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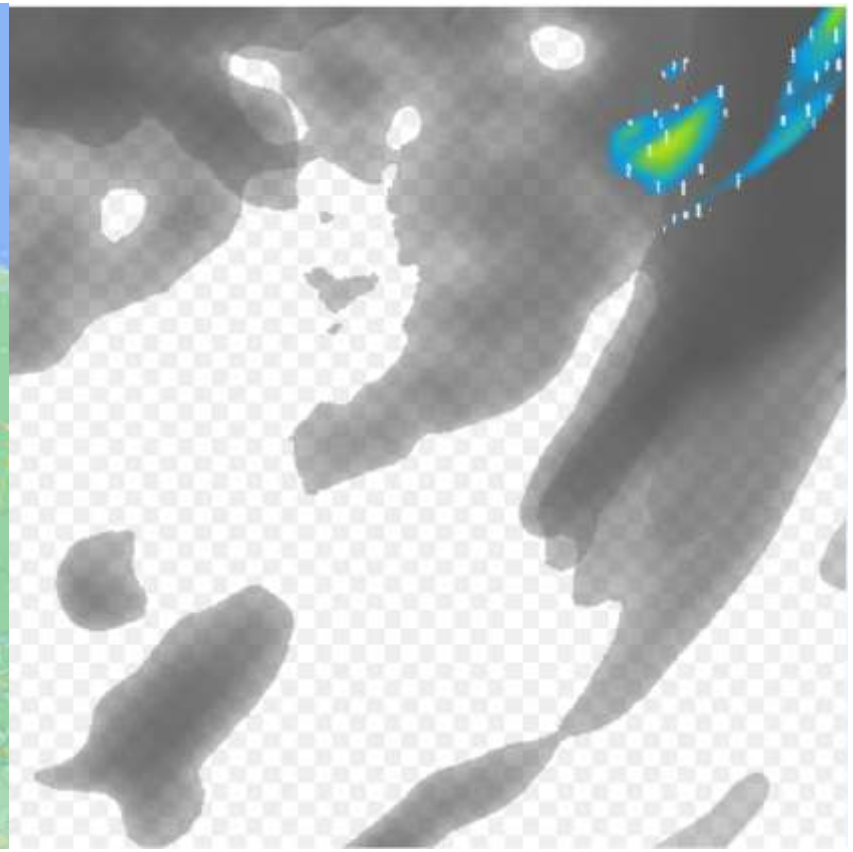
Hybrid Imaging: The Story so Far and What to Expect Next

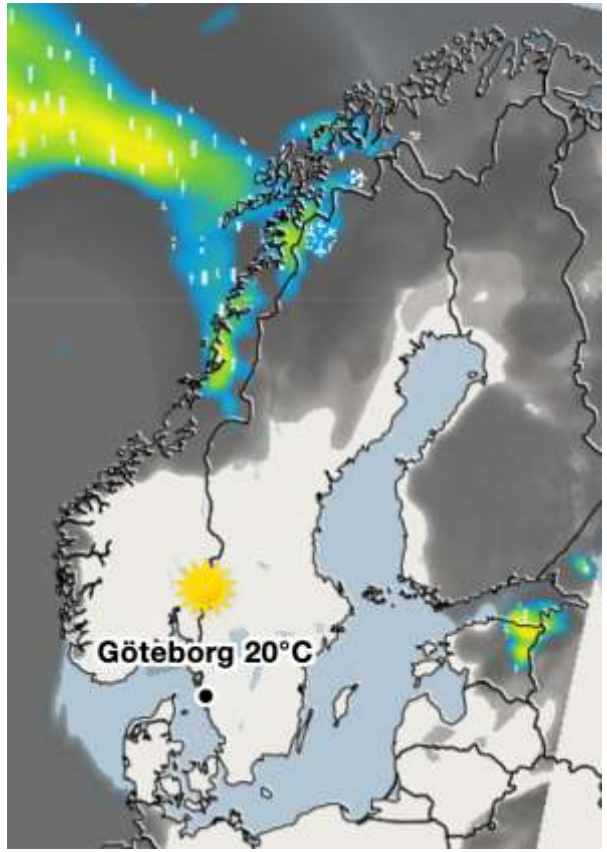
Katrine Riklund

Professor/Consultant, Radiology and Nuclear medicine

Umeå university Hospital Sweden

The Weather





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Hybrid Imaging

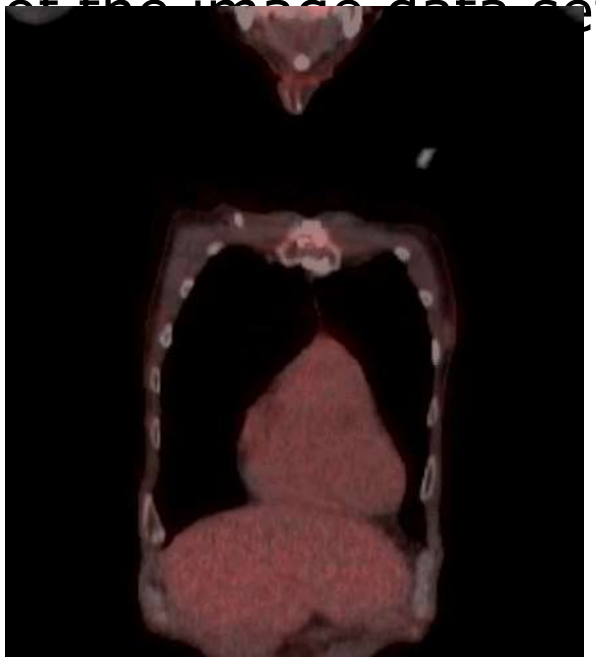
A combination of imaging with different type of information that is synergistic!

→

the whole information is larger than the sum of the image data set

→

= >2



The Nobel Prize in Physics 1901


EINE NEUE ART
DER
STRAHLEN.

Wilhelm Conrad Röntgen
1845-1923

"in recognition of the extraordinary services he has rendered by the discovery of the remarkable rays subsequently named after him"

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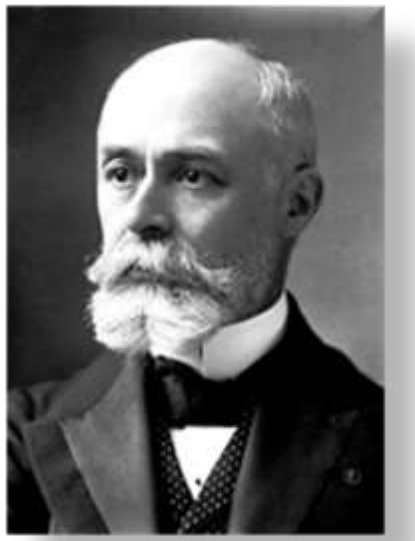
Nobelprize.org

The Nobel Prize in Physics 1903



Henri Becquerel
1852-1908

Pierre Curie
1859-1906

Marie Curie Sklodowska
1867-1934

"in recognition of the extraordinary services he has rendered by his discovery of spontaneous radioactivity"

"in recognition of the extraordinary services they have rendered by their joint researches on the radiation phenomena discovered by Professor Henri Becquerel"

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Nobelprize.org

The Nobel Prize in Chemistry 1911

Marie Curie, born Sklodowska

1867-1934

"in recognition of her services to the advancement of chemistry by the discovery of the elements radium and polonium, by the isolation of radium and the study of the nature and compounds of this remarkable element"

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Nobelprize.org

The Nobel Prize in Chemistry 1935

Irène Joliot-Curie

1897-1956

Frédéric Joliot

1900-1958

"in recognition of their synthesis of new radioactive elements"

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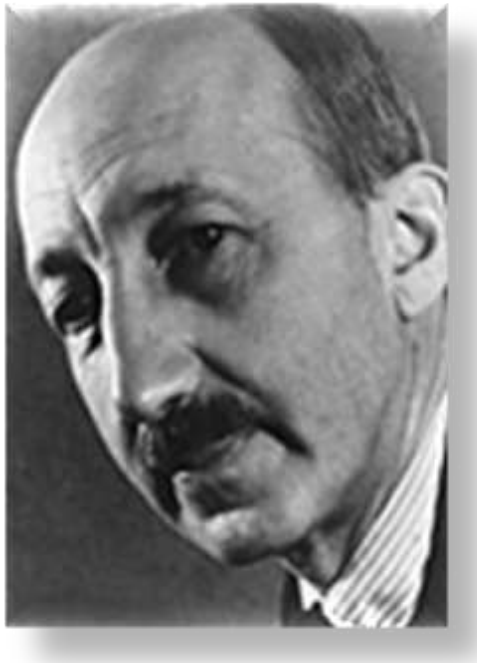
The Nobel Prize in Chemistry 1943

George de Hevesy

Hungary

Stockholm university

1885 - 1966



”for his work on the use of isotopes as tracers in the study of chemical processes"

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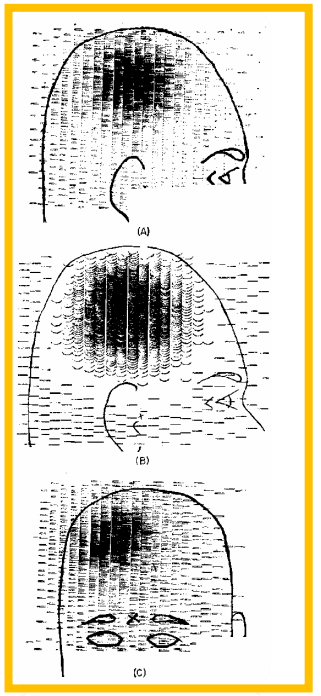
Nobelprize.org

History



Early Theranostic agent - ^{131}I-iodide

The Nobel Prize in Physiology or Medicine 1979

Allan M. Cormack
1924-1998

Godfrey N. Hounsfield
1919-2004

"for the development of computer assisted tomography"

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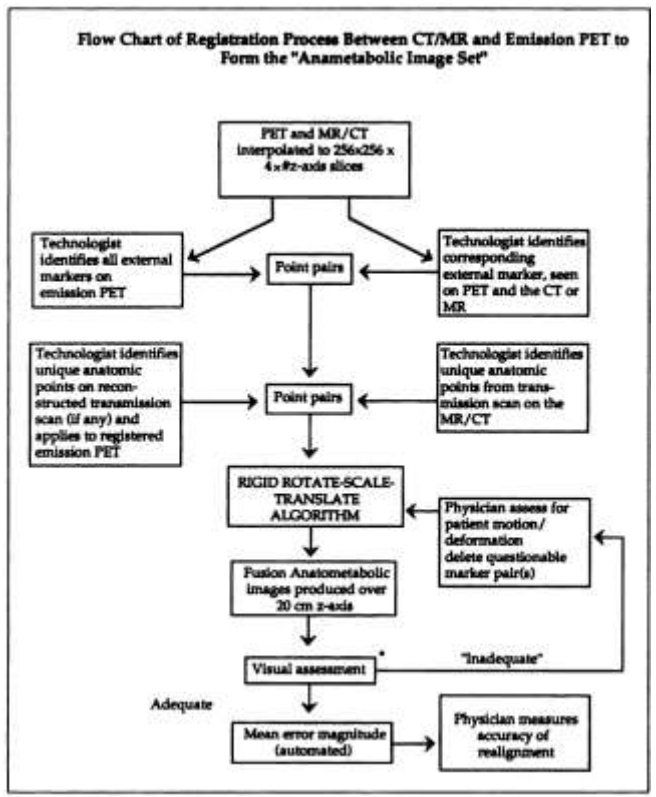
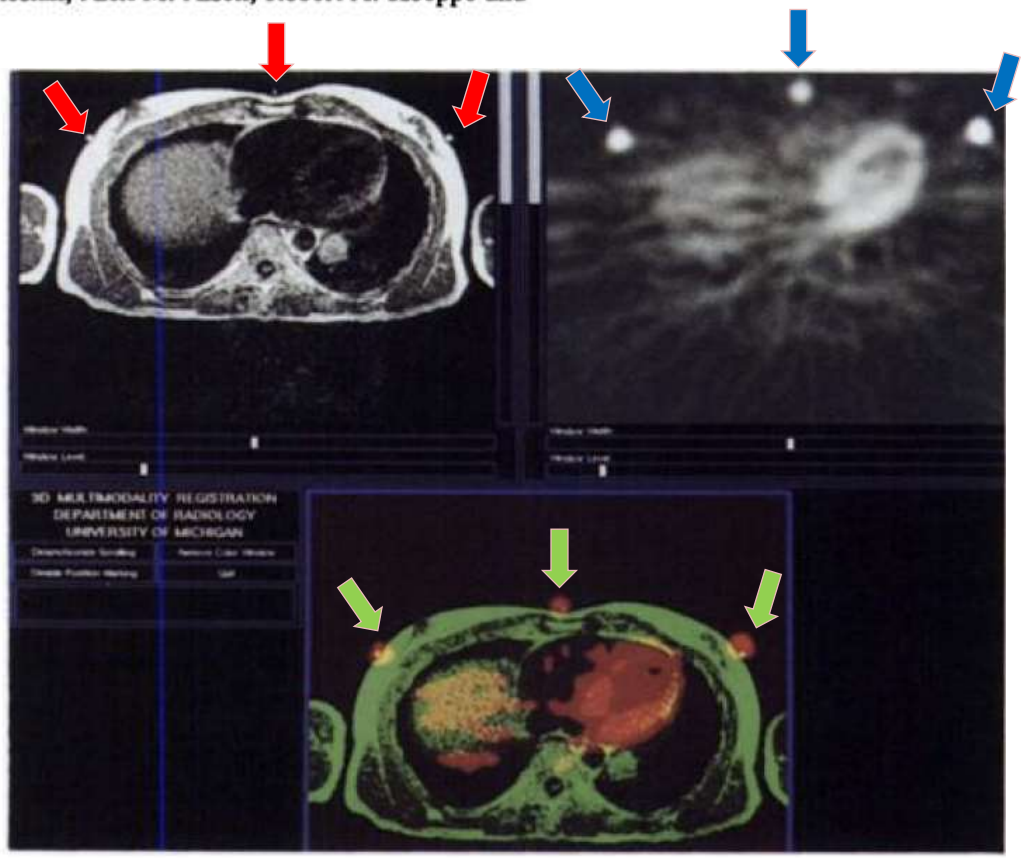
Nobelprize.org

"Anatometabolic" Tumor Imaging: Fusion of FDG PET with CT or MRI to Localize Foci of Increased Activity

Richard L. Wahl, Leslie E. Quint, Richard D. Cieslak, Alex M. Aisen, Robert A. Koeppe and Charles R. Meyer





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Wahl *et al* JNM 1993;34:1190

Commentary

NEWSLINE

Fused Image Tomography: Where Do We Go From Here?

HardWare Fusion

In my recent "Annual Meeting Highlights" (see *Newsline*, August, p. 13N), I suggested that the exact portrayal of anatomy (through CT) and regional biochemistry (PET), obtained with the same imaging gantry without moving the patient, represents an important integrating force in nuclear medicine.

SPECT/CT as well as PET/CT shou
oped, but that fusion of the images fro
PET instruments should be developed
cannot be developed by industry sim

Several qualifying statements need
First, the persons responding to the
were those who are sufficiently inter

—Henry N. Wagner, Jr., MD

THE JOURNAL OF NUCLEAR MEDICINE • Vol. 40 • No. 9 • Oct

(1) The ability to obtain fused PET data and
CT images without moving the
is an important advance. 97%

(2) The quality of the CT images sh
clinically interpretable themselves. 19%
80%

as a team.

"I think fusion is overblown in reputation. Good nuclear physicians can correlate just as well using internal landmarks."

"The PET business will go to the radiologist who will in fact own / control the CT."

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A Combined PET/CT Scanner for Clinical Oncology

Thomas Beyer, David W. Townsend, Tony Brun, Paul E. Kinahan, Martin Charron, Raymond Roddy, Jeff Jerin, John Young, Larry Byars, and Ronald Nutt

PET Facility and Division of Nuclear Medicine, Department of Radiology, University of Pittsburgh, Pittsburgh, Pennsylvania; CTI PET Systems, Knoxville; and Byars Consulting, Oak Ridge, Tennessee

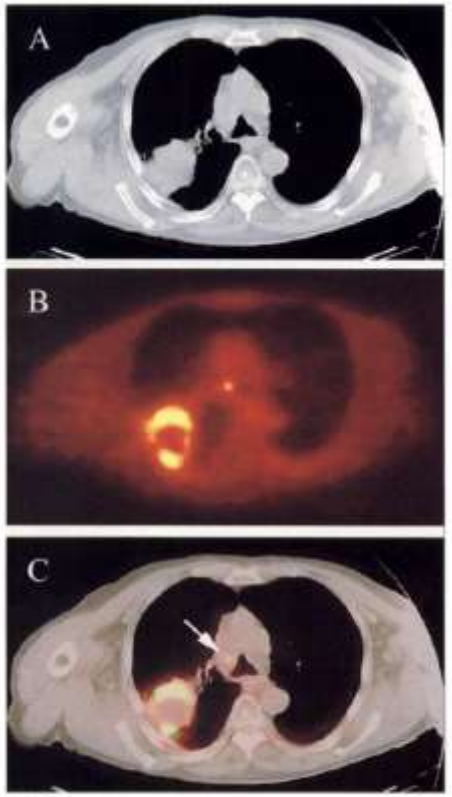

FIGURE 5. A 78-y-old man with squamous cell carcinoma of the lung. (A) Large isodense mass seen on CT appears on (B) PET scan as a hypermetabolic rim of increased FDG uptake, with necrotic center. (C) Fused image shows good alignment of 2 modalities. Lymph node in mediastinum (arrow) also demonstrated increased FDG uptake.

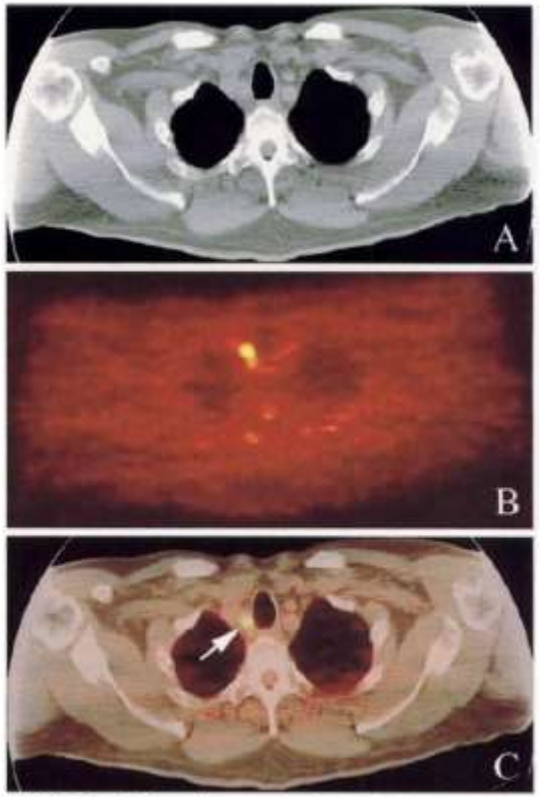

FIGURE 6. A 69-y-old man with diagnosed primary esophageal adenocarcinoma. (A) CT image. (B) PET image shows abnormal FDG uptake in the thorax. (C) Fused PET/CT image localizes uptake to specific lymph node (arrow).

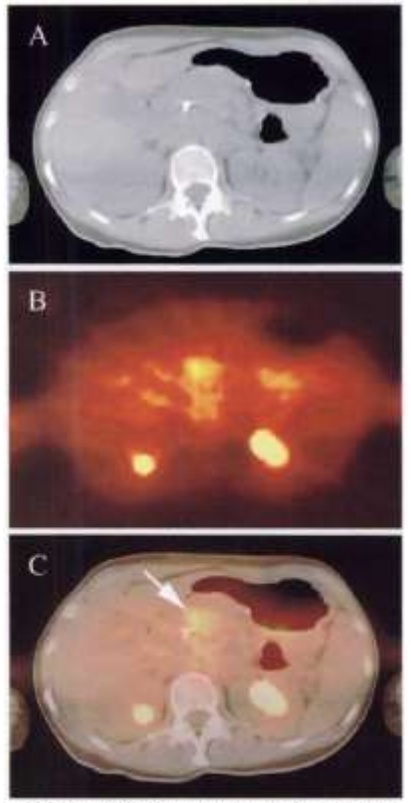

FIGURE 7. A 38-y-old woman with history of unresectable pancreatic cancer. Laparotomy revealed presence of liver metastases. (A) CT image. (B) Difficulty of accurately localizing FDG uptake can be seen from PET image. (C) Fused image enabled uptake to be localized to pancreas and not to transverse colon as had originally been thought.

The combined PET/CT approach offers extensive possibilities for improving the diagnosis and staging of tumors, identification and localization of disseminated disease, improving radiotherapy treatment planning, and monitoring the effects of chemotherapy and radiation therapy.

Beyer *et al* JNM 2000

Staging of Non–Small-Cell Lung Cancer with Integrated PET and CT

- 49 pats
- Extrathoracic metastases were confirmed histopathologically or by at least one other imaging method.
- PET/CT provided 24 items of additional information in 20/49 patients (41 %).

