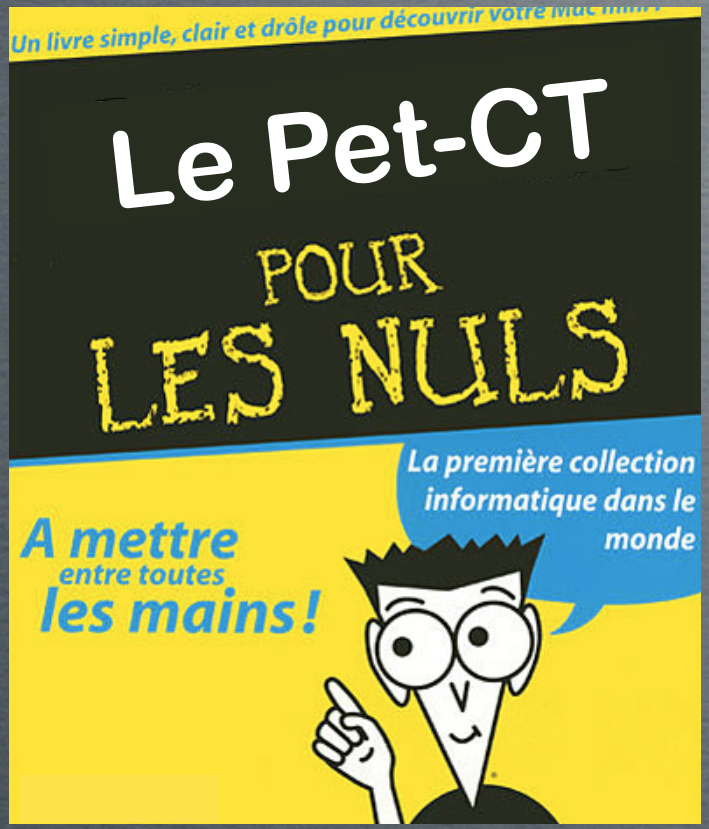


Dr Renaud Lhommel

Service de Médecine Nucléaire

Cliniques Universitaires Saint Luc

UCL

WRDGN 3120

Imaging in Medicine

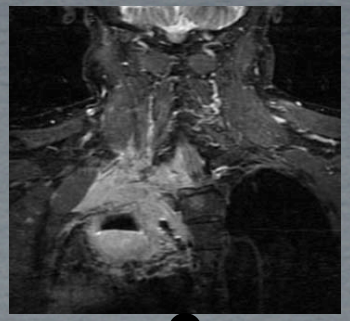
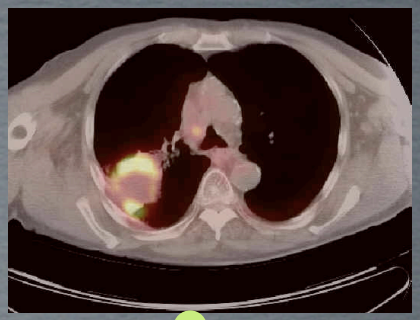
- An effective treatment is depending on :
  - **early diagnosis** : sensitivity
  - **accurate diagnosis** : specificity
  - **accurate evaluation of the severity** of the disease
  - **accurate evaluation of the efficacy** of the therapy

Disease --> altered biology

- Increased/decreased blood flow
- Increased/decreased glucose uptake
- Increased protein synthesis
- Increased/decreased receptor expression
- Increased DNA synthesis
- Increased bone turnover
- Decreased oxygenation
- etc...

Specific probes

- Every altered biological pathway can theoritically be “spied” by a molecular probe
- Nuclear medicine has the unique capability (in a living subject) of using probes at a nanomolar concentration, which means **no impact** on the natural processes

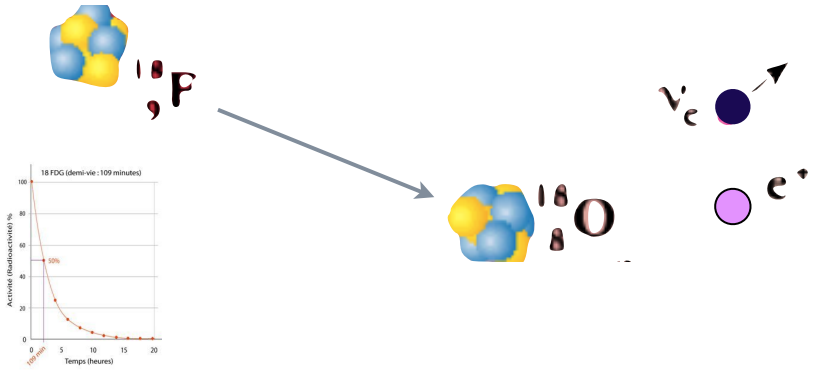




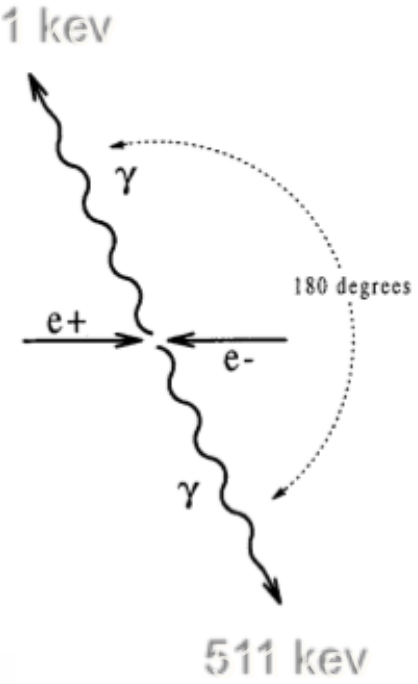
	Anatomic		Functional
	CT	**MRI**	**PET (/CT)**
	Where is the tumor...		**What is the tumor...**
+	• high spatial resolution • air interface contrast • bony structures • no image distortion • dose calculation	• soft tissue contrast • multiplanar acquisitions • bone marrow invasion	• **functional imaging** • tumor behavior • tumor characterization
-	• metallic artifacts • soft tissues contrast • need of iodine contrast	• movement artifacts • metallic artifacts • distortion artifacts • no density map • lower spatial resolution	• functional imaging • poor spatial resolution • low statistics (noise) • tracer sensitivity • tracer specificity

Positron Emmiters and Radionuclide Decay

When a nucleus undergoes positron decay, the result is a new nuclide with 1 fewer proton and 1 more neutron, as well as the emission of a positron and a neutrino:

$$ {}^{A}_{Z}X_{N} \rightarrow {}^{A}_{Z-1}Y_{N+1} + e^{+} + \upsilon. \qquad (1) $$





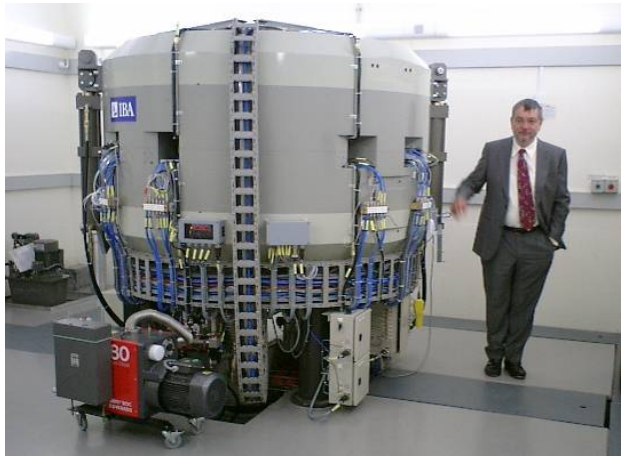
Some Commonly Used PET Radionuclides

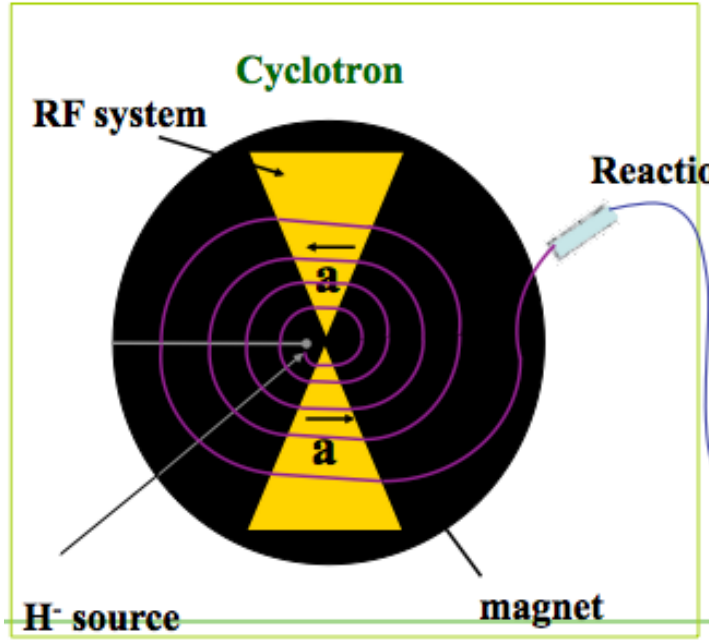
Nuclide	Halflife
^{11}C	20.3 min
^{13}N	9.97 min
^{15}O	124 sec
^{18}F	110 min

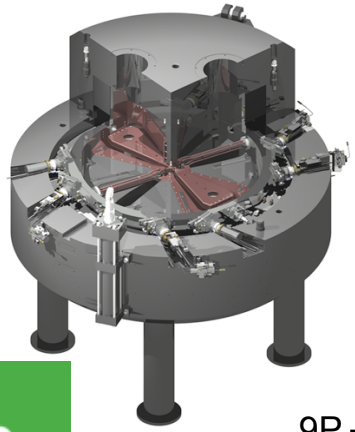
Ccl pratiques: No PET without isotope activity
Time is money

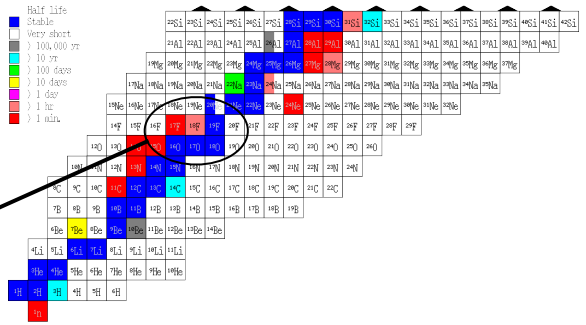
PET FDG: 3-5mSv

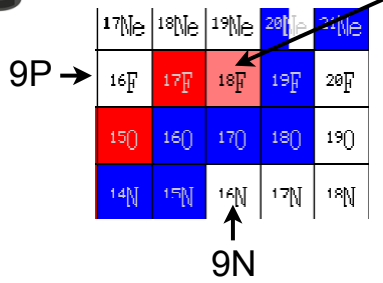
Positron Emmitters Production

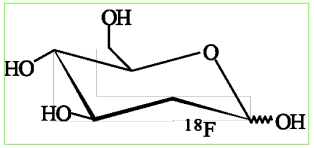












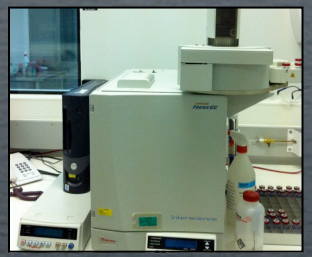
18/9

Préparation des radio-pharmaceutiques selon les normes de l'industrie pharmaceutique (GMP)> salle blanche et modules de synthèse semi-automatiques

Cellules de production

Module de synthèse du traceur PET
(=précurseurs chimiques organiques + isotope β+ venant du cyclotron)

Contrôles de qualité du produit final (HPLC)



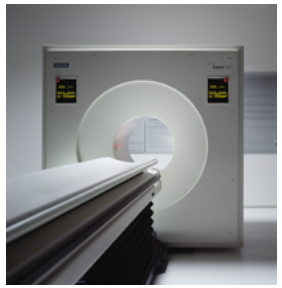
Dispensing & packaging

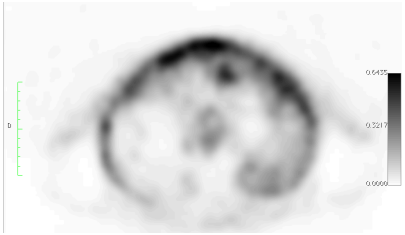
RL- WRDGN3120

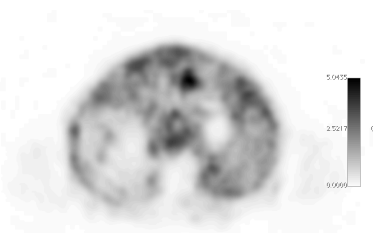
Evolution Darwinienne...

1987...2001& 2001-2007

Durée d'examen
(45 min)

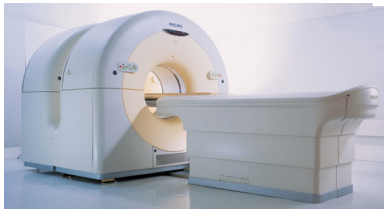


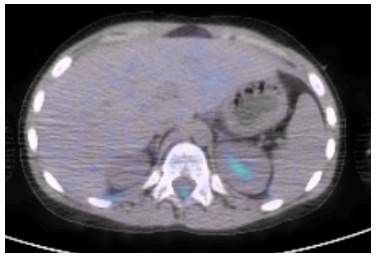


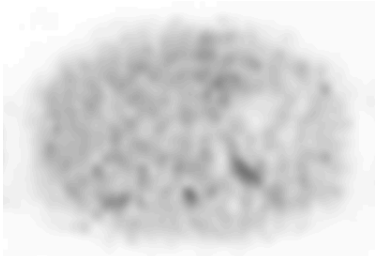


2007 - ?

Durée d'examen
(15 min)



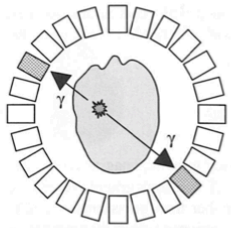


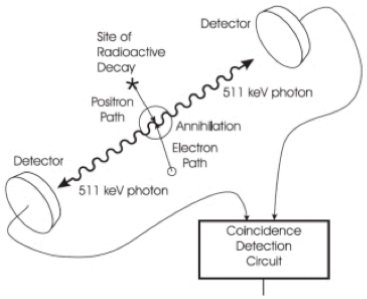


Principes de base d'une caméra PET

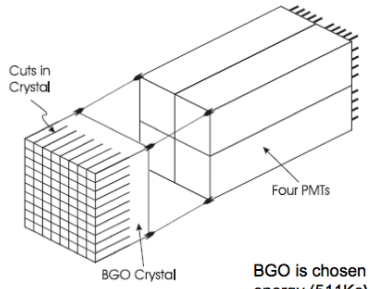
Annihilation Coincidence Detection

- Detect two events in opposite directions occuring "simultaneously"
- Time window is 2-20 ns, typically 12 ns
- No detector collimation is required
  - Higher sensitivity





PET Detector Block



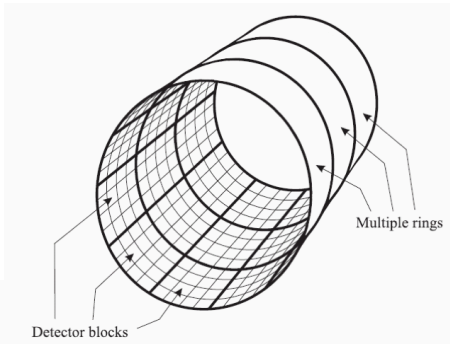
BGO is chosen because of the higher energy (511KeV) of the photons

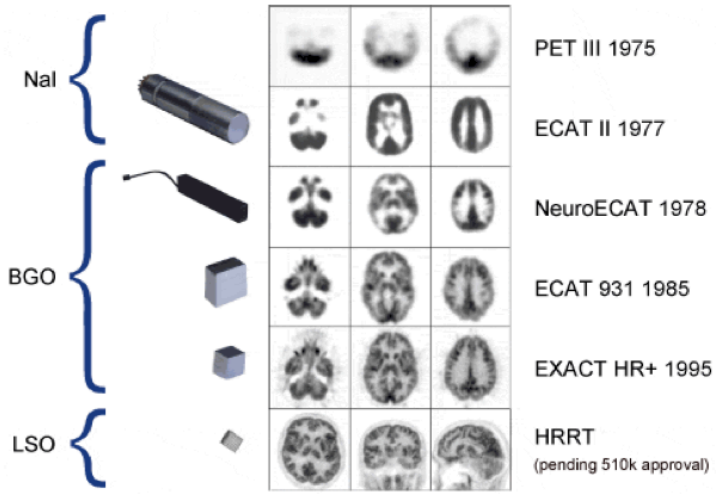
- Crystals plus PMTs
- BGO = Bismuth Germanate
- BGO has 3x stopping power than NaI(Tl)

PET Detector Configuration

- Typical numbers:
  - 8 by 8 blocks; 2 mm × 2 mm element
  - 2 by 2 PMTs per block
  - 3 major rings
  - ⇒ 24 detector rings
  - 48 detector blocks per major ring
  - ⇒ 384 detectors per ring
  - ⇒ 8216 crystals total

Multiple Ring Detector





Reconstruction du signal

LOR

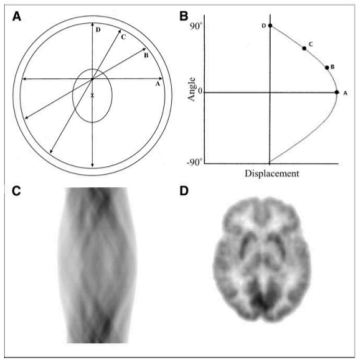
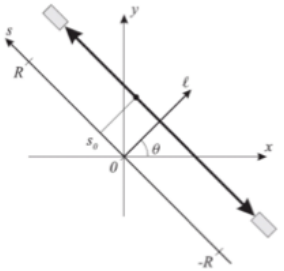


FIGURE 1. Sinogram formation. Coincidence events in PET scanner are categorized by plotting each LOR as function of its angular orientation versus its displacement from center of gantry. (A) Center of gantry is noted by cross (X), and locus of interest (e.g., tumor) is noted by ellipse. Four LORs passing through locus of interest are labeled A, B, C, and D. (B) These 4 LORs are plotted on this sinogram where angular orientation is on *y*-axis and displacement from center of gantry is on *x*-axis. If all possible LORs that pass through this point are plotted, it maps out half of sine wave turned on its side as shown here. (C) Sinograms of more complicated objects, such as sinogram of brain scan shown, are composed of many overlapping sine waves. (D) Reconstructed brain image corresponding to sinogram in (C) is shown.

Imaging Equation



$$N^{+}(s_0) = N_0 \exp\left\{-\int_{s_0}^{R}\mu(x(s'),y(s'));E)ds'\right\}$$

$$N^{-}(s_0) = N_0 \exp\left\{-\int_{-R}^{s_0}\mu(x(s'),y(s'));E)ds'\right\}$$

$$N_c(s_0) = N_0 \exp\left\{-\int_{s_0}^{R}\mu(x(s'),y(s'));E)ds'\right\}$$

$$\bullet \exp\left\{-\int_{-R}^{s_0}\mu(x(s'),y(s'));E)ds'\right\}$$

$$= N_0 \exp\left\{-\int_{-R}^{R}\mu(x(s'),y(s'));E)ds'\right\}$$

$$\varphi(l,\theta) = K\int_{-R}^{R}A(x(s),y(s))\exp\left\{\int_{-R}^{R}\mu(x(s'),y(s'))ds'\right\}ds = K\int_{-R}^{R}A(x(s),y(s))ds \bullet \exp\left\{\int_{-R}^{R}\mu(x(s'),y(s'))ds'\right\}$$

$A(x,y)$ and $\mu(x,y)$ can be separated!

Corrections (Scatter+AC+TOF)

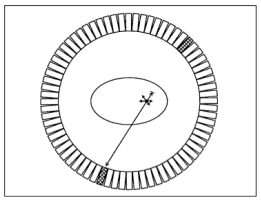


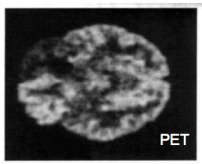
FIGURE 5. Attenuation. One of the photons is stopped or deflected before being detected.

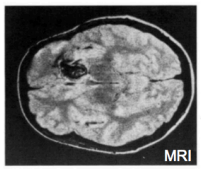
- Corrected sinogram

$$\phi_c(\ell,\theta) = \frac{\phi(\ell,\theta)}{K\exp\left\{-\int_{-R}^{R}\mu(x(s),y(s);E)\,ds\right\}}$$

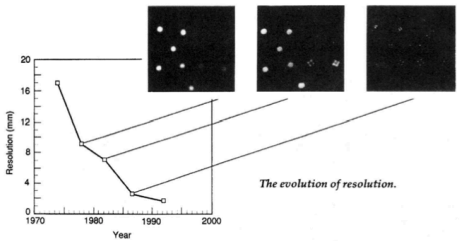
- $\mu(x,y)$ found from CT (transmission PET)

- One can apply filtered backprojection algorithm to reconstruct A(x,y) from the corrected sinogram





- Modern PET ~ 2-3 mm resolution (1.3 mm)



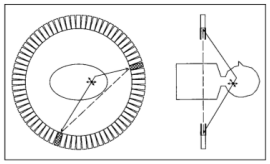
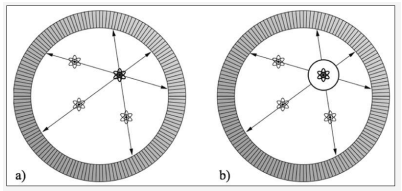
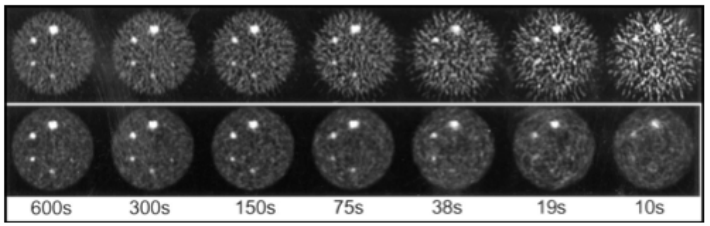


FIGURE 4. Scattered events. At left is in-plane scatter and at right is out-of-plane scatter, rejected by septa.

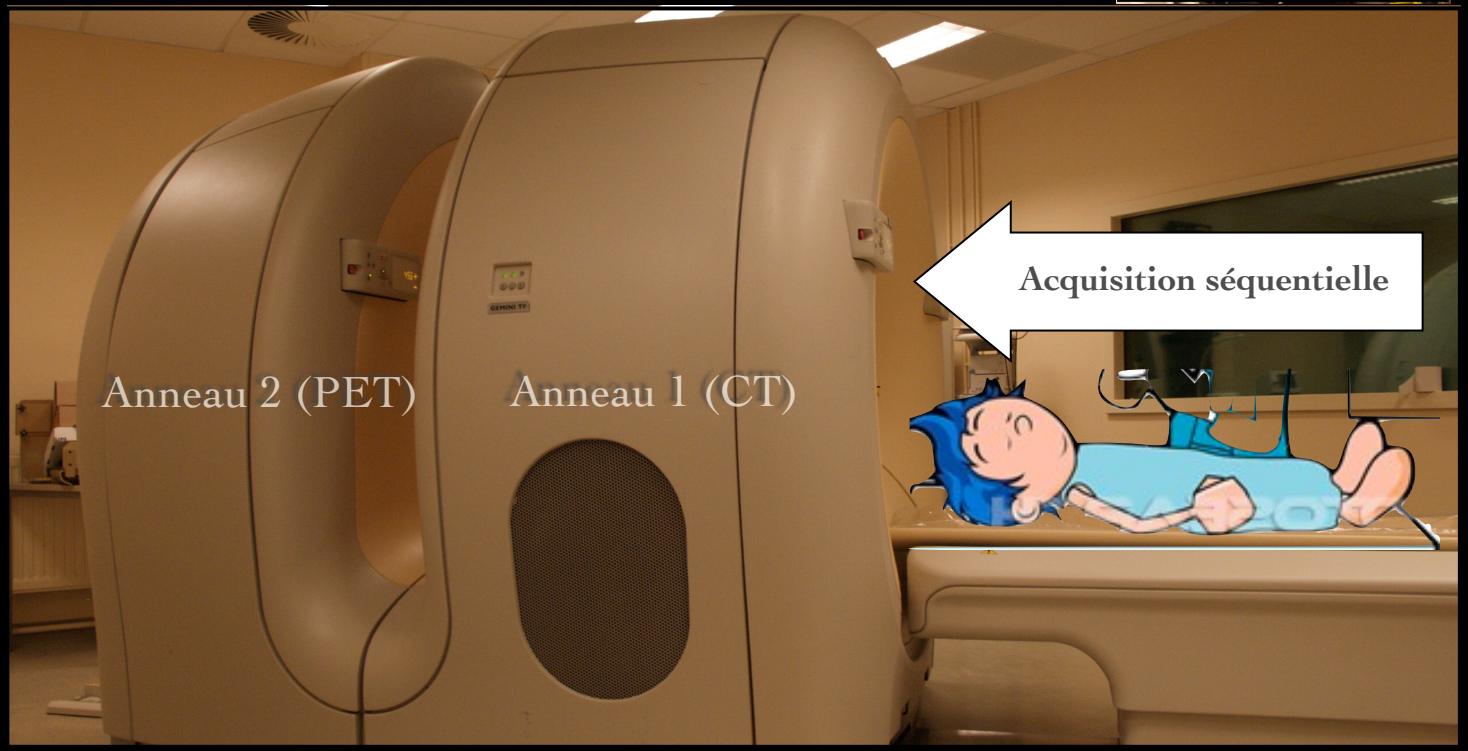


FBP

OSEM3D

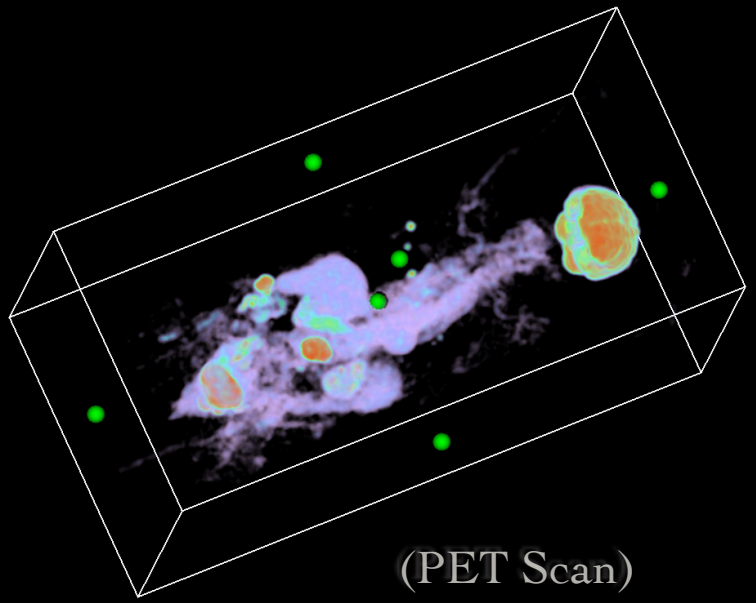


Caméra PET/CT



Acquisition matricielle 3D de la distribution du traceur

Support Anatomique



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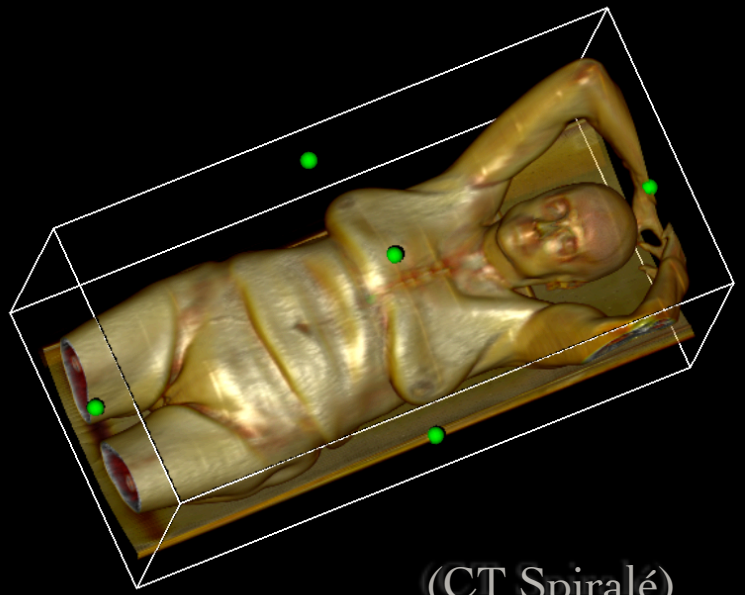
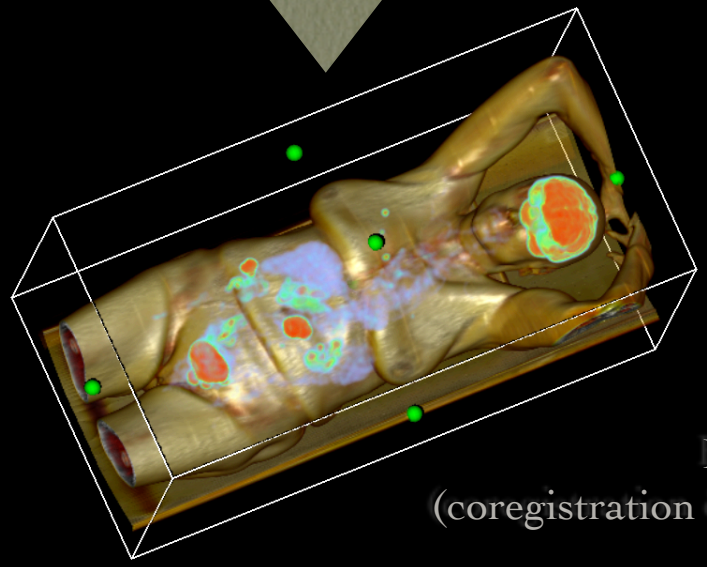


(PET Scan)

(CT Spiralé)



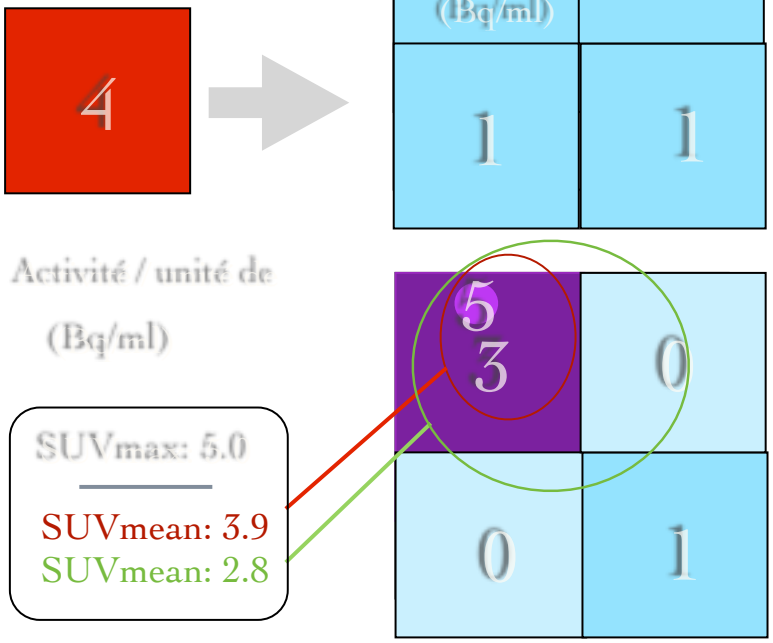
PET/CT
(coregistration & fusion automatiques)

RL- WRDGN3120

Le PET = Instrument de mesure précis et qualibré
> quantification du signal

Standardized Uptake Value (SUV)

Activité/unité de poids

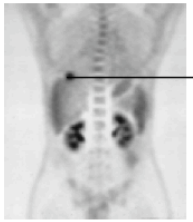


Activité / unité de

(Bq/ml)

SUV_{BW}, SUL, SUV_{BSA}, TLG,

- Index caractérisant la fixation du traceur

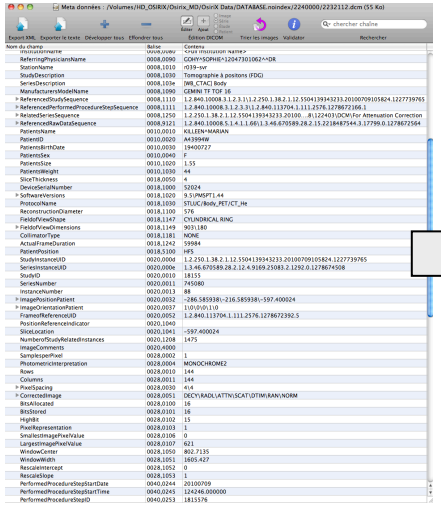


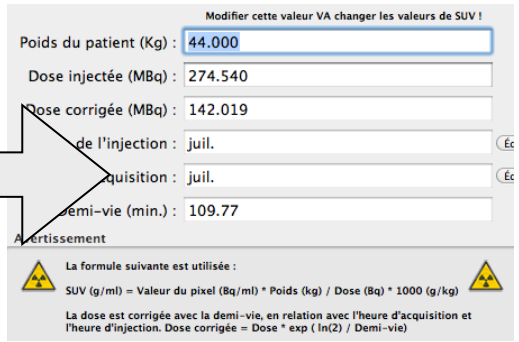
$$SUV = \frac{\text{fixation (kBq/mL)}}{\text{dose injectée (kBq) / poids du patient (g)}}$$

(1mL = 1g)

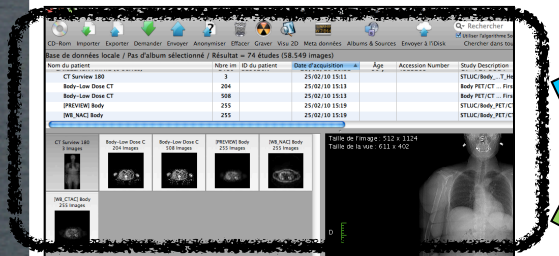
Répartition uniforme du traceur dans tout l'organisme, SUV = 1 partout

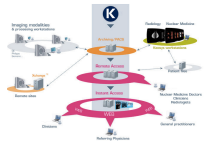
SUV > 1, hyperfixation du traceur





Visualiser un PET/CT implique l'utilisation d'outils adaptés !





