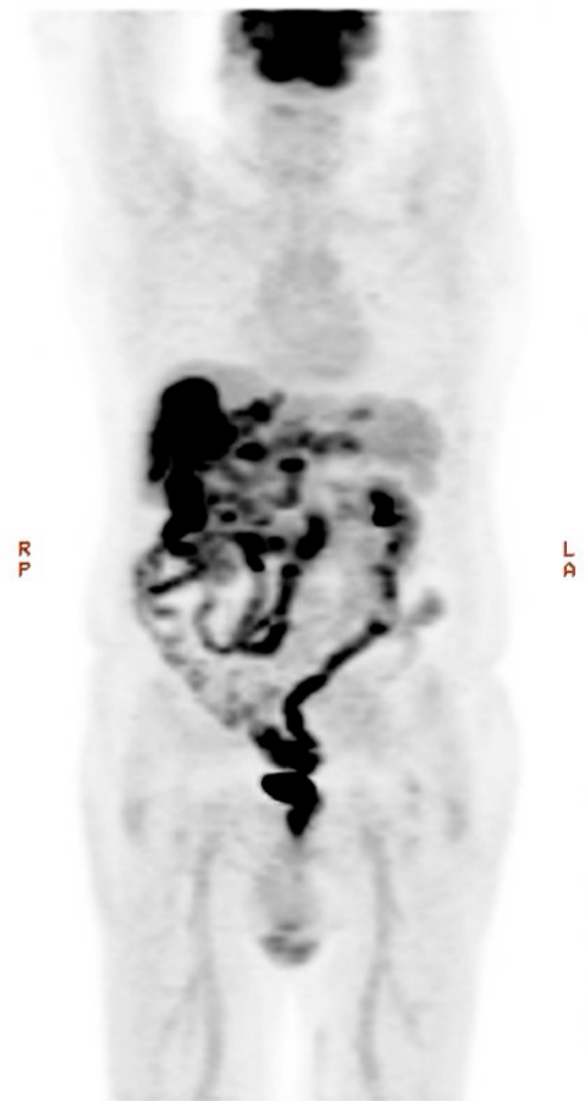


Un ganglion hyper-
métabolique
inter
cave

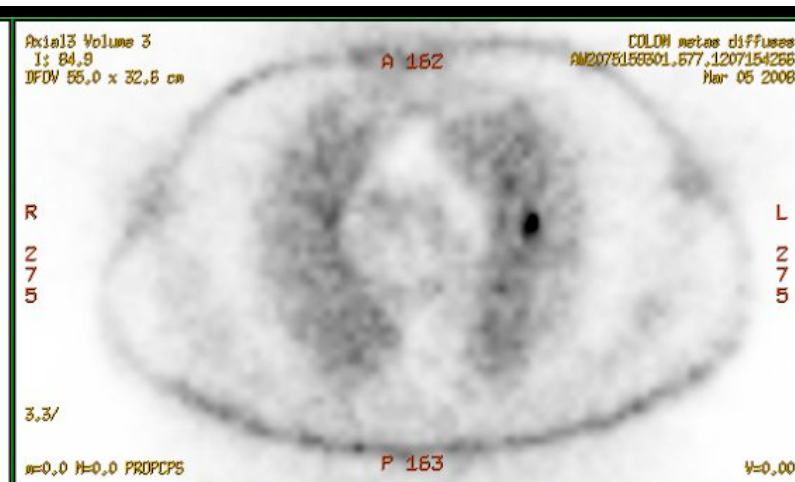
Fixation
gauche
(ce n'est pas de
la carcinose)

Et...

3D Volume 2
S COLON metas diffuses
AM2075159301.677.1207154266
DFOV 60,6 x 138,6 cm
HD MIP No cut
Mar 05 2008



m=0,00 H=5,80 g/ml I V=1,88



Un foyer
pulmonaire
gauche
surtout
images
corrigées

visible
sur les
non



Detection of recurrences

After radiofrequency :

- ✓ After radiofréquency ablation of liver metastases : no uptake.

PET > CT for detection of recurrence after radiofrequency

Travaini LL et al, Eur J Nuc Med Mol Im 2008, 1316-22

PET = MRI for detection of recurrence after radiofrequency

Kuehl H et al, Eur J Radiol 2007, 362-71

- ✓ Evaluation in the first 12 hours (evaluation of efficiency) or after 6 à 8 weeks (recurrence) : inflammation from the 3rd day with hot spot rim (granulation)

Avril N, 2006, 47, 1235-37



Thérapeutic Evaluation

Chemotherapy :

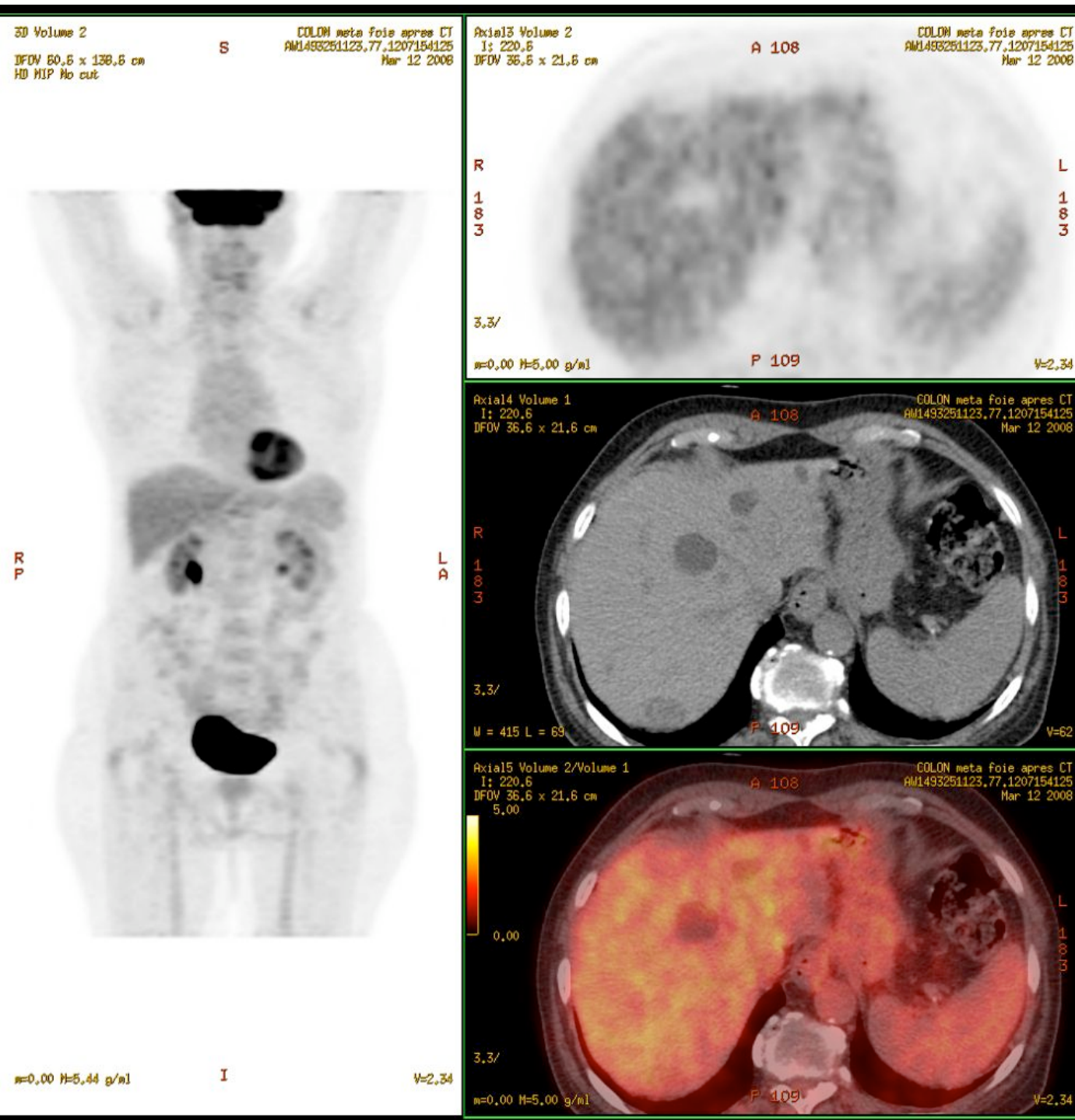
- ✓ Early evaluation of therapeutic to detect answering from non answering patients : evaluation after 1 or 2 administrations (3 or 6 weeks)