Table 1. Comparison of the Diagnostic Accuracy of Integrated PET–CT with CT Alone, PET Alone, and Visual Correlation of PET and CT Images.*

Variable	P Value
Tumor stage (n=40)	
PET–CT vs. CT alone	0.001† ✓
PET–CT vs. PET alone	<0.001† ✓
PET–CT vs. visual correlation of PET and CT	0.013† ✓
Node stage (n=37)	
PET–CT vs. CT alone	0.12 ✓
PET–CT vs. PET alone	0.013† ✓
PET–CT vs. visual correlation of PET and CT	0.021 ✓

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Didier Lardinois *et al.* NEJM 2003;348

FDG-PET/CT in re-staging of patients with lymphoma

Table 1. Region-based (n=135) sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the different imaging modalities in lymphoma

Imaging modality	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
CT	61	89	54	92	84
FDG-PET/CT	96	99	96	99	99

Table 2. Patient-based (n=27) sensitivity, specificity, positive predictive value, negative predictive value and accuracy of the different imaging modalities in lymphoma

Imaging modality	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)	Accuracy (%)
CT	78	54	65	70	67
FDG-PET/CT	93	100	100	93	96

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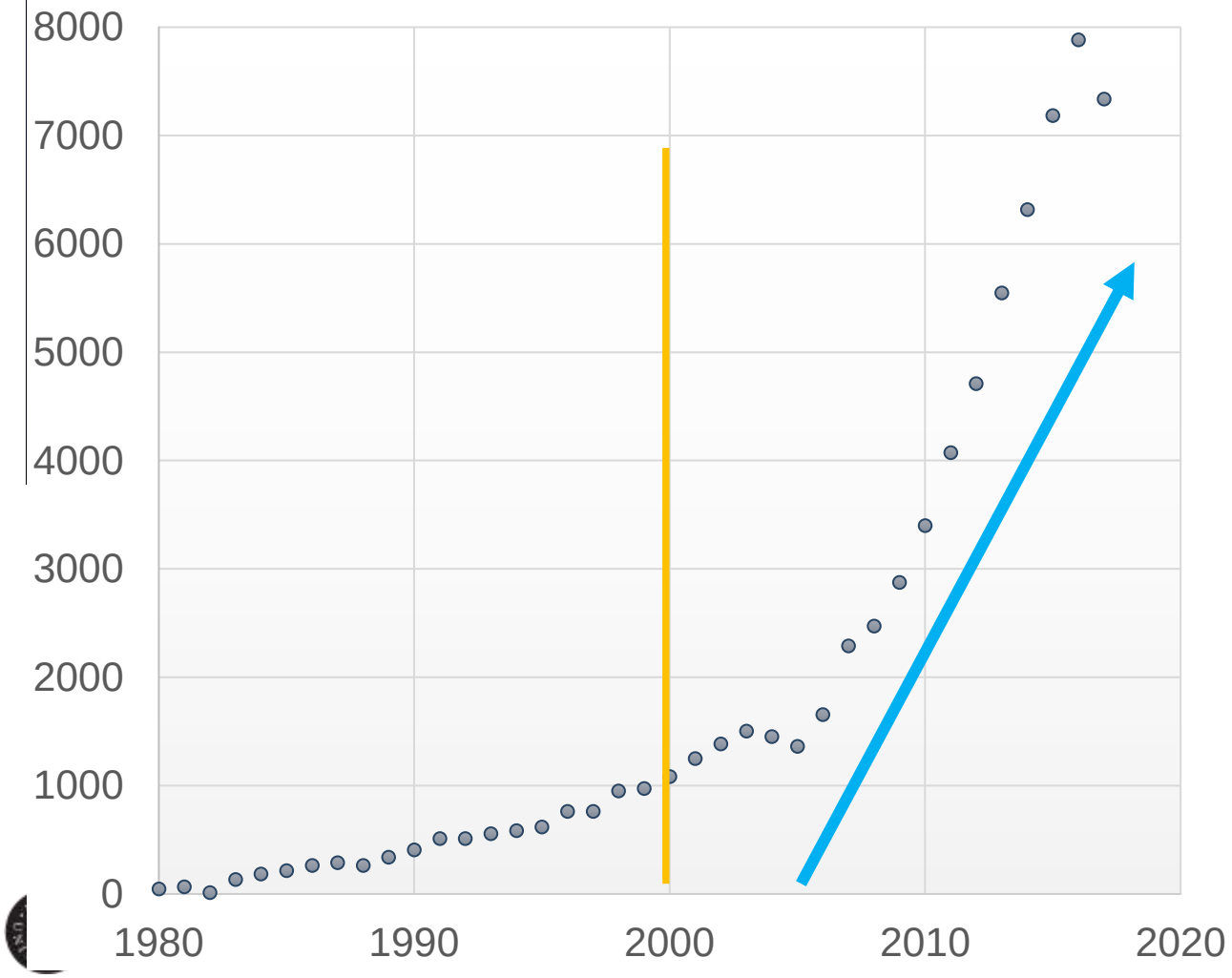
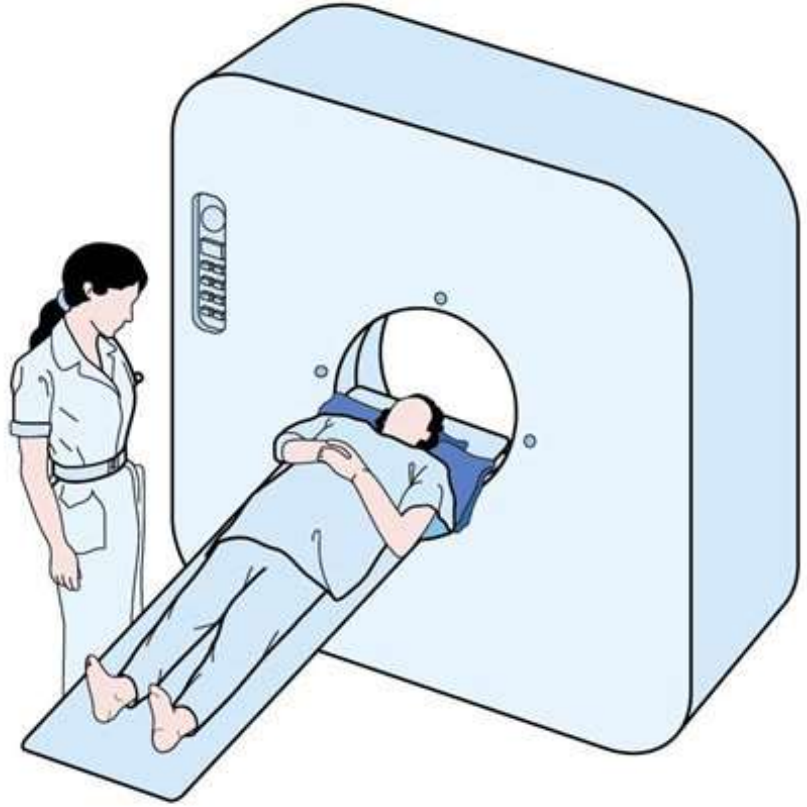
L. S. Freudenberg *et al.* **EJNMMI (2004) 31:**

Scientific Publications





HardWare Fusion

Commercial scanners on the market in 2001!
Last stand alone PET on the market in 2006!

The Nobel Prize in Physiology or Medicine 2003

Paul C. Lauterbur
University of Illinois
Urbana, IL, USA
1929-2007

Sir Peter Mansfield
University of Nottingham, School of Physics and Astronomy
Nottingham, United Kingdom
1919-2017

"for their discoveries concerning magnetic resonance imaging"

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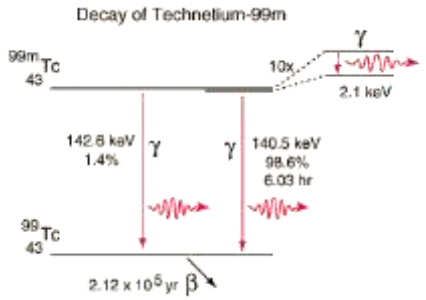
Nobelprize.org

The Tracer is the Key

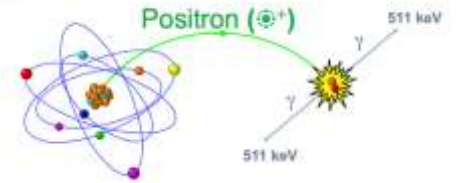
Gamma camera



Radio Pharmacon

Bone
Receptors
Perfusion
Ventilation
Kidney function
Blood cells
….

PET



Tracer

^{18}F or ^{11}C or ^{15}O

and

Active substanse

(FDG or ACE or….)

Metabolism
Receptors
Perfusion
Amino acid
Fatty acid
….

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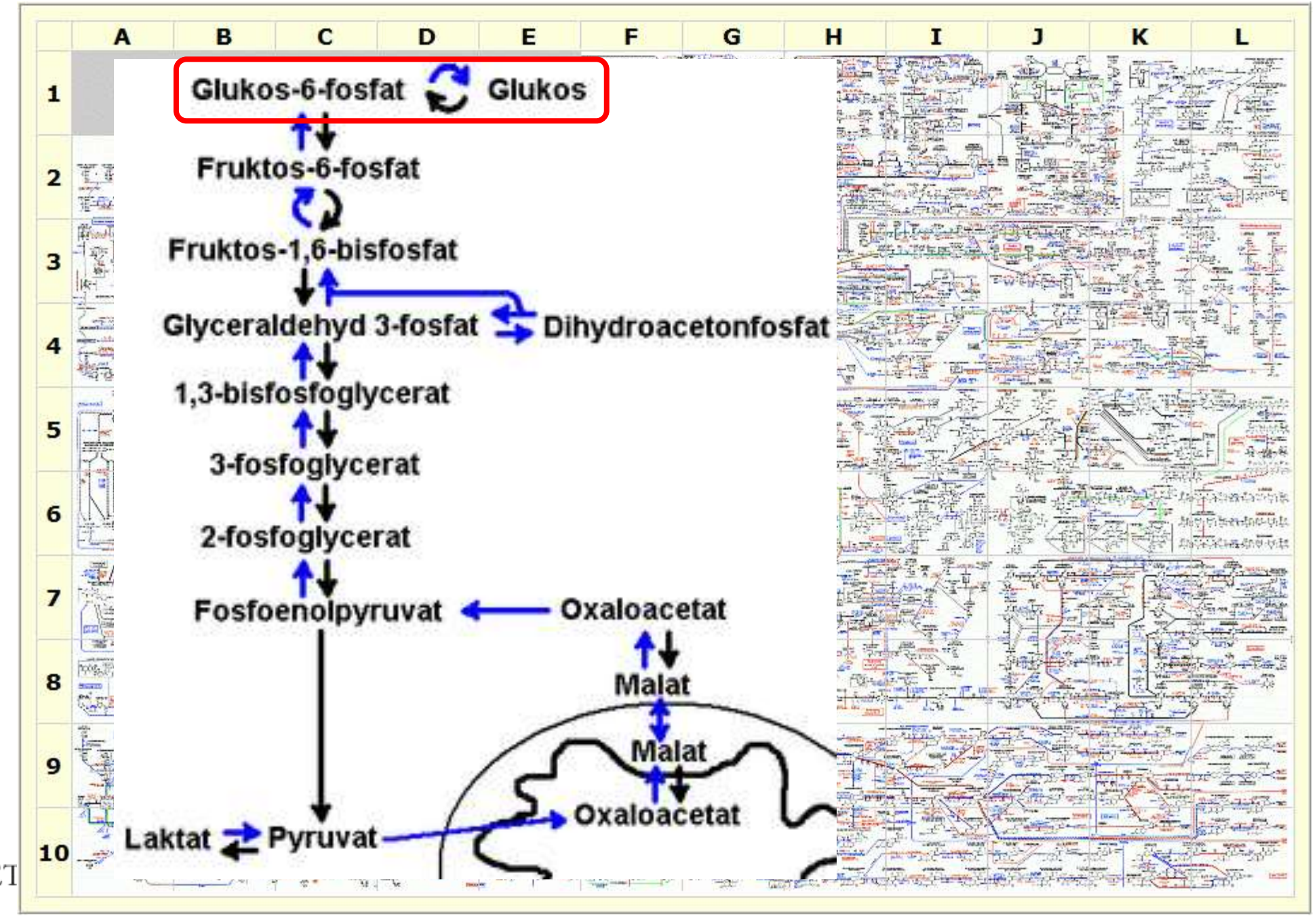

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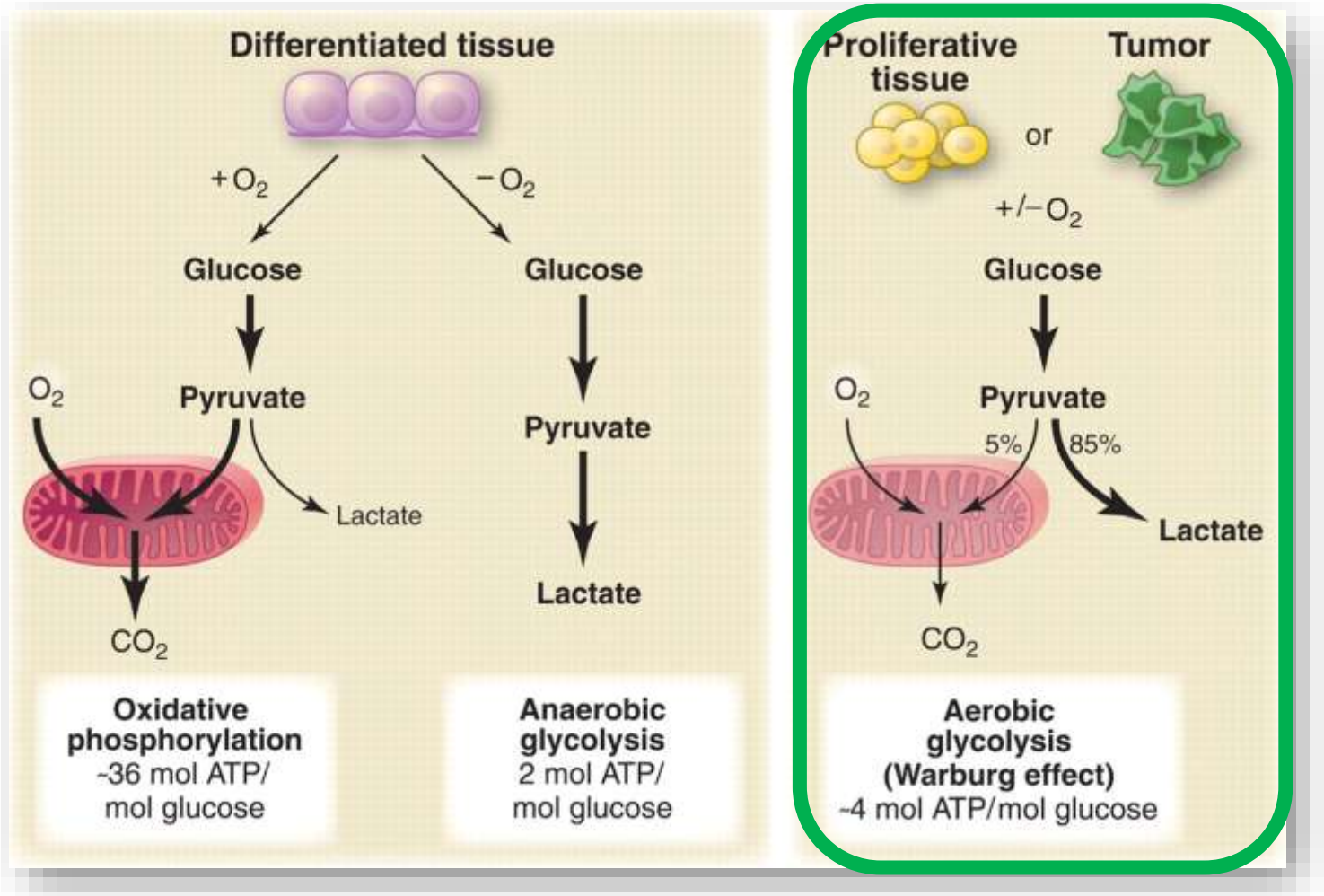
Warburg effect



Published by AAAS

M G Vander Heiden et al. Science 2009;324:1029-1033

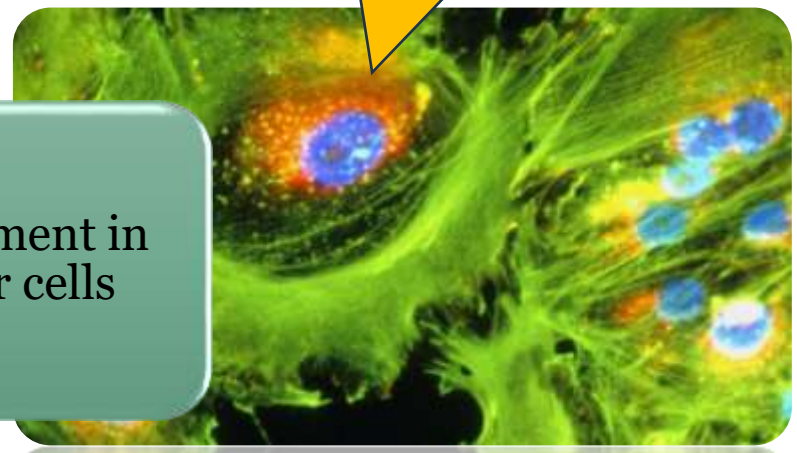
Tumour Cell Biology

Damage to DNA
Activation of oncogenes

Uncontrolled proliferation
Inefficient energy metabolism

Increased energy demands
activation of pathways

Entrapment in cancer cells



FDG can ”see” Cancer

Concentration and Resolution

Modality	Conc at target		Resolution (mm)
PET	picomolar	(10^{-12})	3-6
SPECT	nanomolar	(10^{-9})	4-12
Gd MRI	milli-micromolar	(10^{-3-4})	< 0.5
CE CT	milli	(10^{-3})	< 0.5

PET or SPECT

- Function/molecular/metabolic imaging

CT

- Attenuation correction
- Structural/Morphological imaging

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No pharmacological effect of PET tracer –µg dosage

FDG Dosage

1 sugar lump = 3 000 000 µg

…or….

200 000 sugar grains

Approx 3 µg FDG per patient

…or….

1/5 sugar grain

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FDG PET/CT Makes a Difference

VOLUME 26 · NUMBER 13 · MAY 1 2008

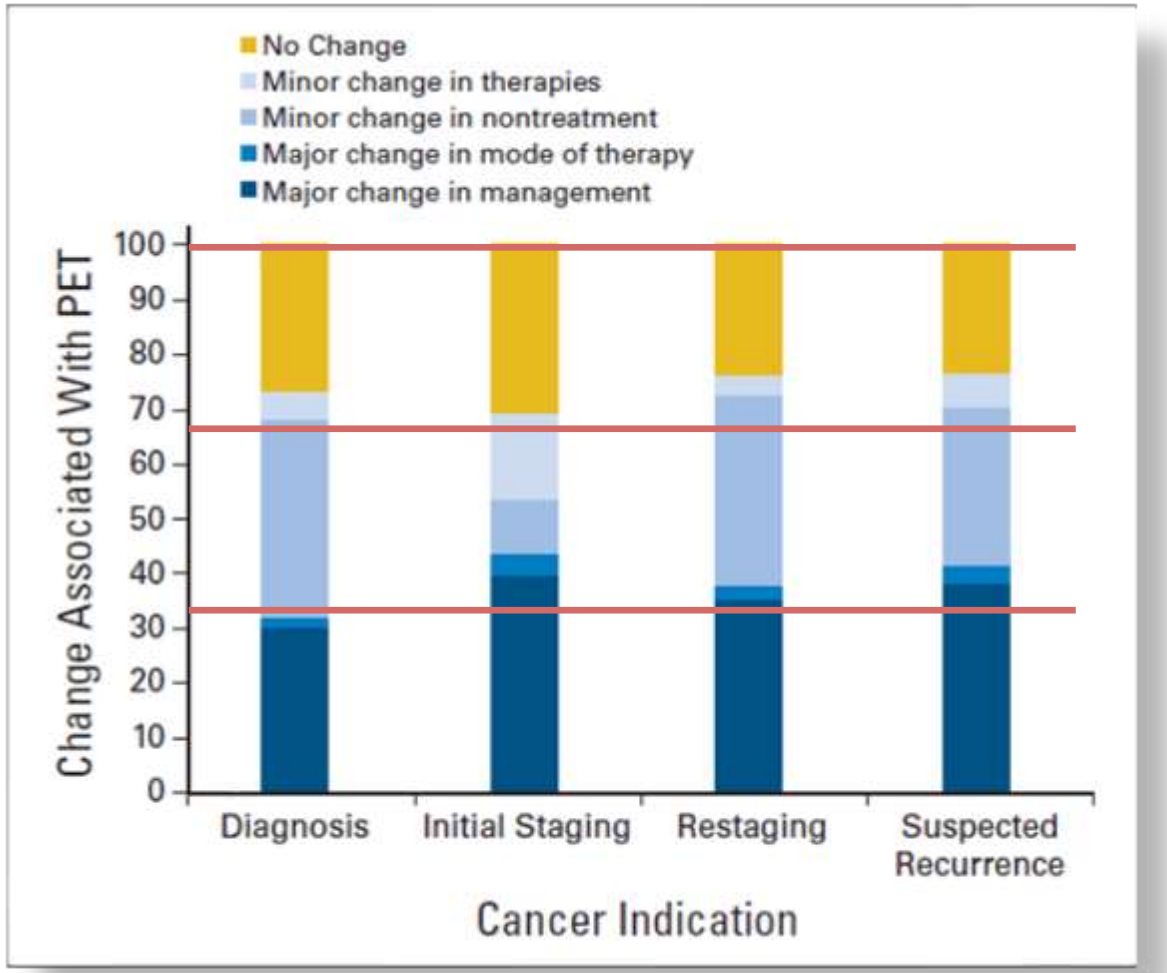
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Impact of Positron Emission Tomography/Computed Tomography and Positron Emission Tomography (PET) Alone on Expected Management of Patients With Cancer: Initial Results From the National Oncologic PET Registry

