Ospedale
Sacro Cuore - Don Calabria

Nuovi traccianti PET-Colina... PET PSMA quale ruolo nel 2019

(Negrar 6/7/2019)

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Semin Nucl Med 41:246-264 © 2011

ELSEVIER

Seminars in
NUCLEAR
MEDICINE

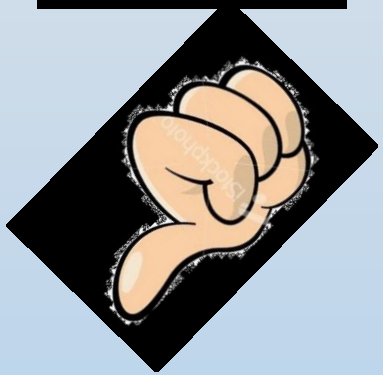
A Broad Overview of Positron Emission Tomography Radiopharmaceuticals and Clinical Applications: What Is New?

Shankar Vallabhajosula, PhD, Lilja Solnes, MD, and Brigitte Vallabhajosula, PhD

Despite the availability of many radiotracers, [18F]fluorodeoxyglucose (FDG) is currently the most widely used radiopharmaceutical in PET, and the field of molecular imaging is anxiously awaiting the introduction of new PET radiopharmaceuticals for routine clinical use.

FDG Weak Points

- ✓HCC
- ✓Breast Cancer
- ✓H&N
- ✓Renal Cancer
- ✓Gastric Cancer
- ✓Lung BAC/Some AdenoCA

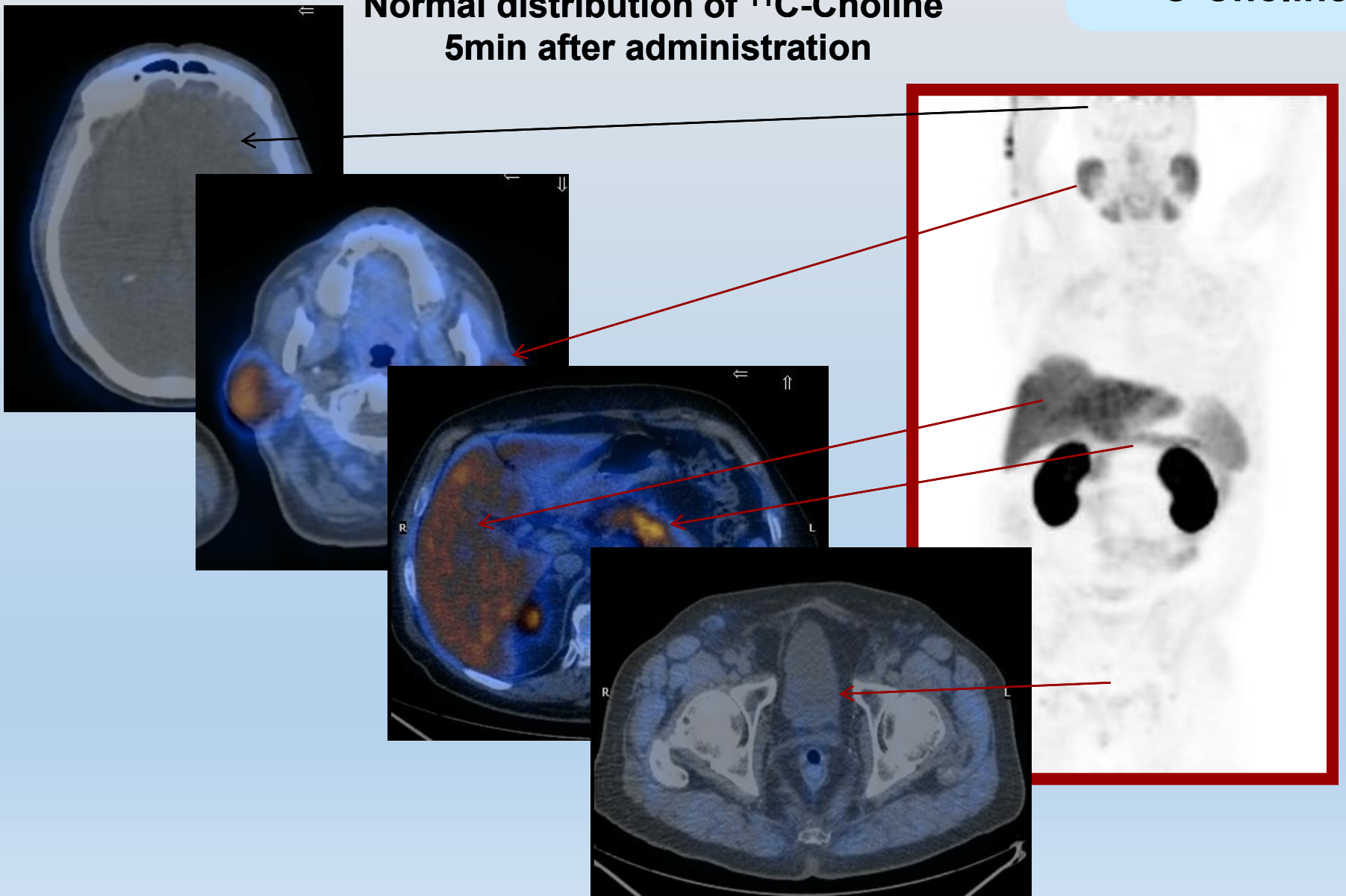


- ✓Differentiated Prostate Cancer
  - $^{11}C/^{18}F$ choline
  - ^{11}C-acetate

PROSTATE CANCER

^{11}C-Choline

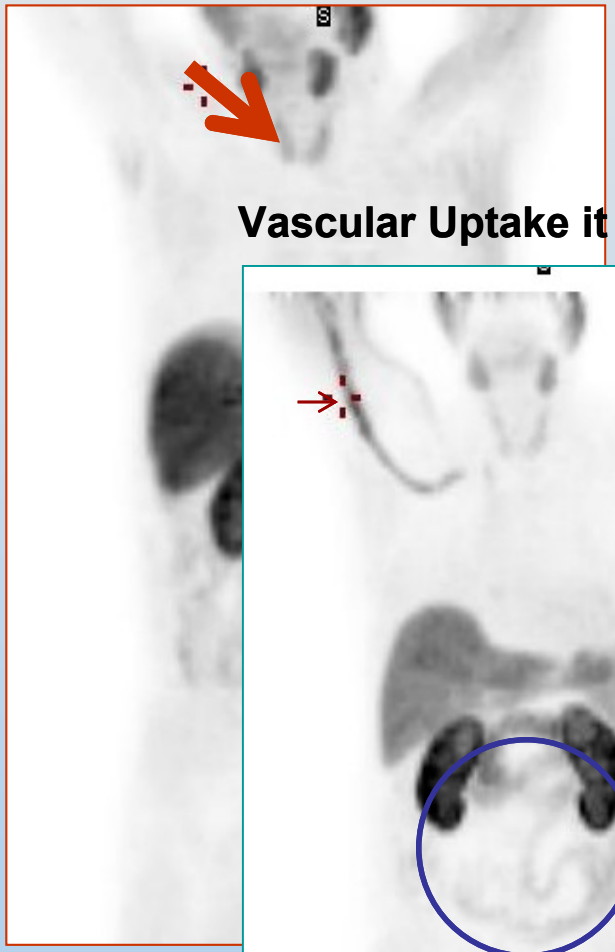
Normal distribution of ^{11}C-Choline
5min after administration



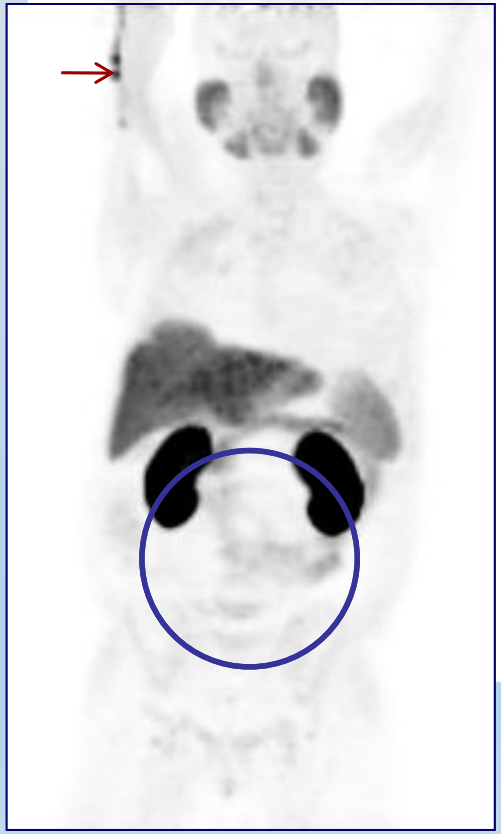
PROSTATE CANCER

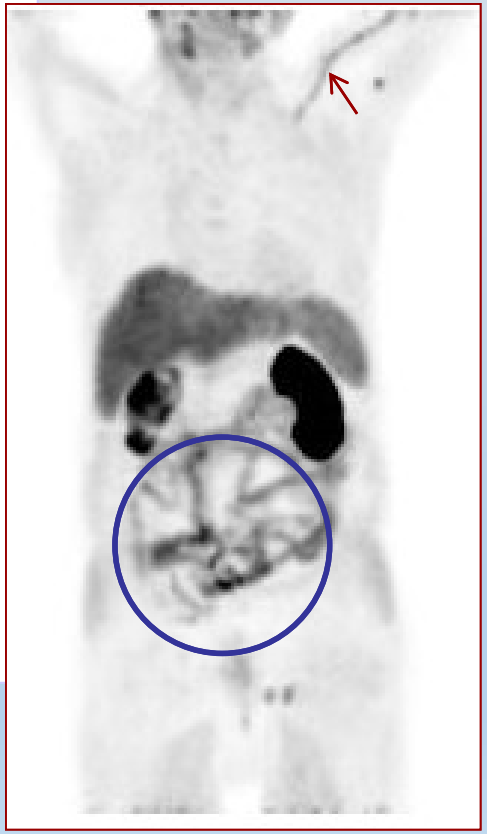
^{11}C-Choline

Faint uptake in the thyroid



Vascular Uptake it is frequently present early after administration of ^{11}C-Choline