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Telemis

Biomedical Image Quantification

PMOD Technologies

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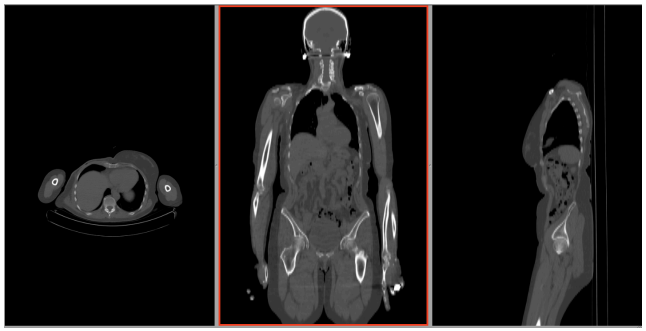
Toile de fond = support anatomique (CT ou IRM)

Surview

Séries CT (5mm,2mm,cCT)...



Distribution d'une activité biologique particulière (+traceur)

NAC

Preview

+ Corrections (scatter, attenuation, TOF...)

(Wb,HN,Be...)

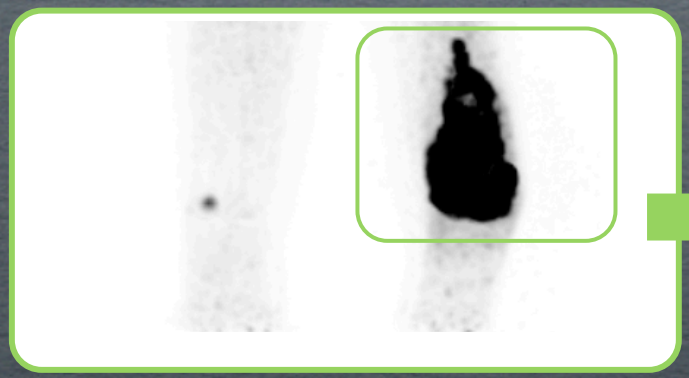
CTAC

Quantifiée ($SUV_{bw/lbm/...}$)

Visual only !

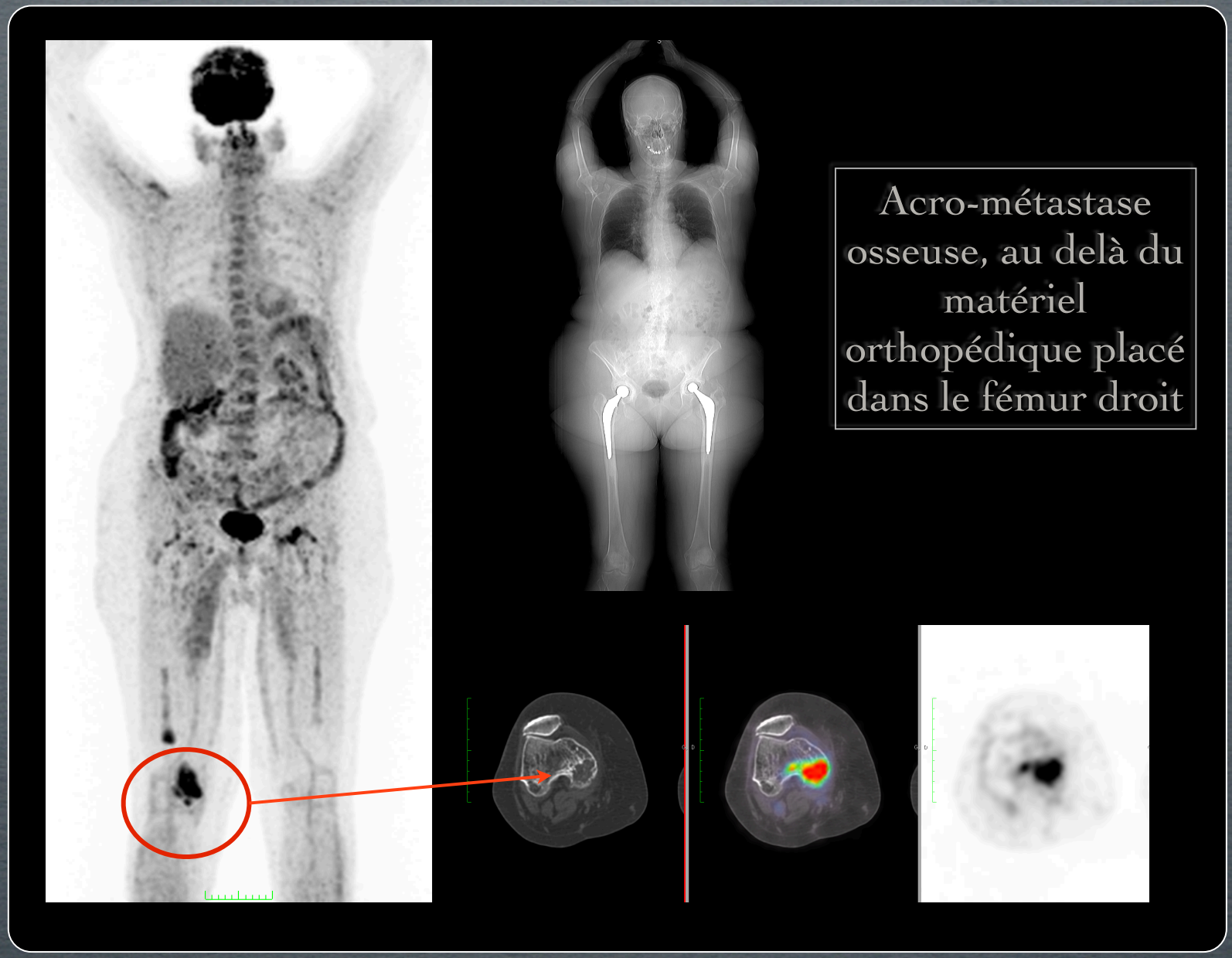
Whole-body acquisition

basal acquisition = from the skull to the mid thight



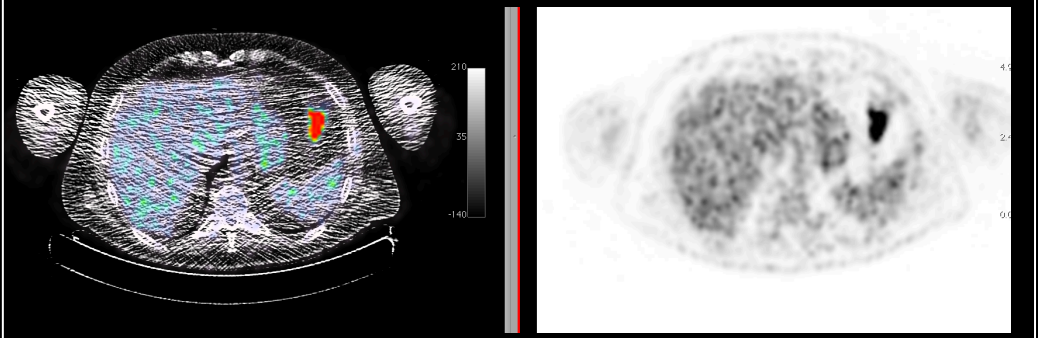
Importance du choix du bon protocole d'acquisition pour ne pas «oublier» de l'information !

Autre exemple: néoplasie du sein, majoration du CA 15.3

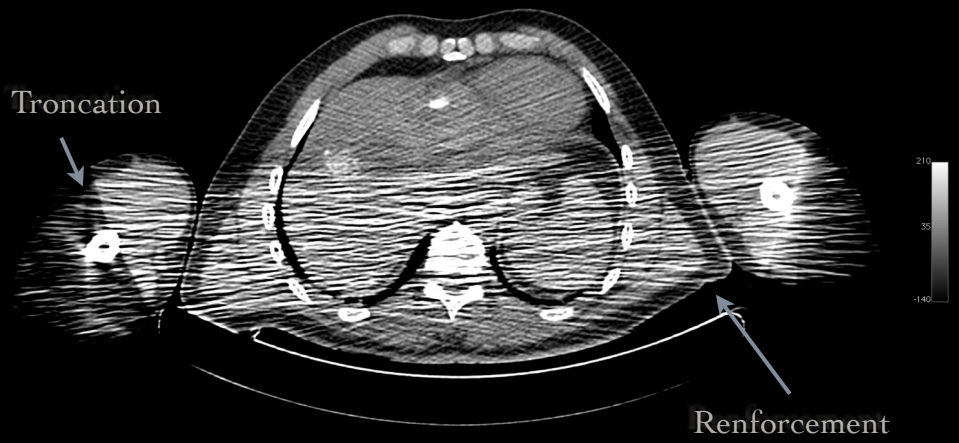


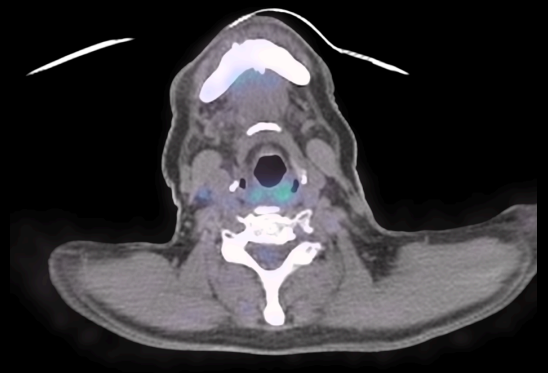
PET/CT: qualité du CT = choix institutionnel

50 mAs / 120 kev

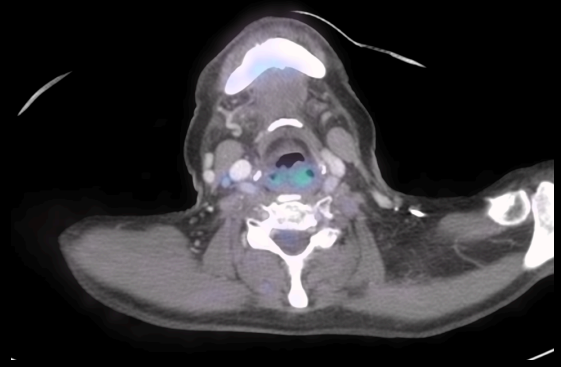


Low-dose...mais pas sous-dosé !





Dose Modulated(+inj)



Technical Pitfalls

PET and PET/CT Artifacts

PET-based errors

- Calibration problems
- Detector failures
- Resolution and partial volume effects
- patient motion

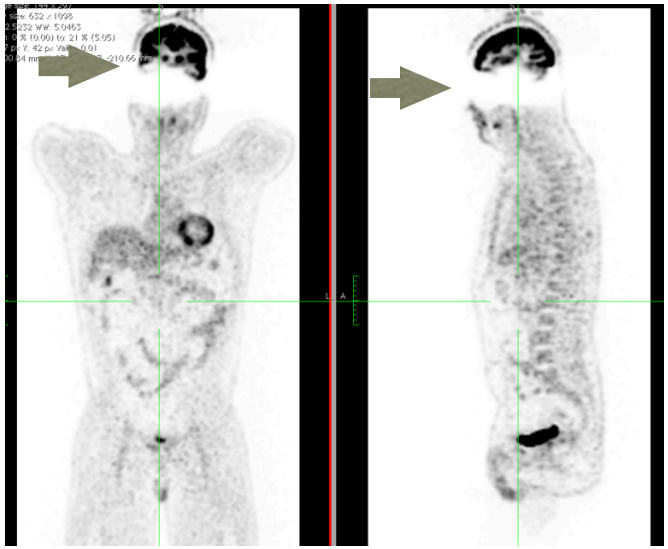
Errors from CT-based attenuation correction in PET/CT

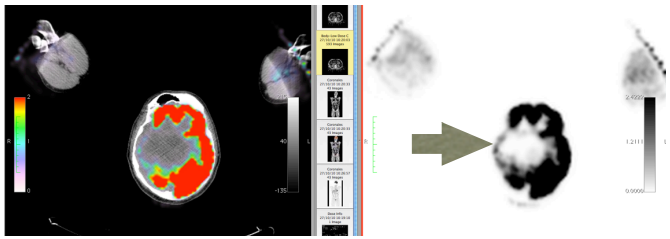
- CT artifacts
- non-biological objects in patients
- respiratory mismatch between PET and CT images
- patient motion

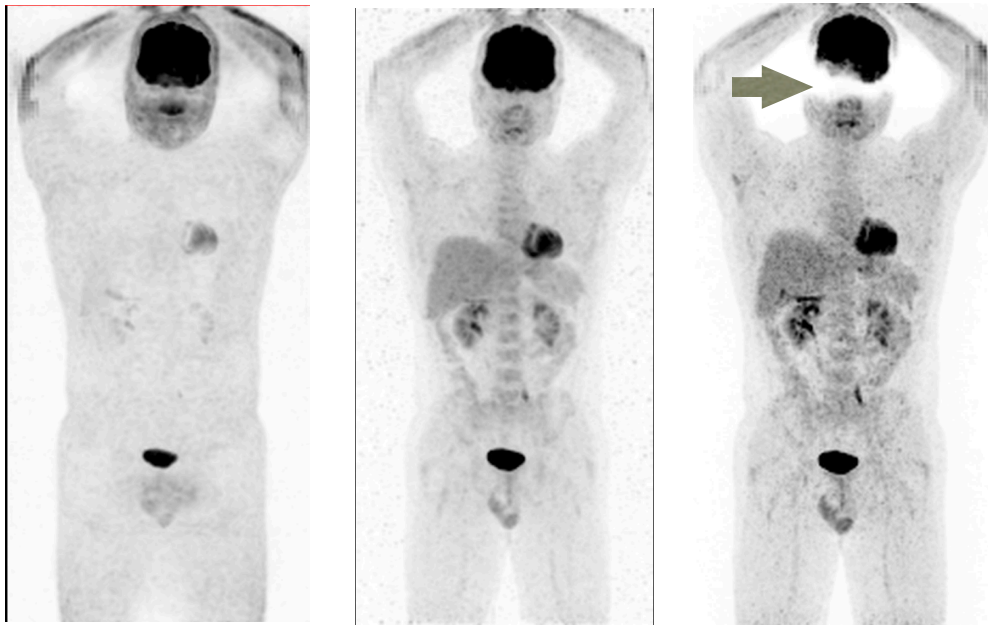
Types of CT Artifacts

- Physics based
  - beam-hardening
  - partial volume effects
  - photon starvation
  - scatter
  - undersampling
- Scanner based
  - center-of-rotation
  - tube spitting
  - helical interpolation
  - cone-beam reconstruction
- Patient based
  - metallic or dense implants
  - motion
  - truncation

Correction de scatter

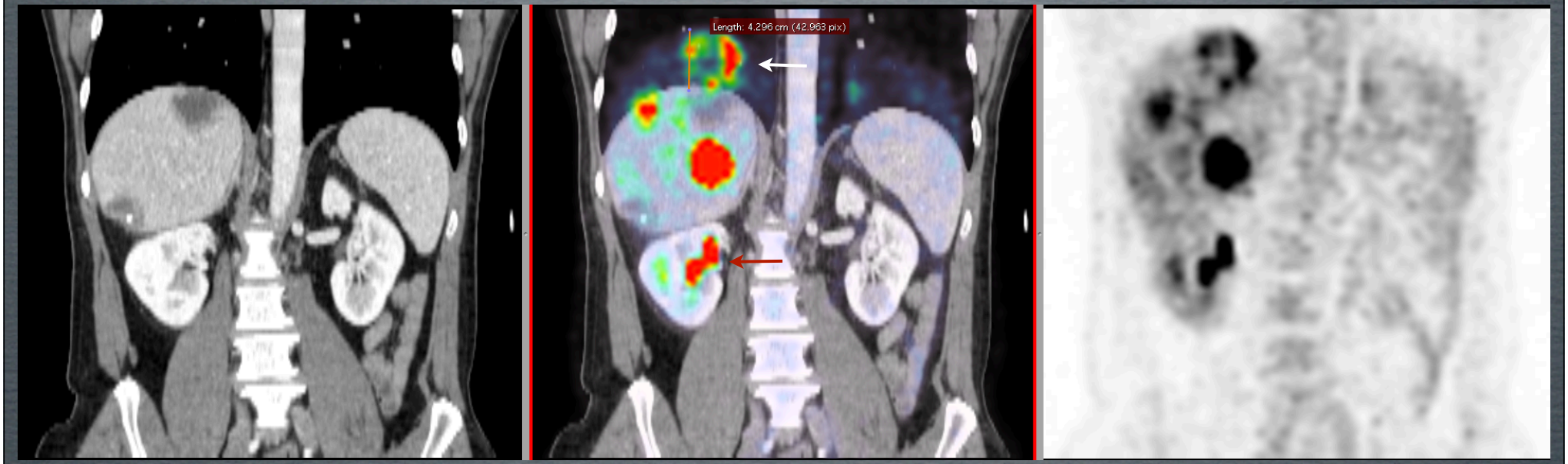






WB_NAC ⇨ WB_Preview ⇨ WB_CTAC

Misregistration (respiration)



Pas de CT en inspiration bloquée !

Partial volume effect

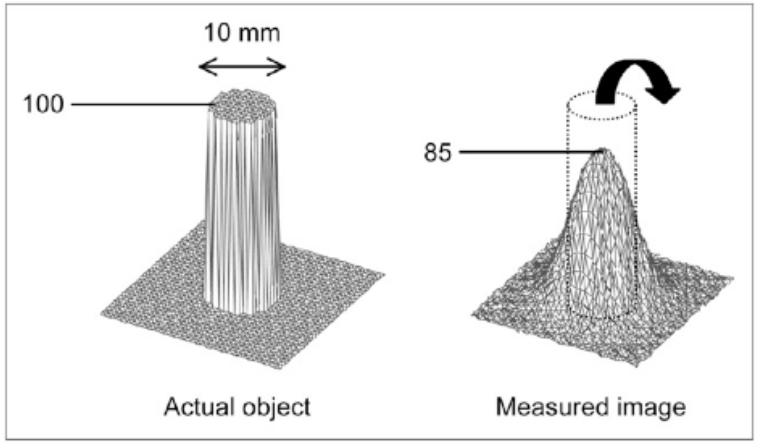


FIGURE 1. Circular source (diameter of 10 mm) of uniform activity (100 arbitrary units) in nonradioactive background yields measured image in which part of signal emanating from source is seen outside actual source. Maximum activity in measured image is reduced to 85.

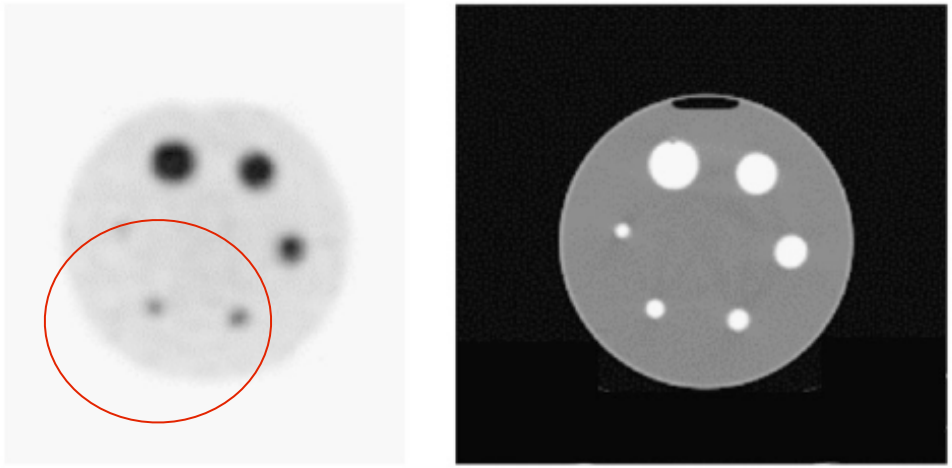


FIGURE 5. Transverse PET slice of 6 radioactive spheres with different diameters (10, 12, 16, 22, 28, and 34 mm) and filled with same radioactivity concentrations in uniform radioactive background (left) and corresponding CT slice (right). PVE makes apparent uptake decrease when sphere size decreases.

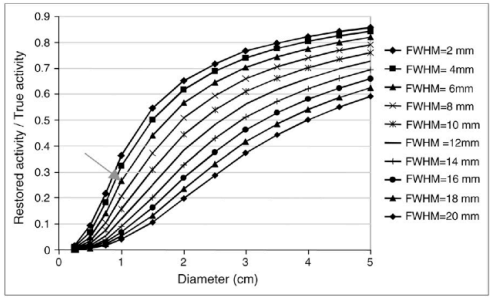


FIGURE 10. Restored activity measured in actual contour of spheres in cold background as function of sphere diameter and spatial resolution of imaging system.

Ccl: attention aux petites métas pulmonaire, aux T1...!
non hypermétabolique= en apparence...

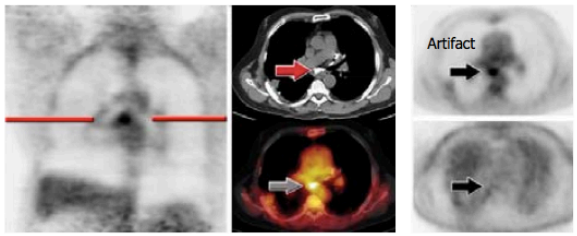
Attenuation correction

(prothèses de hanche, dentiers, clips chirurgicaux, produits de contraste ioniques au CT...)

Metal Clip

Courtesy O Mawlawi MDACC

Calcified Lymph Node

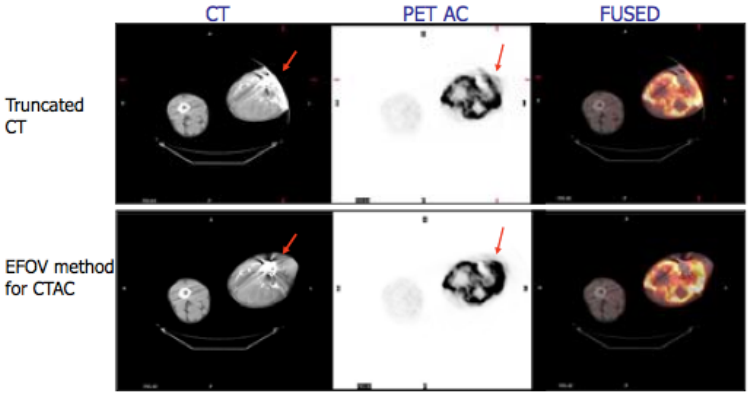


Courtesy T Blodgett UPMC

Truncation

- Standard CT field of view is 50 cm, but many patients exceed this
- Not often a problem for CT, but can be a problem when a truncated CT is used for PET attenuation correction

Truncation Artifacts and Wide-Field CT Methods



Max SUV changed from 3.4 to 12.7 with extended field of view CT

Summary

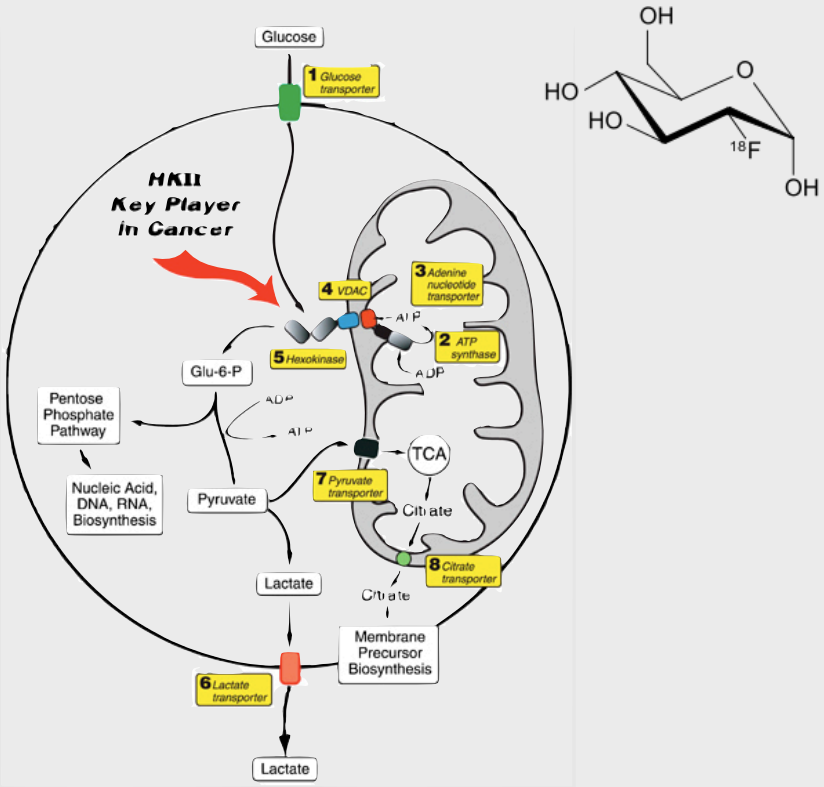
- Look at images with and without attenuation correction if in doubt
- Don't assume correct alignment *always* between PET and CT, at a minimum, patient and/or bed motion is a possibility
- Manufacturers have new methods to help with truncation and respiratory motion artifacts
- CT artifacts and dense objects can propagate errors into the PET image via CTAC
- CINE-CTAC method can help reduce respiratory-induced banana artifacts

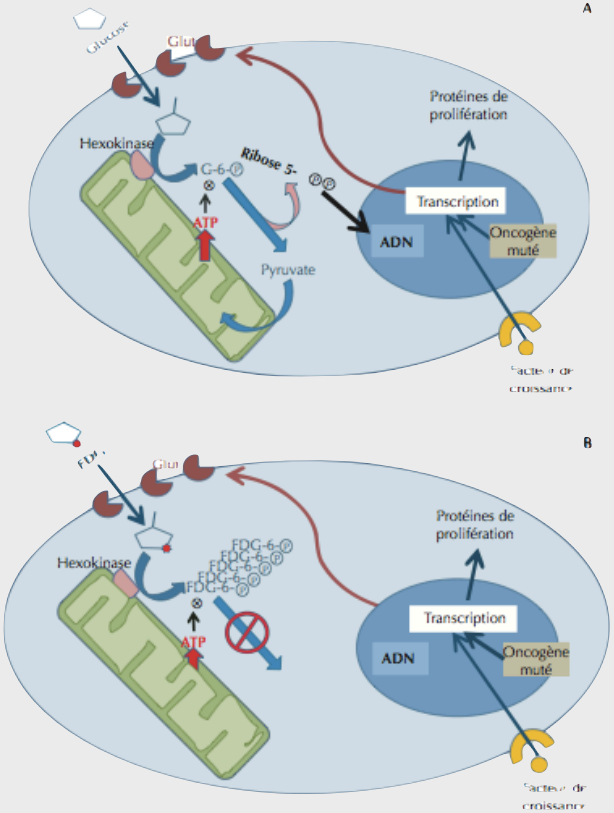
LES TRACEURS PET

RL- WRDGN3120

FDG PET

Fluorodeoxyglucose (2-deoxy-2-(^{18}F)fluoro-D-glucose)





Oncogene (2006) **25,** 4777–4786. doi:10.1038/sj.onc.1209603

Hépato-Gastro. Volume 17, Number 1, 11-9, janvier-février 2010

DOI : 10.1684/hpg.2009.0385

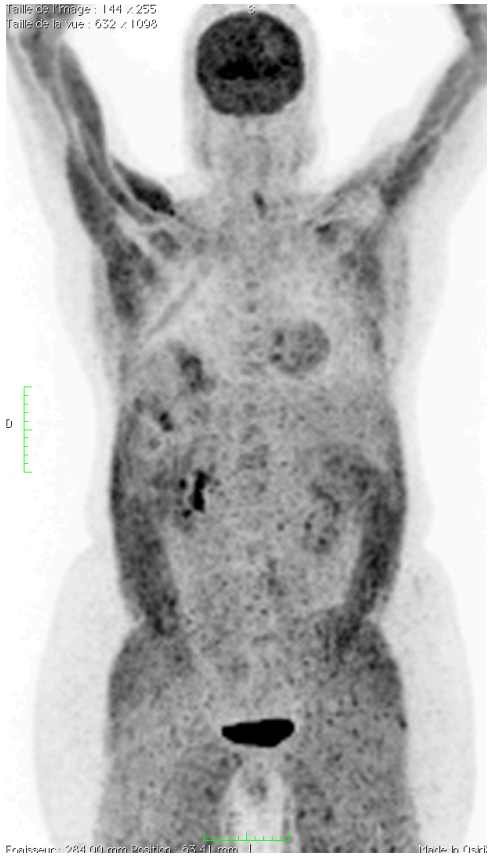
RL- WRDGN3120

UN PET FDG, CELA SE PRÉPARE...

