CLINICAL PET IN OCNOLOGY: current applications and future perspectives

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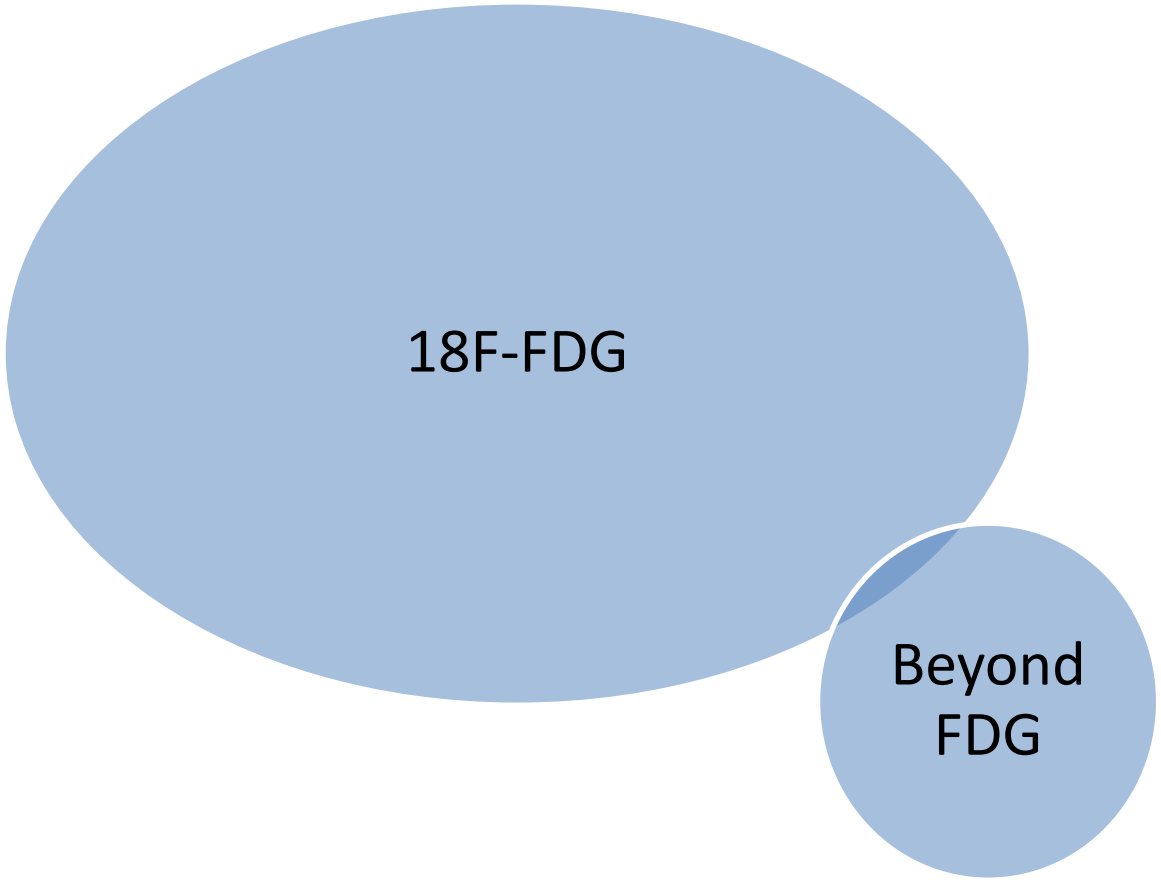
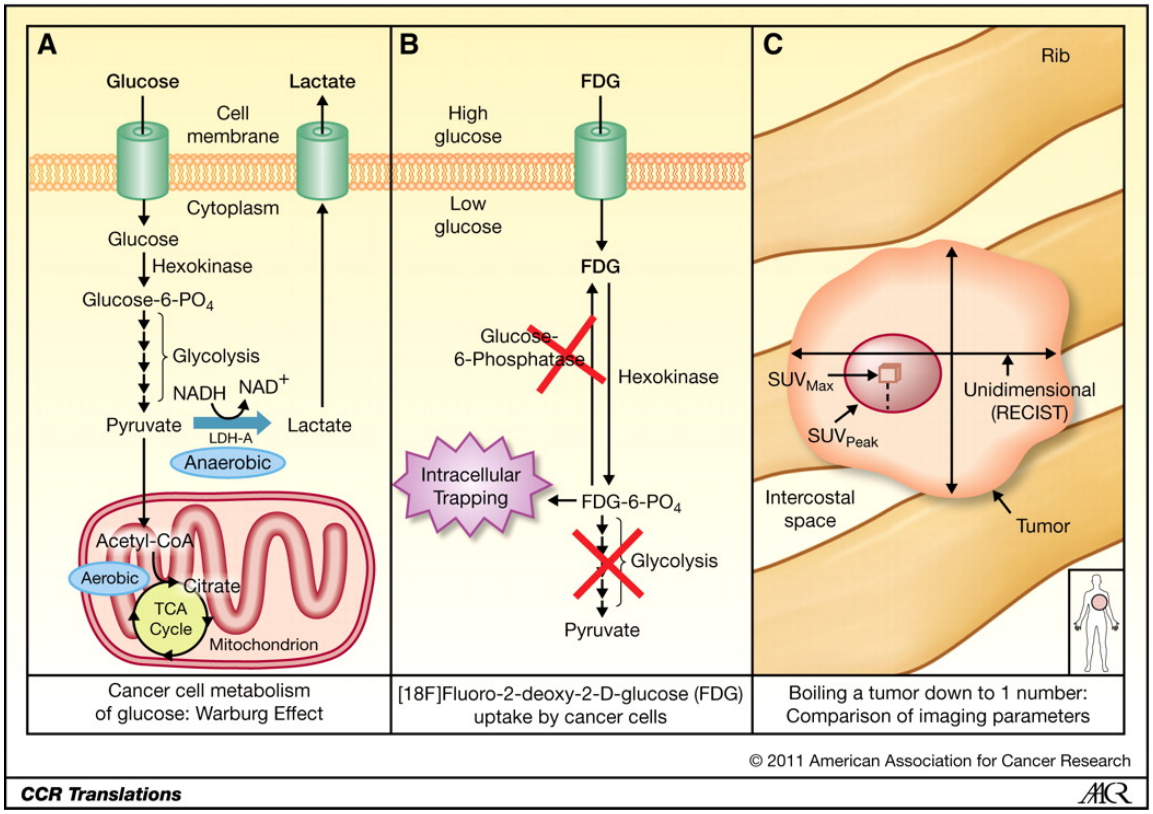
Clinical PET/CT in oncology



Warburg's effect and 18F-FDG PET



Harrison M R , and George D J Clin Cancer Res 2011;17:5841-5843

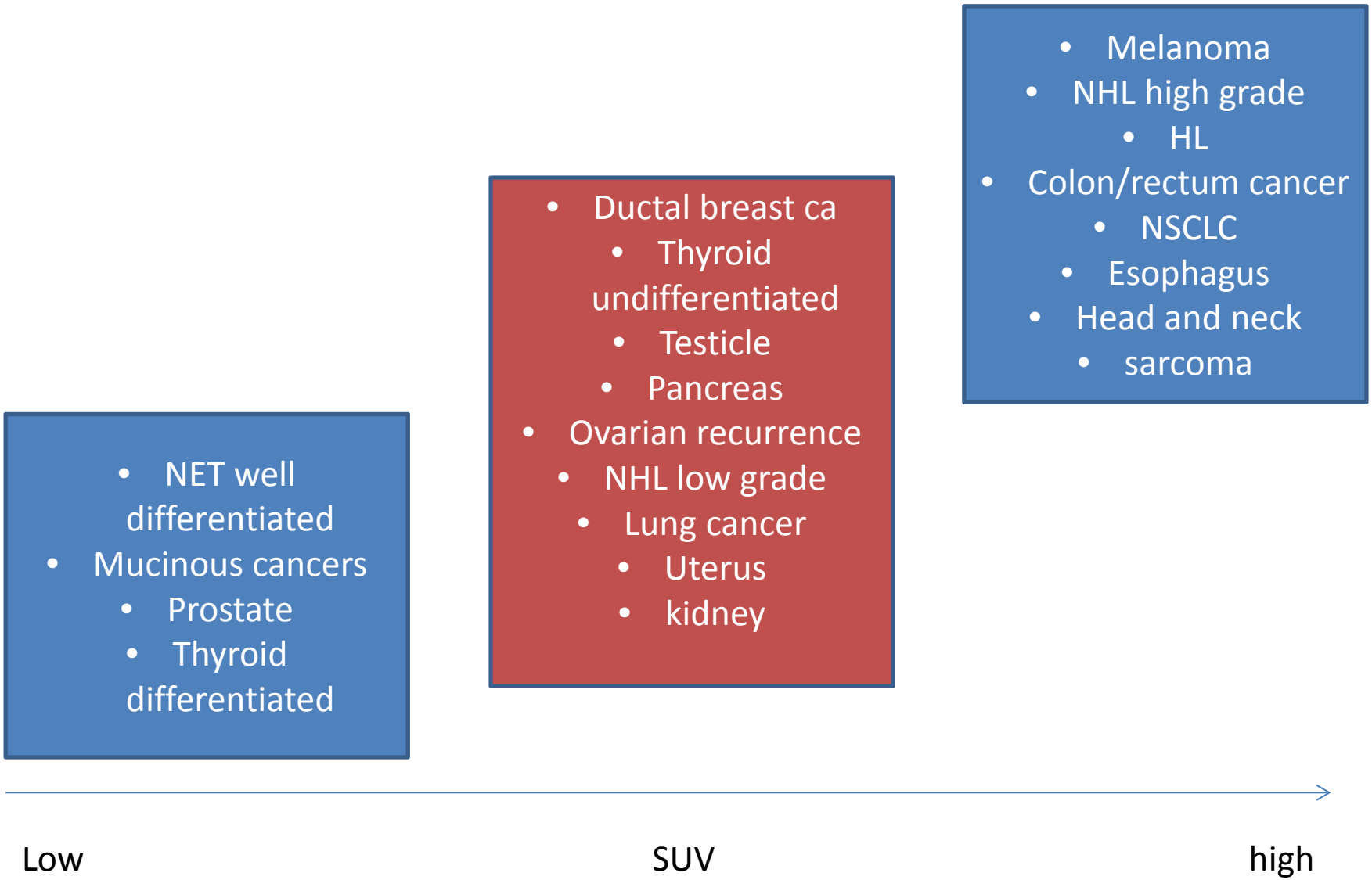
Quantification

Silly

Useless

Value

18F-FDG PET - SUV



18F-FDG PET indications (EANM guidelines)

- Primary presentation:
  - Unknown primary malignancy
  - Differentiation of benign and malignant lesions, eg. Solitary pulmonary nodule, especially of the discrepant clinical and radiological estimates of the likelihood of cancer

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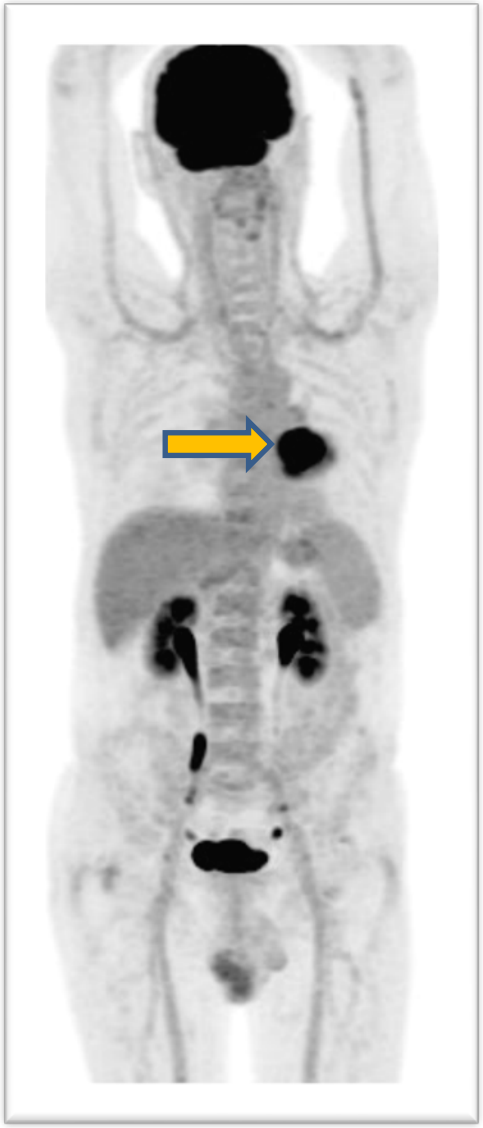
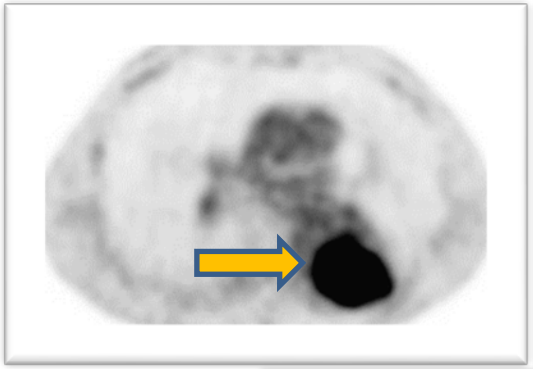
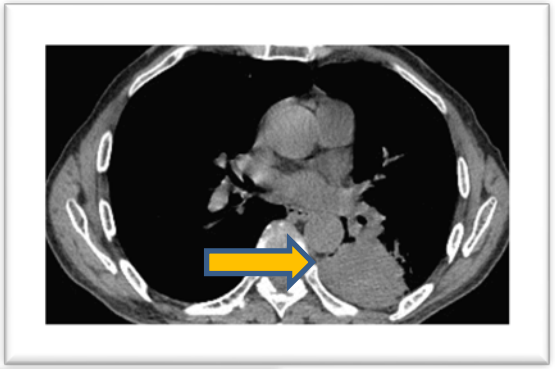
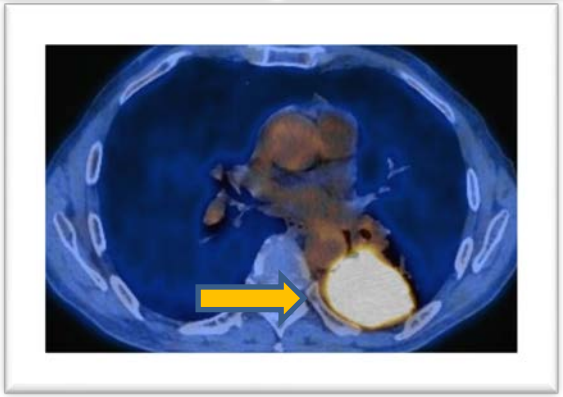
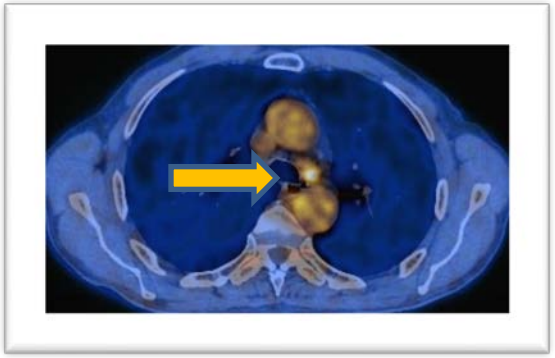
Solitary pulmonary nodule











IJ, male, 49 year-old

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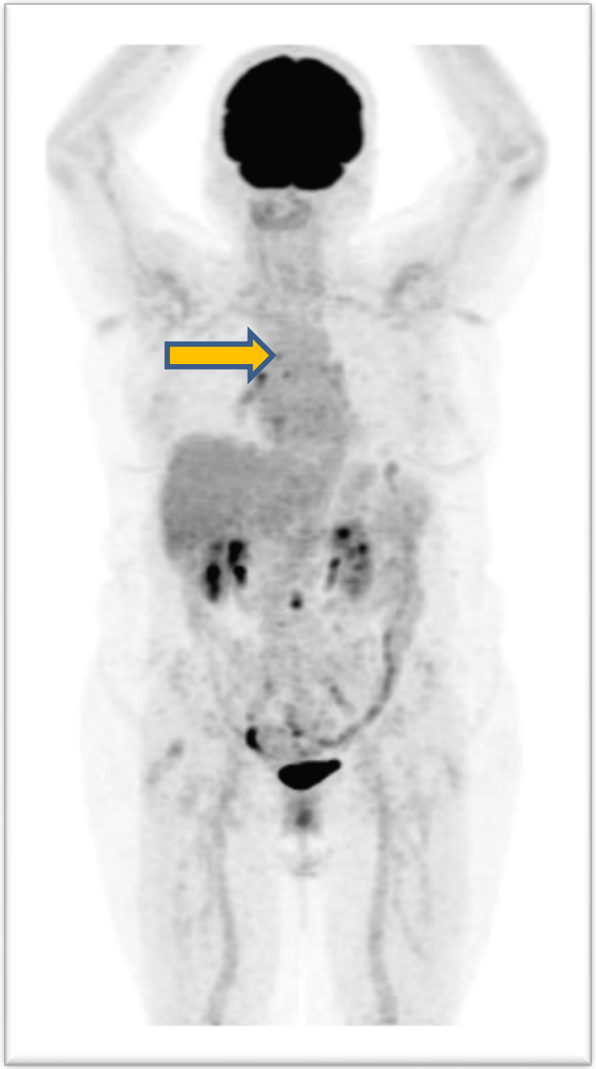
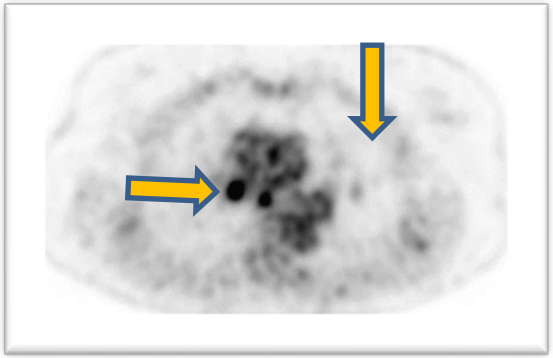
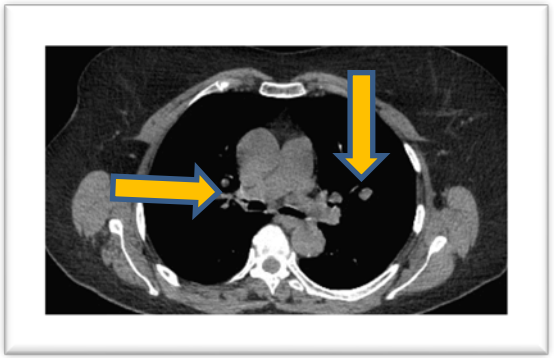
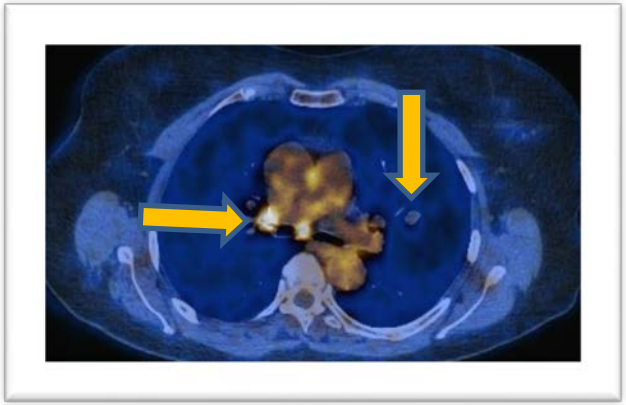
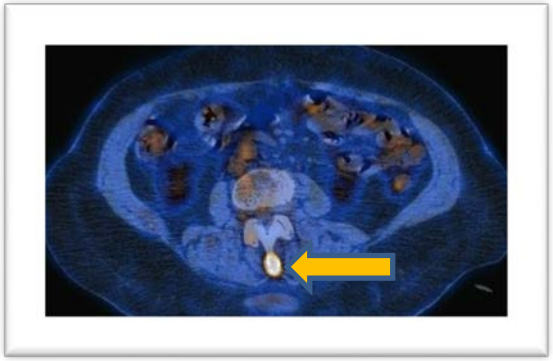
Solitary pulmonary nodule