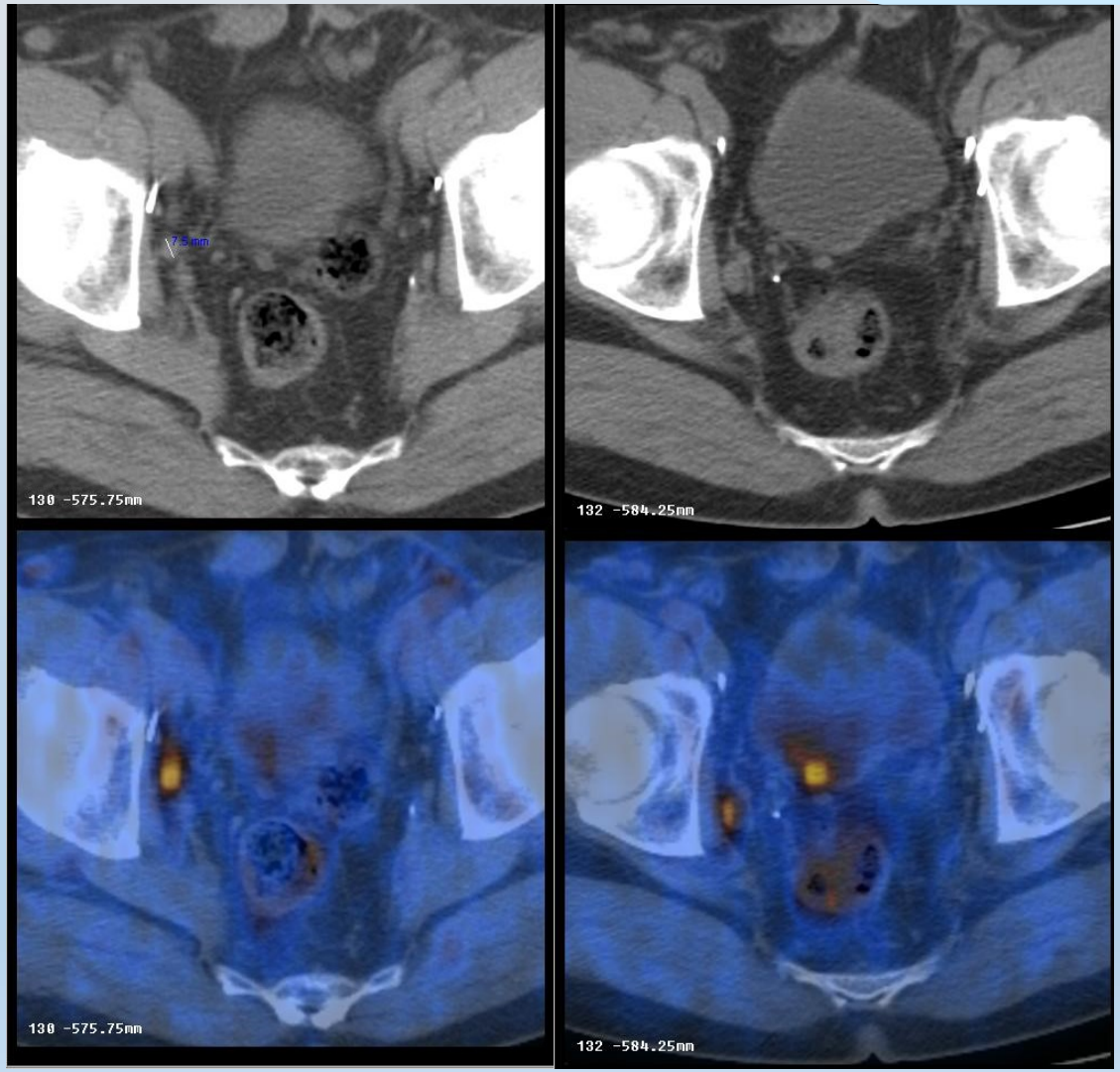


Intestinal uptake of 11C-Choline is variable from patient to patient

PROSTATE CANCER

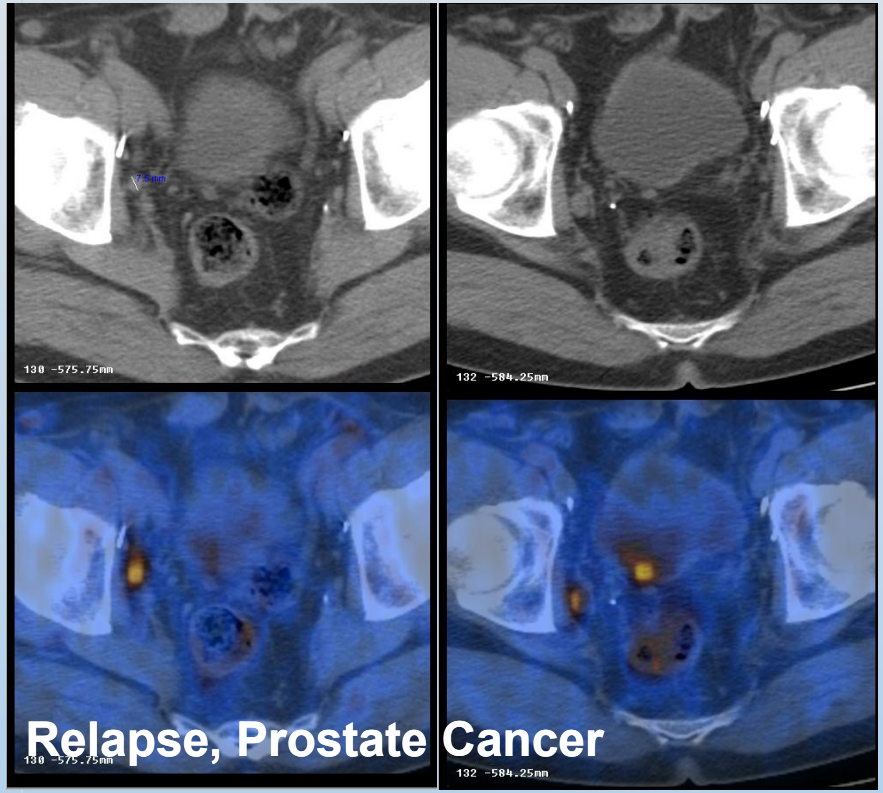
^{11}C-Choline

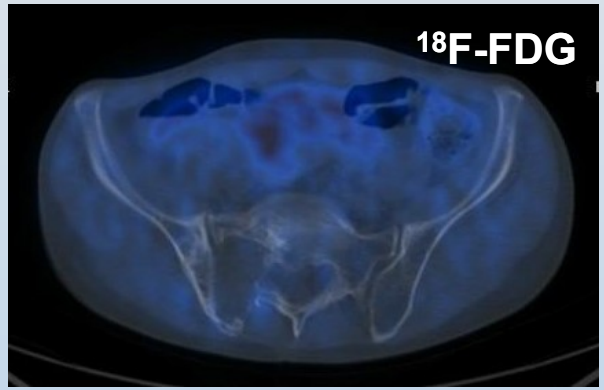
71 y.o.Relapse
PSA 5 ng/mL
prostatectomy 2003

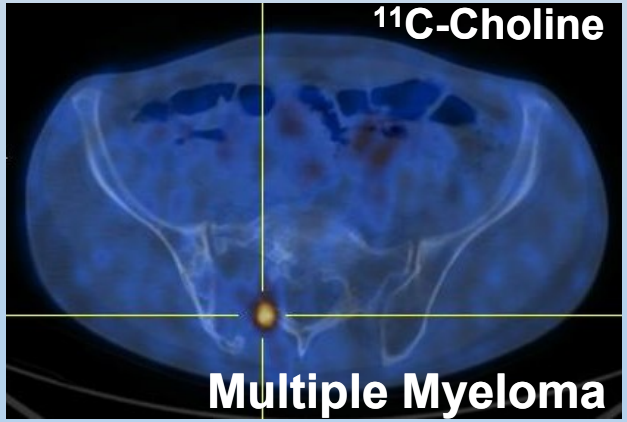


PROSTATE CANCER

^{11}C-Choline







Androgen deprivation therapy influences the uptake of ^{11}C-choline in patients with recurrent prostate cancer: the preliminary results of a sequential PET/CT study

PROSTATE CANCER

^{11}C-Choline

Chiara Fuccio · Riccardo Schiavina · Paolo Castellucci · Domenico Rubello · Giuseppe Martorana · Monica Celli · Claudio Malizia · Marta Barios Profitos · Maria Cristina Marzola · Vincenzina Pettinato · Stefano Fanti

Eur J Nucl Med Mol Imaging (2011) 38:1985–1989

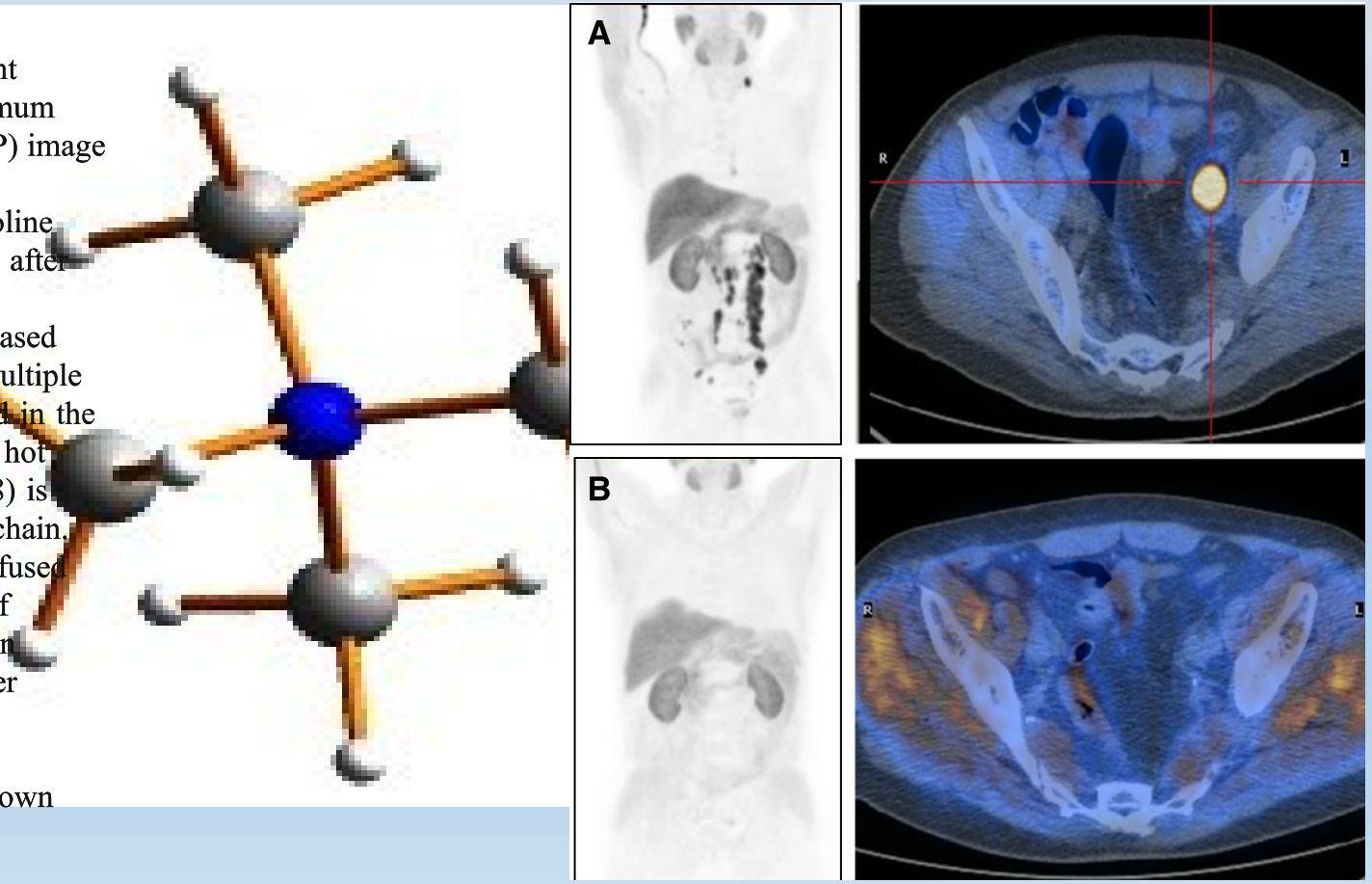


Fig. 1 Patient 13 (see Table 1 indicating patient characteristics). **a** Maximum intensity projection (MIP) image (*left*) and fused PET/CT image (*right*) of ^{11}C-choline PET/CT scan performed after discontinuation of ADT (PSA 12.1 ng/ml). Increased ^{11}C-choline uptake in multiple lymph nodes is observed in the MIP image: a large and hot lymph node (SUV_{max}=8) is evident in the left iliac chain. **b** MIP image (*left*) and fused PET/CT image (*right*) of ^{11}C-choline PET/CT scan performed 6 months after ADT administration. A complete response is evident. PSA dropped down to 0.01 ng/ml

PROSTATE CANCER

Current clinical approach

RT, SURGERY OR SYSTEMIC THERAPY?

About 40% of all patients undergoing radical treatment for localized PCa develop biochemical relapse (BCR)

BUT

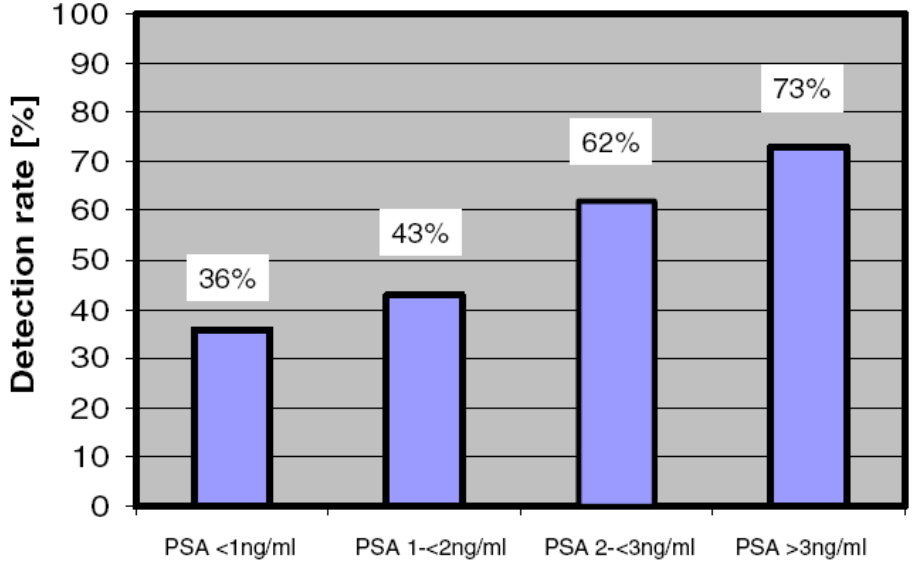
20% of them will show clinically detectable recurrences within 10 yrs

Currently, most of the patients receive androgen deprivation therapy soon after PSA relapse and without any effort to localize the origin of the relapse.

