Actualités concernant les traceurs TEP/Anticorps en Oncologie : ImmunoTEP

Réunion inter-régionale de médecine nucléaire

11 Avril 2015

TORDO Jérémie (IHL)

Hôpitaux de Lyon

Introduction

- Démocratisation récente de l'utilisation de la TEP en imagerie

  ➔ Permet une imagerie **métabolique**

- **Utilisation majoritaire 18-FDG (coût, disponibilité …)**

  ➔ Nombreuses indications en Oncologie

  ➔ Staging, évaluation thérapeutique …

  ➔ Efficacité reconnue, mais …

➔ Peu de spécificité

Introduction

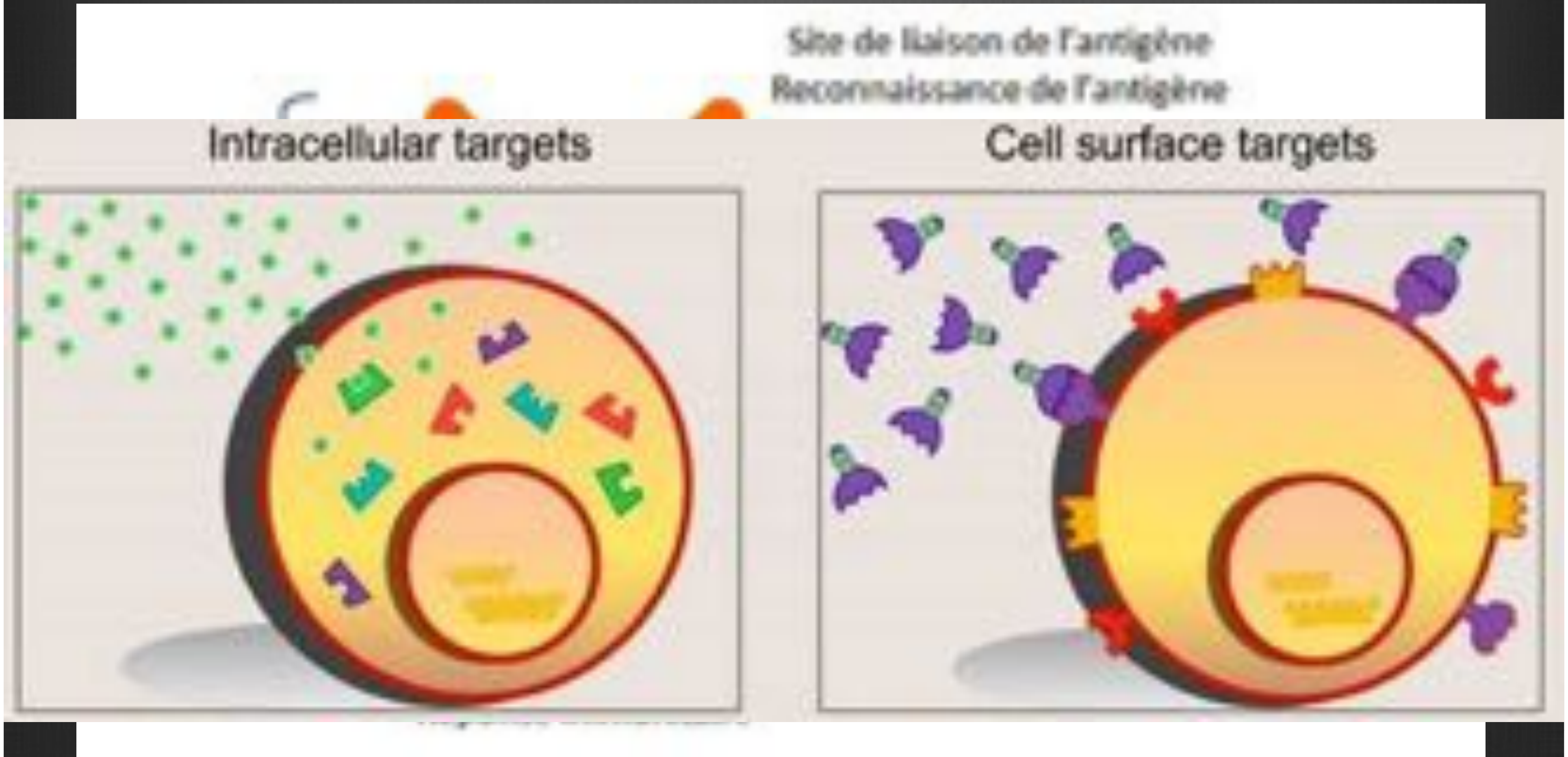
En parallèle :

- Nette augmentation du nombre et de l'utilisation des **thérapies ciblées** (Plan cancer 2014-2019).

- **Amélioration** constante des techniques:
  ➔ Découverte de nouvelles cibles moléculaires
  ➔ Progrès en chimie, ciblage.

- **Utilisation des Anticorps monoclonaux (AcM) ou fragments d'anticorps en tant que vecteurs pour l'imagerie métabolique ?**
  ➔ ImmunoTEP ou Imagerie phénotypique

Anticorps monoclonaux



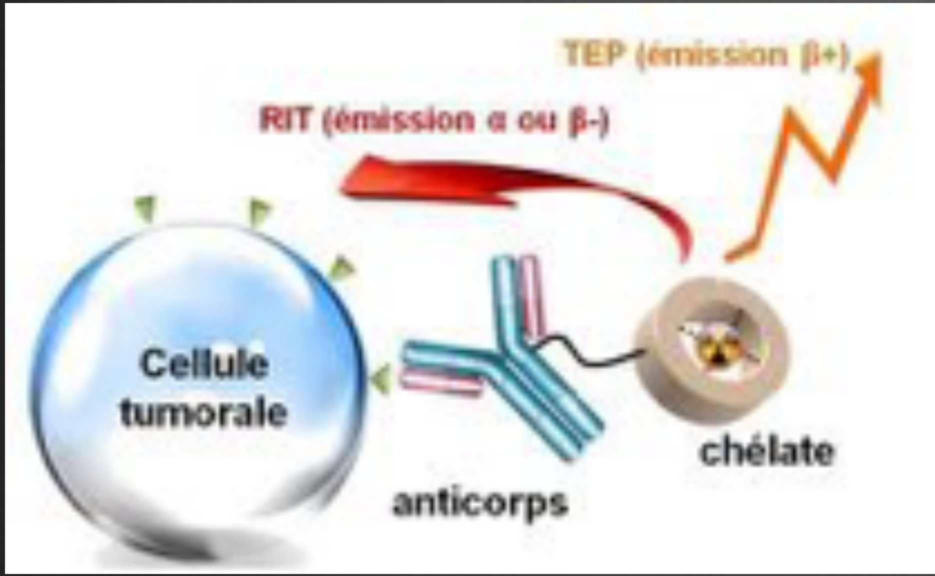
- Glycoprotéines de la famille des **immunoglobulines**
- 4 chaînes polypeptidiques : 2 chaînes lourdes + 2 chaînes légères

Hanahan D, Cell 2011

Liste actuelle des anticorps monoclonaux approuvés par la FDA en Oncologie

Développement exponentiel

Imagerie métabolique ciblée



Associer un vecteur d'une cible moléculaire spécifique à un radioélément TEP (non FDG)

Avantages de la TEP :

- Sensibilité
- Résolution
- Correction d'atténuation
- Possibilité de quantification

Imagerie métabolique ciblée

- Une idée pas si **récente que ça** :

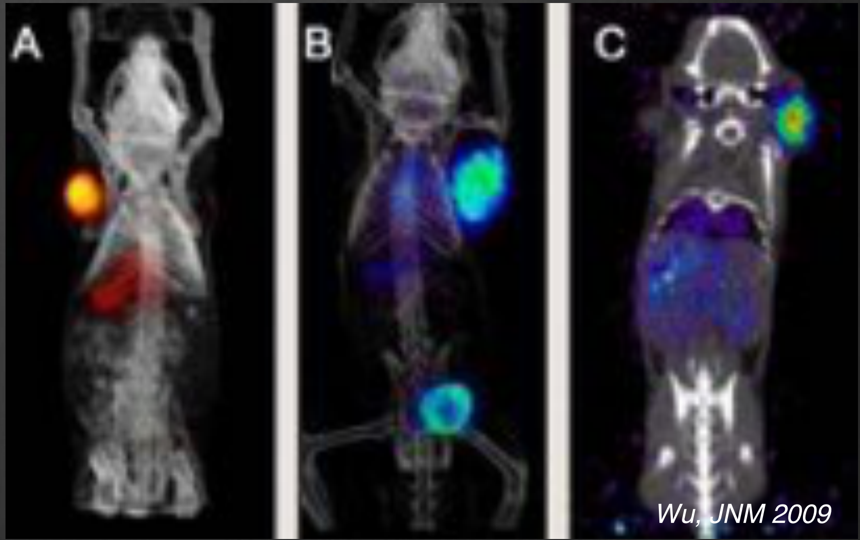
Copper-64-Labeled Antibodies for PET Imaging

Carolyn J. Anderson, Judith M. Connett, Sally W. Schwarz, Pamela A. Rocque, Li Wu Guo, Gordon W. Philpott, Kurt R. Zinn, Claude F. Meares and Michael J. Welch