Bruce E. Hillner, Barry A. Siegel, Dawei Liu, Anthony F. Shields, Ilana F. Gareen, Lucy Hanna, Sharon Hartson Stine, and R. Edward Coleman

Based on 22 975 studies



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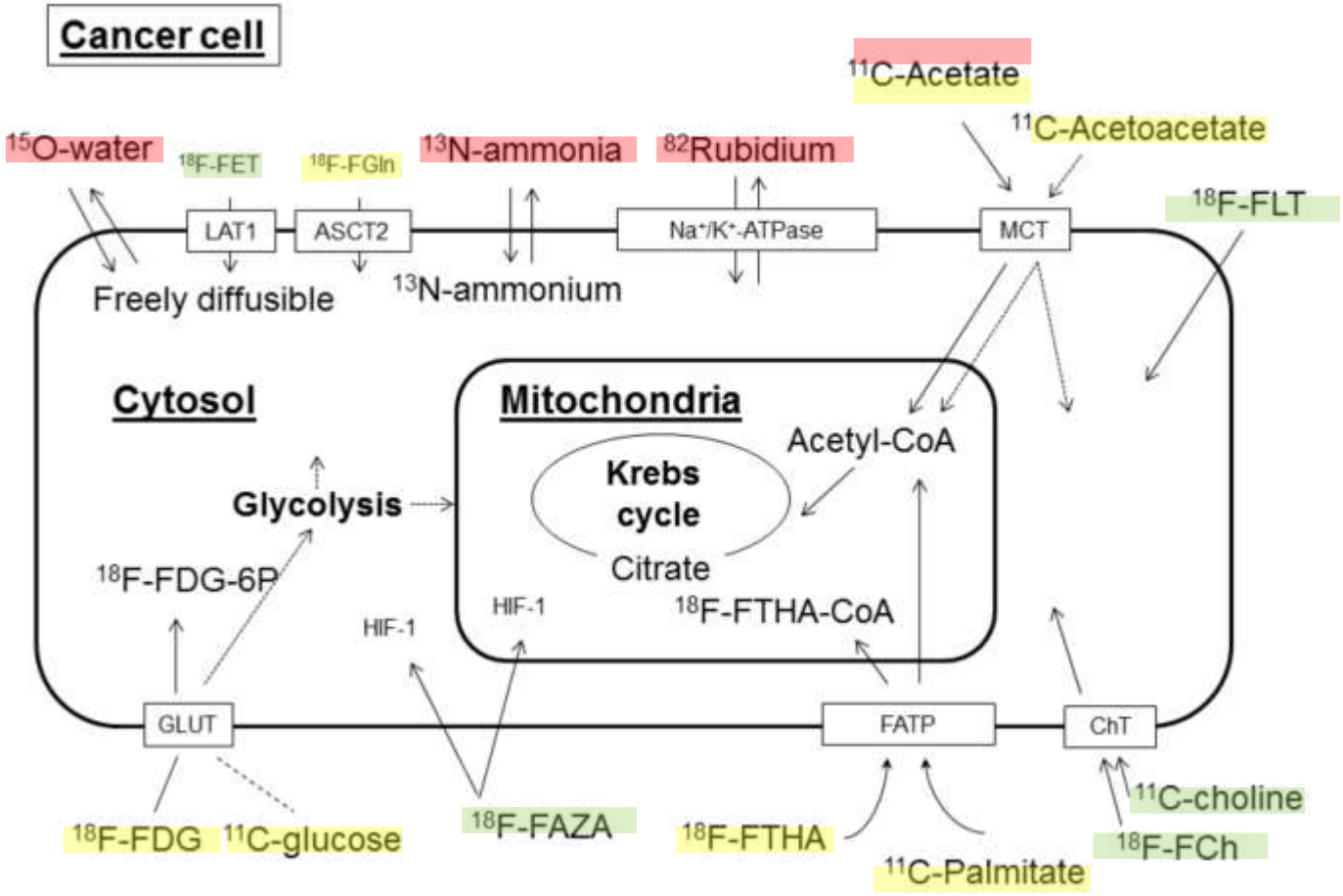
Hillner *et el* JCO 2008

Tracer targets



- PET radiotracers targeting tumors used for the assessment of blood flow (MBF; 15O-water, 13N-ammonia, 82Rubidium, 11C-acetate),
- metabolism (18F-FDG, 11C-glucose, 18F-FTHA, 11C-palmitate, 11C-acetate, 18F-FGln, and 11C-acetoacetate),
- key markers (18F-FAZA, 18F-FLT, 18F-FET, 18F-FCh, and 11C-choline).

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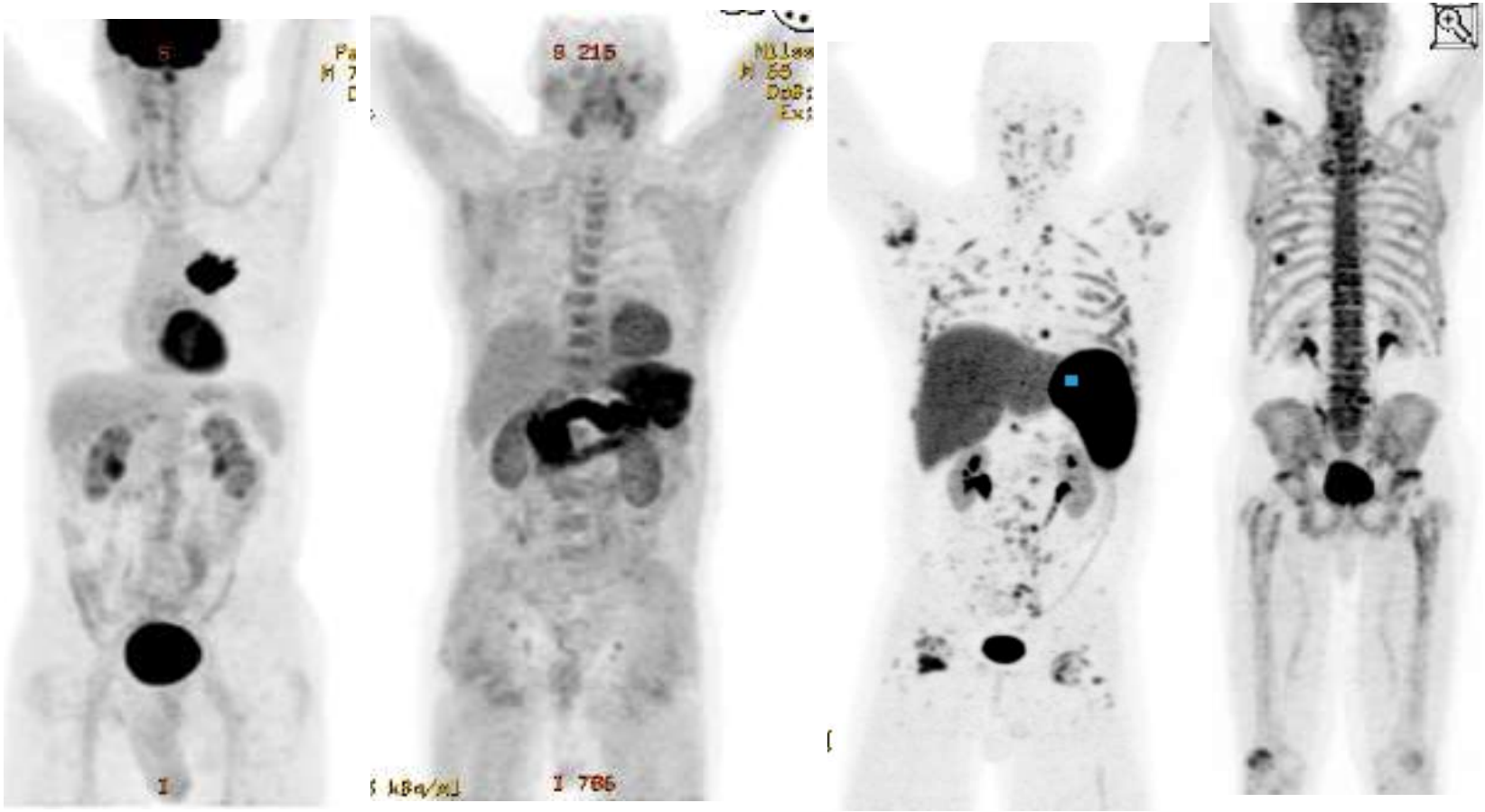
Croteau et al 2016

Tracer Distribution



FDG	Acetat	FLT	NAF
Metabolism	Energy or membranne synthesis	Proliferation	Ostogenesis

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Neuro Applications

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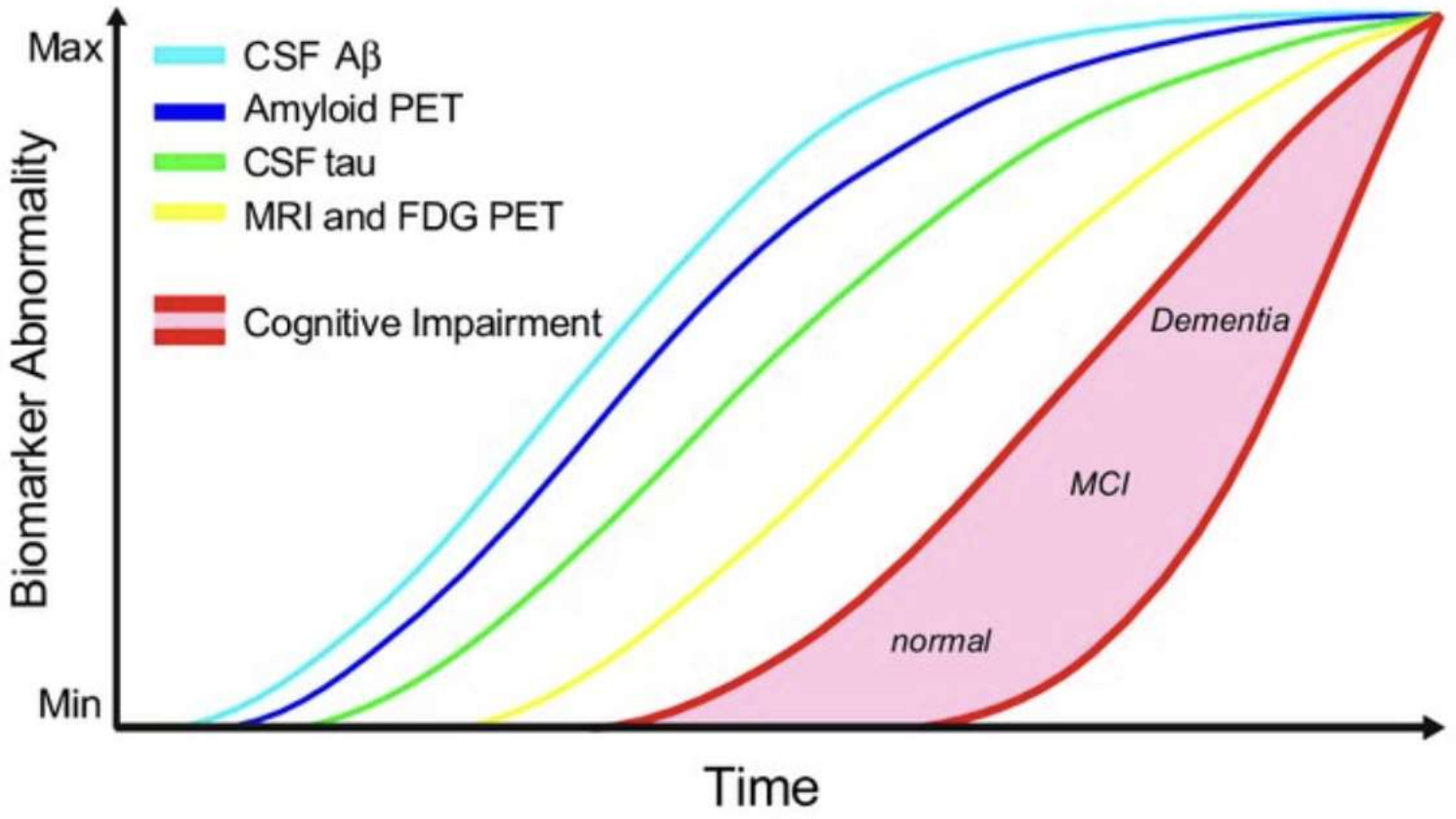
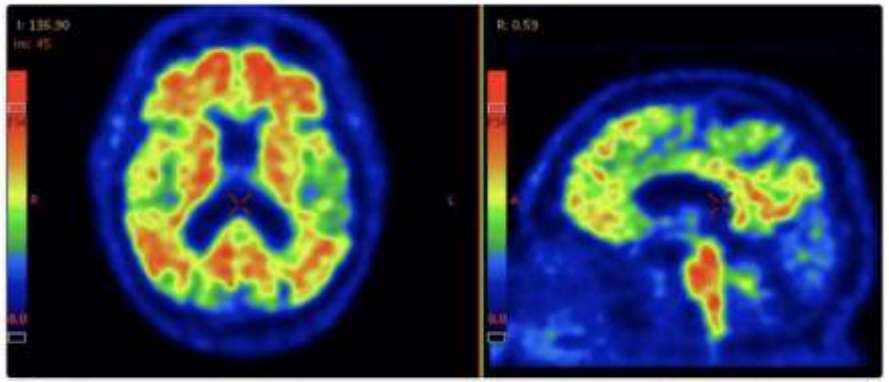
Biomarkers in Dementia



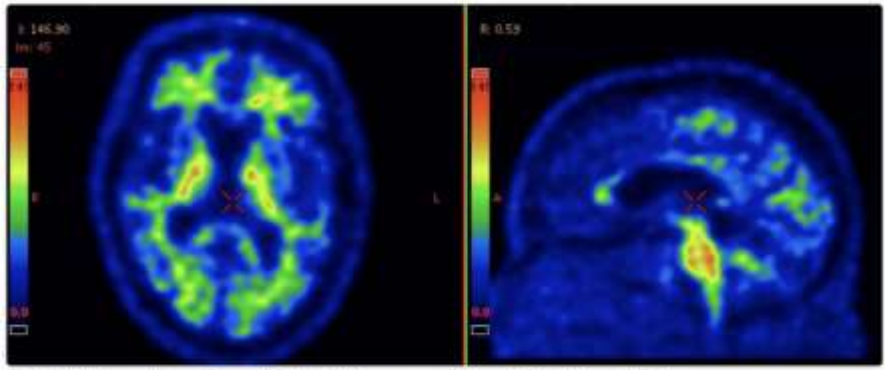
Tracer Distribution

THE SWEDISH BIOFINDER STUDY™

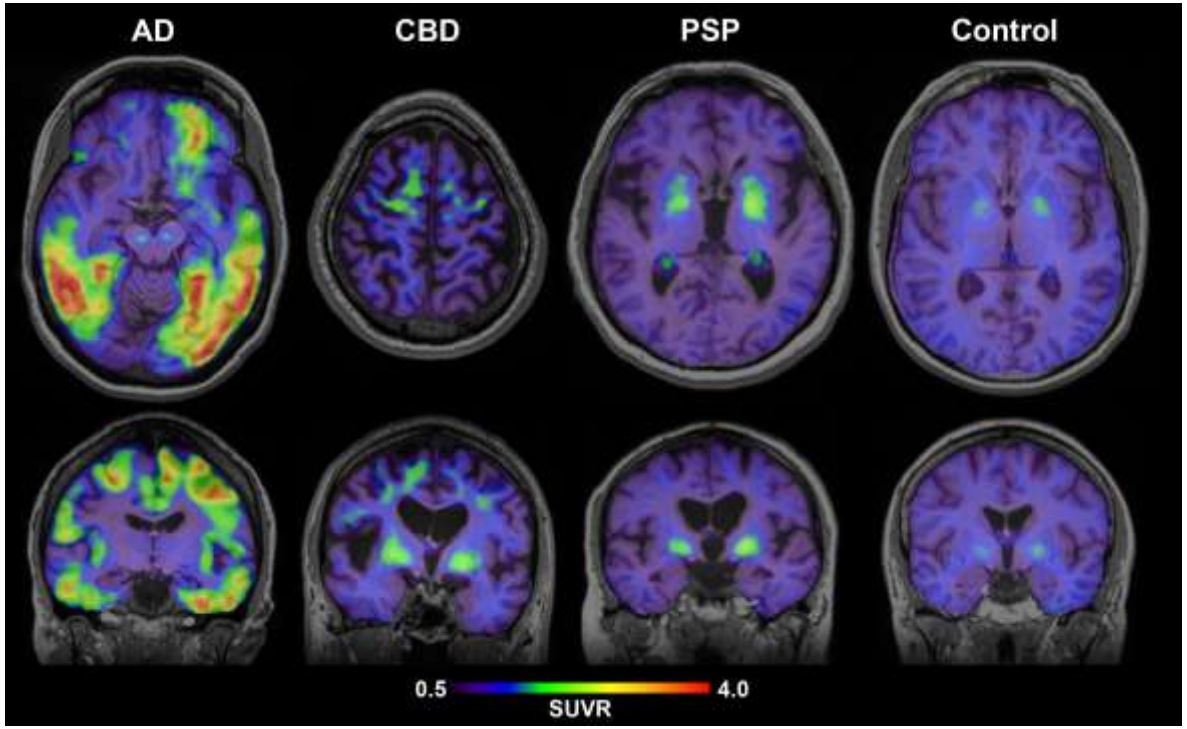
Amyloid PET imaging



[18]F-flutemetamol amyloid PET in an MCI patient that later developed AD



[18]F-flutemetamol amyloid PET in a cognitively healthy elderly



TAU PET

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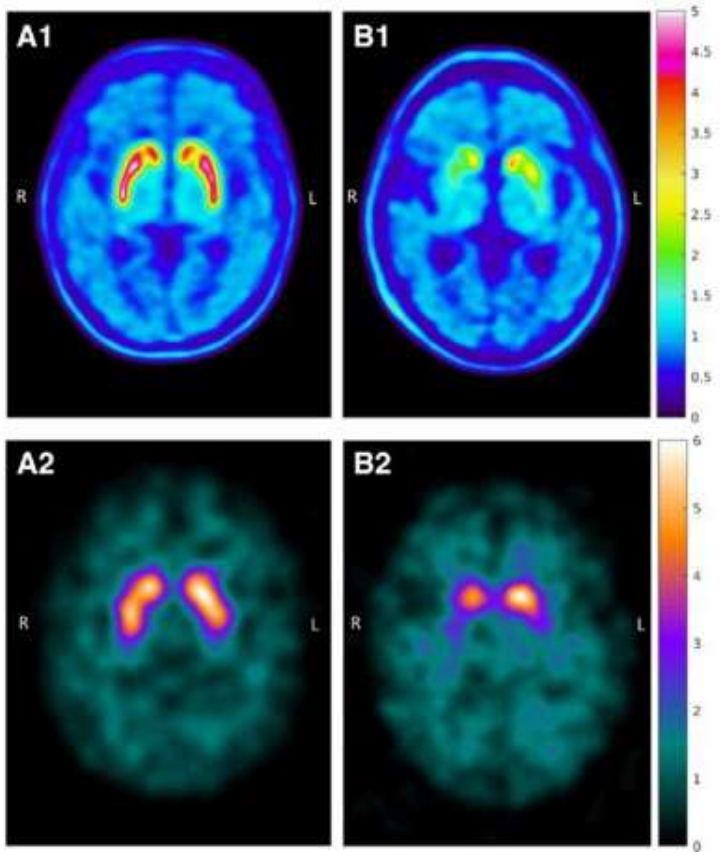
Dopamine transporter imaging with [18F]FE-PE2I PET and [123I]FP-CIT SPECT—a clinical comparison

PE2I-PET

Fp-CIT-SPECT



***Conclusion**: DAT imaging with FE-PE2I PET yields excellent basic diagnostic differentiation in early-stage PS, at least as good as FP-CIT SPECT.*

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Jakobson Mo et al. EJNMMI Research (2018) 8:100

Lymphoma

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Change in Guidelines

VOLUME 32 · NUMBER 27 · SEPTEMBER 20 2014

JOURNAL OF CLINICAL ONCOLOGY

SPECIAL ARTICLE

Recommendations for Initial Evaluation, Staging, and Response Assessment of Hodgkin and Non-Hodgkin Lymphoma: The Lugano Classification

Bruce D. Cheson, Richard I. Fisher, Sally F. Barrington, Franco Cavalli, Lawrence H. Schwartz, Emanuele Zucca, and T. Andrew Lister

Deauville Criteria 2014

Score	Definition	
1	No uptake	CMR
2	Uptake ≤ mediastinum	
3	Uptake > mediastinum but ≤ liver	Prob CMR
4	Moderately increased uptake compared to the liver	
5	Markedly increased uptake compared to the liver and/or new lesions	
X	New areas of uptake unlikely to be related to lymphoma	

- A baseline PET/CT should always be performed prior to initiation of therapy.
- An interim-PET must be performed early on during induction chemotherapy.