Bender H et al, Hybridoma 1999, 18, 87-91

Delbeke D et al, J Nucl Med, 1999, 40, 591-603

Small RM et al, J surg Oncol 2008, 99, 93-98

- ✓ CHIP : pas de protocole particulier



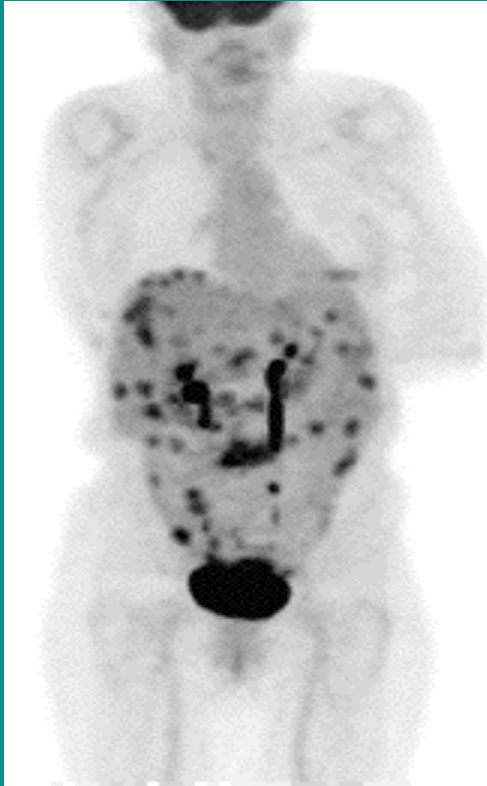
Patiente opérée en
février 2007
d'une lésion
colique. Lésions
secondaires
hépatiques
(synchrones)

CT jusqu'au
23/11/2007

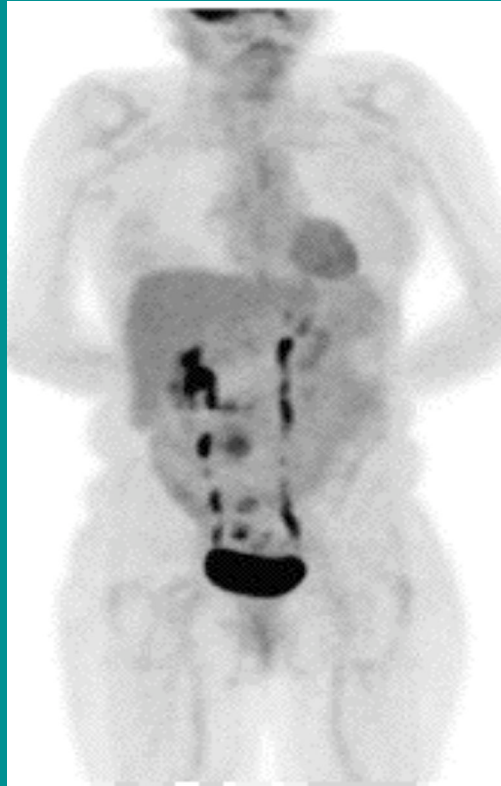
Pas d'image de
référence !!!

Aucune activité
sur les lésions
hépatiques

Erturk et al. Eur J Radiol 2006, 229-235



Before chemotherapy

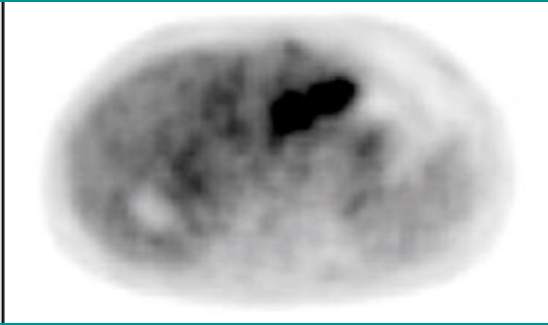
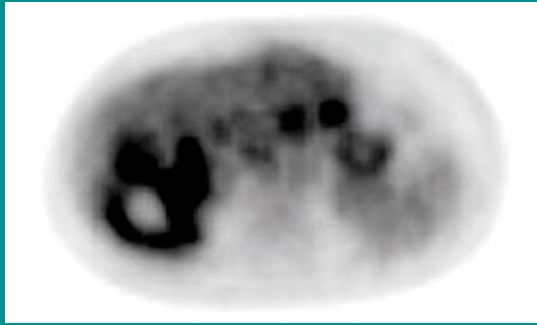


After chemotherapy

Hepatic and peritoneal
metastases

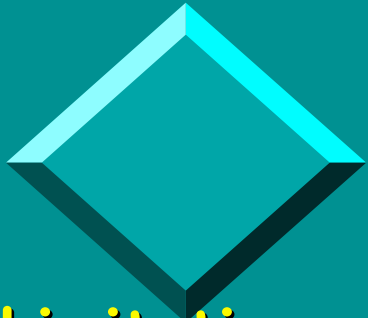
Before therapy

After therapy



After treatment of the
lobe of the liver by intra
arterial injection of
microspheres labeled
Y-90

Bienert et al. Eur J Nucl Med, 2005, 32, 778-87



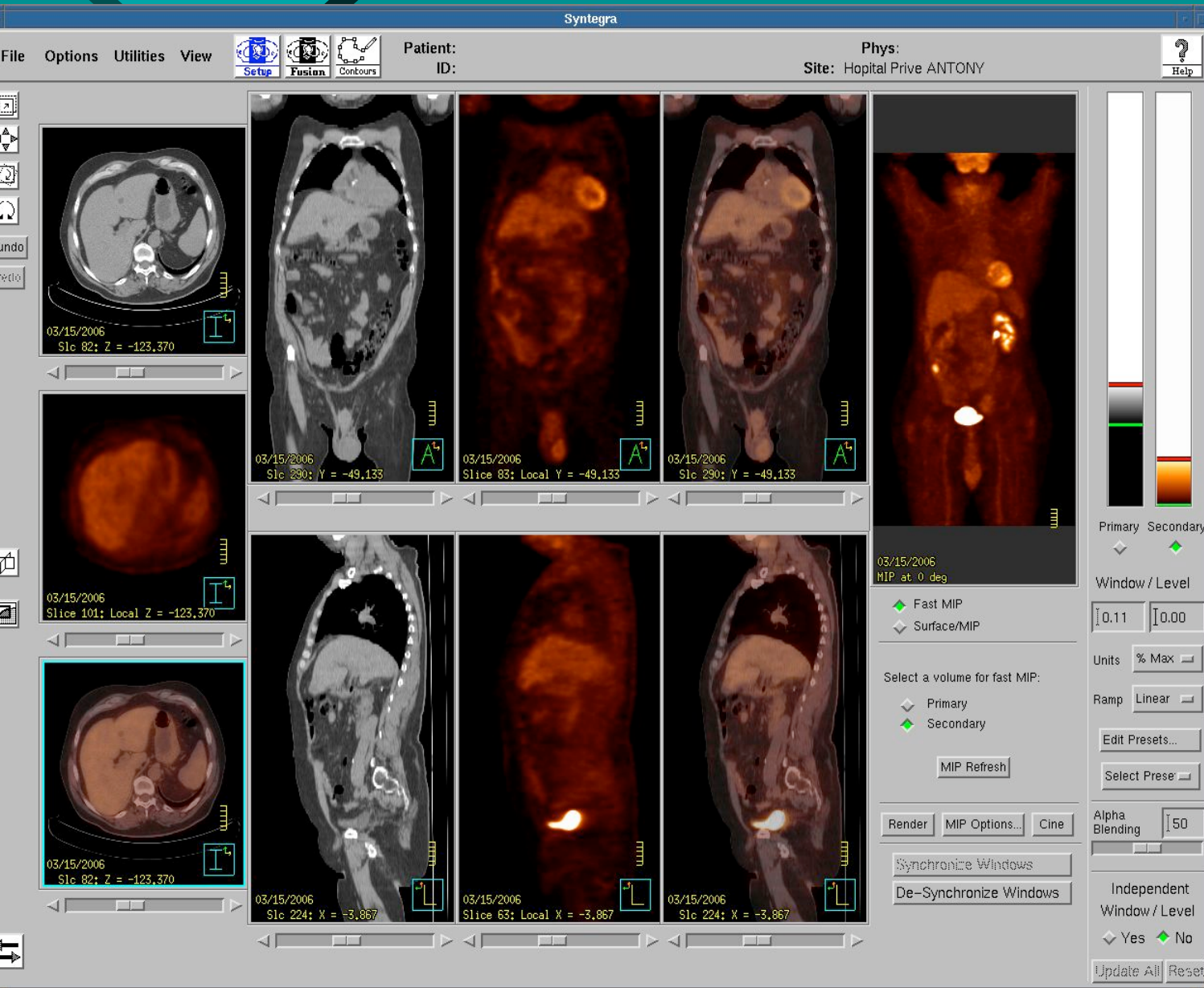
Pitfalls and Artifacts

Limitations of FDG PET (1) :