Dose: 10 ->5 mCi

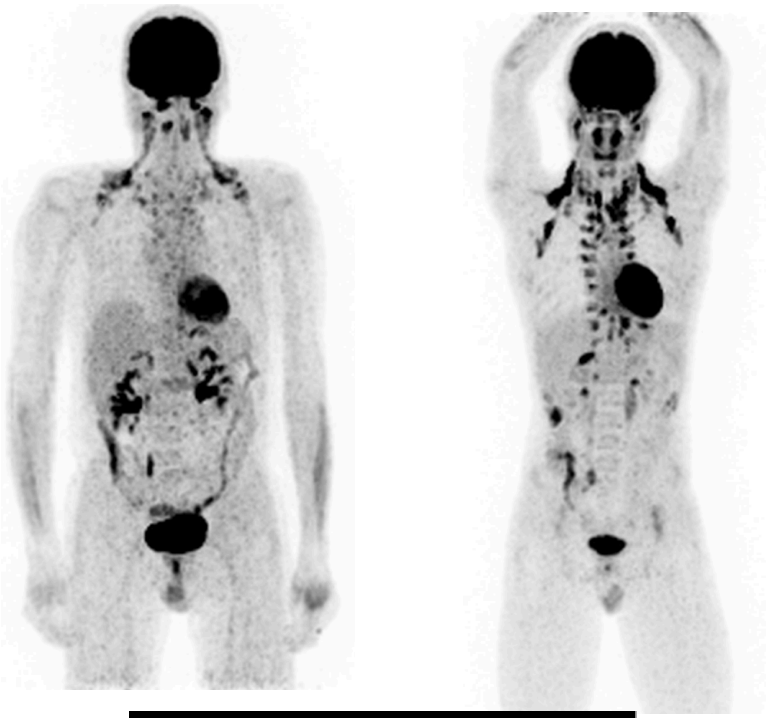
- Délai d'incoporation du FDG: minimum 1 heure
- A jeûn (6 heures)...sauf diabétiques IR
- Au calme (pas de footing/vélo avant le PET)
- Pré/per-hydratation (idéal)
- Vêtements chauds et confortables
- Pas de CT contraste iv et/ou digestif avant le PET

Exemple de captations physiologiques (liées aux conditions de préparation, traitement reçu...)



Patiente diabétique non contrôlé / Patient non à jeun

Imprégnation insulinique

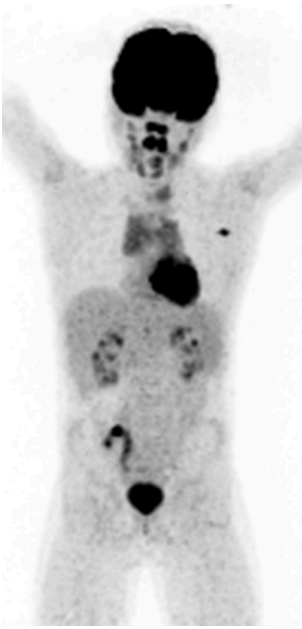


Récidive CMT ?

Récidive lymphome ?

Brown FAT

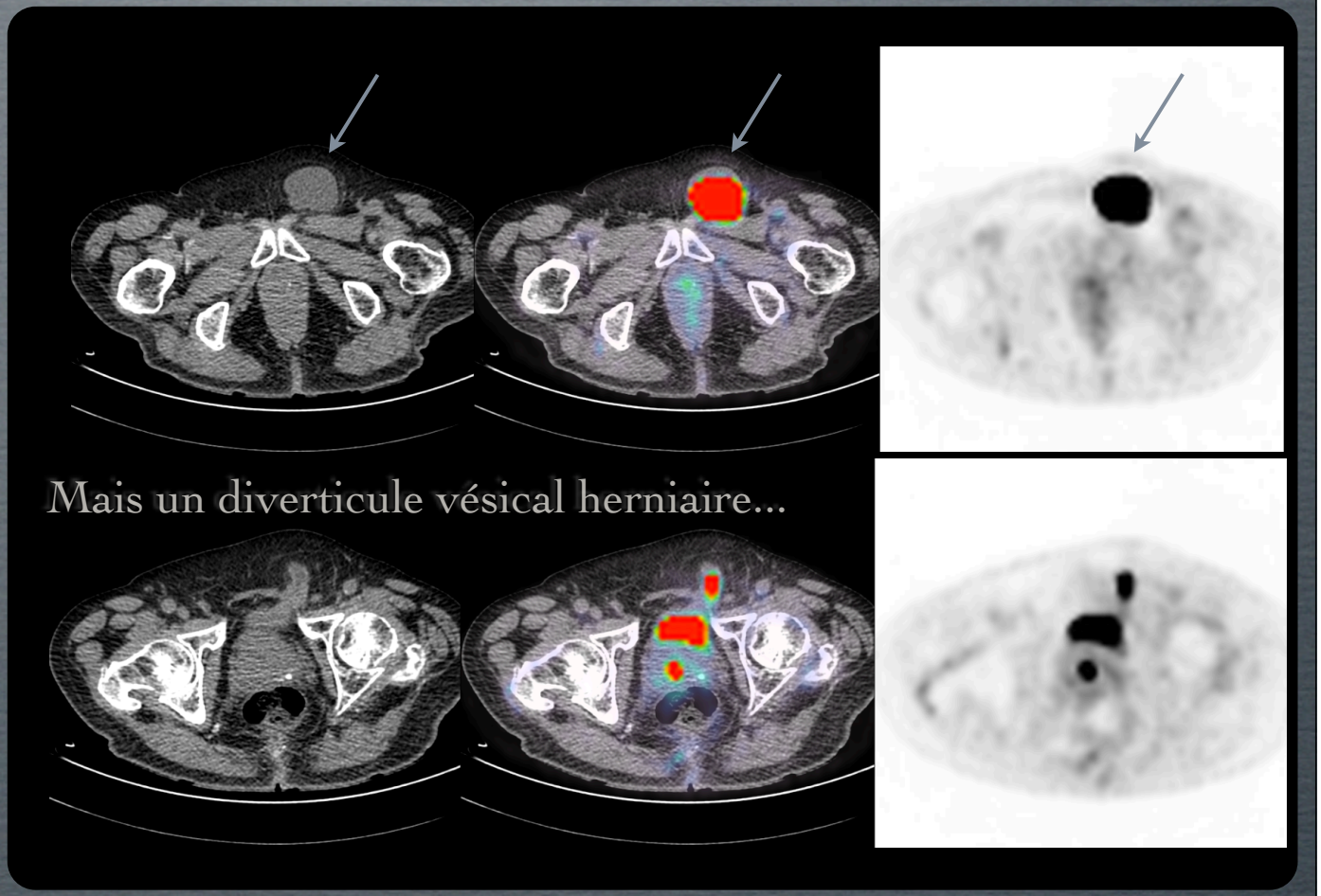
Effort musculaire



Rebond thymique & stase uréthrale

RL- WRDGN3120

Ceci n'est pas une tumeur...

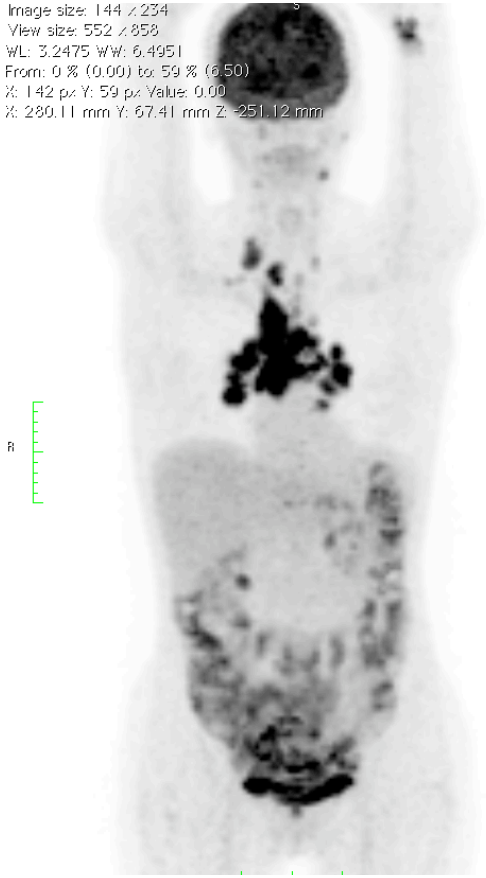


RL- WRDGN3120

F; 61 ans

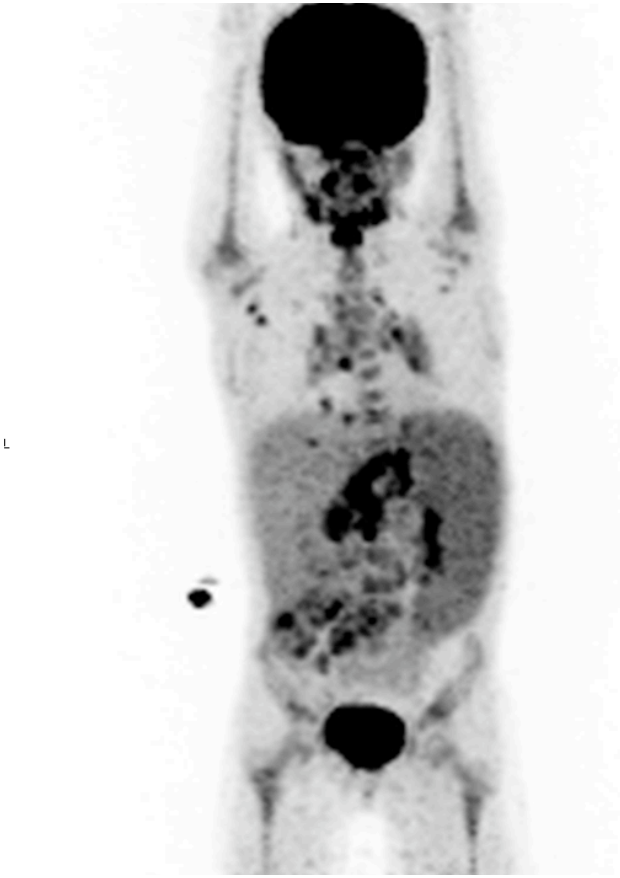
Abcès hépatiques sur neutropénie

M: AEG ; 56 ans



Sarcoïdose

M ; 13 ans



Lympho-histiocytose

Le FDG n'est pas un traceur spécifique !

Masse rétropéritonéale:

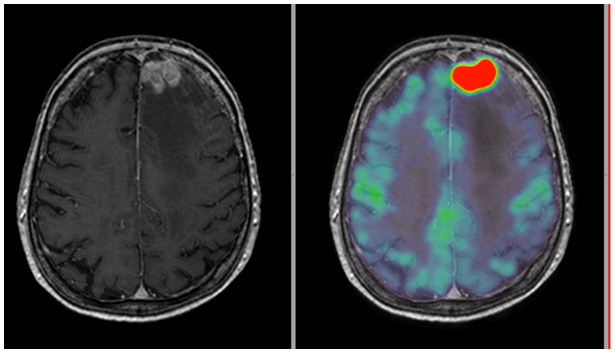
lymphome, sarcôme, GIST,
hypernéphrome....?

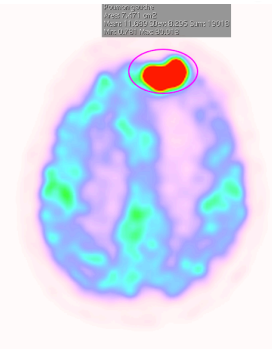
The Tissue is the Issue...

F:76 ANS

IRM cérébrale: métas

PET/CT FDG: lésions+/rien à distance
> primitif high grade type glioblastome
+nodule fille ?

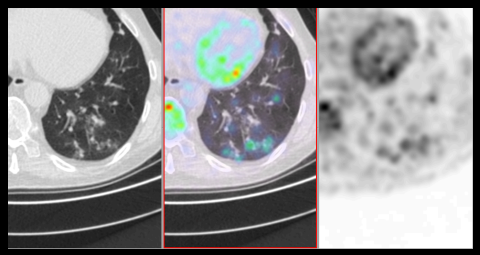


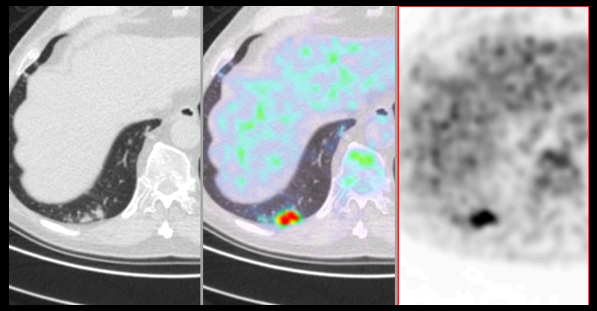


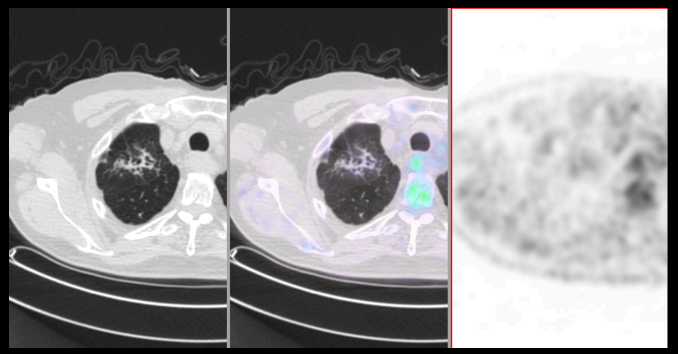
Ccl de l'ana.path: lymphome cérébral (DLBCL)

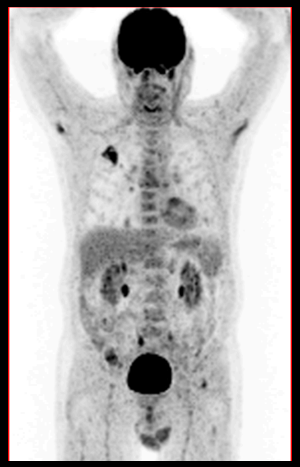
Manque de specificité > protocole «nuancé»...

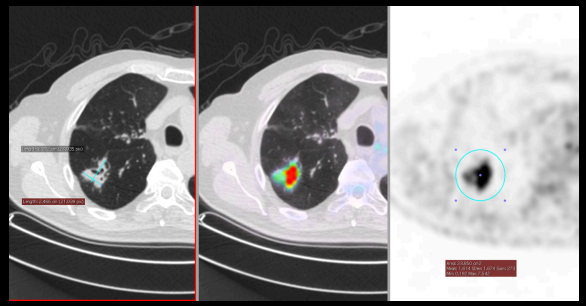
Bilan d'opacité LID chez un patient de 74 ans présentant des ATCDTS de TBC LSD

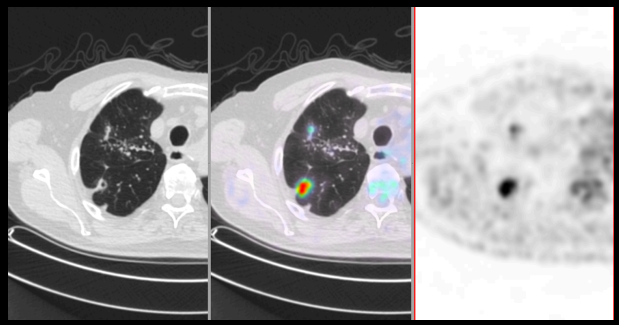


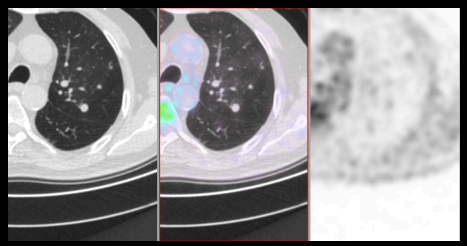






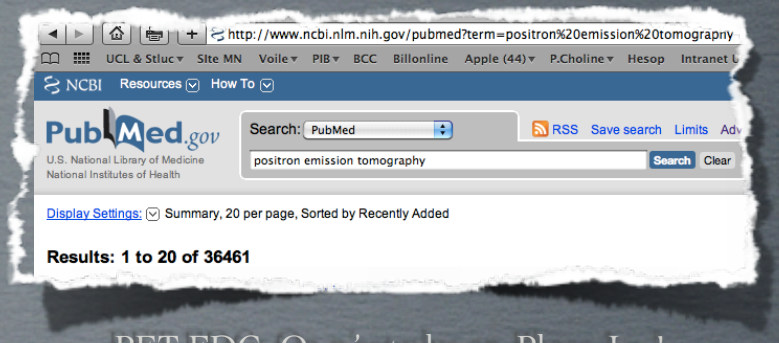






T4M1, T2Nx avec surinfection saisonnière, réactivation de TBC ?? -> contexte clinique...

Items classiques de la littérature PET Onco



PET FDG: On n'est plus en Phase I... !

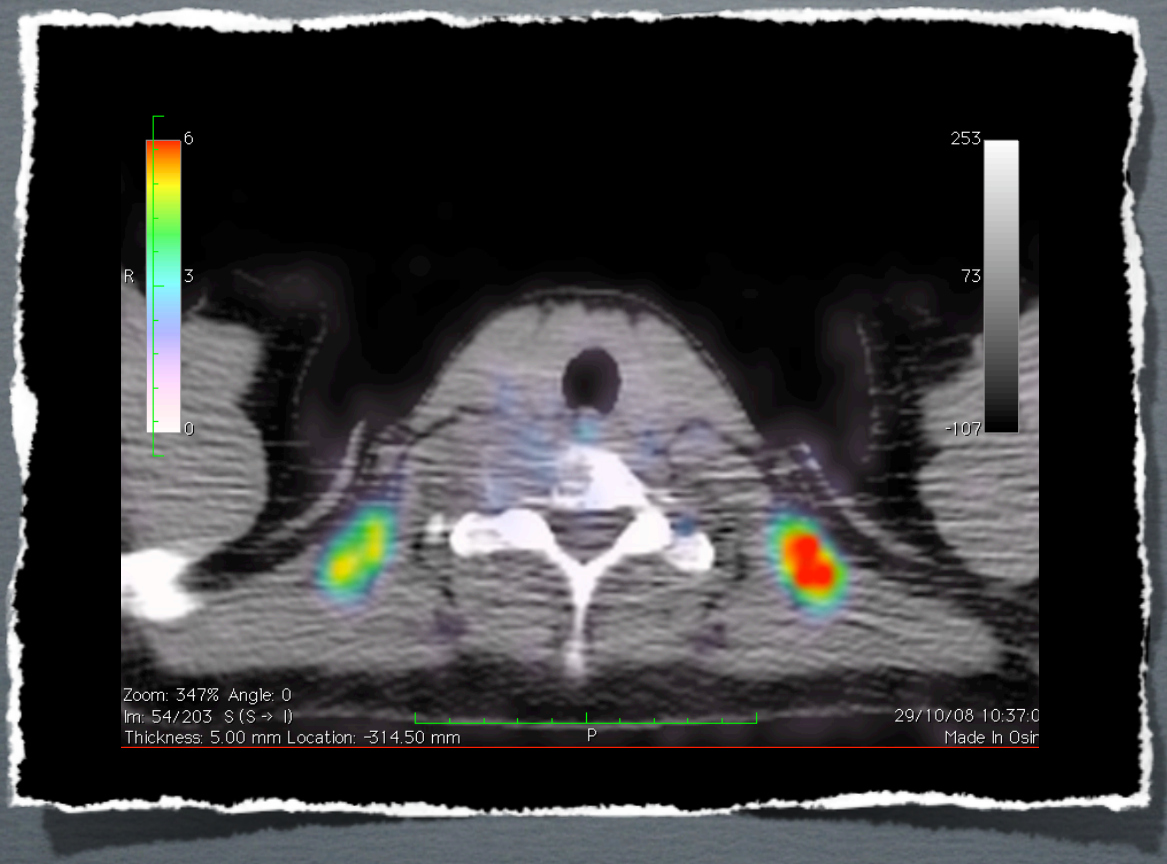
- Bénin/malin
- Staging, restaging, récidive
  - mofications TNM
  - Impact sur la prise en charge du patient
  - Valeur pronostique (réponse précoce, Positif/négatif...)
  - Coûts/bénéfices

- Médecine personalisée / Monitoring Thérapeutique

Items classiques de la littérature PET Onco

- Bénin/malin
- Staging, restaging, récidive
  - Mofications TNM((+stratégie diagnostique X ou Y)
  - Impact sur la prise en charge du patient
  - Valeur pronostique (réponse précoce, positif/négatif…)
  - Coûts/bénéfices
- Médecine personalisée / Monitoring Thérapeutique

Bilan d'extension d'une lésion lytique de C6



Ccl: hémangiome

Nodule pulmonaire: Ceci...

...est un cancer !!

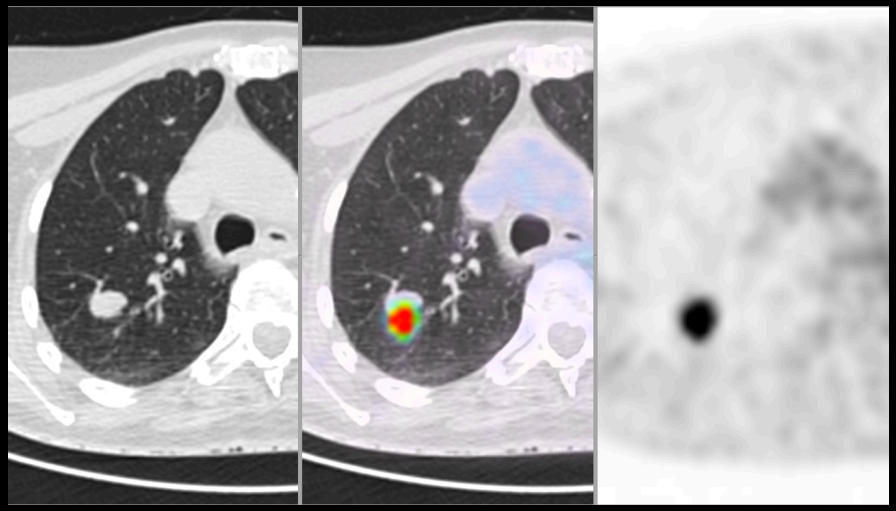
30/06/2010

17/09/2010

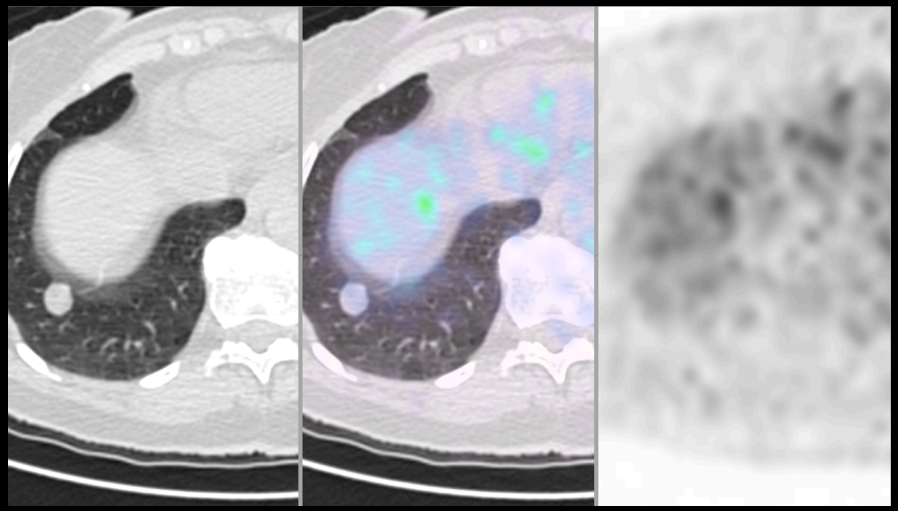
T2a N2 M0

RL- WRDGN3120

Femme 75 ans ;
Lésions pulmonaires suspectes - contexte de mélanome réséqué au niveau de l'aile du nez.



Lésion LSD nettement hypermétabolique (SUVmax: 7.8)
= tumeur plumonaire primitive (épidermoïde)



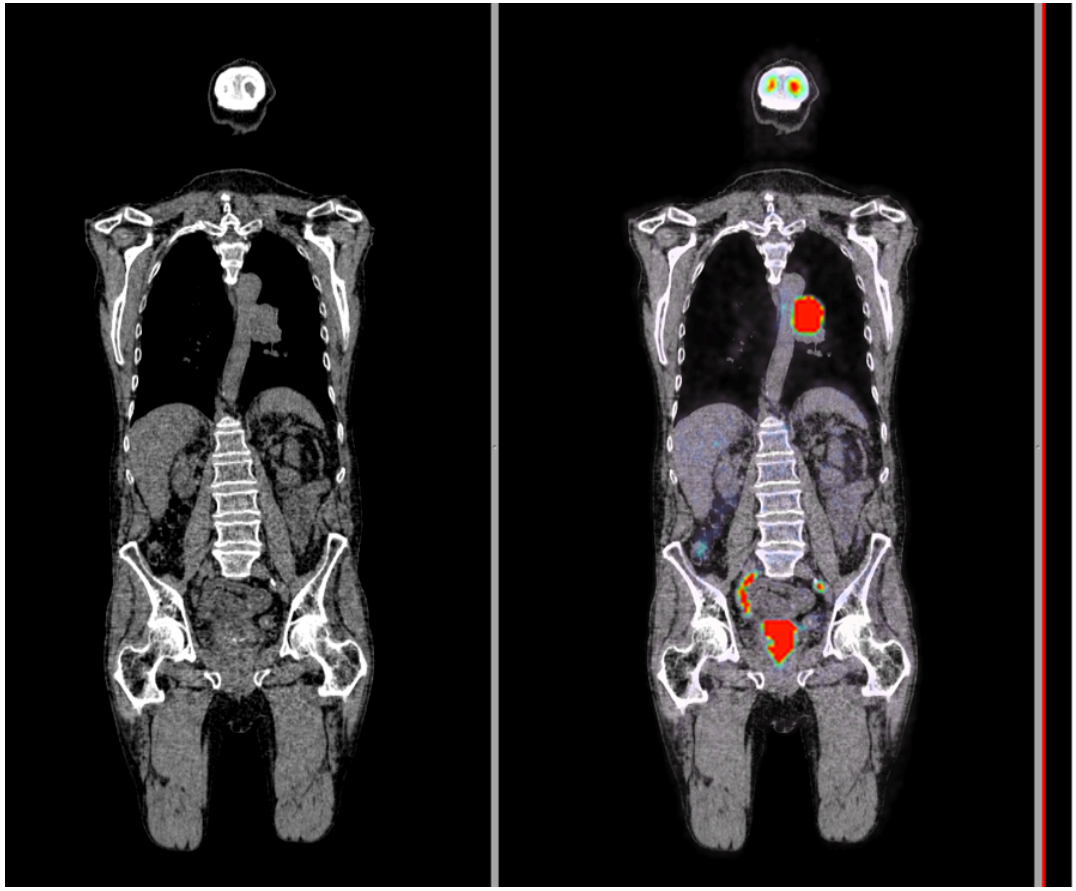
Lésion LID non hypermétabolique
= hamartome (TB)

RL- WRDGN3120

Items classiques de la littérature PET Onco

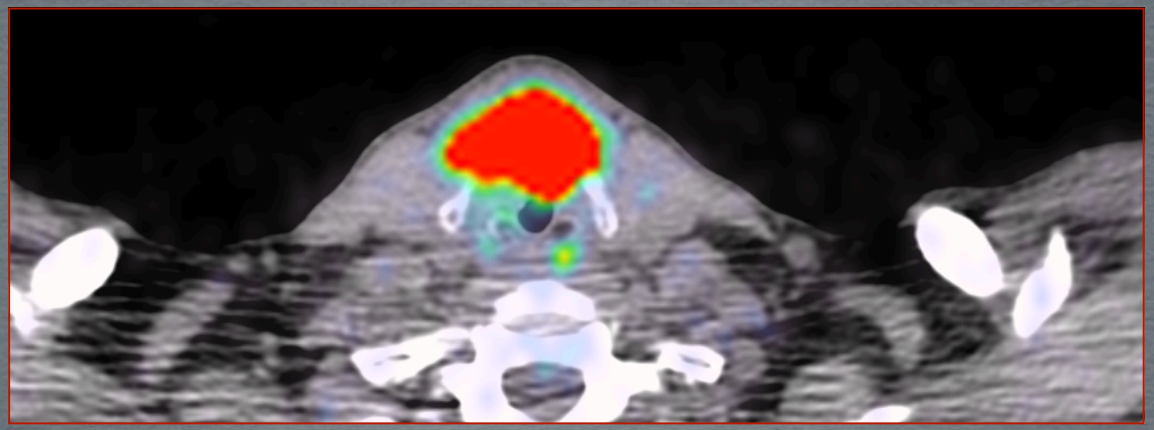
- Bénin/malin
- Staging, restaging, récidive
  - mofications TNM (÷stratégie diagnostique X ou Y)
  - Impact sur la prise en charge du patient
  - Valeur pronostique (réponse précoce, Positif/négatif…)
  - Coûts/bénéfices
- Médecine personalisée / Monitoring Thérapeutique

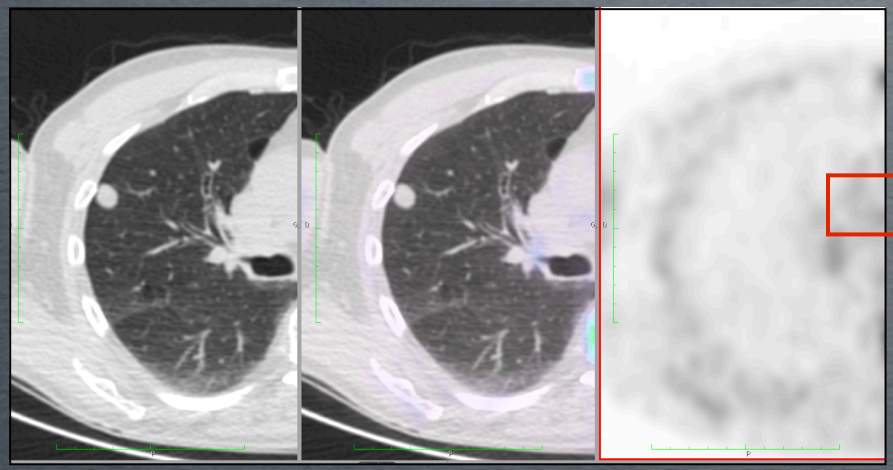
Staging initial

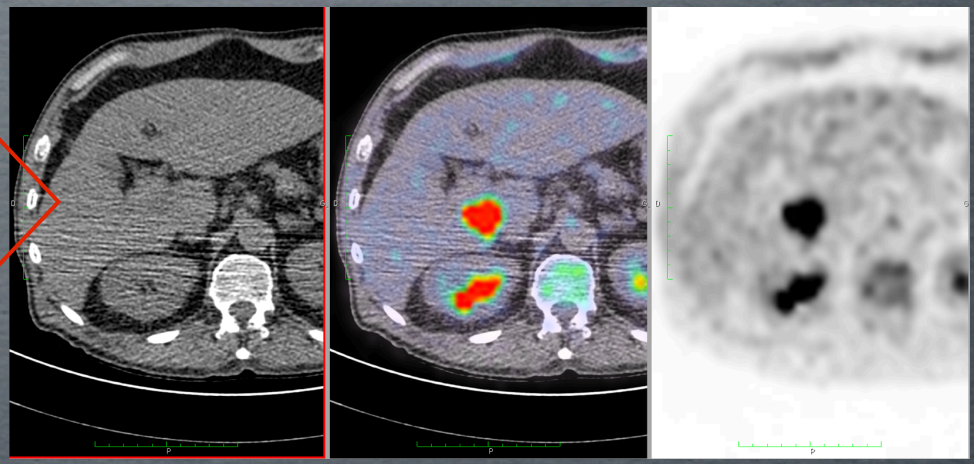


cT2cN2M0 (14/09/2010)

Tumeur ORL (cT4)- suspicion de métastase pulmonaire au CT







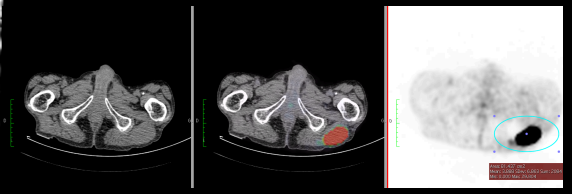
Lesion pulmonaire négative !