FDG-PET/CT in B-cell Lymphoma and Hodgkins disease

- Initial staging → altered therapy occurs in about 9%
- response assessment → residual fibrotic masses vs viable tumor
- Post-treatment PET-neg → more favorable PFS outcomes; (P <.001)
- Interim PET neg → higher 2-year PFS (P=0.0046)
- Interim PET pos → change of treatment
- No bone marrow biopsy if clearly positive focal marrow uptake by PET-CT

Mb Hodgkin!

Sep

First two rounds of chemo

Complete metabolic response after two rounds of ABVD

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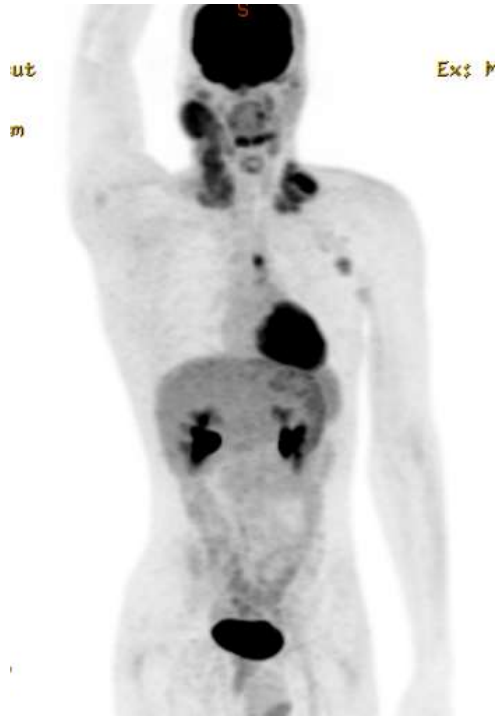
3

2



1

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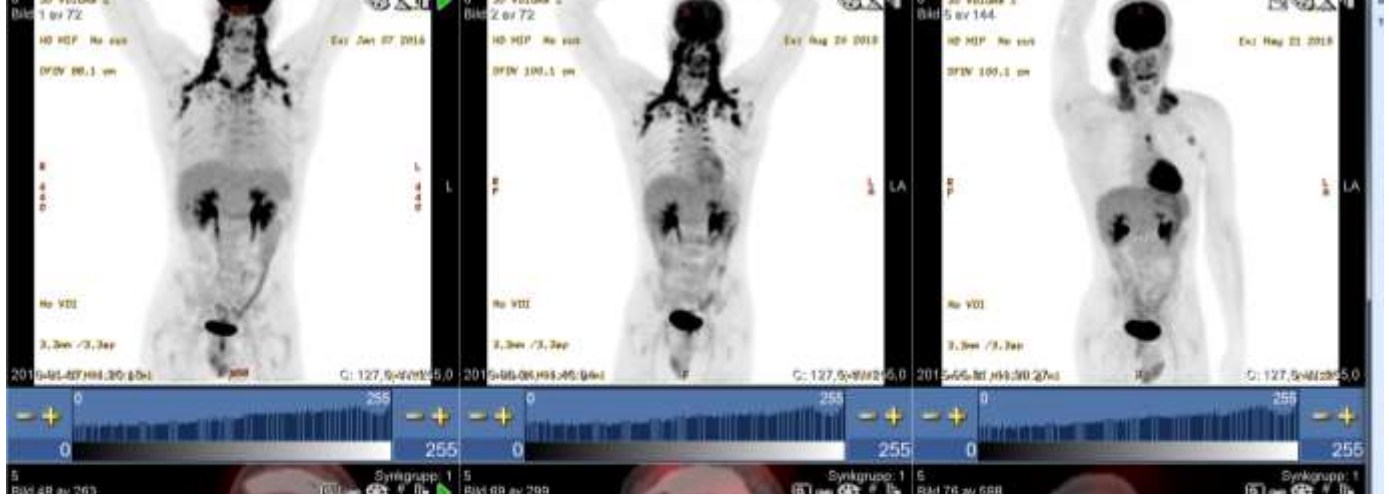
In 17 of the 638 patients (2.5%), increased, symmetrical FDG uptake was found in the shoulder region that was not related to muscular structures on CT.



Short communication

Brown adipose tissue: a factor to consider in symmetrical tracer uptake in the neck and upper chest region

Thomas F. Hany[1], Esmaiel Gharehpapagh[1], Ehab M. Kamel[1], Alfred Buck[1], Jean Himms-Hagen[2], Gustav K. von Schulthess[1]

[1] Department of Medical Radiology, Division of Nuclear Medicine, University Hospital Zurich, Rämistrasse 100, 8091 Zurich, Switzerland
[2] Department of Biochemistry, Microbiology and Immunology, University of Ottawa, Canada

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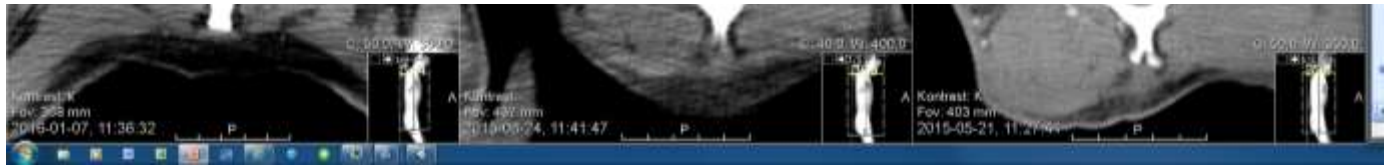
Eur J Nucl Med (2002) 29:1393–1398



Lung Cancer

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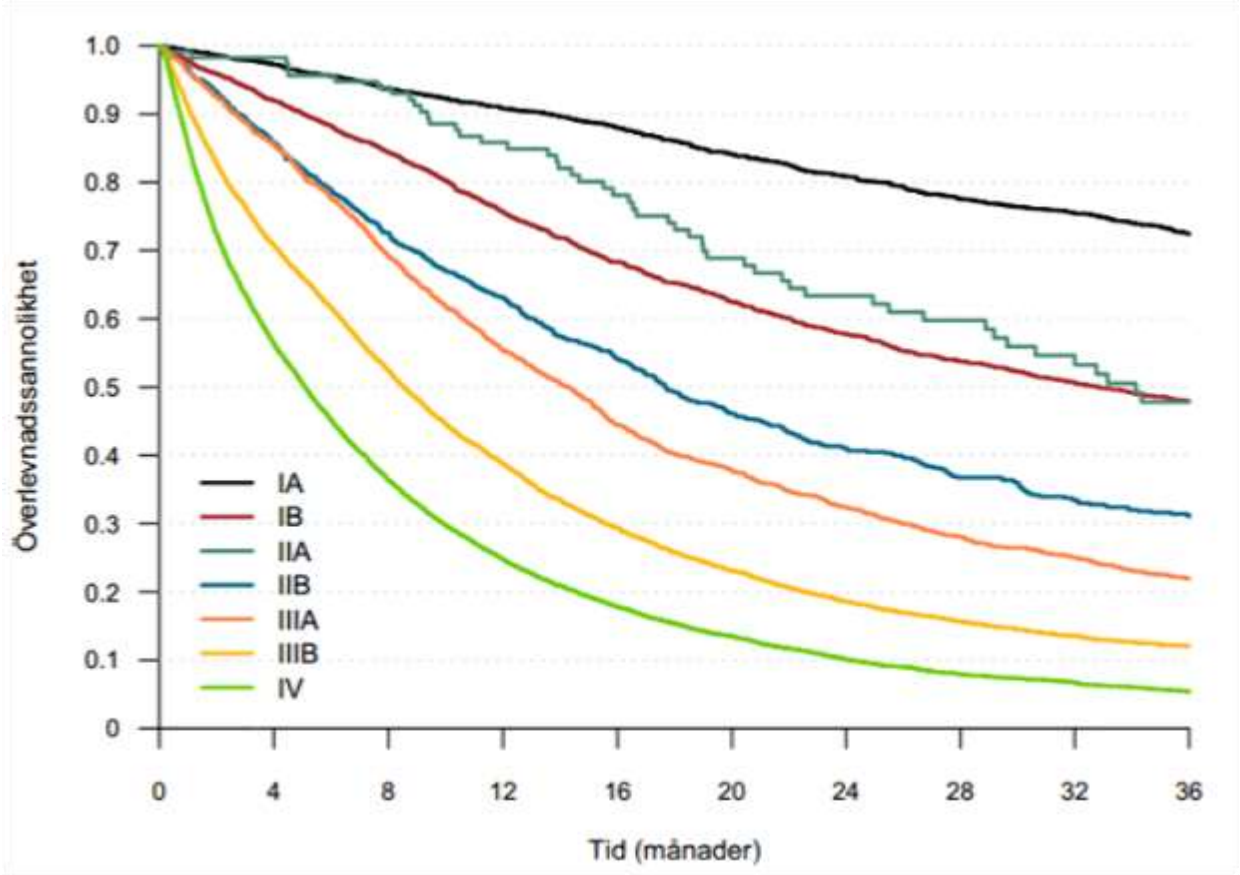
FDG-PET/CT in NSCLC

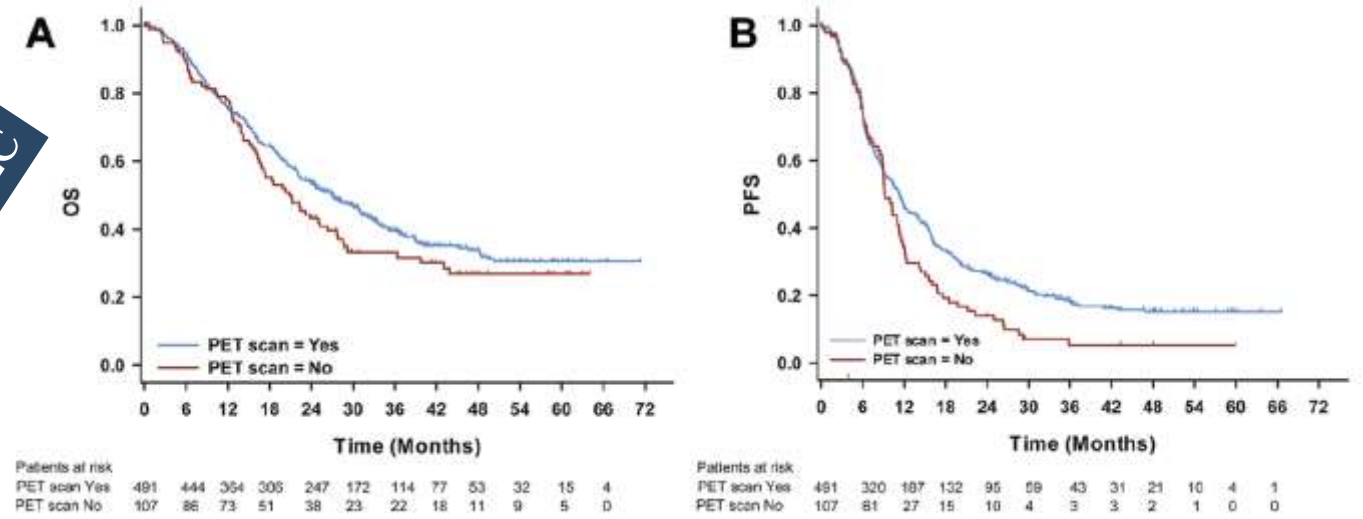
- 590 292 pat – 6118 with NSCLC
- Unsuspected distant metastases in 11-16.5% of patients
- Changes in stage in 27-62%
- Changes in medical management in 25-37%



Morgensztern et al 2008 J Thor Surg

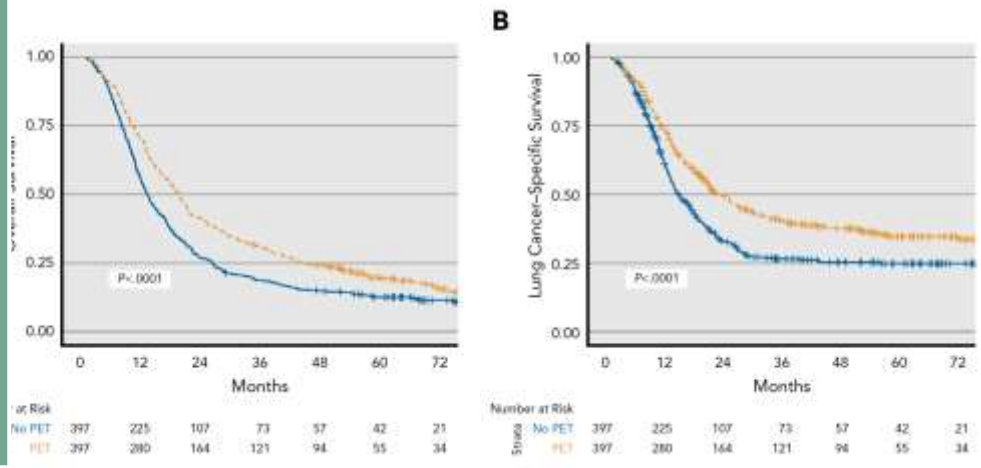
Stage Migration in Lung Cancer

NSCLC

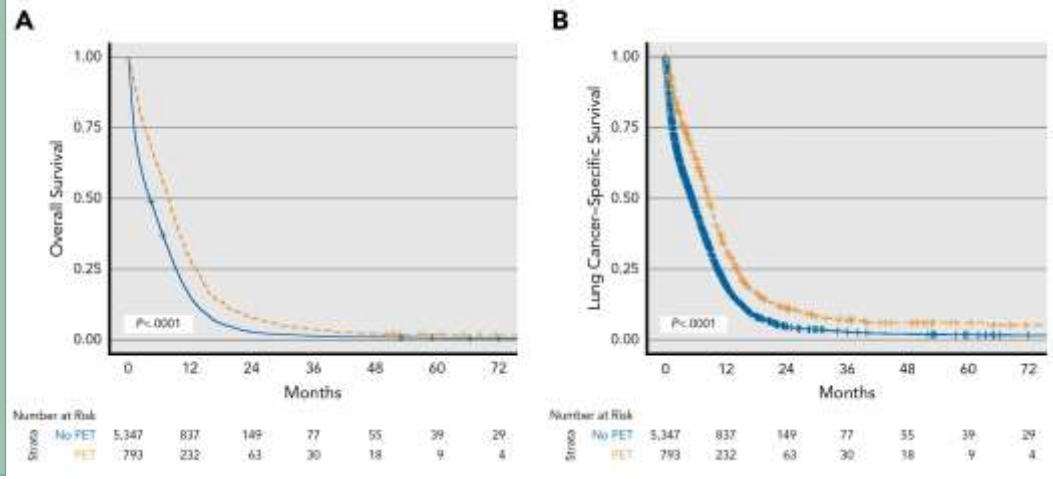


Vokes et al *Journal of Thoracic Oncology 2018 Vol. 13 No. 8: 1183*

limited-stage small cell lung cancer treated with chemoradiation.



Extensive stage small cell lung cancer treated with chemoradiation.



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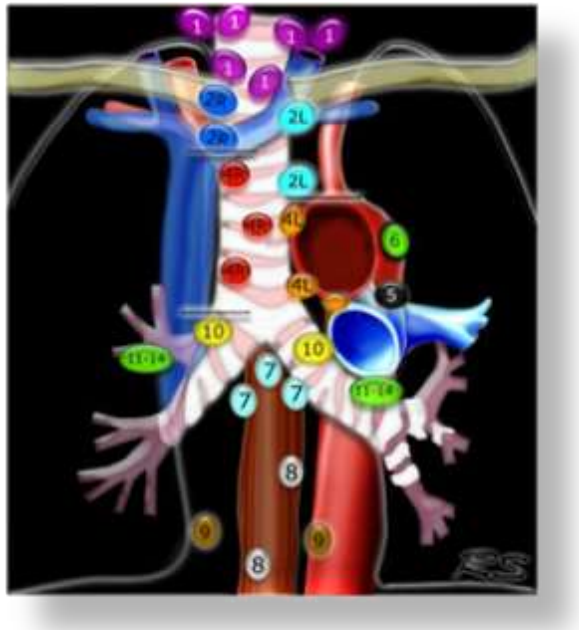
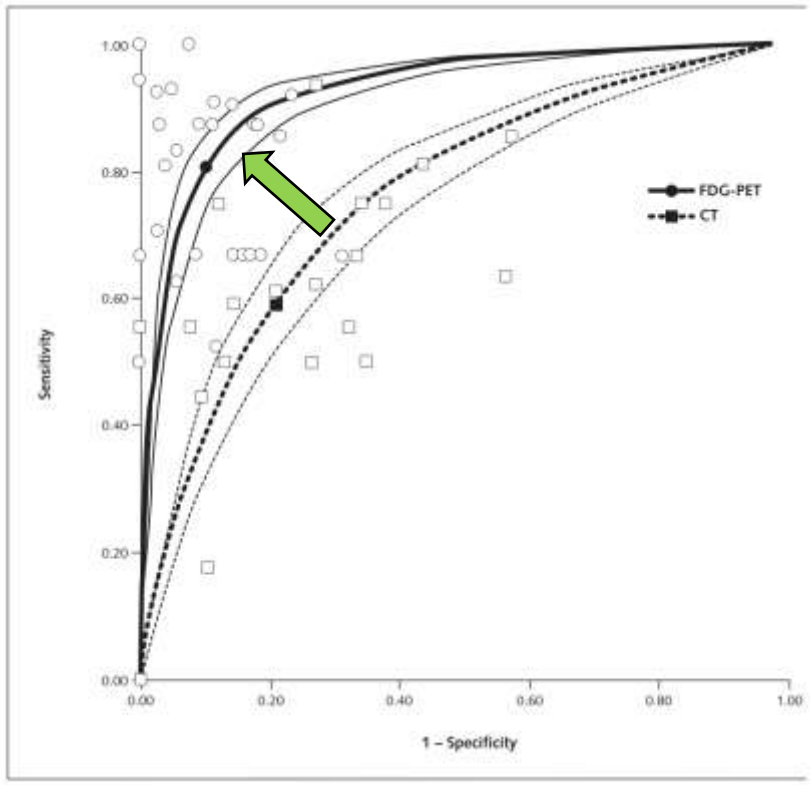
Hong et al *J Natl Compr Canc Netw 2019;17(2):127*

Test Performance of Positron Emission Tomography and Computed Tomography for Mediastinal Staging in Patients with Non–Small-Cell Lung Cancer

A Meta-Analysis

- 39 studies - 1959 patients – unknown number of lymph nodes





	Sens (%)	Spec (%)
CT	61	79
PET normal sized nodes	82	93
PET enlarged nodes	100	78

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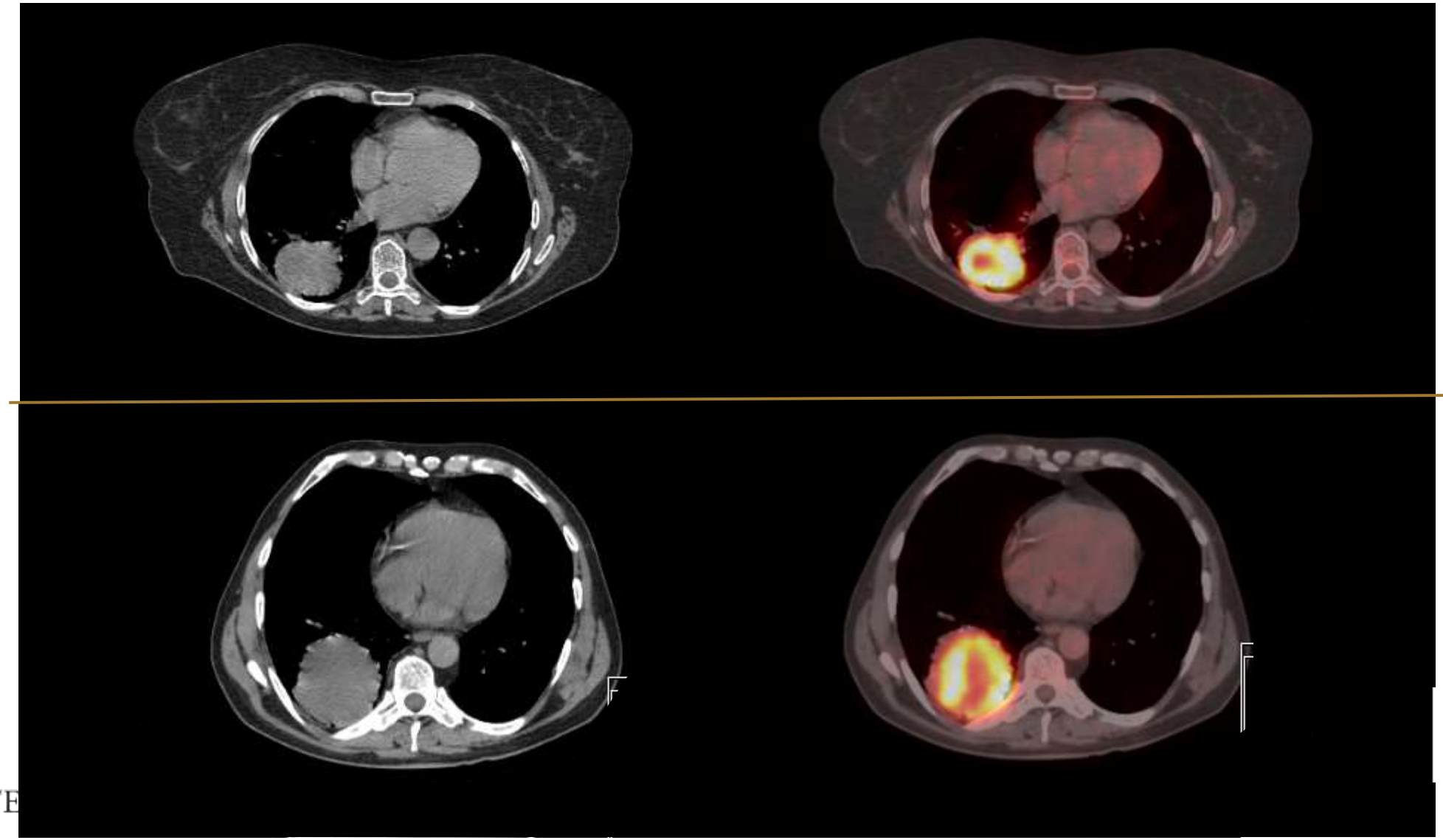
Gould *et al* Ann Intern Med. 2003;13:879