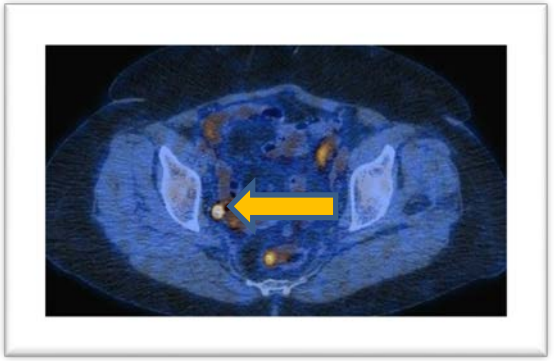












FK, female, 76 year-old

PET-CT evaluation of soliary pulmonary nodules: correlation with maximum standard uptake value and pathology

SUV >2,5

N	Accuracy	sensitivity	specificity	PPV	NPV
186	81	86.7%	50%	90,7%	40%

BUT for SUV <2,5 – 62% chance that the nodule nis malignant

SIM YT, et al. Lung 2013

18F-FDG PET indications (EANM guidelines)

- Staging at presentation:
  - Non-small cell lung cancer; T3 esophageal cancer; Hodgkin's disease, NHL; locally advanced cervical cancer, ENT tumours with risk factors, locally advanced breast cancer

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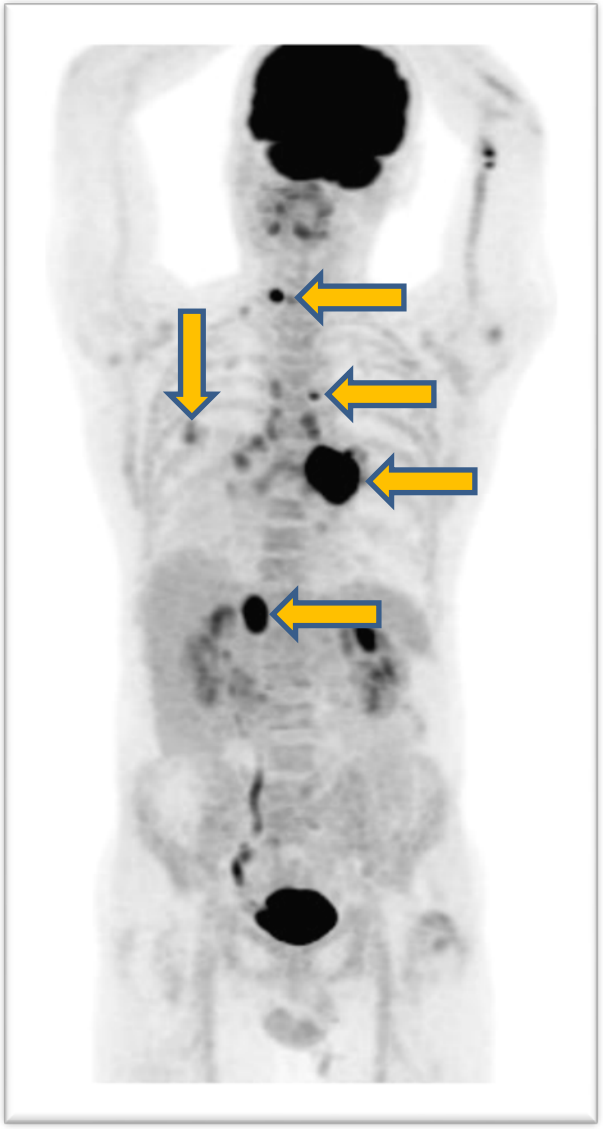
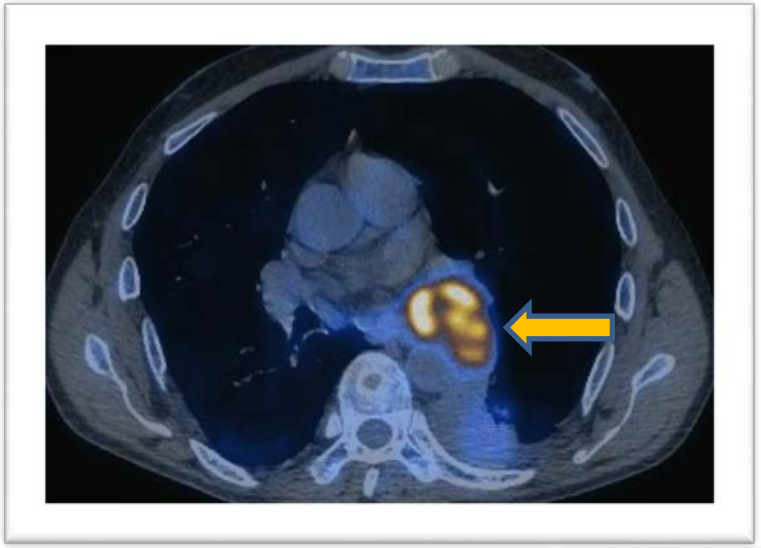
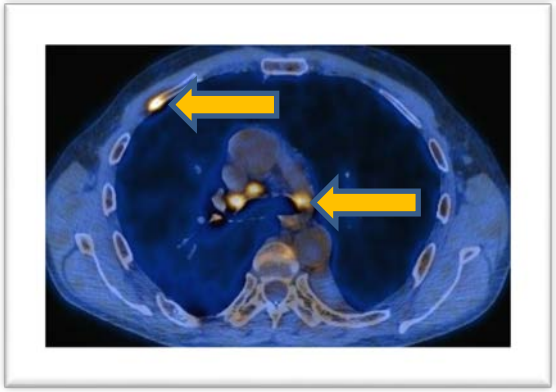
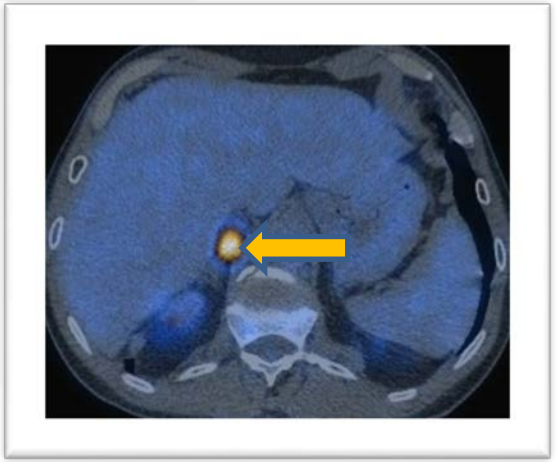
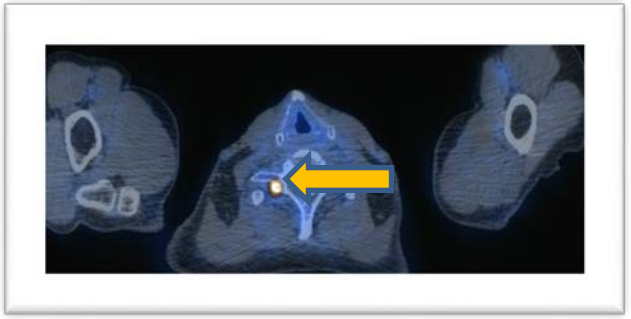
Lung cancer











JK, male, 48 year-old

Effect of PET/CT on Management of Patients with Non–Small Cell Lung Cancer: Results of a Prospective Study with 5-Year Survival Data

Deborah L. Gregory[1], Rodney J. Hicks[2], Annette Hogg[2], David S. Binns[2], Poh Lin Shum[1], Alvin Milner[3], Emma Link[3], David L Ball[1], and Michael P. Mac Manus[1]

Impact of PET/CT on Patient Management Plan

Before PET/CT		After PET/CT		PET/CT impact			
Management plan	No. of patients	Management plan	No. of patients	High	Medium	Low	None
Observation	1	Surgery	1	1	0	0	0
Invasive biopsy	28	Invasive biopsy	9	19	0	9	0
		Observation	1				
		Surgical	9				
		Radical RT*	3				
		Palliative†	6				
Surgery	80	Surgery	54	26	0	50	4
		Diagnostic (invasive biopsy)	2				
		Observation	2				
		Radical RT‡	8				
		Radical RT, for both NSCLC and PET-detected pharynx cancer	1				
		Palliative§	13				
Radical RT	49	Radical RT as planned‖	19	23	7	18	1
		Radical CRT, field increased	6				
		Radical CRT, field decreased	1				
		Surgery	4				
		Induction chemotherapy, followed by surgery	1				
		Palliative chemotherapy or RT¶	18				
Palliative	10	Palliative chemotherapy or RT, as planned#	8	2	2	6	0
		Palliative CRT, RT field increased	2				
Total	168		168	71 (42%)	9 (5%)	83 (49%)	5 (3%)

JNM, 2012

Effect of PET/CT on Management of Patients with Non–Small Cell Lung Cancer: Results of a Prospective Study with 5-Year Survival Data

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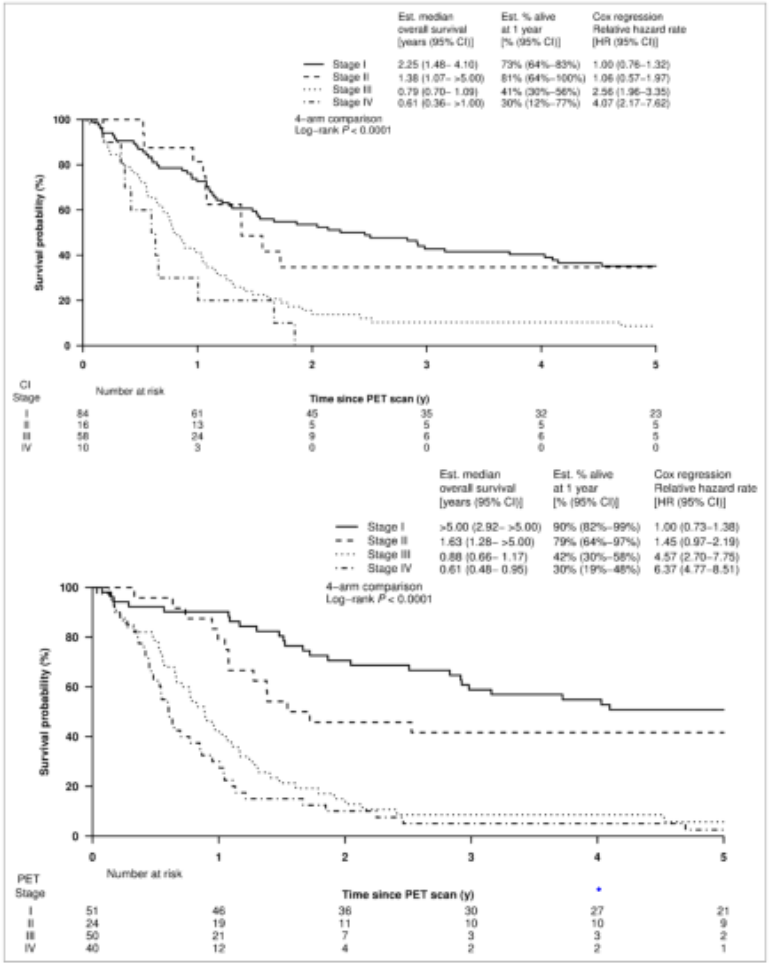

FIGURE 1. Survival according to stage groupings determined by conventional imaging (top) or PET/CT (bottom). Est = estimated.

JNM, 2012

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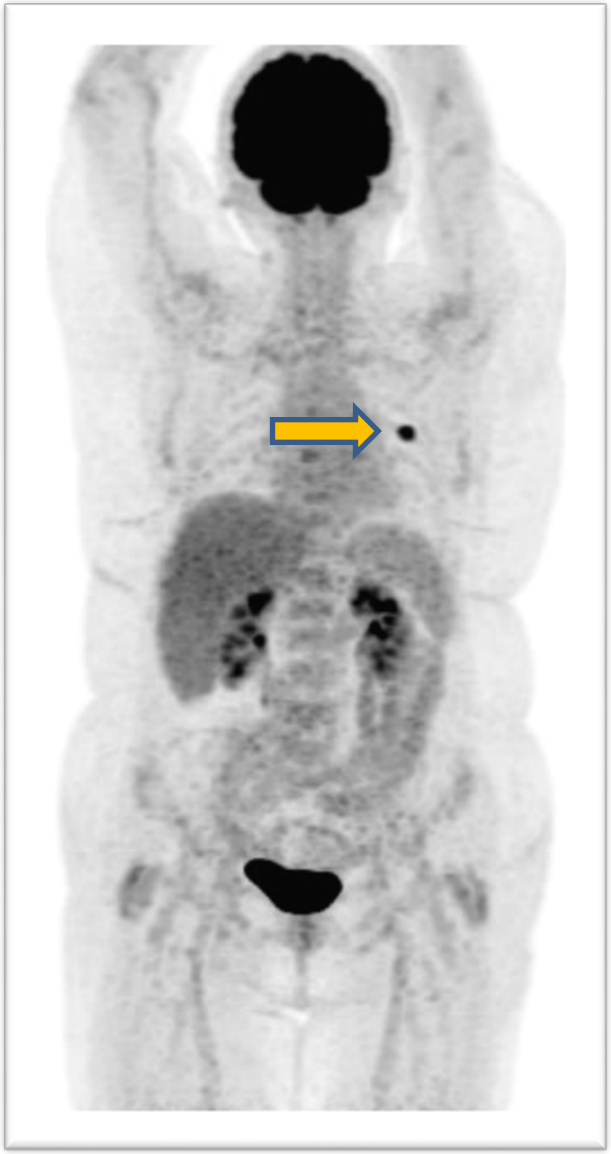
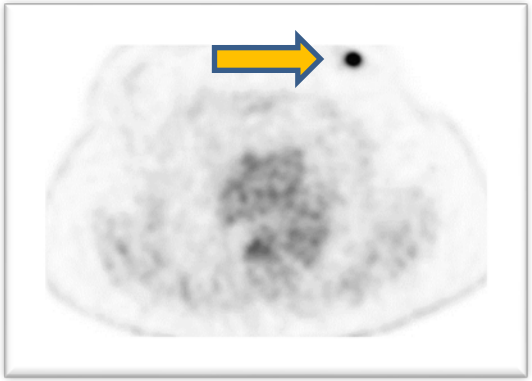
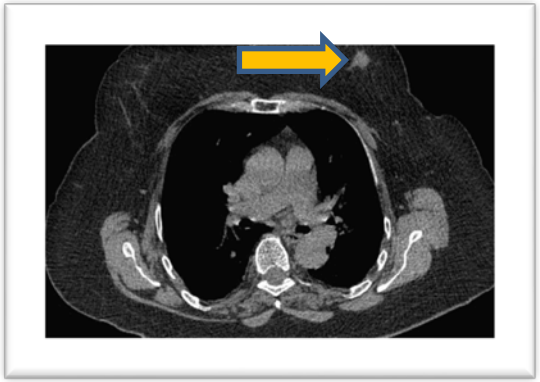
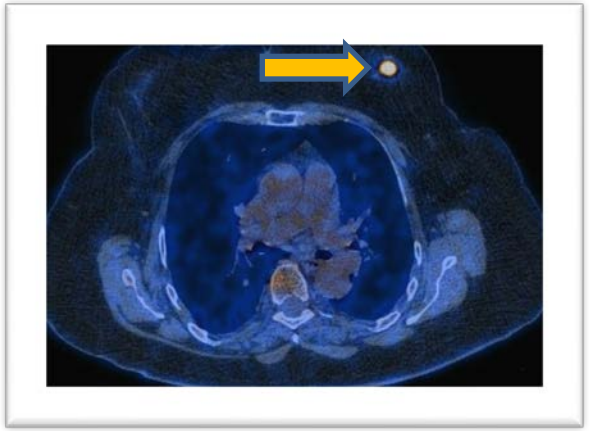
Breast cancer









ABB, female, 67 year-old

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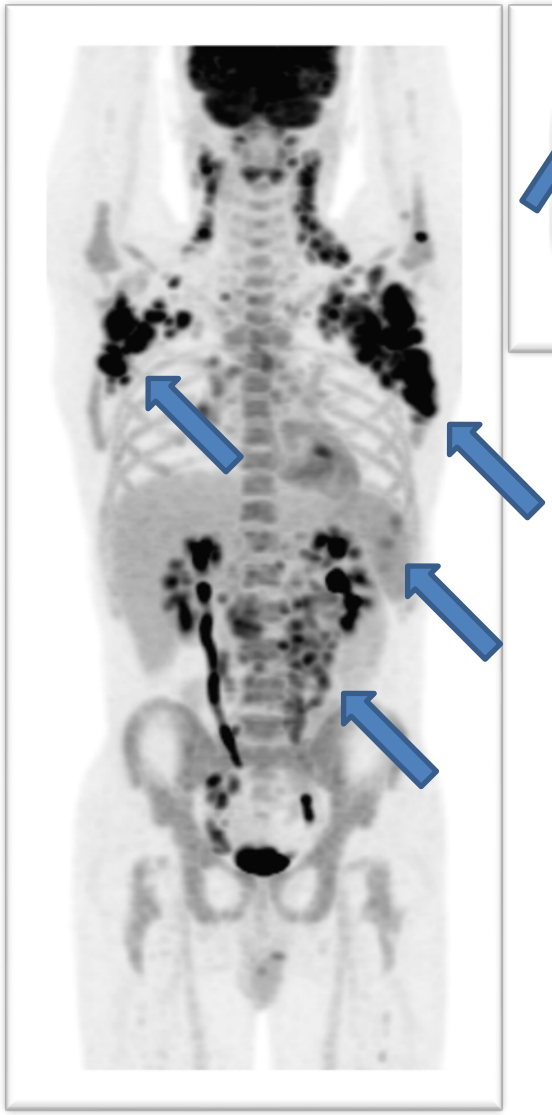
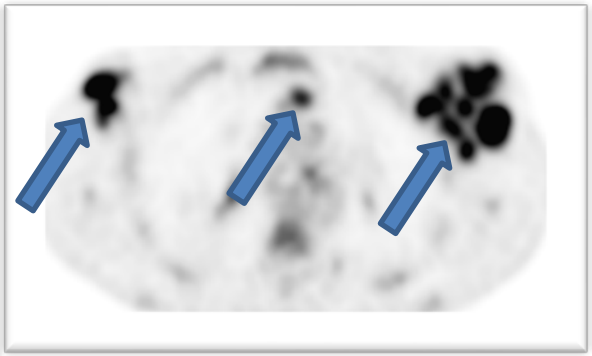
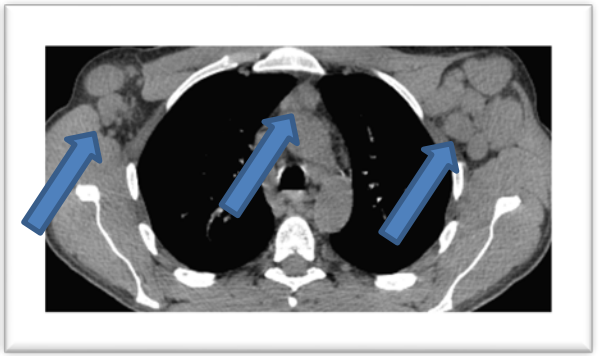
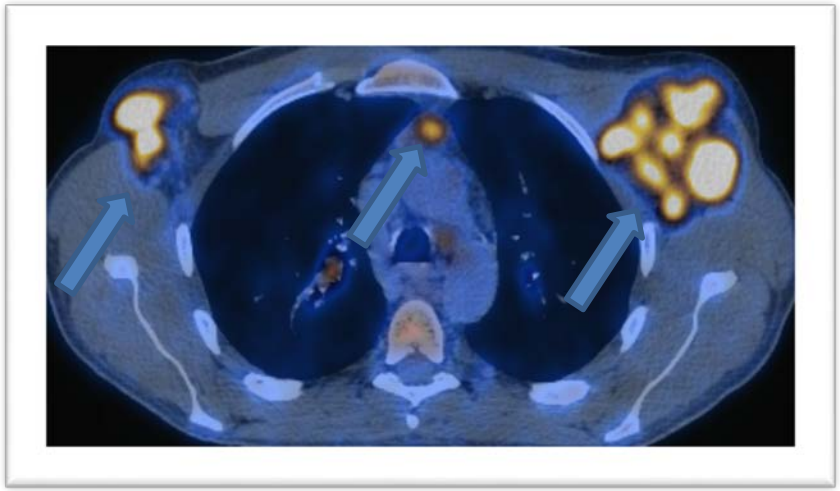
Hodgkings disease - staging