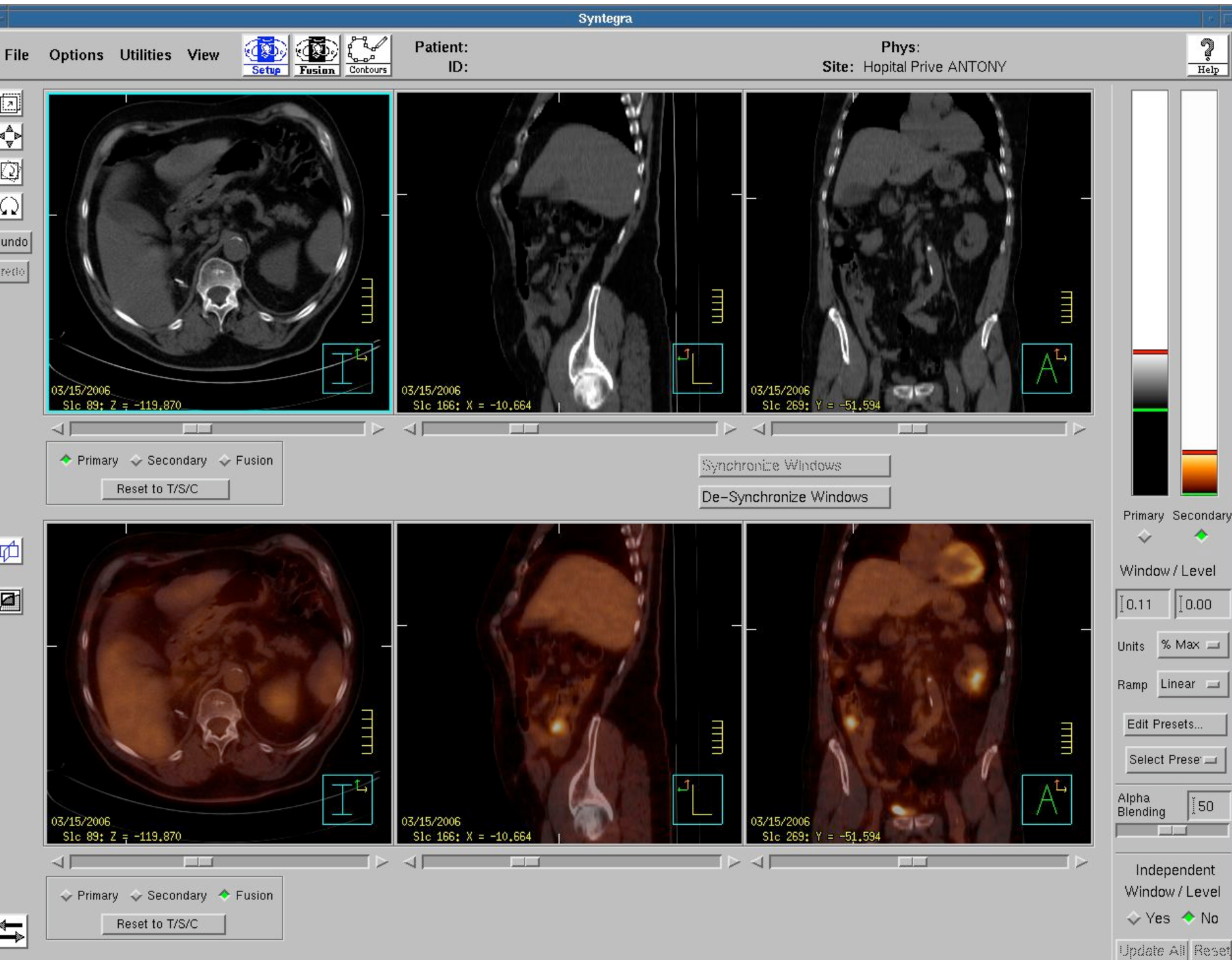
- ✓ HISTOLOGICAL PATTERN : Mucinous adenocarcinoma : Se = 58 % VS 92 % for non mucinous
Whiteford MH et al, Dis Colon Rectum, 2000, 43, 759-67
- ✓ SIZE : poor sensitivity (25 %) for lésions < 1 cm
Fong Y et al, Am J Surg 1999; 178, 282-7
- ✓ CHEMOTHERAPY : cell sideration in the 3 weeks after administration

Cas Clinique

H 67 ans (LEGUI)



- K rein opéré en 08/06
- Apparition de 2 masses hépatiques (II et III) en 02/06
- Bilan d'opérabilité