Lung Cancer x 2



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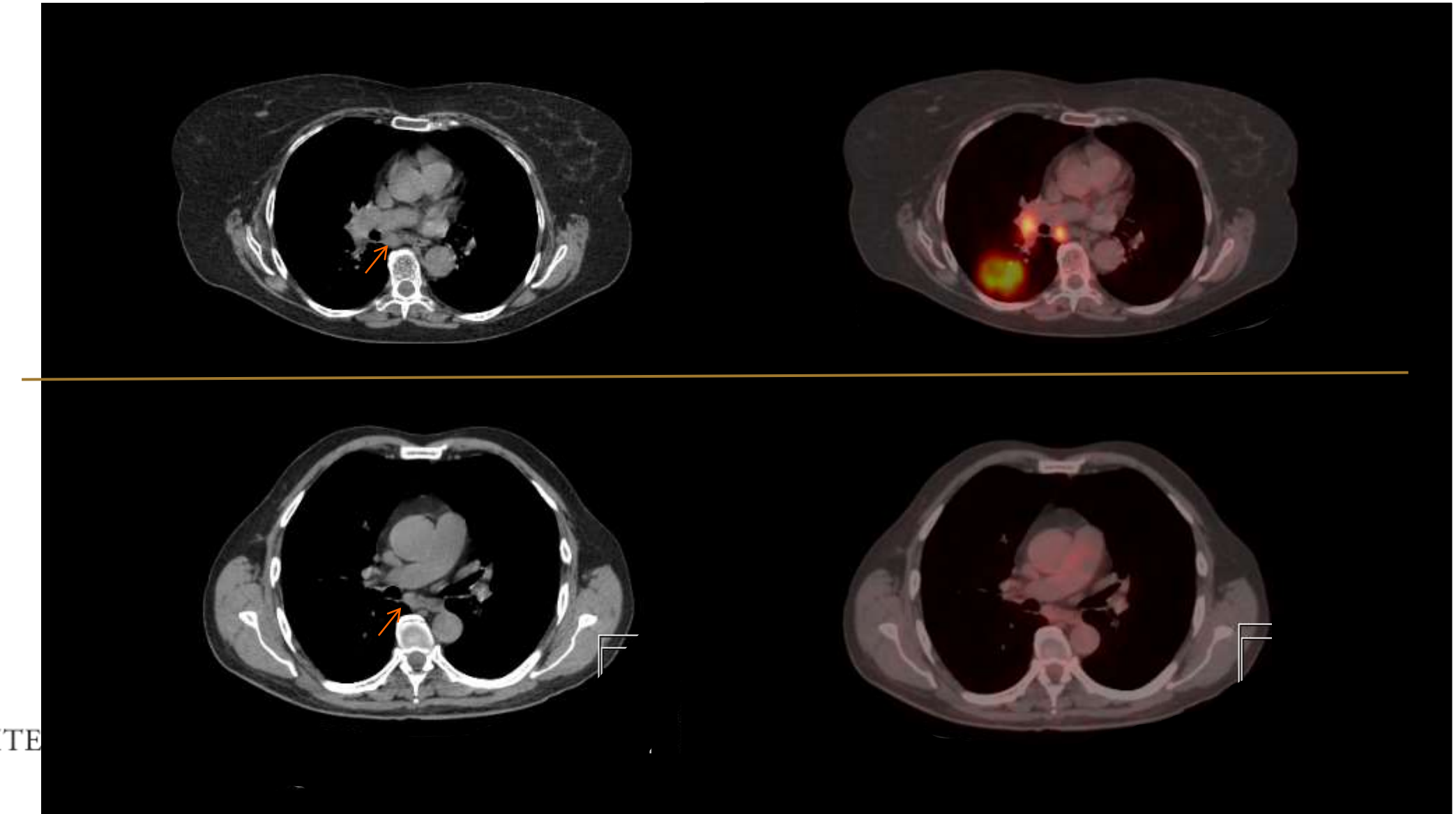
Lung Cancer x 2



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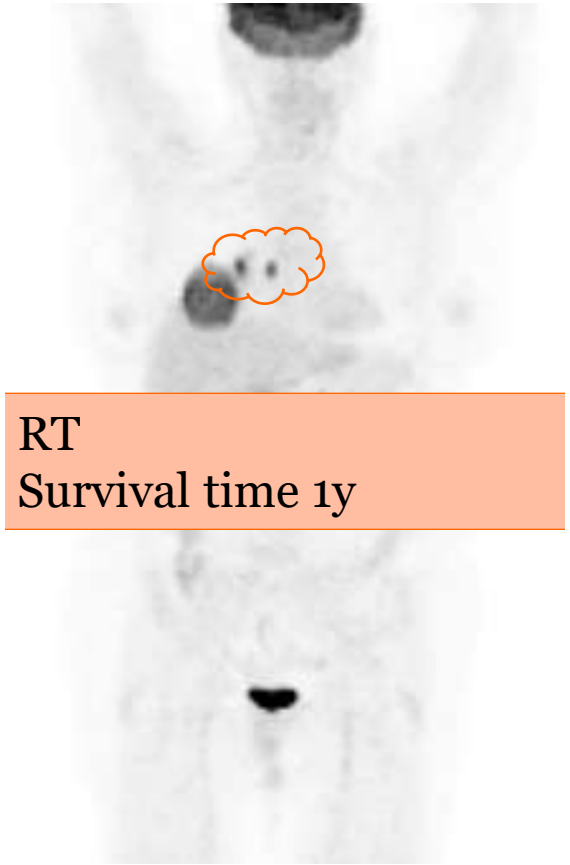
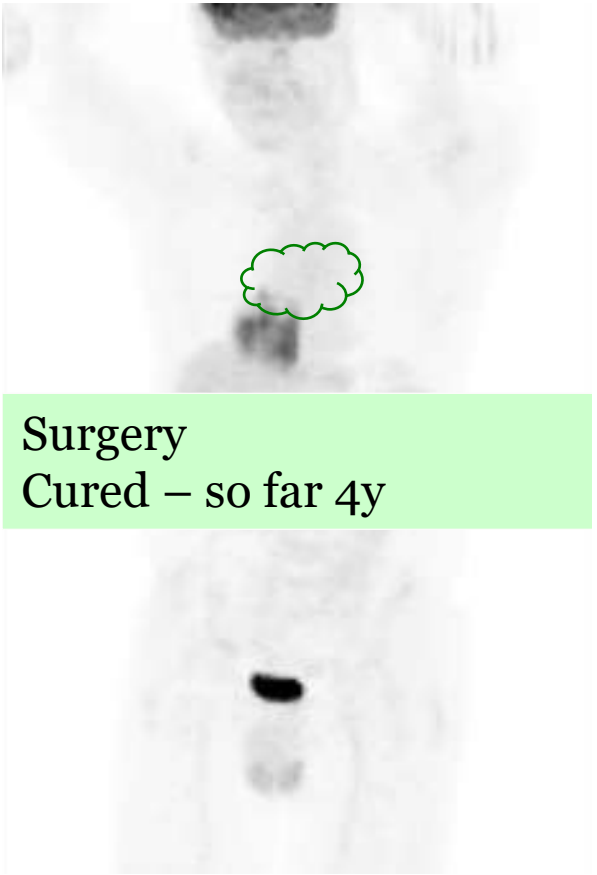
Lung Cancer x 2



RT
Survival time 1y



Surgery
Cured – so far 4y

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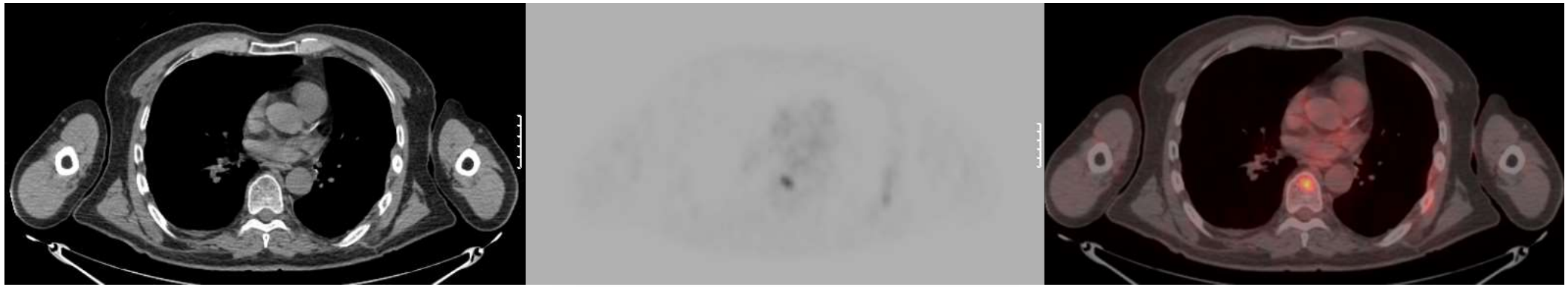
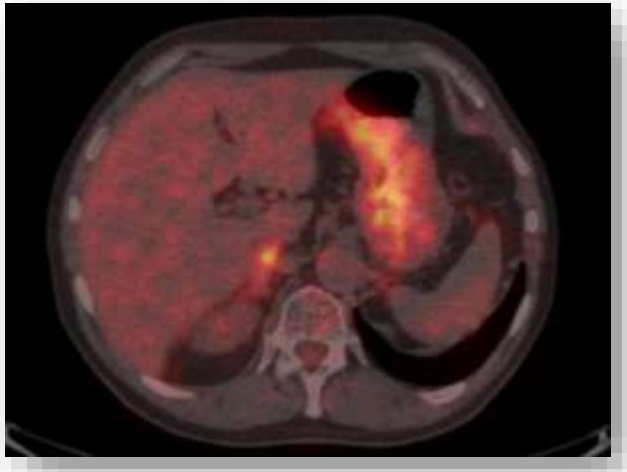
Distant Metastases in Lung Cancer

- FDG PET/CT to rule out metastatic disease in Stage I, II and IIIA Disease, as well as IIIB (T1-2, N3 and T3-4, N2) and IV (M1b)





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MacMahon et al
Radiology 2017;
284:228–243

Guidelines for Management of Incidental Pulmonary Nodules Detected on CT Images: From the Fleischner Society 2017[1]

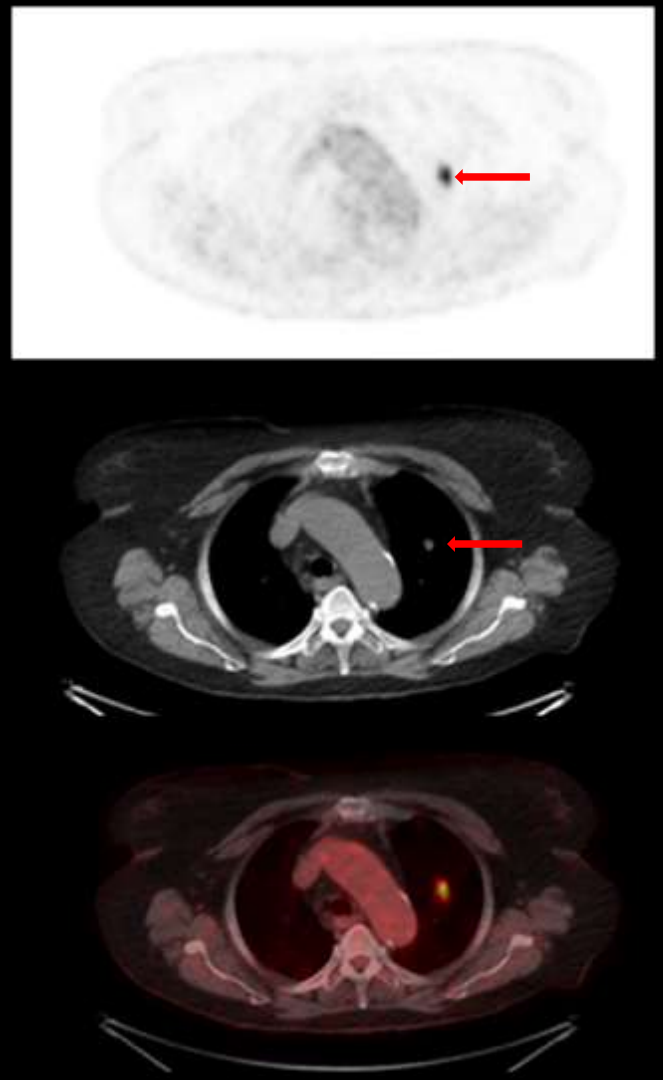
Radiology

Fleischner Society 2017 Guidelines for Management of Incidentally Detected Pulmonary Nodules in Adults

A: Solid Nodules*

Nodule Type	Size			Comments
	<6 mm (<100 mm³)	6–8 mm (100–250 mm³)	>8 mm (>250 mm³)	
Single				
Low risk†	No routine follow-up	CT at 6–12 months, then consider CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients (recommendation 1A).
High risk†	Optional CT at 12 months	CT at 6–12 months, then CT at 18–24 months	Consider CT at 3 months, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-month follow-up (recommendation 1A).

Small Lung nodules



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Prostate Cancer

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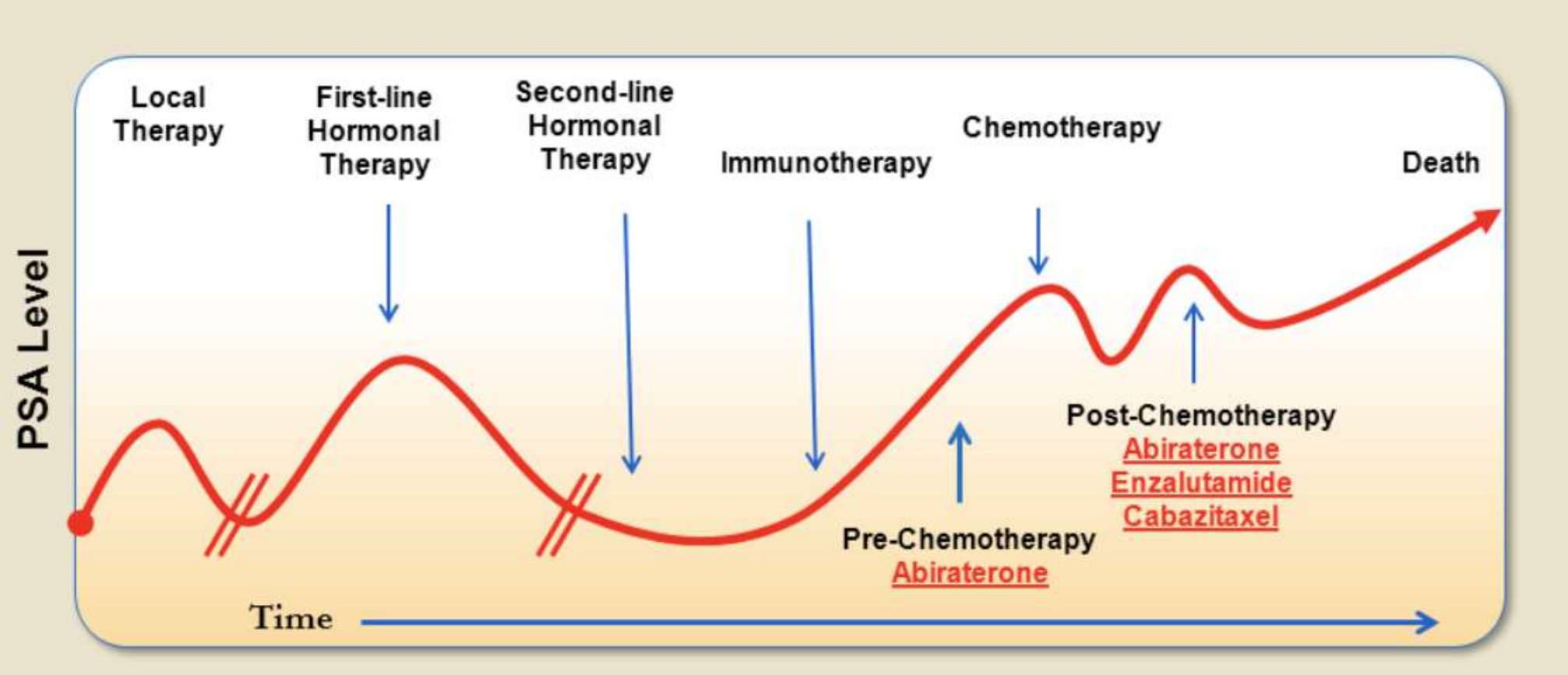
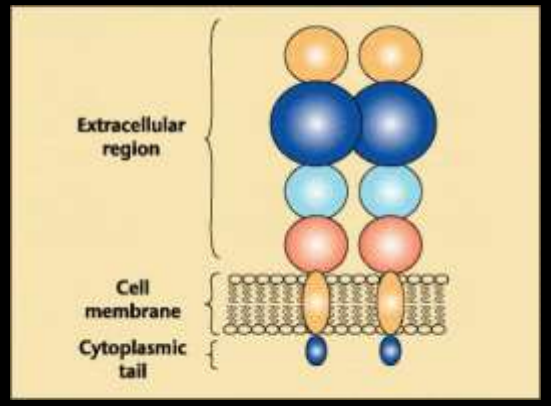
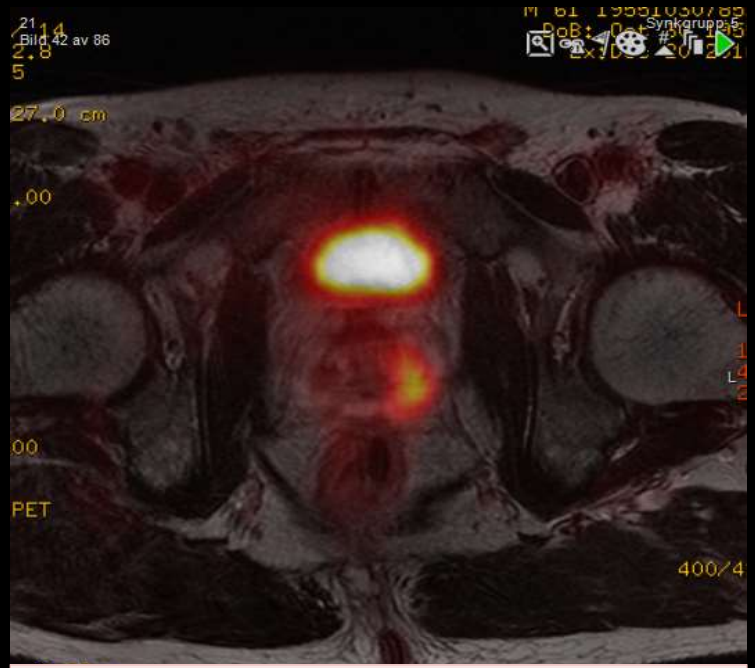
PROGRESSION OF PCA