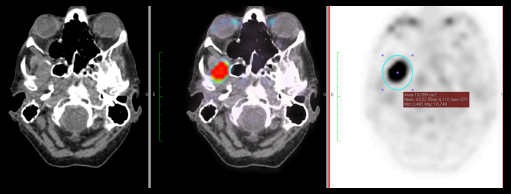
(M1-> M0)

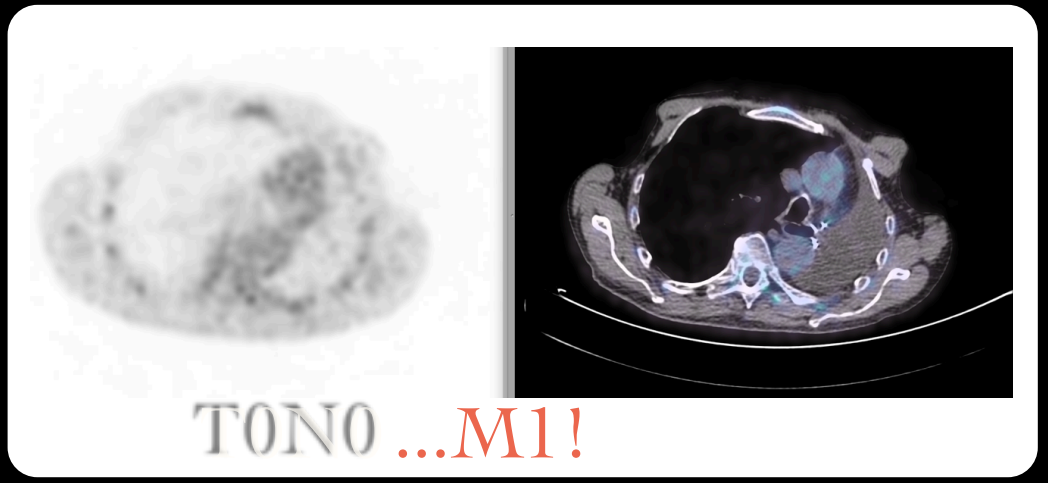
mais... métastase hépatique méconnue !

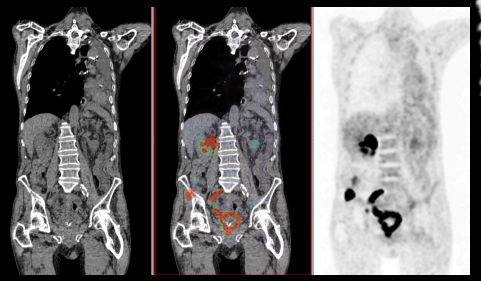
(M0 -> M1 !)

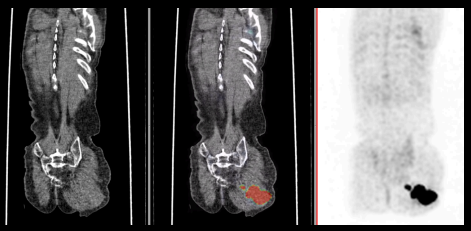
... Re-staging post traitement (23/02/11)

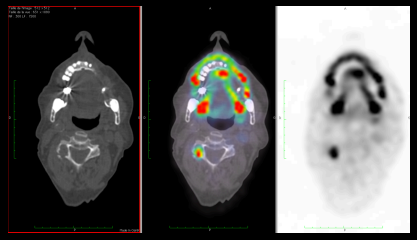


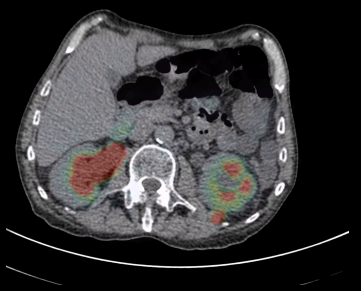






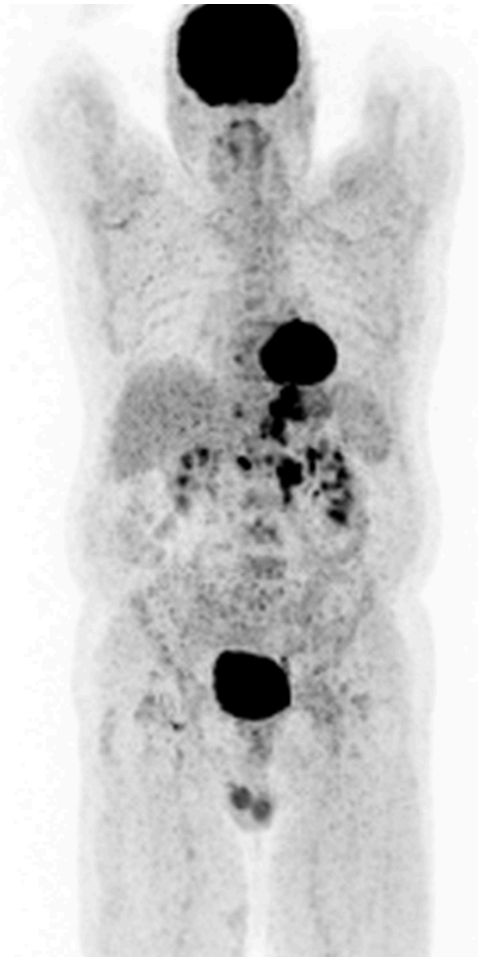


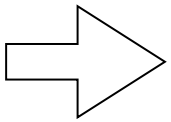




Restaging post Traitement

Cancer de l'oesophage

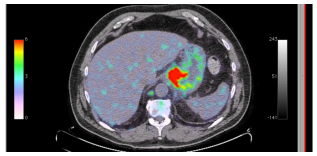


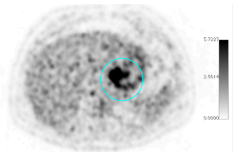


Inopérable

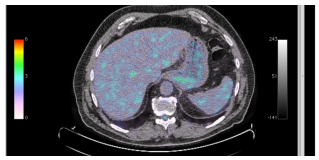
↓

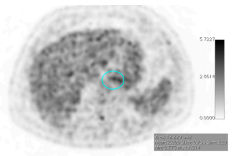
«Opérabilisable»





14/10/10

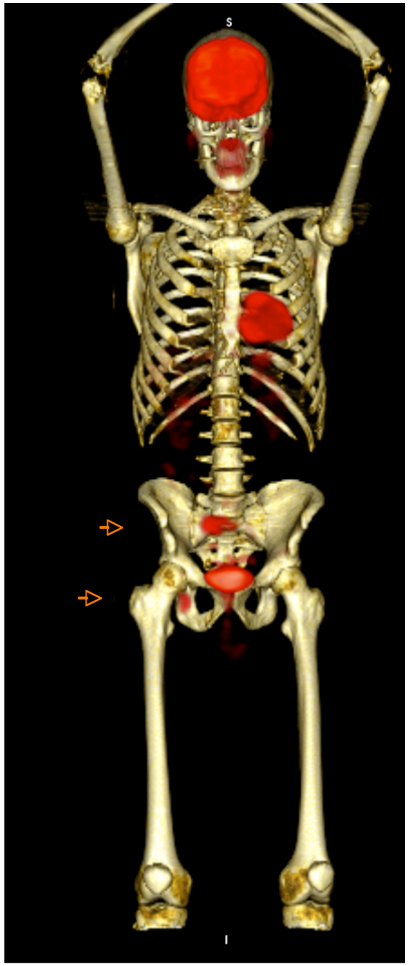




23/02/10

FDG PET/CT to guide biopsy samples

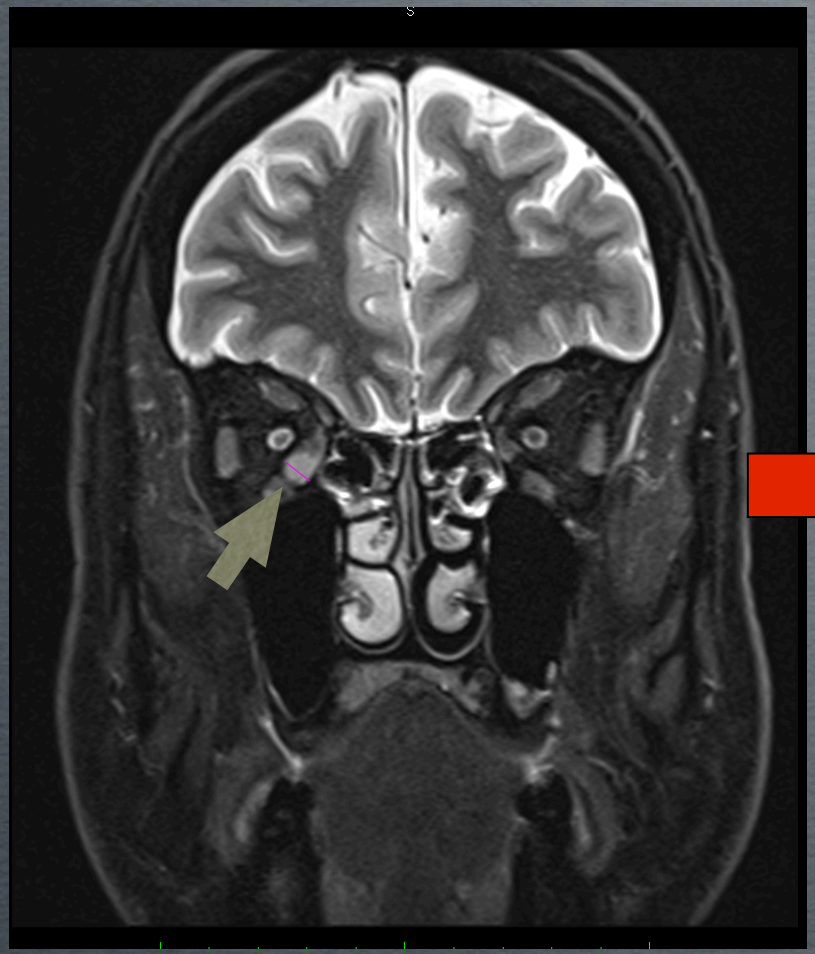
Diffuse M+ Bone lesions > patient irradiated without diagnosis



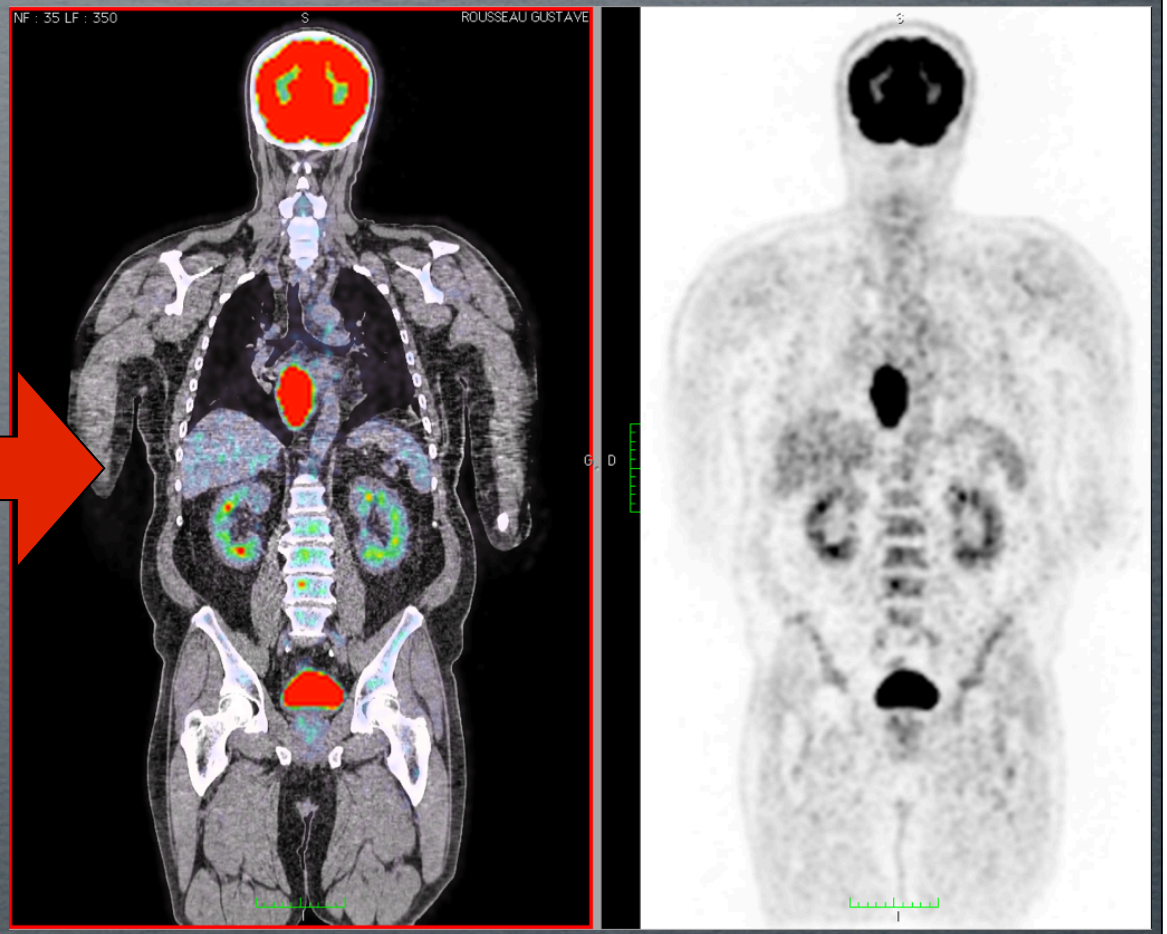
Ccl: Hodgkin Lymphoma > chemotherapy !

Bilan d'une lésion d'allure Métastatique, d'origine indéterminée (CE3998E)

Diminution de l'acuité visuelle



Nodule m.occulo-moteur interne



Néo. oesophage

Items classiques de la littérature PET Onco

- Bénin/malin
- Staging, restaging, récidive
  - Modifications TNM (+stratégie diagnostique X ou Y)
  - Impact sur la prise en charge du patient
  - Valeur pronostique (réponse précoce, positif/négatif…)
  - Coûts/bénéfices

- Médecine personalisée / Monitoring Thérapeutique

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Journal of Nuclear Medicine Vol. 47 No. 6 901-903
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Invited Perspective

^{18}F-FDG PET as a Candidate for "Qualified Biomarker": Functional Assessment of Treatment Response in Oncology

Steven M. Larson and Lawrence H. Schwartz

Memorial Sloan-Kettering Cancer Center New York, New York

clinical trials with traditional endpoints (Phase I>III, OS...) are very expensive (>100.10^6 $)

↓

«Surrogate endpoints for survival»: RR, TTP, PFS..

↓

Biomarkers / marker of cancer activity

↓

FDG PET submitted to FDA authorities

↕

Only if better Procedure Standardization

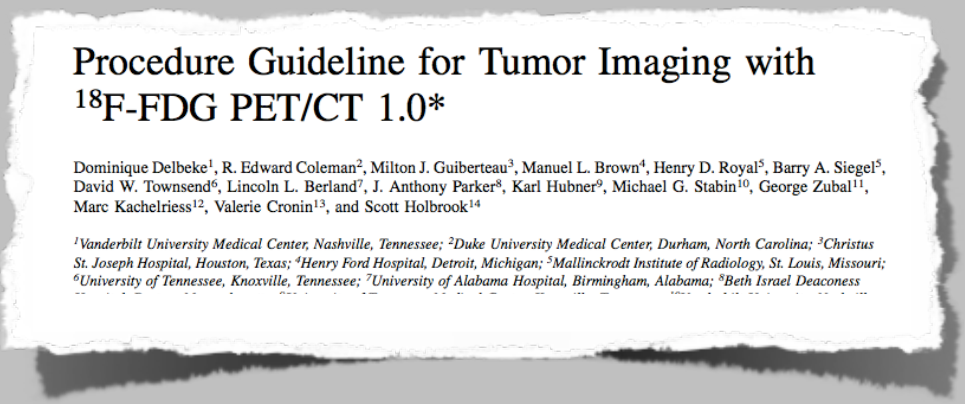
PET/CT FDG: l'âge de raison...

NCI-SNM
(2006)

Et en Europe... ?

EORTC - Accreditation EANM

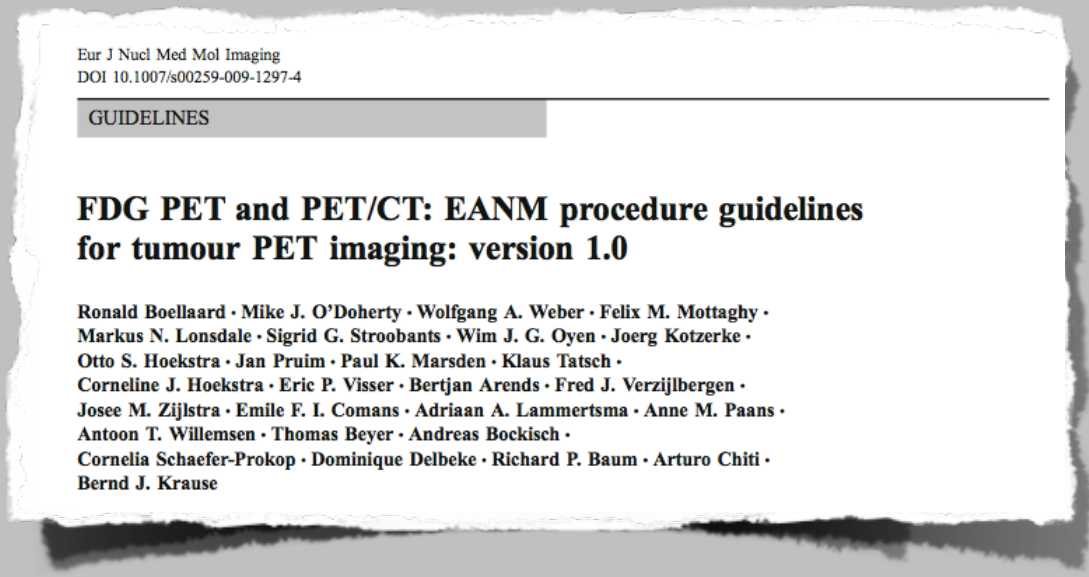
(Amsterdam/Vienna 2010 > 2011)



Procedure Guideline for Tumor Imaging with ^{18}F-FDG PET/CT 1.0*

Dominique Delbeke[1], R. Edward Coleman[2], Milton J. Guiberteau[3], Manuel L. Brown[4], Henry D. Royal[5], Barry A. Siegel[5], David W. Townsend[6], Lincoln L. Berland[7], J. Anthony Parker[8], Karl Hubner[9], Michael G. Stabin[10], George Zubal[11], Marc Kachelriess[12], Valerie Cronin[13], and Scott Holbrook[14]

[1]Vanderbilt University Medical Center, Nashville, Tennessee; [2]Duke University Medical Center, Durham, North Carolina; [3]Christus St. Joseph Hospital, Houston, Texas; [4]Henry Ford Hospital, Detroit, Michigan; [5]Mallinckrodt Institute of Radiology, St. Louis, Missouri; [6]University of Tennessee, Knoxville, Tennessee; [7]University of Alabama Hospital, Birmingham, Alabama; [8]Beth Israel Deaconess



Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-009-1297-4

GUIDELINES

FDG PET and PET/CT: EANM procedure guidelines for tumour PET imaging: version 1.0

Ronald Boellaard · Mike J. O'Doherty · Wolfgang A. Weber · Felix M. Mottaghy · Markus N. Lonsdale · Sigrid G. Stroobants · Wim J. G. Oyen · Joerg Kotzerke · Otto S. Hoekstra · Jan Pruim · Paul K. Marsden · Klaus Tatsch · Corneline J. Hoekstra · Eric P. Visser · Bertjan Arends · Fred J. Verzijlbergen · Josee M. Zijlstra · Emile F. I. Comans · Adriaan A. Lammertsma · Anne M. Paans · Antoon T. Willemsen · Thomas Beyer · Andreas Bockisch · Cornelia Schaefer-Prokop · Dominique Delbeke · Richard P. Baum · Arturo Chiti · Bernd J. Krause

En parallèle...

From RECIST to PERCIST: Evolving Considerations for PET Response Criteria in Solid Tumors

Richard L. Wahl[1,2], Heather Jacene[1], Yvette Kasamon[2], and Martin A. Lodge[1]

[1]*Division of Nuclear Medicine, Department of Radiology, Johns Hopkins University School of Medicine, Baltimore, Maryland; and*
[2]*Department of Oncology, Johns Hopkins University School of Medicine, Baltimore, Maryland*

The purpose of this article is to review the status and limitations of anatomic tumor response metrics including the World Health Organization (WHO) criteria, the Response Evaluation Criteria in Solid Tumors (RECIST), and RECIST 1.1. This article also reviews qualitative and quantitative approaches to metabolic tumor response assessment with ^{18}F-FDG PET and proposes a draft framework for PET Response Criteria in Solid Tumors (PERCIST), version 1.0. **Methods:** PubMed searches, including searches for the terms *RECIST, positron, WHO, FDG, cancer* (including specific types), *treatment response, region of interest,* and derivative references, were performed. Abstracts and articles judged most relevant to the goals of this report were reviewed with emphasis on limitations and strengths of the anatomic and PET approaches to treatment response assessment. On the basis of these data and the authors' experience, draft criteria were formulated for PET tumor response to treatment. **Results:** Approximately 3,000 potentially relevant references were screened. Anatomic imaging alone using standard WHO, RECIST, and RECIST 1.1 criteria is widely applied but still has limitations in response assessments. For example, despite effective treatment, changes in tumor size can be minimal in tumors such as lymphomas, sarcoma, hepatomas, mesothelioma, and gastrointestinal stromal tumor. CT tumor density, contrast enhancement, or MRI characteristics appear more informative than size but are not yet routinely applied. RECIST criteria may 3-cm-diameter region of interest in the liver, using a consistent PET protocol, using a fixed small region of interest about 1 cm^3 in volume (1.2-cm diameter) in the most active region of metabolically active tumors to minimize statistical variability, assessing tumor size, treating SUV lean measurements in the 1 (up to 5 optional) most metabolically active tumor focus as a continuous variable, requiring a 30% decline in SUV for "response," and deferring to RECIST 1.1 in cases that do not have ^{18}F-FDG avidity or are technically unsuitable. Criteria to define progression of tumor-absent new lesions are uncertain but are proposed. **Conclusion:** Anatomic imaging alone using standard WHO, RECIST, and RECIST 1.1 criteria have limitations, particularly in assessing the activity of newer cancer therapies that stabilize disease, whereas ^{18}F-FDG PET appears particularly valuable in such cases. The proposed PERCIST 1.0 criteria should serve as a starting point for use in clinical trials and in structured quantitative clinical reporting. Undoubtedly, subsequent revisions and enhancements will be required as validation studies are undertaken in varying diseases and treatments.

Key Words: molecular imaging; oncology; PET/CT; anatomic imaging; RECIST; response criteria; SUV; treatment monitoring

J Nucl Med 2009; 50:122S–150S
DOI: 10.2967/jnumed.108.057307

Critères morphologiques

WHO criteria (1979)

RECIST (2001)

RECIST 1.1 (2009)

Nouveaux agents biologiques cystatiques >< cytotoxiques

-> décrochage entre outcome & non-évolution morphologique tumorale

(ex: HCC dans SHARP, GIST & Glivec...)

PERCIST (Delta SUV)

VOLUME 25 · NUMBER 5 · FEBRUARY 10 2007

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Revised Response Criteria for Malignant Lymphoma

Bruce D. Cheson, Beate Pfistner, Malik E. Juweid, Randy D. Gascoyne, Lena Specht, Sandra J. Horning, Bertrand Coiffier, Richard I. Fisher, Anton Hagenbeek, Emanuele Zucca, Steven T. Rosen, Sigrid Stroobants, T. Andrew Lister, Richard T. Hoppe, Martin Dreyling, Kensei Tobinai, Julie M. Vose, Joseph M. Connors, Massimo Federico, and Volker Diehl

From the Division of Hematology/ Oncology, Georgetown University Hospital, Washington, DC; University of

VOLUME 25 · NUMBER 5 · FEBRUARY 10 2007

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Use of Positron Emission Tomography for Response Assessment of Lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma

Malik E. Juweid, Sigrid Stroobants, Otto S. Hoekstra, Felix M. Mottaghy, Markus Dietlein, Ali Guermazi, Gregory A. Wiseman, Lale Kostakoglu, Klemens Scheidhauer, Andreas Buck, Ralph Naumann, Karoline Spaepen, Rodney J. Hicks, Wolfgang A. Weber, Sven N. Reske, Markus Schwaiger, Lawrence H. Schwartz, Josee M. Zijlstra, Barry A. Siegel, and Bruce D. Cheson

From the Department of Radiology, University of Iowa, Iowa City, IA; Department of Nuclear Medicine,

Critères de fin de traitement !

Etudes interventionelles sur base des résultats PET intermédiaires

Work in Progress/Validation... (5point scale, deltaSUV...)

Deauville 2009

Menton 2010

Menton 2011

Third international workshop on interim-PET in lymphoma
Menton (France), Palais de l'Europe,
September 26-27th, 2011

Under the auspices of GELA, IIL, SFMN, EANM, EHA

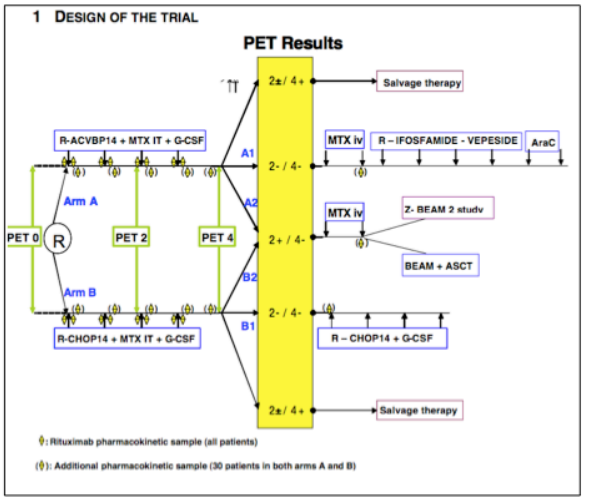
Organization Committee
M.Meignan (France), A.Gallamini (Italy), C.Haioun (France)

Scientific committee

M.Meignan (France), A.Gallamini (Italy), C.Haioun (France), A.Polliack (Israel), B.Cheson (USA), A. Lister (UK), U.Duhrsen (Germany), Th.Vander Borght (Belgium), L.Kostakoglu (USA), M. Juweid (USA), S.Barrington (UK), E.Itti (France).