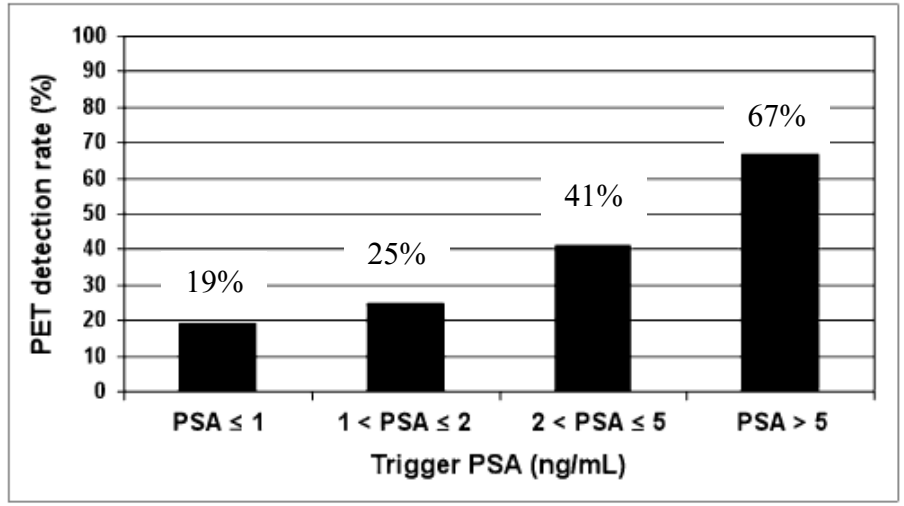
PROSTATE CANCER

11C-Choline PET/CT

Krause et al. Eur J Nucl Med Mol Imaging (2008) 35:18-23



Castellucci et al. JNM (2009) 50:1394–1400

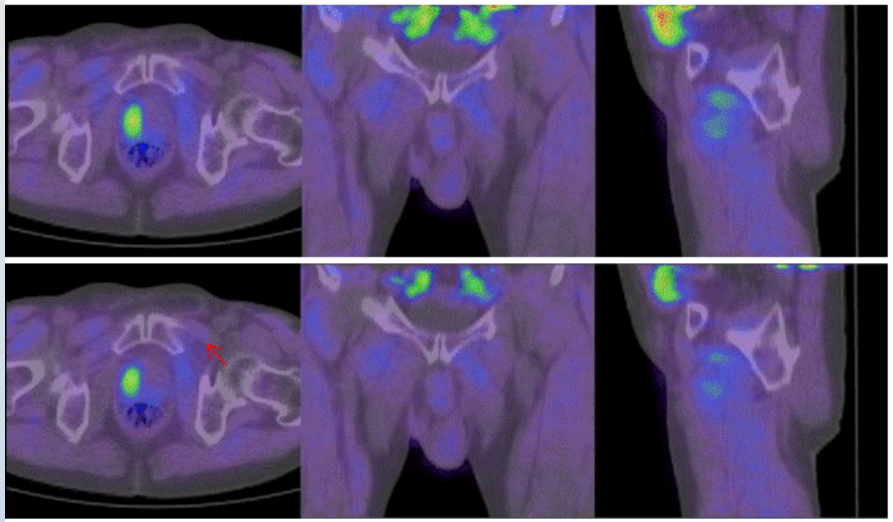


THE DETECTION RATE OF ^{11}C-CHOLINE IS THE BEST AVAILABLE BUT STILL SUBOPTIMAL ESPECIALLY FOR RELATIVELY LOW PSA LEVELS

PROSTATE CANCER

11C-Choline PET/CT

Low resolution OSEM



Lesion-absent

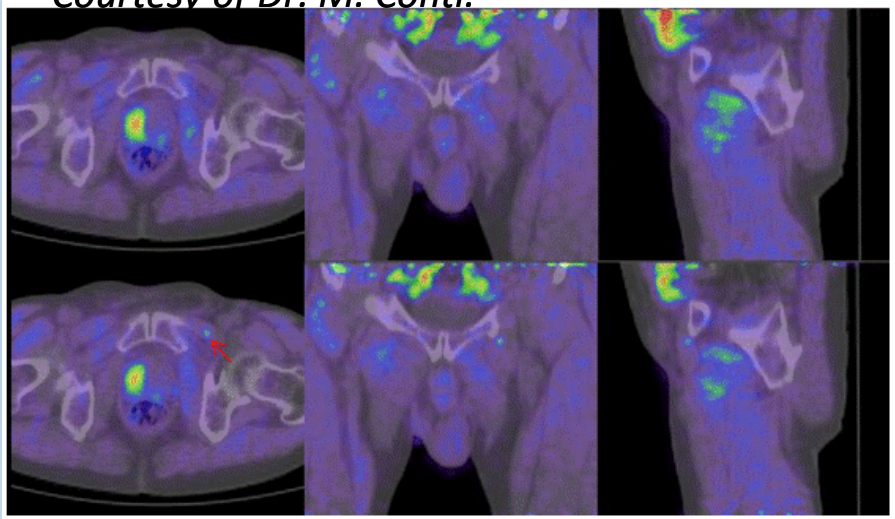
Lesion-present

IMPROVING TECHNOLOGY

Improving PET spatial resolution and detectability for prostate cancer imaging.
Bal H. et al. Phys Med Biol. 2014 Aug 7;59(15):4411-26.

High resolution PSF+TOF (4mm filter)

Courtesy of Dr. M. Conti.



Lesion-absent

Lesion-present

IMPROVING SENSITIVITY

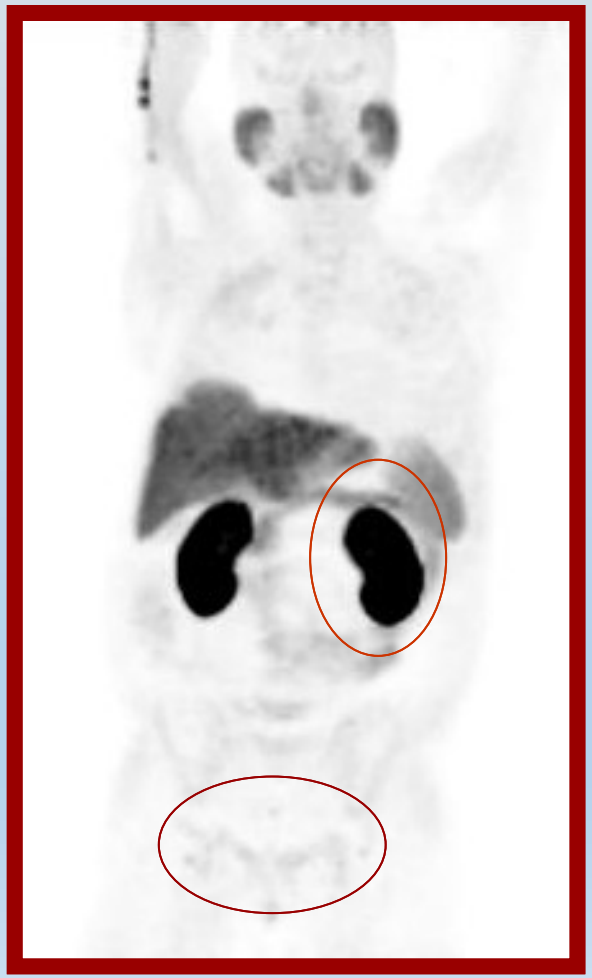
PROSTATE CANCER

^{18}F/^{11}C choline

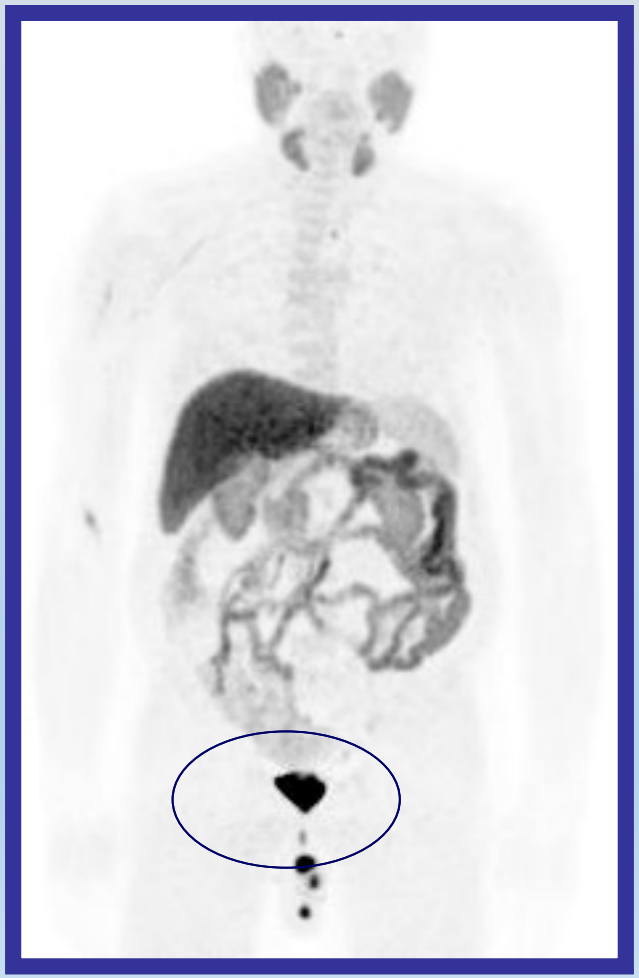
Biodistribution

Is there any difference between ^{11}C-Choline and ^{18}F-Fluorocholine

^{11}C-Choline



^{18}F-Choline



PROSTATE CANCER

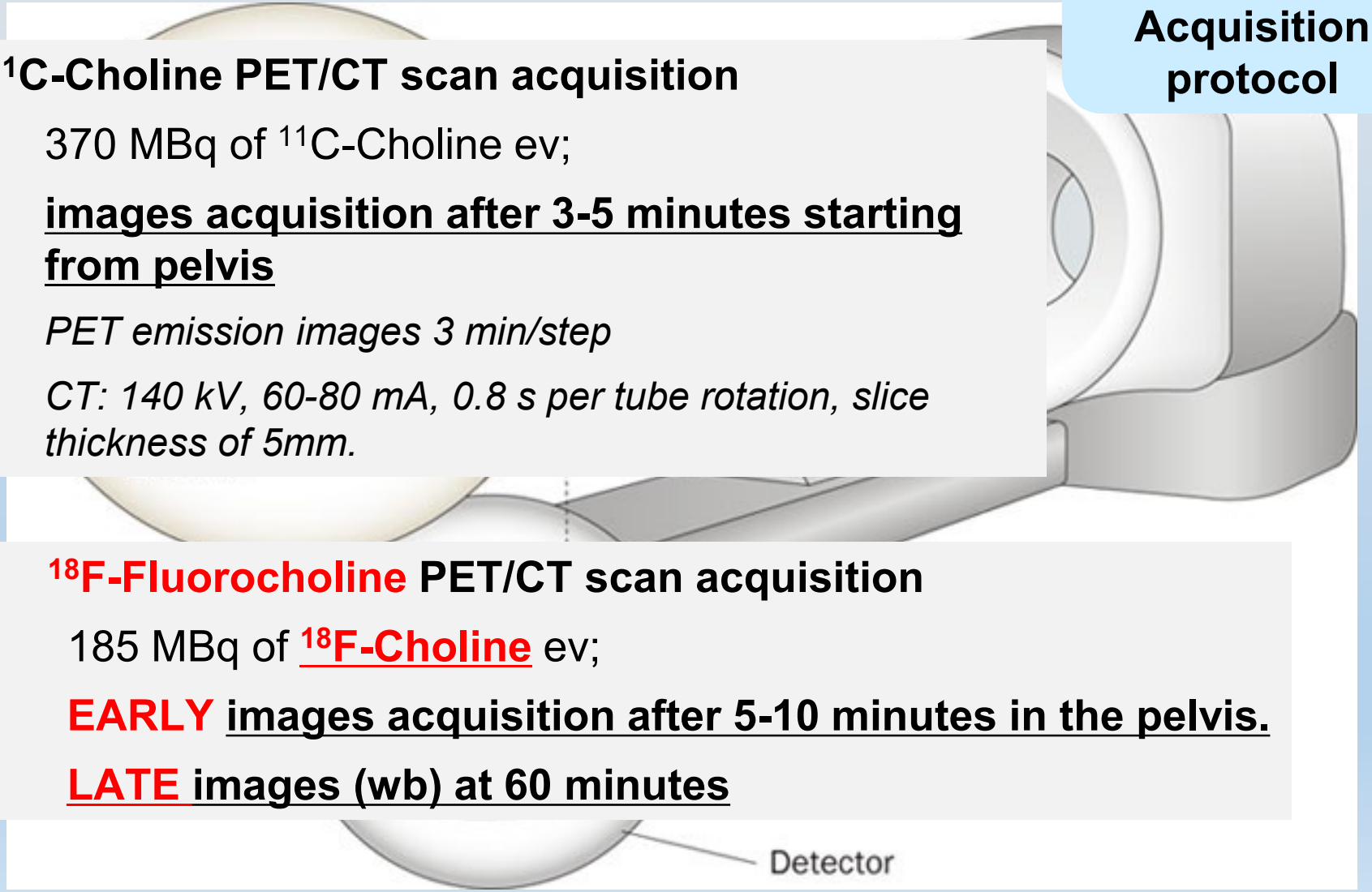
^{18}F/^{11}C choline

Acquisition protocol

Is there any difference between ^{11}C-Choline and ^{18}F-Fluorocholine

^{11}C-Choline PET/CT scan acquisition

- 370 MBq of ^{11}C-Choline ev;
- **<u>images acquisition after 3-5 minutes starting from pelvis</u>**
- *PET emission images 3 min/step*
- *CT: 140 kV, 60-80 mA, 0.8 s per tube rotation, slice thickness of 5mm.*