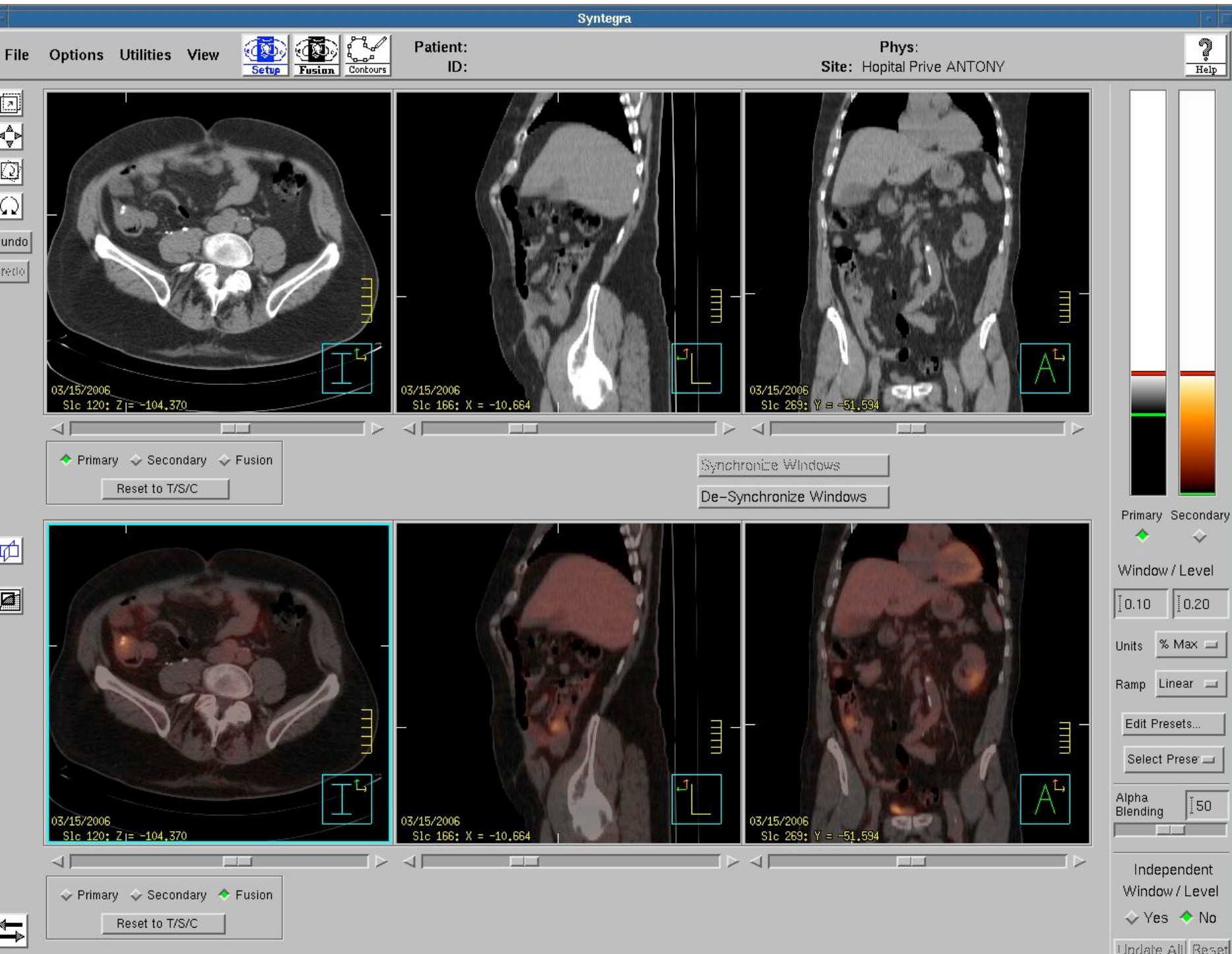


**TEP-
FDG:**

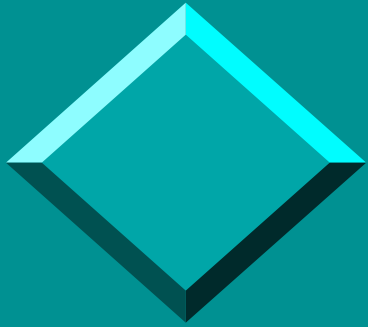
**Foie
RAS**

MAIS

**fixation
colique
droite**



*kystes
parasi-
taires
+
cancer
du
colon
(colo-
scopie
négati-
ve !!!)
...*

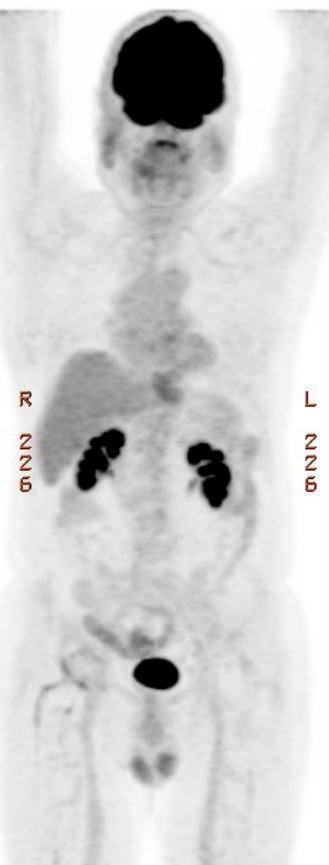


Pitfalls and Artifacts

Limitations of FDG PET (2) :

- ✓ MELLITUS DIABETES : competition between FDG blood glucosis. Back
tissular penetration ; poor sensitivity
- ✓ BRAIN : Intense uptake because of poor glucose-6 phosphatase activity
- ✓ Localization beside a natural hot spot (bladder) : signal is not
distinguished from the hot spot

303 Volume 2 META CEREBRALE POUND
 AME625470.508.1196878894
 DFOV 45,1 x 180,5 cm Dec 05 2007
 HD NIP No cut



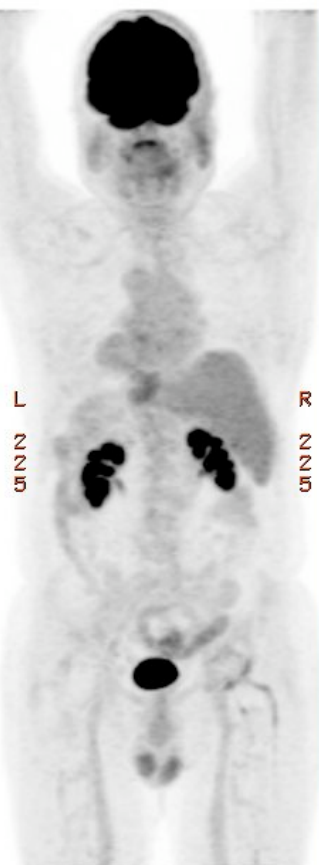
m=0,00 H=5,98 g 1411 V=1,22

304 Volume 2 META CEREBRALE POUND
 AME625470.508.1196878894
 DFOV 45,1 x 180,4 cm Dec 05 2007
 HD NIP No cut



m=0,00 H=5,98 g 1411 V=1,25

305 Volume 2 META CEREBRALE POUND
 AME625470.508.1196878894
 DFOV 45,1 x 180,4 cm Dec 05 2007
 HD NIP No cut



m=0,00 H=5,98 g 1411 V=1,25

306 Volume 2 META CEREBRALE POUND
 AME625470.508.1196878894
 DFOV 45,1 x 180,4 cm Dec 05 2007
 HD NIP No cut



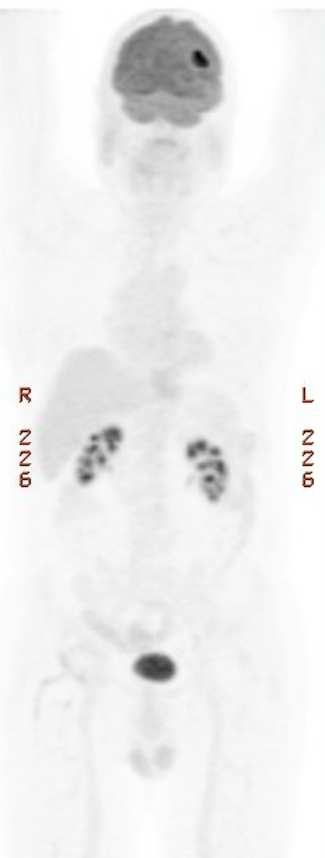
m=0,00 H=5,98 g 1411 V=1,25

Patient de 66 ans
 opéré en 2000 d'une
 lésion pulmonaire
 gauche

Découverte d'une
 lésion cérébrale
 frontale supérieure
 gauche

Recherche d'autres
 localisations

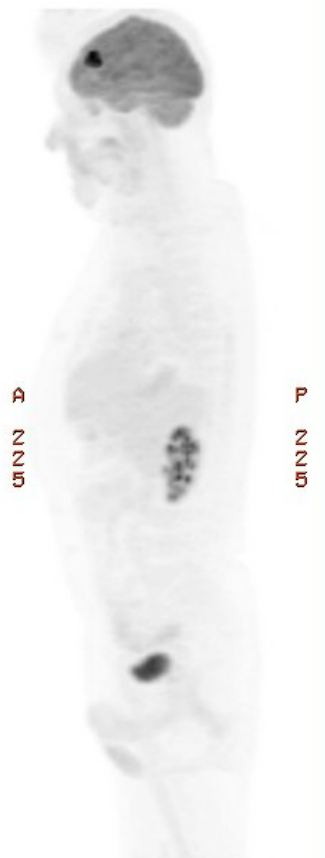
303 Volume 2 META CEREBRALE POUND
 AMB 62570.508.1196678894
 DFOV 45.1 x 180.5 cm Dec 05 2007
 HD HIP No cut



R 2 2 6 L 2 2 6

m=0.00 H=18.49 g 1411 V=1.22

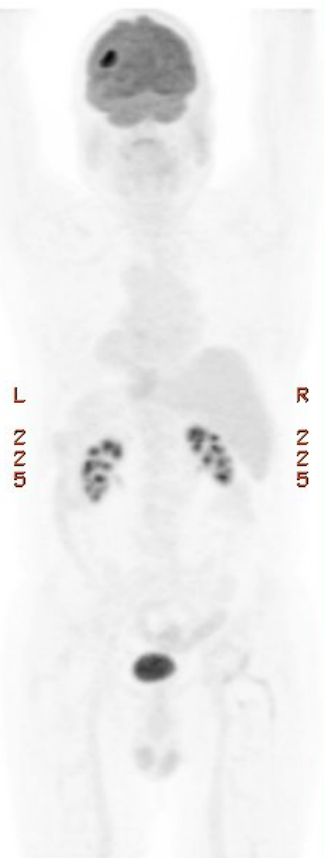
304 Volume 2 META CEREBRALE POUND
 AMB 62570.508.1196678894
 DFOV 45.1 x 180.4 cm Dec 05 2007
 HD HIP No cut



A 2 2 5 P 2 2 5

m=0.00 H=18.49 g 1411 V=1.26

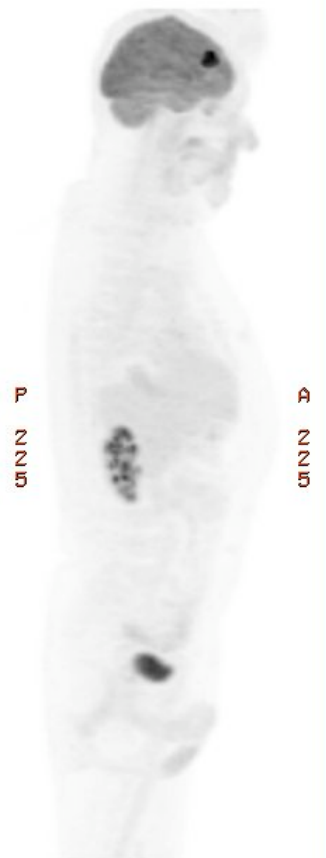
305 Volume 2 META CEREBRALE POUND
 AMB 62570.508.1196678894
 DFOV 45.1 x 180.4 cm Dec 05 2007
 HD HIP No cut



