

Place de l'imagerie isotopique dans la prise en charge de l'endocardite infectieuse

François Rouzet

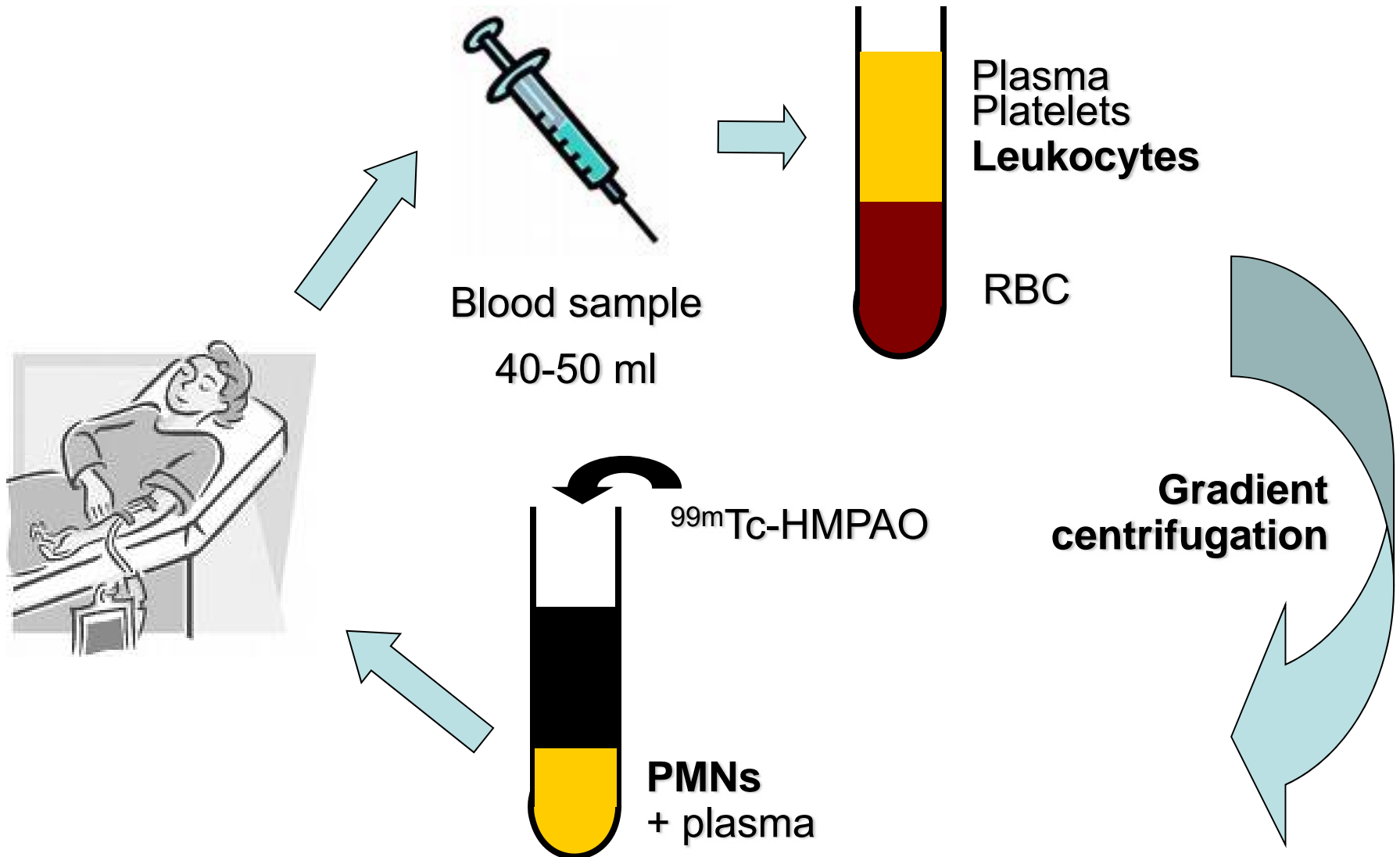
- Service de Médecine Nucléaire, GH Bichat-Claude Bernard, Paris
- Inserm U698, Remodelages cardiovasculaires
- Université Paris Diderot, Sorbonne Paris cité

Imagerie isotopique de l'infection

Quels sont les examens actuellement disponibles ?

- ^{67}Ga Gallium
- Leucocytes marqués
- TEP au ^{18}F Fluoro-deoxyglucose (FDG)

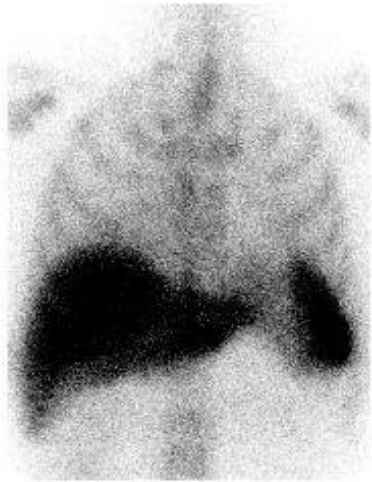
Leucocytes marqués : méthodes



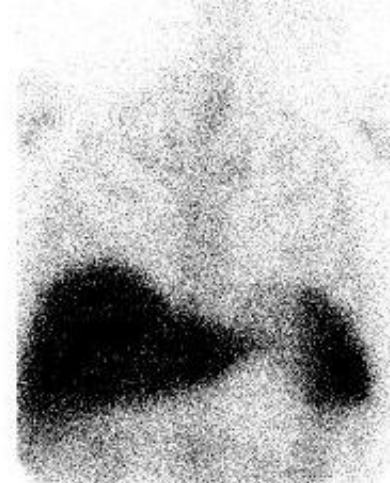
Leucocytes marqués

- La procédure de marquage dure 120-180 min, dans des conditions aseptiques (hotte à flux laminaire)
- Par sécurité : 1 seul patient par jour
- Imagerie : 1h (vasculaire), 4h, **24h**
- Biodistribution normale : système réticulo-endothélial

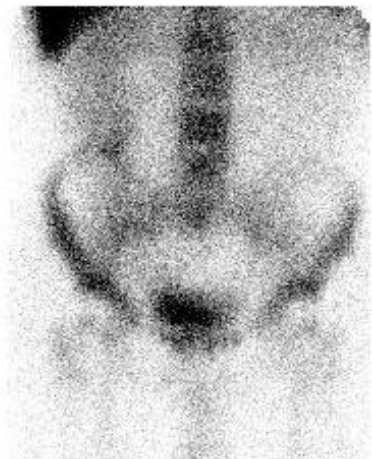
Leucocytes marqués : biodistribution



4 h



24 h



- Homme de 54 ans
- Pacemaker ancien
- Fièvre au décours d'un remplacement valvulaire aortique
- Découverte d'une masse (ETO) sur la sonde atriale



RAO



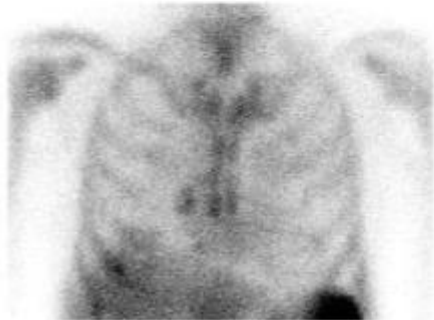
LAO



RAO



LAO



4 H

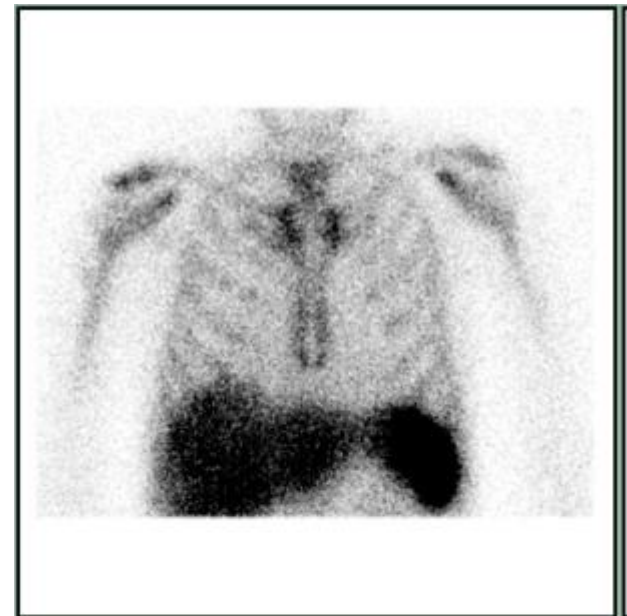


24 H

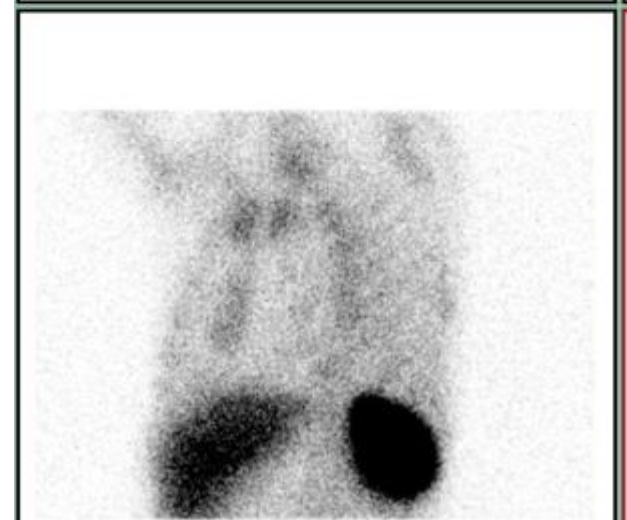
Homme 77 ans, RVAo (07/12/2010), bactériémie Staph Méti-S, ablation du pacemaker, hyperleucocytose persistante, ETO : épaissement de l'anneau de la prothèse aortique