LNH-2007-38

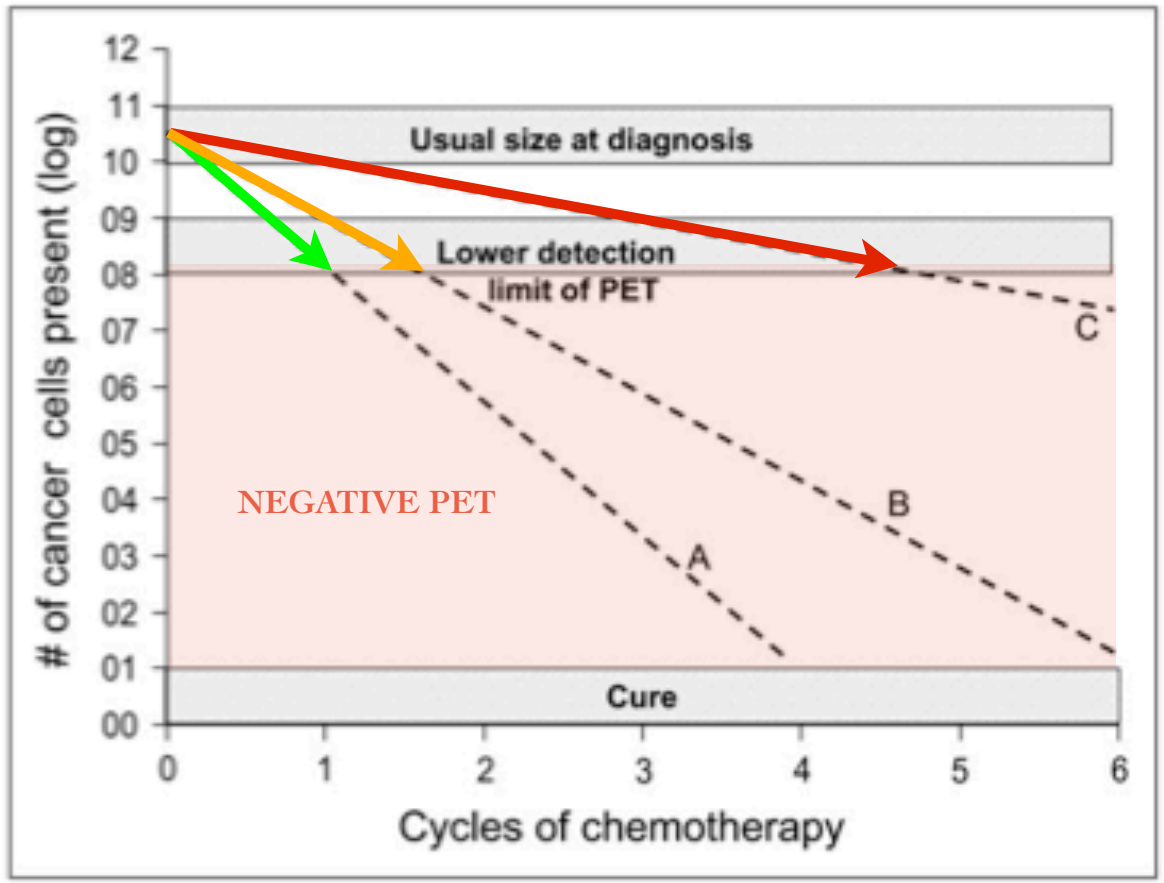
RANDOMIZED PHASE II STUDY OF TWO ASSOCIATIONS OF RITUXIMAB AND CHEMOTHERAPY, WITH A PET-DRIVEN STRATEGY, IN PATIENTS FROM 18 TO 59 WITH DLBCL CD 20+ LYMPHOMA AND 2 OR 3 ADVERSE PROGNOSTIC FACTORS OF THE AGE-ADJUSTED IPI



EORTC European Organisation for Research and Treatment of Cancer

Gela

Seuil de détectabilité tumorale par PET	0.4-1.0 cm
...quand la T+ atteint	0.1-0.5 to 1g 10^8-10^9 cellules



cT0≠pT0

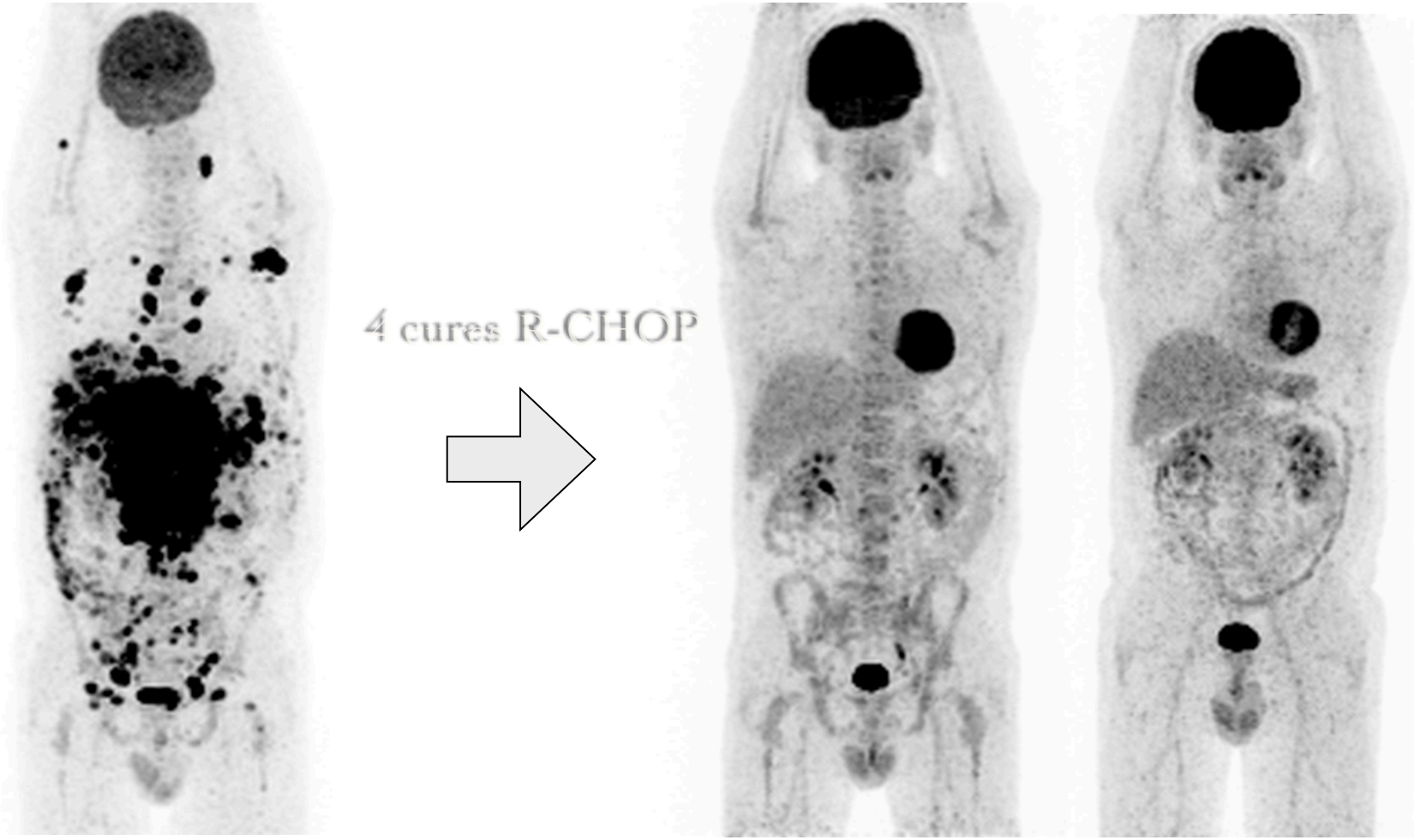
Un PET négatif en fin de traitement ne signifie pas nécessairement l'absence de cellule tumorale résiduelle ([0-10^7 cells] ...mais est de bon pronostic !

Ex: métas hépatiques colo-rectales

T+ Pauci-cellulaires:

VBEH, urothéliales, kystiques, mucoïdes....

DLBCL - M; 50 ans



06/08/08 17/11/08 01/07/09

LNH Folliculaire - M; 59 ans

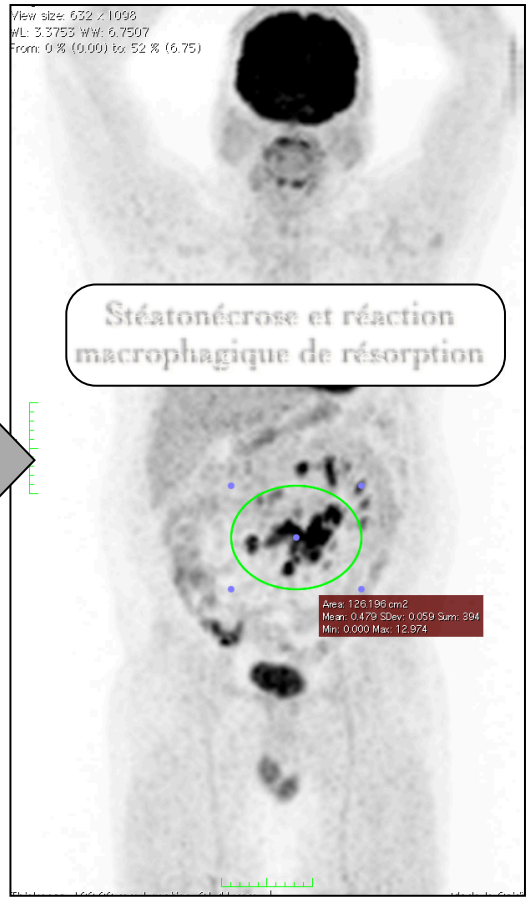
16/02/10

R-CHOP
4cures

20/04/10

?

Infiltrat mésentérique mal défini



22/10/10

Discordances- complications infectieuses du R/ (HIV+)

Quid des critères pour les tumeurs solides ?

Pergamon

European Journal of Cancer, Vol. 35, No. 13, pp. 1773–1782, 1999
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0959-8049/99/$ - see front matter

PII: S0959-8049(99)00229-4

Position Paper

Measurement of Clinical and Subclinical Tumour Response Using [^{18}F]-fluorodeoxyglucose and Positron Emission Tomography: Review and 1999 EORTC Recommendations

H. Young,[1] R. Baum,[2] U. Cremerius,[3] K. Herholz,[4] O. Hoekstra,[5] A.A. Lammertsma,[5] J. Pruim[6] and P. Price[1] on behalf of the European Organization for Research and Treatment of Cancer (EORTC) PET Study Group

[1]CRC PET Oncology Research Group, MRC Cyclotron Unit, Imperial College School of Medicine, Hammersmith Hospital, Du Cane Rd, London W12 ONN, U.K.; [2]Bad Berka PET Centre, Zentralklinik Bad Berka GmBH, Bad Berka; [3]Department of Nuclear Medicine, Aachen University of Technology, Aachen; [4]Max Planck Institut für Neurologische Forschung und Neurologische Universitatsklinik, Koln, Germany; [5]PET Centre, Academisch Ziekenhuis Vrije Universiteit, Amsterdam; and [6]PET Centrum, Academisch Ziekenhuis Groningen, Groningen, The Netherlands

- mCR: complete metabolic response

  Complete resolution of FDG uptake within the tumour, indistinguishable from surrounding normal tissue.

- mPR: partial metabolic response

  Reduction of more than 15% of the tumour SUVmax

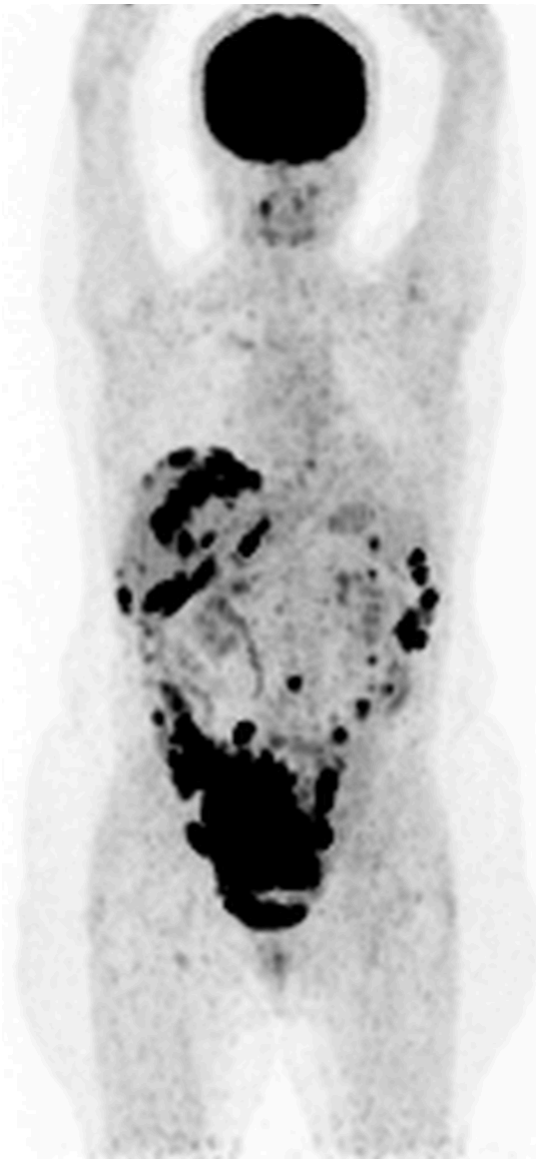
- mSD: stable metabolic disease

  Increase of < 25% in tumour SUVmax or decrease of <15 % in tumour SUVmax

- mPD: progressive metabolic disease

  Increase of > 25% in tumour SUVmax or of > 20% in the extent (longest dimension), or the appearance of a new suspected lesion.

F 74 ans ; Néo ovarien



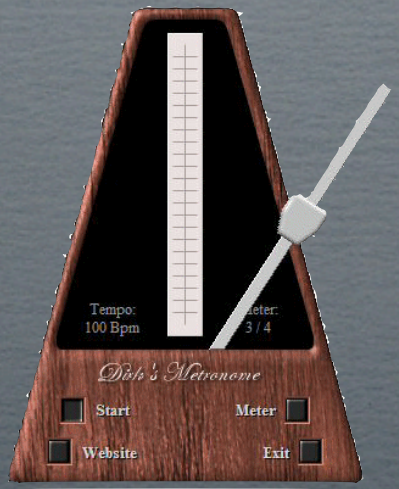
08/03/10

6 cures de Carbo-taxol

17/09/10

IMPORTANCE DU TIMING

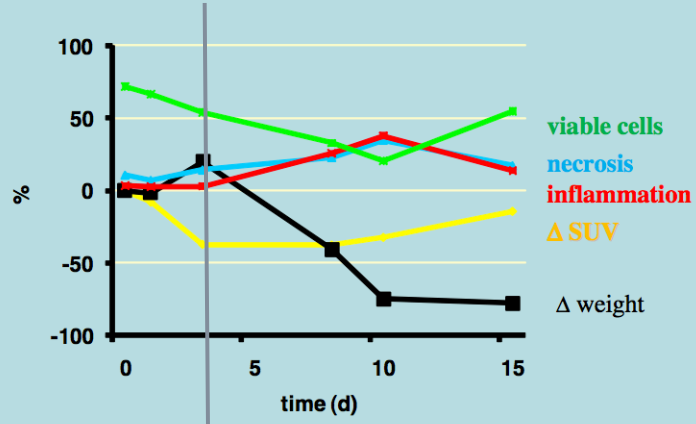
dans le monitoring thérapeutique



RL- WRDGN3120

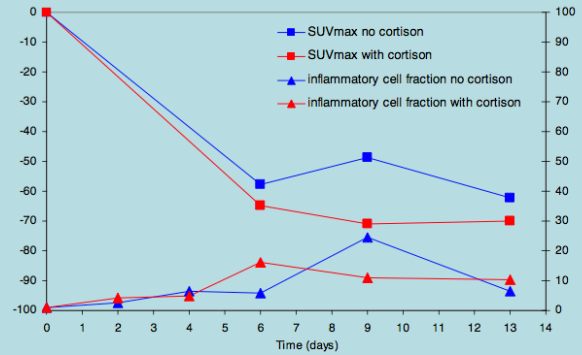
Inflammation and its interference with early response assessment

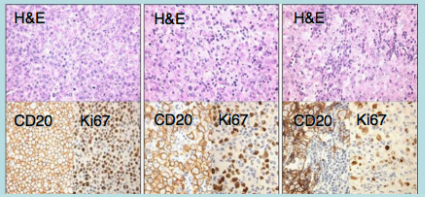
Spaepen, EJNM 2003
SCID mice with cyclophosphamide, ex-vivo measurements



// non //

Does the presence of anti-inflammatory drugs (corticosteroids) influences the FDG-uptake and the cellular respons after chemotherapy?





Cyclophosphamide
Cyclophosphamide + hydrocortisone

Brepoels L, Stroobants S, et al. J Nucl Med. 2007

Recommendations:

Chimiothérapie: PET minimum 10j après... (idéalement juste avant la prochaine cure)

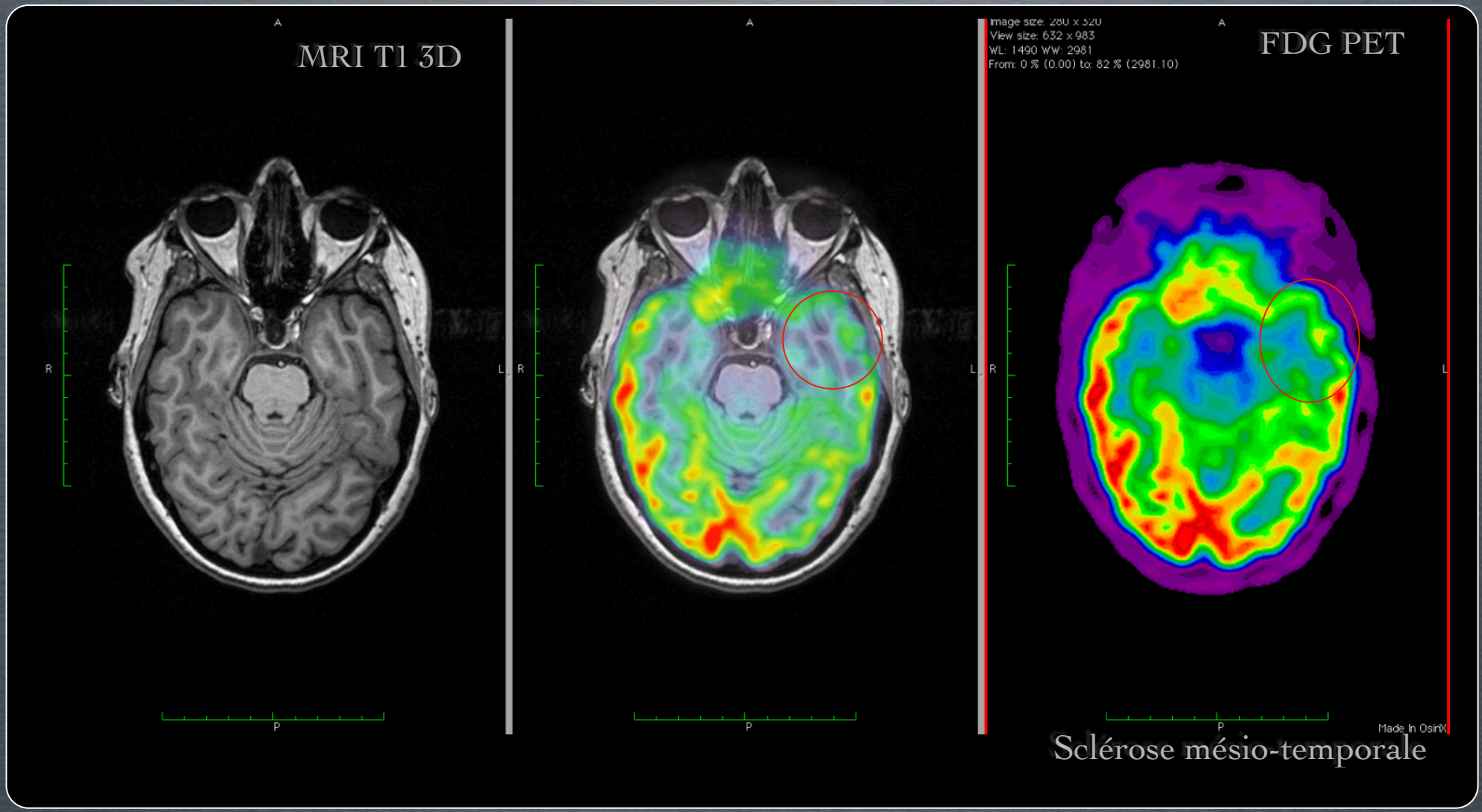
Radiothérapie externe: 8 - 12 semaines !

Autres champs d'application du PET/CT

- Neurologie (épilepsie réfractaire, démences, tumeurs...)
- Cardiologie (Viabilité myocardique/flux coronarien)
- Médecine Interne Générale: inflammation & infection
- Radiothérapie (délimitation des volumes à irradier)

Neurologie

Localisation d'un foyer épileptogène (épilepsie réfractaire)



Sclérose mésio-temporale

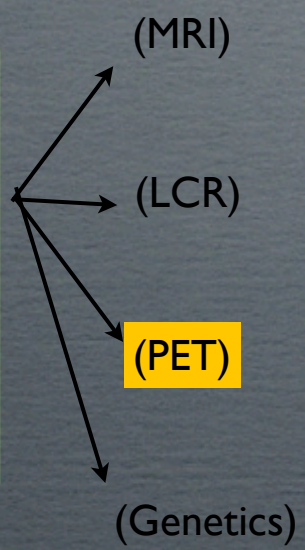
RL- WRDGN3120

Bilan des Démences

Clinical
(A)

+

one or more biomarker criteria
(B,C,D or E)



Panel 2: Diagnostic criteria for AD

Probable AD: A plus one or more supportive features B, C, D, or E

Core diagnostic criteria

A. Presence of an early and significant episodic memory impairment that includes the following features:

1. Gradual and progressive change in memory function reported by patients or informants over more than 6 months
2. Objective evidence of significantly impaired episodic memory on testing: this generally consists of recall deficit that does not improve significantly or does not normalise with cueing or recognition testing and after effective encoding of information has been previously controlled
3. The episodic memory impairment can be isolated or associated with other cognitive changes at the onset of AD or as AD advances

Supportive features

B. Presence of medial temporal lobe atrophy

- Volume loss of hippocampi, entorhinal cortex, amygdala evidenced on MRI with qualitative ratings using visual scoring (referenced to well characterised population with age norms) or quantitative volumetry of regions of interest (referenced to well characterised population with age norms)

C. Abnormal cerebrospinal fluid biomarker

- Low amyloid β_{1-42} concentrations, increased total tau concentrations, or increased phospho-tau concentrations, or combinations of the three
- Other well validated markers to be discovered in the future

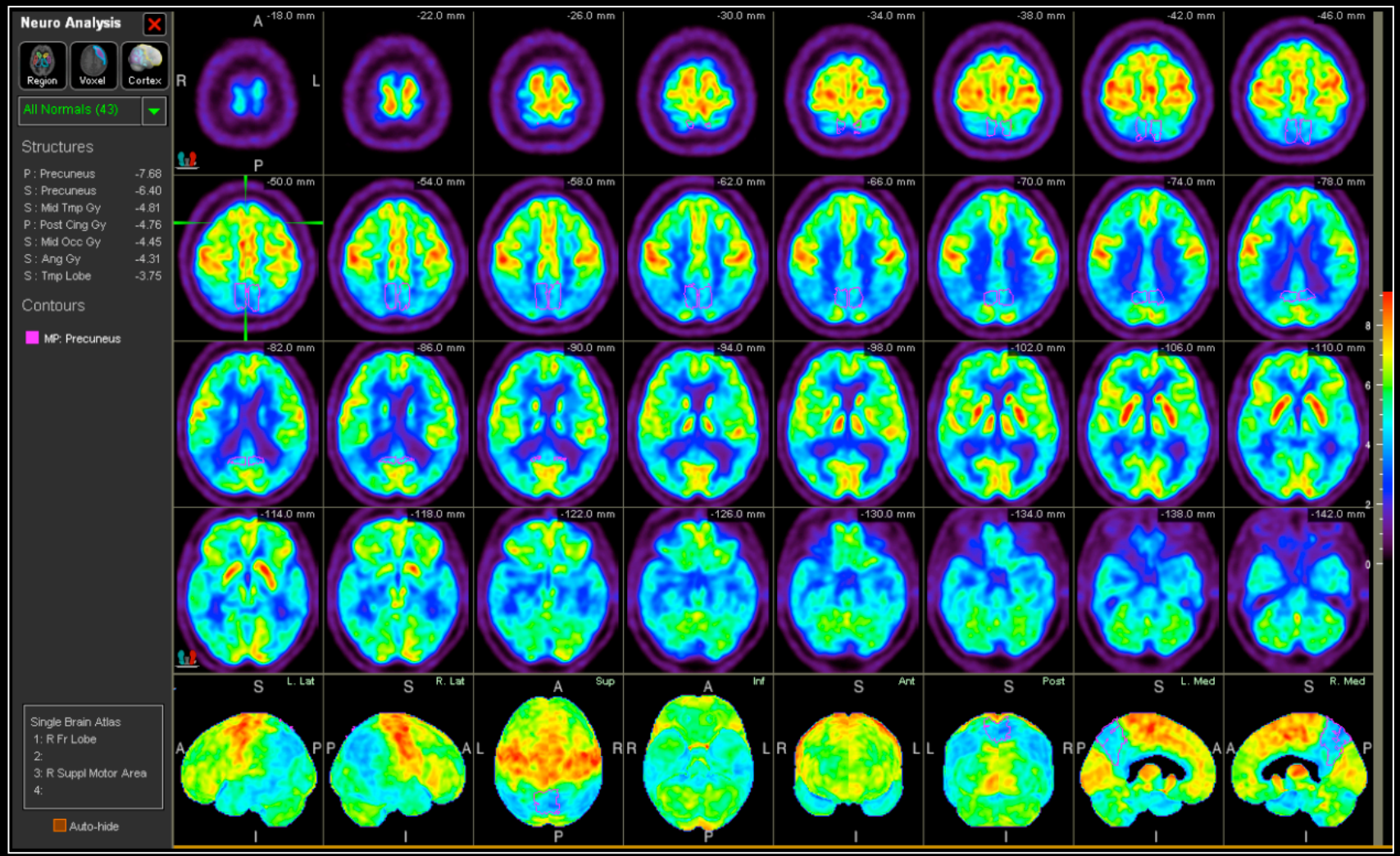
D. Specific pattern on functional neuroimaging with PET

- Reduced glucose metabolism in bilateral temporal parietal regions
- Other well validated ligands, including those that foreseeably will emerge such as Pittsburg compound B or FDDNP

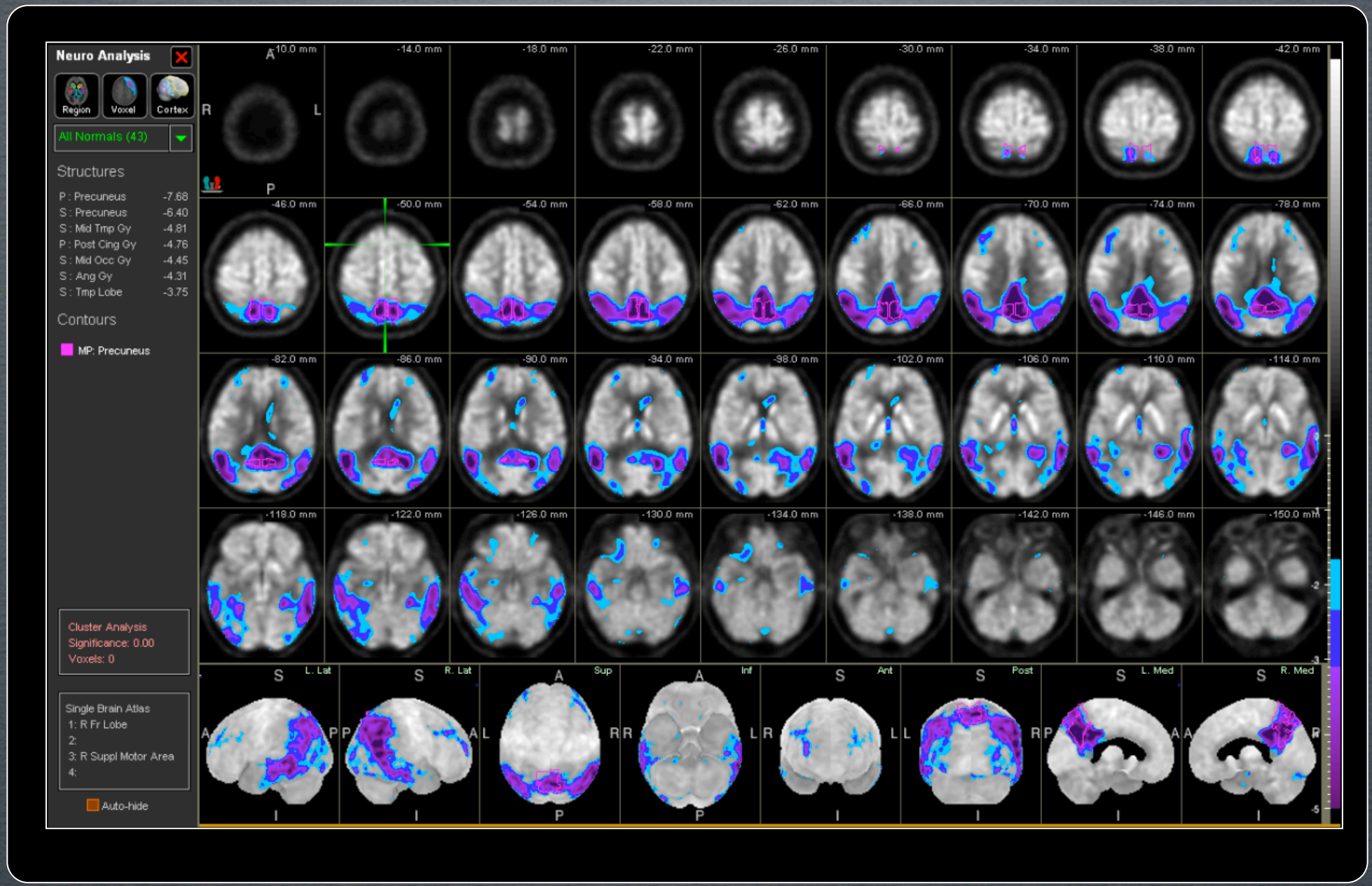
E. Proven AD autosomal dominant mutation within the immediate family