L 2 2 5 R 2 2 5

m=0.00 H=18.49 g 1411 V=1.26

306 Volume 2 META CEREBRALE POUND
 AMB 62570.508.1196678894
 DFOV 45.1 x 180.4 cm Dec 05 2007
 HD HIP No cut

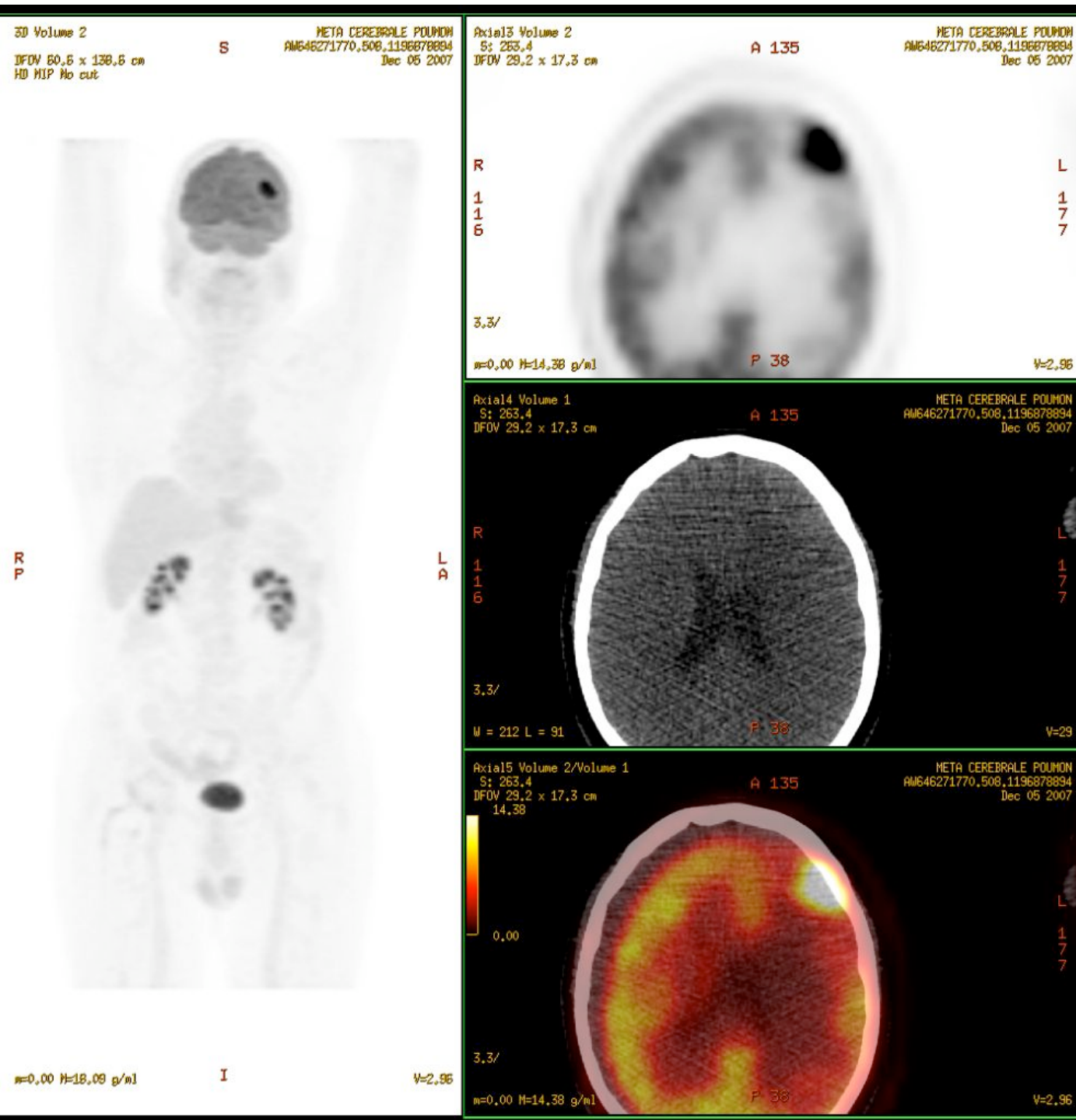


P 2 2 5 A 2 2 5

m=0.00 H=18.49 g 1411 V=1.26

Localisation
 cérébrale visible en
 TEP

Pas d'autre foyer en
 particulier
 pulmonaire
 surrénalien ou
 osseux



Foyer frontal gauche



Patient opéré
d'une lésion
sigmoïdienne
en octobre
2006

CT jusqu'en
juin 2007

Unique
ganglion
iliaque
primitif
gauche sur
le scanner
et l'IRM

Fixation sur
LE ganglion
iliaque
primitif
gauche

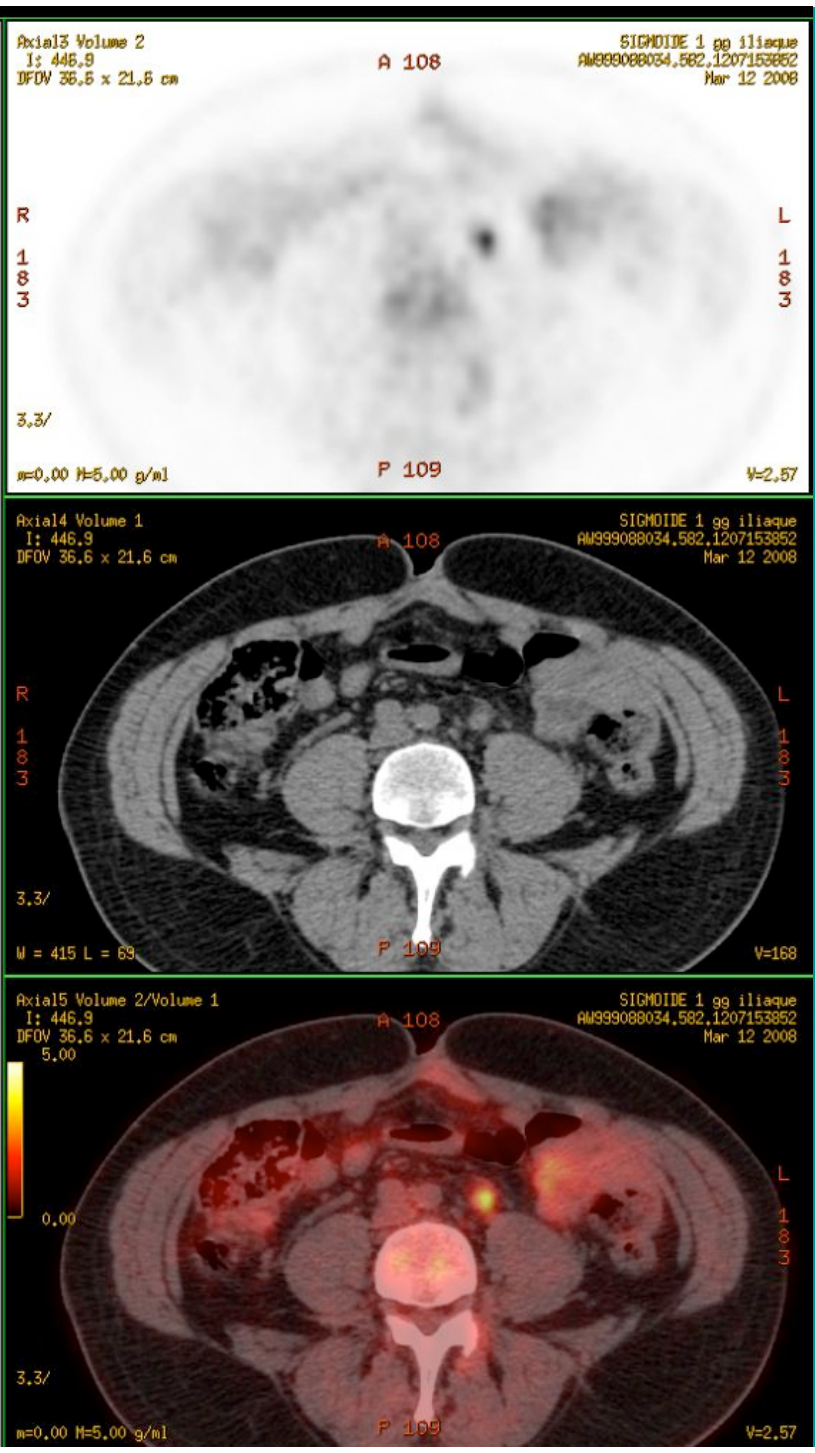
Aspect
confirmé
sur
images
tardives



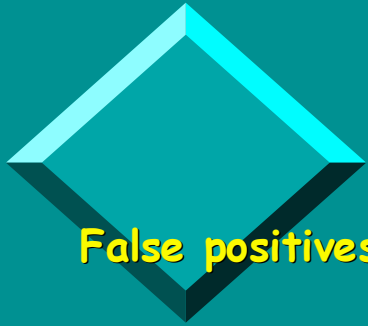
m=0,00 H=3,60 g/ml

I

V=2,57



Pitfalls and Artifacts



False positives :

✓ INFLAMMATION :