**Face
antérieure**



**Oblique
antérieure
gauche**

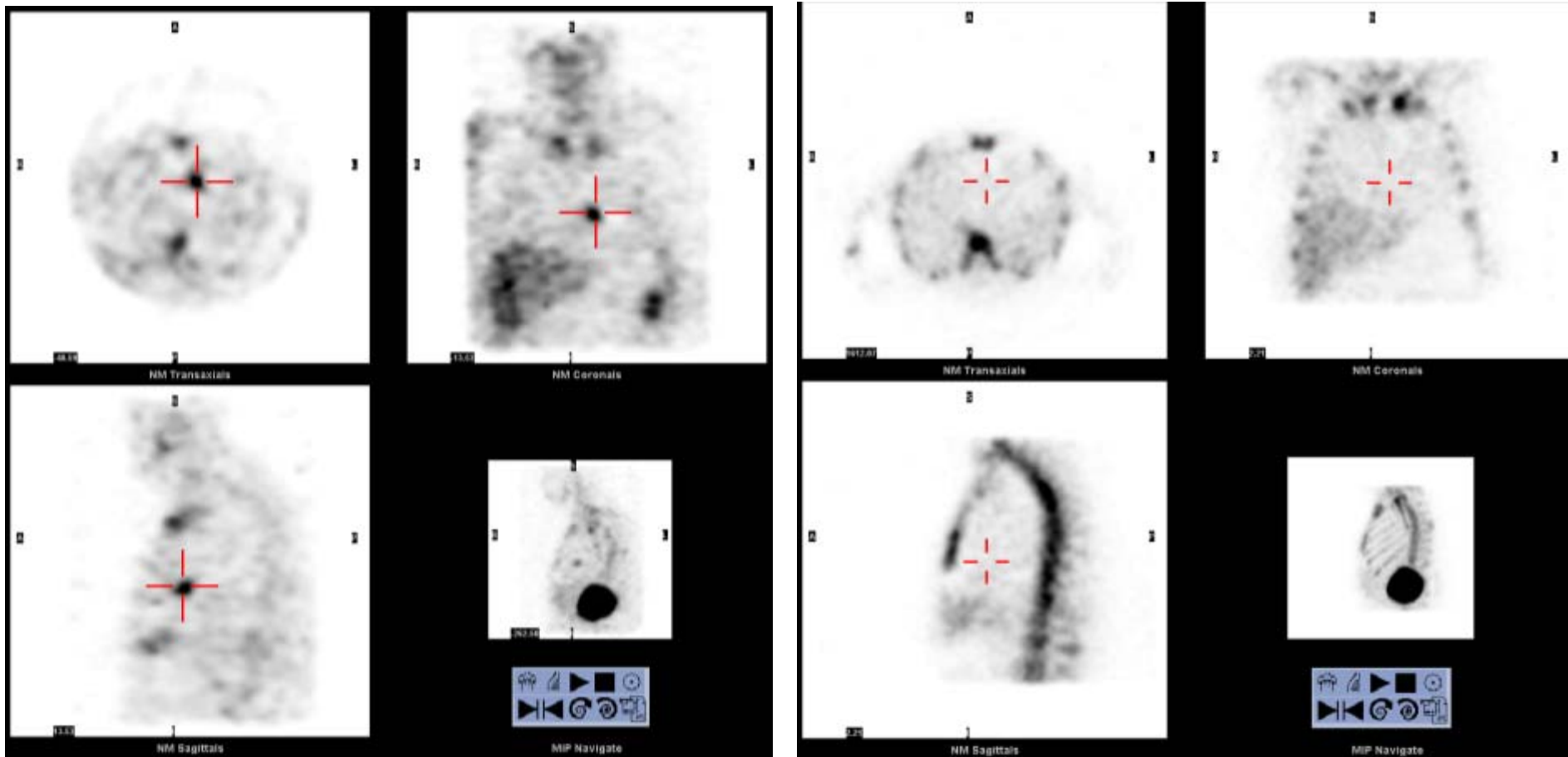


03/01/2011

Redux

14/02/2011

Tomographie (SPECT)



03/01/2011 → 14/02/2011

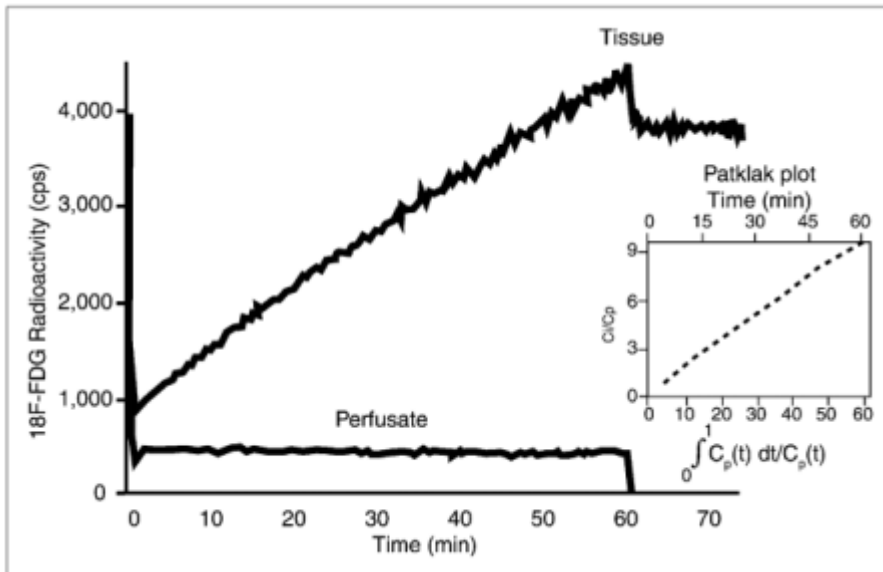
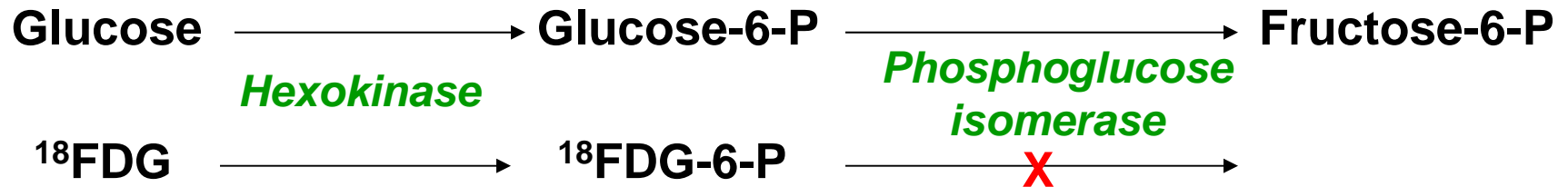
Redux

leucocytes marqués : indications

- Examen validé dans les infections osseuses, prothèses vasculaires, médiastinites
- Très spécifique (images à 24h), bonne sensibilité
- Pas d'indication dans les infections patentes
- En complément de l'imagerie morphologique
- A venir : évaluation prospective dans les endocardites infectieuses

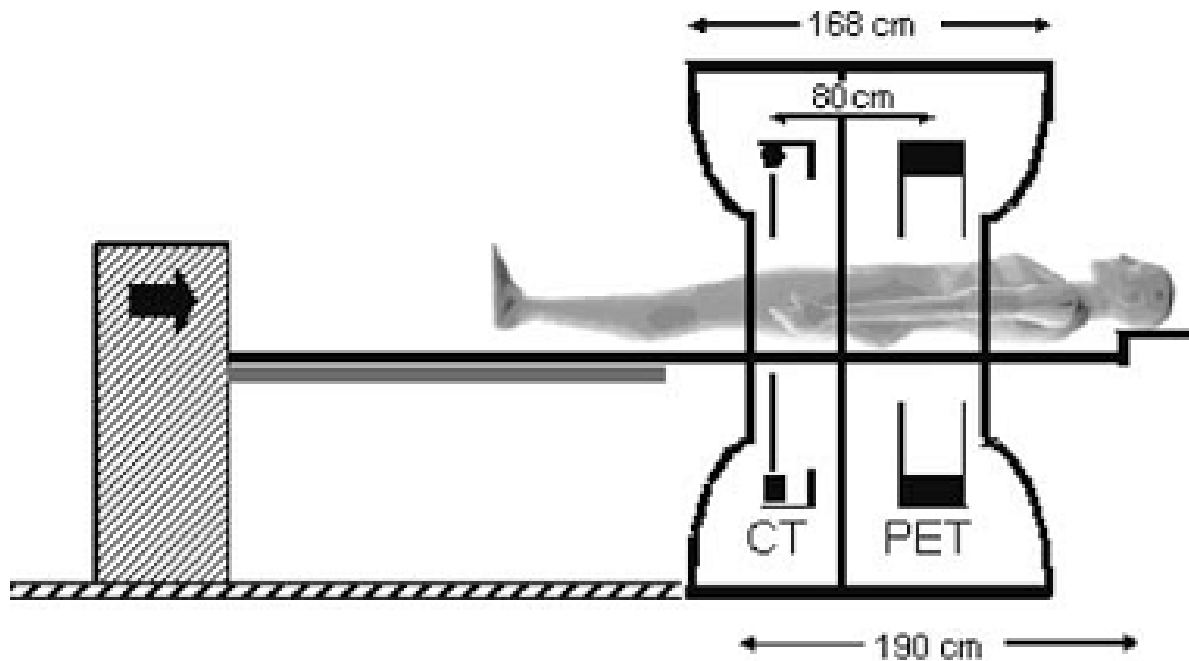
^{18}F -deoxyglucose (FDG)

^{18}F -deoxyglucose (FDG)



L'accumulation de ^{18}F FDG-6-P
témoigne de l'activité
glycolytique cellulaire

TEP/TDM : caméra hybride



Pour quoi faire?