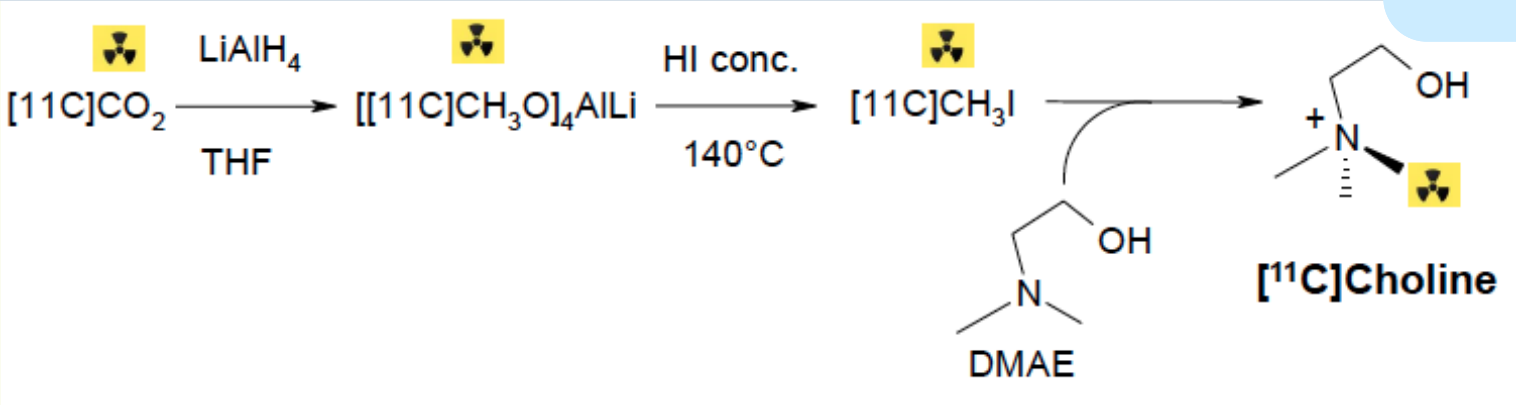
- **^{18}F-Fluorocholine PET/CT scan acquisition**
- 185 MBq of **^{18}F-Choline** ev;
- **EARLY <u>images acquisition after 5-10 minutes in the pelvis.</u>**
- **<u>LATE images (wb) at 60 minutes</u>**

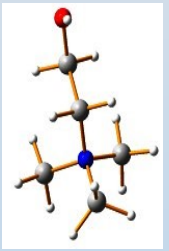
PROSTATE CANCER

$^{18}F/^{11}C$ choline

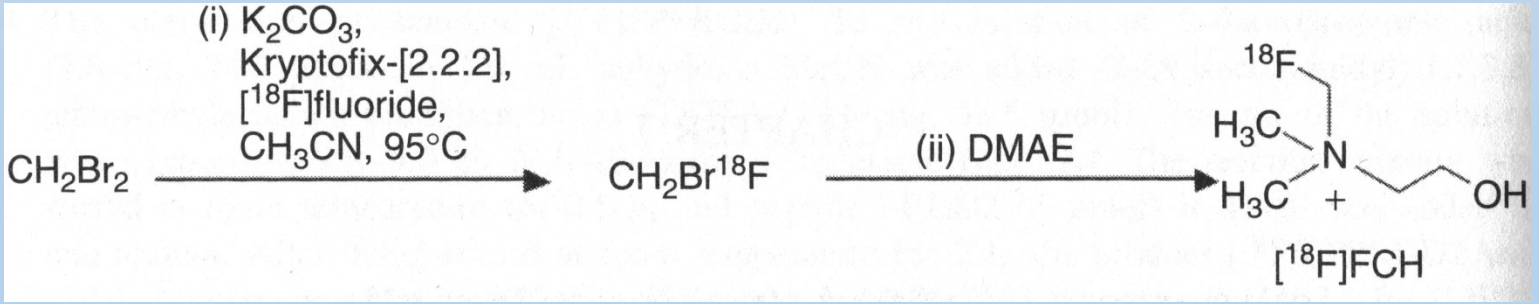
Synthesis

Radiochemical synthesis of [^{11}C]choline.

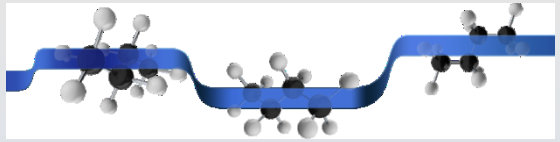




Radiochemical synthesis of [^{18}F]Fluorocholine.



Council of Europe



Clinical Impact

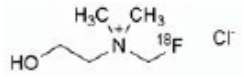
^{11}C-Choline

^{18}F-fluorocholine

DRAFT

FLUOROCHOLINE (^{18}F) CHLORIDE INJECTION

Fluorocholini (^{18}F) chloridi solutio iniectabilis



$C_5H_{13}ClFNO$ M_r 156.6

DEFINITION

Sterile solution of *N*-([^{18}F]fluoromethyl)-2-hydroxy-*N*,*N*-dimethylethanaminium chloride ([^{18}F]fluorocholine chloride). It may contain a suitable buffer.

Limiti dell’attuale imaging (11F/18F-colina)

- Riduzione della sensibilità per livelli di PSA < 1
- La mancanza di tessuto/specificità neoplastica
- Mancato approccio alla via terapeutica del radiofarmaco (la colina non mostra sviluppi possibili verso la terapia)

PROSTATE CANCER

$^{18}F/^{11}C$ choline

Is there any difference between ^{11}C-Choline and ^{18}F-Fluorocholine

	^{18}F-Fluorocholine	^{11}C-Choline
Urinary excretion		+
Half-life	+++	
Dosimetry		+
Labelling		+
Cost		+*
FDA approved		+**

NON E'PIU' COSI'

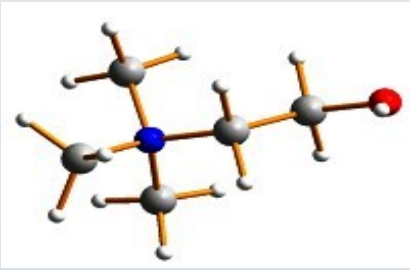
** with onsite cyclotron*
*** in case of biochemical relapse*

FDA Approves PET Imaging Agent for Prostate Cancer Detection

Mayo Clinic is first facility approved to manufacture agent

By Ian Ingram | 20 settembre 2012

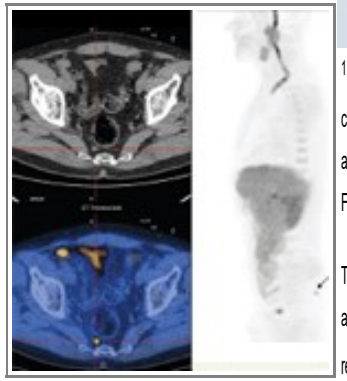
Web Editor, *Cancer Network*



The US Food and Drug Administration (FDA) has **approved** the production and use of ^{11}C choline, an agent shown to be effective in detecting recurrent prostate cancer during positron emission tomography (PET) imaging.

PET imaging with ^{11}C choline is performed in patients previously treated for prostate cancer who have elevated prostate-specific antigen (PSA) levels. A rising PSA can signal a recurrence even when computerized tomography (CT) imaging shows no sign of disease.

(**MORE:** FDA Approves PET Imaging Agent for Alzheimer's Evaluation)



Radical prostatectomy was performed on a 65-year-old patient. Top left: pararectal positive subcentimetric lymph node. Lower left: MIP Projection sagittal view ^{11}C choline PET/CT, performed 5 minutes after injection of 370 MBq of ^{11}C choline, detected metastatic pararectal lymph node. Source: Castellucci P

^{11}C choline "provides an important imaging method to help detect the location of prostate cancer in patients whose blood tests suggest recurrent cancer when other imaging tests are negative," said Charles Ganley, MD, director of the office of drug evaluation at the FDA, in a **press release**.

The results of four independent studies led to the approval of ^{11}C choline as an imaging agent. In total, 98 patients with elevated PSA levels, but no sign of prostate cancer recurrence during CT scans, underwent PET imaging with ^{11}C choline. Biopsies were performed on all abnormalities found during the PET scan.

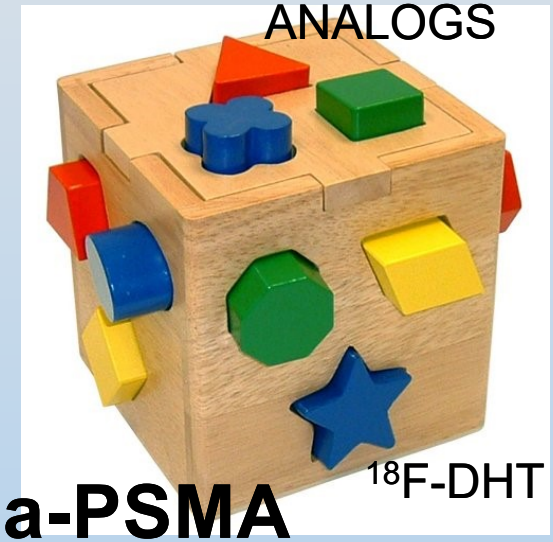
Roughly 50% of patients biopsied within each study were ultimately found to have recurrent prostate cancer. False positives varied by study, ranging from 15% to 47% of patients, confirming the need for biopsies. Other than a mild skin reaction at the site of injection, no side effects were reported.

The Mayo Clinic PET Radiochemistry Facility in Rochester, Minnesota is the first facility approved for manufacturing ^{11}C choline, which must be administered to patients shortly after production.

PROSTATE CANCER

TRACERS

^{68}Ga-BOMBESIN AND ANALOGS



^{68}Ga-PSMA

^{18}F-DHT

RECEPTORS

^{18}F-CHOLINE ^{18}F-FLT

^{18}F-FDG

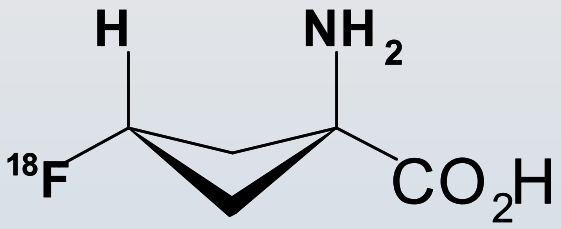
^{11}C-ACETATE

^{18}F-FMAU

METABOLISM

PROSTATE CANCER

^{18}F-FACBC



^{18}F-Amino-3-fluorcyclobutane-1-carboxylic Acid

^{18}F-FACBC

SYNTHETIC AA
L-LEUCINE ANALOGUE
FLUORINATED

Synthesis and Evaluation of [^{18}F]1-Amino-3-fluorocyclobutane-1-carboxylic Acid to Image Brain Tumors

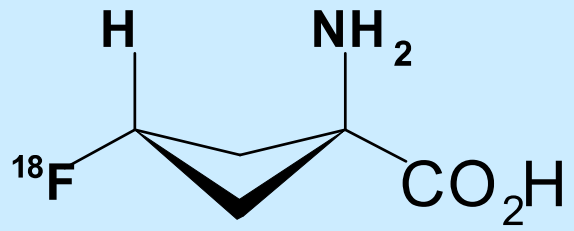
Timothy M. Shoup, Jeffrey Olson, John M. Hoffman, John Votaw, Dennis Eshima, Lori Eshima, Vernon M. Camp, Michael Stabin, Delicia Votaw and Mark M. Goodman

J Nucl Med. 1999;40:331-338.