AS, male, 38 year-old

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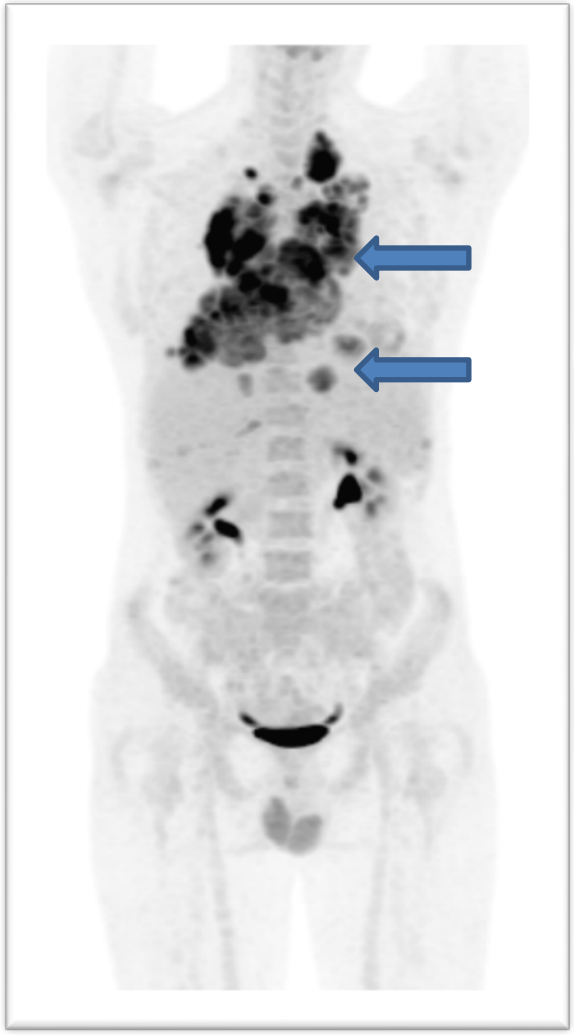
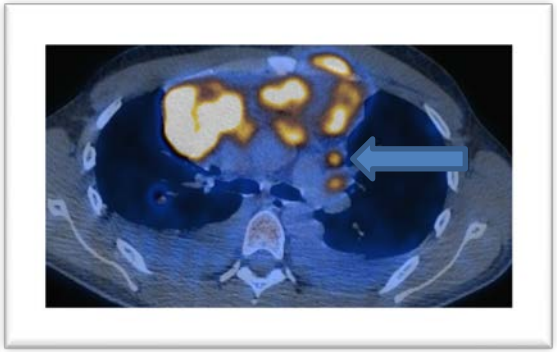
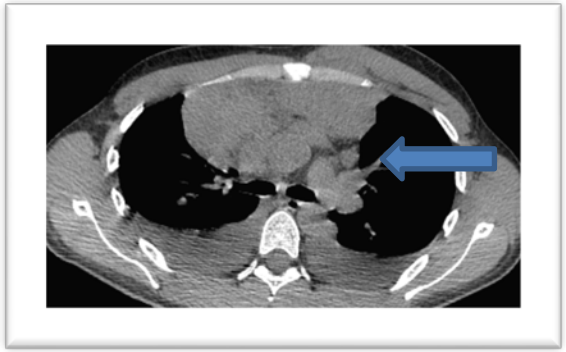
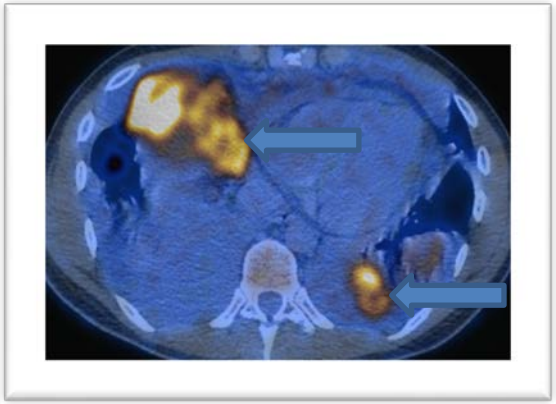
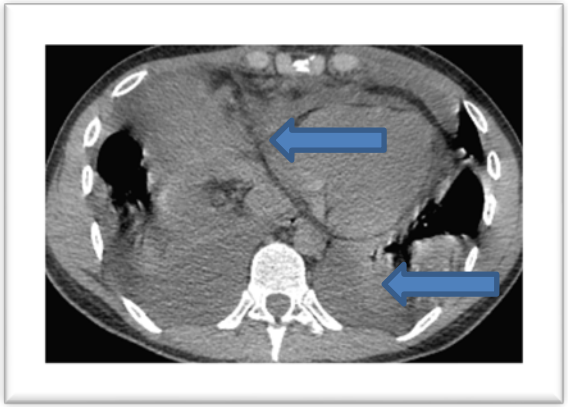
Hodgkings disease - staging









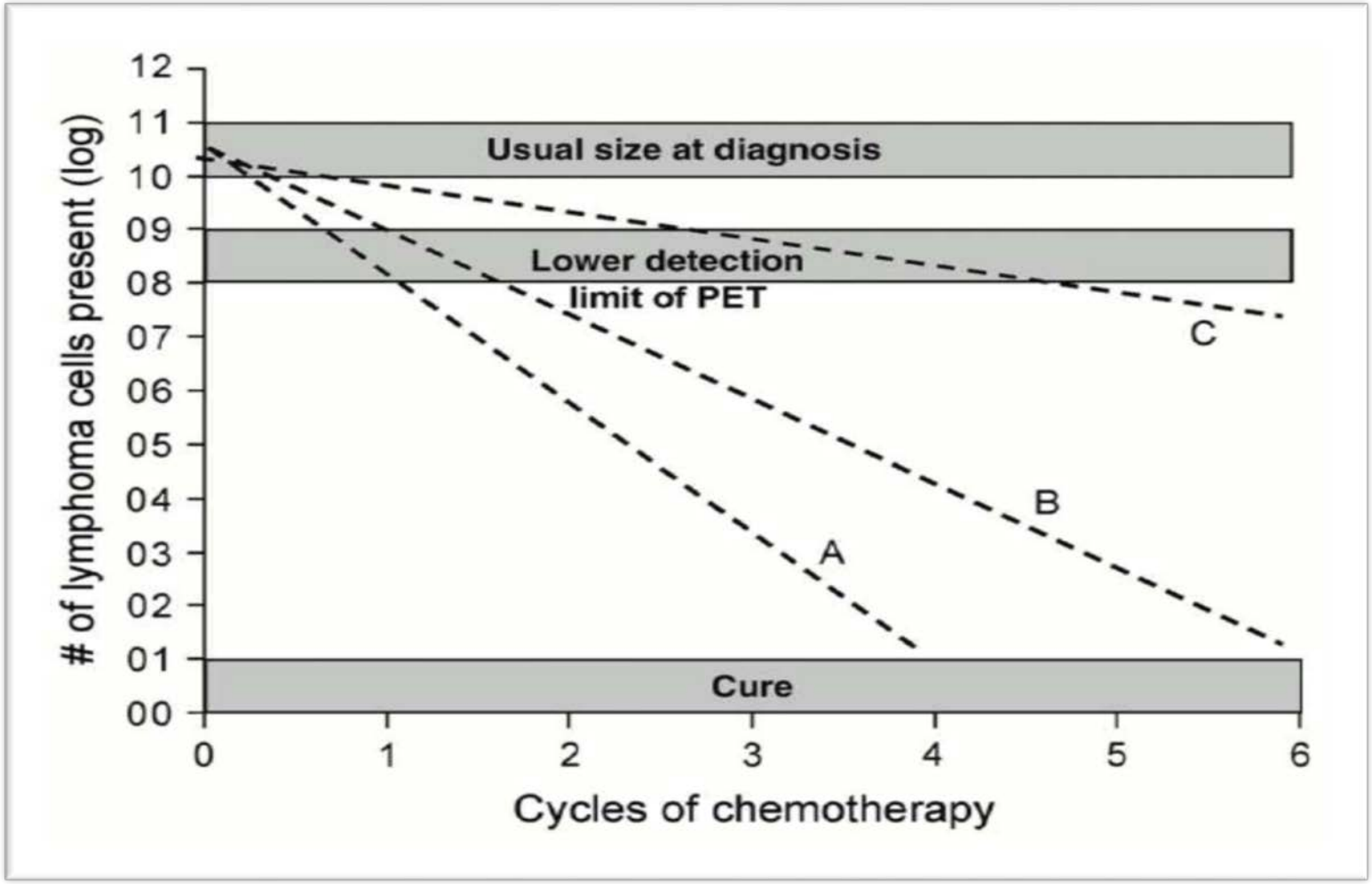


AM, male, 26 year-old

18F-FDG PET indications (EANM guidelines)

- Response evaluation:
  - Malignant lymphoma ; GIST

PET/CT and the response to the therapy



Kasamon YL. Integrating PET and PET/CT into the risk-adapted therapy of lymphoma. J Nucl Med 2007,48 (suppl 1)

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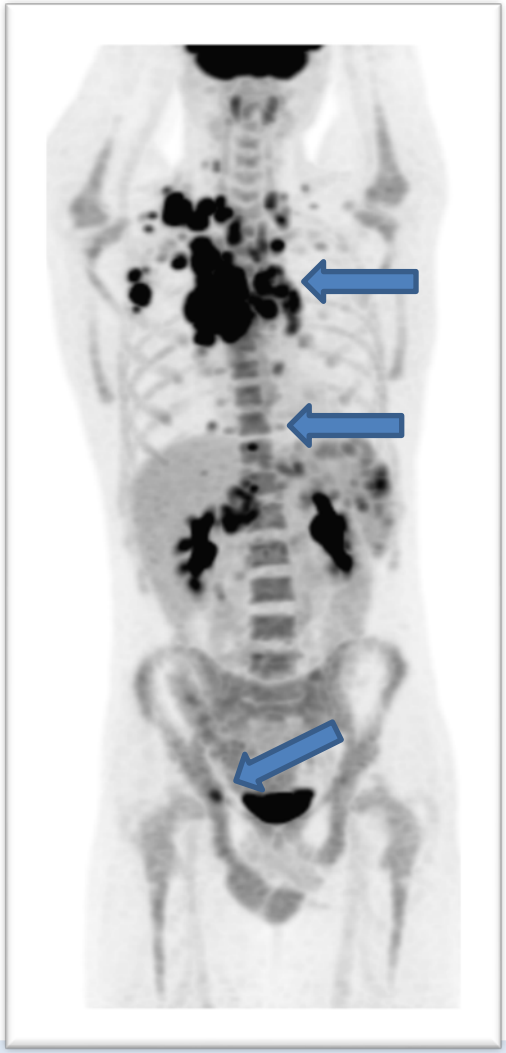
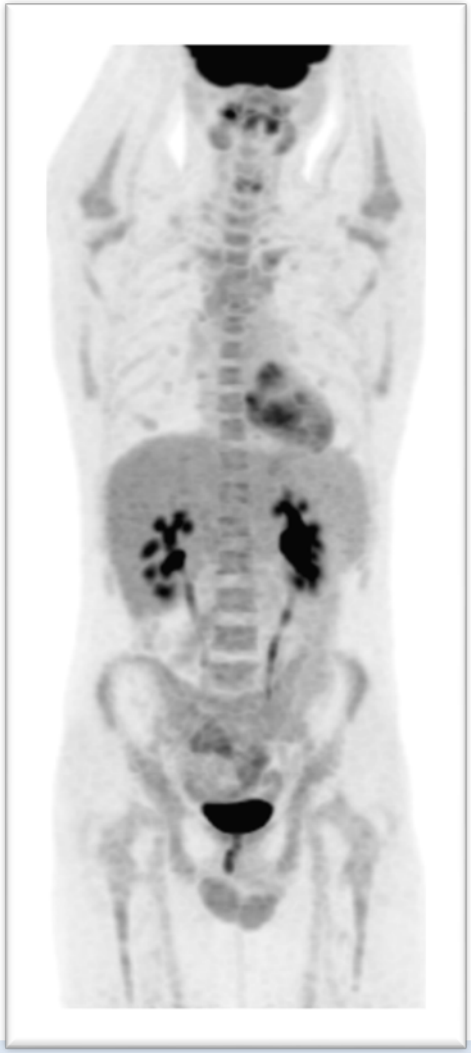
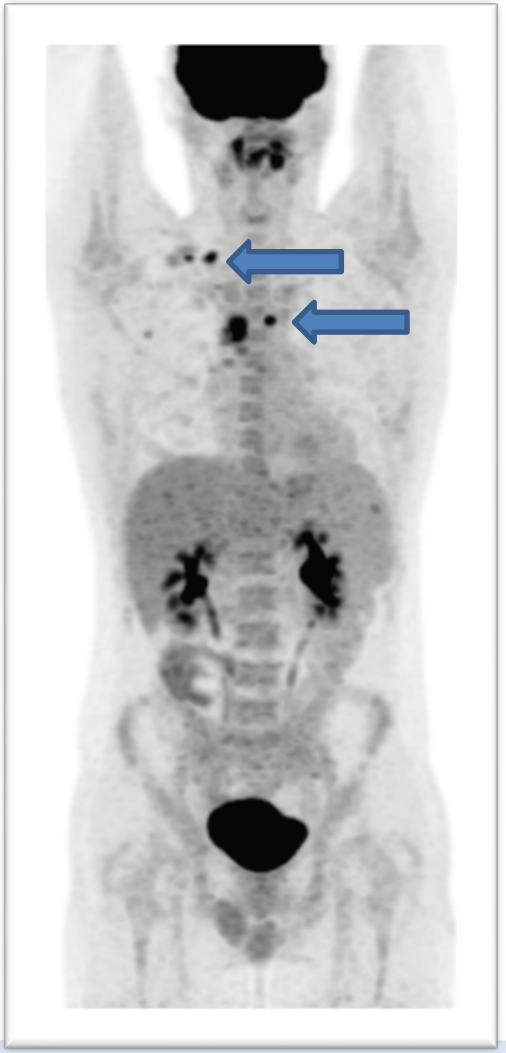
Hodgking's disease – response evaluation

Ann Arbor IV







MK
male
20 year-old

20.12.2012	11.02.2013	08.08.2013
before treatment	I control examination	II control examination

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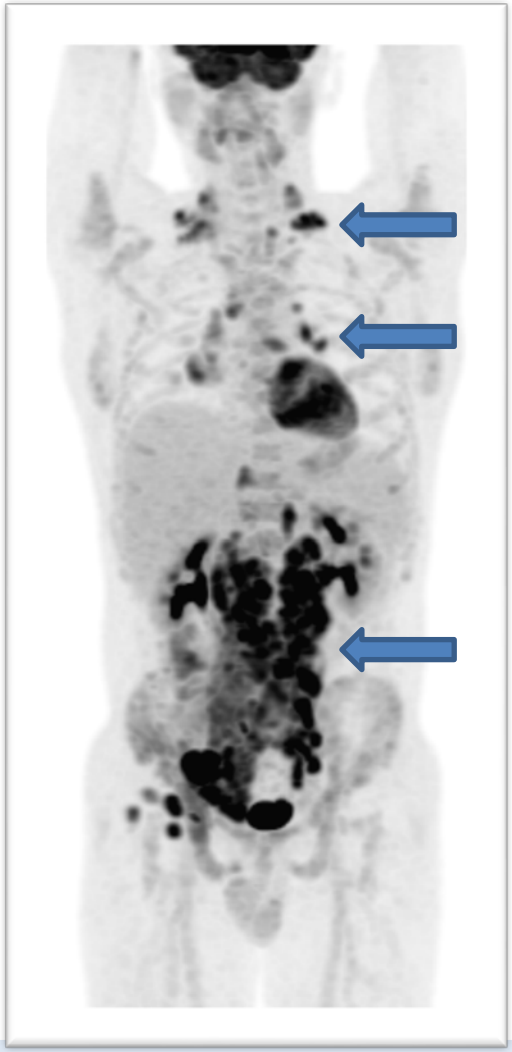
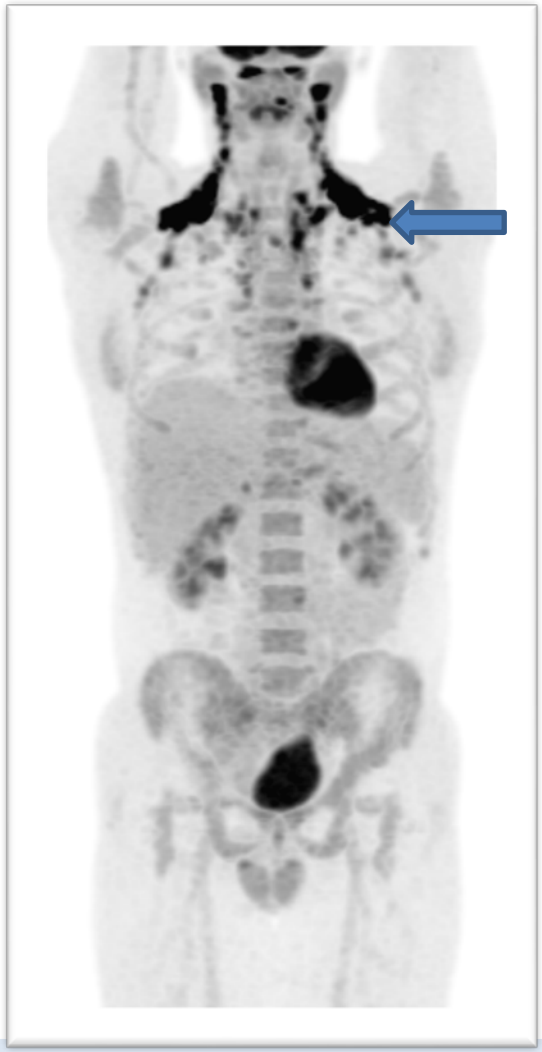
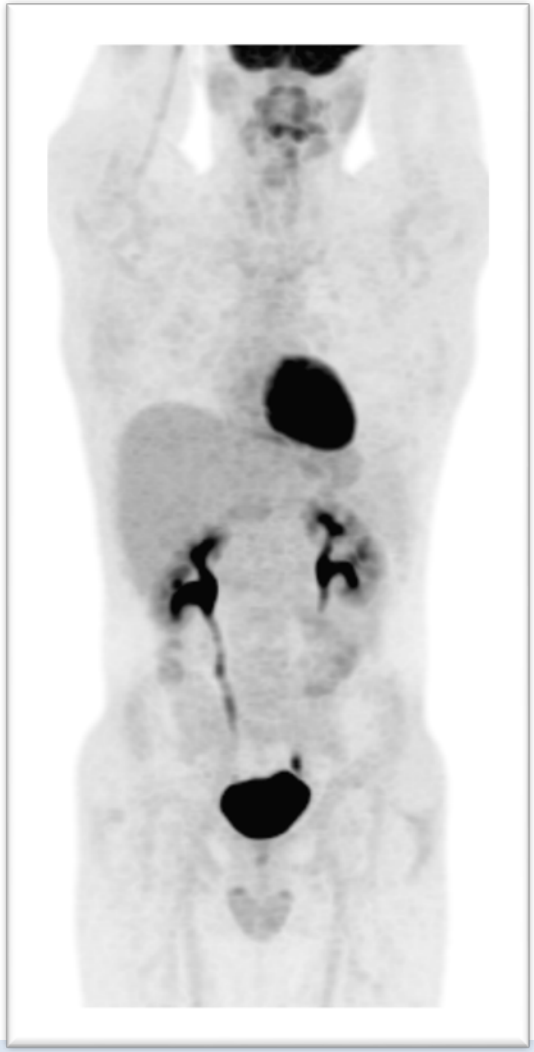
Hodgking's disease – response evaluation