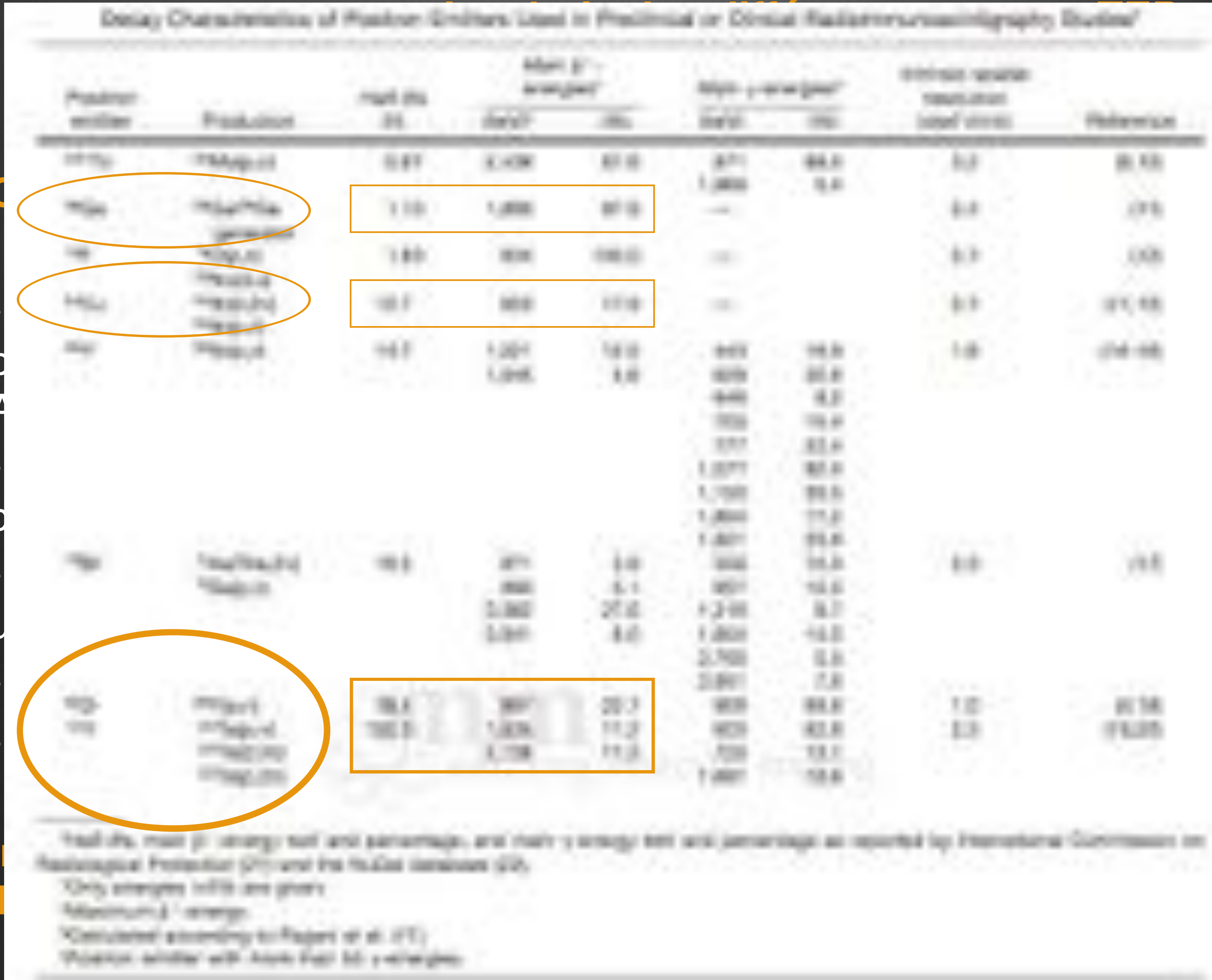
Division of Radiation Sciences, Washington University Medical School, St. Louis, Missouri; Department of Surgery, Jewish Hospital, St. Louis, Missouri; University of Missouri Research Reactor, Columbia, Missouri; and Department of Chemistry, University of California, Davis, Davis, California

In conclusion, we have developed and evaluated a ^{64}Cu-labeled anticolorectal antibody that appears very promising for utilization with PET for the evaluation of colon cancer. An amendment to our IND for ^{111}In-BrΦHBED-1A3 (*23*) to include ^{64}Cu-benzyl-TETA-1A3 administration in colorectal cancer patients is currently underway.

Received Jan. 22 1992; revision accepted Apr. 21, 1992.
For reprints contact: Michael J. Welch, PhD, Division of Radiation Sciences, Washington University School of Medicine, Box 8131, 510 S. Kingshighway Blvd., St. Louis, MO 63110.



- Mais une utilisation uniquement en recherche pré-clinique ?



Un des traceurs les plus utilisés :

^{89}Zirconium

Figure 1: Schematic overview of ^{89}Zr labeled antibody using DFO as chelator.

Decay data of ^{89}Zr.

Radiation type	Energy (keV)	Radiation intensity (%)
β^{+}*	395.5	22.74
Auger-L	1.91	79.00
Auger-K	12.7	19.47
γ-annihilation	511.0	45.48
γ	909.15	99.04
γ	1620.8	0.07
γ	1657.3	0.11
γ	1713.0	0.75
γ	1744.5	0.12

Un des radioélément les plus utilisés en immunoTEP :

- Période de 78,4 heures
- Rendement énergétique suffisant pour l'obtention d'images avec contraste suffisant

^{89}Zirconium

Figure 1: Schematic overview of ^{89}Zr-labeled antibody using DFO as chelator.

Review Article

Table 1: Overview of the described preclinical and clinical studies using ^{89}Zr-labeled antibodies.

Target	Type of tumor	Targeting vector
CD147	Pancreas	059-053
CD20*	Non-Hodgkin's lymphoma	Ibritumomab tiuxetan
CD44v6*	Head and neck squamous cell carcinoma	cmAb U36
EGFR	Multiple	Cetuximab
EGP-1	Prostate	hRS7
GPC3	Liver	αGPC3
HER1	Colorectal	Panitumumab
HER2*	Breast and ovarian	Trastuzumab
IGF-1R	Triple negative breast cancer	R1507
MET	Head and neck squamous cell carcinoma and gastric	DN30
MN/CA IX	Renal cell carcinoma	cG250
PSMA	Prostate	7E11
PlGF	Liver	RO5323441
VEGF*	Breast, head, and neck squamous cell carcinoma and ovarian	Bevacizumab

*Targets evaluated in clinical studies.

- PSMA
- CD44V6 (cancer ORL : ganglions, métastases)
- VEGF (Bevacizumab)

^{89}Zirconium

IgG antiCD44v6

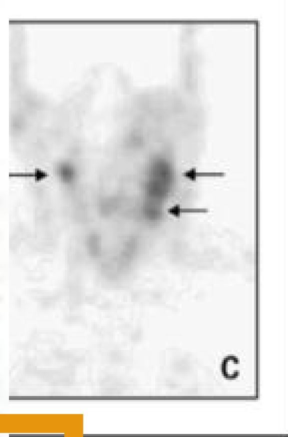
Figure 1: Schematic overview of ^{89}Zr-labeled antibody using DFO as chelator