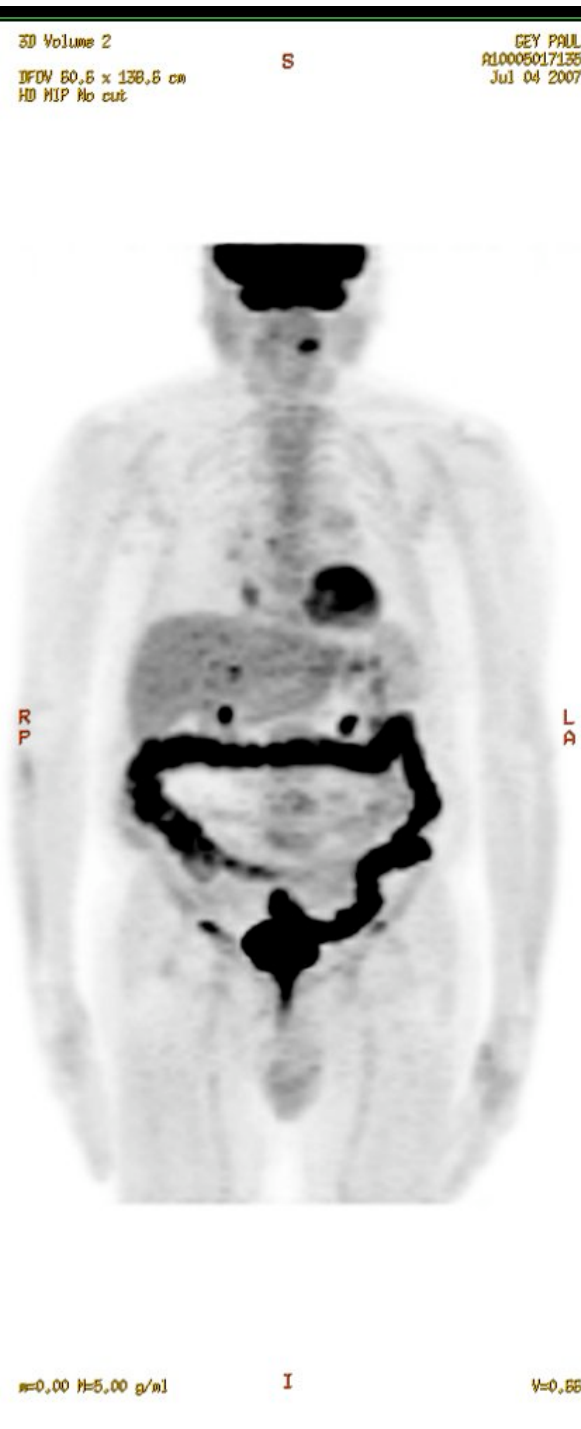
- Uptake is effective on inflammatory nodes : granulomatosis, sarcoïdosis, infection, etc...
- post-surgical inflammation
- Diverticulitis
- (MICI et adenomas)

✓ Radiotherapy : uptake in the field during 4 to 6 months

✓ Brown adipose tissue

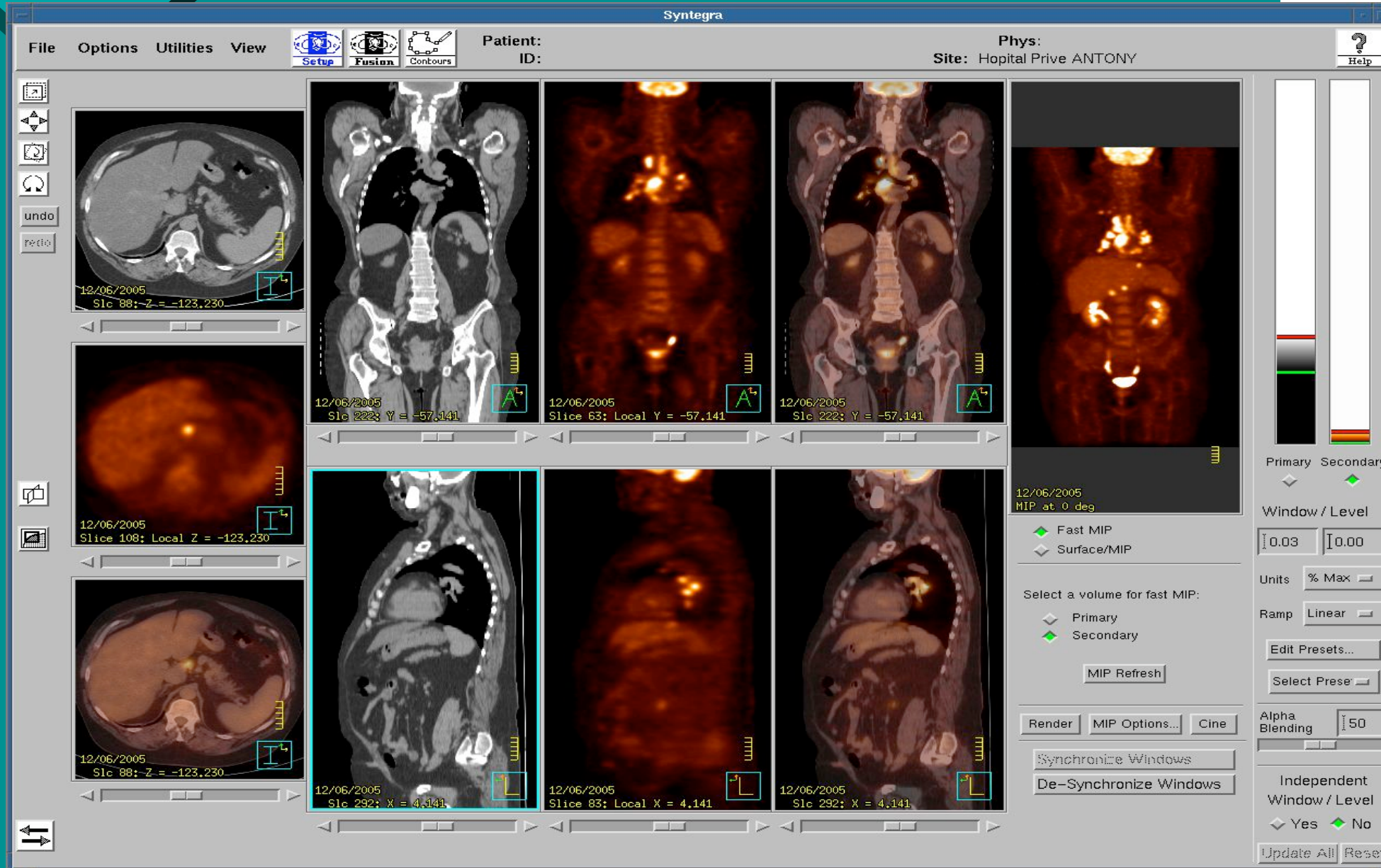
✓ INFECTION : hepatic abscess, other infections