Dubois, Lancet Neurology 2007

F; 55 ans - Typical pattern of Alzheimer (early onset)



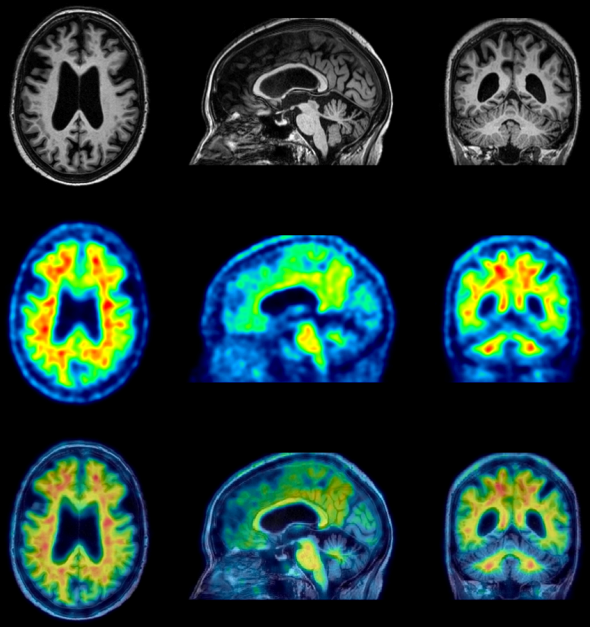
Complex Voxel based analysis (Zscore ÷normal DB)

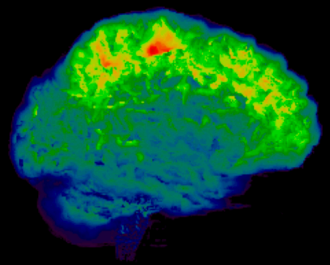


Amyloid plaques imaging

^{11}C-PIB ^{18}F-Flumetamol ^{18}F-AVID$_{21,28}$ ^{18}F-BAY 94-9172

Negative ^{18}F-Flutemetamol PET





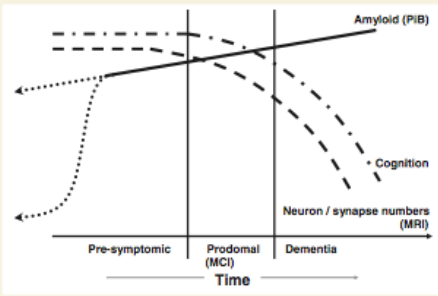
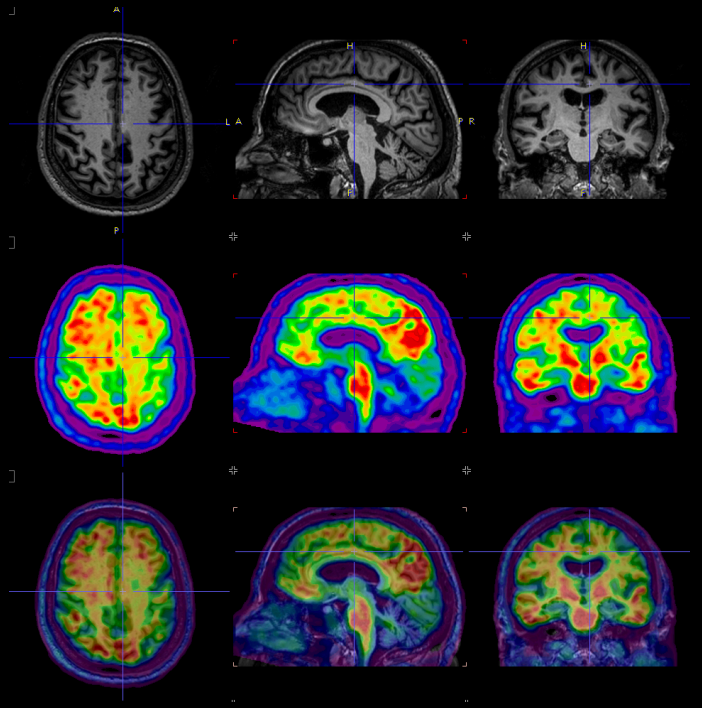
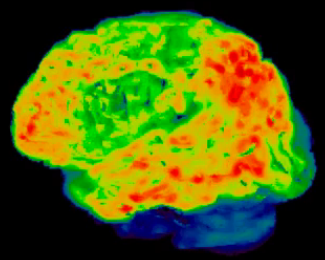


Figure 3 Proposed model relating imaging, pathology and clinical presentation over an individual's adult lifetime. The lifetime clinical course of the disease is divided into pre-symptomatic, prodromal and dementia phases. Neurodegeneration, detected by MRI, is indicated by a dashed line. Cognitive function is indicated by a dot-dash line. Amyloid deposition, detected by PIB, is indicated by a solid line late in life (i.e. that portion of the disease for which we have data). The time course of amyloid deposition early in life is represented as two possible theoretical trajectories (dotted lines), reflecting uncertainty about the time course of early PIB deposition.

Jack. Brain 2009

Positive ^{18}F-Flutemetamol PET

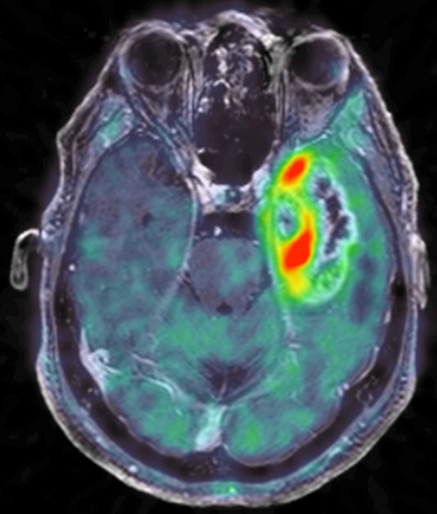




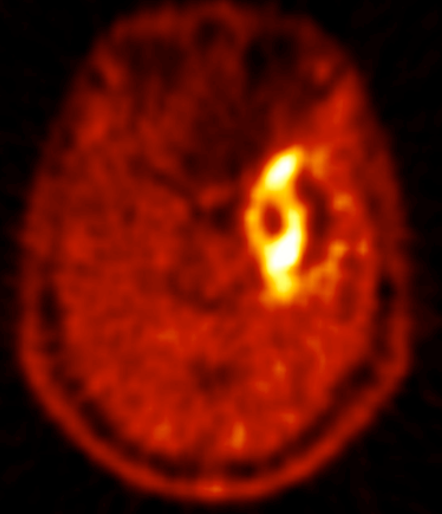
Bilan des tumeurs cérébrales primitives

Problème du FDG= activité cérébrale physiologique élevée > autres traceurs utilisés.

MRI MKM-1.2mmS



Coreg & Fusion PET - MRI



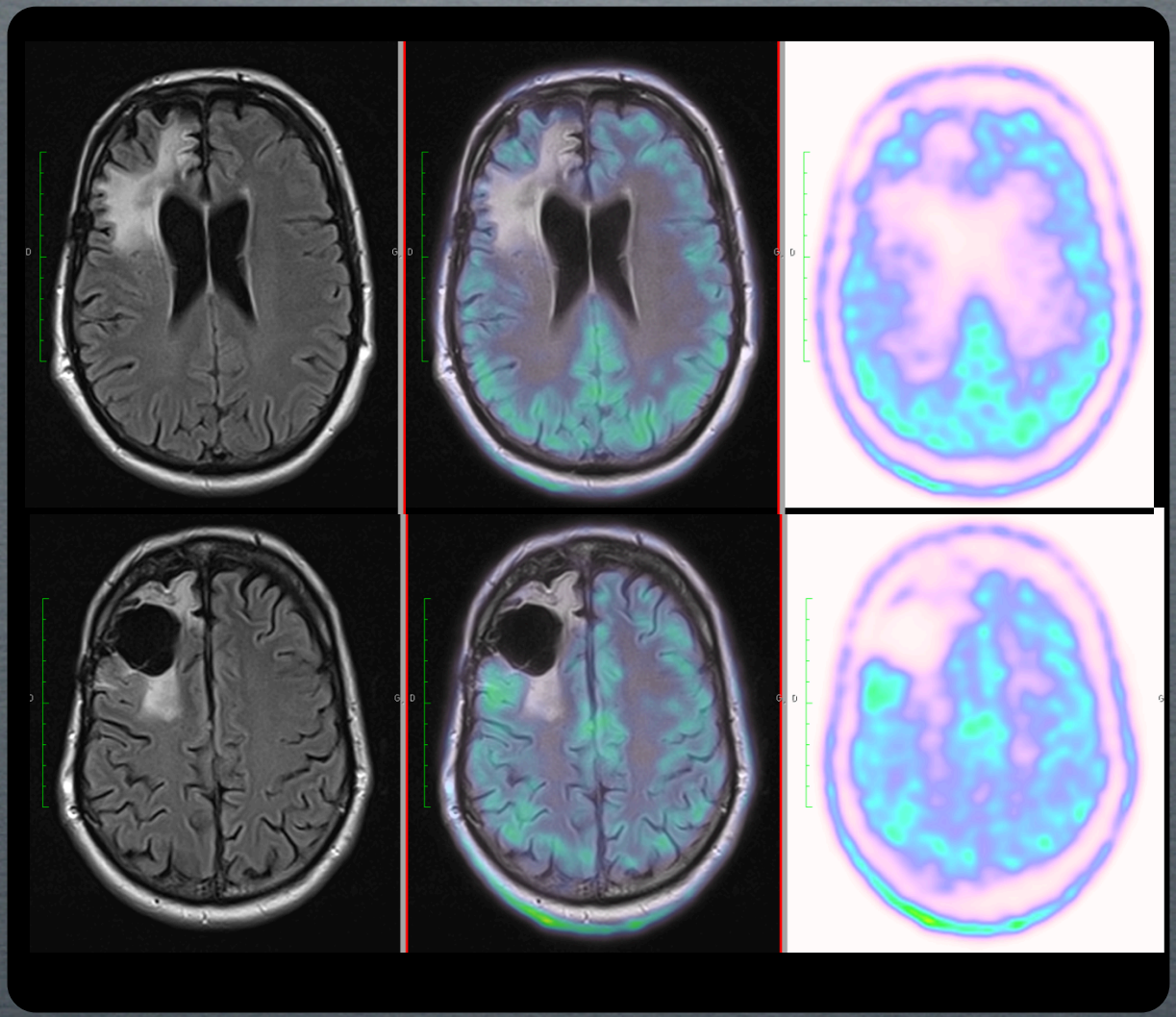
^{11}C-Methionine

↓

^{18}F-FET

Pseudo-progression radiologique versus récidive

Astro.anaplasique 3 ans post chir/radiothérapie (P93879F)



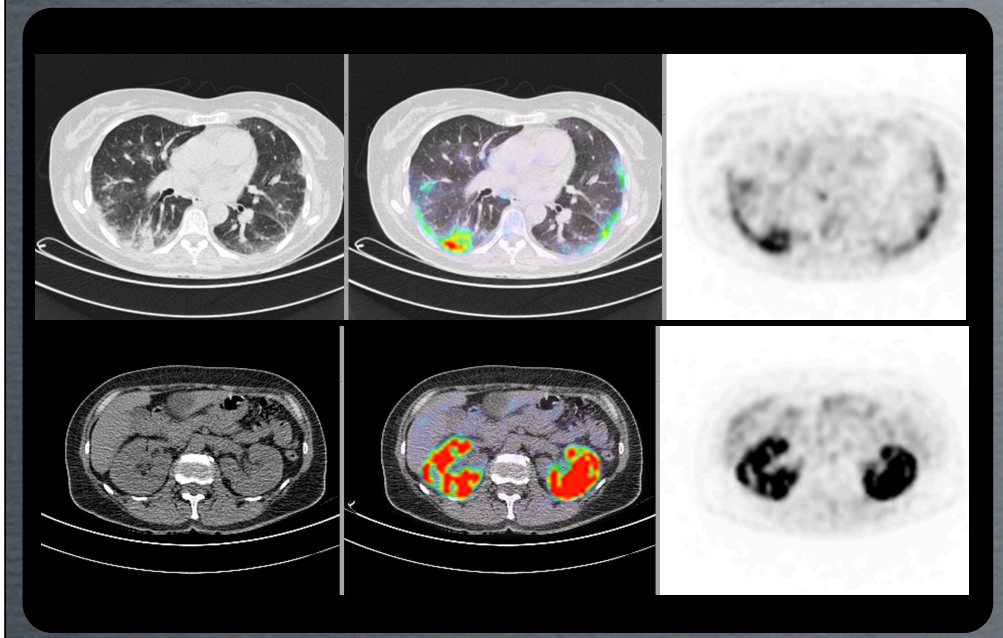
MIG

BACKGROUND

- ✓ «False positive» in cancer patients : most correspond to some degree of inflammation / infection
- ✓ GLUT 1 and 3 are present on WBCs:
  - Acute reaction (GLUT1&3)
  - Chronic inflammation with macrophages+++ (GLUT 3>GLUT 1)

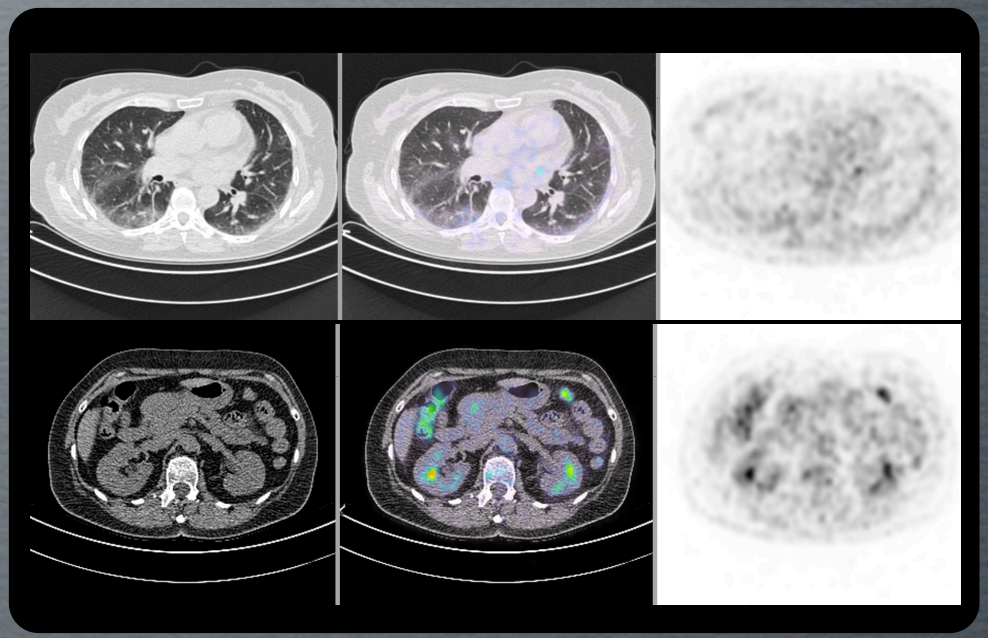
Inflammation/Fiever of Unknown Origin (FUO)

Female : 62 Y



At the time of diagnosis

28/08/09

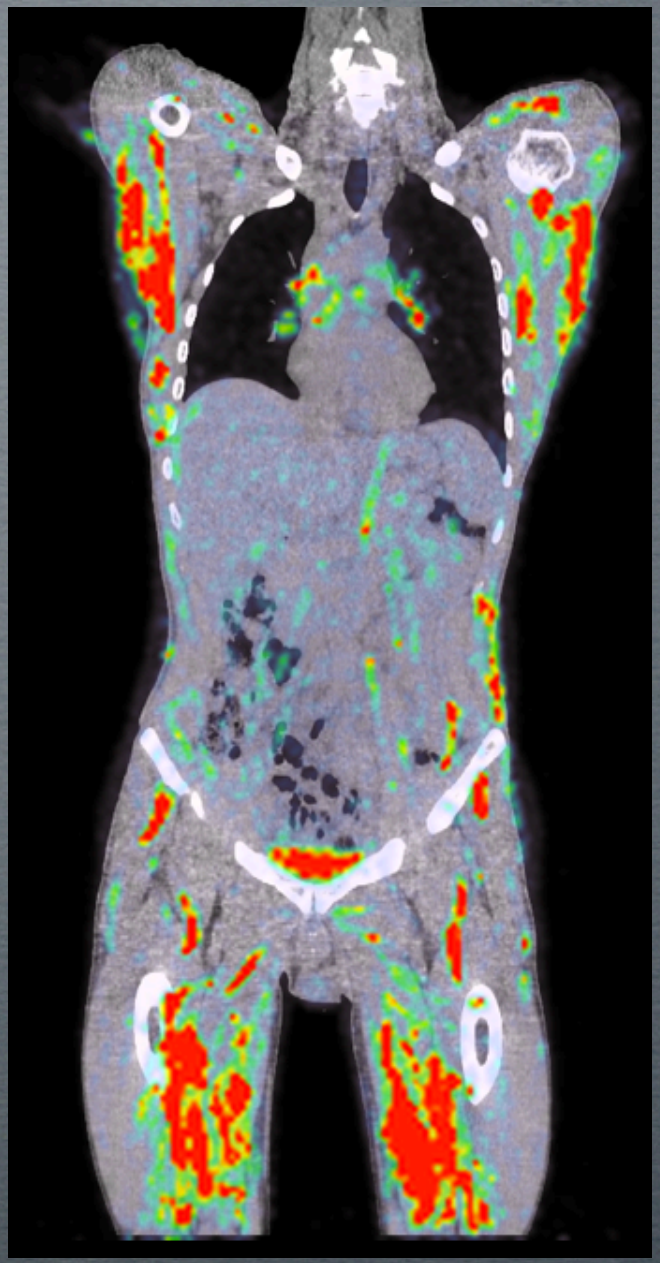


Post R/

02/12/09

Sarcoïdosis ! → Cortico-therapy

Sarcoïdose musculaire (BY5400J): hypercalcémies, troubles psychiatriques et myoclonies



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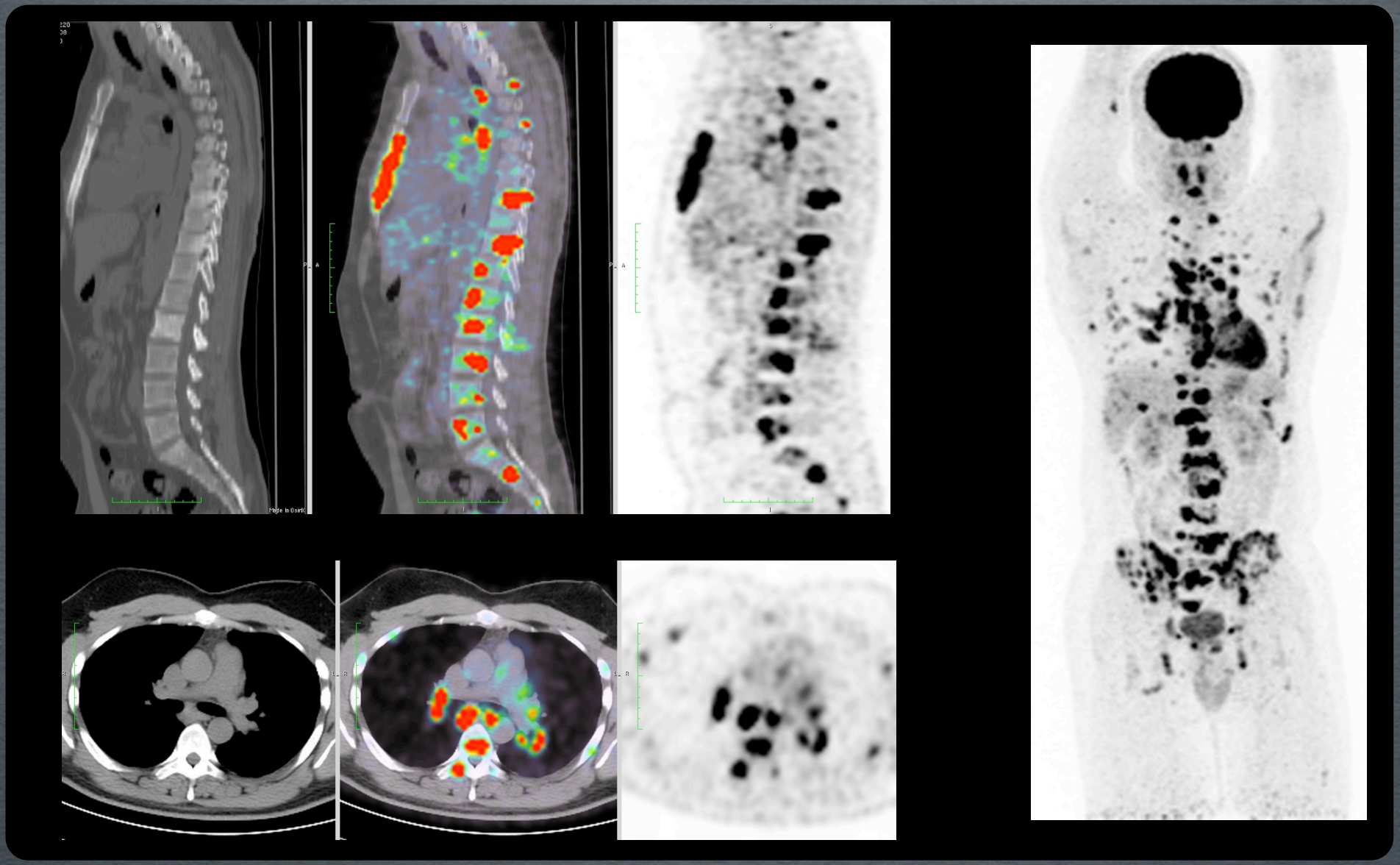
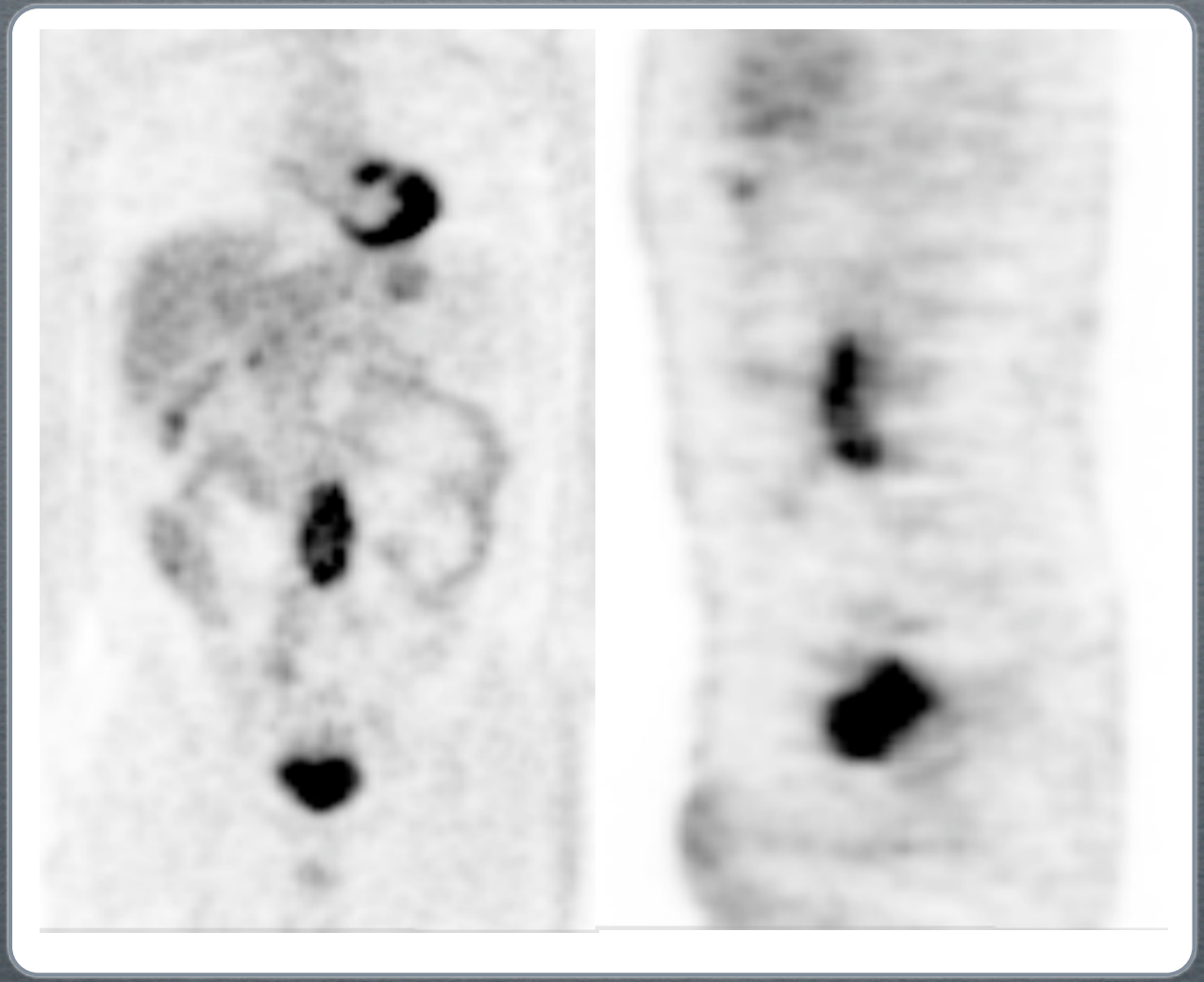
Tuberculose active



Bactériémie+FUO > Infection de prothèse aortique



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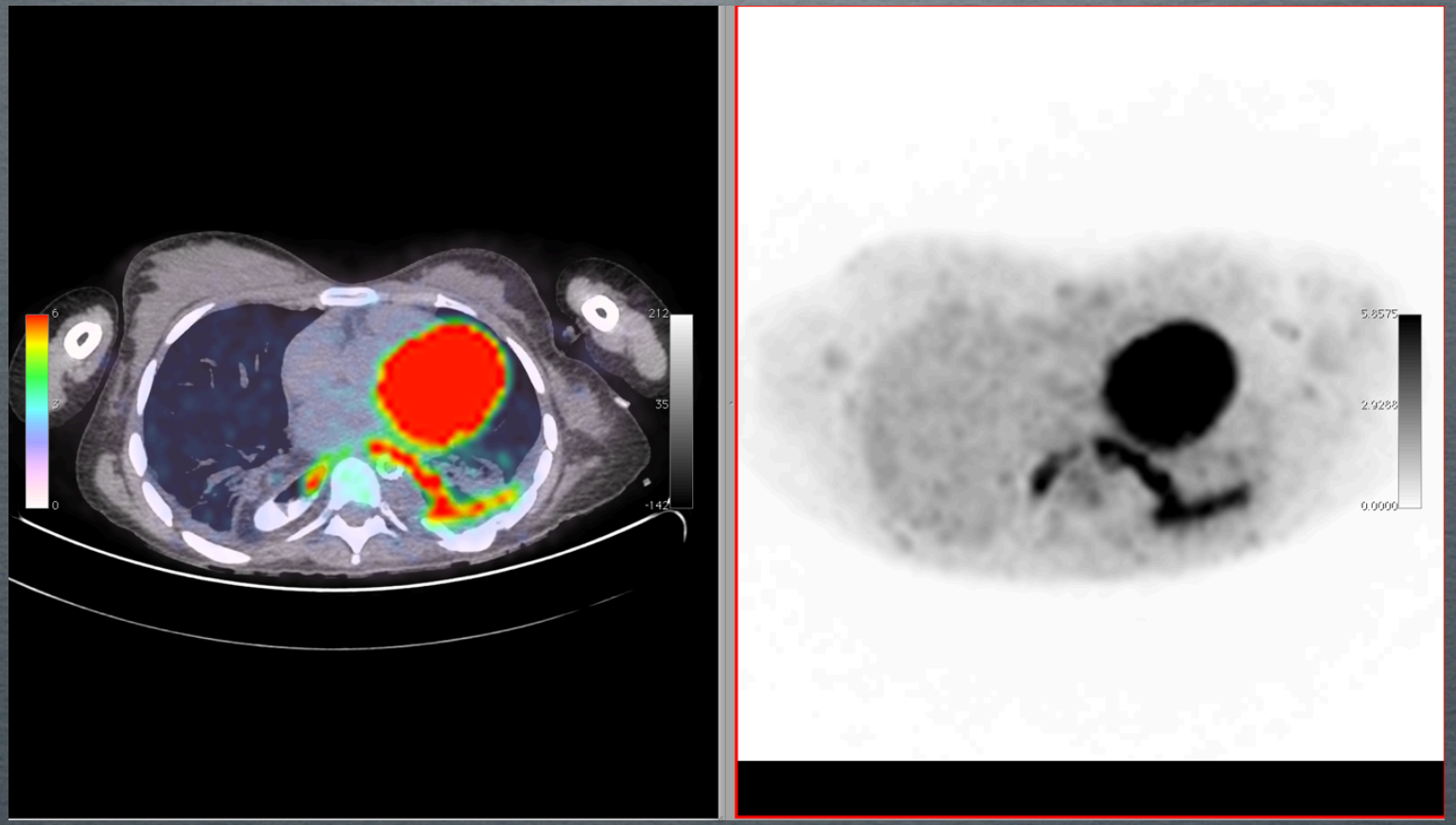
DIAGNOSIS OF INFECTION

- Usual clinical presentation
  - fever
  - "bacteriemia of unknown origin"
  - sometimes specific clinical signs (pain) with unconclusive imaging results

FUO/septicémie:

Activité marquée d'un trajet fistuleux au départ d'une plastie colique (lachage de suture) avec infiltration de l'aorte thoracique prothésée (=voie d'entrée d'une septicémie à ecoli multiR/)