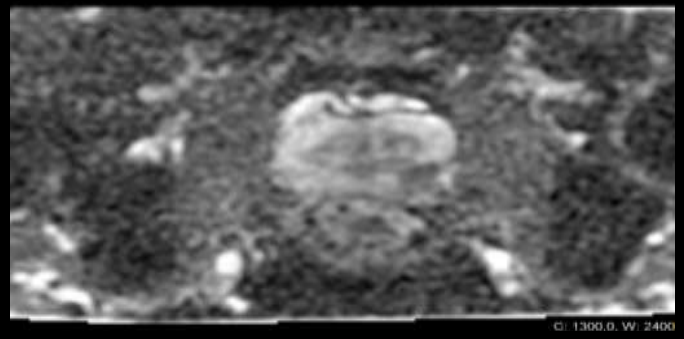




^{68}Ga- & ^{177}Lu-labelled PSMA targeting agents



PSMA PET/MR: Uptake PZ left



DWI

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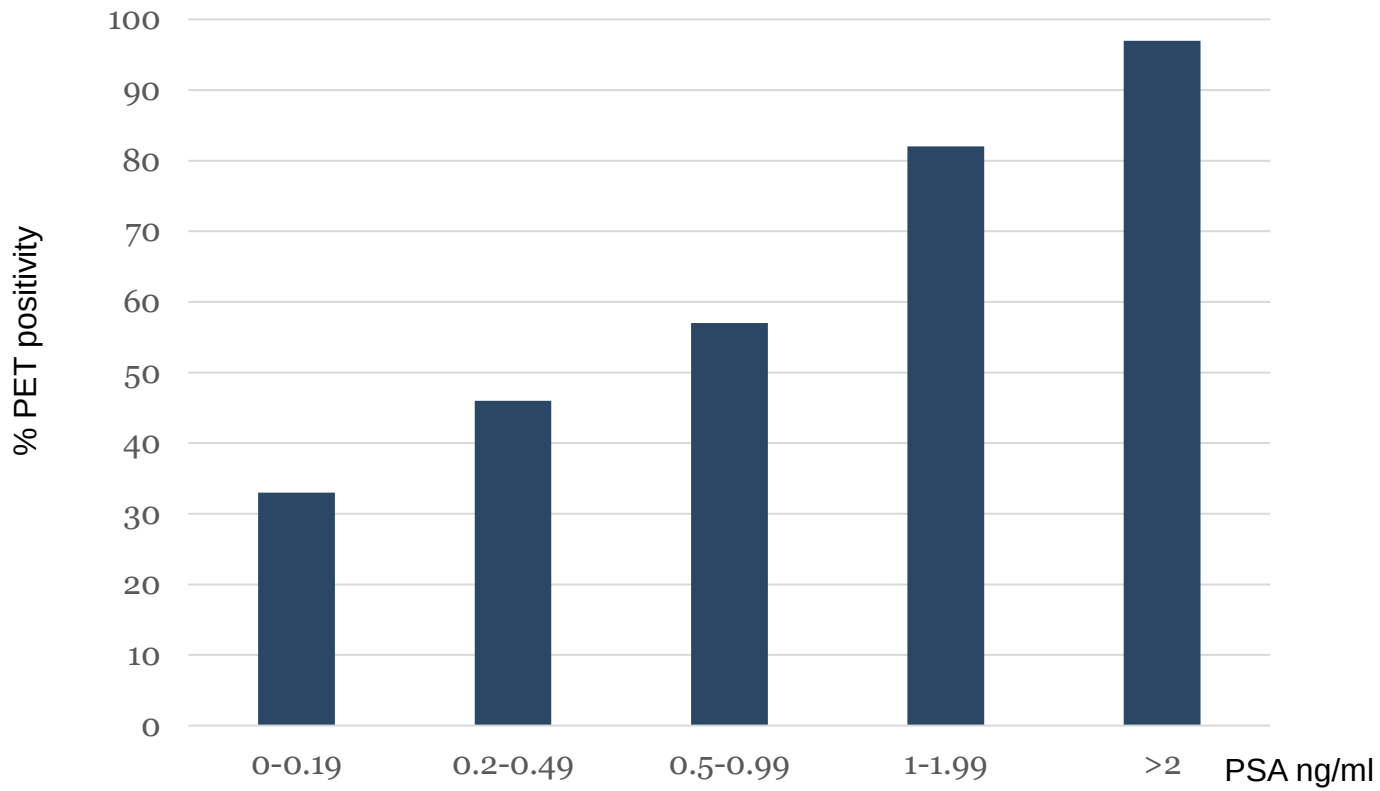
Gallium-68 Prostate-specific Membrane Antigen Positron Emission Tomography in Advanced Prostate Cancer—Updated Diagnostic Utility, Sensitivity, Specificity, and Distribution of Prostate-specific Membrane Antigen-avid Lesions: A Systematic Review and Meta-analysis



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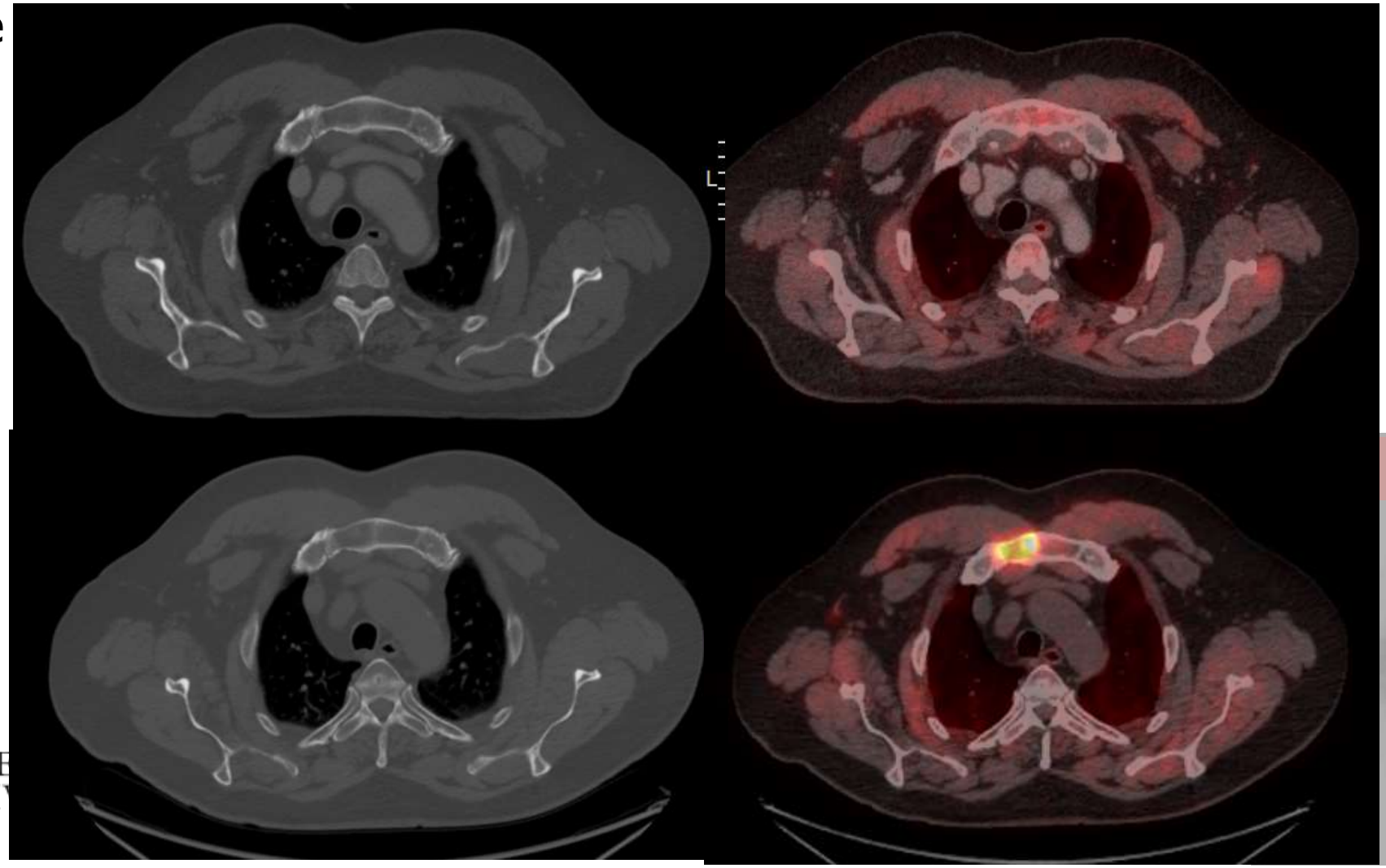
37 papers including 4790 patients

Perera et al Eur Urol, 2020. 77: 403.

Prostate cancer with PSMA PET CT

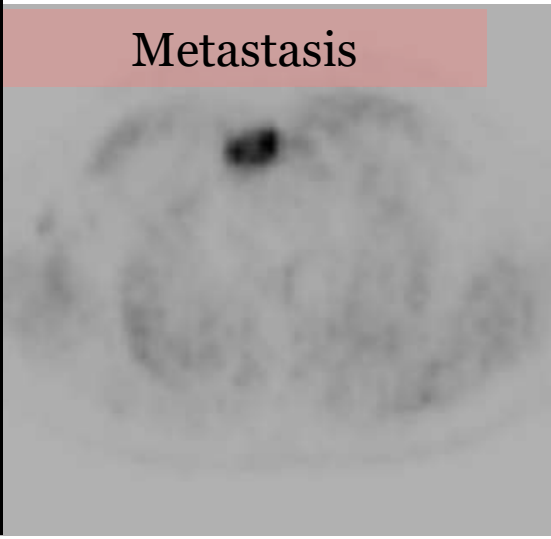
Baseline

FU@2.5 y



3. Finding?

Metastasis



UME
UNI

ColoRectal Cancer

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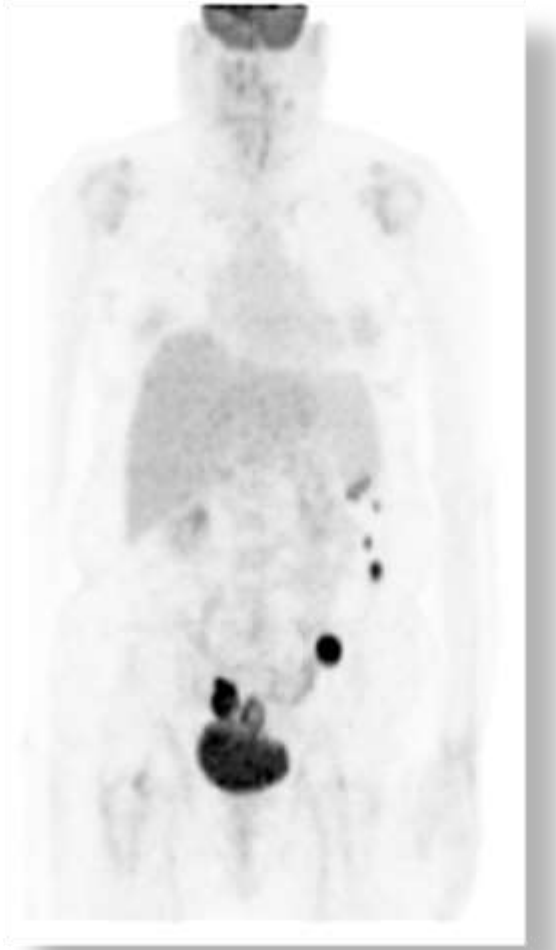
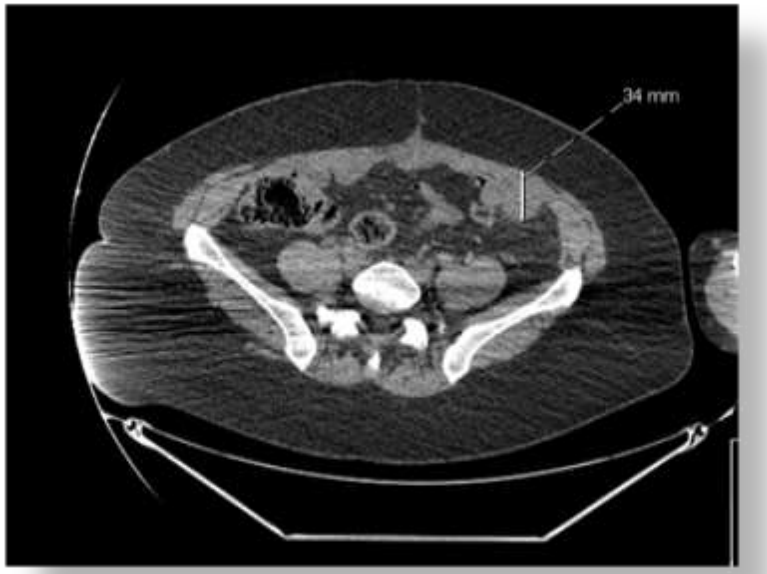
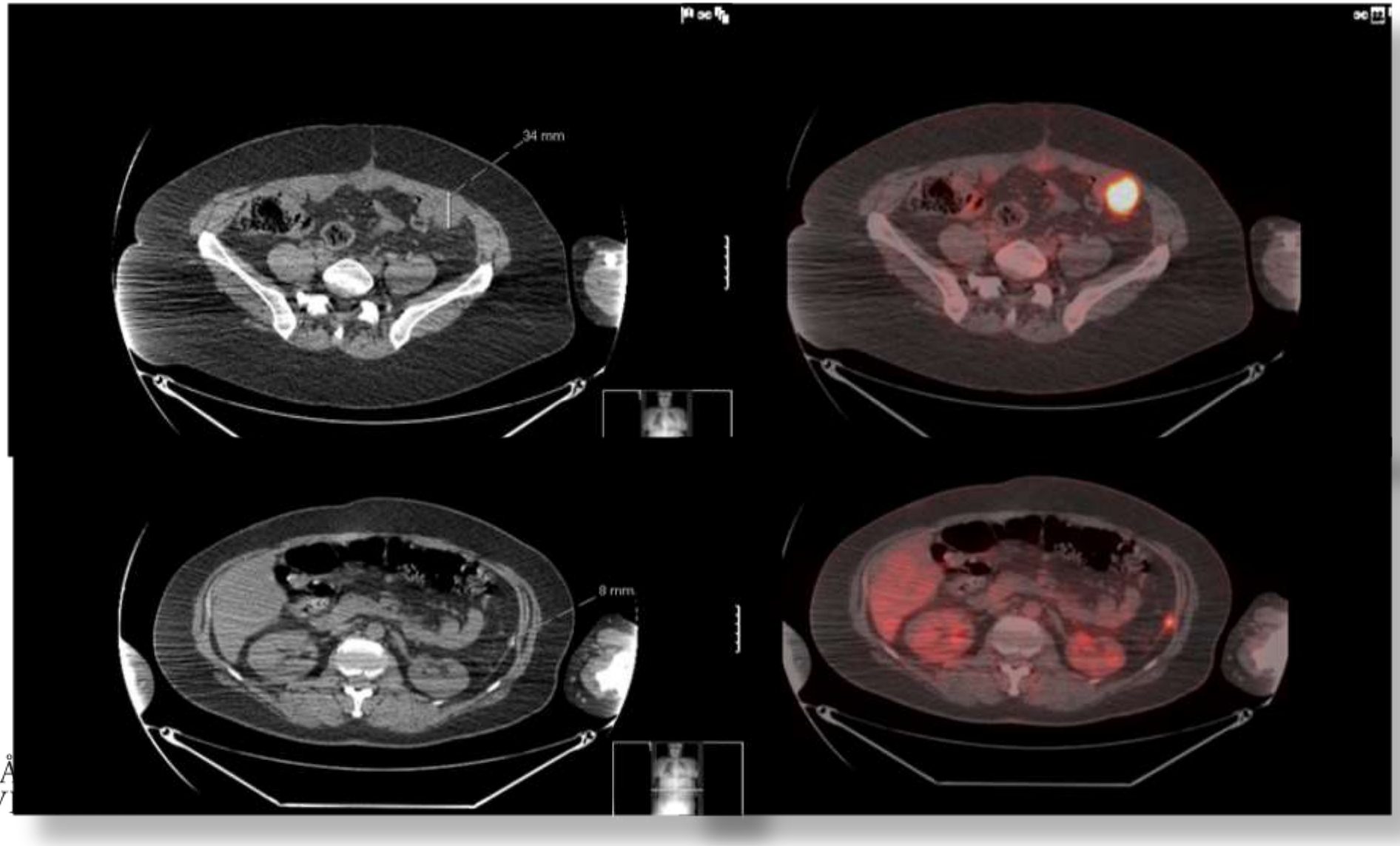
Coloncancer - Uppföljning





Vänstersidig hemicolektomi för en avancerad tumör med överväxt på laterala bukväggen för 1 år sedan. PAD visade tveksam radikalitet - Dukes C. Adjuvant cyt. CT-kontroll visar 2,5 cm stor tumör ventralt till vänster i bukväggen. I övrigt ingen metastasering.

Metastast - Recidiv



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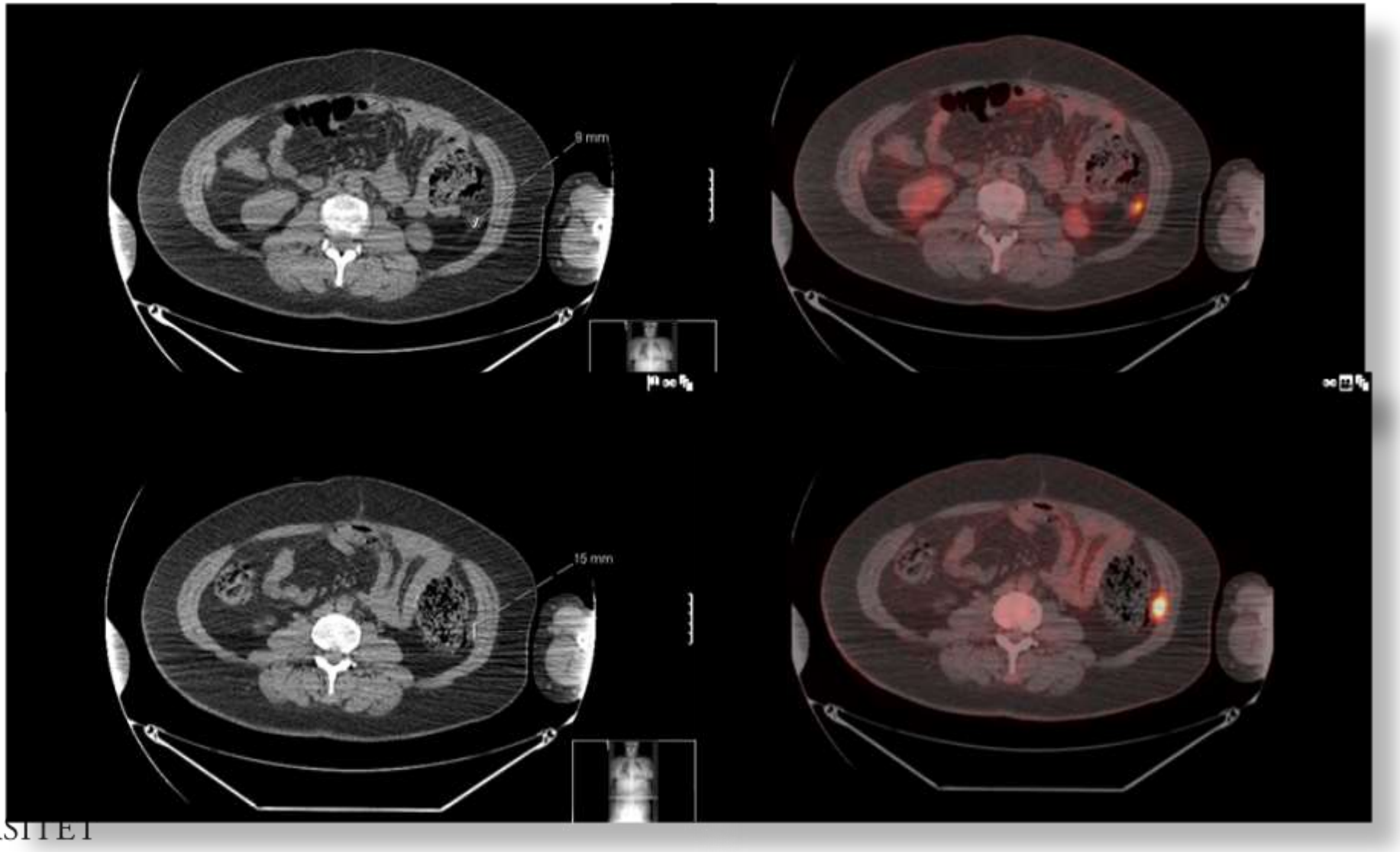
Metastas - Recidiv



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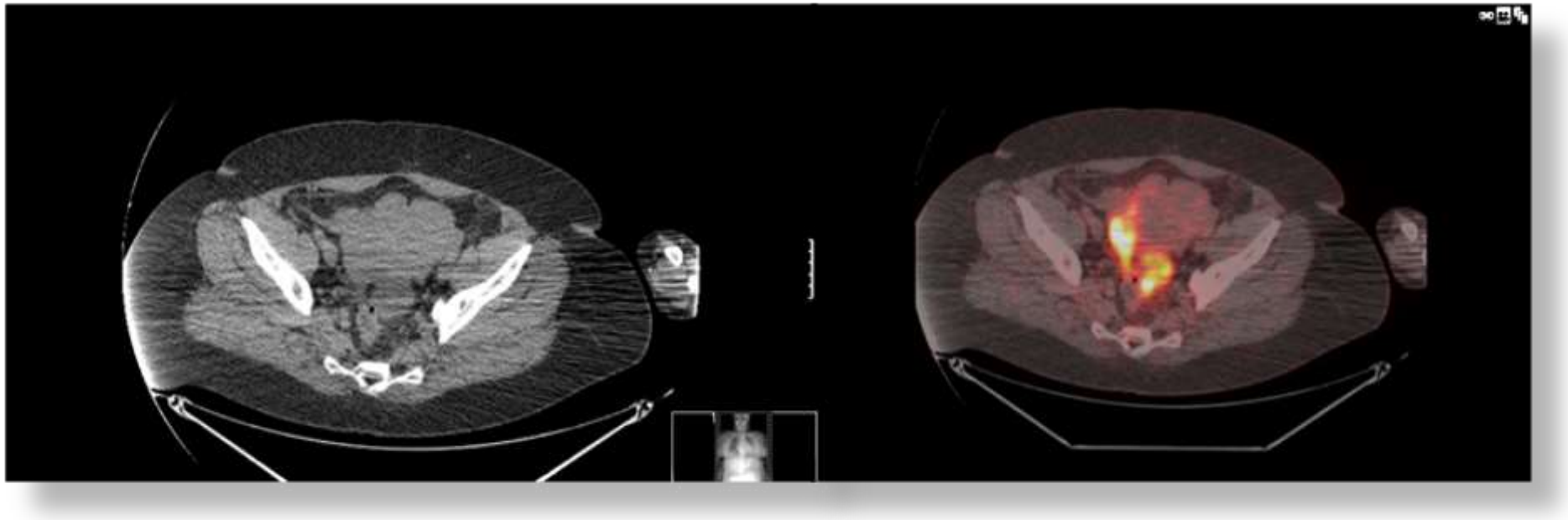
Metastas - Recidiv