Ann Arbor III







PB
male
34 year-old

6.12.2012	17.1.2013	27.06.2013
before treatment	I control examination	II control examination

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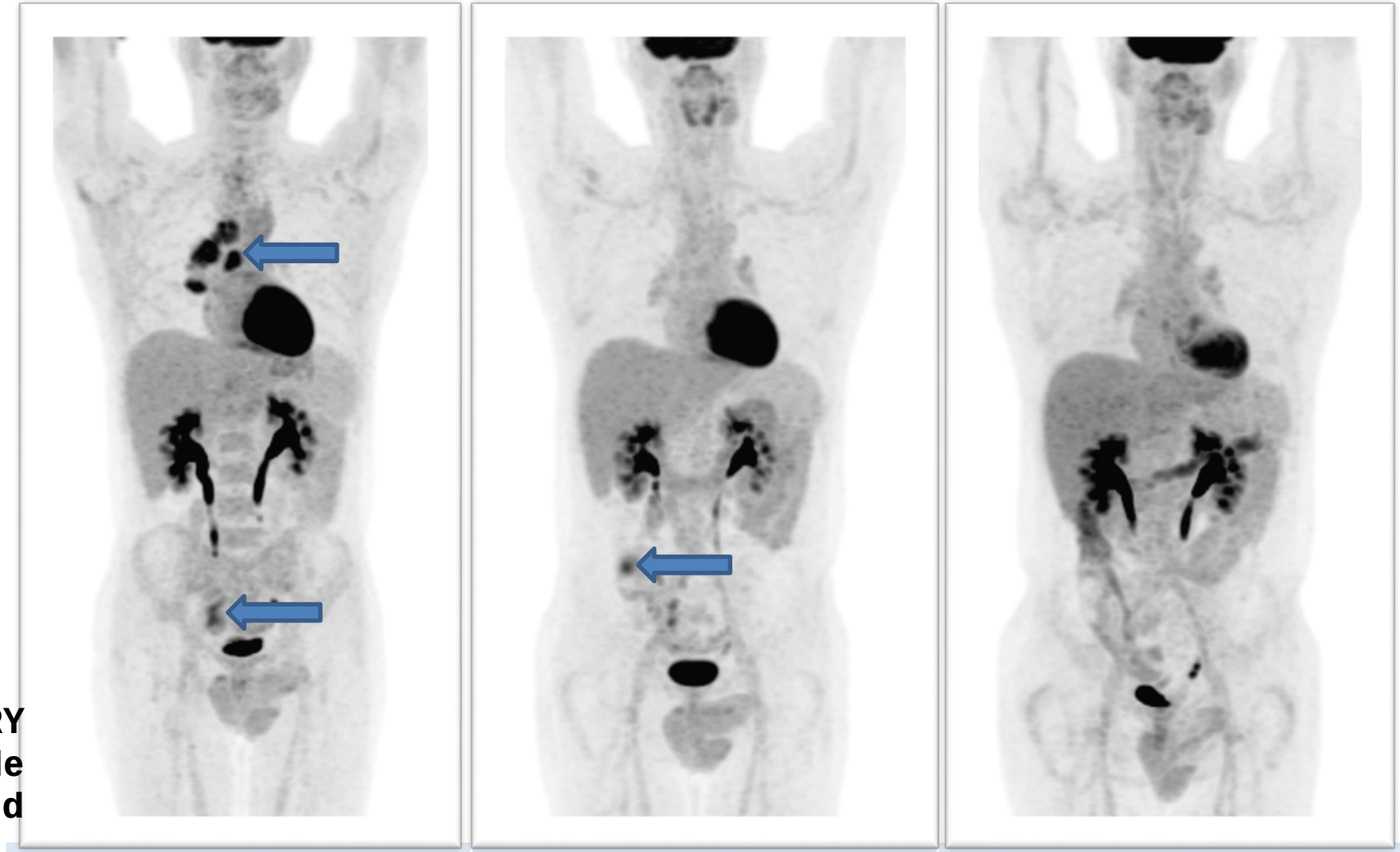
Hodgking's disease – response evaluation

Ann Arbor II



ARY
male
44 year-old

4.2.2013	8.4.2013	29.07.2013
before treatment	I control examination	II control examination

Eur J Nucl Med Mol Imaging (2012) 39:4–12
DOI 10.1007/s00259-011-1916-8

ORIGINAL ARTICLE

Early interim ^{18}F-FDG PET in Hodgkin's lymphoma: evaluation on 304 patients

Pier Luigi Zinzani · Luigi Rigacci · Vittorio Stefoni · Alessandro Broccoli · Benedetta Puccini · Antonio Castagnoli · Luca Vaggelli · Lucia Zanoni · Lisa Argnani · Michele Baccarani · Stefano Fanti

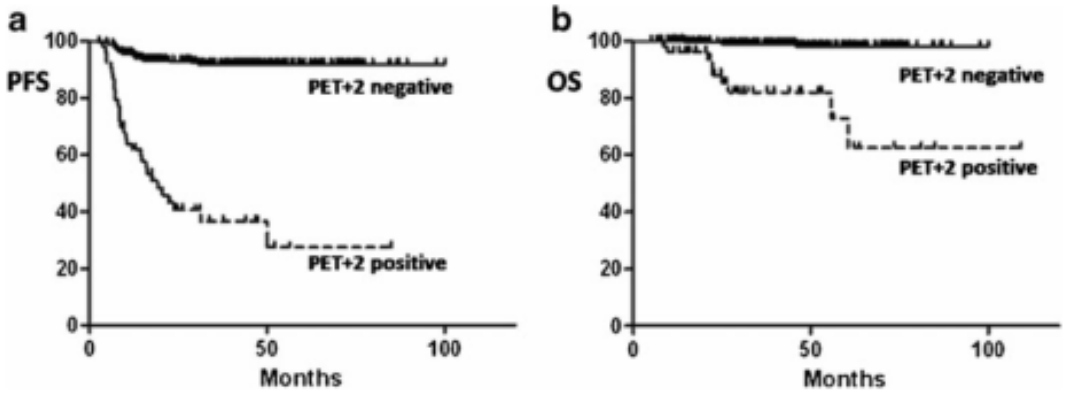


Fig. 2 PFS (**a**) and OS (**b**) curves for the entire study population in relation to the PET+2 results

18F-FDG PET indications (EANM guidelines)

- Relapse for in the event of potentionally curable disease

18F-FDG PET indications (EANM guidelines)

- Establishing and localizing disease sites as a cause of elevated serum markers: colorectal, thyroid, ovarian, cervix, melanoma, breast and germ-cell tumors

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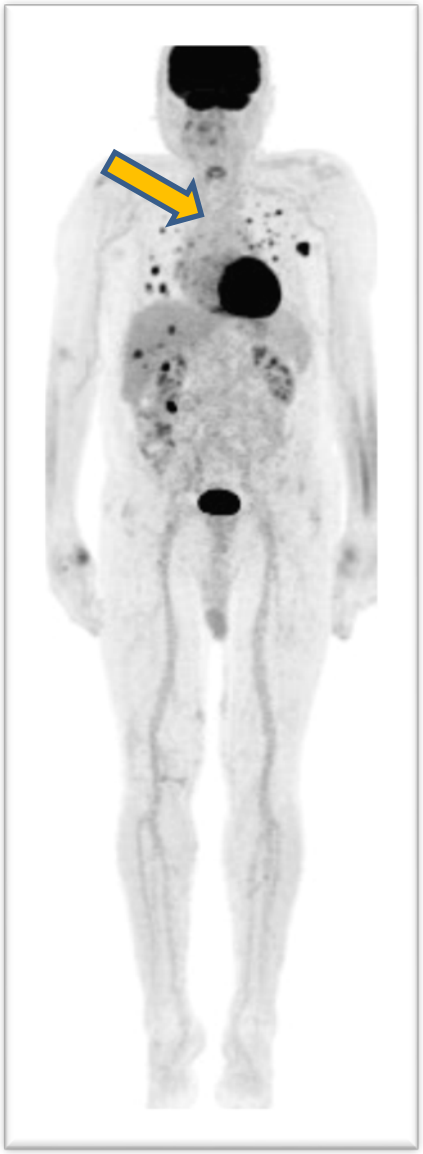
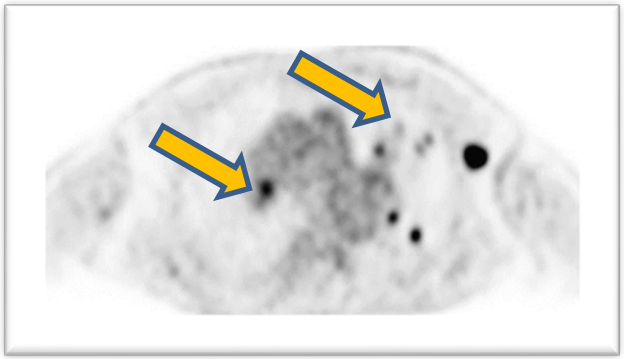
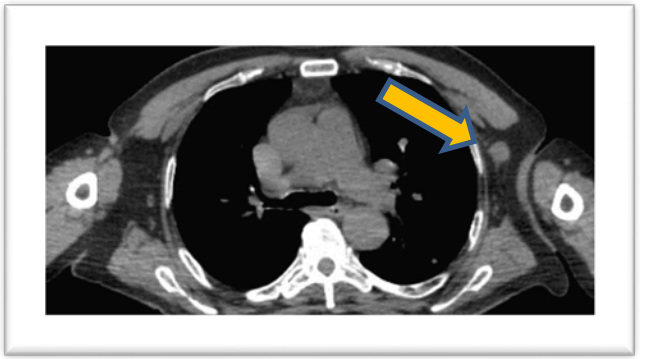
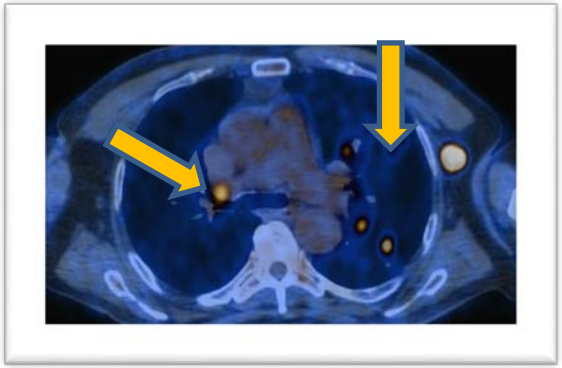
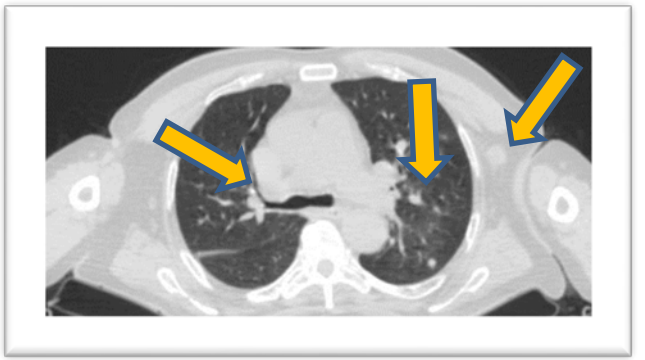
Melanoma











AH, male, 74 year-old

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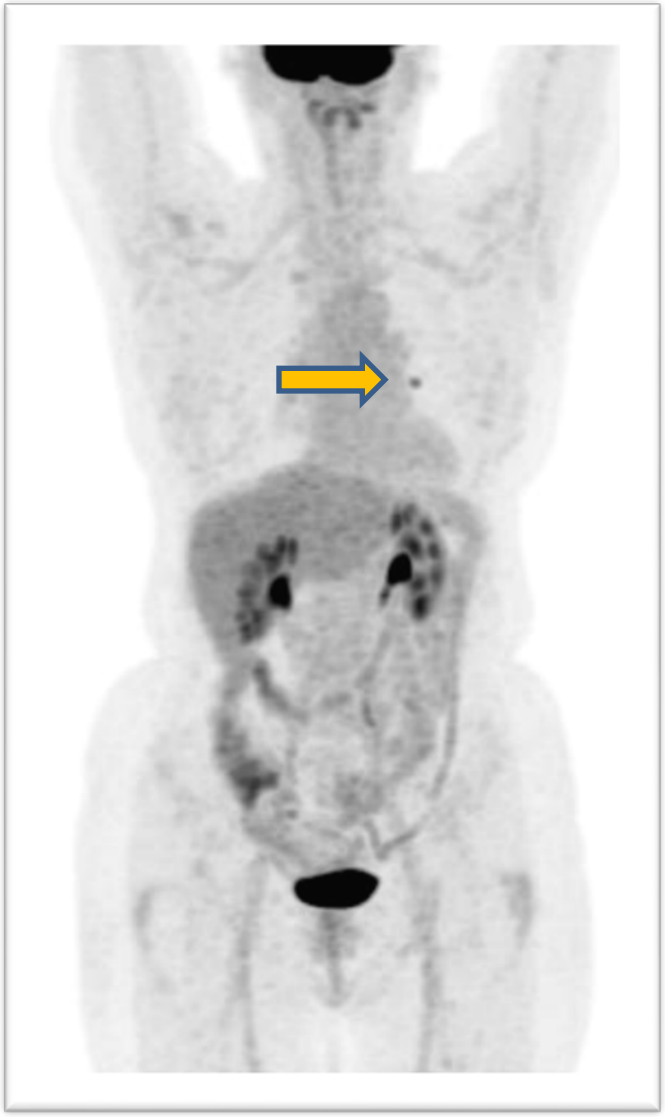
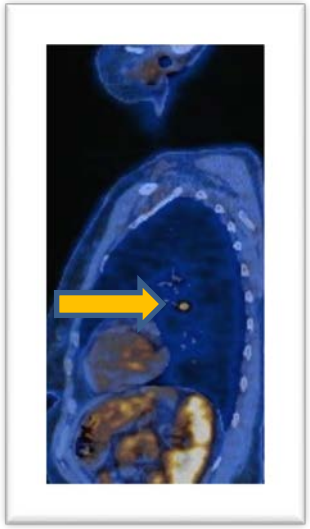
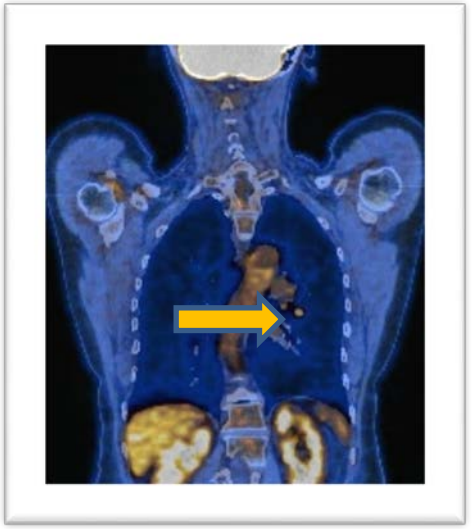
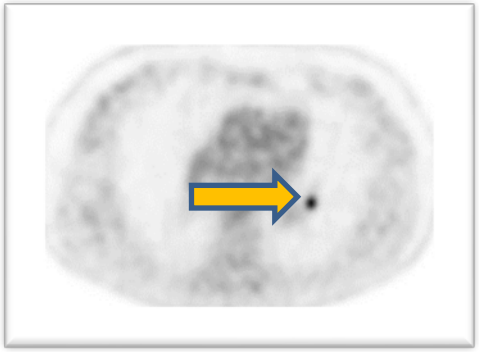
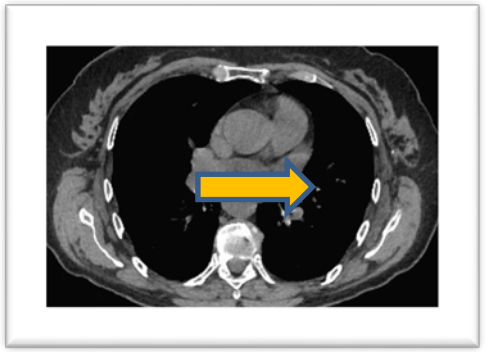
Thyroid cancer