✓ ARTIFACTS : physiologic uptake on gut, or ureters

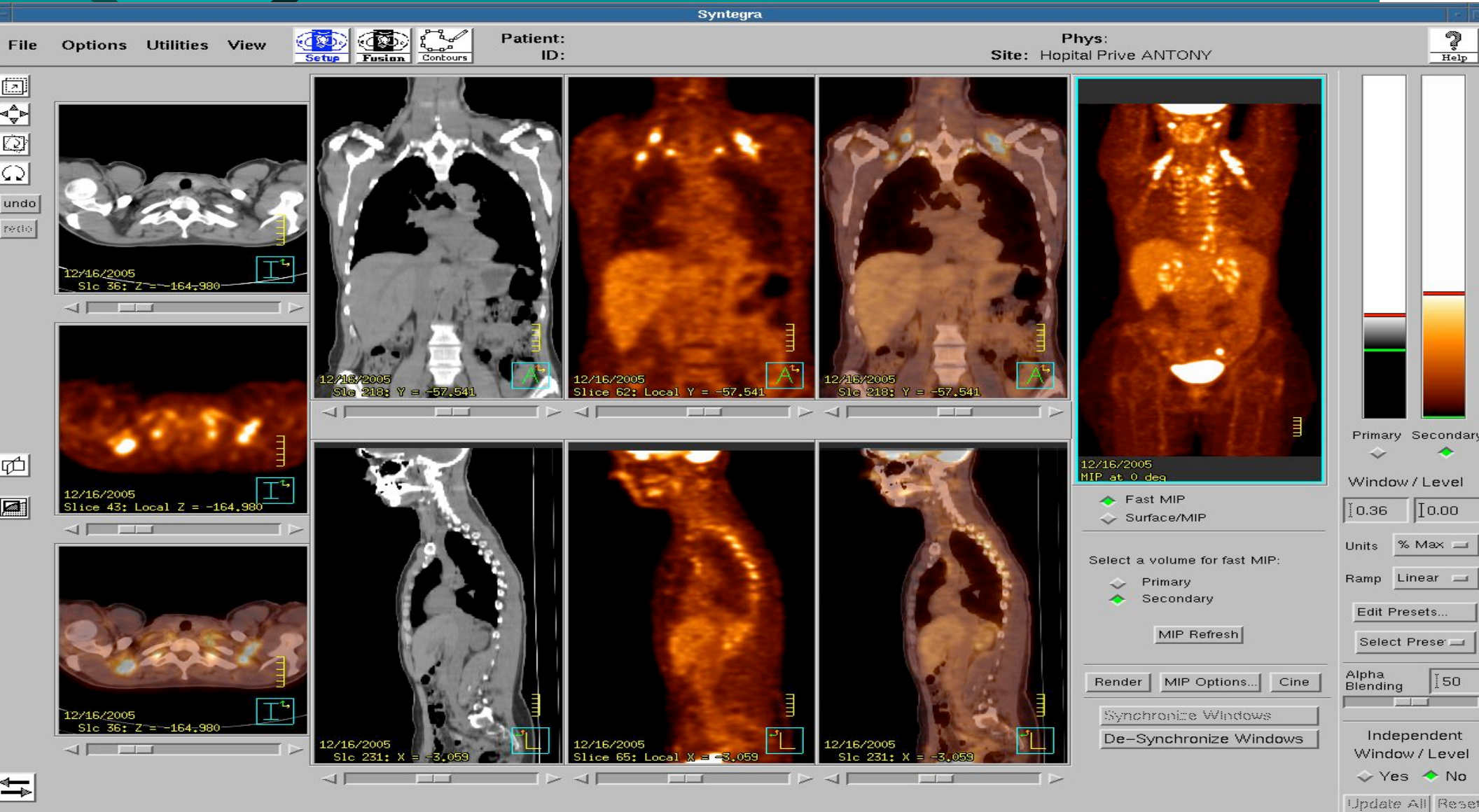


Réalisation
d'une TEP
dans le
cadre d'un
cancer du
poumon
chez un
patient
présentant
une maladie
de Crohn
connue

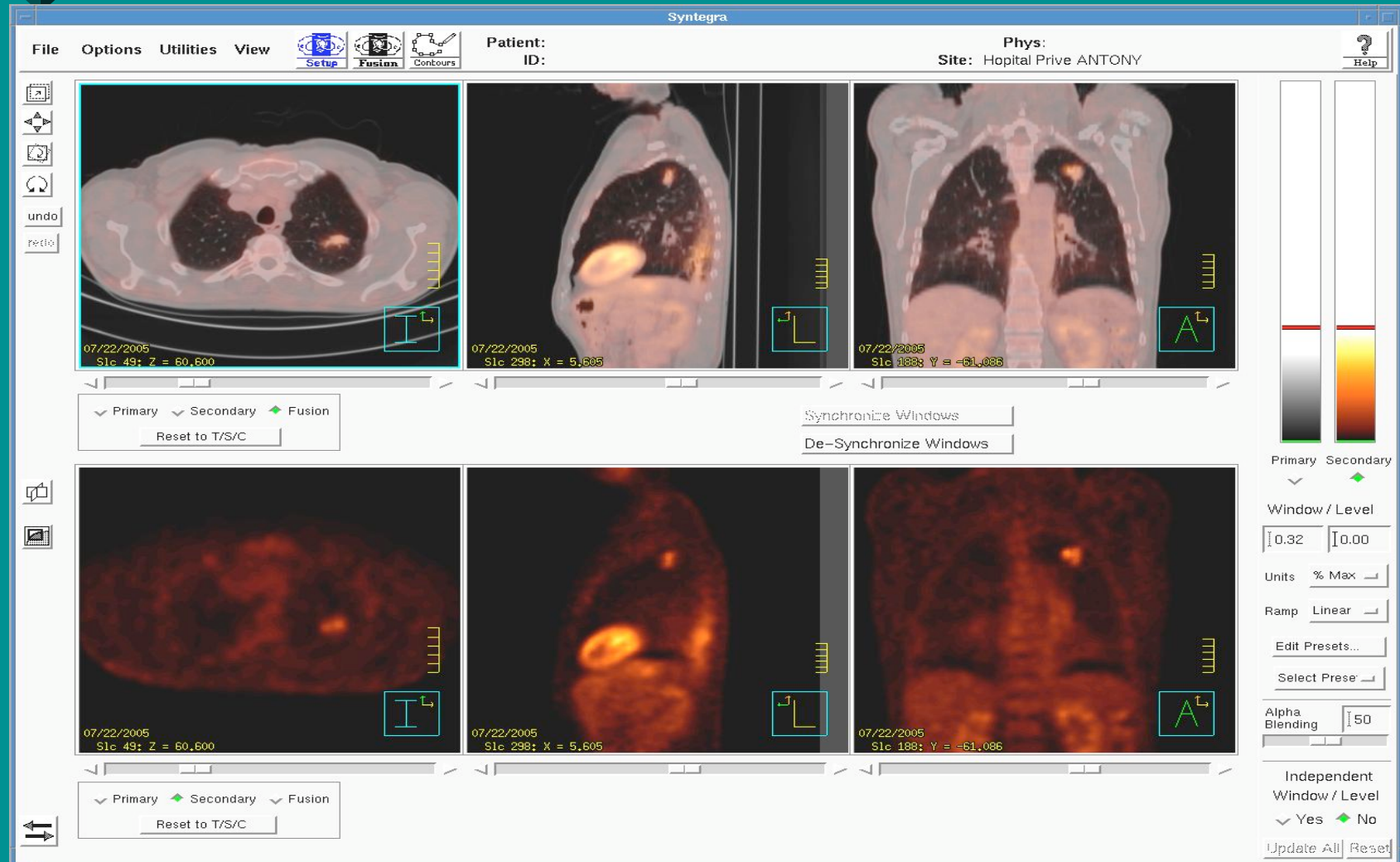
Sarcoidosis



Brown fat uptake

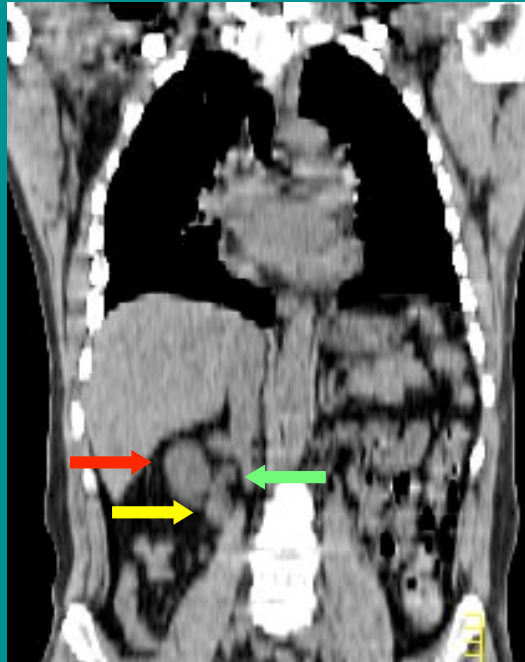
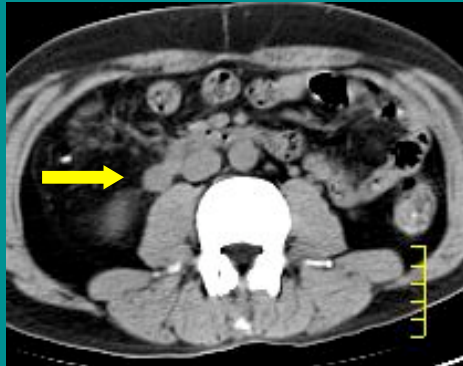