- Correction d'atténuation
- Co-localisation

Biodistribution of ^{18}F -deoxyglucose (FDG)



PET non corrected

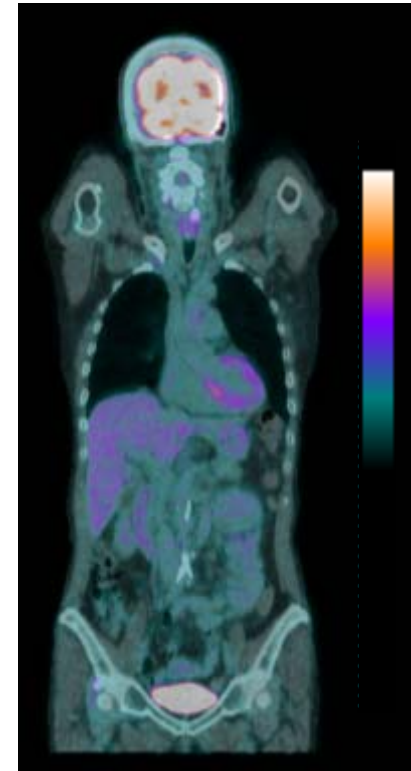


CT: attenuation map (μ)

=



PET attenuation corrected



Coregistration PET/CT

TEP au ^{18}F FDG

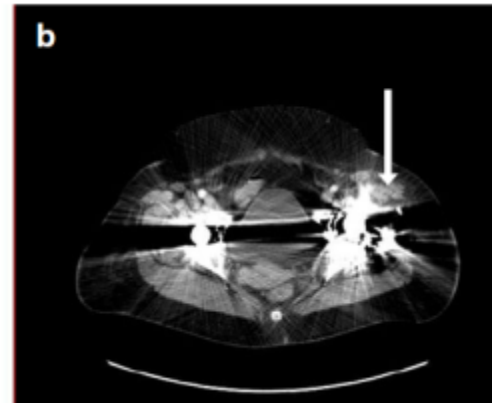
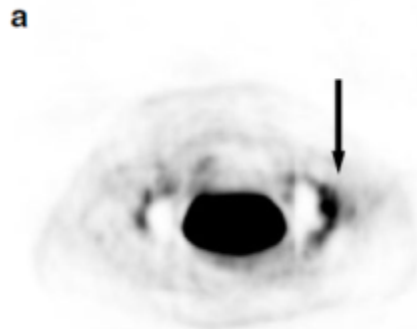
- Glucose marqué = intensité de l'activité métabolique (glycolytique) des tissus
- Non spécifique : inflammation, infection, prolifération cellulaire
- Captation physiologique par le myocarde, variable selon les conditions métaboliques (substrats, insulinémie...)
- TEP/CT : avantage technique sur la SPECT(/CT)
 - Sensibilité (3D corps entier en 20 minutes)
 - Résolution spatiale (localisation du signal)
 - Quantification du signal (SUV)

Endocardite : recherche de localisations secondaires

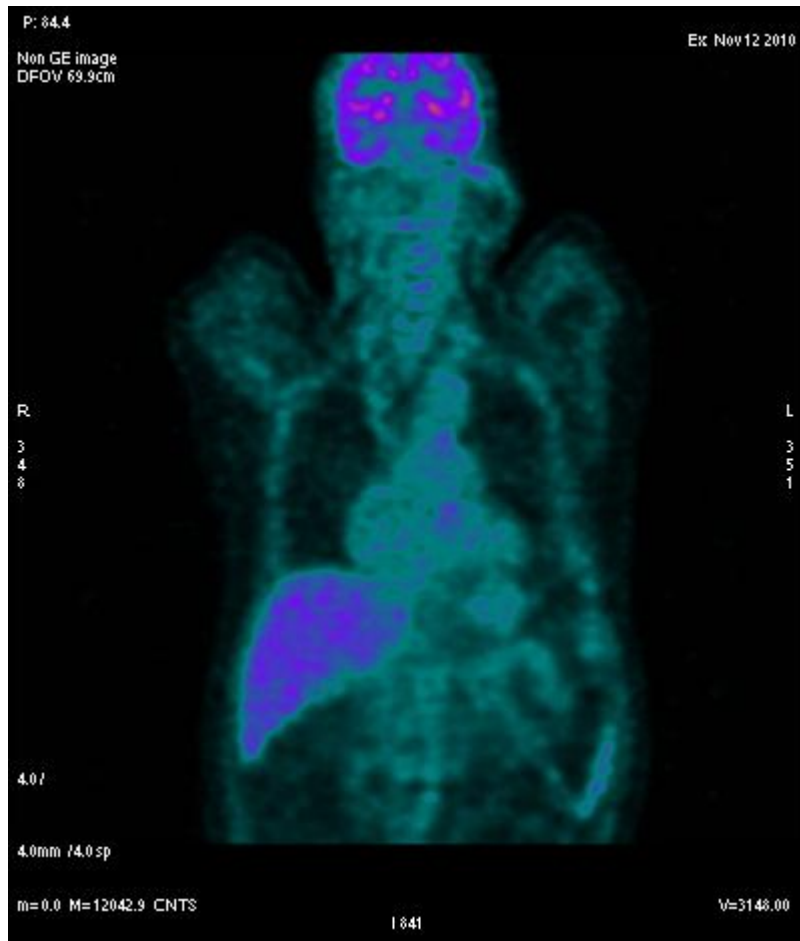
- 24 patients (25 épisodes d'endocardite)
 - TEP/TDM réalisé <2 semaines après le diagnostic d'EI
 - Suivi : 6 mois
 - TEP \oplus dans 11 épisodes (44%), dont 7 (28%) en l'absence de symptômes (1 faux-positif)
 - TEP \ominus dans 14 épisodes : pas d'événement au bout de 6 mois
- *Sensibilité : 100% ; Spécificité : 91%*

Endocardite : recherche de localisations secondaires

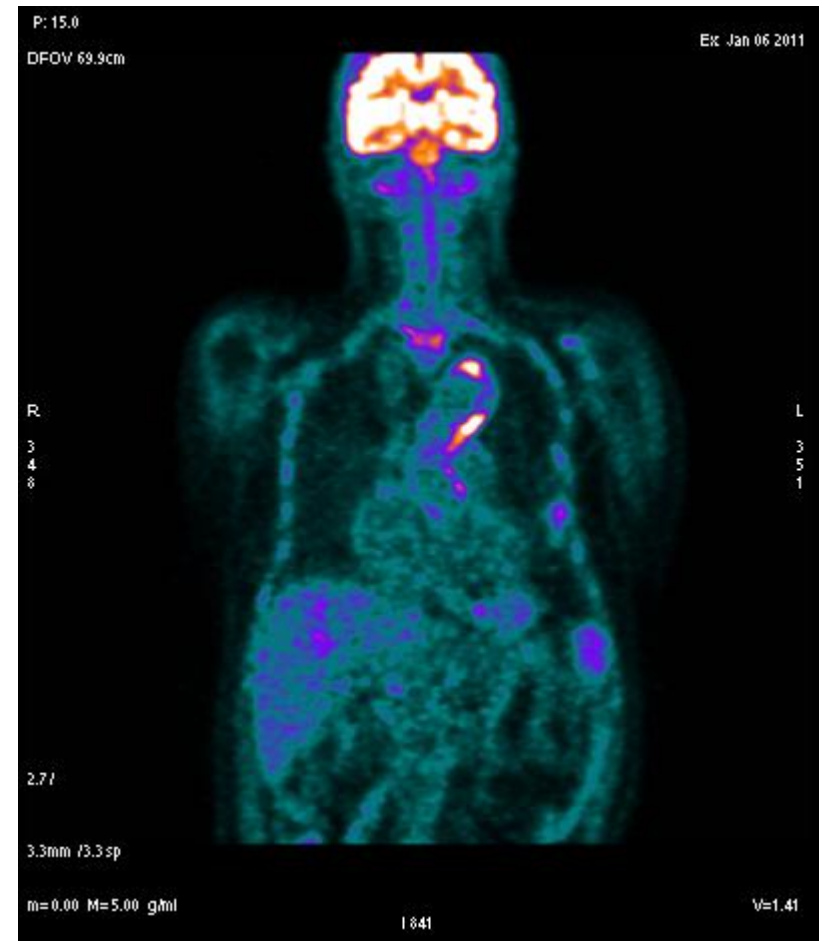
- Modification de la prise en charge thérapeutique chez 7 patients
 - chirurgie anticipée en présence d'emboles périphériques
 - traitement spécifique pour infections de prothèses articulaires



Homme 62 ans, Marfan, Bentall + tube aortique + prothèse mécanique mitrale.
Septicémie à Candida

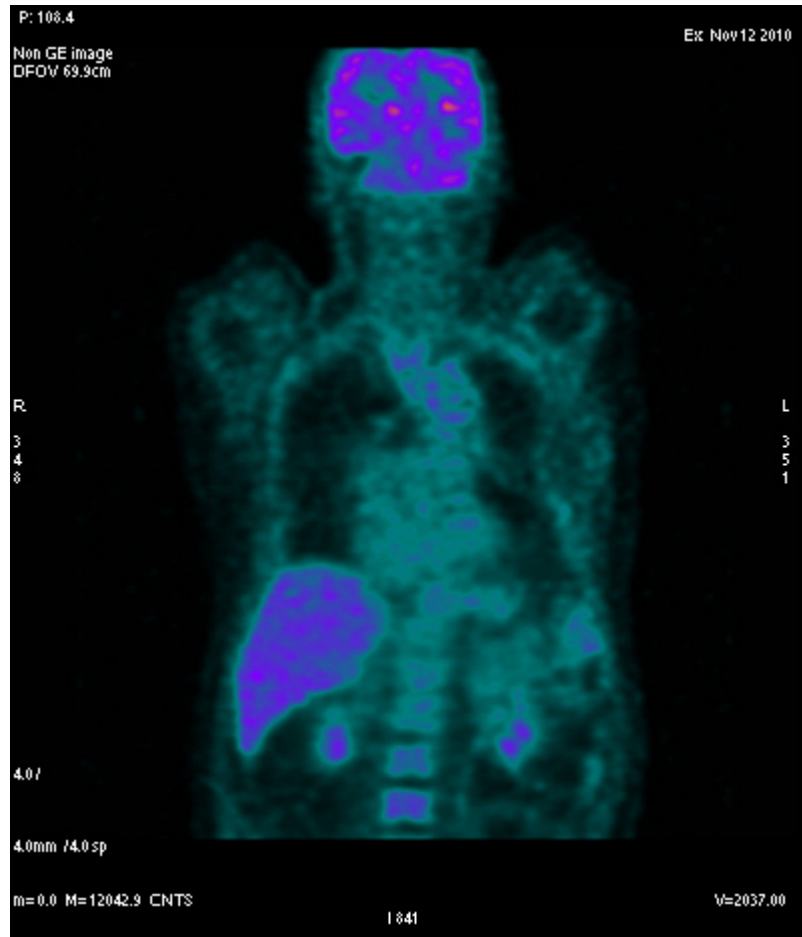


12/12/2010



06/01/2011

Homme 62 ans, Marfan, Bentall + tube aortique + prothèse mécanique mitrale.
Septicémie à Candida