FLUORINATED
SYNTHETIC AA
L-LEUCINE ANALOGUE

PROSTATE CANCER

^{18}F-FACBC

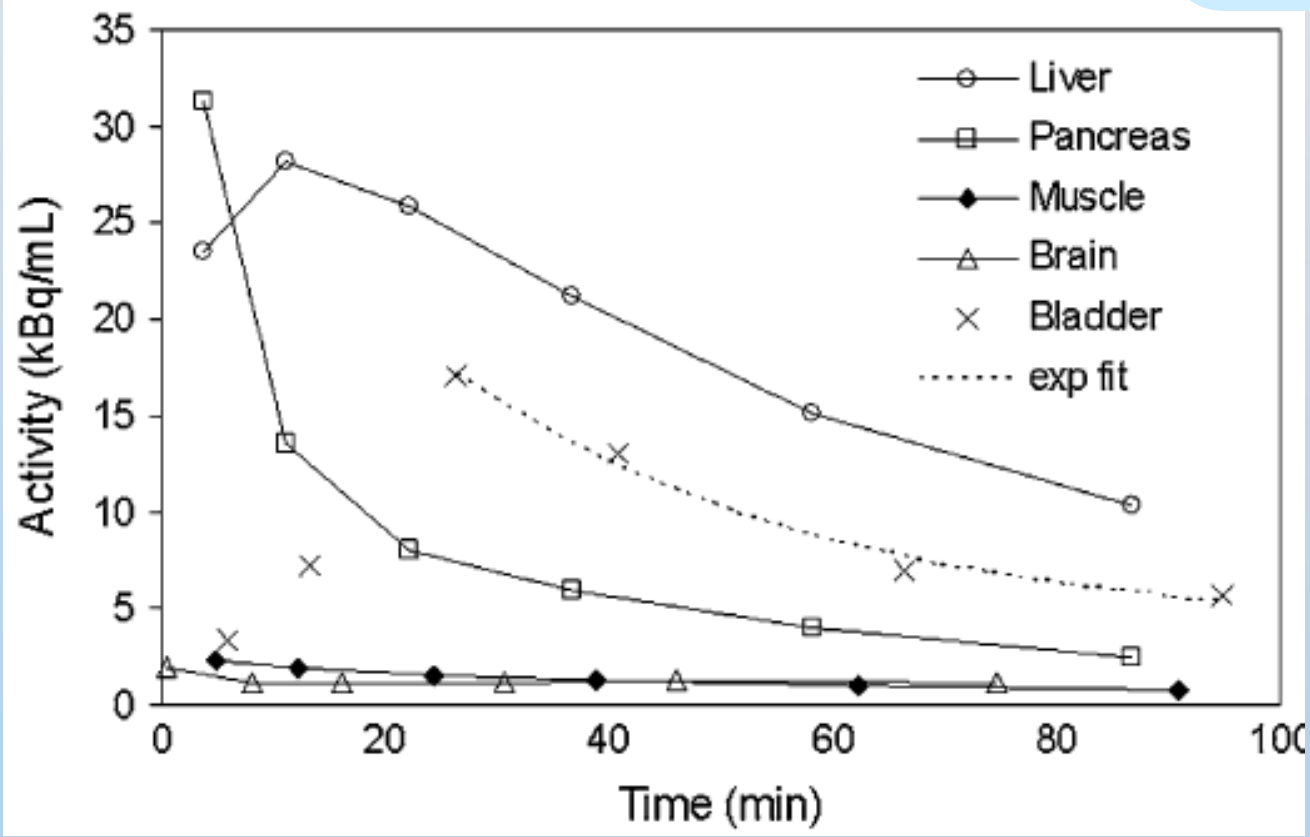


anti-1-amino-3-[^{18}F]fluorocyclobutane
-1-carboxylic acid
(anti-3-[^{18}F]FACBC)

- **Total of ^{18}F-FACBC uptake in PCa cells is probably related to the expression level of system ASC, a Na^+-dependent AAT, in PCa cells and is a likely explanation for the higher uptake of anti-[14C]FACBC in PCa cells compared with normal cells.**
- **LAT1, a Na^+ independent AAT, is also an important transport system for anti-[14C]FACBC uptake, especially in acidic pH environments such as that present in an intra-tumoural environment.**
- **FACBC is translocated from inside cell with cold leucine**
- **Not incorporated into proteins**
- **No significant metabolite formation**
- **Relatively low uptake of anti-[^{18}F]FACBC in inflammatory cells**
- **Little renal excretion or brain uptake compared to FDG**

NORMAL SUBJECT

^{18}F-FACBC

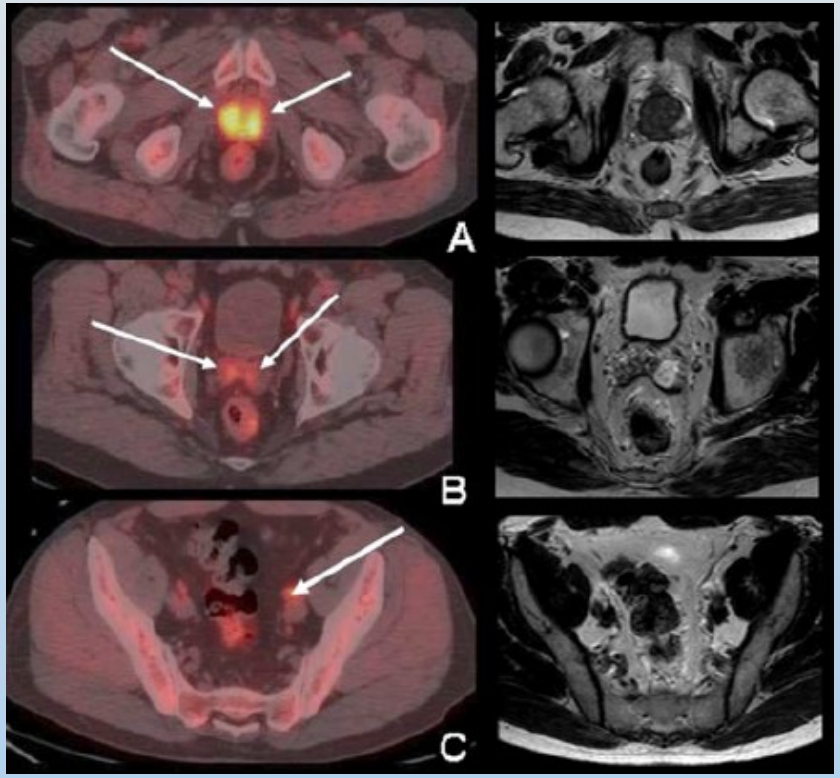


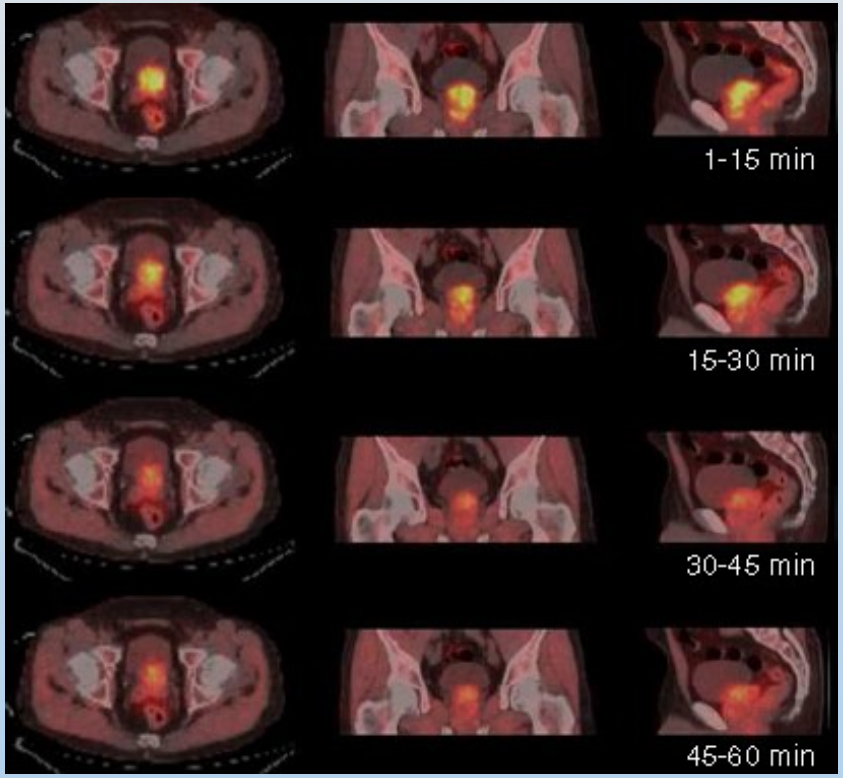
Biodistribution and Radiation Dosimetry of the Synthetic Nonmetabolized Amino Acid Analogue *Anti*-^{18}F-FACBC in Humans **J Nucl Med 2007; 48:1017–1020**

Jonathon A. Nye, David M. Schuster, Weiping Yu, Vernon M. Camp, Mark M. Goodman, and John R. Votaw

PROSTATE CANCER

^{18}F-FACBC





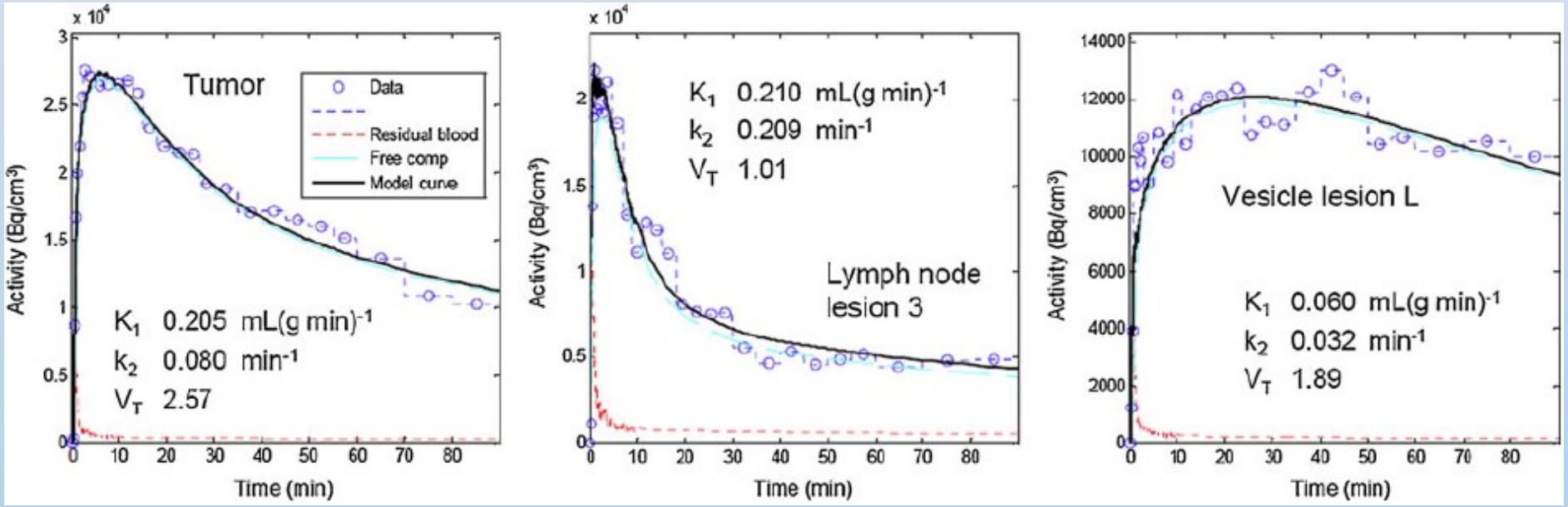
Regional distribution and kinetics of [^{18}F]fluciclovine (anti-[^{18}F]FACBC), a tracer of amino acid transport, in subjects with primary prostate cancer