Performance of Immuno – Positron Emission Tomography with
Zirc
in th
Hea

Pontus
Jan C.
Adriaa

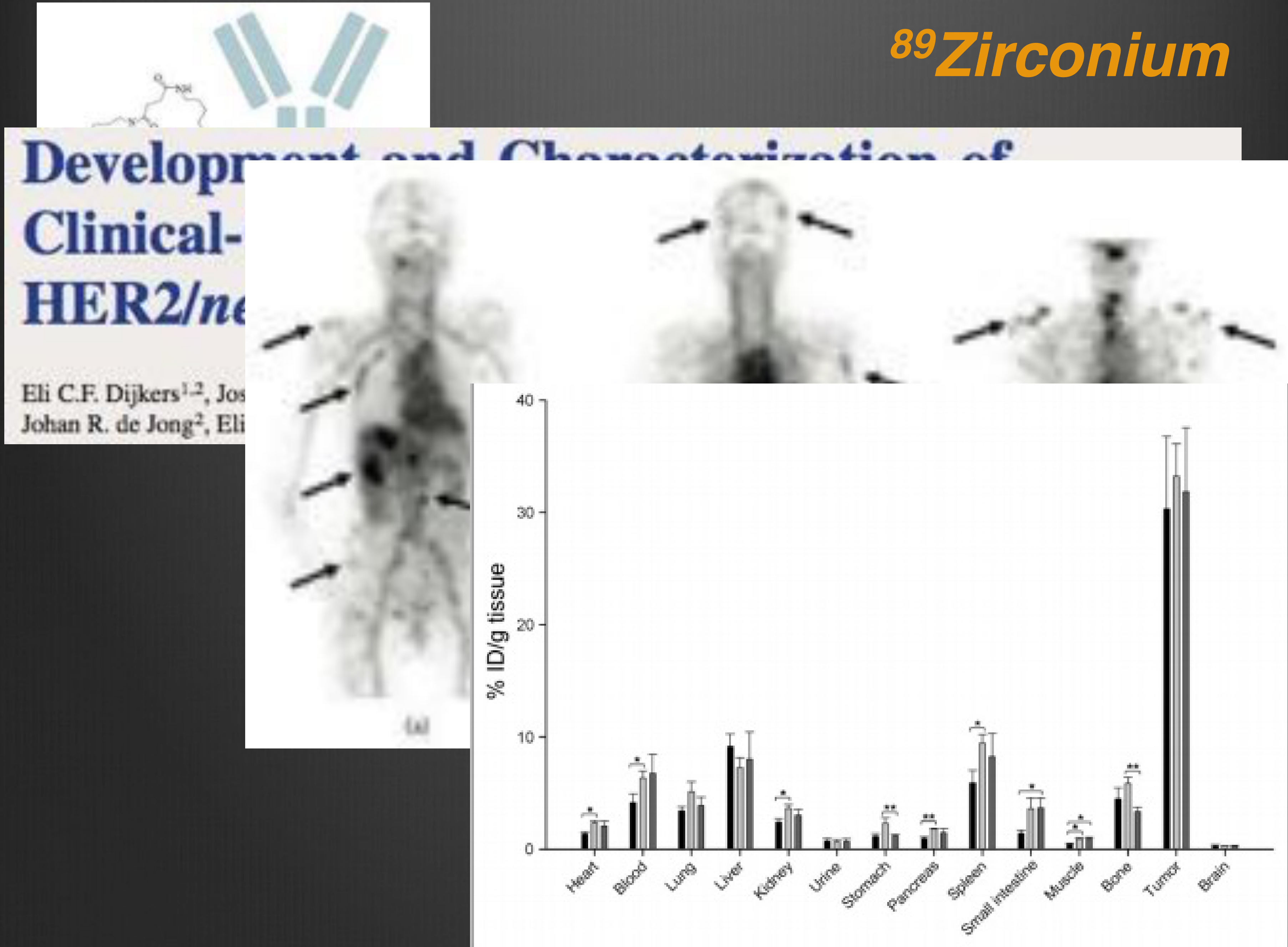
Table 4. Correlation of preoperative findings with histopathologic findings per level in six patients who received FDG-PET

40 operated levels, 13 tumors involved	Sensitivity	Specificity	Accuracy
Palpation	7/13 (54%)	27/27 (100%)	34/40 (85%)
CT/MRI	10/13 (77%)	27/27 (100%)	37/40 (93%)
FDG-PET	8/13 (62%)	27/27 (100%)	35/40 (88%)
^{89}Zr-immuno-PET	11/13 (85%)	27/27 (100%)	38/40 (95%)

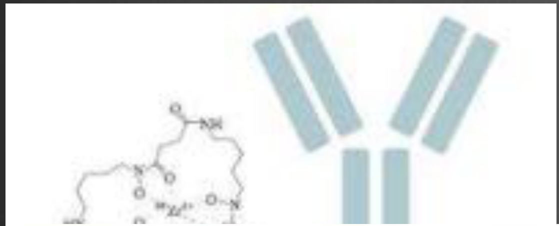


Cl cancer 2006

^{89}Zirconium



^{89}Zirconium



^{89}Zr-Bevacizumab PET Imaging in Primary Breast Cancer

Sietske B ... is[4],
Hetty Ti ... R. de Jong[2],
Joost Ba ... er[1]

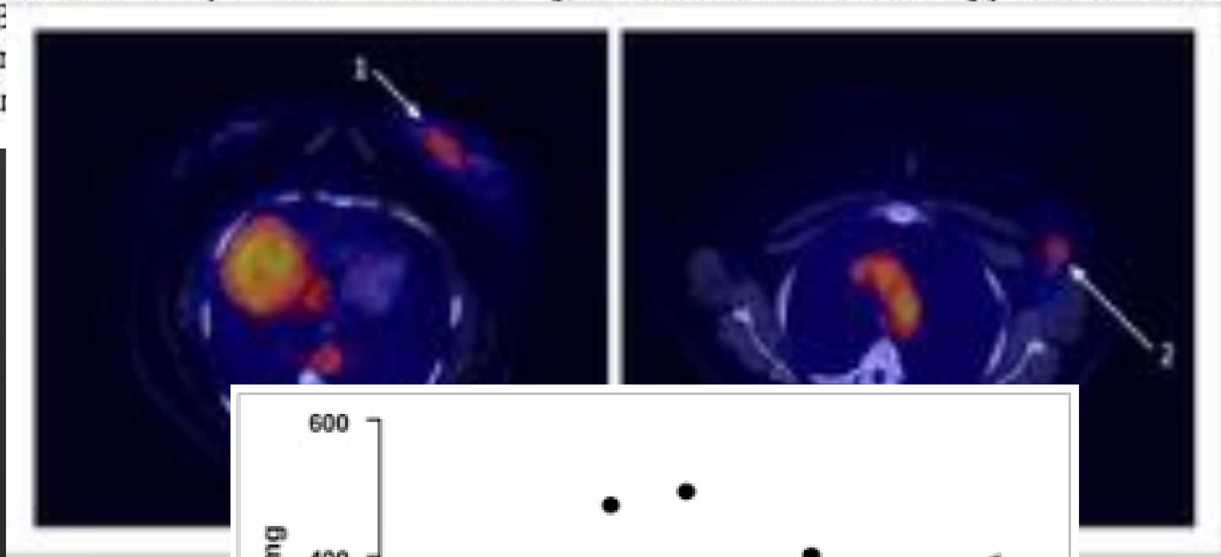
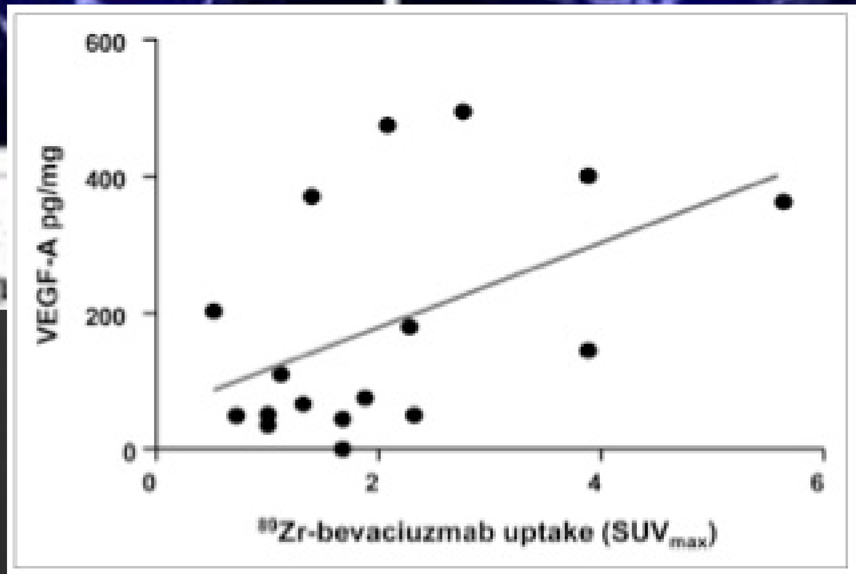