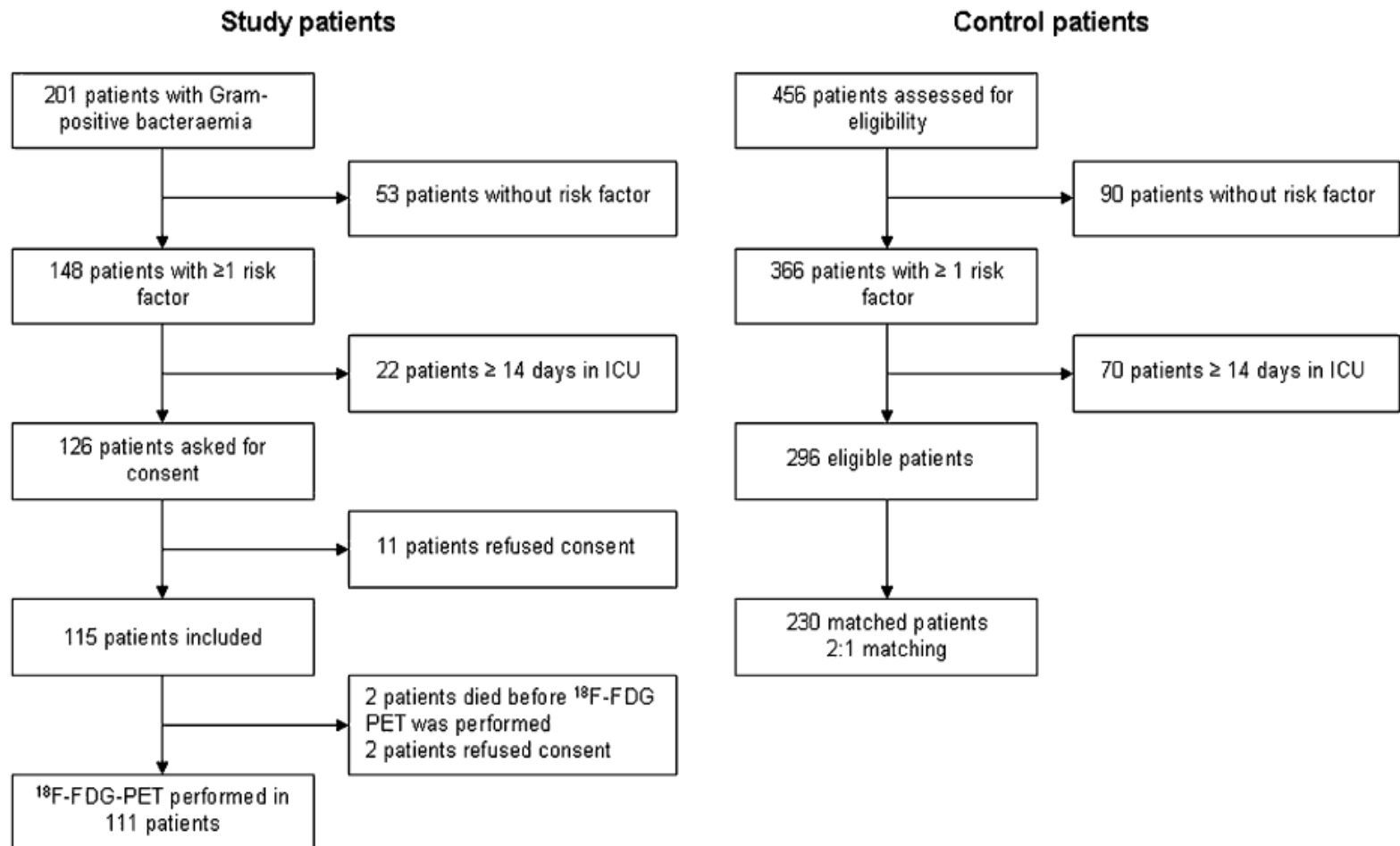


12/12/2010



06/01/2011

^{18}F -FDG PET/CT for Detection of Metastatic Infection in Gram-Positive Bacteremia



¹⁸F-FDG PET/CT for Detection of Metastatic Infection in Gram-Positive Bacteremia

TABLE 1. Baseline Characteristics of Study Patients and Historical Controls

Parameter	Study patients (n = 115)	Controls (n = 230)	P
Male	56%	52%	0.57
Mean age ± SD (y)	59 ± 16	58 ± 16	
Matching criteria			
<i>S. aureus</i>	n = 73 (64)	n = 146 (64)	1.0
<i>Streptococcus</i> species	n = 30 (26)	n = 60 (26)	1.0
<i>Enterococcus</i> species	n = 12 (10)	n = 24 (10)	1.0
Community acquisition	70%	68%	0.71
Additional risk factors			
Treatment delay	27%	45%	0.01
Persistent fever	46%	37%	0.13
Remaining possible risk factors			
Portal of entry unknown	52%	46%	0.30
Central venous catheter not removed within 48 h	5%	8%	0.50
Persistent positive blood cultures	16%	6%*	0.006
Immune suppression	22%	17%	0.30

*Not routinely obtained in control group.

Data presented in parentheses are percentages.

TABLE 2. Localization of Metastatic Foci and Number of Foci First Detected by ¹⁸F-FDG PET/CT

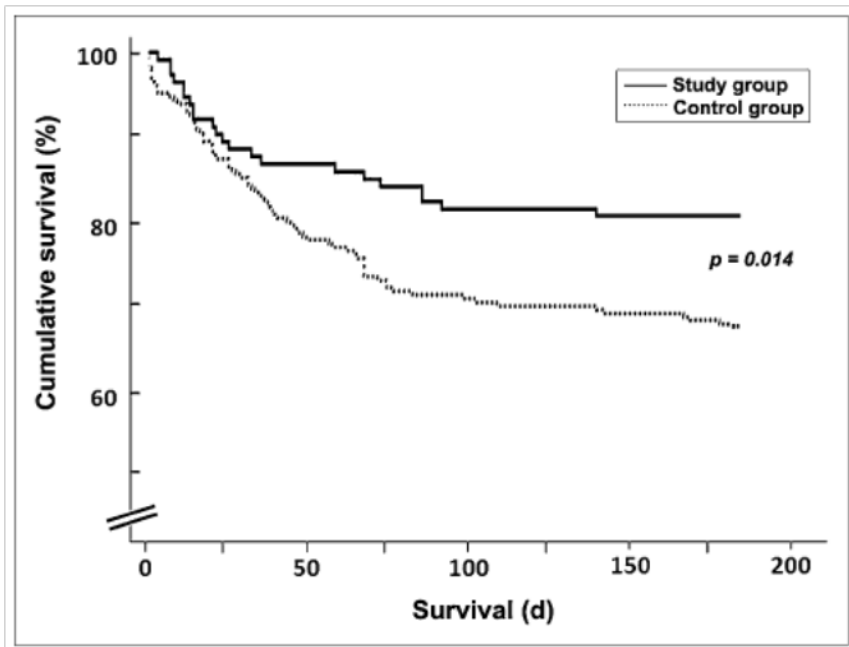
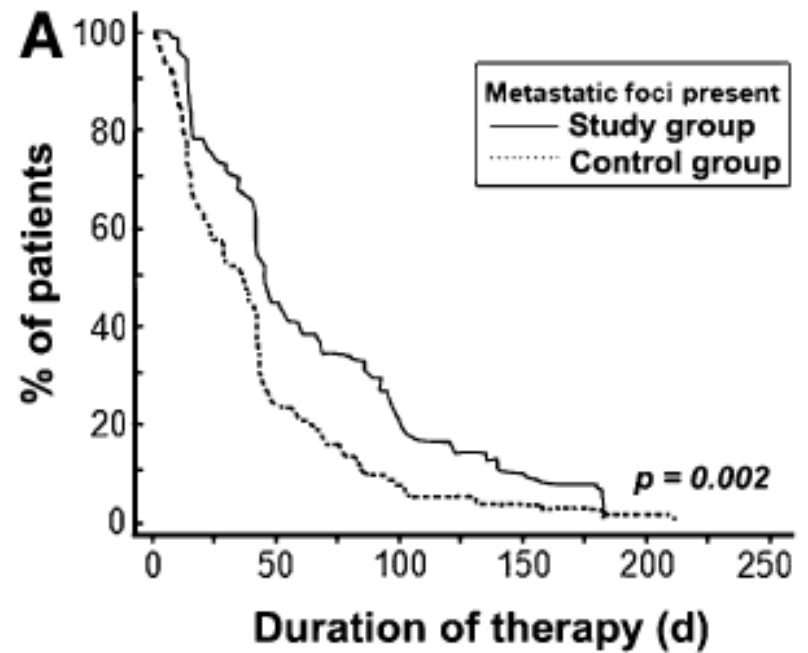
Metastatic foci	Study patients (n = 115)			Controls (n = 230)		P
	Total number	%	First detected by ¹⁸ F-FDG PET	Total number	%	
Patients with foci identified	78	67.8		82	35.7	<0.01
Total number of foci	124			113		
Endocarditis	21	18.3	0	19	8.3	0.01
Endovascular	20	17.4	12	9	3.9	<0.01
Lung	12	10.4	6	8	3.5	0.01
Liver	1	0.9	0	1	0.4	1.0
Spleen	1	0.9	1	0	0	1.0
Arthritis	10	8.7	3	28	12.2	0.37
Spondylodiskitis	11	9.6	8	10	4.3	0.09
Osteomyelitis	6	5.2	1	3	1.3	0.06
Psoas abscess	3	2.6	2	1	0.4	0.11
Soft tissue	11	9.6	4	12	5.2	0.18
Central nervous system	11	9.6	3*	7	3.0	0.02
Eye	3	2.6	0	0*	0	0.04
Joint prosthesis	9	7.8	3	5	2.2	0.02
Intraabdominal	4	3.5	1	6	2.6	0.74
Kidney	1	0.9	0	4	1.7	0.67

*Epidural extension of ¹⁸F-FDG uptake in 3 patients with spondylodiskitis, confirmed by MRI.
In 30 study patients and 22 controls, more than 1 metastatic localization was identified.