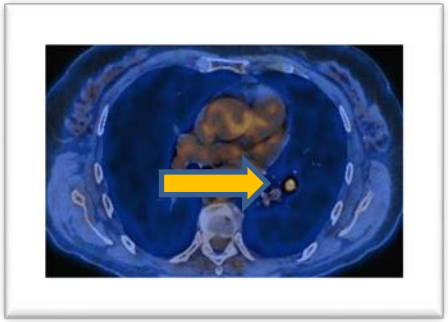








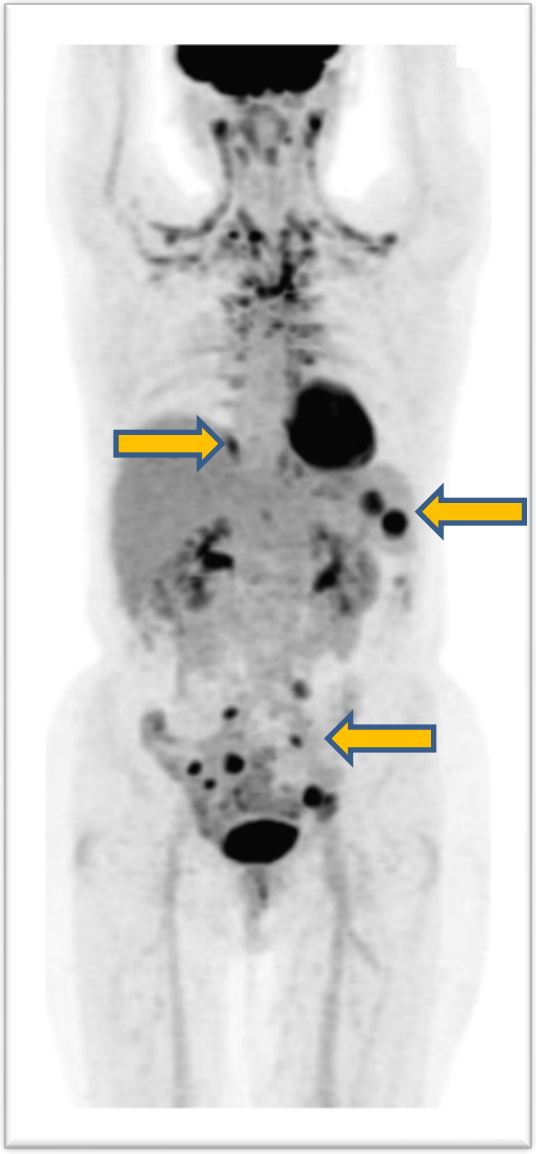


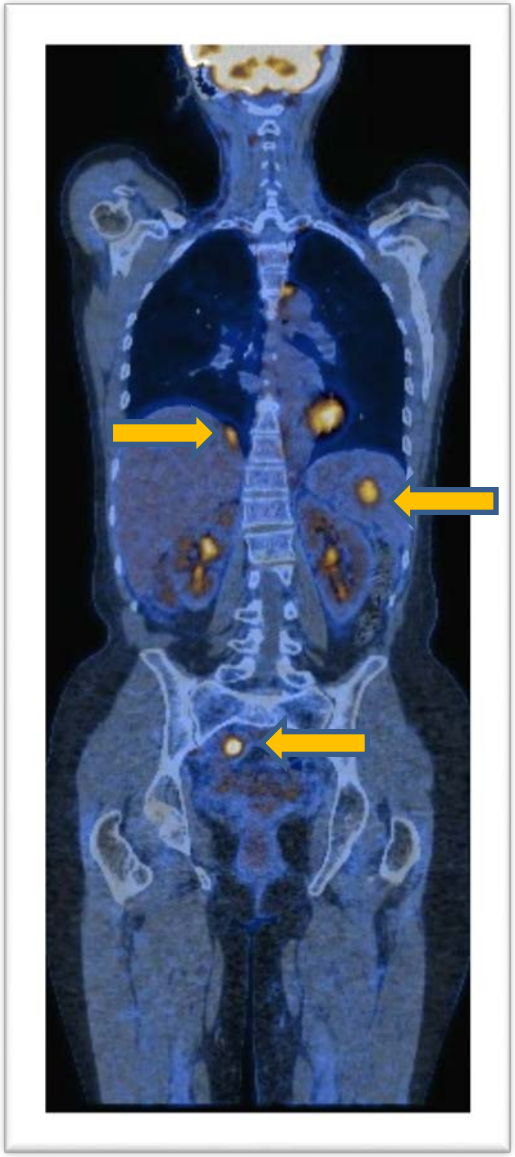


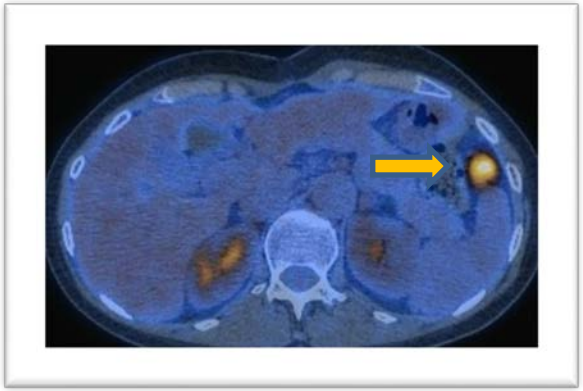
DP, female, 68 year-old

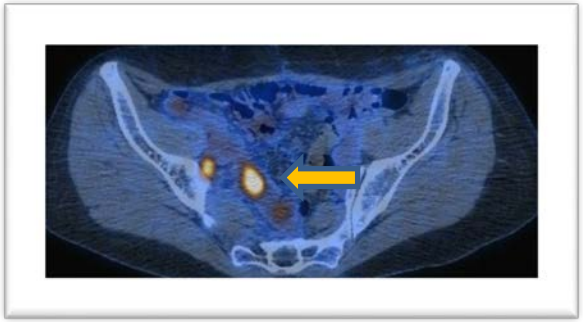
Szpital Uniwersytecki w Krakowie

Ovarian tumor





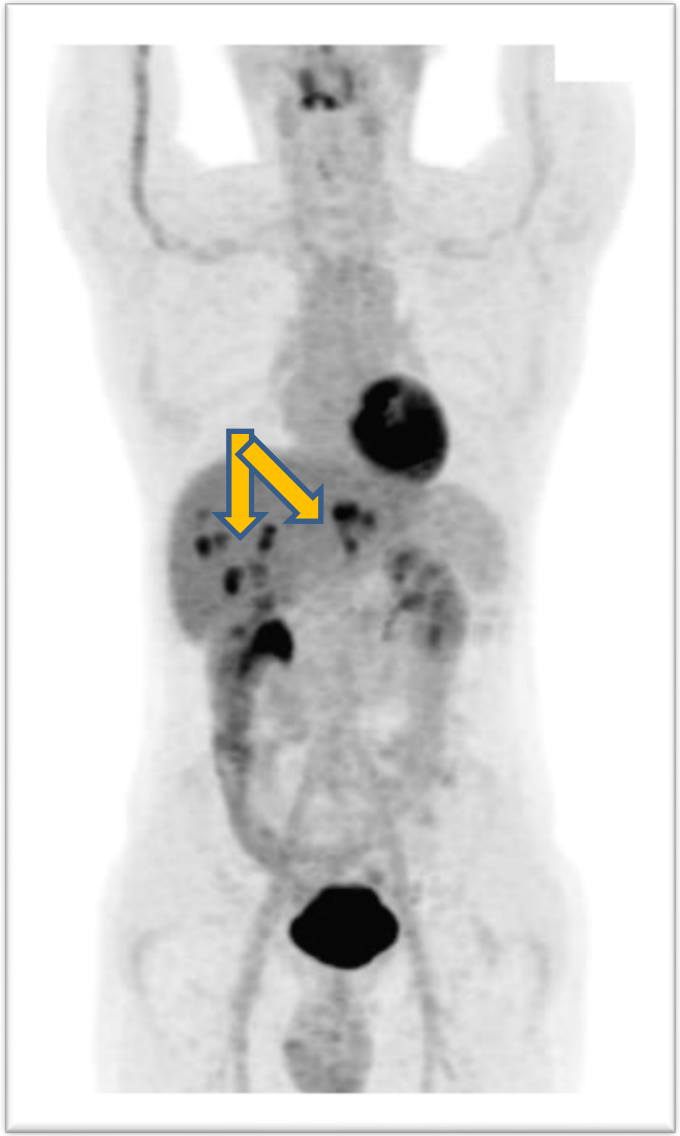


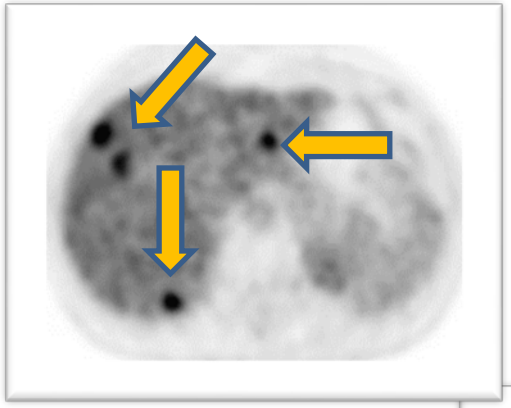


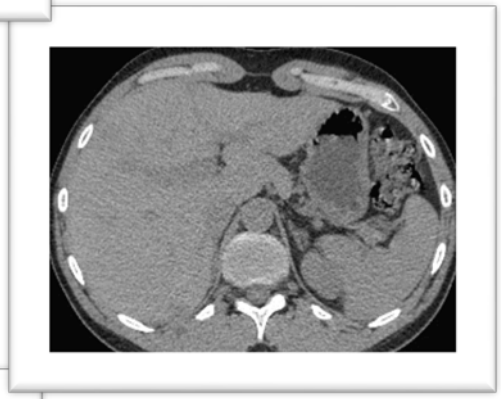
HB, female, 49 year-old

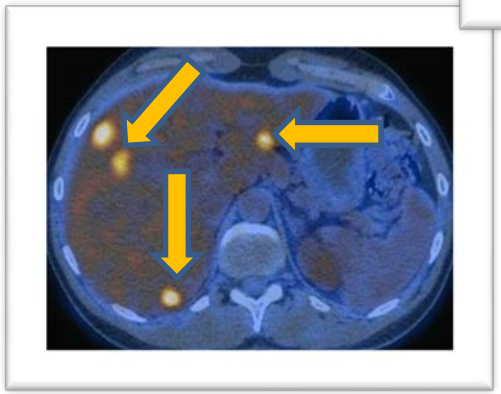
Szpital Uniwersytecki w Krakowie

Colorectal cancer









JT, male, 38 year-old

18F-FDG PET indications (EANM guidelines)

- Image guided biopsy and radiation planning

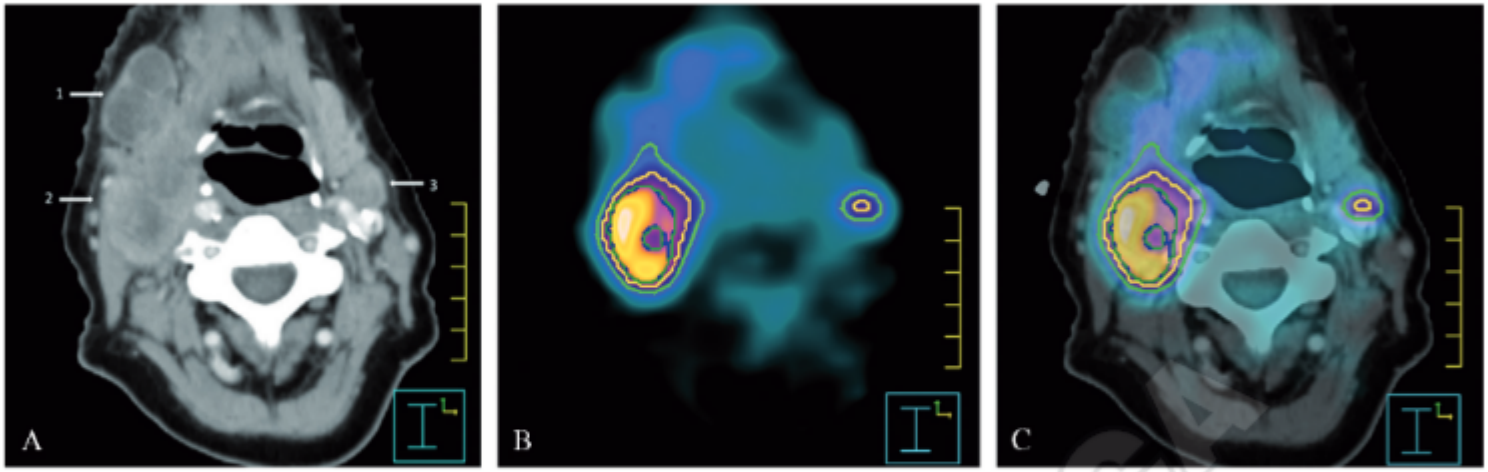


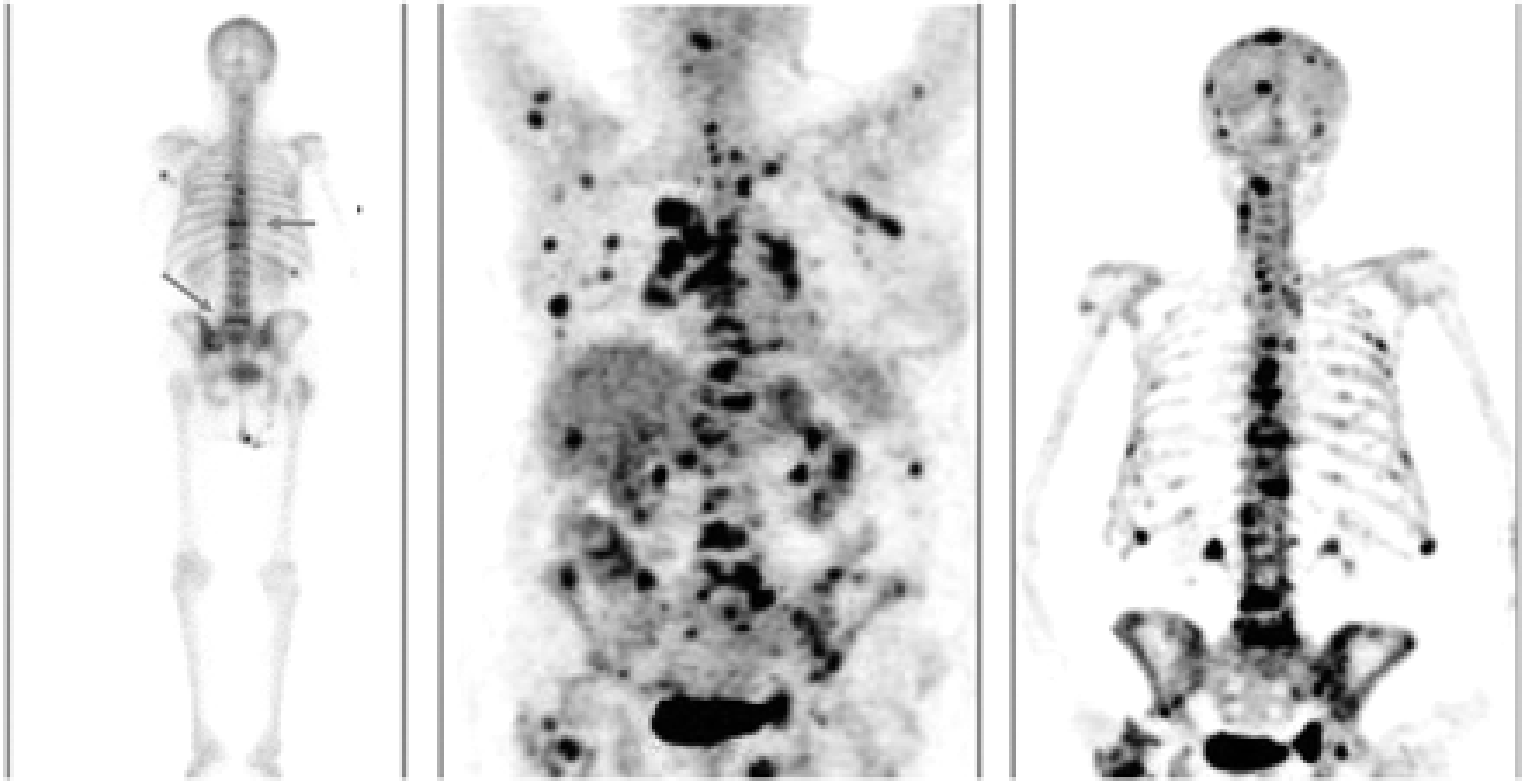
Figure 3.—A-C) CT-scan, corresponding FDG-PET scan, and fused image of a patient with a T4 oropharyngeal carcinoma showing three lymph nodes. Right (arrow 1): an overtly metastatic node of 21 mm in the shortest axial diameter with central necrosis that was not identified by FDG-PET. Right (arrow 2): a node of 23 mm in the shortest axial diameter that was included in the PET-based GTV obtained by visual interpretation (light green), fixed threshold of 40% of maximum signal intensity (yellow), fixed threshold of 50% of maximum signal intensity (blue) and when applying adaptive threshold based on signal-to-background ratio (dark green). The pattern of FDG uptake in this particular node suggests intranodal tumor heterogeneity. Left (arrow 3): a node of 13 mm in the shortest axial diameter included in the PET-based GTV obtained by visual interpretation (light green) and the fixed threshold of 40% of maximum signal intensity (yellow).

Clinical practice – beyond 18F-FDG PET

- 18F-fluoride
- 68Ga-somatostatin analogues
- 18F or 11C- choline
- Labelled aminoacids

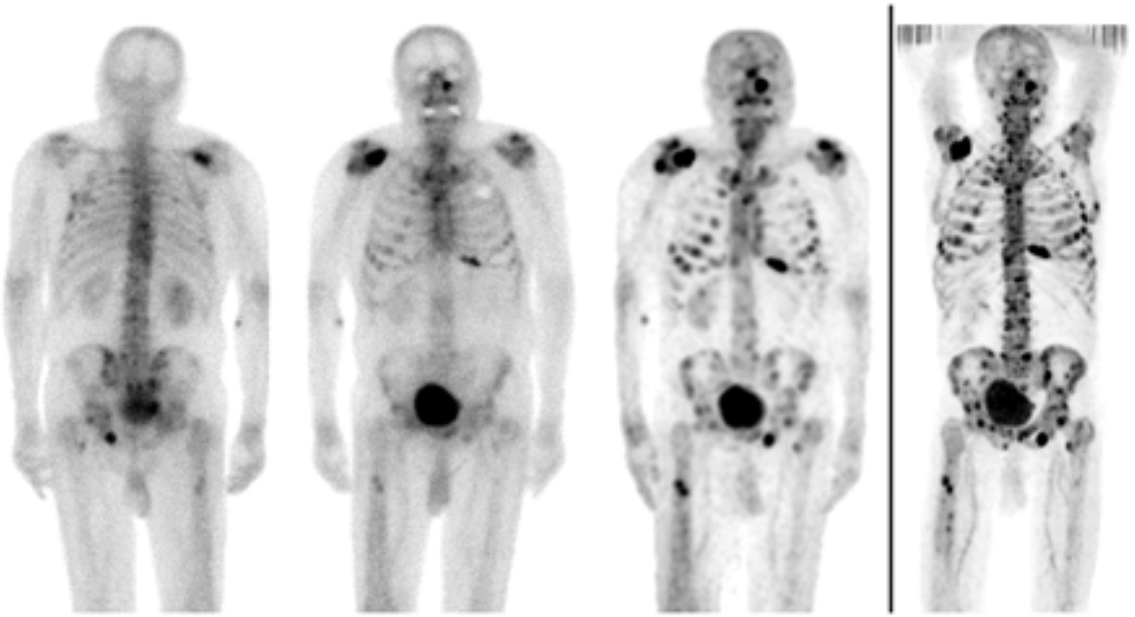
J Nucl Med January 2008 vol. 49 no. 1 68-78

99mTcMDP vs 18F-FDG vs 18F-NaF

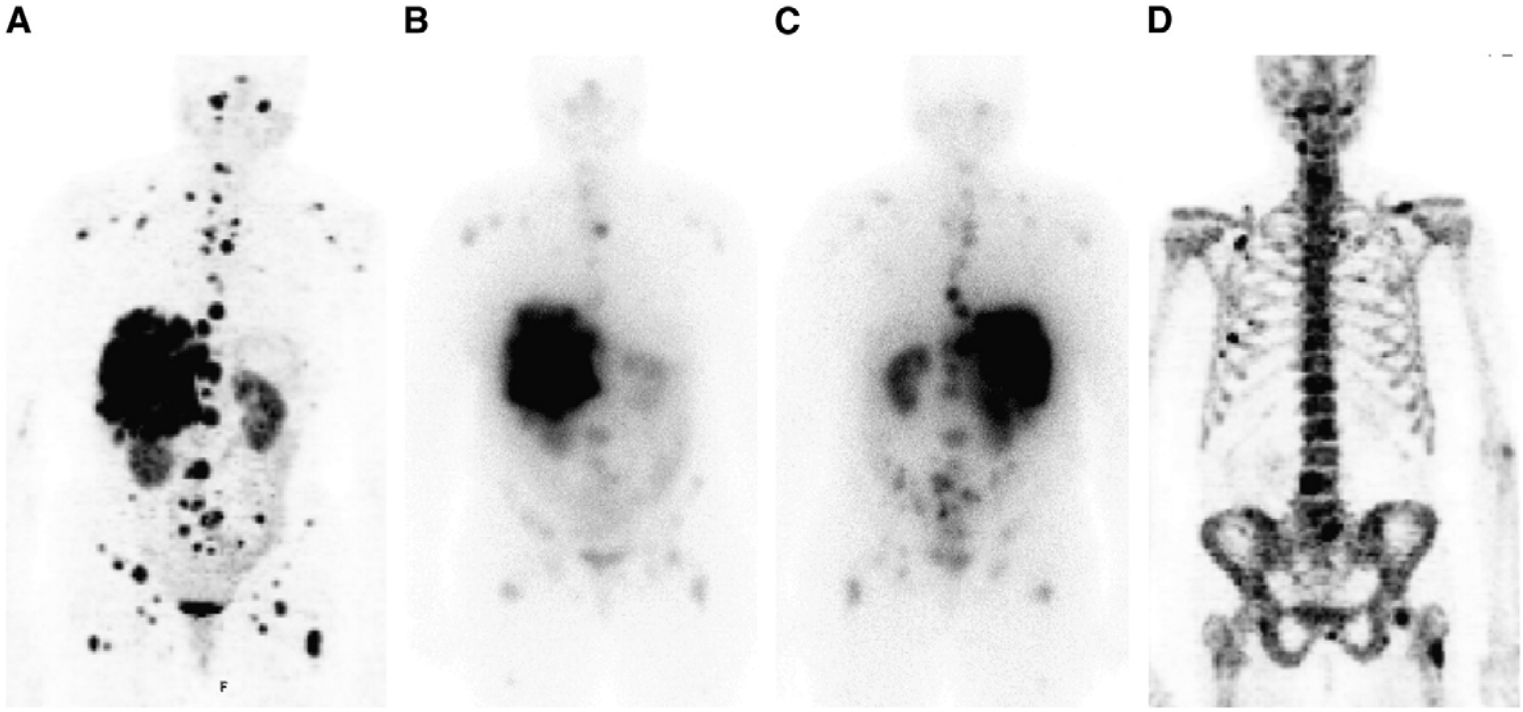


J Nucl Med January 2008 vol. 49 no. 1 68-78

99mTcMDP vs. 18F-fluoride



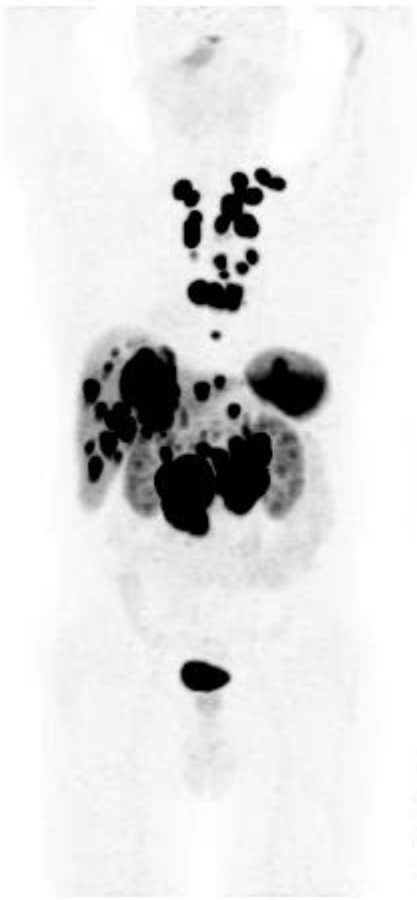
68Gallium SRS PET vs 111In –SRS vs 18F-fluoride