FIGURE 1.
primary brea ... ient with



JNM 2013

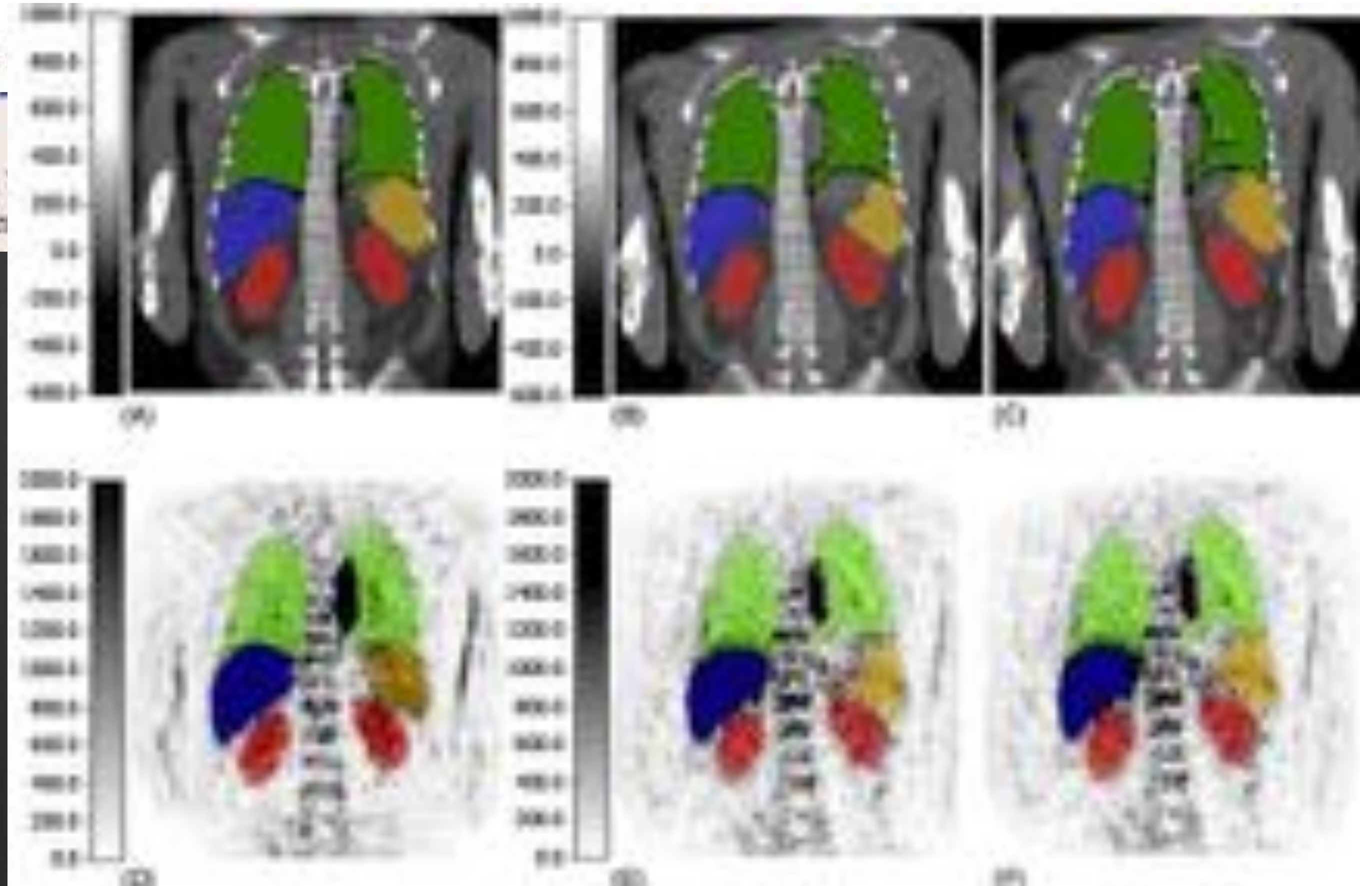
^{89}Zirconium

Validation of simplified dosimetry approaches in 89 Zr-PET/CT: The use of manual versus semi-automatic delineation methods to estimate organ absorbed doses

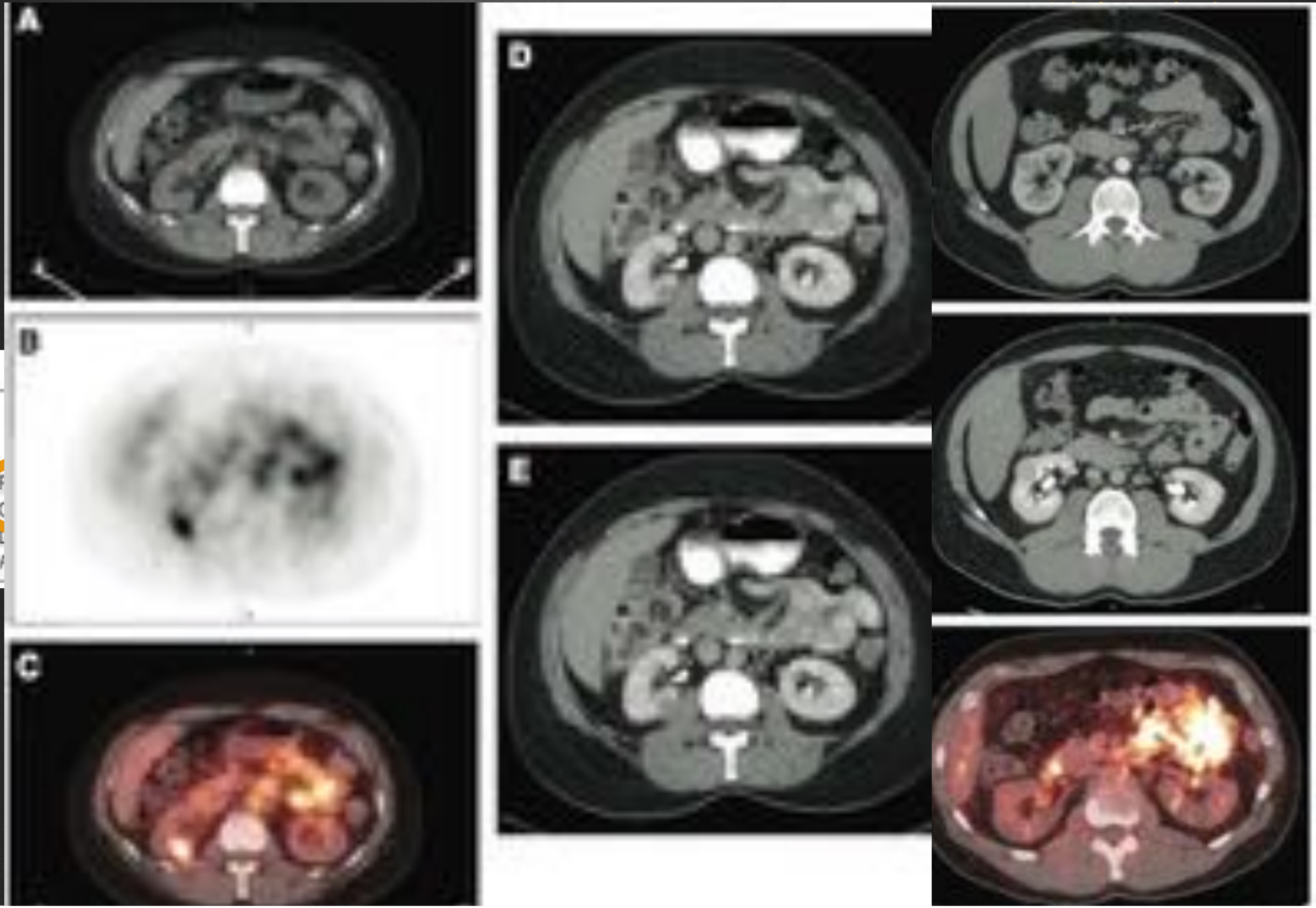
N. E. Makris, F. H. P. van Velden, M. C. Huisman, C. W. Menke, A. A. Lammertsma, and R. Boellaard