- Plus de la moitié des patients avec endocardite avaient au moins 1 localisation II
- 50% des localisations secondaires étaient asymptomatiques

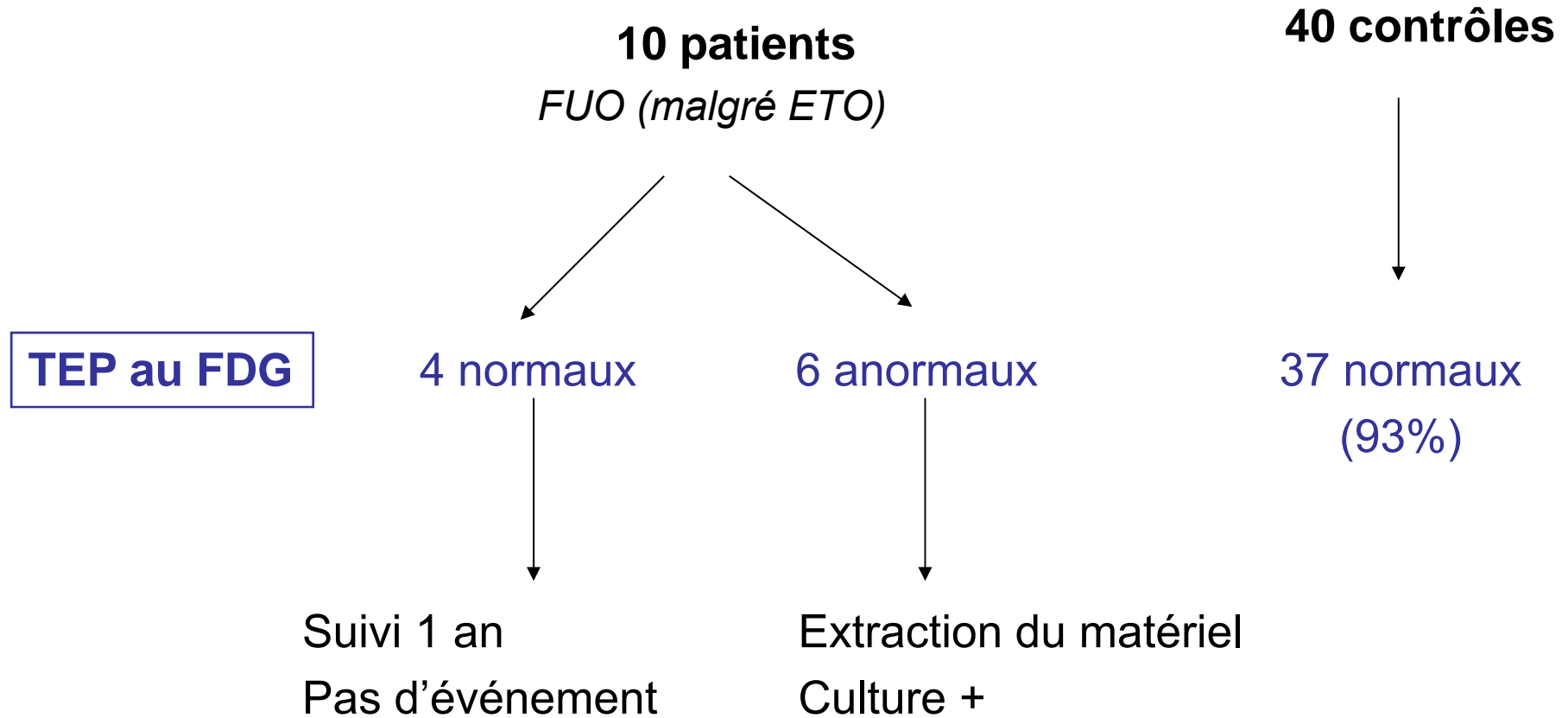
Récidive à 3 mois : 2.6% vs. 7.4%

Sous-groupe *S. aureus* : 1.4% vs. 8.9%



**Mortalité globale à 6 mois :
19% vs. 32%**

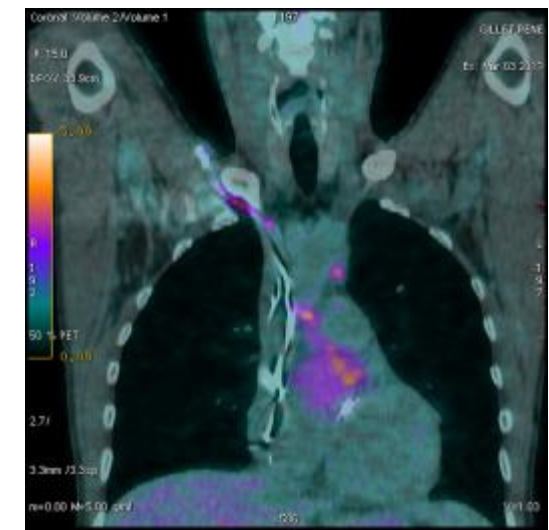
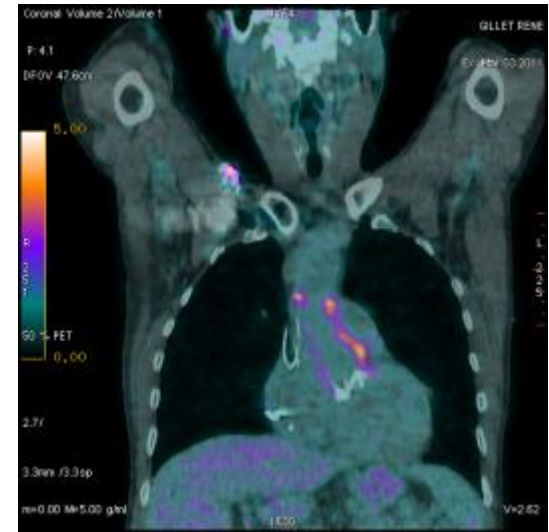
Infection de pacemaker



Homme 42 ans, pacemaker ancien, hémocultures + (Staph méti-R) dans les suites d'une chirurgie de Bentall (12/01/2011)

Scintigraphie aux leucocytes marqués : négatif

TEP au FDG le 03/03/2011



TEP au ^{18}F FDG

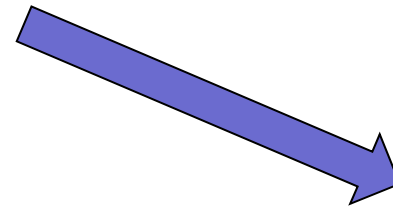
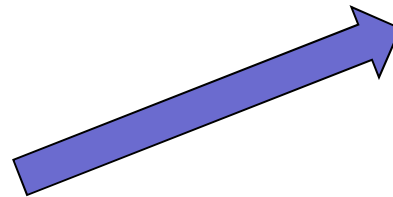
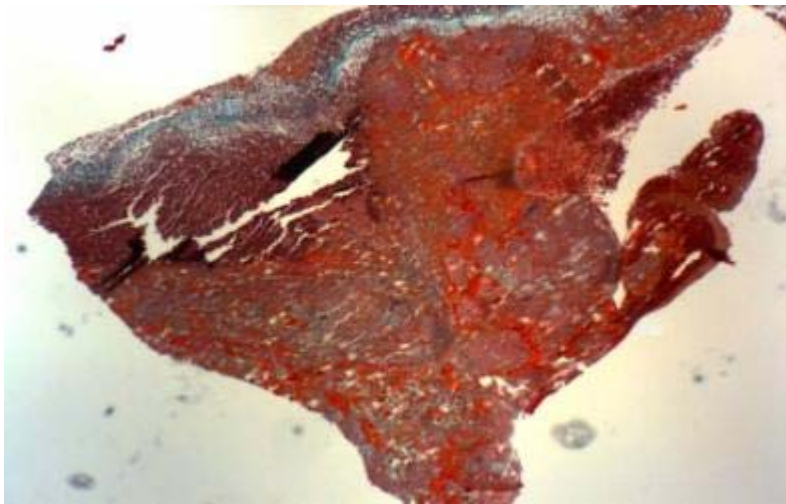
- Valeur prédictive négative+++
- Mais faible spécificité, en particulier sur matériel prothétique
- Intérêt dans la recherche d'embolies septiques
- Impact thérapeutique (\pm pronostique)

Perspectives

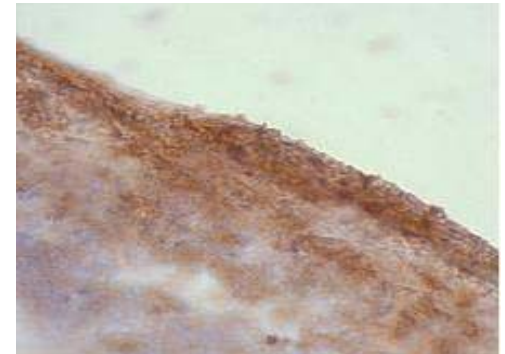
- Leucocytes marqués en TEP
- Annexine V radiomarquée