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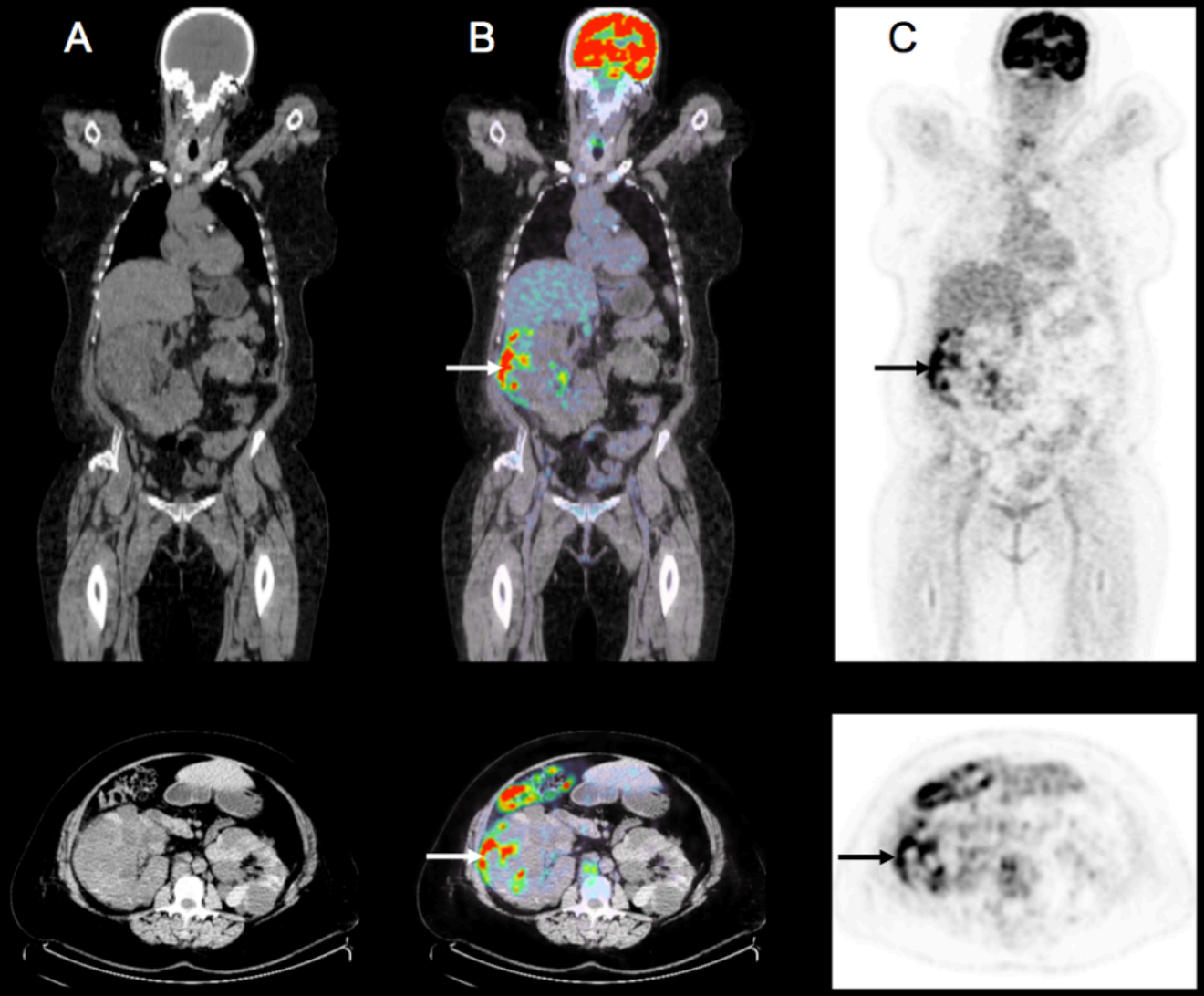
Bactériémie à G- ; Contexte de polykystose rénale

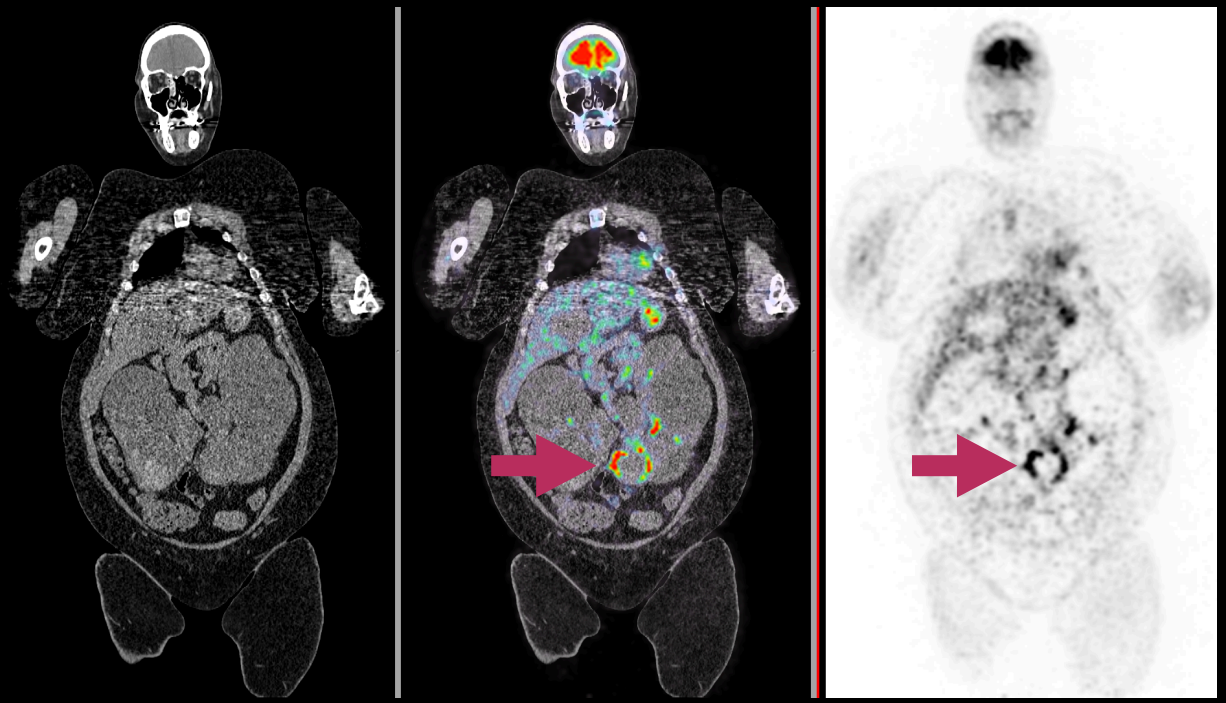


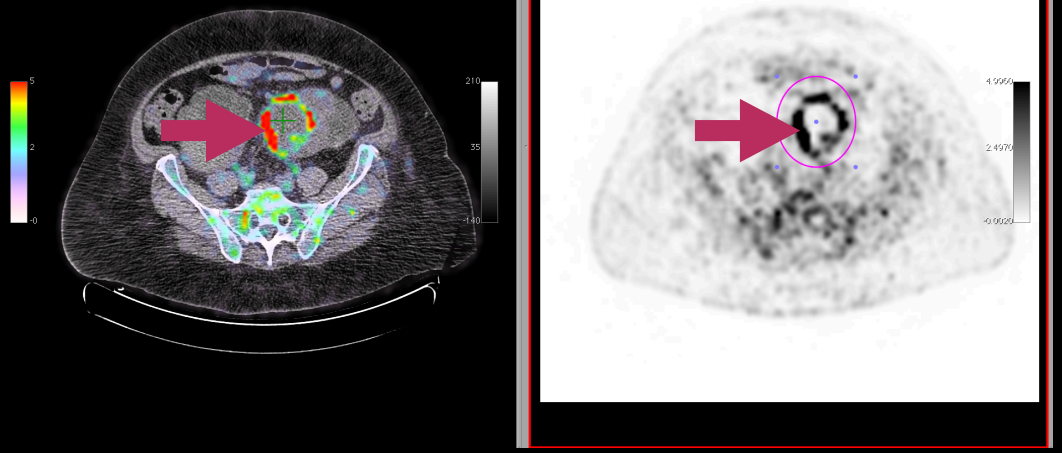
Ccl: Infection de kyste dans contexte d'ADPKD

CJASN July 2011

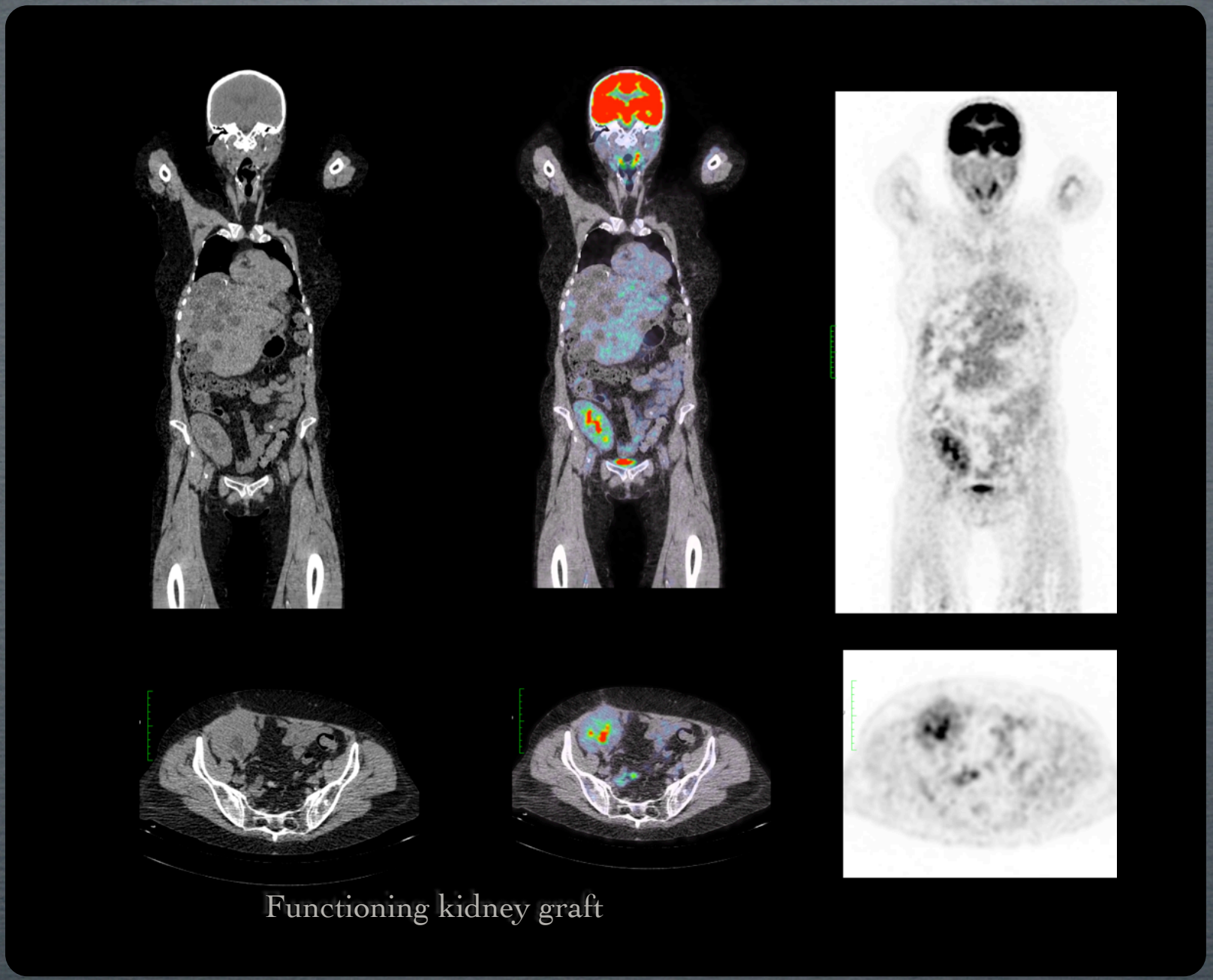
Autre patient…

Intérêt +++ de la combinaison anatomique et métabolique pour la mise en évidence de la bonne structure pathogène au sein d'organes morphologiquement très remaniés.

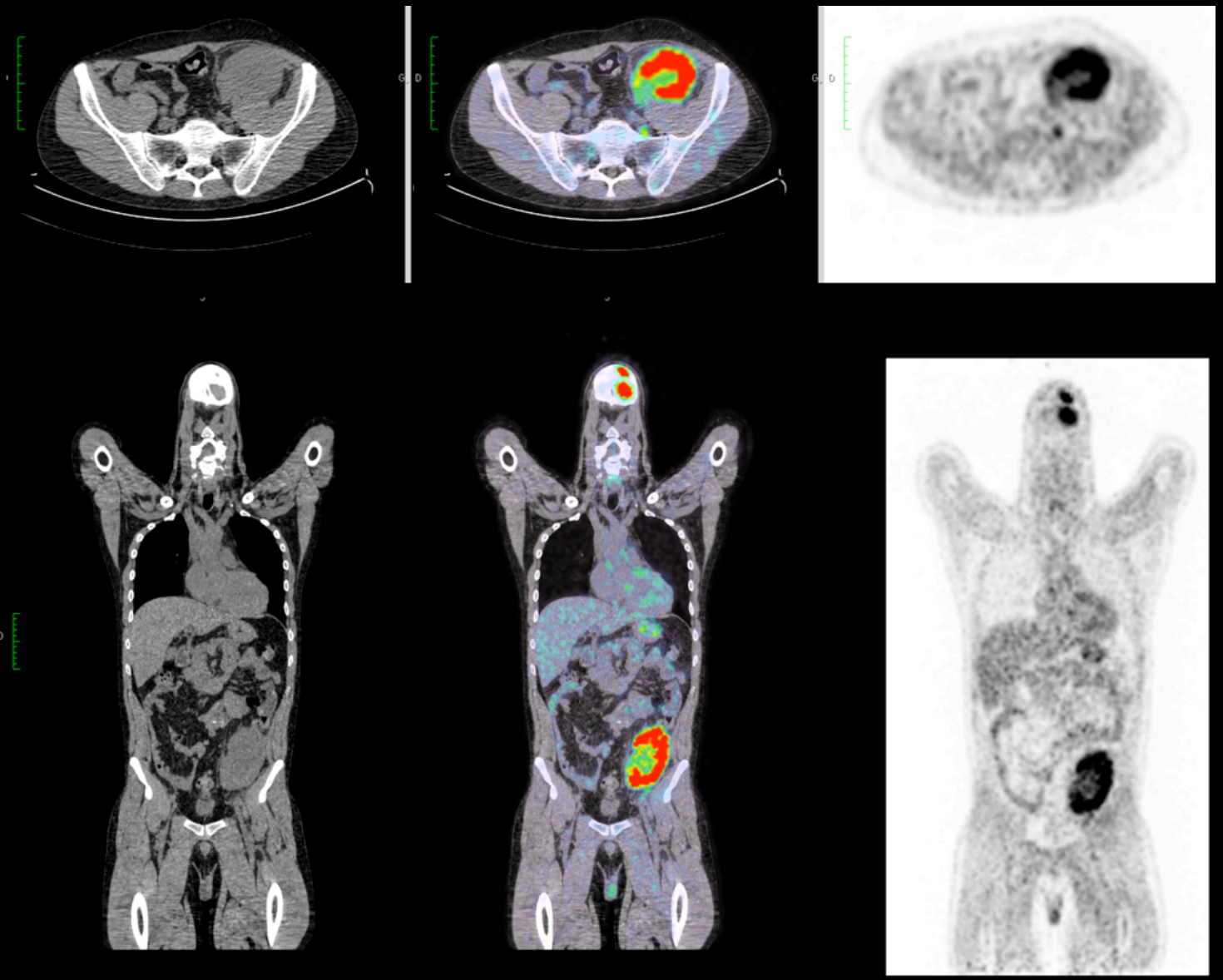




CJASN July 2011



Functioning kidney graft



Acute reject of the kidney
graft + Infl.syndrom and T°

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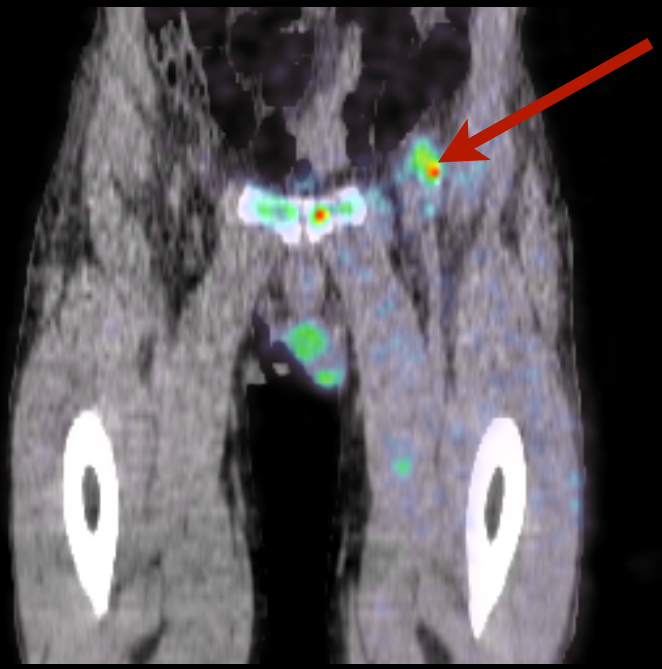
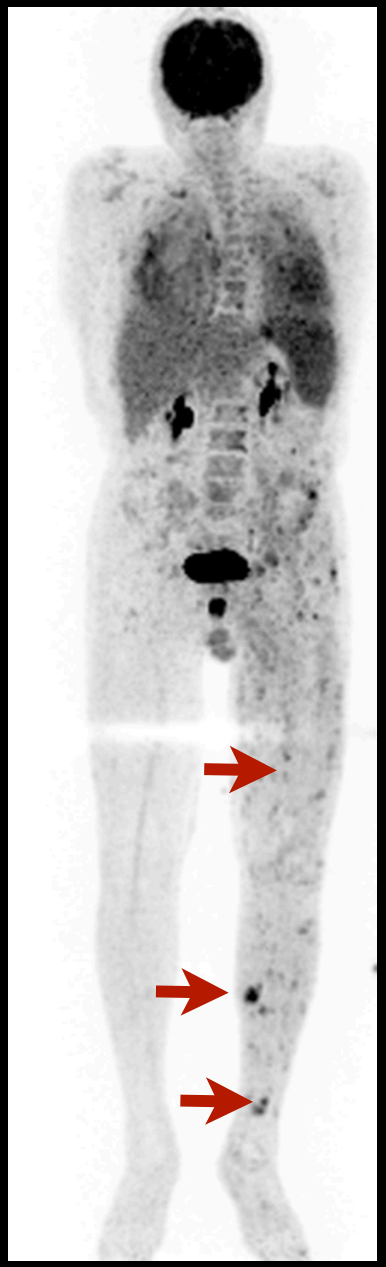
Contexte de polyarthrite rhumatoïde traité par inhibiteur de IL-6 mais gros SI et T°/prothèse vasculaire ilio-fémorale gauche

Ccl:
Embols septiques multiples sur infection de prothèse





Connectivites : vasculite giganto-cellulaire (Horton)

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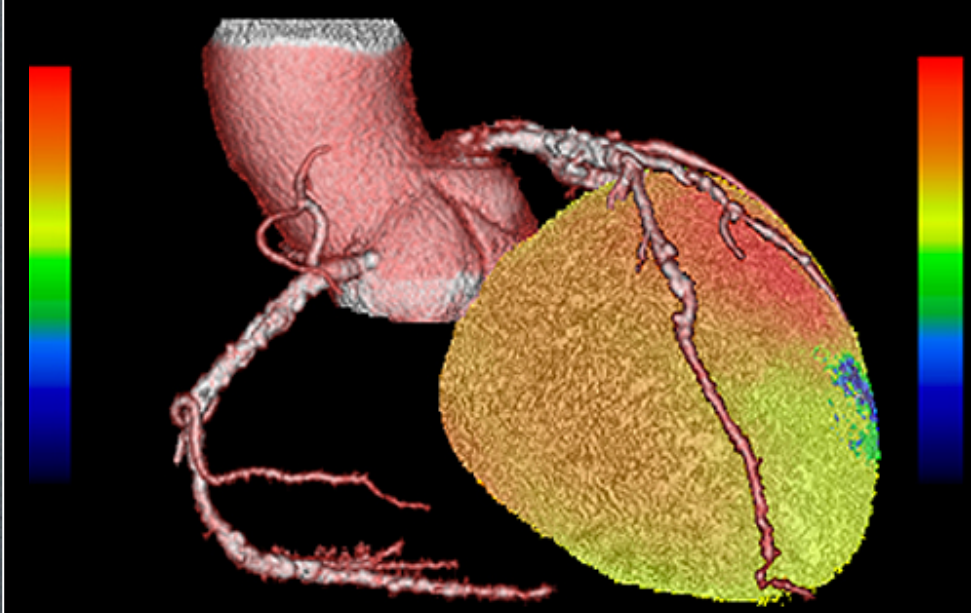
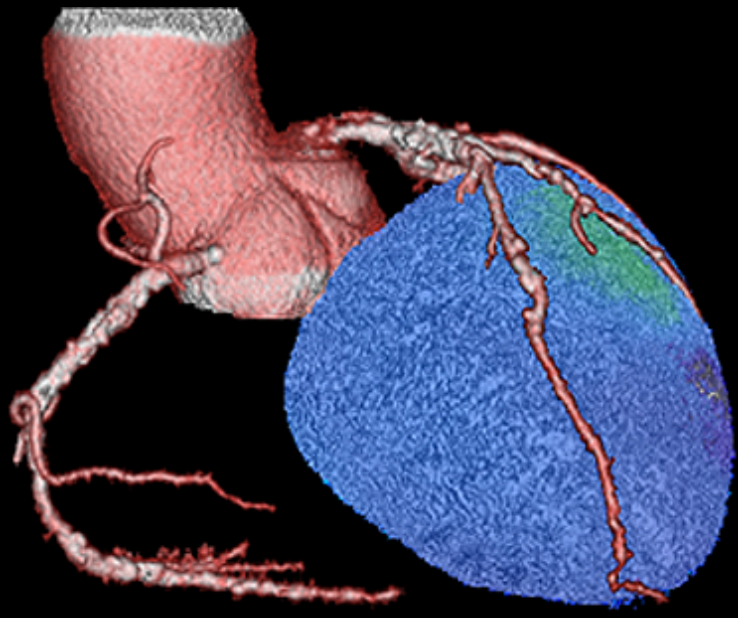
Cardiologie

Quantification absolue du flux coronarien (^{82}Ru, $^{13}NH_3$, $H_2{}^{15}O$)

Typical indication : diffuse triple vessels coronary disease



PET/CT image with relative color scale for myocardial stress perfusion



Same PET/CT with absolute color scale for myocardial stress perfusion

Myocardial relative stress perfusion was homogenous (left image) but absolute perfusion measured as ml/g/min was very low in all myocardial regions (1.0-1.3 ml/g/min). Perfusion was analyzed using CARIMAS Turku software.

http://www.gehealthcare.com/euen/molecular-imaging/products/pet_ct_imaging/clinical_cases/triple-vessel-coronary.html

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Viabilité myocardique

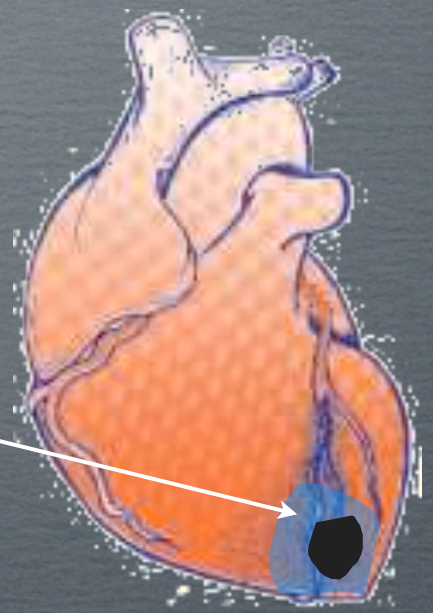
Acute coronary occlusion induces a myocardial necrosis.

Nevertheless, infarct don't imply that all the cells within the infarct area are dead.

> some viable cells will "hibernate" and further benefit from a rescue procedure of revascularization

(angioplasty or surgical bypass)

Hibernating Myocardium

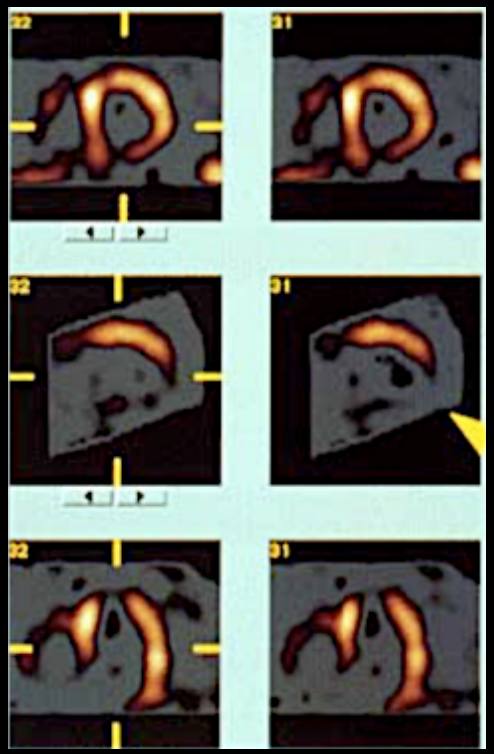


Necrosis (scar)

How to reveale hibernating myocardium ?

Tracers of perfusion

(^{82}Ru, $^{13}NH3$,$H_2{}^{15}O$)

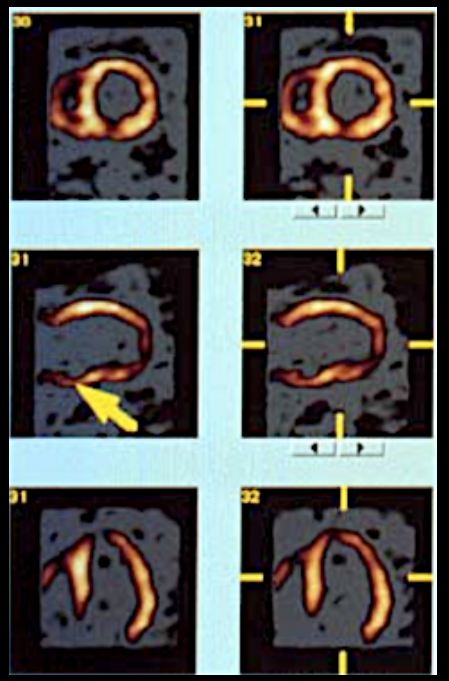


Inferior infarct

><

Metabolism Tracers

(FDG PET)



Divers

Radiotherapy and Oncology 96 (2010) 277–279

Contents lists available at ScienceDirect

Radiotherapy and Oncology

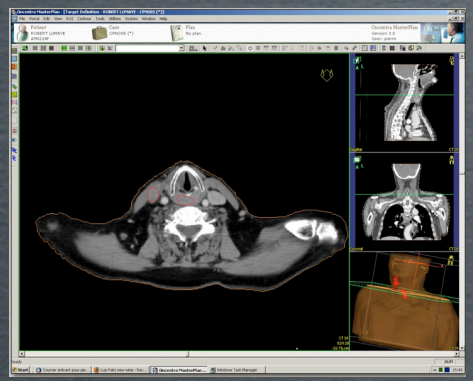
journal homepage: www.thegreenjournal.com

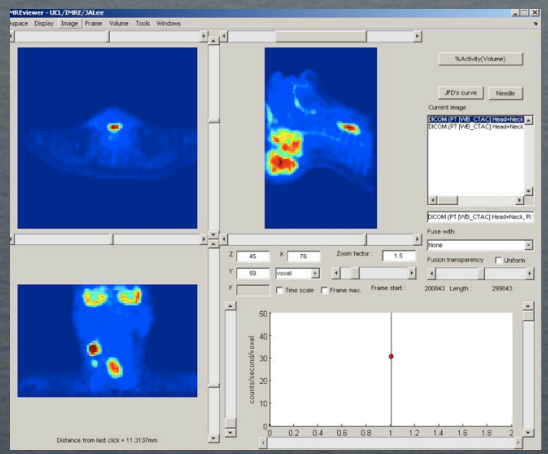
Editorial

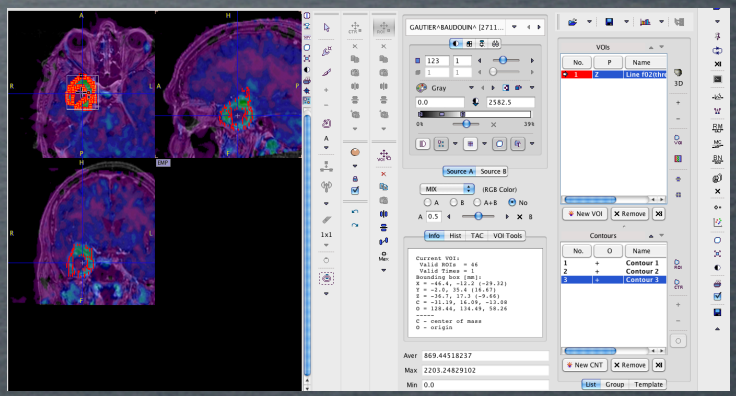
Clinical use of PET-CT data for radiotherapy planning: What are we looking for?