Citation: Medical Physics

Pontus K.E. Börjesson[1],
Guus A.M.S. van Donge



^{124}Iode

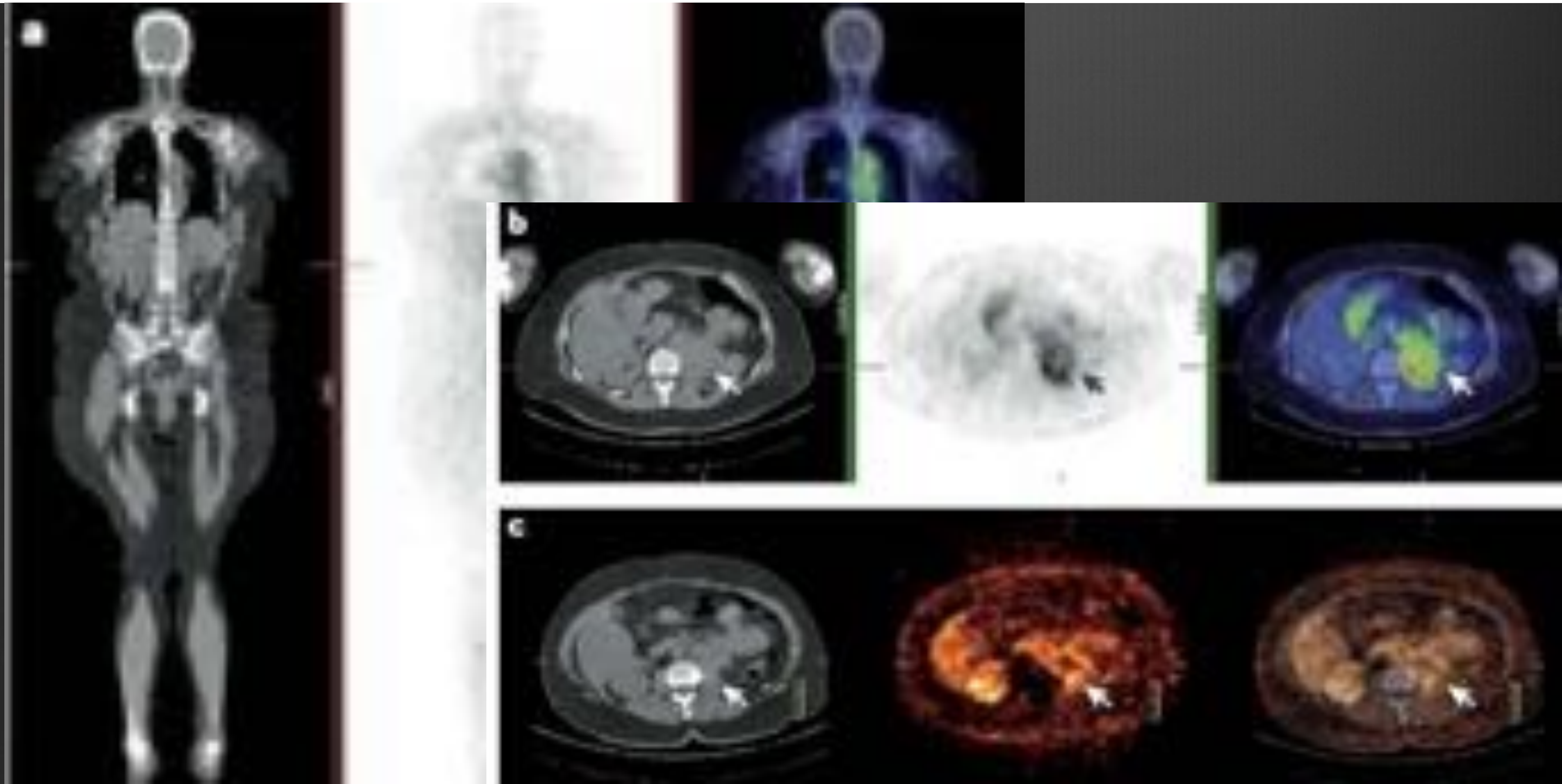


^{124}Iode

cG250 CAIX specific

Antibody therapy of cancer

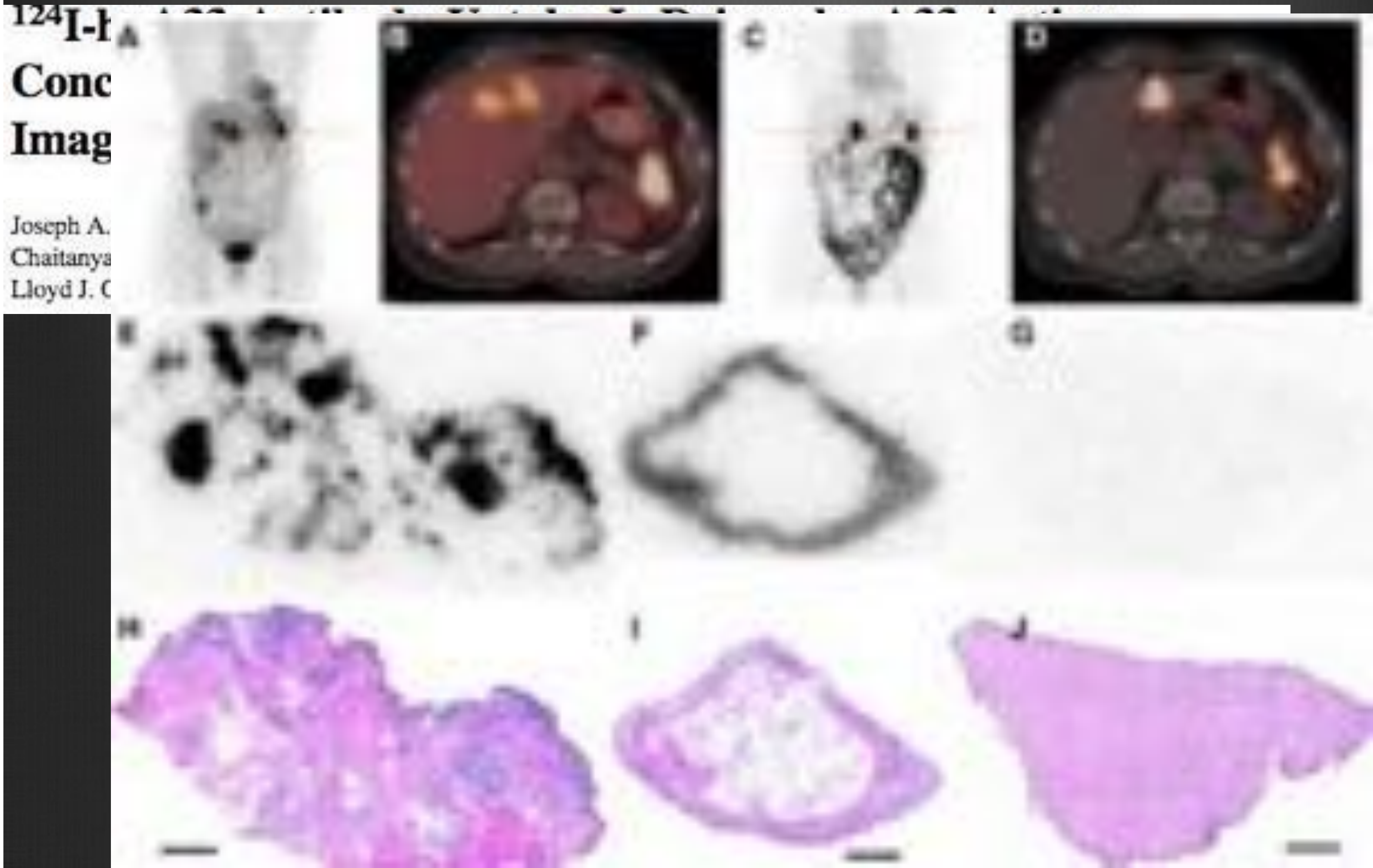
Andrew M. Scott[1], Jedd D. Wolchok[2,3,4,5] and Lloyd J. Old[3,4,5]



Nature 2012

^{124}Iode

AcM chimérique cG250 (anti-carbonic anhydrase-IX)