Activation plaquettaire

Végétation = Thrombus fibrino-plaquettaire



Phosphatidylsérine

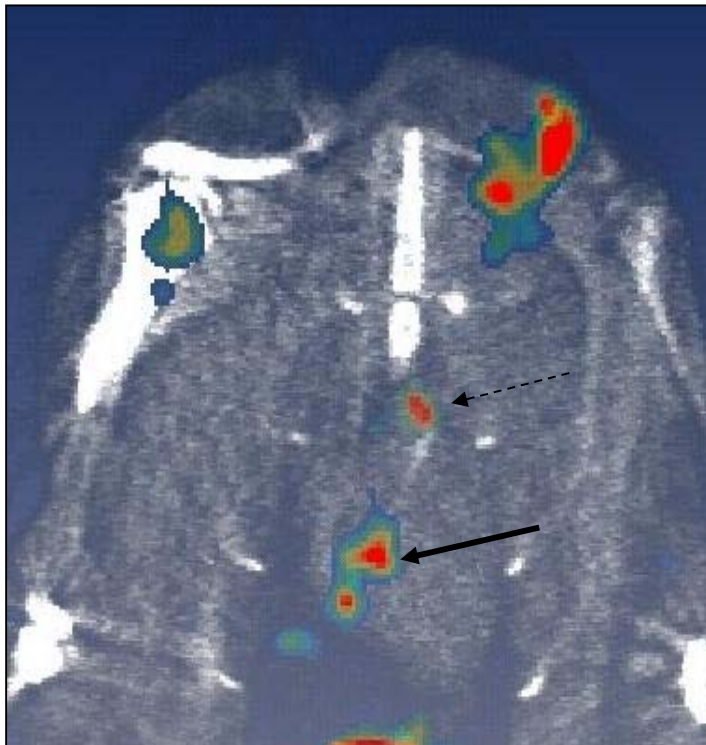


P-sélectine

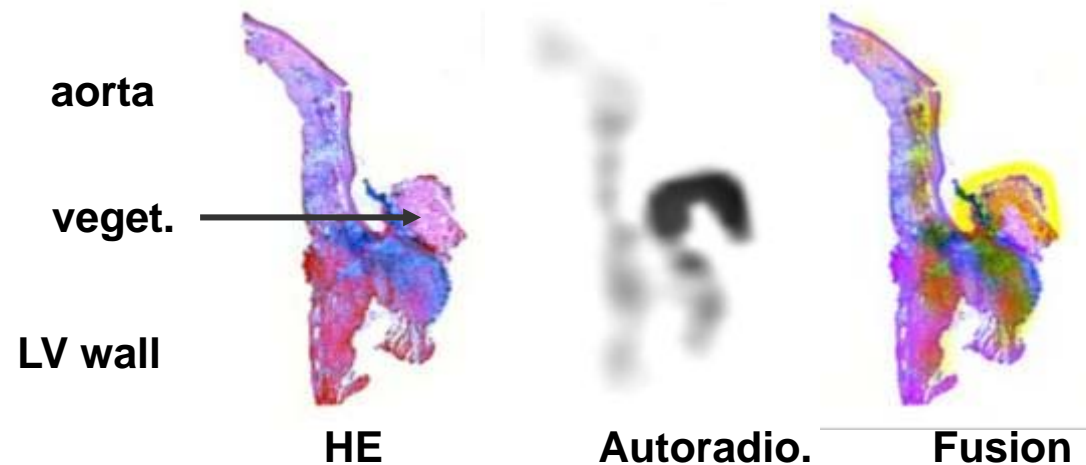


Annexine V radiomarquée

Endocardite chez le rat



SPECT/CT (rat)



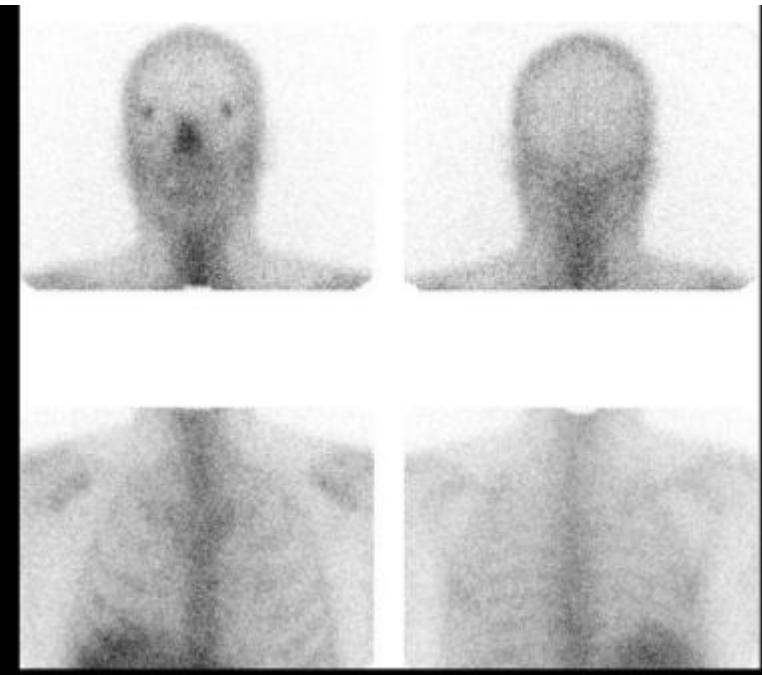
Conclusions

- Imagerie isotopique de l'endocardite :
 - en complément de l'imagerie morphologique (ETO)
 - dans les diagnostics litigieux
- Evaluer la place respective des leucocytes marqués et de la TEP au FDG (valves natives / prothétiques)
- Évaluation clinique de l'annexine V radiomarquée (Promotion Inserm, Coordination : D. Le Guludec, X. Duval)
 - Valeur diagnostique
 - Localisations secondaires

Gallium 67 imaging: normal uptake

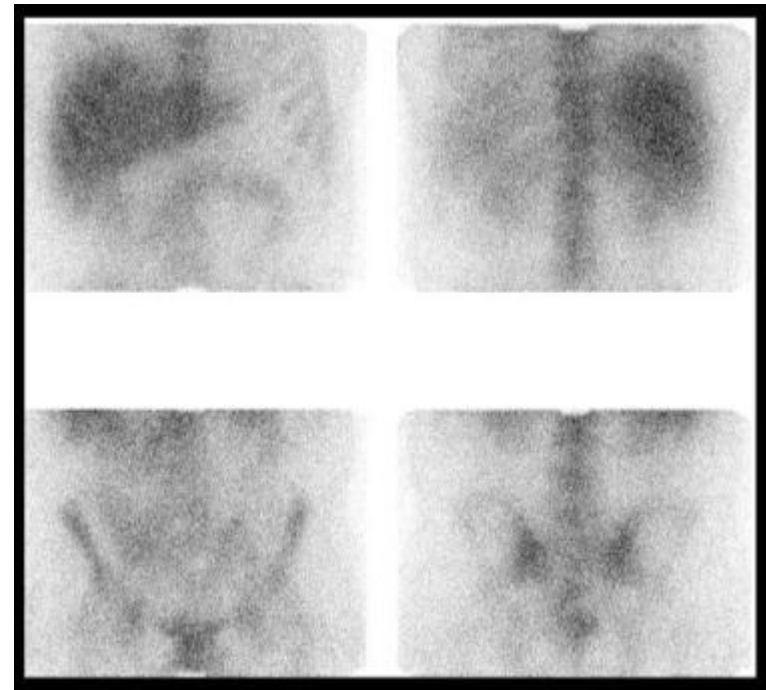
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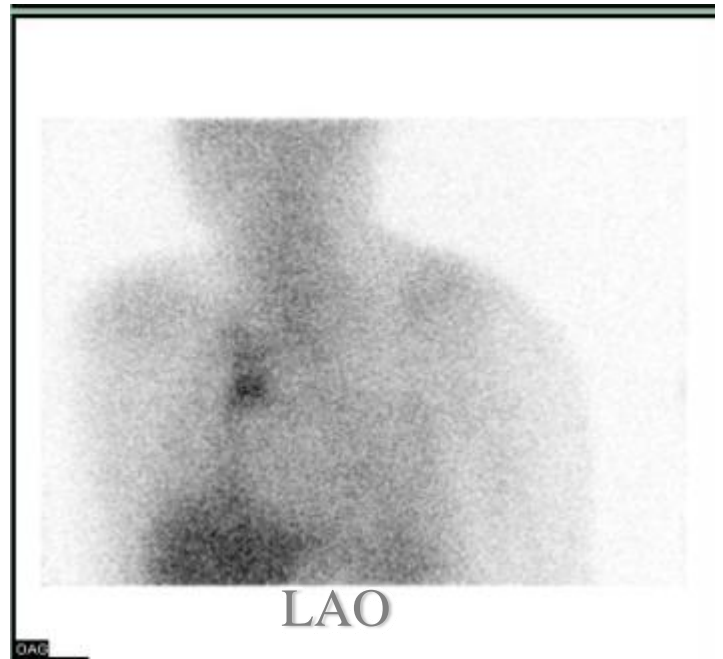


- 37 year-old patient
- 1997 aortic valve replacement (homograft) secondary to endocarditis (SAMS) on bicuspidia
- 2006 Bentall / degenerescence of the homograft
- 2007 Fever resolutive under Amoxicillin but blood culture positive SAMS
- TTE, TEE, CT: aorta root thickening