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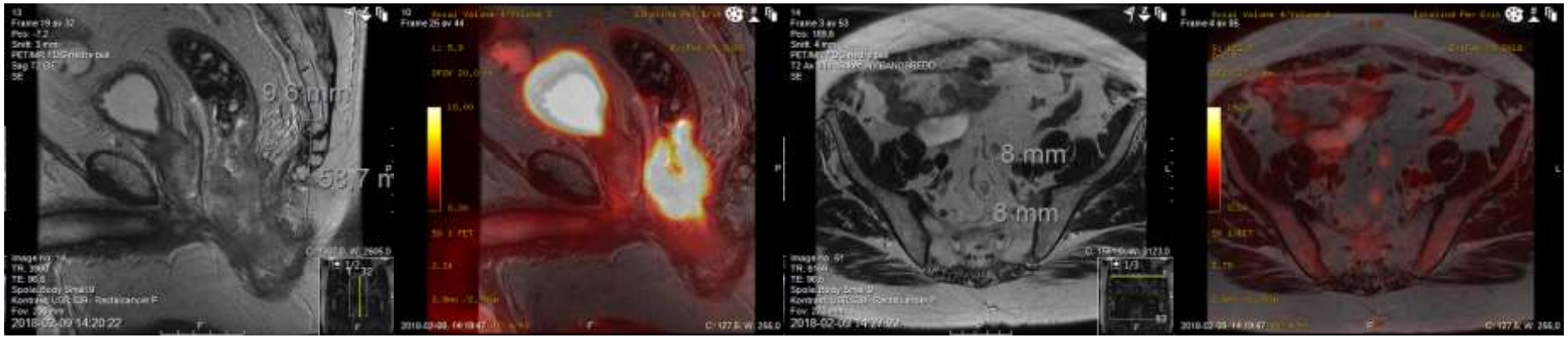
FDG PET/MR in Rectal Cancer



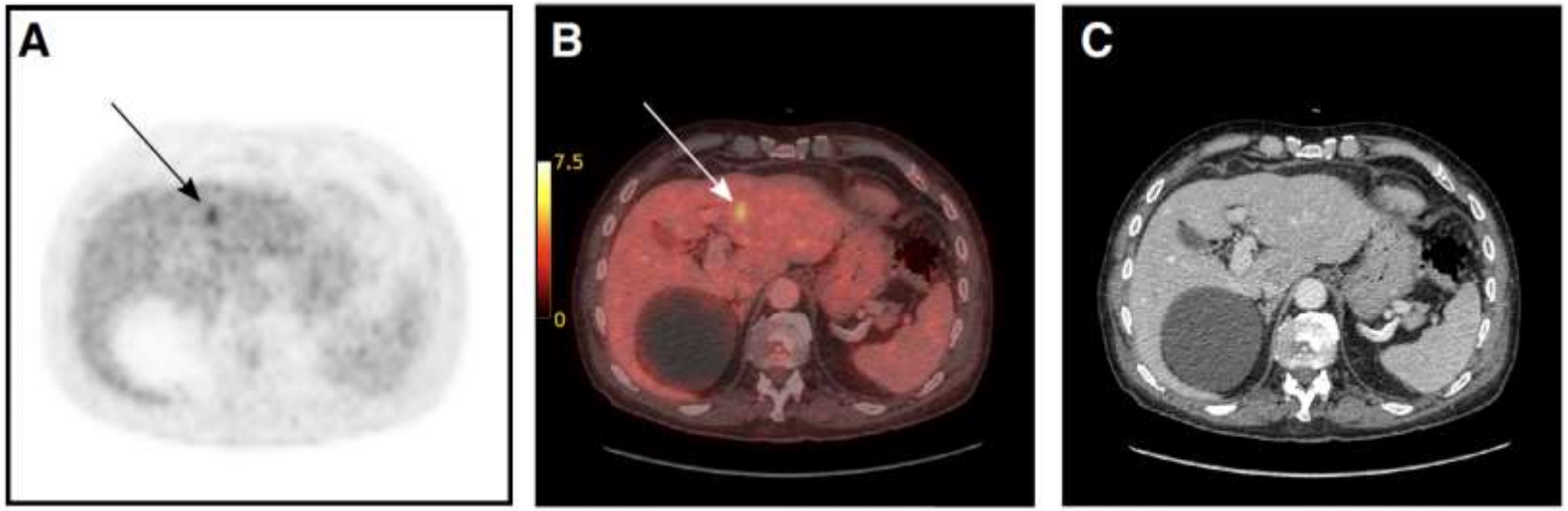


Fig. 3 Focally increased metabolic activity in the right liver lobe without corresponding morphological changes in the second FDG-PET/CT imaging after neoadjuvant treatment. **a** FDG-PET; **b** FDG-PET/CT; **c** CT

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Rutegård et al. Cancer Imaging (2019)

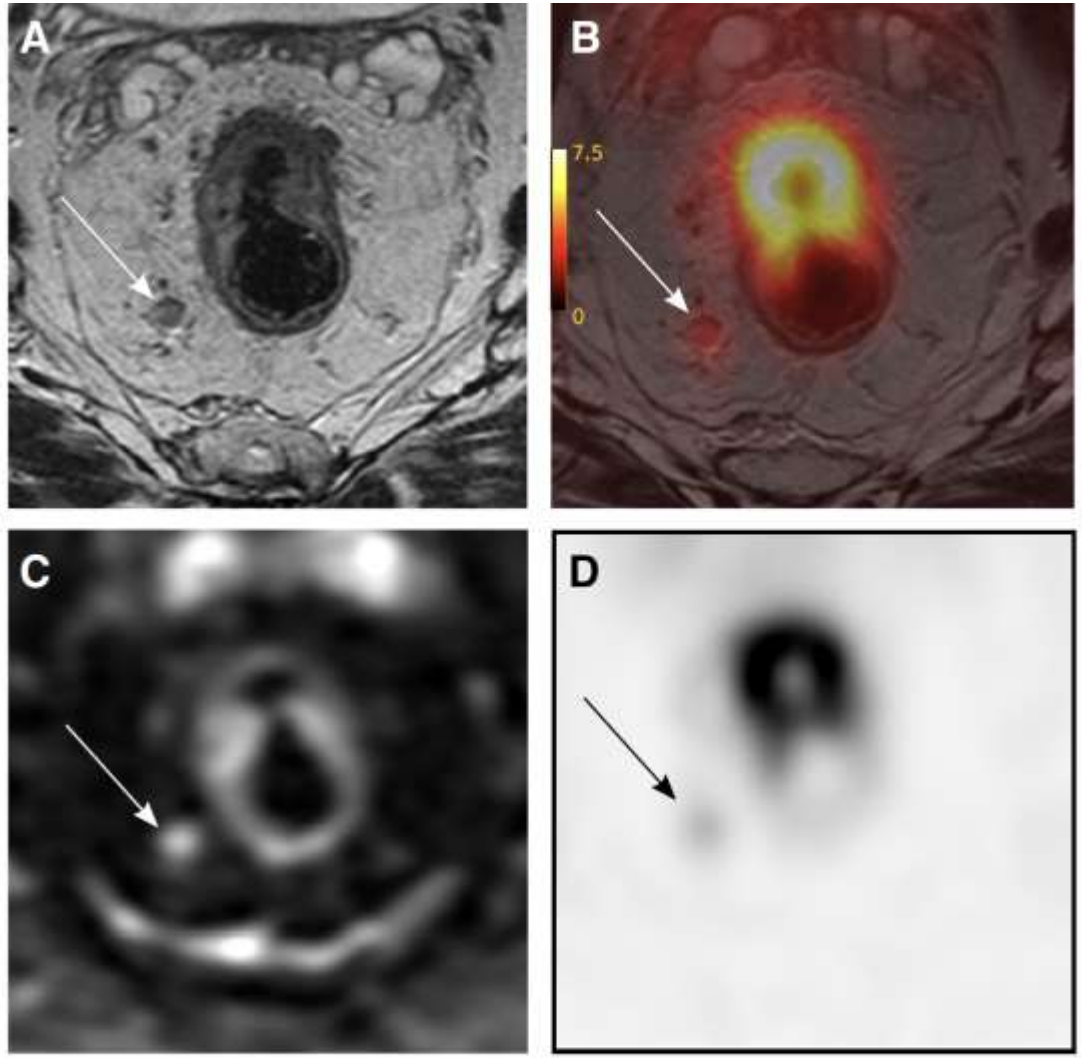
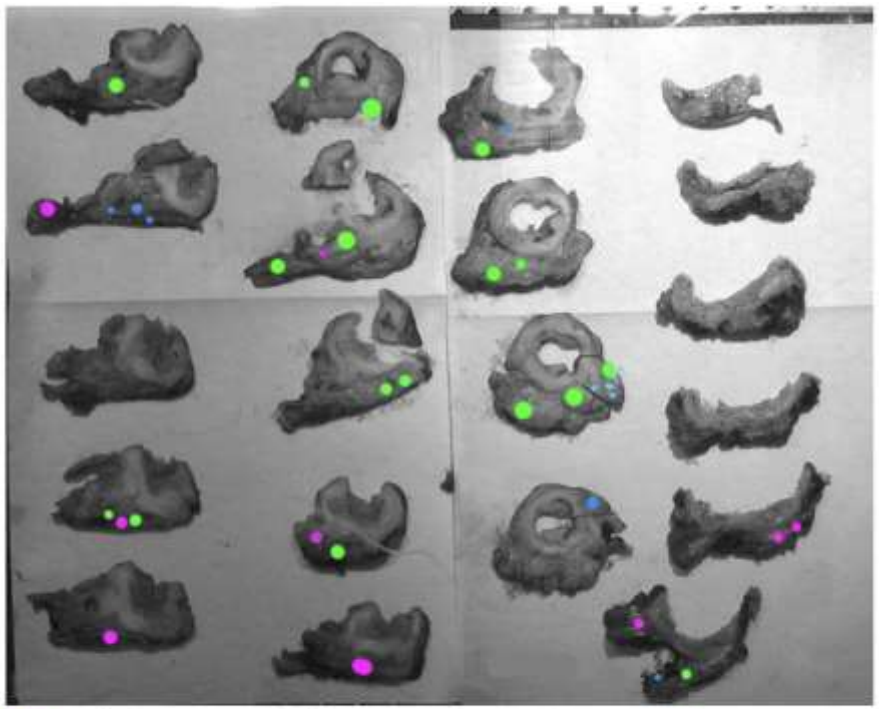


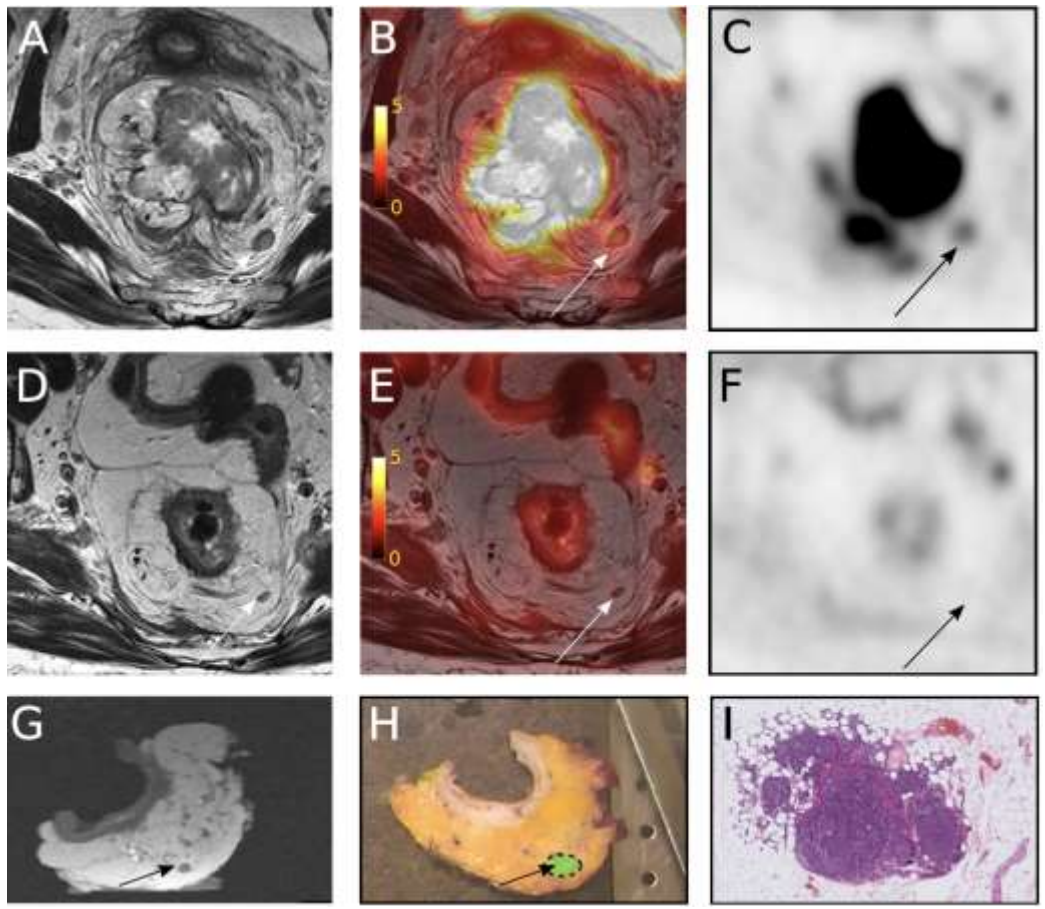
Fig. 5 A PET/MR image of the same patient as that in Fig. 3. **a** Transaxial T2 weighted sequence perpendicular to the tumour; **b** FDG-PET/MR image with a T2 weighted MR sequence; **c** Transaxial diffusion-weighted sequence (b = 800 s/mm2) **d** Static 3D MAC PET image

RESEARCH ARTICLE

Rectal cancer: a methodological approach to matching PET/MRI to histopathology



Both histopathology and MRI (surgical specimen)
Only in MRI (surgical specimen)
Only in histopathology



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Rutegård et al. Cancer Imaging (2020) 20:80

What about the size?

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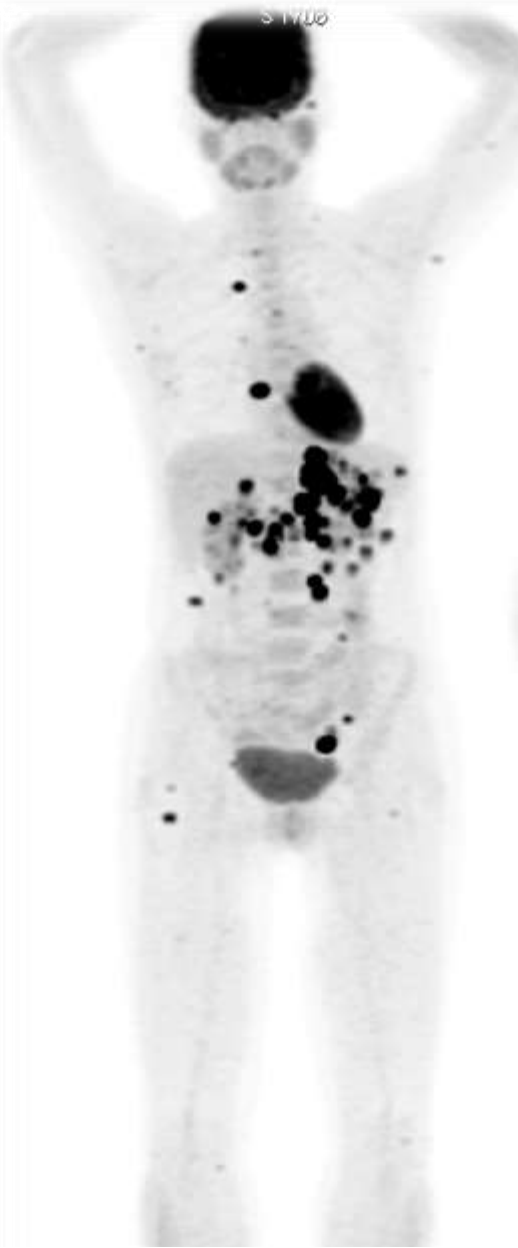
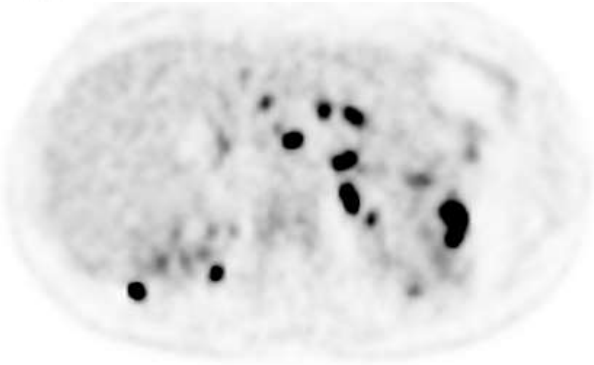
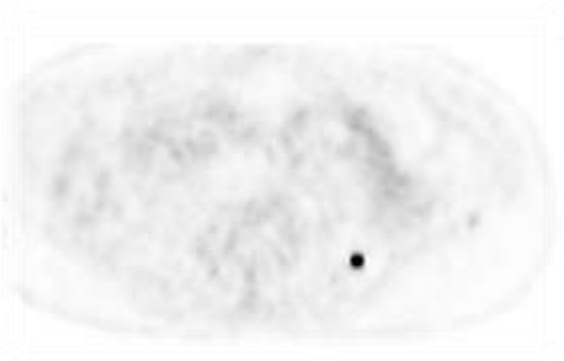
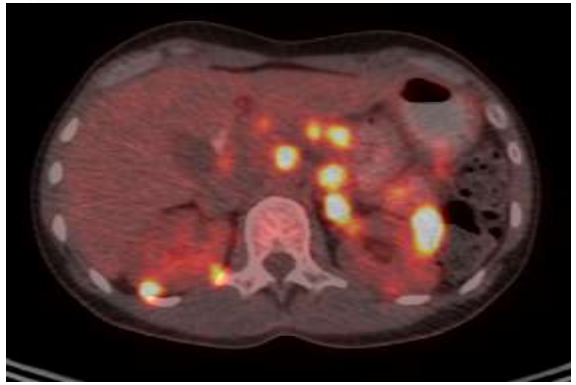
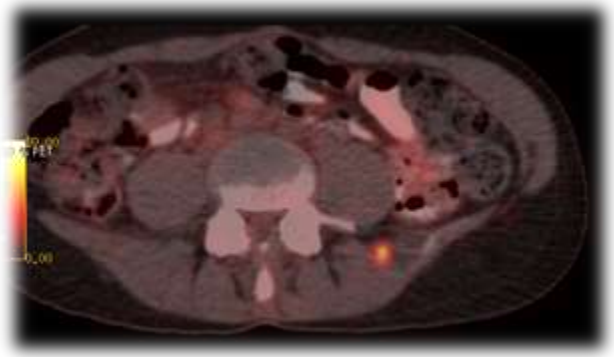
Very Small Tumours











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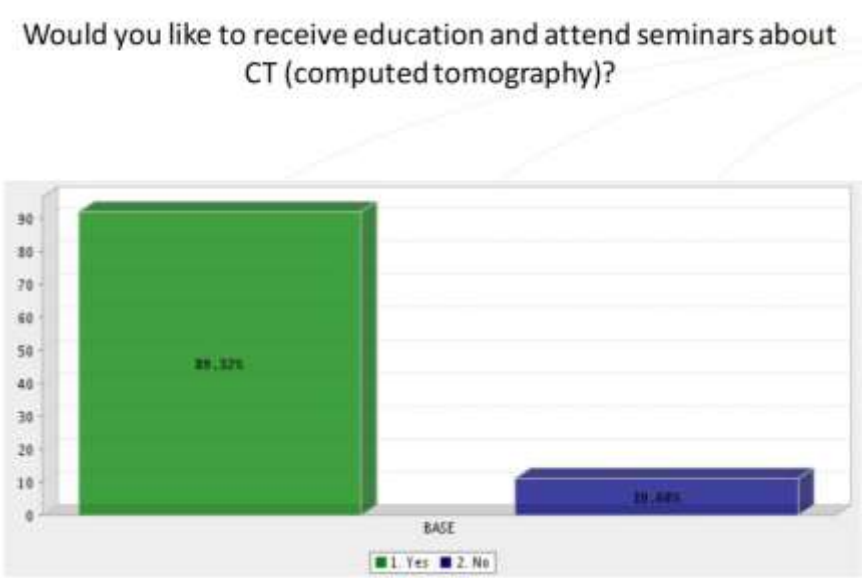
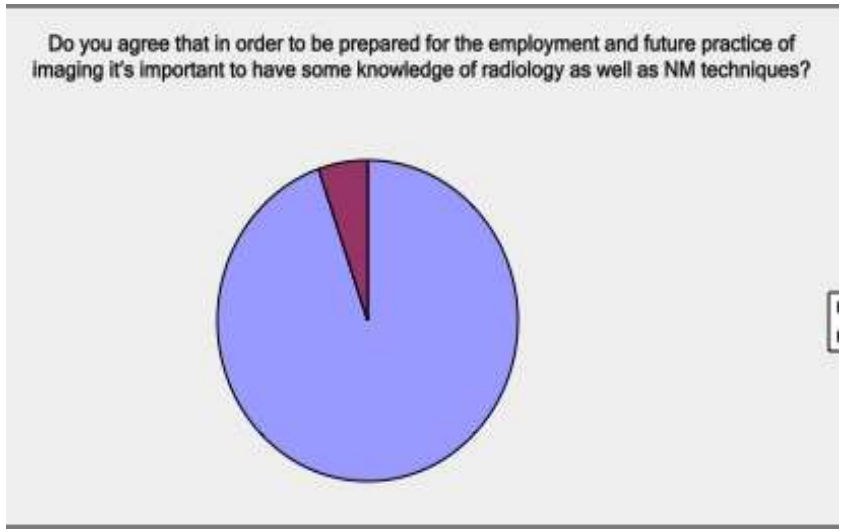
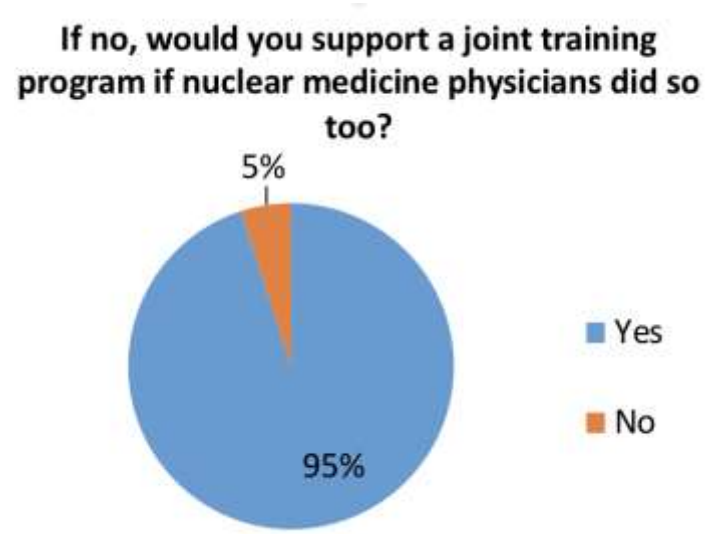
Education and Training?