Arturo Chiti [a,*], Margarita Kirienko [a], Vincent Grégoire [b]

[a] Department of Nuclear Medicine, Istituto Clinico Humanitas, Milan, Italy; [b] Department of Radiation Oncology, St-Luc University Hospital, Brussels, Belgium

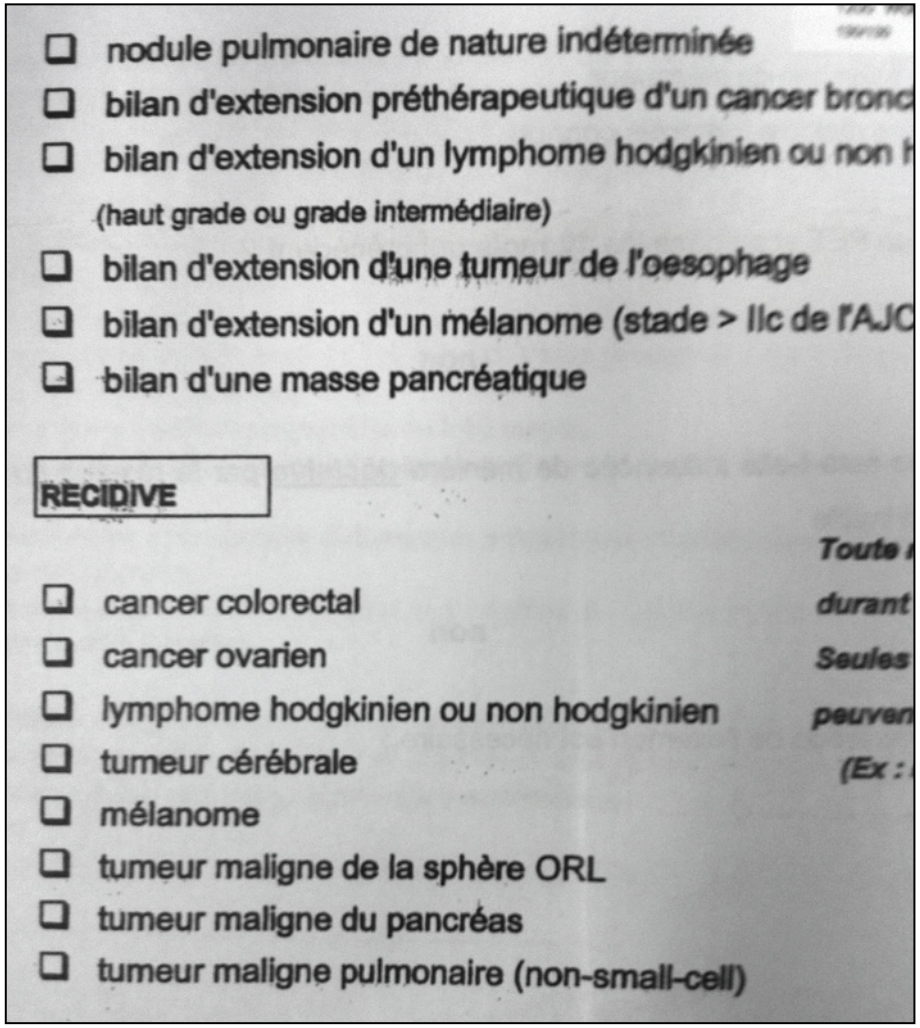







Le PET en Belgique...
RL- WRDGN3120

16 indications prises en charge par l'INAMI



- ☐ nodule pulmonaire de nature indéterminée
- ☐ bilan d'extension préthérapeutique d'un cancer bronc
- ☐ bilan d'extension d'un lymphome hodgkinien ou non h
  (haut grade ou grade intermédiaire)
- ☐ bilan d'extension d'une tumeur de l'oesophage
- ☐ bilan d'extension d'un mélanome (stade > IIc de l'AJC
- ☐ bilan d'une masse pancréatique

RECIDIVE

Toute r
durant
Seules
peuven
(Ex :

- ☐ cancer colorectal
- ☐ cancer ovarien
- ☐ lymphome hodgkinien ou non hodgkinien
- ☐ tumeur cérébrale
- ☐ mélanome
- ☐ tumeur maligne de la sphère ORL
- ☐ tumeur maligne du pancréas
- ☐ tumeur maligne pulmonaire (non-small-cell)

- ☐ viabilité myocardique (en vue d'une éventuelle revascul
- ☐ localisation d'un foyer épileptogène (épilepsie résistante

Nouveautés en perspectives ?

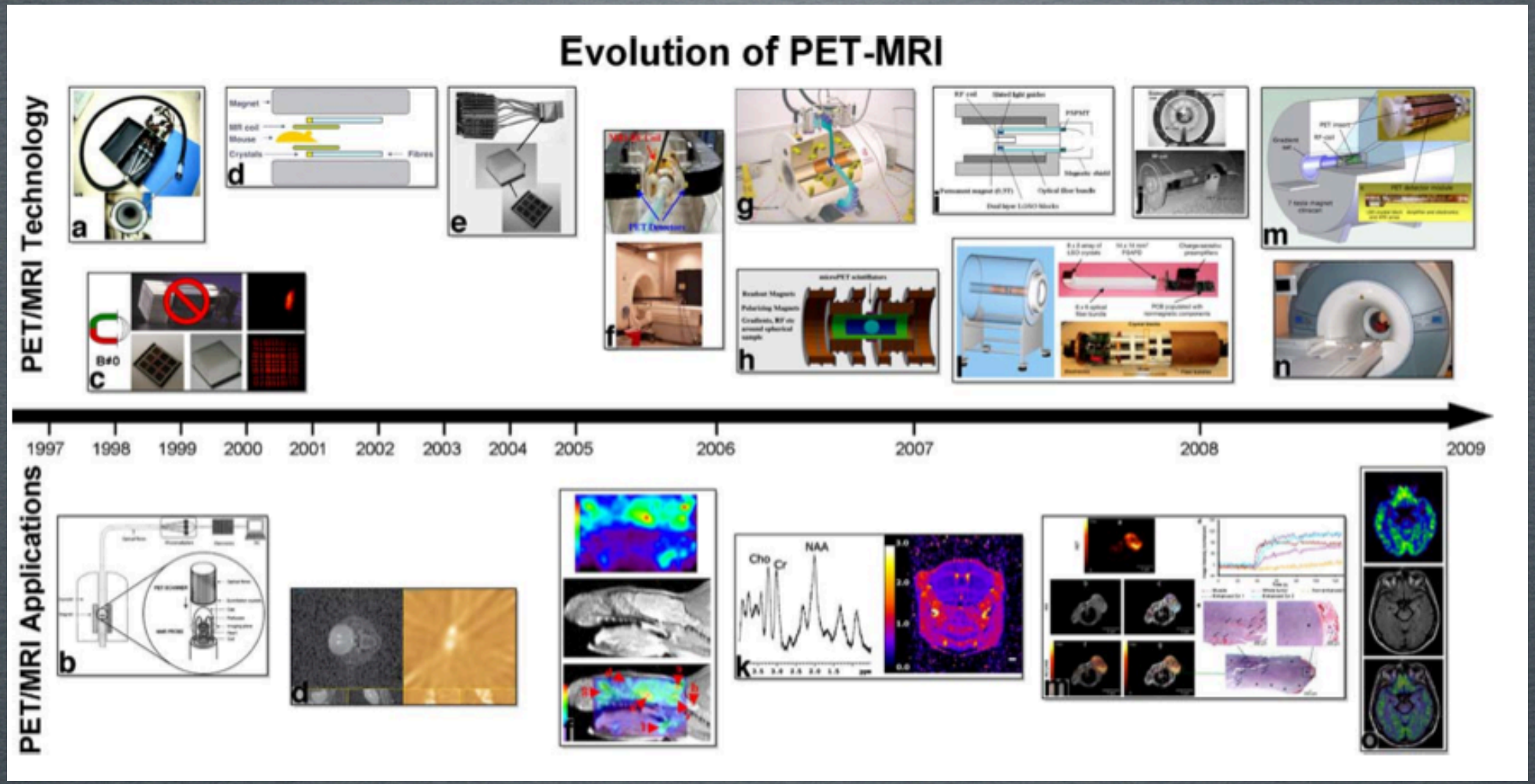
Du côté des équipementiers…

Sequential whole body PET-MR for determining clinical potential of PET-MRI

Achieva 3T MRI and PET Gemini TF

+	-
Easier for service and production	Not simultaneous
Standard technology	2 acquisitions
No performance loss for MR and PET	Large room
No interference	No motion correction

Installed in Mount Sinai NY dec 2009



EJNM (2009) 36 (Suppl 1):S56-68

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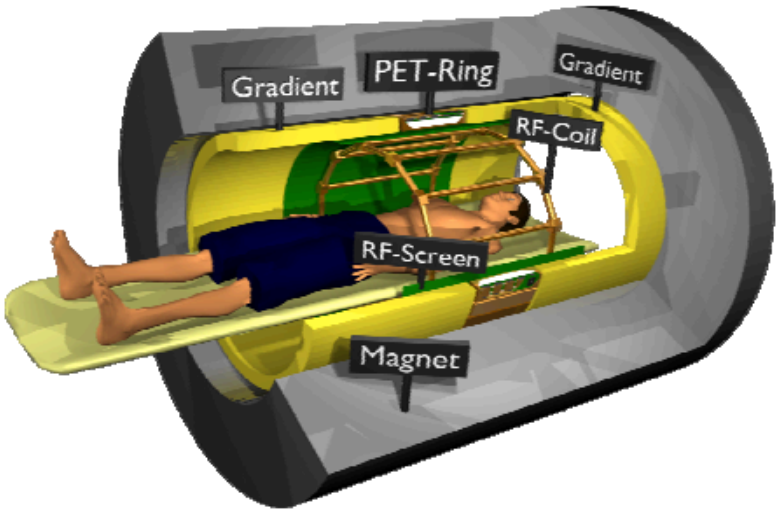
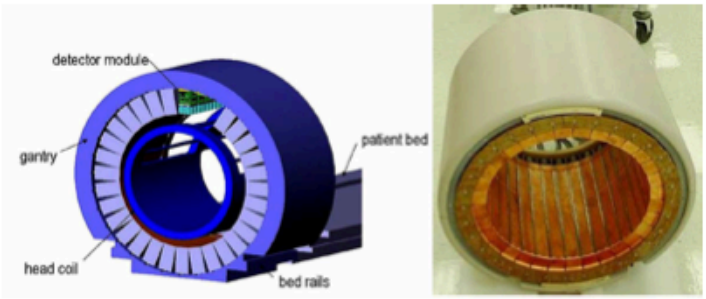
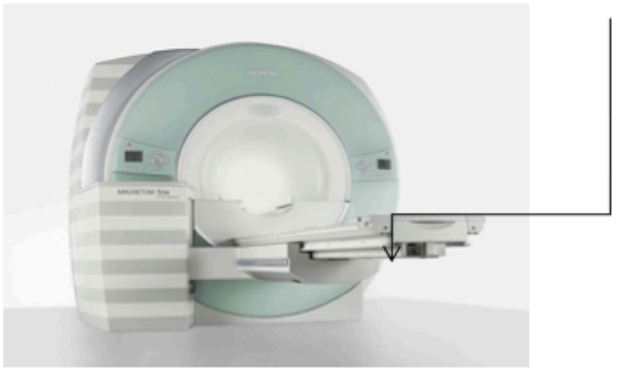
Towards simultaneous whole body PET-MR



Philips research EU-FP7 collaboration
MR design based on linac MRI (Utrecht)
PET SiPM based
Timing first prototype to be determined



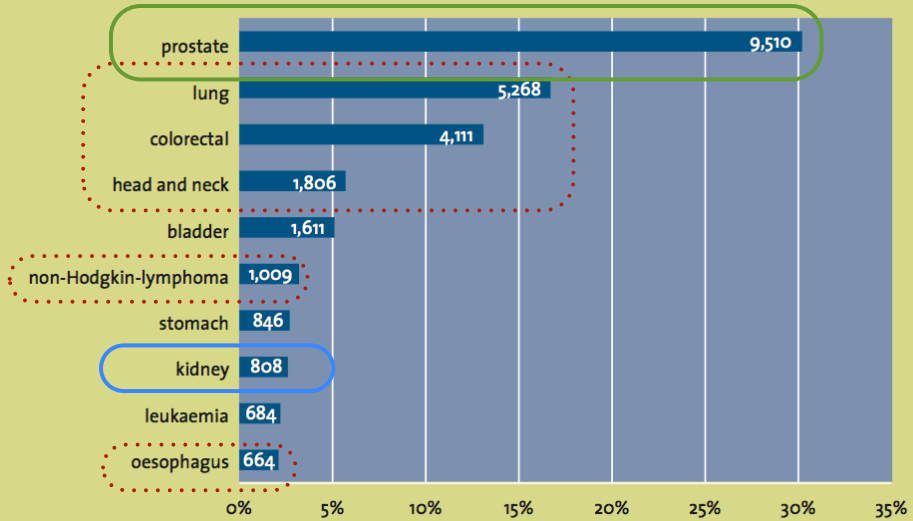


Siemens Healthcare Knoxville (USA)
–Tuebingen group (Pichler/Clausen):
first full-body PET-MRI prototype
built during 2009/2010, ready in 2011.
PET APD based

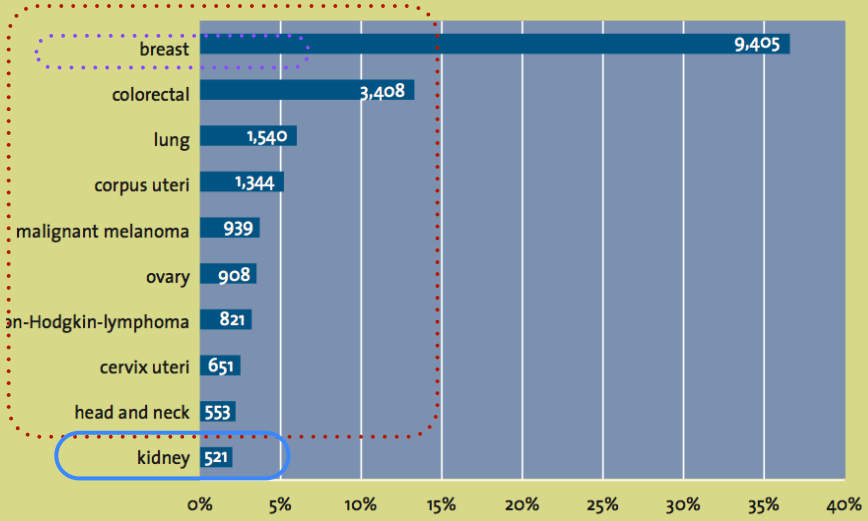
Nouveaux Radiopharmaceutiques ?

Registre national du cancer 2004-2005

Figure 7 The 10 most frequently occurring invasive tumours in males, Belgium 2005



8 The 10 most frequently occurring invasive tumours in females, Belgium 2005



FDG

^{18}F-Choline

^{124}I-cG250

Figure 9 The 10 most frequent causes of death from cancer in males, Belgium 2004

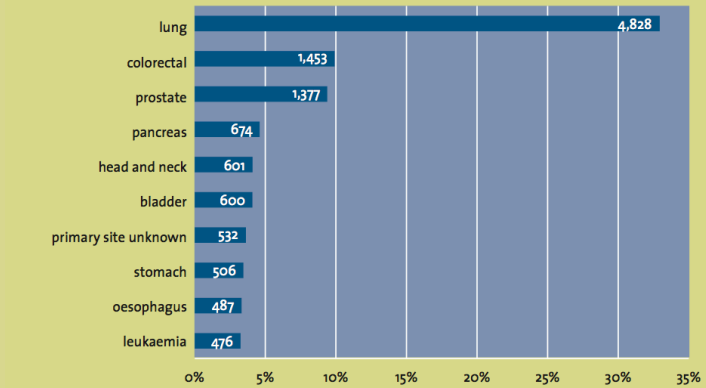
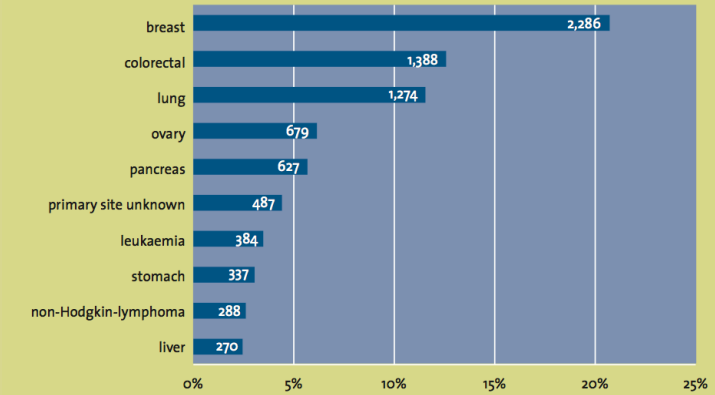


Figure 10 The 10 most frequent causes of death from cancer in females, Belgium 2004



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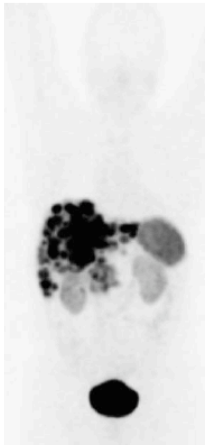
Ge/^{68}Ga generator

IGG100 Gallium-68 Generator

Product Information

^{68}Ga-OctreoPET



^{18}F-DOPA

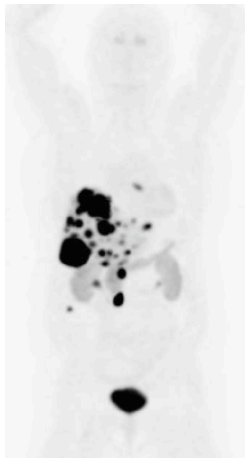


TABLE 5
Comparison of 3 Imaging Modalities: PET, SPECT, and CT

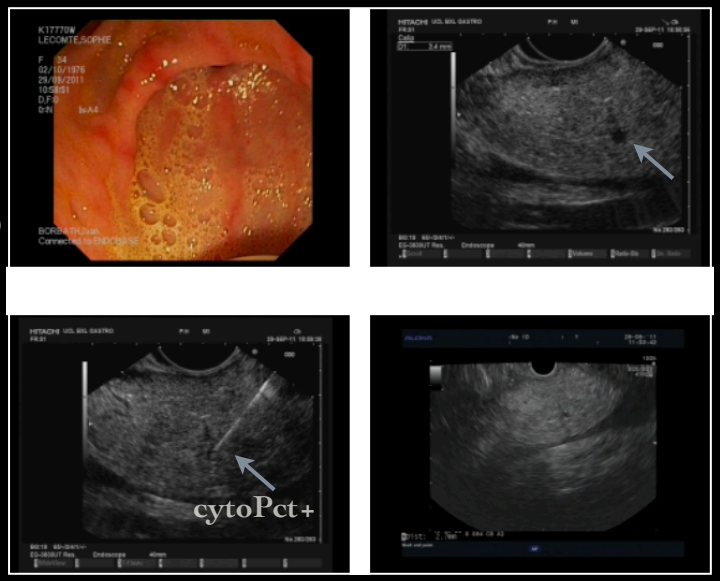
Parameter	PET (%)	SPECT (%)	CT (%)
Sensitivity	97 (69/71)	52 (37/71)	61 (41/67)
Specificity	92 (12/13)	92 (12/13)	71 (12/17)
Accuracy	96 (81/84)	58 (49/84)	63 (53/84)

F; 35 y.o
Severe diarrhea

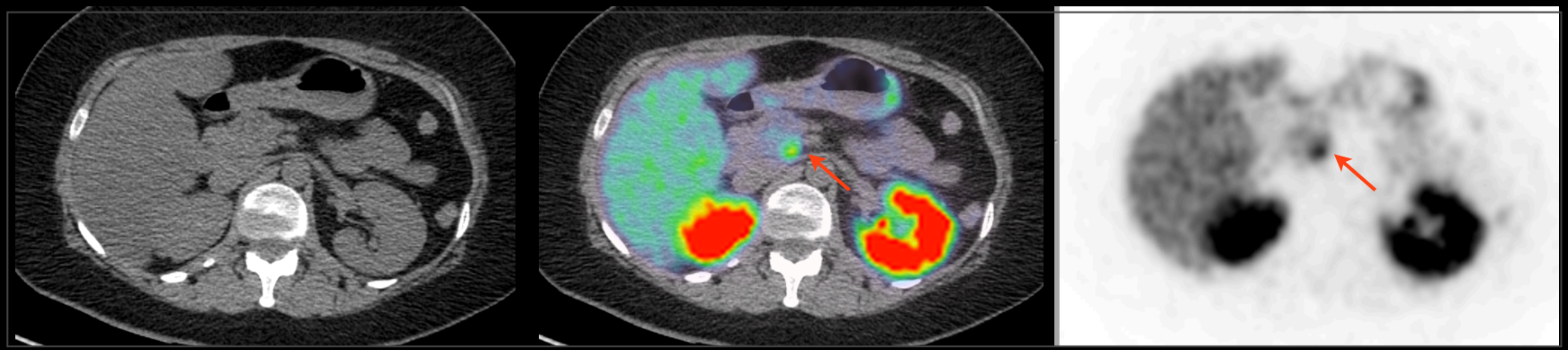
Gastrin: 505.2 pg/ml (nl: 25-111)

Chromogranin: 70.3 pg/ml (nl<23)

Echo-endoscopy



^{68}Ga-octreotate PET/CT (Bordet)



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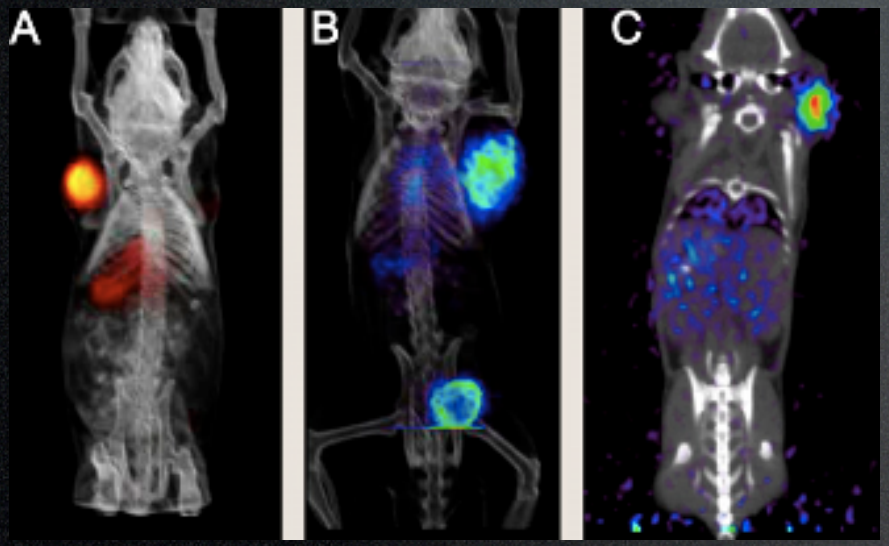
ImmunoPET

TABLE 1. Positron-Emitting Radionuclides for immuno-PET

Radionuclide	Half-life	Positron yield
^{68}Ga	68 min	89%
^{18}F	109 min	97%
^{64}Cu	12.7 h	18%
^{86}Y	14.7 h	17.5%
^{76}Br	16.0 h	55%
^{89}Zr	78.4	22.7%
^{124}I	100.2 h	23%

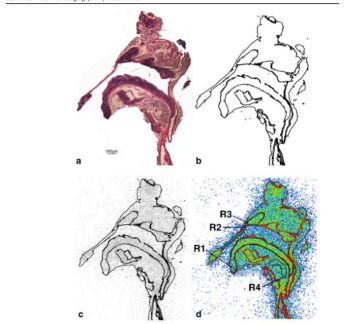


Eur J Nucl Med Mol Imaging (2009) 36:2058–2067
DOI 10.1007/s00259-009-1220-z

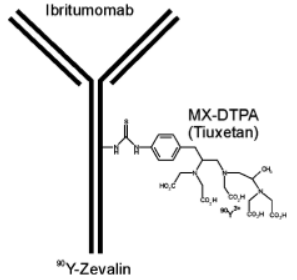
ORIGINAL ARTICLE

^{68}Ga-DOTA-RGD peptide: biodistribution and binding into atherosclerotic plaques in mice

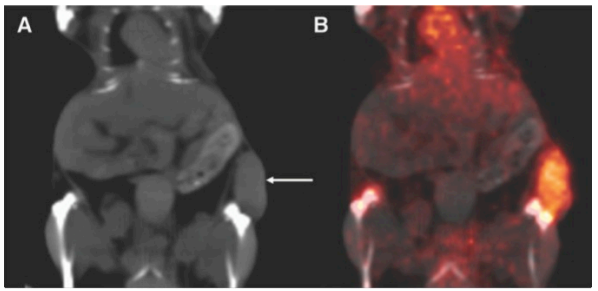
Johanna Haukkala · Iina Laitinen · Paullina Luoto · Peter Iveson · Ian Wilson · Hege Karlsen · Alan Cuthbertson · Jukka Laine · Pia Leppänen · Seppo Ylä-Herttula · Juhani Knuuti · Anne Roivainen



^{89}Zr-Anti CD20



^{89}Zr-Bevacizumab (Avastin)



- Target : VEGF
- Ovarian human cancer
- 168 h pi

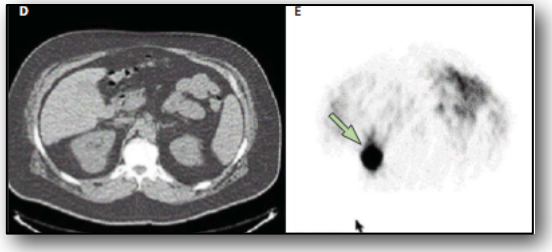
Nagengast et al, JNM 2007;48:1313-1319 (Groningen)

cG250

Preoperative characterisation of clear-cell renal carcinoma using iodine-124-labelled antibody chimeric G250 (^{124}I-cG250) and PET in patients with renal masses: a phase I trial

Chaitanya R Divgi, Neeta Pandit-Taskar, Achim A Jungbluth, Victor E Reuter, Mithat Gönen, Shutian Ruan, Christine Pierre, Andrew Nagel, Daniel A Pryma, John Humm, Steven M Larson, Lloyd J Old, Paul Russo

Lancet Oncol 2007; 8: 304–10



Sensitivity	94%
NPV	90%
PPV	100%
Accuracy	100%

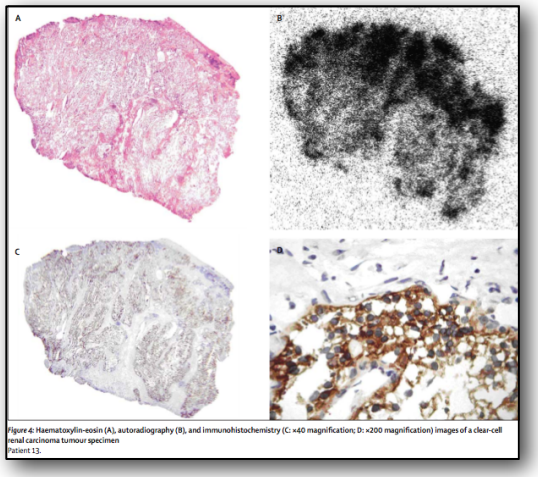


Figure 4: Haematoxylin-eosin (A), autoradiography (B), and immunohistochemistry (C: ×40 magnification; D: ×200 magnification) images of a clear-cell renal carcinoma tumour specimen
Patient 13.

Correlation of In Vivo and In Vitro Measures of Carbonic Anhydrase IX Antigen Expression in Renal Masses Using Antibody ^{124}I-cG250

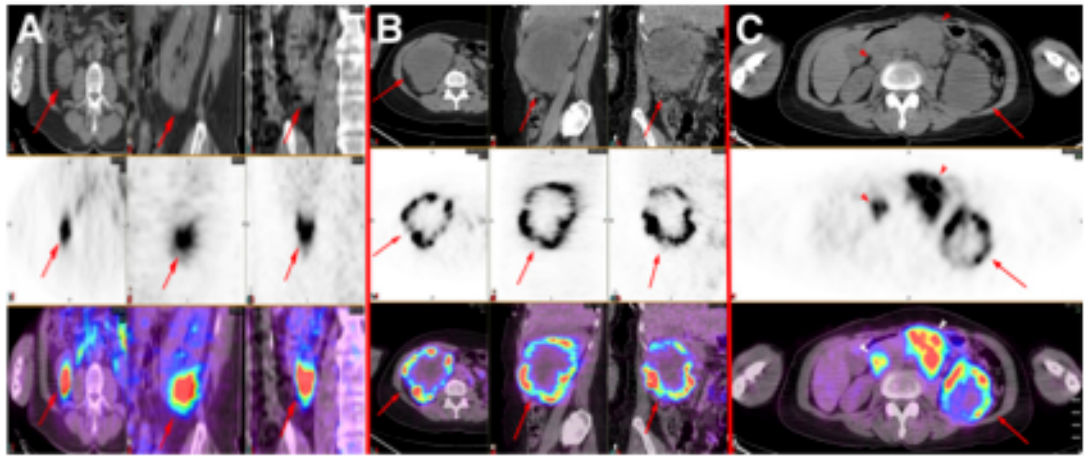


FIGURE 1. (A and B) Axial, sagittal, and coronal CT (top), PET (middle), and fused PET/CT (bottom) images of patient with clear cell renal cancer with relatively homogeneous distribution of antigen (arrows) (A) and patient with large, centrally necrotic clear cell renal cancer with marked heterogeneity of antigen distribution within mass (arrows) (B). (C) Axial CT (top), PET (middle), and fused PET/CT (bottom) images of patient with advanced clear cell renal cancer. Antigen distribution within primary tumor is heterogeneous (arrows), whereas distribution within metastatic nodes is relatively homogeneous (arrowheads).

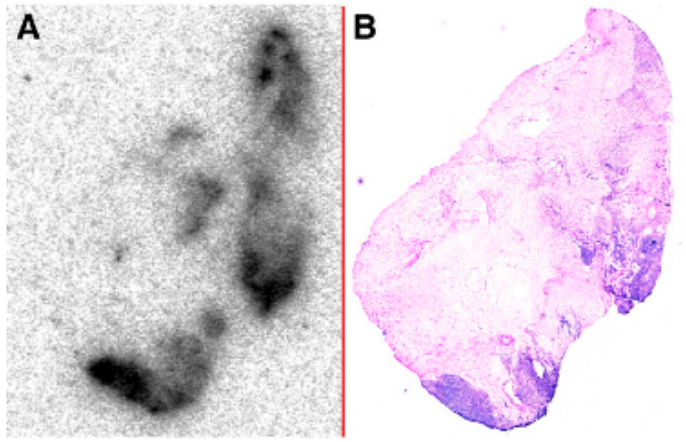


FIGURE 2. Autoradiographic (A) and histologic (B) sections from patient with clear cell renal cancer. Marked heterogeneity of antibody binding seen on autoradiography correlates with areas of densest tumor cells on histology.

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^{18}F-ML10 (IBA) Aposense®

IBA and Aposense Sign Strategic Collaboration to Commercialize Aposense® ML-10 for Molecular Imaging of Apoptosis

18F]-ML-10 is a small molecule radiotracer which allows the imaging of apoptosis, a fundamental biological process of controlled cell death, from the early stages of the death process. Given the broad, cross disease role of apoptosis in a wide range of medical disorders, molecular imaging with [18F]-ML-10 is expected to play an important role in early detection of disease, monitoring of disease course, assessment of effect of treatment or development of novel therapies. In particular, [18F]-ML-10 may assist oncologists in evaluating tumor response to treatment much earlier than conventional imaging modalities such as CT or MRI. This may allow clinicians to identify earlier the most effective treatment within their therapeutic arsenal and provide personalized, safer and more cost-effective care. Among other clinical fields of potential applications of [18F]-ML-10 are Cardiology and Neurology.