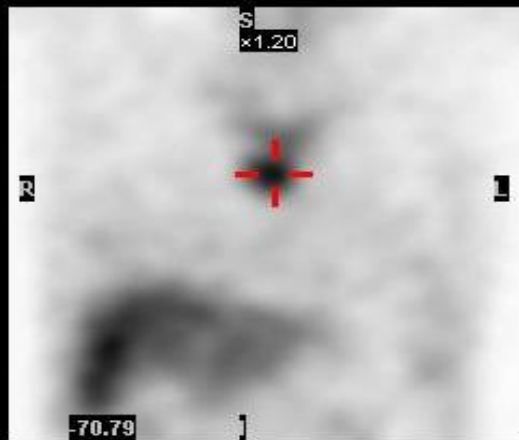
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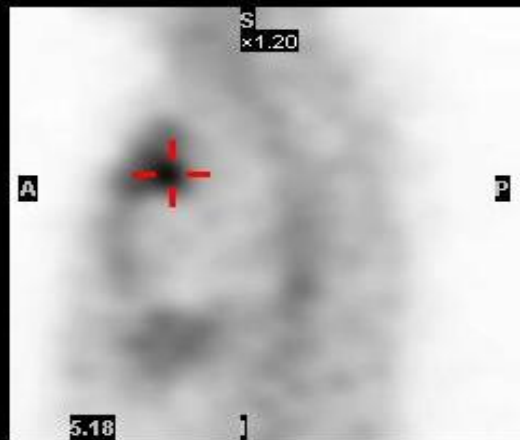


LAO

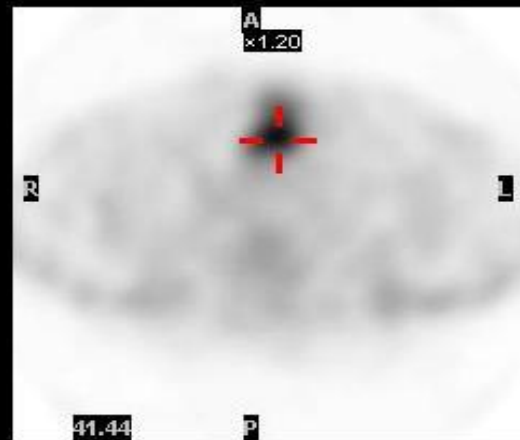
OAG



NM Coronals



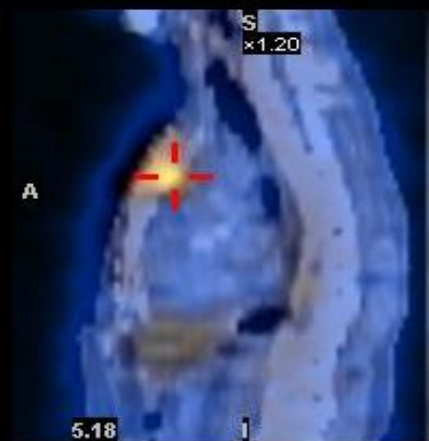
NM Sagittals



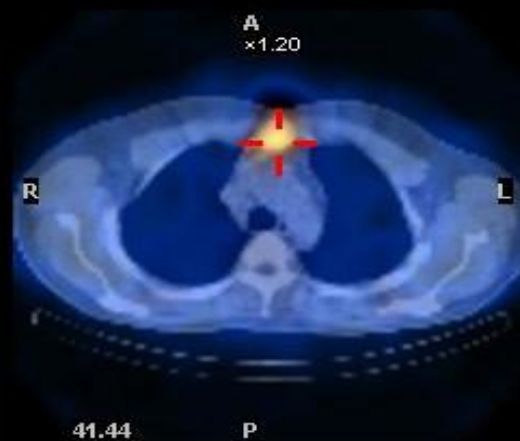
NM Transaxials



Fused Coronals



Fused Sagittals



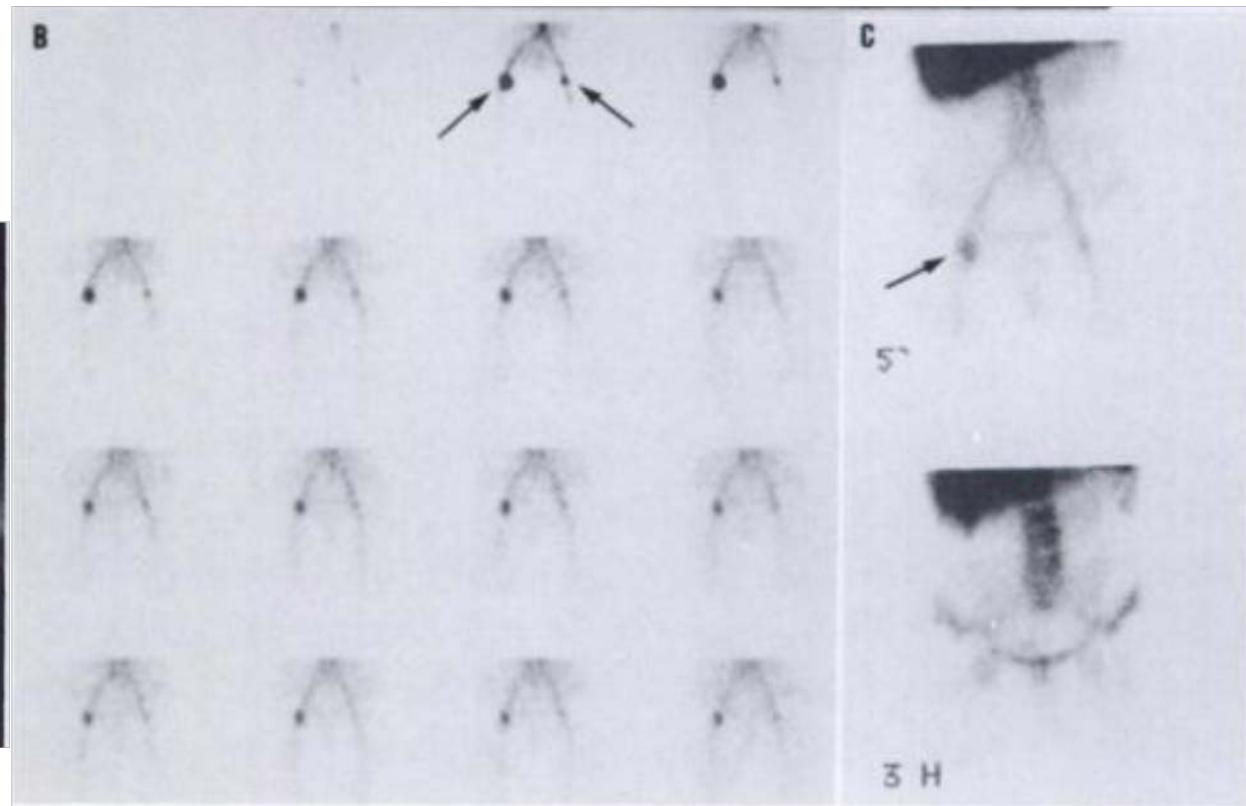
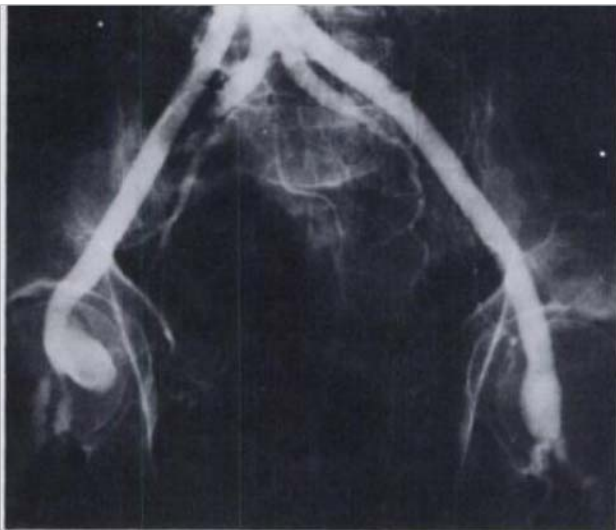
Fused Transaxials

Results : Abdominal aortic graft

- Liberatore et al. *J Nucl Med* 1998: WBCS-^{99m}Tc HMPAO in 129 pts
 - Sensitivity 100%, specificity 92% et accuracy 97%
- Fiorani et al *J Vasc Surg* 1993: WBCS- ^{99m}Tc HMPAO in 37 pts
 - Sensitivity 100%, specificity 94% et PPV 90% and NPV 100% (1 false positive: aneurysm)

Results : Abdominal aortic graft

- Prats et al. J Nucl Med 1994: WBCs- ^{99m}Tc HMPAO in 36 pts, 20 infected pts



Results : Abdominal aortic graft

- Liberatore et al. Med Sci Monit 2006.
 - 23 pts with endovascular graft preoperative and postoperative period (WBCS at 1week and 1 month):
 - WBCS do not provide false positives results in the first month
 - 1 positive one week lymphorrhage and normal at 1 month
 - 3 positives in one patient : sepsis confirmed by surgery at 19 months

Koen S. Simons
Peter Pickkers
Chantal P. Bleeker-Rovers
Wim J. G. Oyen
Johannes G. van der Hoeven

F-18-fluorodeoxyglucose positron emission tomography combined with CT in critically ill patients with suspected infection

- 33 mechanically ventilated patients with FUO
- PET/CT performed additionally to usual diagnostic procedures (CT, US...)
- Final diagnosis made by ICU staff with knowledge of PET/CT results

Table 3 4 × 4 diagram of FDG-PET/CT results compared to follow-up

	Follow-up+	Follow-up–	Total
FDG-PET/CT+	21	3	24
FDG-PET/CT–	0	11	11
Total	21	14	35

Sensitivity : 100%

Specificity : 79%

PPV : 88%

NPV : 100%

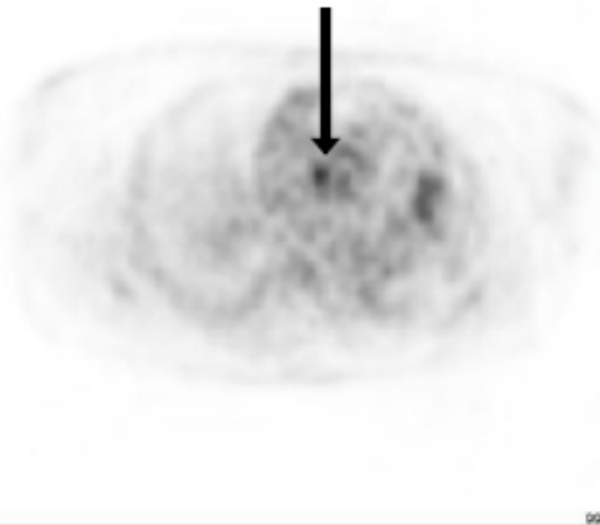
- Negative PET/CT seems to exclude a focal infection as a cause of symptoms
- False positive results : iatrogenic risk increase