Eur J Nucl Med Mol Imaging (2013) 40:394–402

Jens Sörensen · Rikard Owenius · Michelle Lax · Silvia Johansson

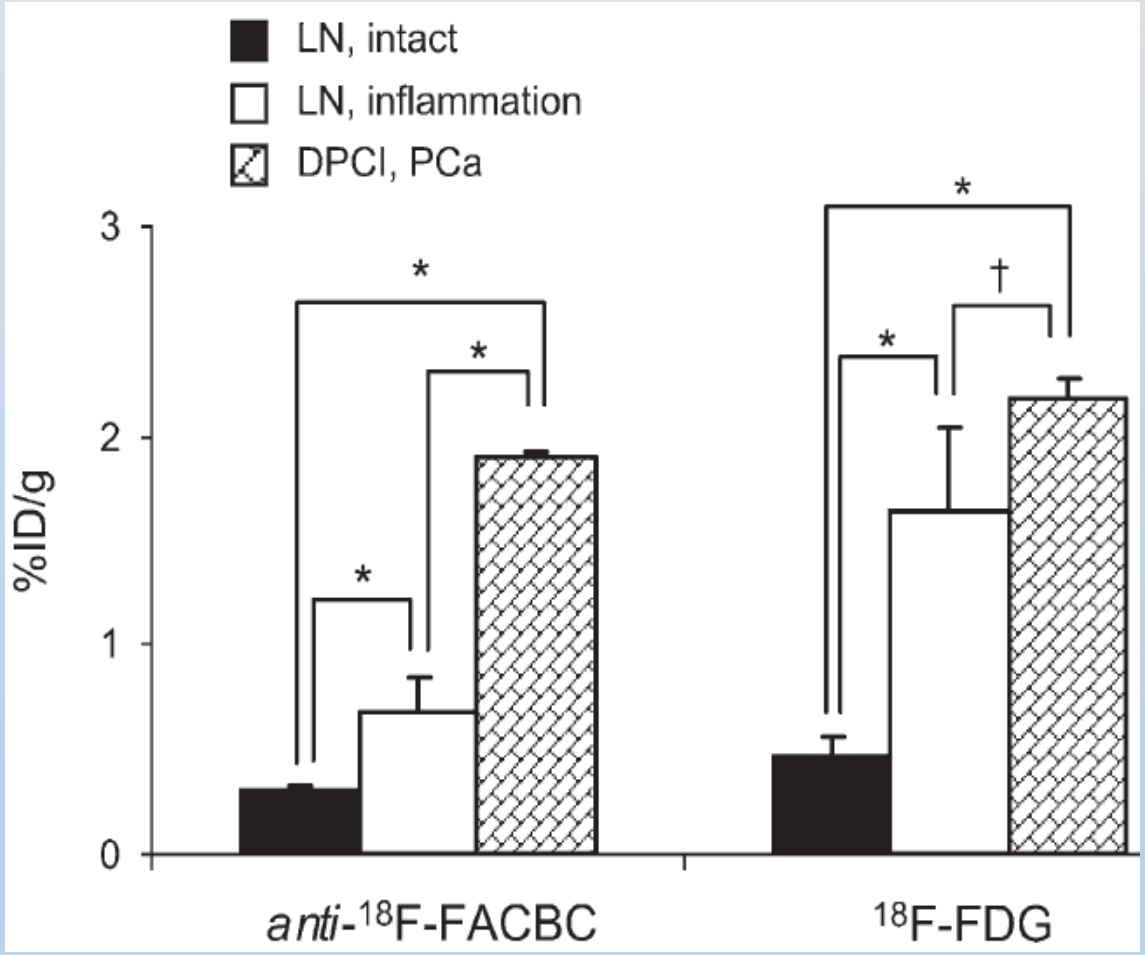
PROSTATE CANCER

^{18}F-FACBC

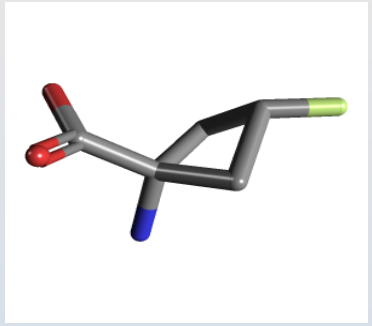


J Nucl Med 2007; 48:46–55

+++ Specificity



Relatively low uptake in inflammation: ^{18}F-FACBC may be useful to separate areas of inflammation from tumor



PROSTATE CANCER

^{18}F-FACBC vs ^{11}C-choline

Biodistribution

Eur J Nucl Med Mol Imaging. 2013 Jul;40 Supp1:S11-7.

Comparison of 18F-FACBC and 11C-choline PET/CT in patients with radically treated prostate cancer and biochemical relapse: preliminary results.

Nanni C, Schiavina R, Boschi S, Ambrosini V, Pettinato C, Brunocilla E, Martorana G, Fanti S.

Clin Genitourin Cancer. 2013 Oct 14

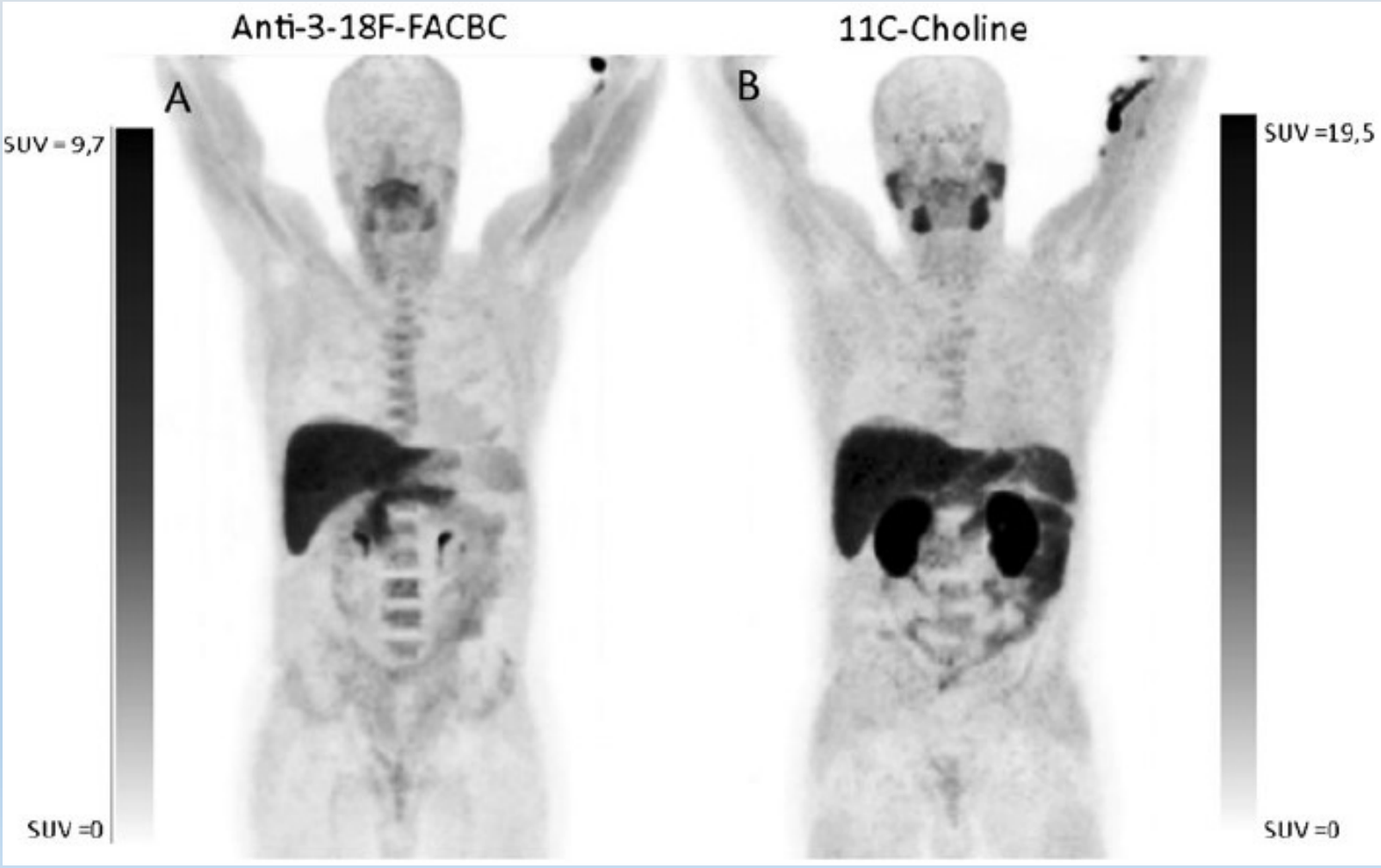
18F-FACBC Compared With 11C-Choline PET/CT in Patients With Biochemical Relapse After Radical Prostatectomy: A Prospective Study in 28 Patients.

Nanni C, Schiavina R, Brunocilla E, Borghesi M, Ambrosini V, Zanoni L, Gentile G, Vagnoni V, Romagnoli D, Martorana G, Fanti S.

Fluciclovine (18F-FACBC) PET/CT for the detection of prostate cancer relapse: a comparison to 11c-choline PET/CT.

Cristina Nanni°, Riccardo Schiavina*, Eugenio Brunocilla*, Stefano Boschi°, Marco Borghesi*, Lucia Zanoni*, Cinzia Pettinato^, Giuseppe Martorana*, Stefano Fanti*. **Eur J Nucl Med Mol Imaging 2013.**