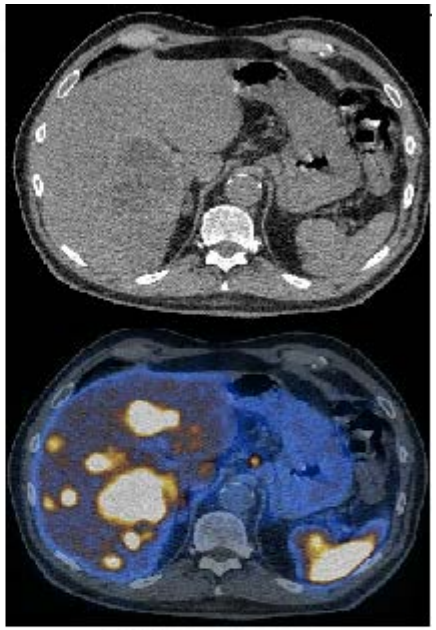


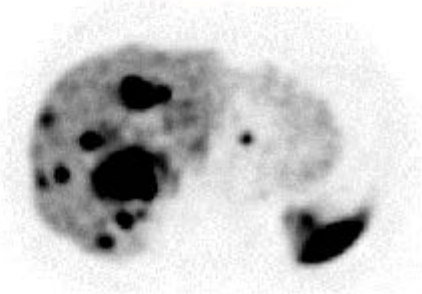
J Nucl Med April 2007 vol. 48 no. 4 508-518

68Ga-labelled somatostatin analogues

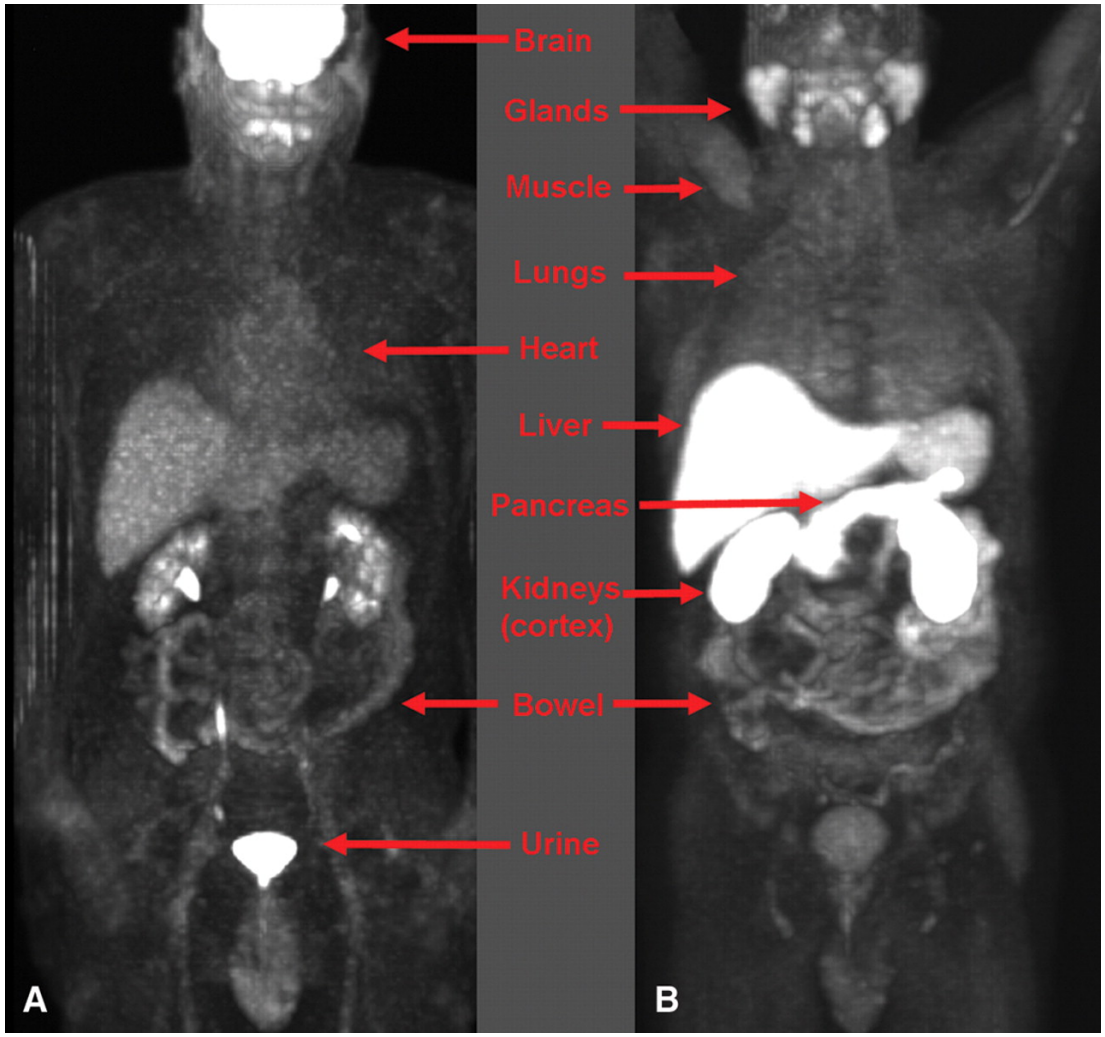
- Indications (according to EANM):
  - Neuroendocrine tumors imaging:
    - To localise primary tumors
    - Follow up of patients with known disease to detect residual, recurrent or progressive disease (restaging)
    - To determine somatostatin receptor status
    - To select the patients with metastatic disease suitable for peptide receptor radionuclide therapy
    - To monitor the response to the therapy





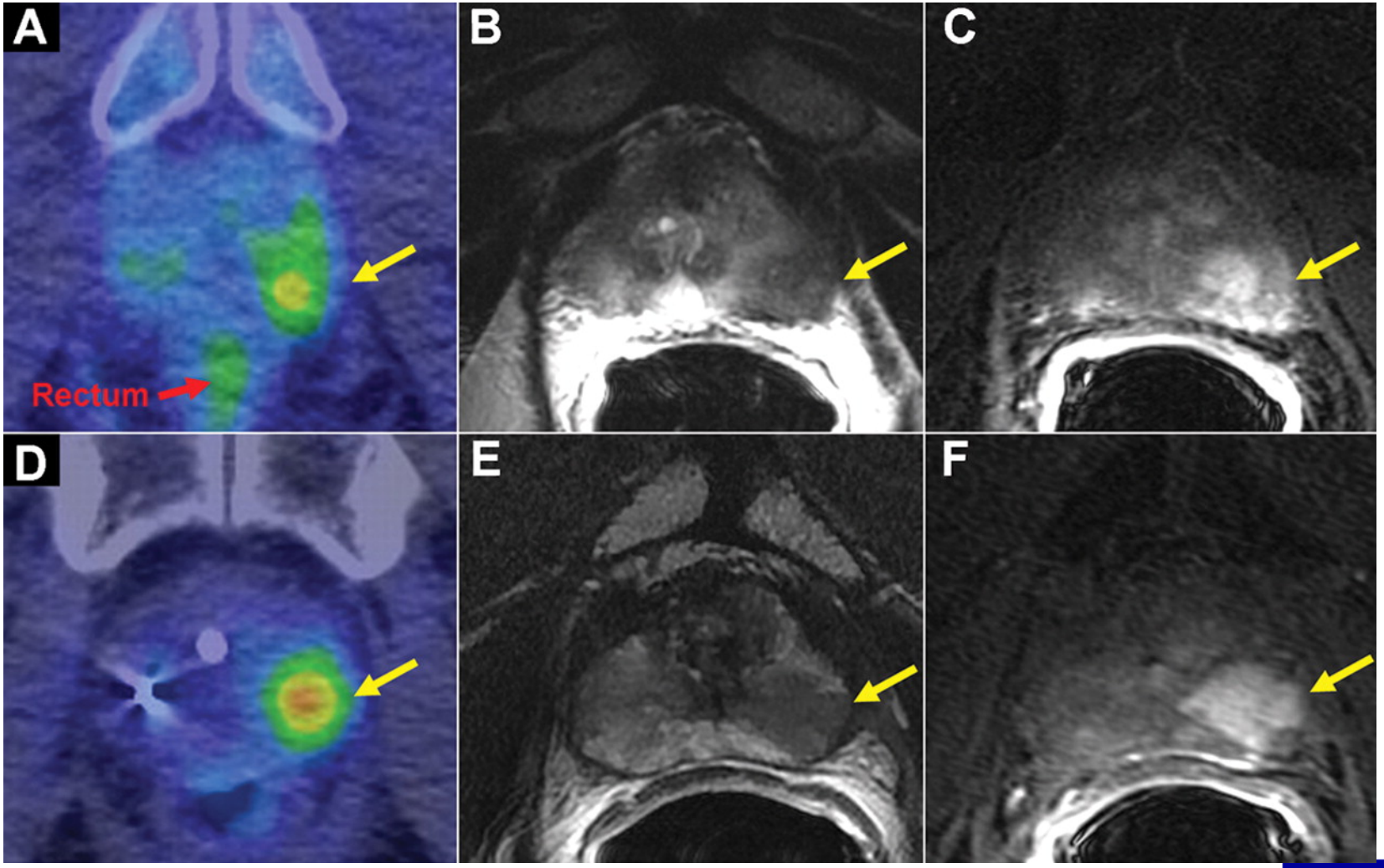


—Comparison of physiologic 18F-FDG distribution (A) with physiologic 11C-choline distribution (B).



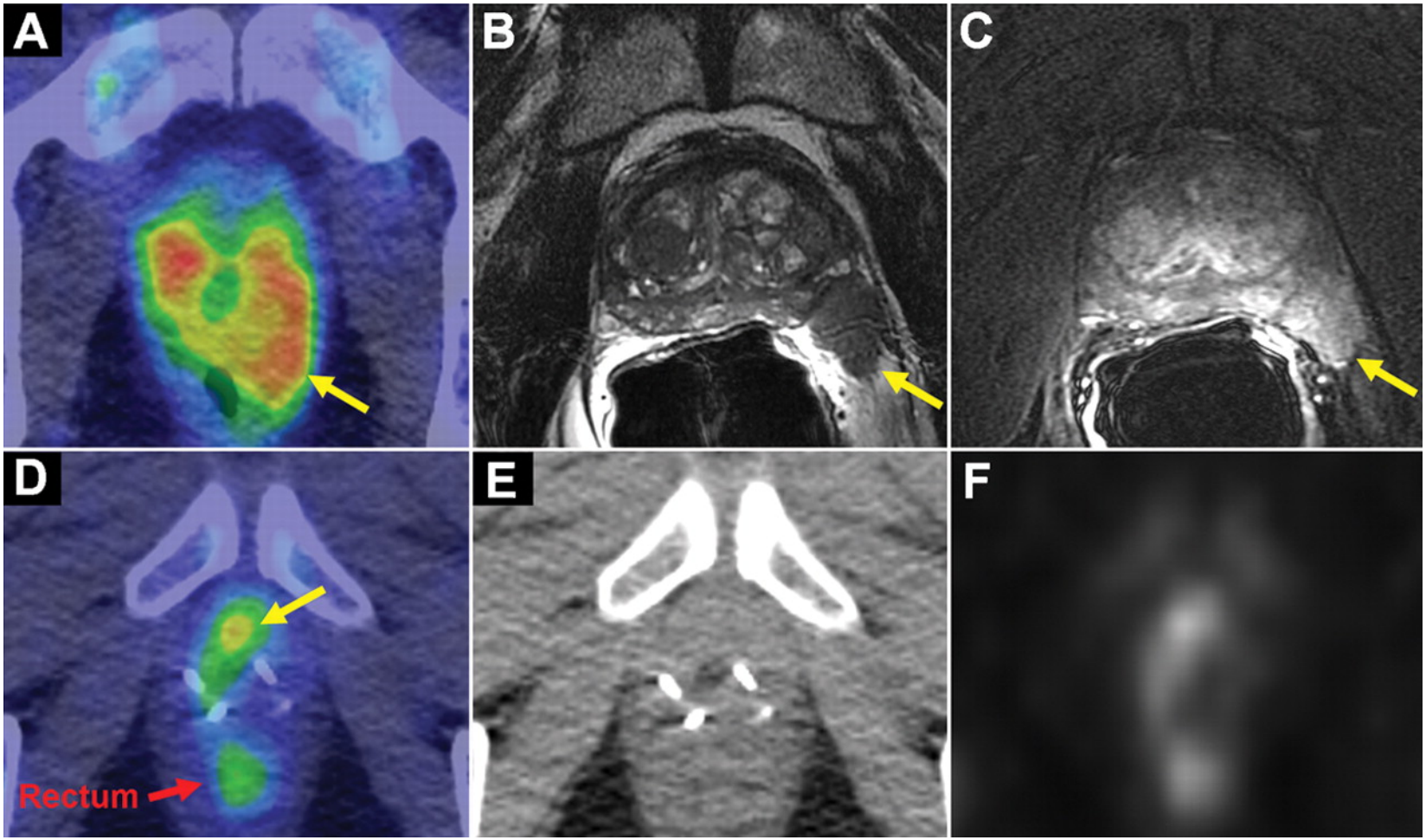
Murphy R C et al. AJR 2011;196:1390-1398

—Typical local patterns of malignant 11C-choline uptake shown in two patients with prostate cancer: 73-year-old man with biopsy-proven prostate cancer (A–C) and 78-year-old man with biopsy-proven recurrent prostate cancer (D–F).



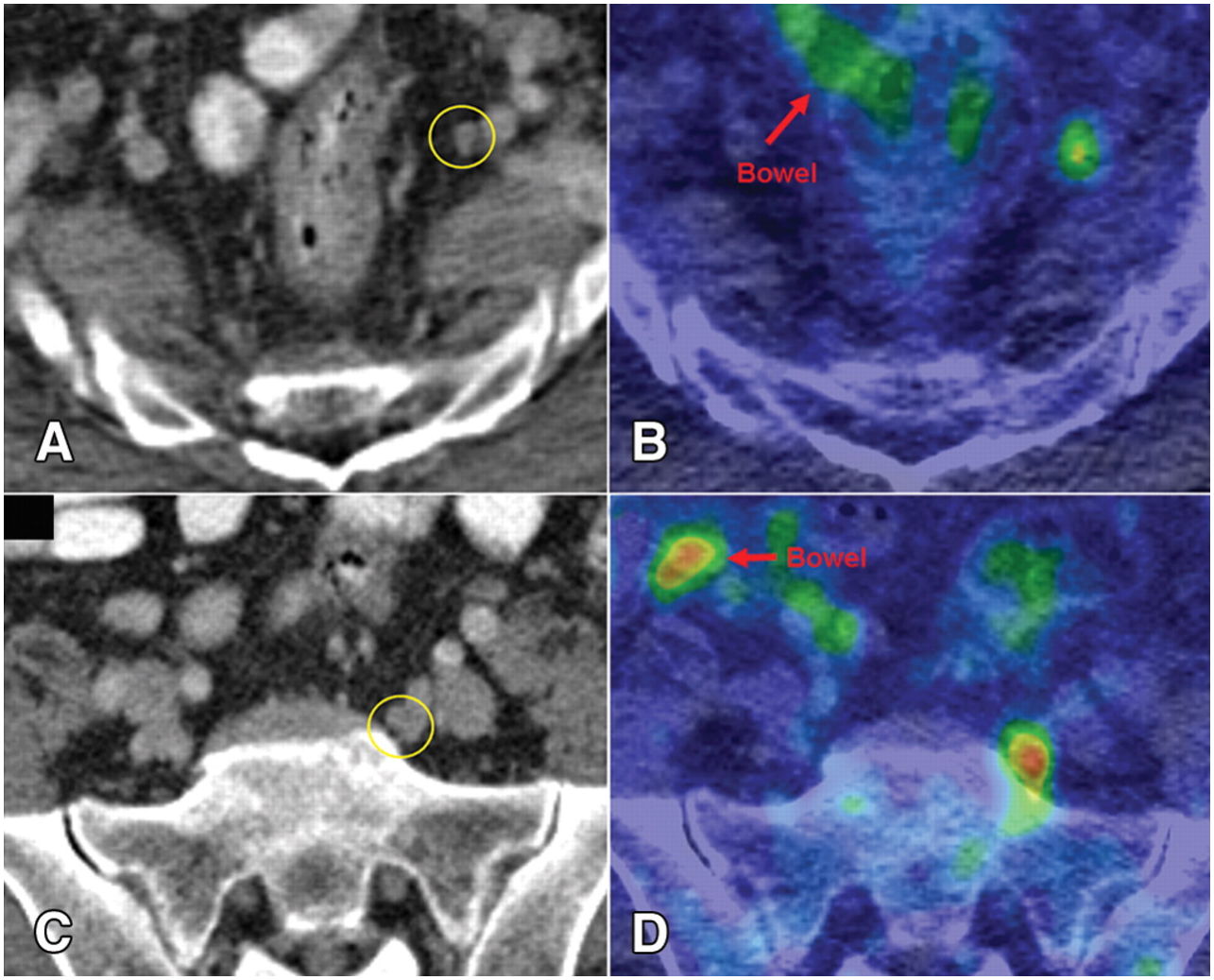
Murphy R C et al. AJR 2011;196:1390-1398

—Typical local patterns of malignant 11C-choline uptake in two patients with prostate cancer.



Murphy R C et al. AJR 2011;196:1390-1398

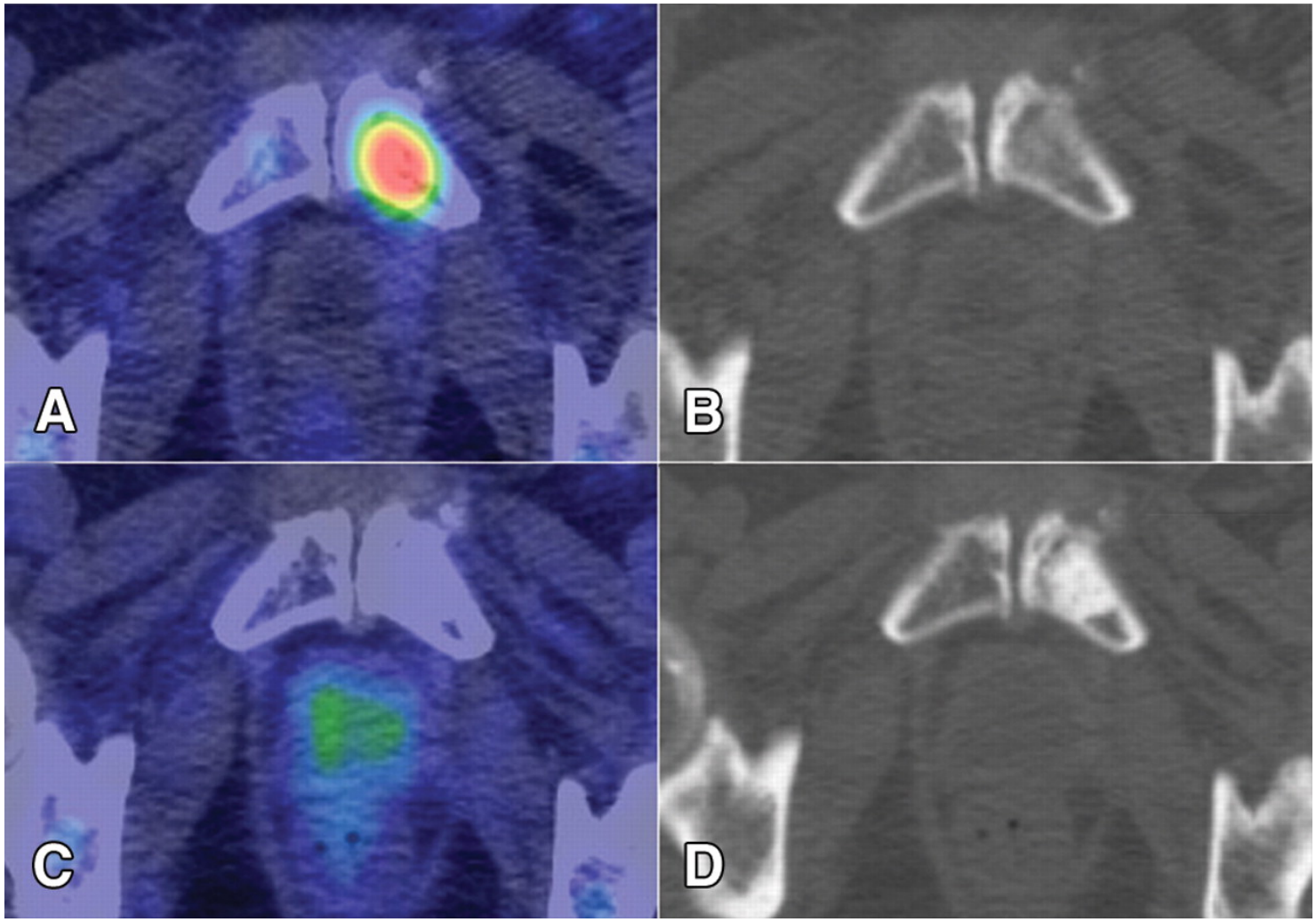
—67-year-old man with prostate cancer (Gleason 3 + 4) treated in 2002 with brachytherapy and external beam radiation who presented for evaluation of biochemical recurrence.