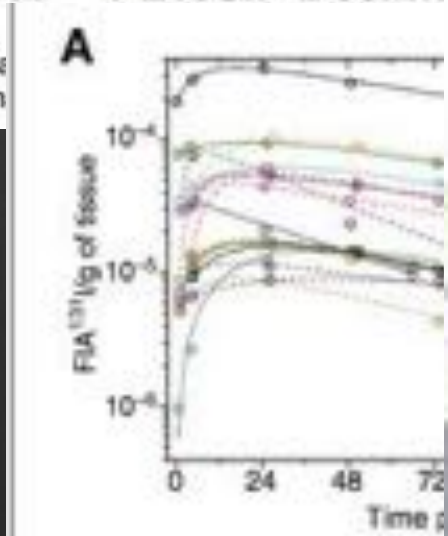


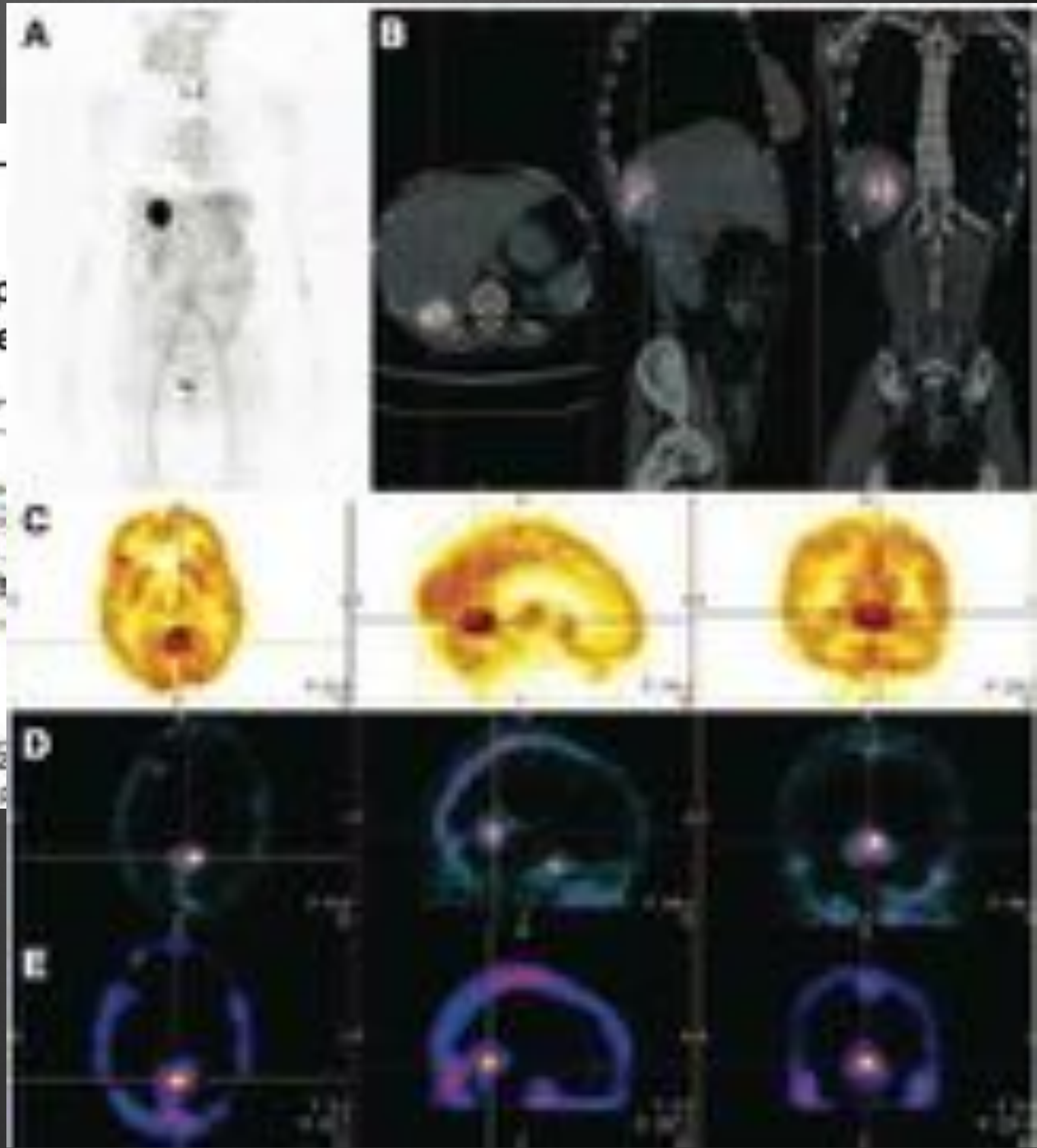
JNM 2011

Research Article

Radretumab Radioimmunotherap
Metastasis: A ^{124}I-L19SIP Dosime

Gian Luca Poli[1], Cla
Giuliano Elia[3], Leon

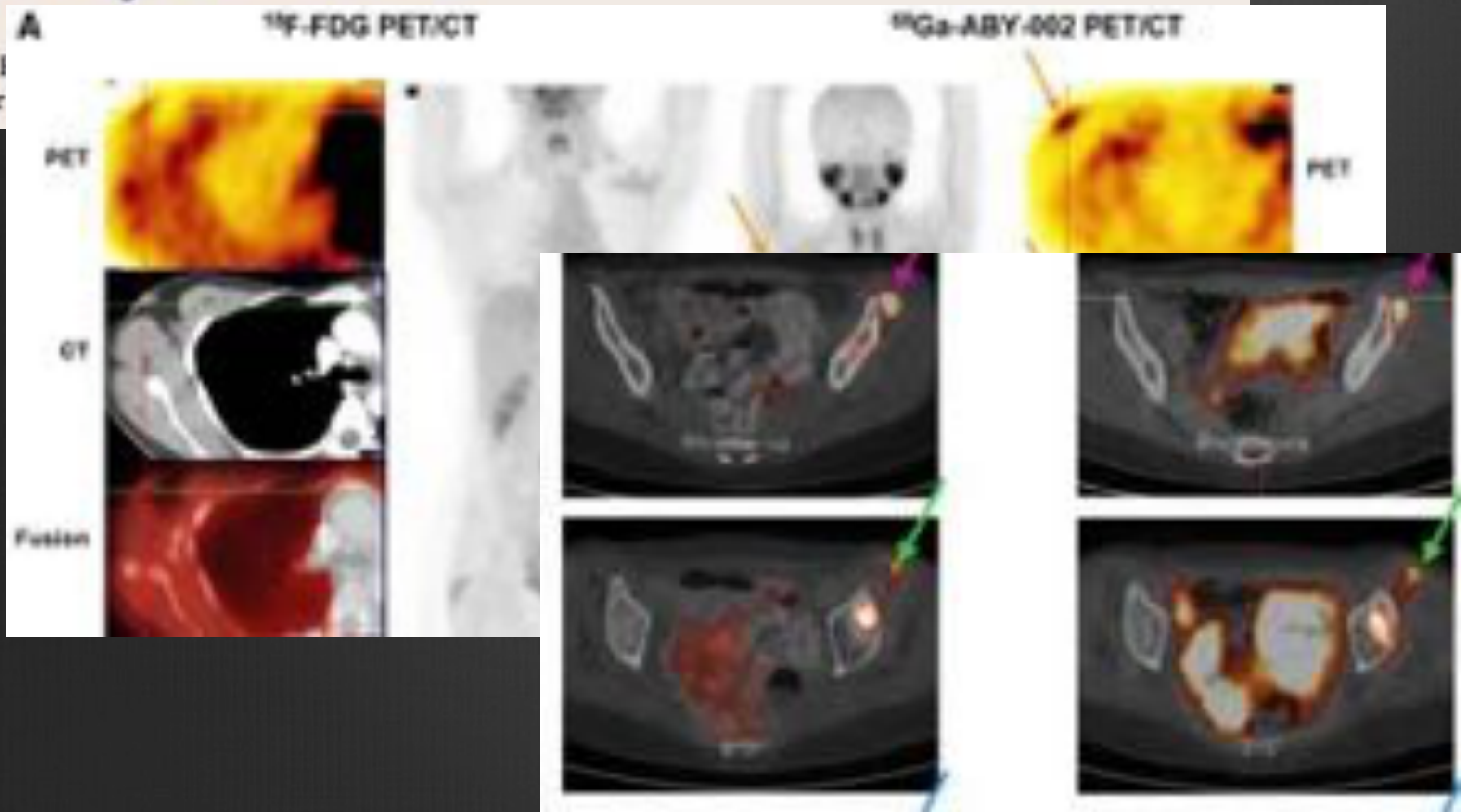




^{68}Gallium

Molecular Imaging of *HER2*-Expressing Malignant Tumors in Breast Cancer Patients Using Synthetic ^{111}In- or ^{68}Ga-Labeled Affibody Molecules

Richard
Vladimir



JNM 2010

Avantages imagerie métabolique ciblée

- Utilisation d’un vecteur **spécifique** de la cible recherchée :
  - information obtenue plus **pertinente**
  - étude du processus moléculaire

- Permet de **prédire** et **d’évaluer l’efficacité** des thérapies ciblées

- Possibilité de développer des “**traceurs compagnons**” aux thérapies ciblées
  ➔ Approche **théragnostique** de la médecine nucléaire

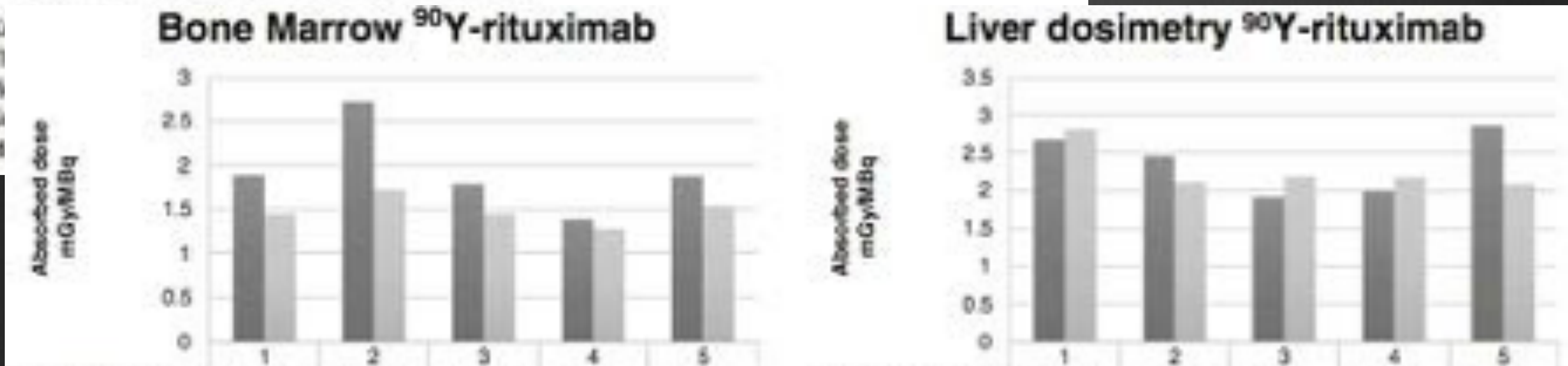
- Association RIV et ImmunoTEP

Association RIV et ImmunoTEP :

Eur J Nucl Med Mol Imaging
DOI 10.1007/s00259-015-3023-6

ORIGINAL ARTICLE

Tumour targeting and radiation dose of radioimmunotherapy with ^{90}Y-rituximab in CD20+ B-cell lymphoma as predicted by ^{89}Zr-rituximab immuno-PET: impact of preloading with unlabelled rituximab