18F-FACBC vs 11-Choline

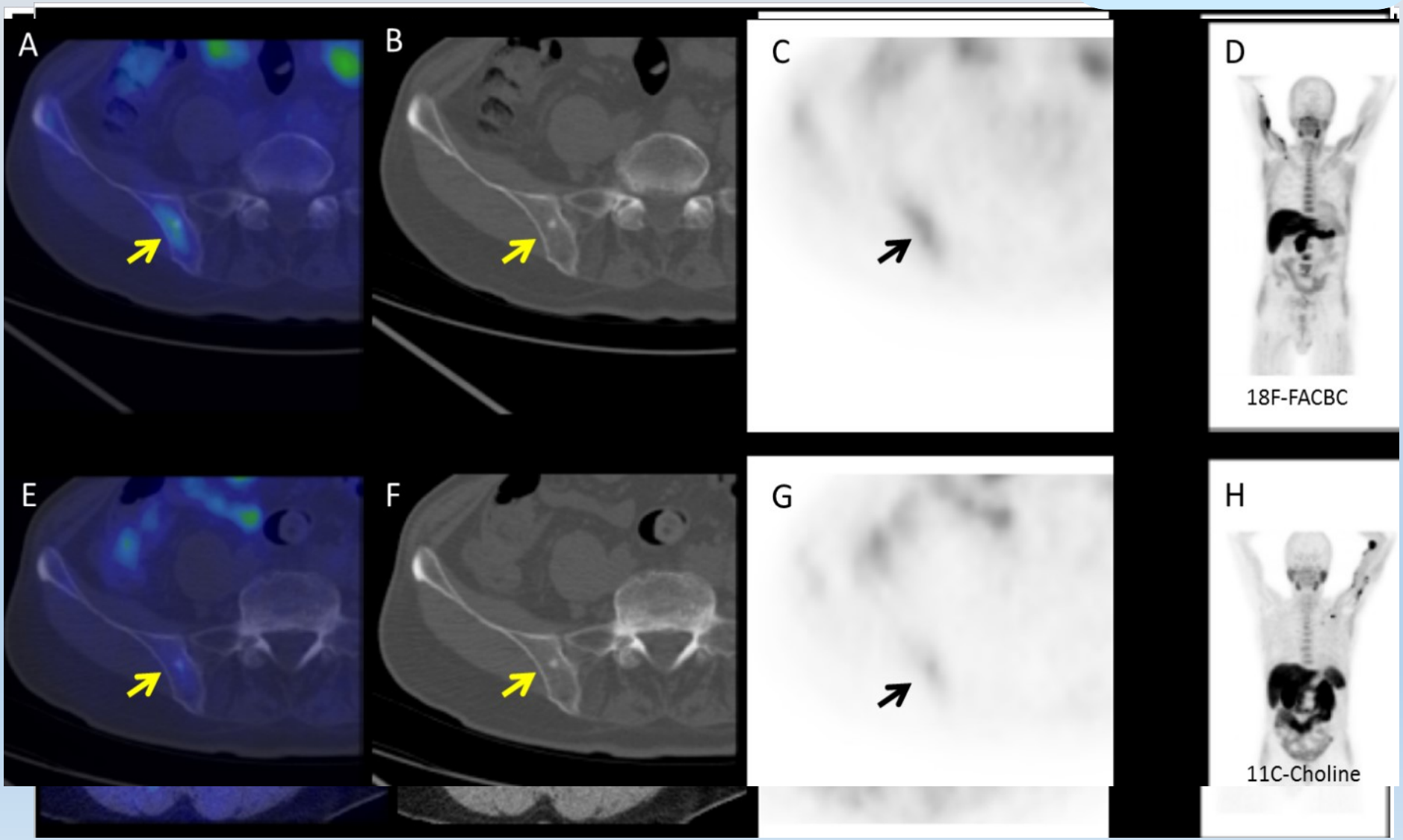


PROSTATE CANCER

^{18}F-FACBC vs ^{11}C-choline

LYMPHNODE

BONE LOCAL RELAPSE



PROSTATE CANCER

^{18}F-FACBC vs ^{11}C-choline

ORIGINAL ARTICLE

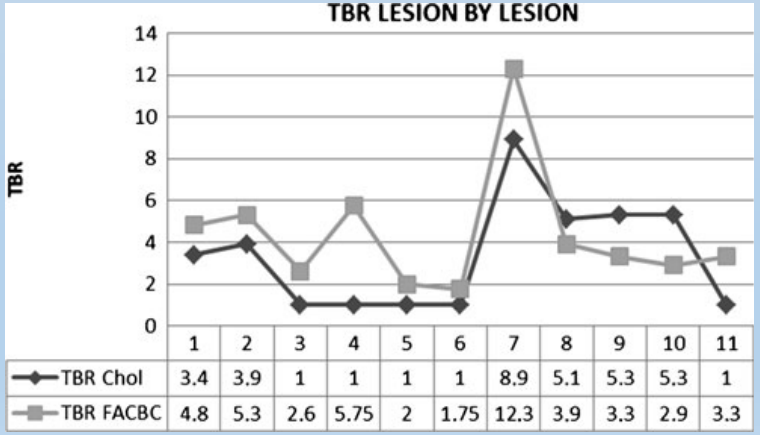
Comparison of ^{18}F-FACBC and ^{11}C-choline PET/CT in patients with radically treated prostate cancer and biochemical relapse: preliminary results

Cristina Nanni · Riccardo Schiavina · Stefano Boschi · Valentina Ambrosini · Cinzia Pettinato · Eugenio Brunocilla · Giuseppe Martorana · Stefano Fanti

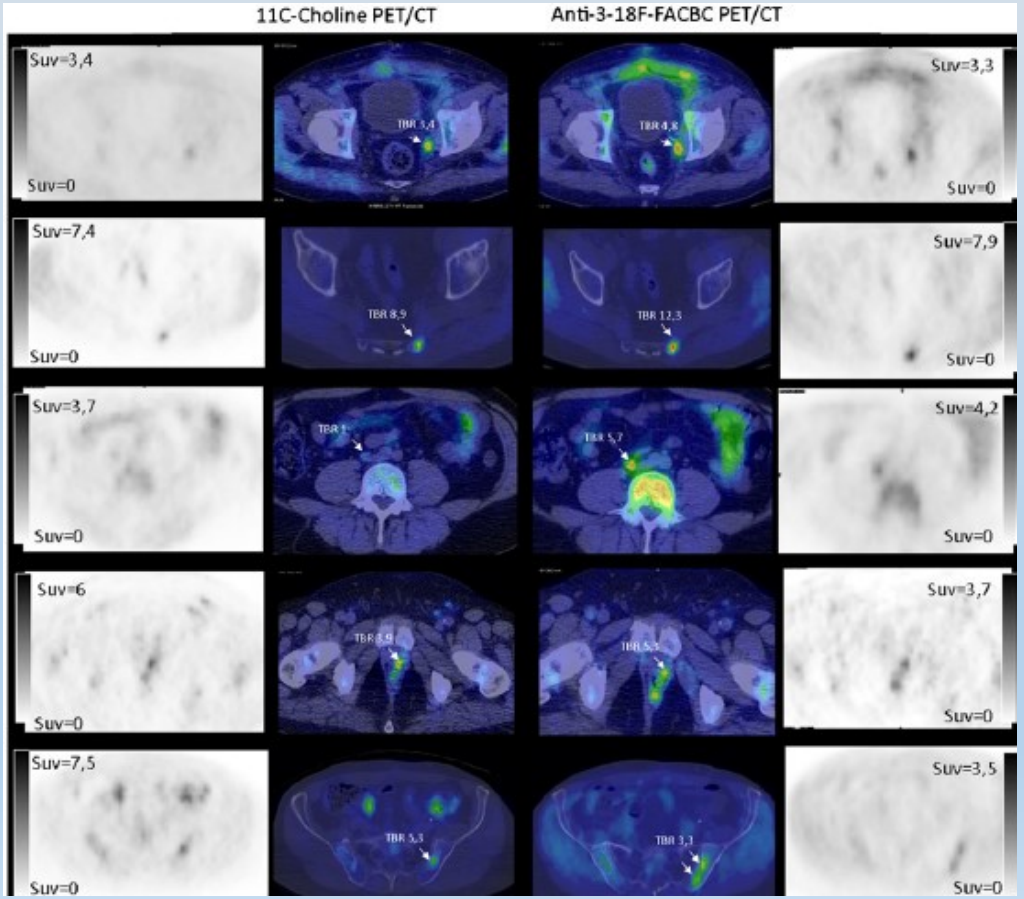
Eur J Nucl Med Mol Imaging (2013) 40 (Suppl 1):S11–S17
DOI 10.1007/s00259-013-2373-3

Table 2 Patient-based analysis

	^{11}C-Choline-positive	^{11}C-Choline-negative	Total
Anti-3-^{18}F-FACBC-positive	3	3	6
Anti-3-^{18}F-FACBC-negative	0	9	9
Total	3	12	15



None of ^{11}C-choline positive lesions was negative with ^{18}F-FACBC



Clinical Nuclear Medicine 2015

PROSTATE CANCER

^{18}F-FACBC vs ^{11}C-choline

^{18}F-Fluciclovine PET/CT for the Detection of Prostate Cancer Relapse

A Comparison to ^{11}C-Choline PET/CT

Cristina Nanni, MD, Riccardo Schiavina,† Eugenio Brunocilla,† Stefano Boschi,* Marco Borghesi,† Lucia Zanoni,† Cinzia Pettinato,‡ Giuseppe Martorana,† and Stefano Fanti†*

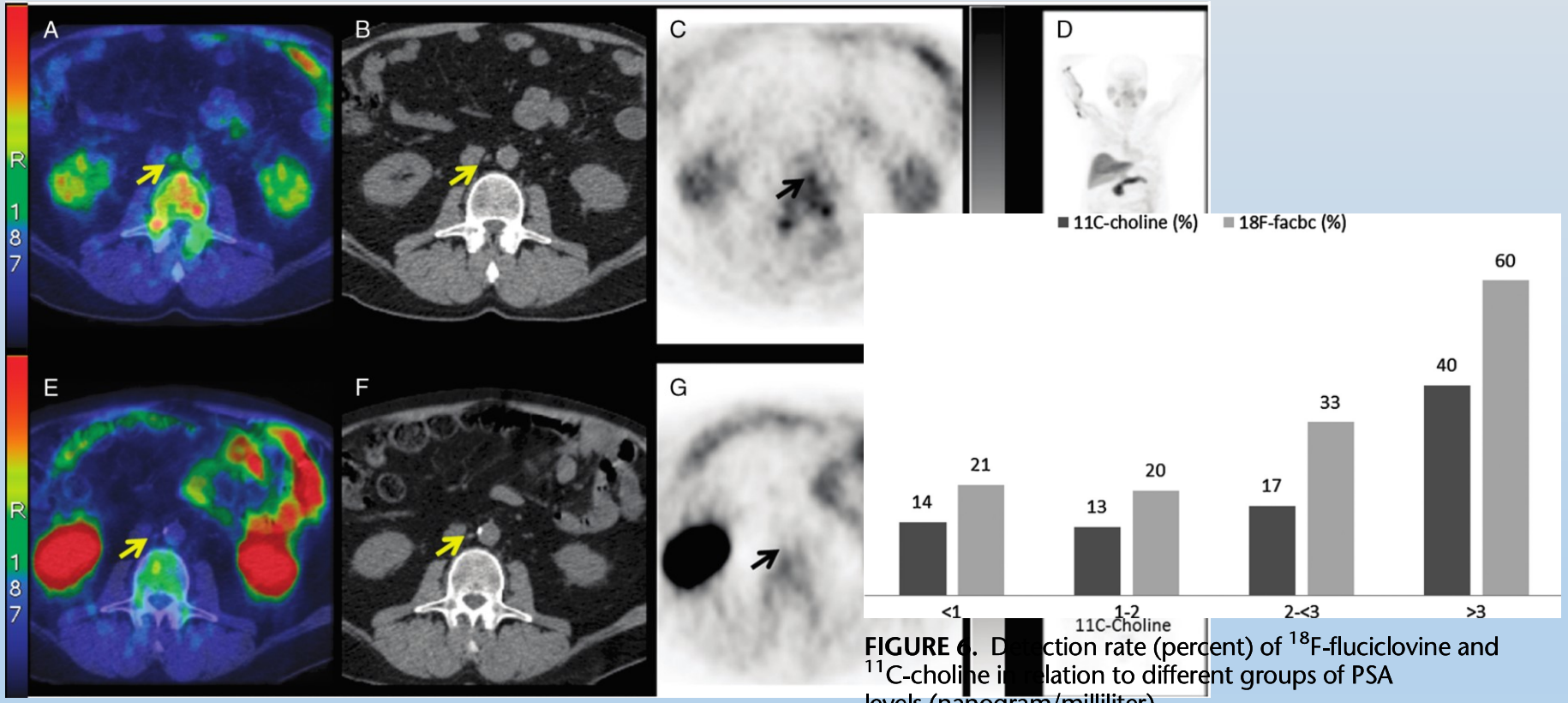
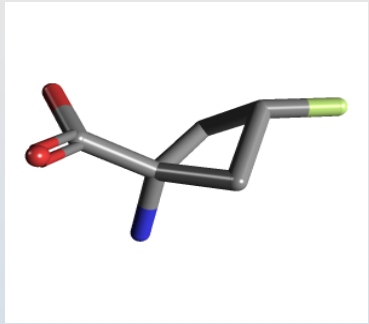


FIGURE 6. Detection rate (percent) of ^{18}F-fluciclovine and ^{11}C-choline in relation to different groups of PSA levels (nanogram/milliliter).

^{18}F-fluciclovine axial cut (A,fusion;B,CT;C,PET;D,MIP) showing increased uptake in 1 small positive interaortocaval lymph node (arrow). Corresponding ^{11}C-choline axial cut (A, fusion; B, CT; C, PET; D, MIP) resulted completely negative.