EANM
European Association of Nuclear Medicine
BIOMEDICAL IMAGING AND THERAPY FOR PERSONALIZED HEALTHCARE

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ESR
EUROPEAN SOCIETY OF RADIOLOGY

ESHI
EUROPEAN SOCIETY FOR HYBRID MEDICAL IMAGING

FDA-Approved PET Radiopharmaceuticals 2023

^{11}C choline	^{64}Cu dotatate (Detectnet™)	^{18}F florbetaben (Neuraceq™)	^{18}F florbetapir (Amyvid™)	^{18}F flortaucipir (Tauvid™)
^{18}F fluciclovine (Axumin™)	Fluorine-18 fludeoxyglucose (FDG)	^{18}F fluorodopa	^{18}F fluoroestradiol (Cerianna™)	^{18}F flutemetamol (Vizamyl™)
^{18}F piflufolastat (PYLARIFY®)	^{18}F sodium fluoride	^{68}Ga DOTATATE (Netspot™)	^{68}G DOTATOC	^{68}Ga gozetotide (Illuccix®, Locametz®)
^{13}N ammonia	^{82}Rb chloride (Cardiogen-82®)			

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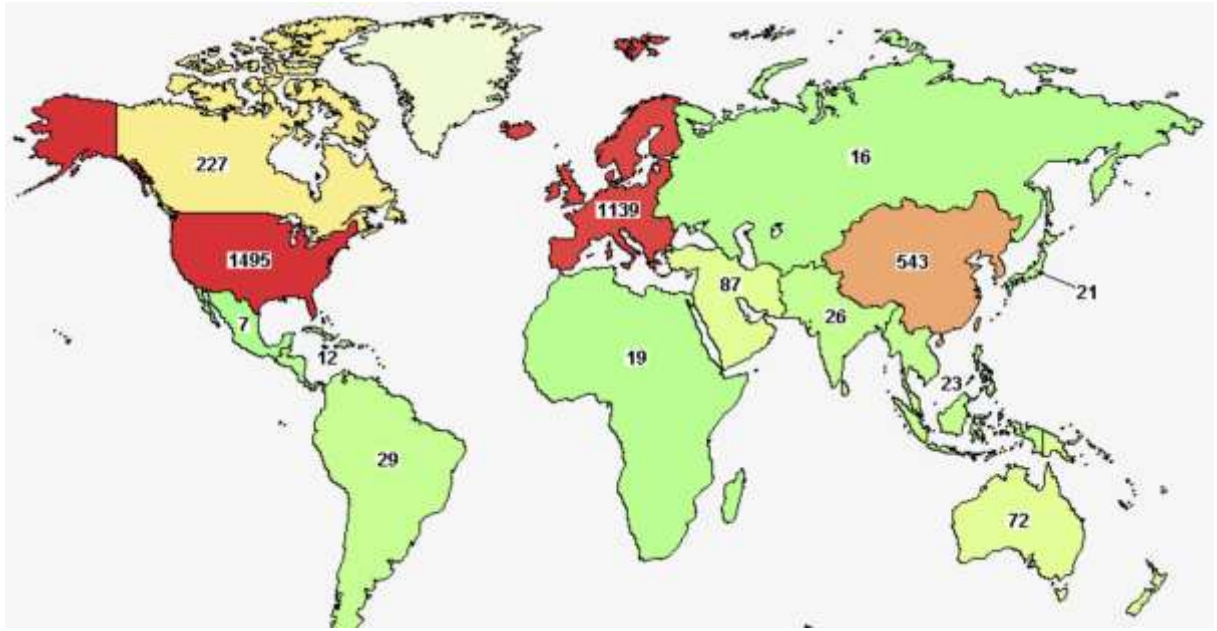
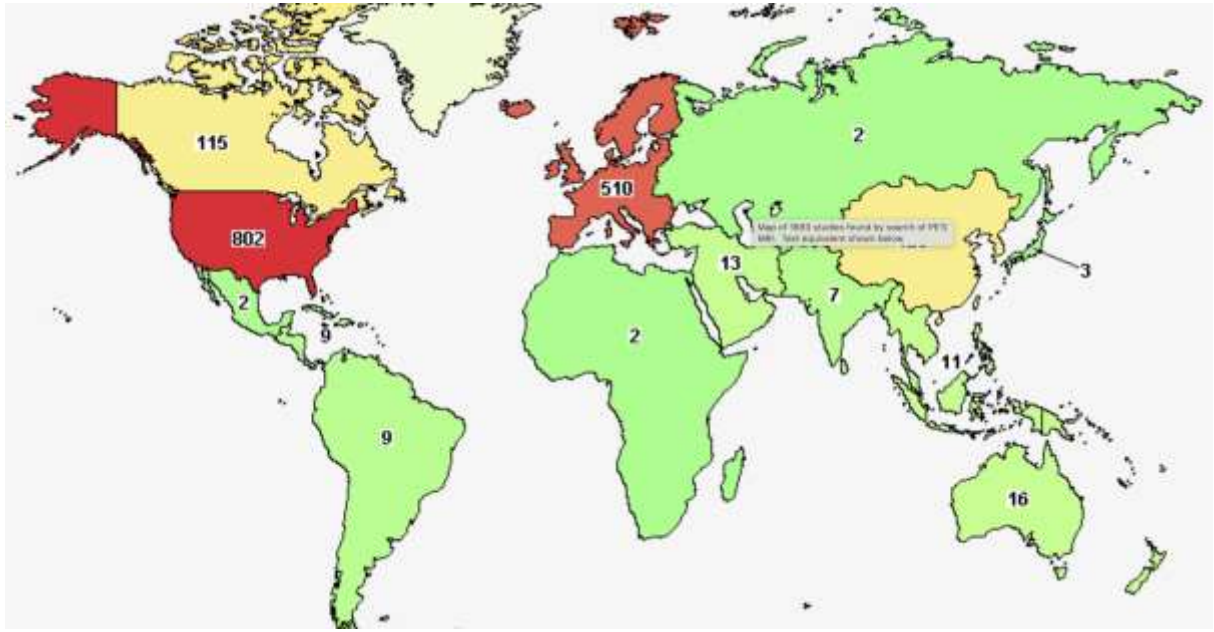
2023 PET/CT and PET/MRI clinical studies





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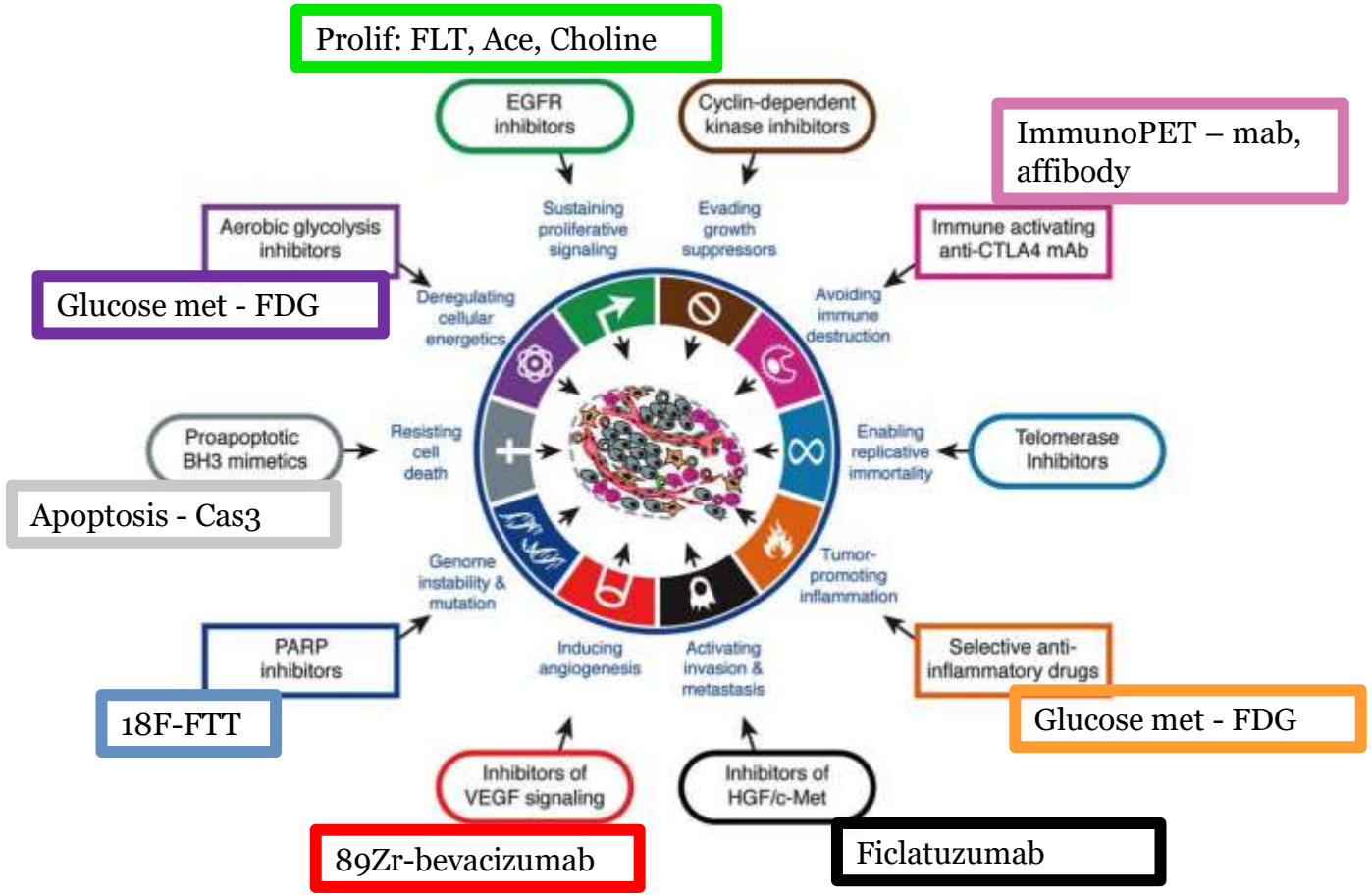
Hallmarks of Cancer



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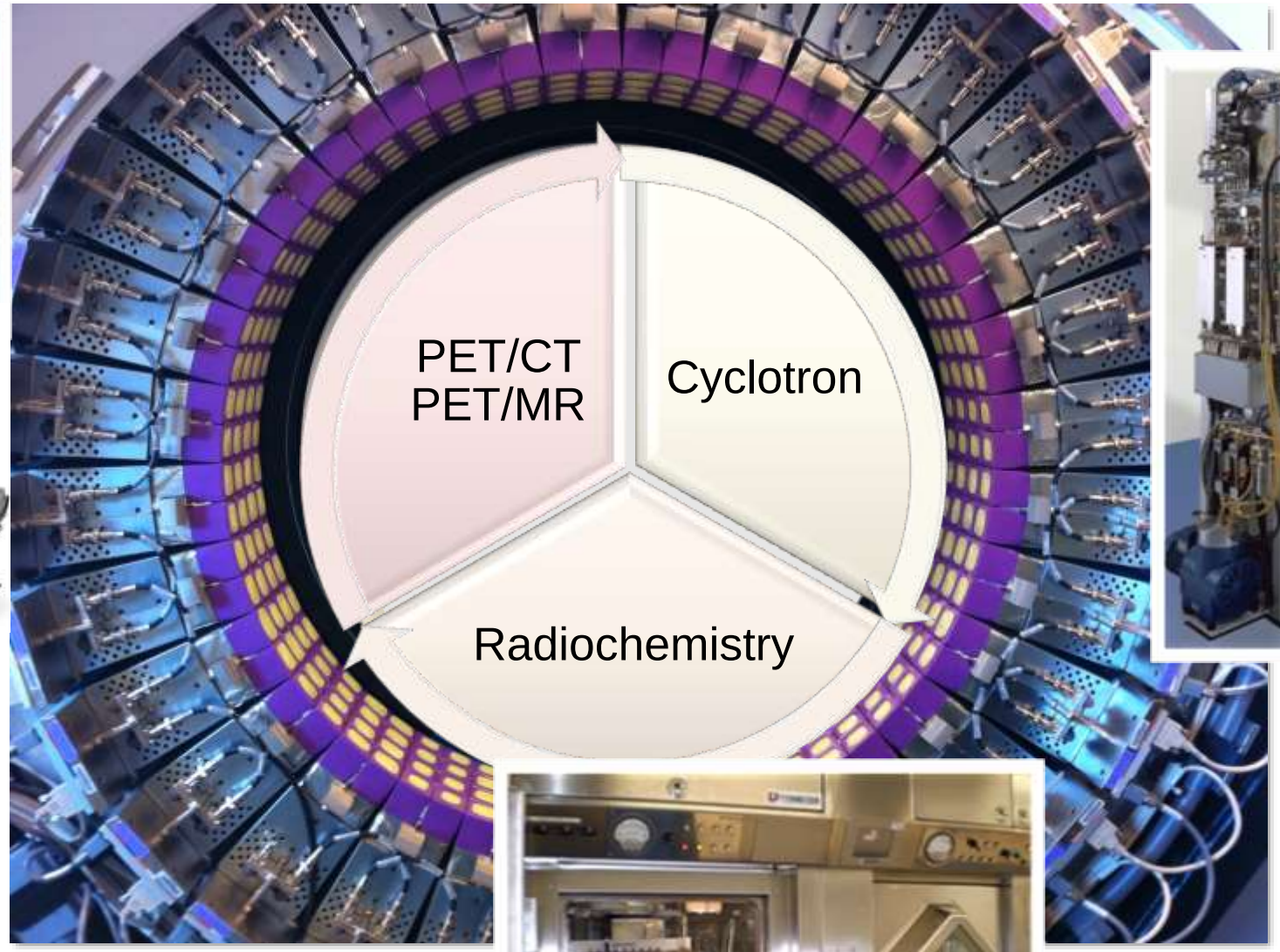
Hanahan and Weinberg. Cell 2011



^{18}F-FDG

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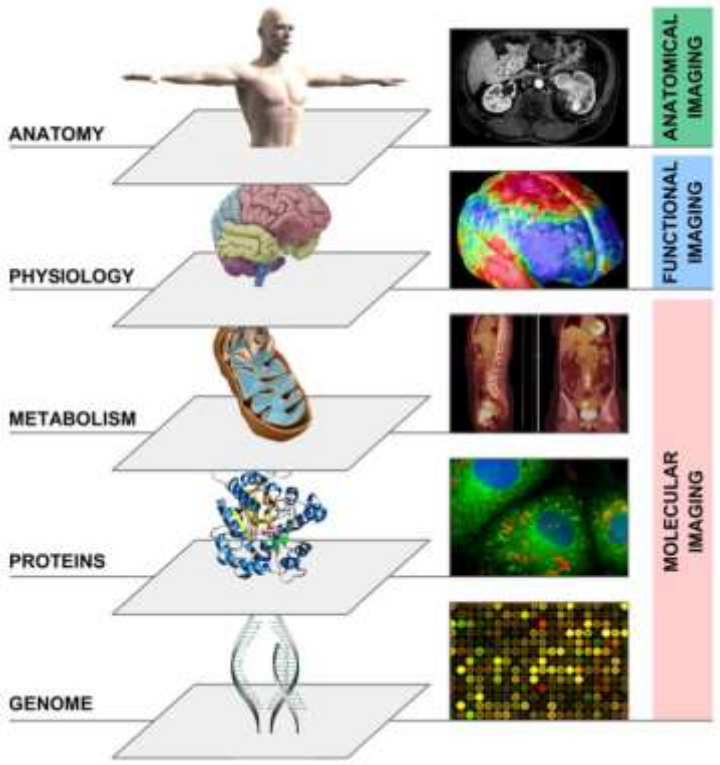
How to use Hybrid Imaging

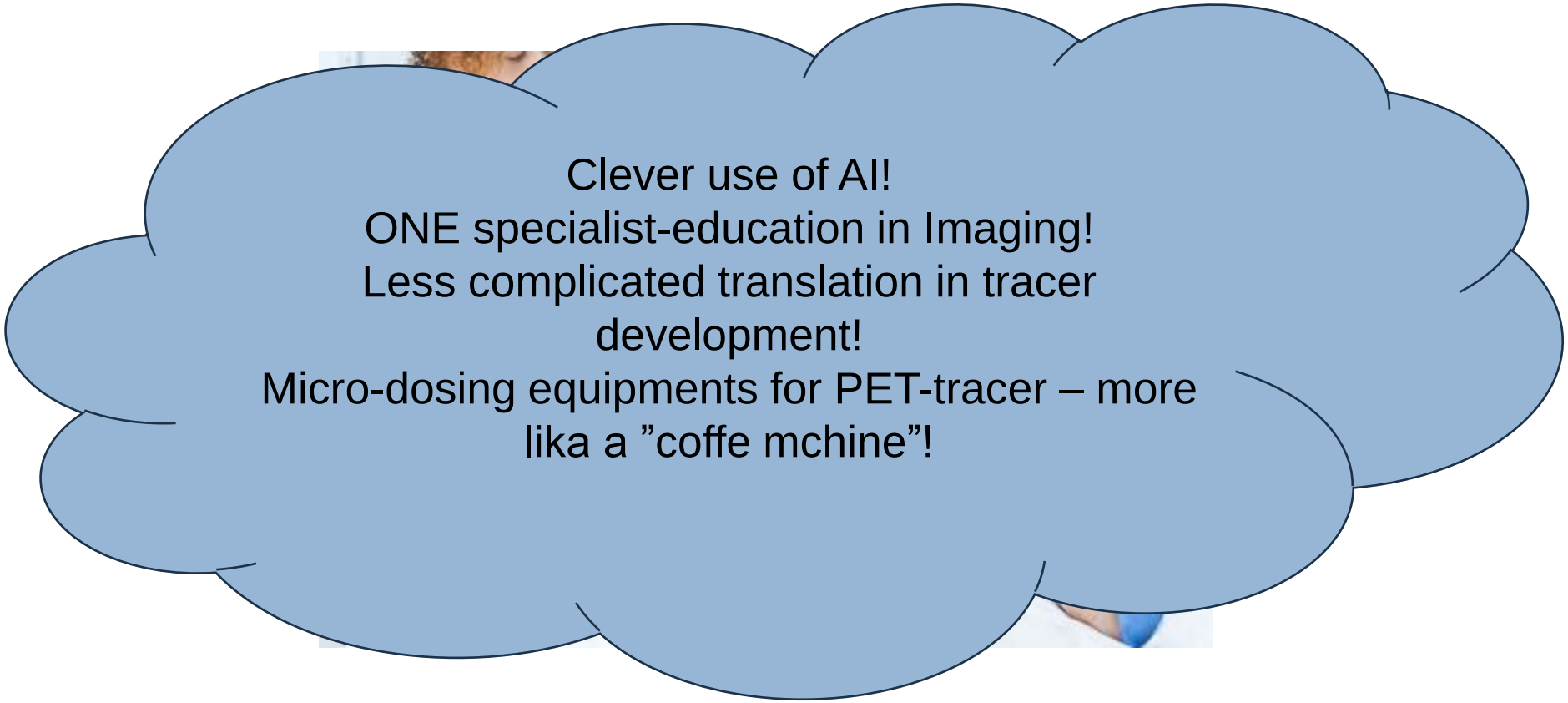


Lambin et al EJC 2012

- Use information from both PET and CT/MR!
- Structure the report
  1. PET-pathology with corresponding CT/MR-findings
  2. CT/MR-pathology without PET pathology
  3. Summary of the disease

PET/CT
PET/MR

Wishes for the Future!



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Collaborators at:

- Umeå university,
- Umeå university hospital
- Umeå center for functional Brain imaging
- Grant givers
- ESR
- ESHI
- Others

Tack!

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