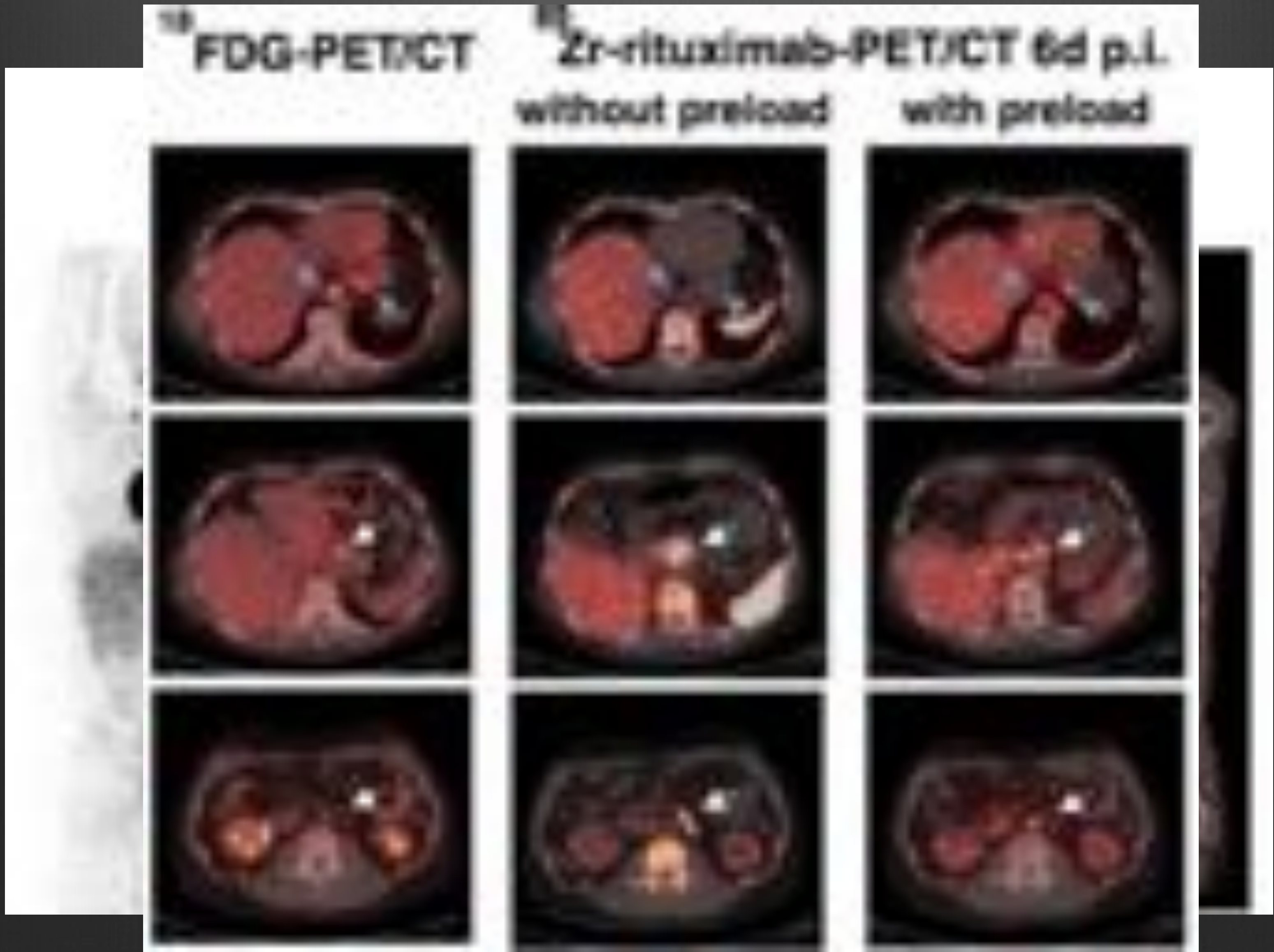


	1	2	3	4	5
Without predosing	1.89	2.73	1.79	1.39	1.88
With predosing	1.45	1.73	1.45	1.28	1.54

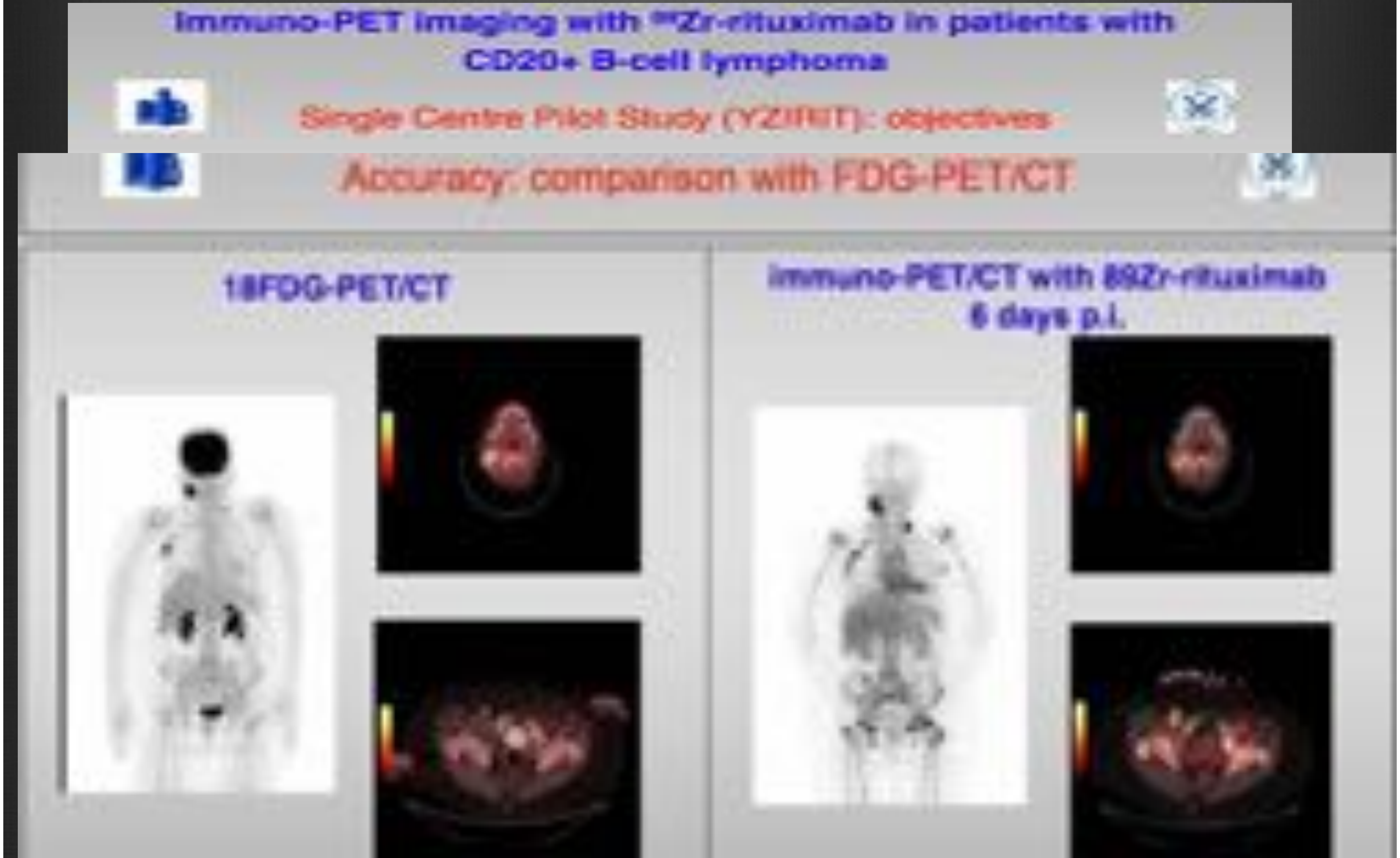
	1	2	3	4	5
Without predosing	2.68	2.46	1.92	2.01	2.86
With predosing	2.82	2.11	2.19	2.18	2.09

Associé au pré-ciblage

Association RIV – ImmunoTEP et Pré-ciblage :



Association RIV et ImmunoTEP :



Un intérêt croissant global :

Int. J. Mol. Sci. **2015**, *16*, 3932-3954; doi:10.3390/ijms16023932
Review

Tumor Immunotargeting Using Innovative Radionuclides

Françoise Kraeber-Bodéré [1,2,3,*], Caroline Rousseau [1,3], Caroline Bodet-Milin [1,2], Cédric Mathieu [2], François Guérard [1], Eric Frampas [1,4], Thomas Carlier [1,2], Nicolas Chouin Ferid Haddad [6], Jean-François Chatal [6], Alain Faivre-Chauvet [1,2], Michel Chérel [1,3] and Jacques Barbet [1,6]

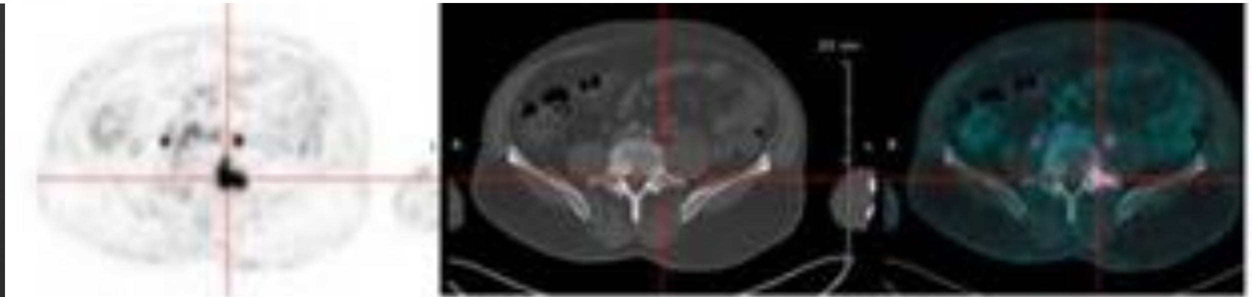


Figure 3. Positron emission tomography (PET) in a patient with a relapse of medullary thyroid carcinoma recorded after injection of the TF2 anti-carcino-embryonic antigen (CEA) bispecific antibody and the ^{68}Ga-IMP-288 peptide. Image shows a good detection of a bone lesion.