Murphy R C et al. AJR 2011;196:1390-1398

AJR

—Patterns of metastatic skeletal disease.



Murphy R C et al. AJR 2011;196:1390-1398

Nucl Med Commun. 2013 Oct;34(10):935-45.

A literature review of 18F-fluoride PET/CT and 18F-choline or 11C-choline PET/CT for detection of bone metastases in patients with prostate cancer.

Wondergem M, van der Zant FM, van der Ploeg T, Knol RJ.

On a lesion basis, we found a sensitivity and **specificity of 84.0 and 97.7% for C-choline and F-choline and 88.6 and 90.7% for F-fluoride**, respectively. On a patient basis, the sensitivity and specificity were **85.2 and 96.5% for C-choline and F-choline and 86.9 and 79.9% for F-fluoride**, respectively. No significant differences were found between the sensitivity and specificity of C-choline or F-choline and F-fluoride.

BJU Int. 2012 Dec;110(11):1666-71..

[18F]fluoromethylcholine (FCH) positron emission tomography/computed tomography (PET/CT) for lymph node staging of prostate cancer: a prospective study of 210 patients.

Poulsen MH, Bouchelouche K, Høilund-Carlsen PF, Petersen H, Gerke O, Steffansen SI, Marcussen N, Svolgaard N, Vach W, Geertsen U, Walter S.

- **RESULTS:**

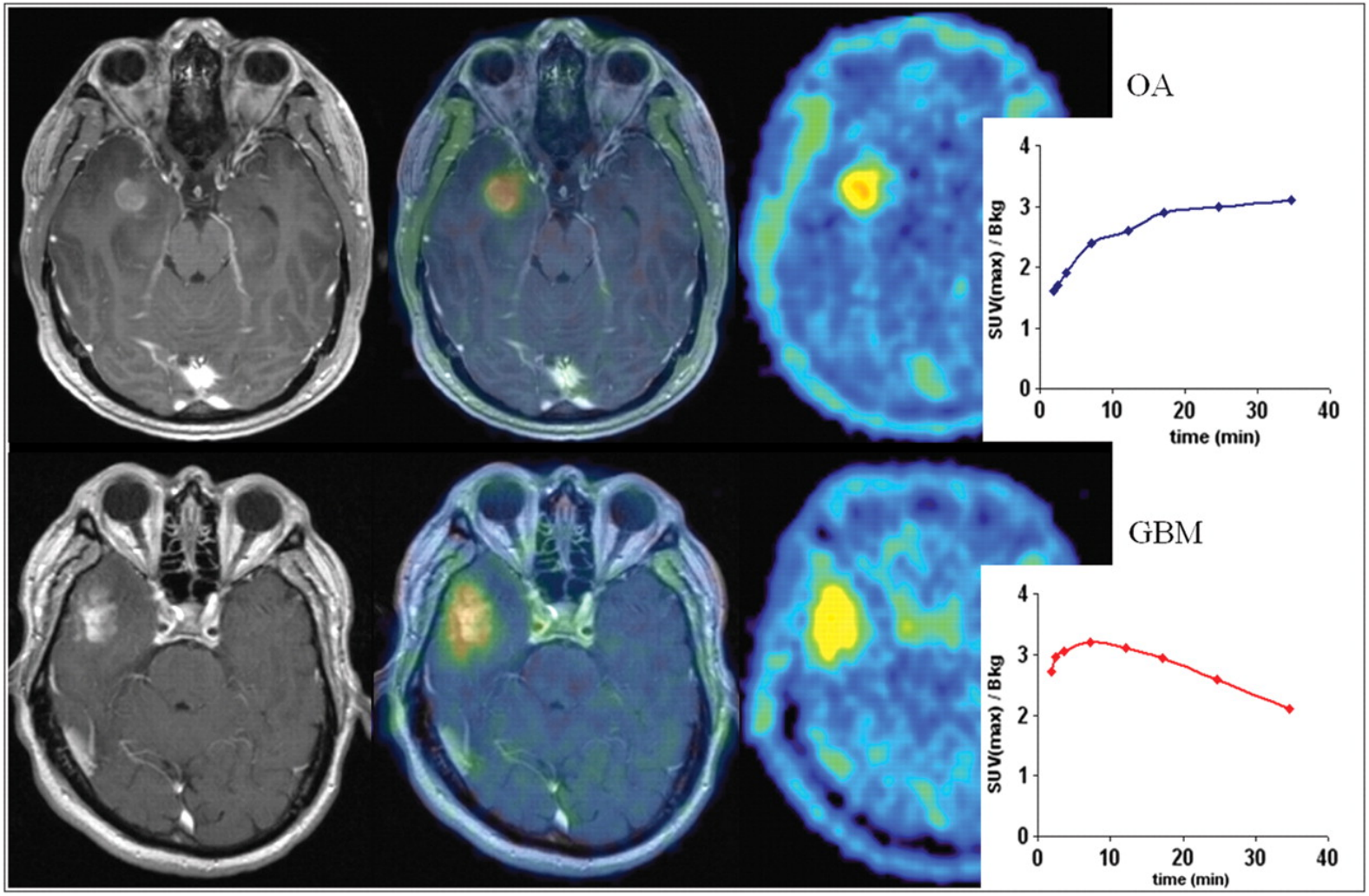
Of the 210 patients, 76 (36.2%) were in the intermediate-risk group and 134 (63.8%) were in the high-risk group. A medium (range) of 5 (1-28) LNs were removed per patient. • Histological examination of removed LNs showed metastases in 41 patients. Sensitivity, specificity, PPV, and NPV of FCH PET/CT for patient-based LN staging were 73.2%, 87.6%, 58.8% and 93.1%, respectively. • Corresponding values for LN-based analyses were 56.2%, 94.0%, 40.2%, and 96.8%, respectively. • The mean diameter of the true positive LN metastases was significantly larger than that of the false negative LNs (10.3 vs 4.6 mm; $P < 0.001$). • In addition, FCH PET/CT detected a high focal bone uptake, consistent with bone metastases, in 18 patients, 12 of which had histologically benign LNs.

- **CONCLUSIONS:** Due to a relatively low sensitivity and a correspondingly rather low PPV, FCH PET/CT is not ideal for primary LN staging in patients with prostate cancer. • However, **FCH PET/CT does convey important additional information otherwise not recognised, especially for bone metastases.**

Labeled aminoacids – brain tumours (EANM guideline) 18F-FET

- Detection of the viable tumour tissue
- Tumour delineation
- Selecting of the biosy site
- Non-nvasive tumour grading (although 18F-FDG performs better)
- Therapy planning
- Tumour response

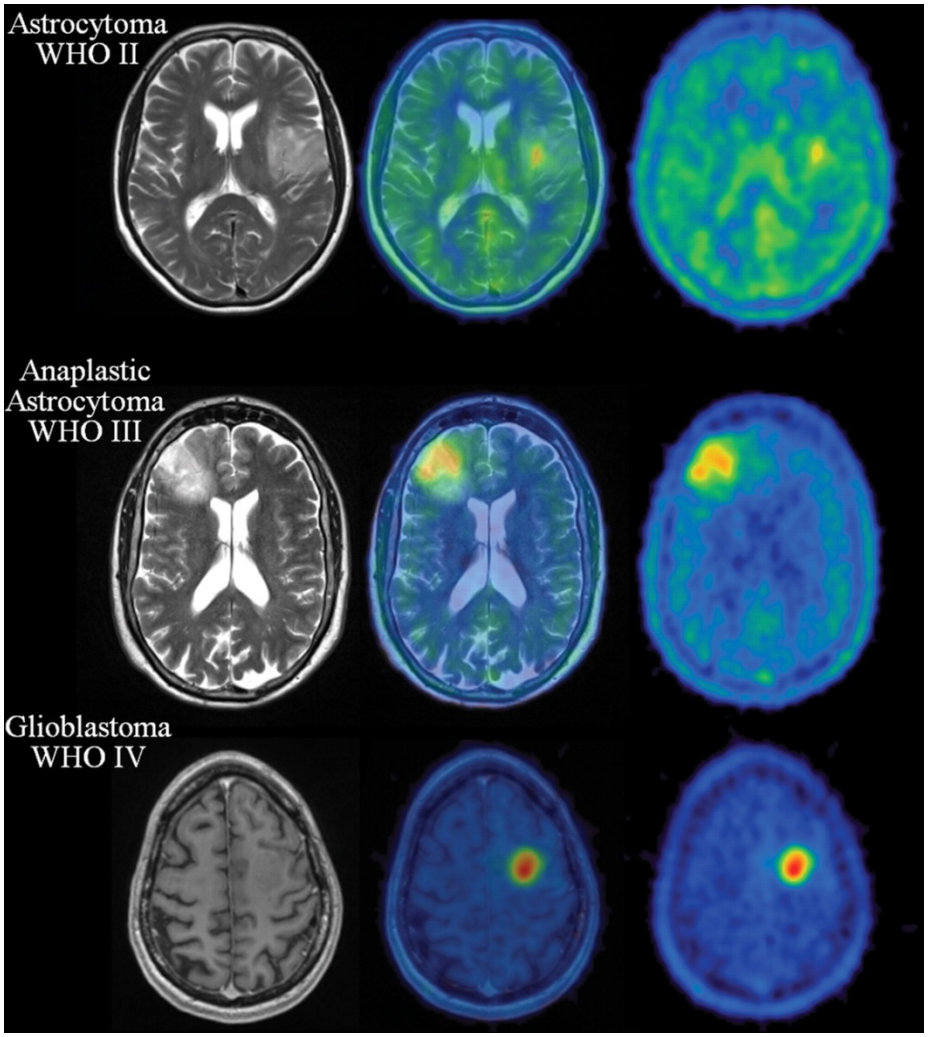
Transversal [18F]FET PET, fused PET MR, and contrast-enhanced T1-weighted MR images are shown.



la Fougère C et al. Neuro Oncol 2011;13:806-819

Neuro-Oncology

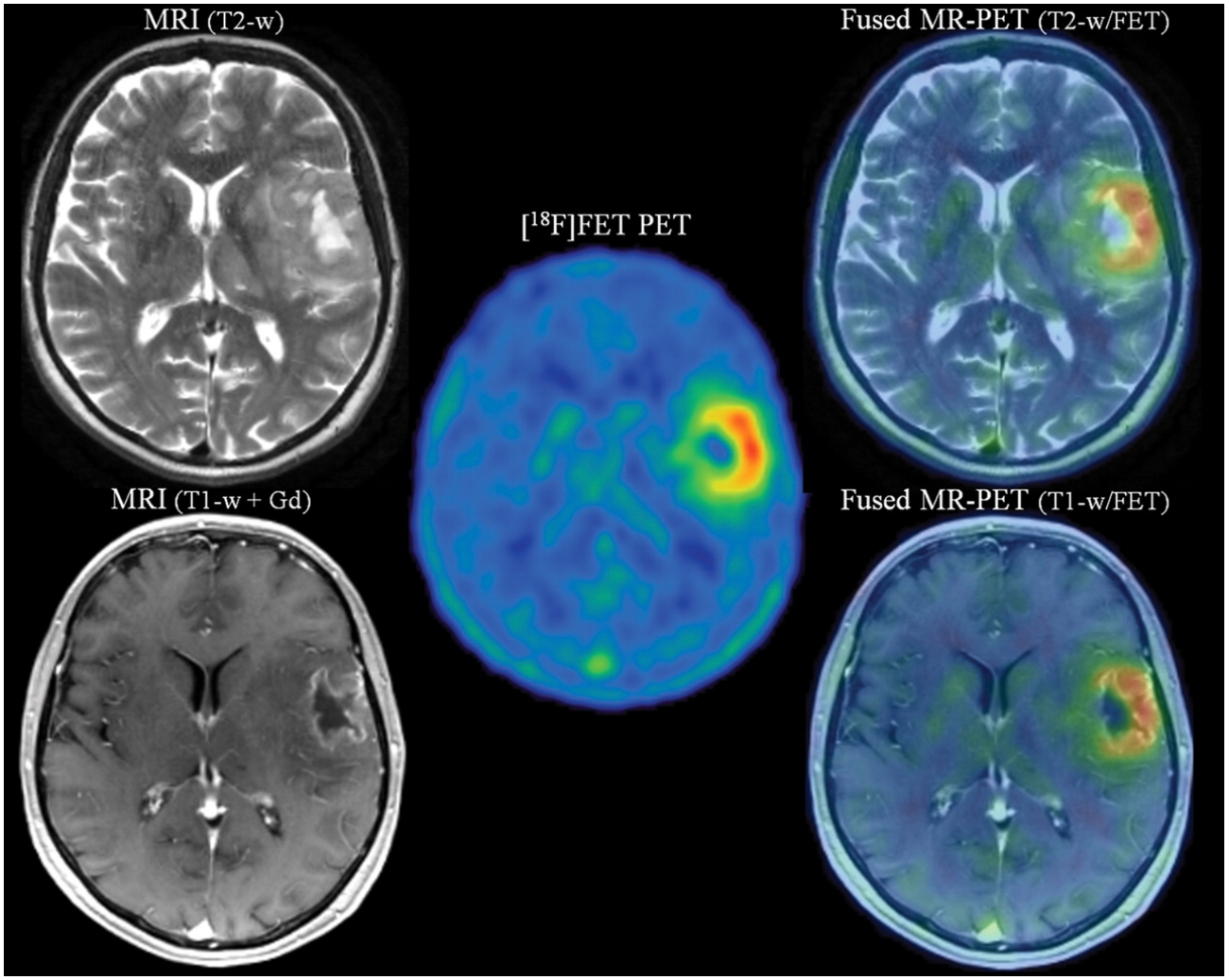
Transversal MR, fused PET MR, and [18F]FET PET images are shown.



la Fougère C et al. Neuro Oncol 2011;13:806-819

Neuro-Oncology

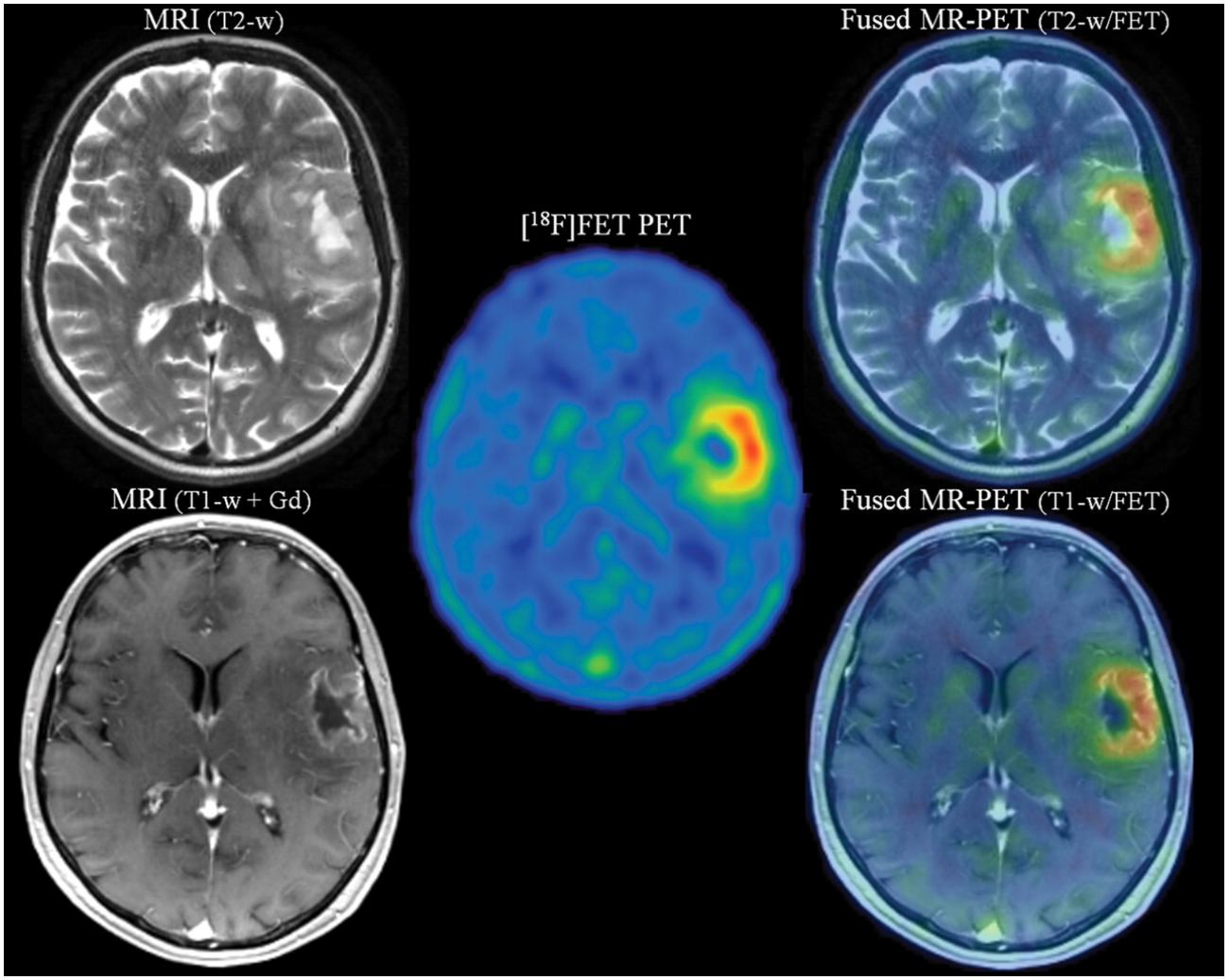
Tumor delineation and target volume definition for treatment planning substantially differs, depending on the image modality used.



la Fougère C et al. Neuro Oncol 2011;13:806-819

Neuro-Oncology

Tumor delineation and target volume definition for treatment planning substantially differs, depending on the image modality used.