Table 4 Review of the literature on the utility of FDG-PET in patients with FUO and comparison with the present study

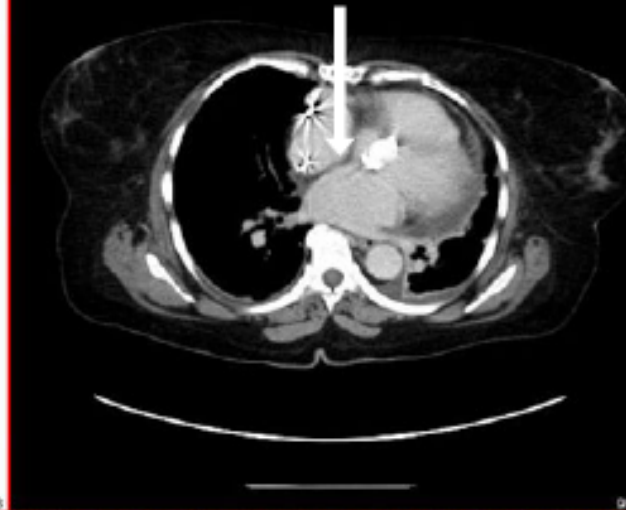
First author (year)	Study design	FUO-definition	FDG-PET technique	Conclusions
Meller (2000) [14]	Prospective ($n=20$): comparison of FDG-PET and ^{67}Ga -citrate ($n=18$)	Temp. $>38.3^{\circ}\text{C}$ for >3 weeks No diagnosis after 1 week of diagnostic work-up and referral to nuclear medicine department	Dual-headed coincidence camera	FDG-PET helpful in 55%, PPV 92%, NPV 75%, FDG-PET superior to ^{67}Ga -citrate
Blockmans (2001) [13]	Prospective ($n=58$): comparison to ^{67}Ga -citrate ($n=40$)	Temp. $>38.3^{\circ}\text{C}$ for >3 weeks No diagnosis after 3 days of in-hospital investigation	Full-ring PET scanner	FDG-PET helpful in 41%, FDG-PET superior to ^{67}Ga -citrate
Lorenzen (2001) [15]	Retrospective ($n=16$)	Temp. $>38.0^{\circ}\text{C}$ for >3 weeks Increased ESR and CRP Inconclusive diagnostic tests	Full-ring PET scanner	FDG-PET helpful in 69%, PPV 92%, NPV 100%
Bleeker-Rovers (2004) [16]	Retrospective ($n=35$)	Temp. $>38.3^{\circ}\text{C}$ for >3 weeks No diagnosis after 1 week of evaluation in the hospital or in the out-patient department	Full-ring PET scanner	FDG-PET helpful in 37%, PPV 87%, NPV 95%
Kjaer (2004) [17]	Prospective ($n=19$): comparison with ^{111}In -granulocyte	Temp. $>38.3^{\circ}\text{C}$ for >3 weeks No diagnosis after 1 week of evaluation in the hospital or in the out-patient department and referral for ^{111}In -granulocyte scintigraphy	Full-ring PET scanner	FDG-PET helpful in 16%, PPV 30%, NPV 67%; ^{111}In -granulocyte scintigraphy helpful in 26%
Buysschaert (2004) [18]	Prospective ($n=74$)	Temp. $>38.3^{\circ}\text{C}$ for >3 weeks No diagnosis after 3 days in hospital or 3 out-patient visits and referral for FDG-PET	Full-ring PET scanner	FDG-PET helpful in 26%
Bleeker-Rovers (present study)	Prospective, multi-centre ($n=70$)	Temp. $>38.3^{\circ}\text{C}$ for >3 weeks No diagnosis after certain obligatory initial investigations	Full-ring PET scanner	FDG-PET helpful in 33%, PPV 70%, NPV 92%

Category	No. of cases	True positive	True negative	False positive	False negative
Infection	12 (17%)	11	–	–	1
Bronchiectasia/pneumonia	2	2	–	–	–
Diverticulitis	1	1	–	–	–
Pyelonephritis	1	–	–	–	1
Abdominal abscesses	1	1	–	–	–
Osteomyelitis	2	2	–	–	–
Tonsillitis	1	1	–	–	–
Chronic persistent yersiniosis	4	4	–	–	–
Neoplasm	5 (7%)	5	–	–	–
Non-Hodgkin's lymphoma	3	3	–	–	–
Metastatic breast cancer	1	1	–	–	–
Adenocarcinoma with unknown primary	1	1	–	–	–
Non-infectious inflammatory disease	16 (23%)	6	7	1	2
Large-vessel vasculitis	2	2	–	–	–
Polymyalgia rheumatica	3	–	3	–	–
Henoch-Schönlein purpura	1	–	1	–	–
Microscopic polyangiitis	1	–	1	–	–
Psoriatic arthritis	1	1	–	–	–
Adult-onset Still's disease	3	1	2	–	–
Systemic lupus erythematosus	4	2	–	–	2
Cryoglobulinaemia	1	–	–	1	–
Miscellaneous	2 (3%)	1	1	–	–
Drug fever	1	1	–	–	–
Hypertriglyceridaemia	1	–	1	–	–
No diagnosis	35 (50%)	–	26	9	–

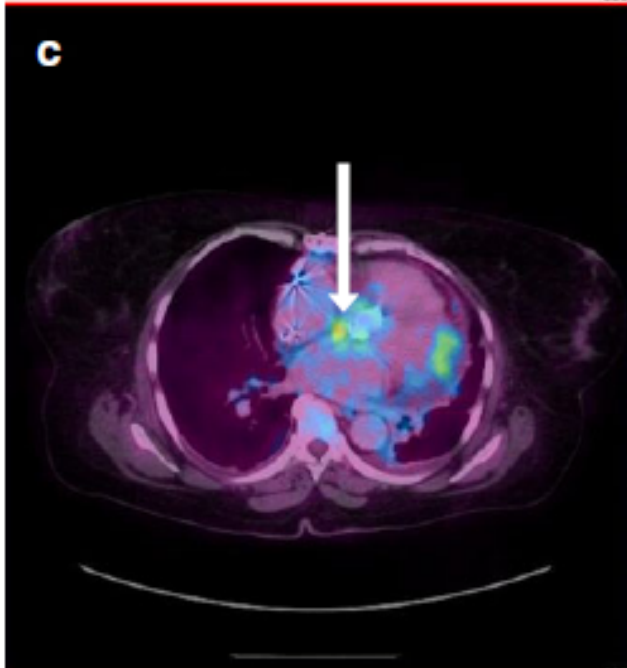
a Elevated FDG uptake in
valve prosthesis



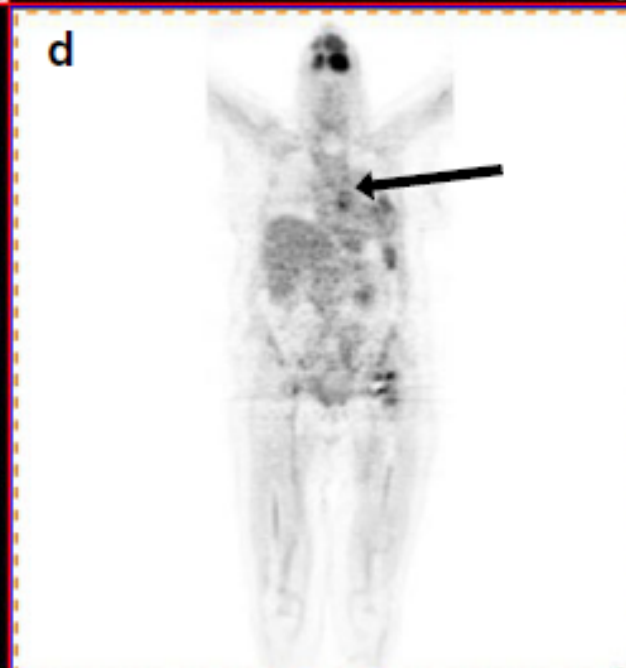
b



c



d



In vitro human leukocyte labeling with ^{64}Cu : an intraindividual comparison with ^{111}In -oxine and ^{18}F -FDG[☆]

Kuldeep K. Bhargava^a, Raj K. Gupta^b, Kenneth J. Nichols^a, Christopher J. Palestro^{a,*}

Nuclear Medicine and Biology 36 (2009) 545–549

Intérêt d'associer

- Les performances techniques de la TEP
- à l'information physiologique provenant des leucocytes
- nécessite un isotope à $\frac{1}{2}$ vie longue (^{64}Cu = 12,7 heures)

Viability			
Radionuclide	1 h	3 h	24 h
^{64}Cu -WBC	99±1%	98±1%	61±8%
^{111}In -WBC	99±1%	96±2%*	48±5%*
^{18}F -FDG-WBC	99±1%	96±2%*	50±7%*

* $P < .05$ vs. ^{64}Cu -WBC.

Retention (%)					
Radionuclide	1 h	2 h	3 h	4 h	24 h
^{64}Cu -WBC	91±4%§	89±4%§	88±4%§	86±4%§	79±6%
^{111}In -WBC	94±2%*	93±3%*	92±3%*	91±3%*	88±4%*
^{18}F -FDG-WBC	85±4%	81±4%	76±4%	68±7%	—

* $P < .05$ for ^{111}In -WBC higher than ^{64}Cu -WBC and ^{18}F -FDG-WBC.

§ $P < .05$ for ^{64}Cu -WBC higher than ^{18}F -FDG-WBC.