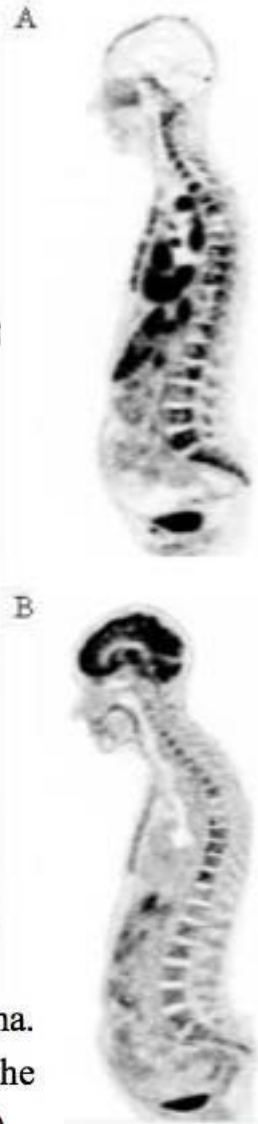
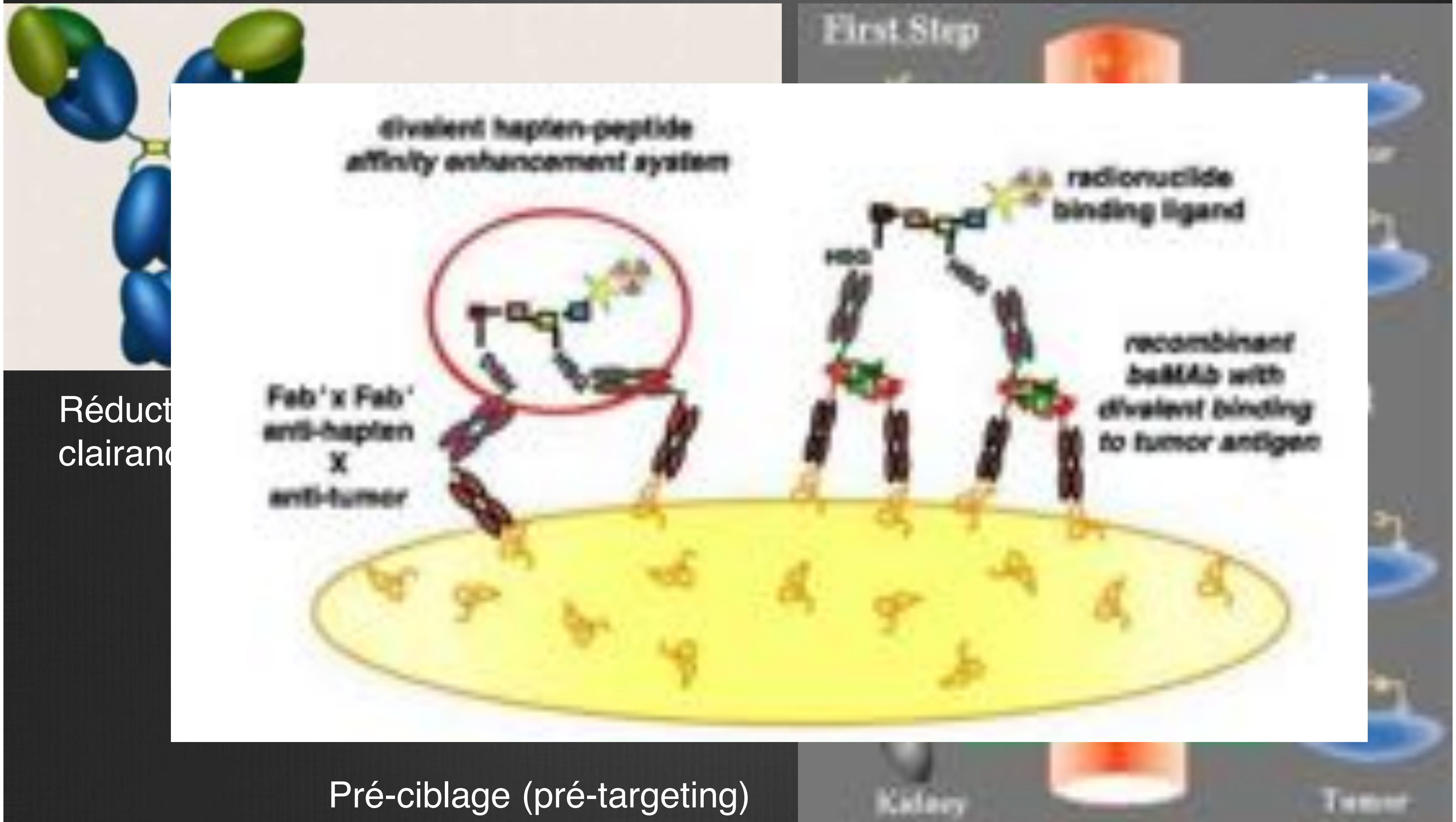


Figure 4. Imaging performed in a patient with a metastatic breast carcinoma. (**A**) Immuno-PET performed using the TF2 anti-CEA bispecific antibody and the ^{68}Ga-IMP-288 peptide detects a more diffuse bone marrow involvement that FDG-PET (**B**).

Amélioration de l'immunociblage



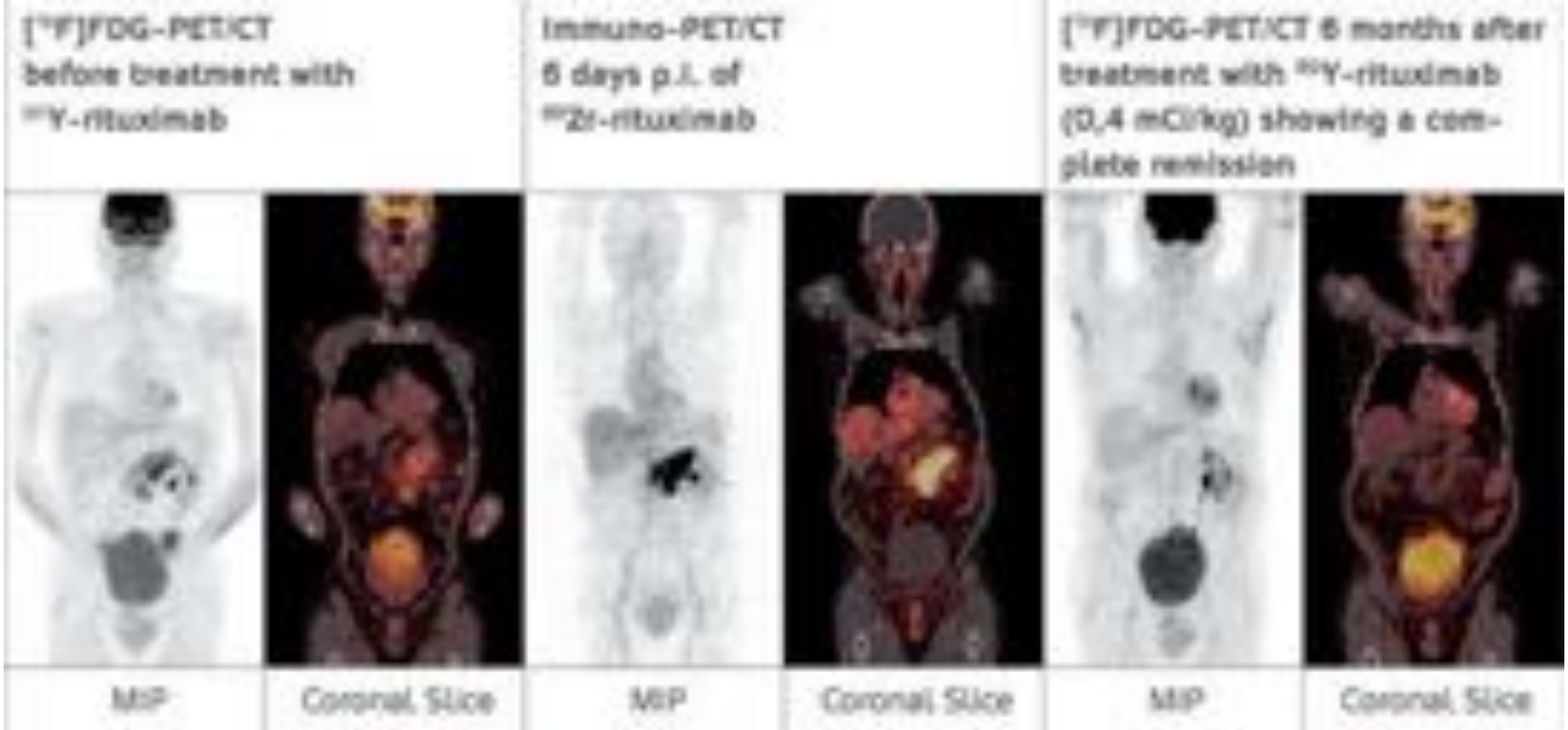
Réduct
clairanc

Pré-ciblage (pré-targeting)

Applications cliniques de l'imagerie ciblée :

- Diagnostique :
  - Détection
  - Caractérisation
  - Staging
  - Intérêt pronostique du ciblage
- Thérapeutique :
  - Sélection des patients à traiter :
    - *Exemple : HER2 et Herceptin*
  - Evaluation de l'étendue des lésions à traiter ➔ Evaluation pré-dose
  - Possibilité de quantification et de dosimétrie si RIV associée envisagée
  - Concept de médecine personnalisée
- Surveillance et évaluation post-thérapeutique

Conclusion



Aspect fondamental et avenir de la médecine nucléaire ? Concept de médecine personnalisée.

Merci de votre attention