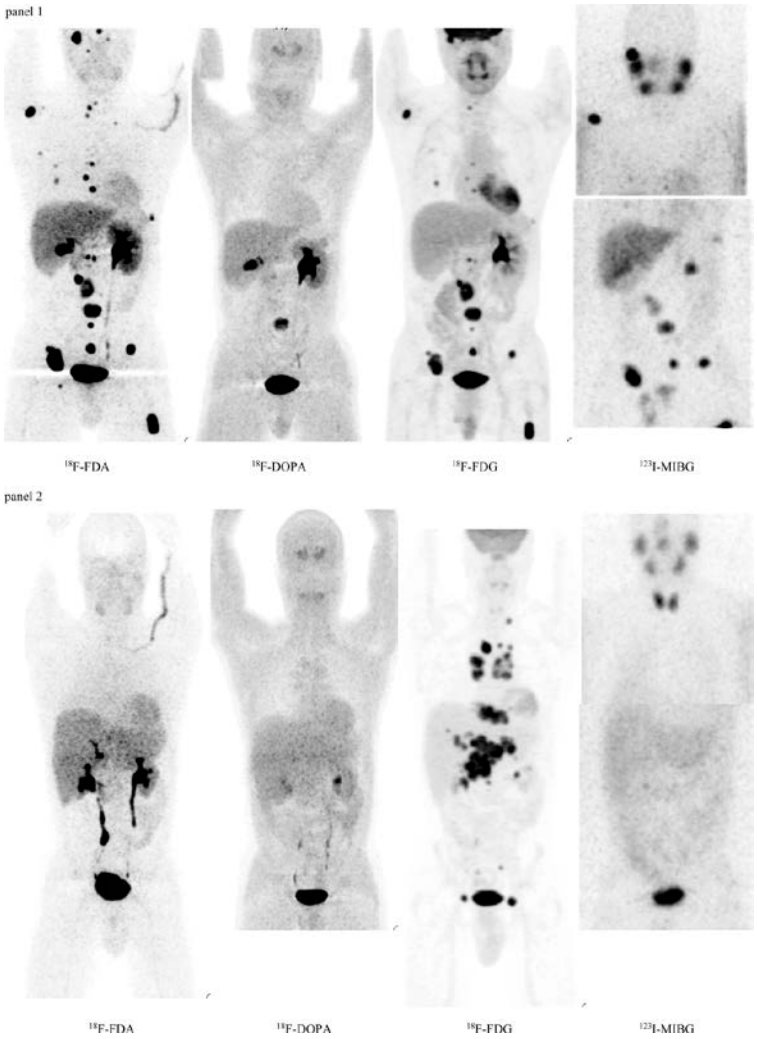
la Fougère C et al. Neuro Oncol 2011;13:806-819

Neuro-Oncology


UNASSUMED
ROAD
USE AT
OWN RISK
NO
EXIT

Functional imaging in patients no. m4 with metastatic SDHB PGL (panel 1), m15 with metastatic SDHB PGL (panel 2), and m6 with metastatic RET PGL (panel 3).

Funcional imaging vs. genetics

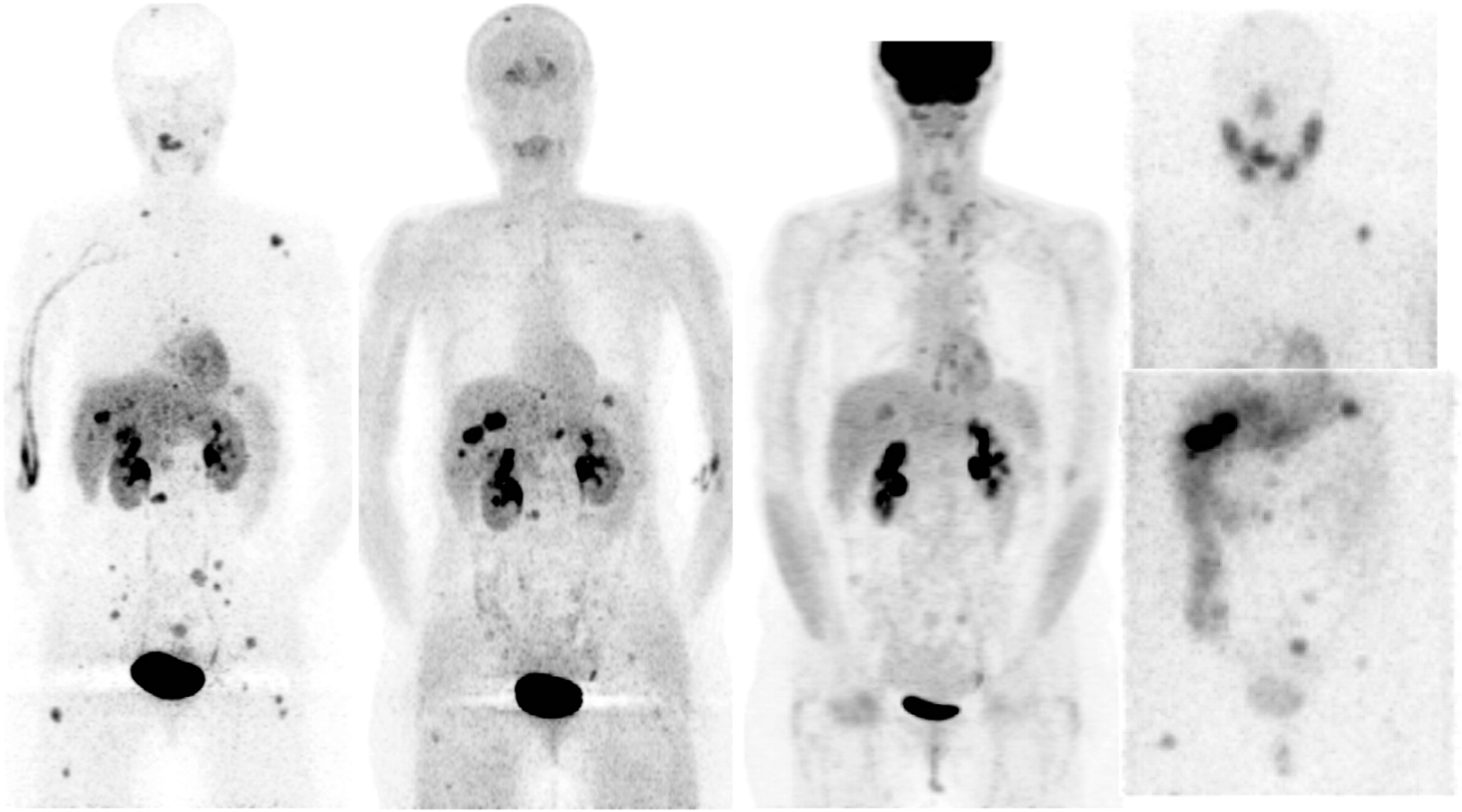


Timmers H J L M et al. JCEM 2009;94:4757-4767

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

Functional imaging in patients no. m4 with metastatic SDHB PGL (panel 1), m15 with metastatic SDHB PGL (panel 2), and m6 with metastatic RET PGL (panel 3).

panel 3



^{18}F-FDA ^{18}F-DOPA ^{18}F-FDG ^{123}I-MIBG

Timmers H J L M et al. JCEM 2009;94:4757-4767

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

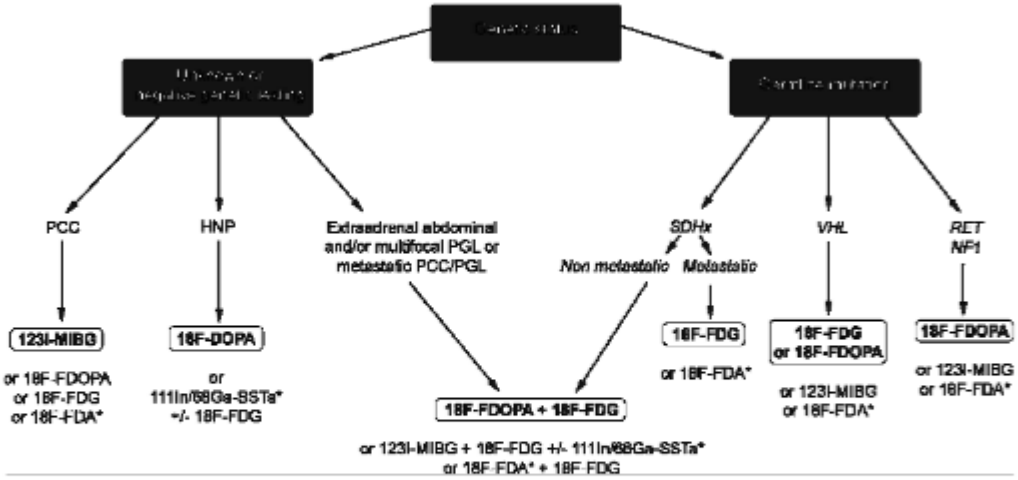


Fig. 1 Clinical algorithm for imaging investigations in PCC/PGL. Based on the above considerations, the following algorithm can be proposed based on the clinical situation. This algorithm should be adapted to the practical situation in each institution, and should evolve with time. *In bold* First-line imaging procedures according to accessibility of tracers and clinical approvals in European countries. ^{18}F-FDA and ^{68}Ga-DOTA-SSTa (*asterisks*) are experimental tracers that should be used in the setting of clinical trials. ^{18}F-FDA PET is currently used at the NIH only. ^{68}Ga-DOTA-SSTa is now accessible in many clinical and research centres in Europe

EANM 2012 guidelines

Hypoxia imaging

- Nitroimidazole derivates (18F-MISO, 18F-FAZA; diacetylmethymshiosemicarbazone 64Cy-ATSM).
- Radiation planning

PET Imaging of Tumor Hypoxia Using ^{18}F-Fluoroazomycin Arabinoside in Stage III–IV Non–Small Cell Lung Cancer Patients

Vikram R. Bollineni[1], Gerald S.M.A. Kerner[2], Jan Pruim[3,4], Roel J.H.M. Steenbakkers[1], Erwin M. Wiegman[1], Michel J.B. Koole[3], Eleonore H. de Groot[3], Antoon T.M. Willemsen[3], Gert Luurtsema[3], Joachim Widder[1], Harry J.M. Groen[2], and Johannes A. Langendijk[1]

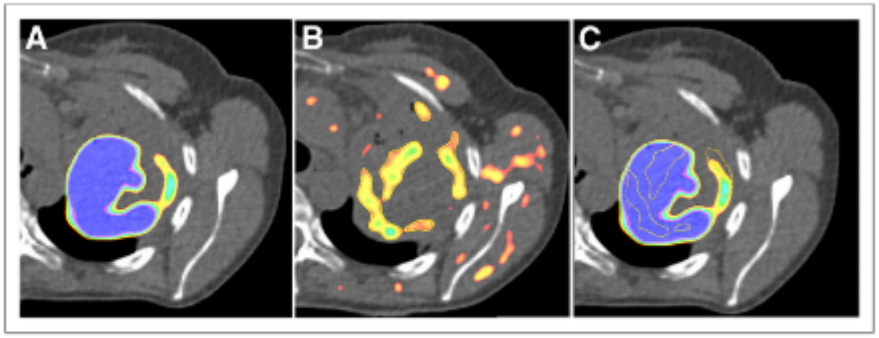


FIGURE 2. Representative transaxial ^{18}F-FDG and ^{18}F-FAZA PET/CT images of patient 4. (A) Thirty-four percent of maximum ^{18}F-FDG accumulation is shown on corresponding CT image. (B) ^{18}F-FAZA accumulation is shown on corresponding CT image. (C) Transposition of areas with ^{18}F-FAZA accumulation onto areas with ^{18}F-FDG accumulation.

2013

Proliferation imaging

PET Imaging of Proliferation with Pyrimidines

Omid S. Tehrani and Anthony F. Shields

CONCLUSION

Imaging tumor proliferation with labeled pyrimidine analogs, such as ^{18}F-FLT PET, offers a new approach to assessing tumor growth kinetics. Several studies have demonstrated that ^{18}F-FLT can detect cancers, but so far it does not appear likely to replace ^{18}F-FDG for this use with most tumor types. The ability of ^{18}F-FLT imaging to provide an early measure of treatment response has been demonstrated in several preclinical and clinical studies with a variety of tumor types. This approach requires further validation to find routine clinical use.

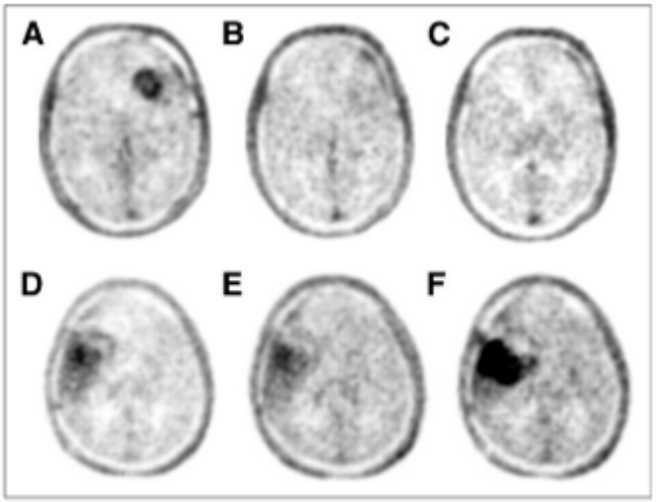


FIGURE 4. ^{18}F-FLT PET at baseline, 2 wk, and 6 wk for responding patient (A–C, patient 25) and nonresponding patient (D–F, patient 9). (Reprinted from (*34*)).

JNM 213

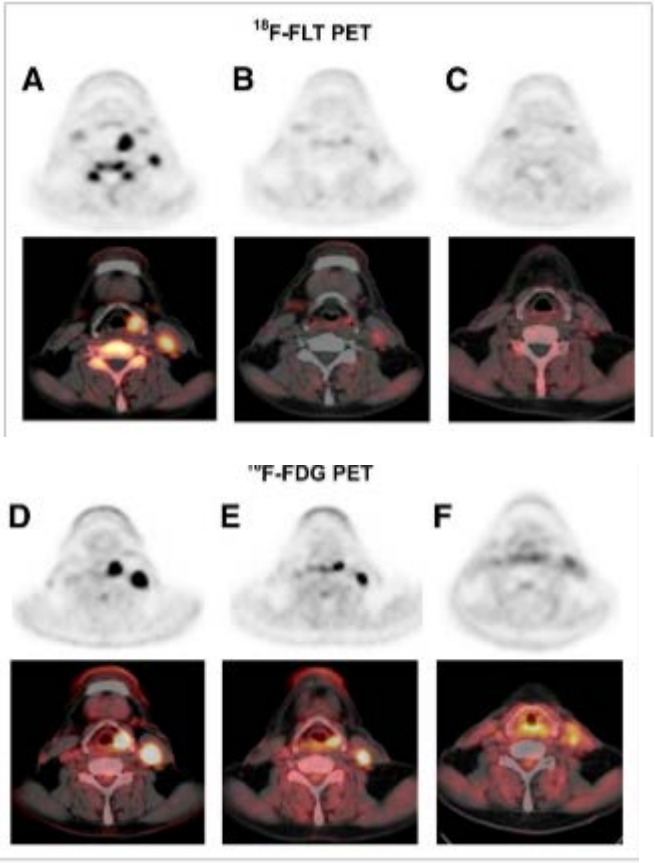


FIGURE 5. PET images of patient with hypopharyngeal cancer (patient 14) before radiation therapy (A and D), 3 wk after initiation of radiation therapy (B and E), and 4 wk after end of radiation therapy (C and F). Pretreatment ^{18}F-FLT and ^{18}F-FDG axial PET images showed increased metabolism in primary tumor and metastatic lymph node (^{18}F-FLT SUVs, 9.16 and 6.06, respectively; ^{18}F-FDG SUVs, 21.81 and 13.37, respectively). ^{18}F-FLT and ^{18}F-FDG SUVs decreased after 30 Gy of irradiation (^{18}F-FLT SUVs, 2.86 and 2.14, respectively; ^{18}F-FDG SUVs, 11.44 and 6.39, respectively). ^{18}F-FLT uptake in primary site and lymph nodes was same as in surrounding muscle (SUVs of 0.93, 0.9, and 0.9, respectively) at 4 wk after completion of treatment, whereas increased uptake of ^{18}F-FDG persisted (SUV of 4.66 in primary lesion and 3.75 in lymph node). Patient was alive and without evidence of recurrent disease 19 mo after therapy. (Reprinted from (*66*).)

Antibodies and Antimatter: The Resurgence of Immuno-PET

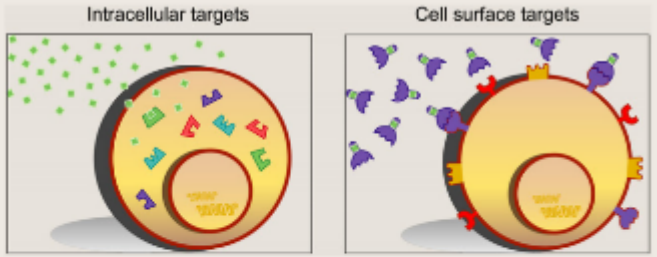
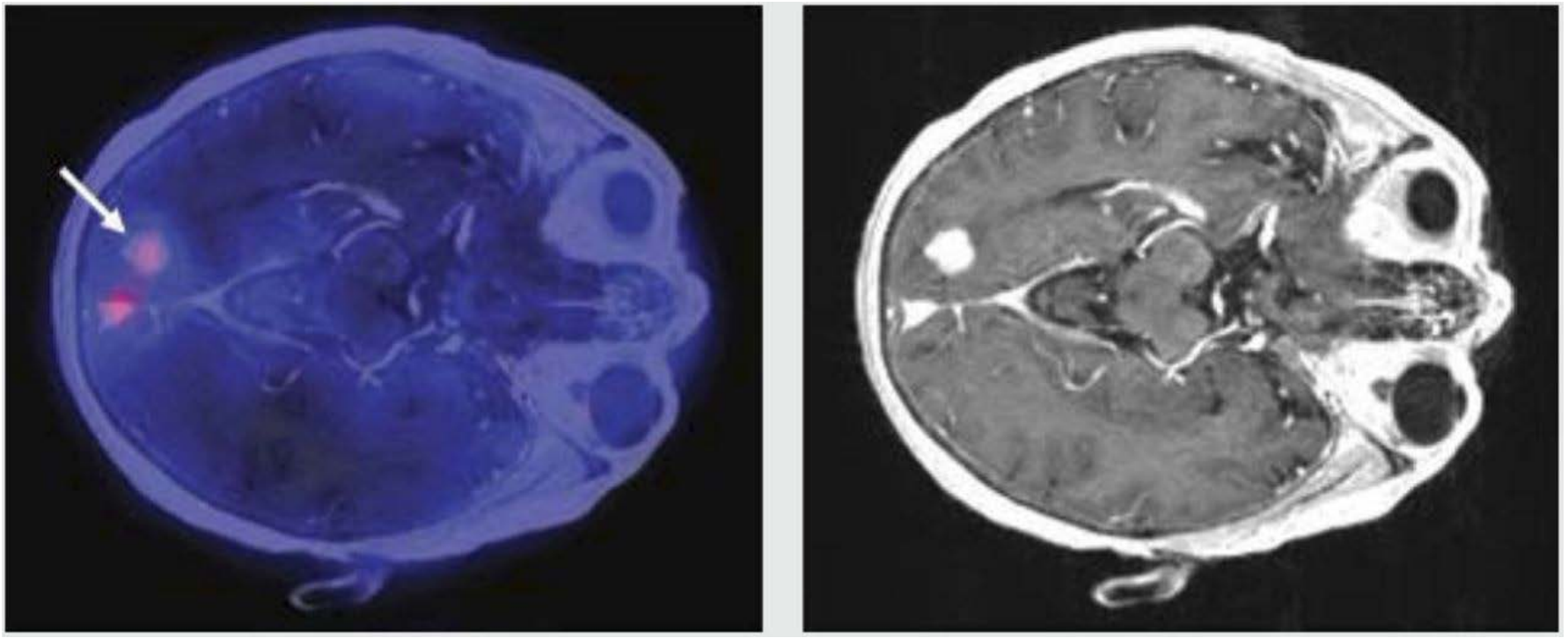


FIGURE 1. Molecular imaging targets include intracellular and cell surface proteins. Antibodies and engineered fragments are particularly suited for detection of cell surface biomarkers (right), which can include highly informative proteins such as growth factor receptors, ligands, adhesion molecules, proteases, and differentiation and activation markers.

JNM 2009

Example of HER2-positive brain lesion undetected by conventional scans, revealed with ^{89}Zr-trastuzumab imaging and subsequently confirmed by MR imaging.



JNM

The real clinical impact?