Caractérisation d'un nodule pulmonaire du LSG - Tuberculose

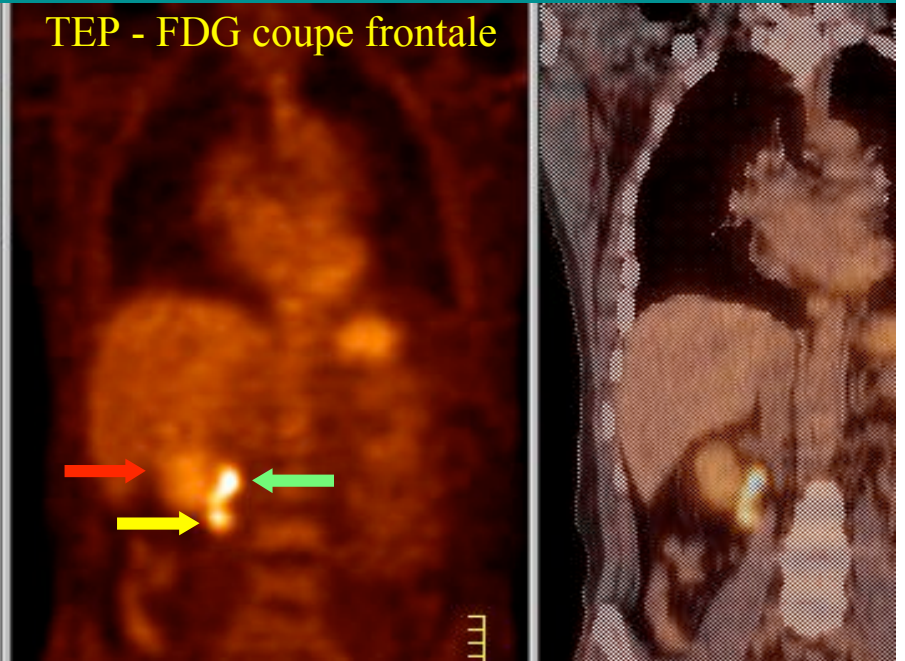


Pitfalls and artifacts

Antécédent de cancer colique opéré: diagnostic de malignité d'un ganglion rétropéritonéal



TEP - FDG coupe frontale



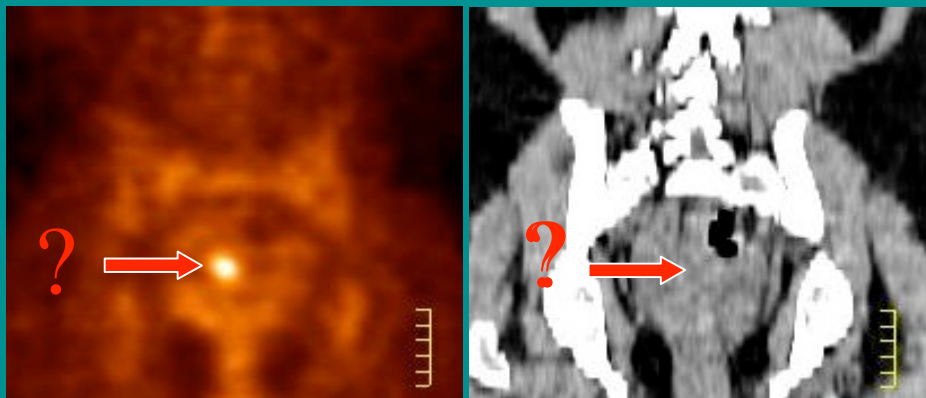
Adénopathie maligne

Rein

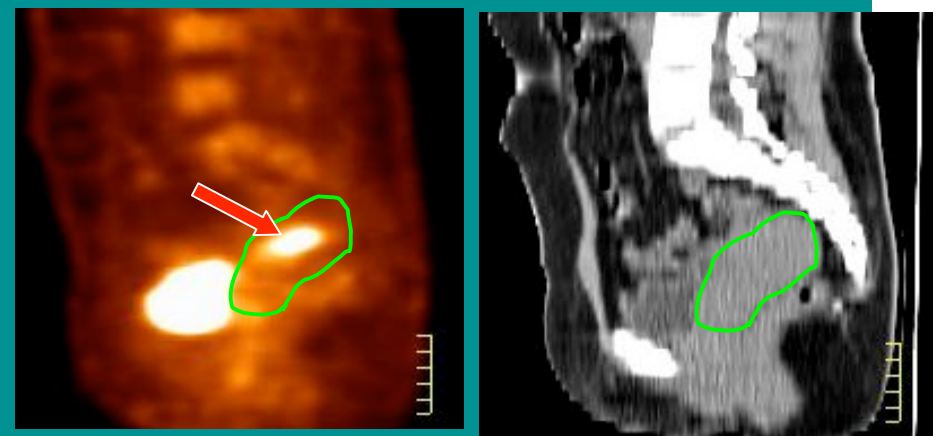
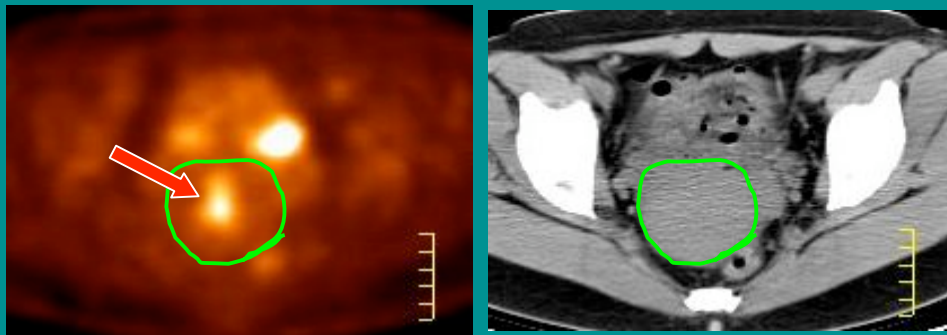
Stase urétérale de traceur

Pitfalls and artifacts

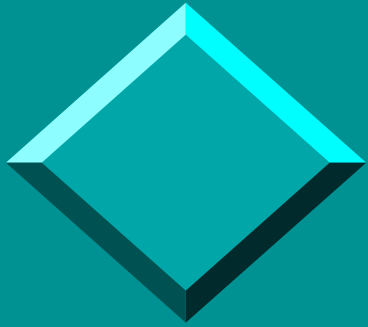
Bilan d'extension d'un lymphome



Cavité utérine en phase menstruelle,
= fixation muqueuse



Utérus

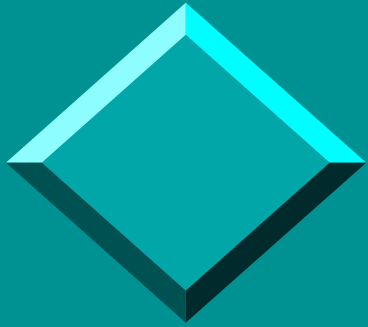


Perspectives

Autres traceurs TEP en oncologie :

- ❖ Prolifération cellulaire : ^{18}F -Fluoro-thymidine
- ❖ Synthèse protéique : ^{11}C -méthionine
- ❖ Hypoxie cellulaire : ^{18}F -Fluoromisonidazole
- ❖ Captation médicamenteuse : ^{18}F -Fluorouracil
- ❖ Et encore... La ^{11}C -Choline, le ^{18}F -Choline...

TEP - FDG, TEP - FLT, TEP - Choline, etc....



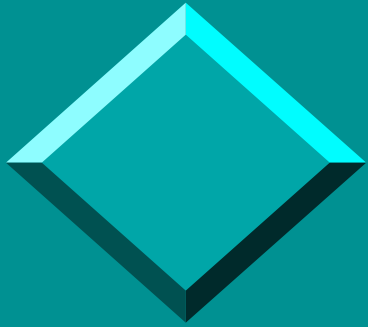
Impact économique :

- * **Examen cher**, remboursé par la SS:

1 000 € / 1000 examen (forfait technique) puis 550 €
+ 89,54 € / examen (honoraires médecin)

2,5 M€ l'appareil TEP-TDM
400 € la dose de FDG

- * **Economie de santé prouvée** dans tous les pays, par la diminution du nombre de procédures invasives et le meilleur ajustement du traitement
- * Beaucoup plus d'indications remboursables par *Medicare* aux USA
(**économie grâce au TEP** en 2004: 3003 \$/patient)



Perspectives :

- * Etudes TEP avec de **nouveaux traceurs** plus spécifiques des métabolismes des cellules néoplasiques (18F-Choline, 11C-Choline, 11C-Acétate, 18F-Fluorothymidine, 18F-Fluorodopa, 18F-FNa...)
- * Dosimétrie **patient**:
 - 18 mSv/ex (1/3 TEP-2/3 TDM)
 - irradiation naturelle: 2,4 mSv/an
 - radio pulmonaire: 0,1 mSv
- * Dosimétrie **personnel** soignant: 3 μ Sv/ex (LMA: 20 mSv/an)



Conclusion

FDG PET-CT and liver metastases from colorectal cancer

- ❖ FDG PET-CT is not the illustration of the Holy Bible
- ❖ This is in an other hand a wonderful tool for cancerologic investigations and specially for colorectal cancer management giving informations for liver and whole body staging with high accuracy
- ❖ Artifacts and pitfalls must be known by every one and the clinical history of the patient well known by the nuclear medicine physician
- ❖ Importance of PET before liver surgery (other localization) and probably more and more for therapeutic evaluation