PROSTATE CANCER

^{18}F-FACBC vs ^{11}C-choline

- **Late urinary excretion**, that allows to acquire images without any significant urinary activity;

- **Lower background.**

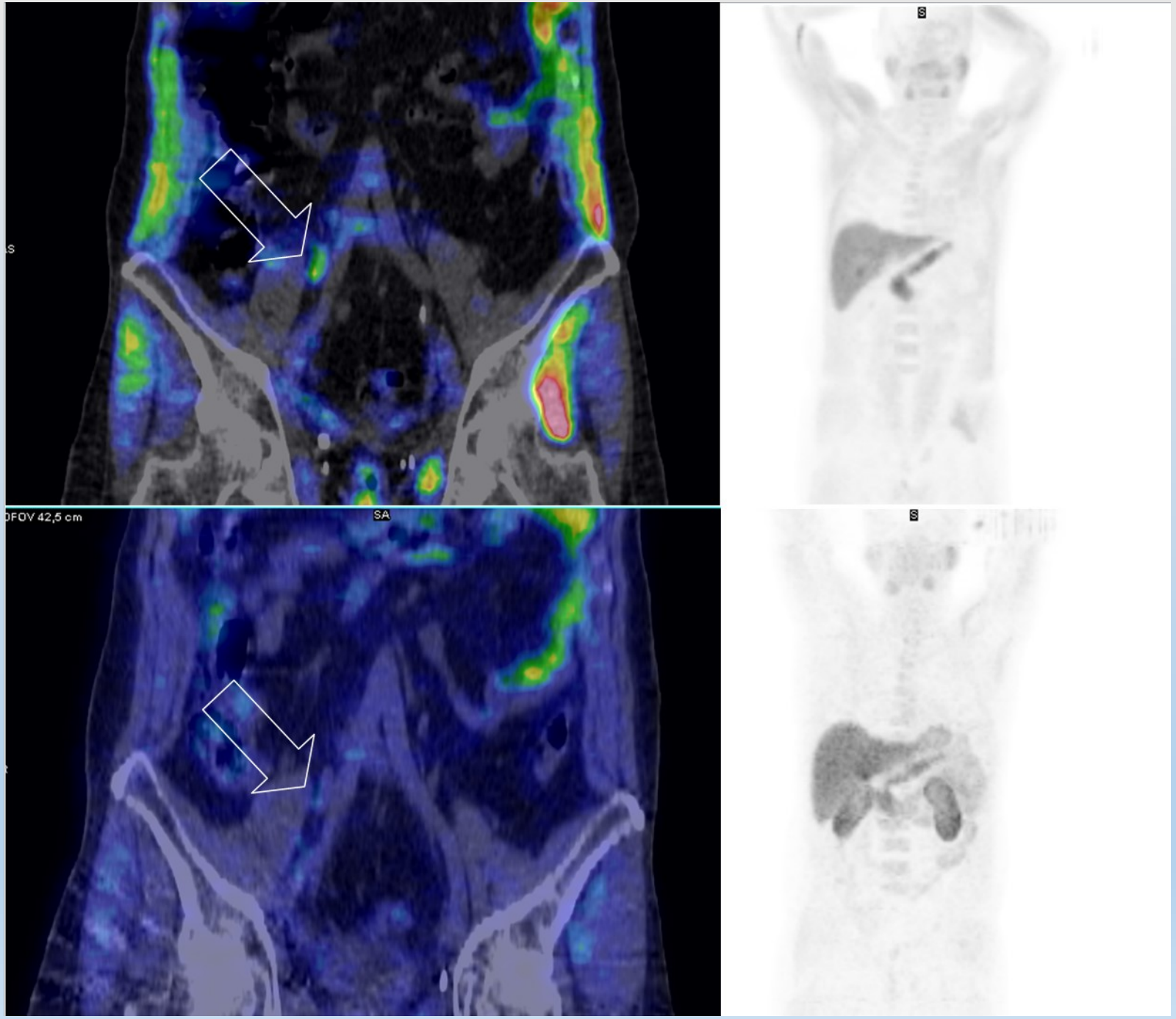
⇨ **Better contrast in positive lesions**

Superior detection rate of Fluciclovine (18F) over 11C-Choline, both on patient basis and on lesion basis

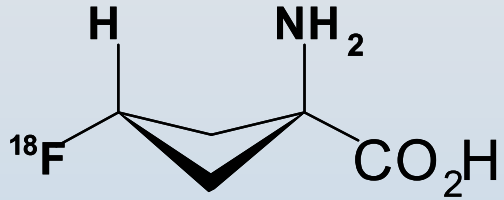
CLINICAL CASE

2009	pT3aN0M0	GS 9
2010	RT PELVIS (POST SURGICAL)	
2013	RISING PSA	2,25 ng/dl
2013	BONE SCAN + TRUS	NEG
2013	PET/CT CHOLINE	NEG
2013	PET/CT FACBC	POS LN
2013	PLNR	

… After surgery a topographic correspondence between histological result and 18F-FACBC positivity was found.


S
SA
S

^{18}F-FACBC



^{18}F-FACBC

J Nucl Med. 2011; 52 (Supplement 1):1433

The development of an automated and optimized synthesis of [18F]Fluciclovine on a FASTlab synthesizer utilising chemometric design

Torild Wickstrøm[1], Anders Svadberg[2], Olav Ryan[3], Roger Smeets[4], Kristine Romøren[1], Liane Ochsenfeld[1] and Knut Dyrstad[1]

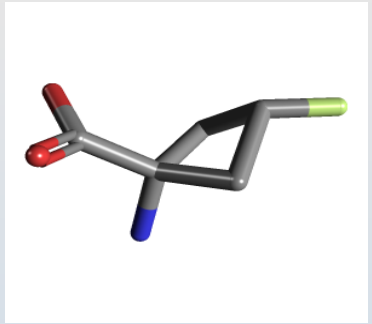
[1] GE Healthcare, Oslo, Norway [2] Univ. of Tromsø, Tromsø, Norway [3] Algeta, Oslo, Norway [4] IFE, Lillestrøm, Norway

Abstract No. 1433

blue earth DIAGNOSTICS

PROSTATE CANCER

^{18}F-FACBC vs ^{11}C-choline



- Longer Halflife
- Tracer stability
- Simple synthesis
- Better biodistribution in the abdomen and pelvis
- Higher TBR
- Apparently higher detection rate

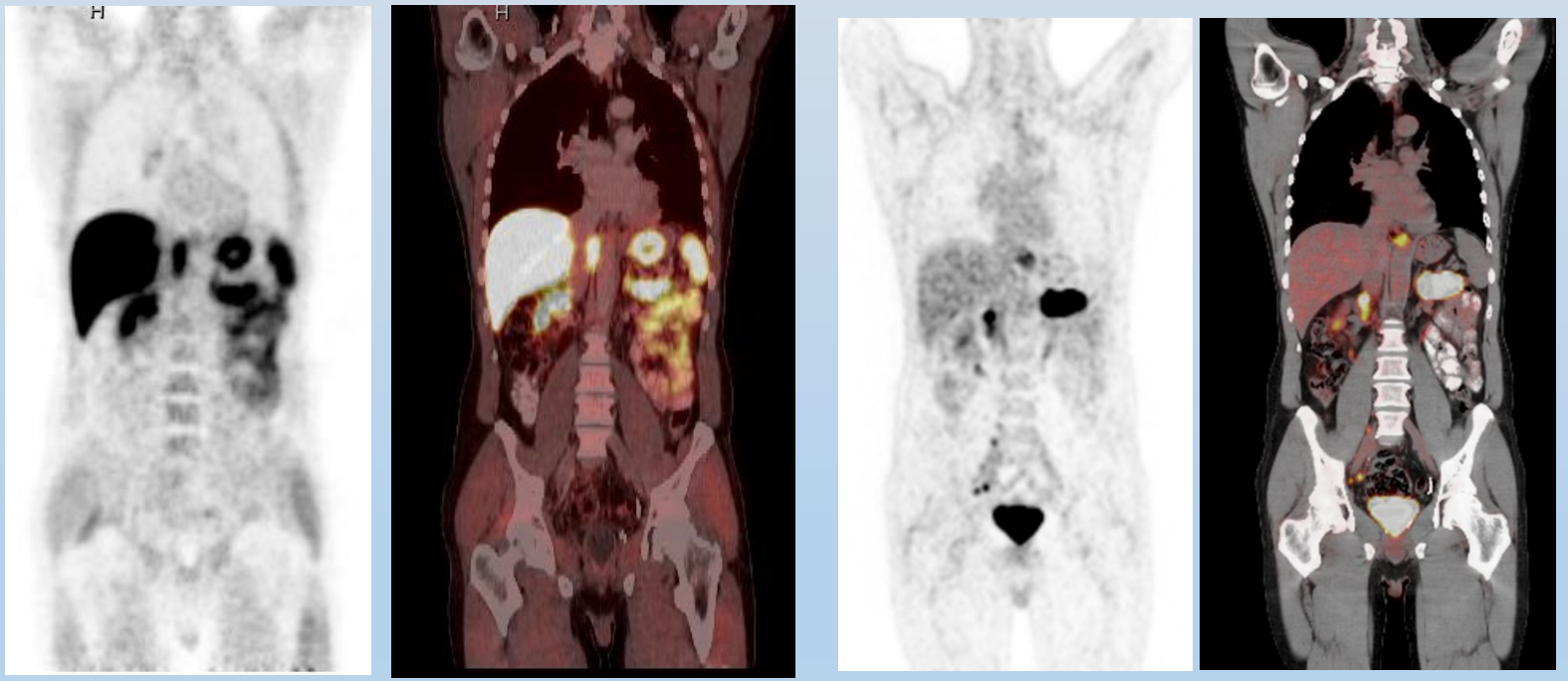
New Targets

^{68}Ga-labeled DOTA-4- amino-1-carboxymethyl-piperidine-*D*-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH2

^{68}Ga-labeled RP's for PC

Bombesin

^{68}Ga-Bombesin Antagonist (RM2) and Choline PET/CT in a patient with PSA recurrence



0 SUV 5

Choline PET/CT

0 SUV 6

Bombesin PET/CT

Courtesy Prof.H.R.Maecke

New Targets

^{68}Ga-labeled RP's for PC

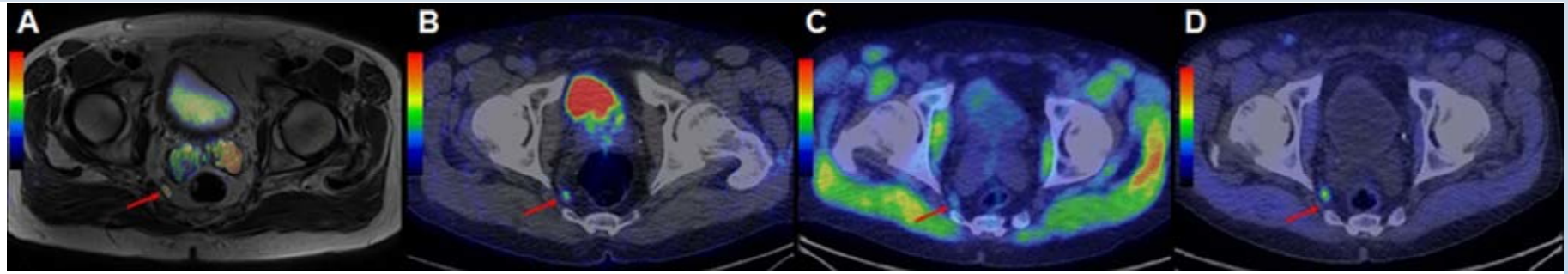
Bombesin

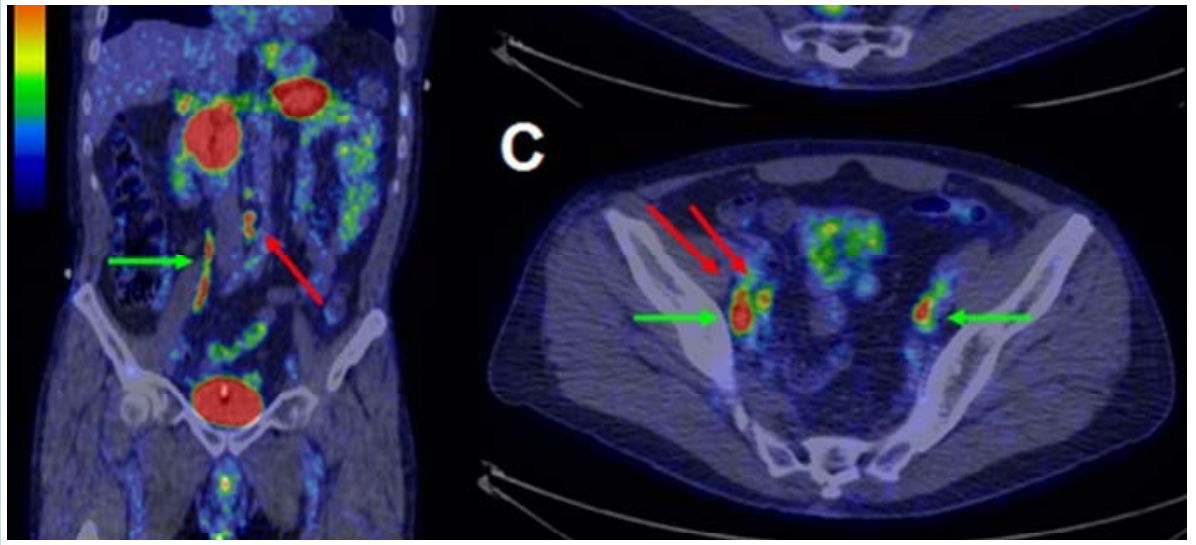
In vivo imaging of prostate cancer using [^{68}Ga]-labeled bombesin analog BAY86-7548

Esa Kahkonen, Ivan Jambor, Jukka Kemppainen, et al.

Clin Cancer Res Published OnlineFirst August 9, 2013.

^{68}Ga-labeled DOTA-4- amino-1-carboxymethyl-piperidine-*D*-Phe-Gln-Trp-Ala-Val-Gly-His-Sta-Leu-NH2





New Targets

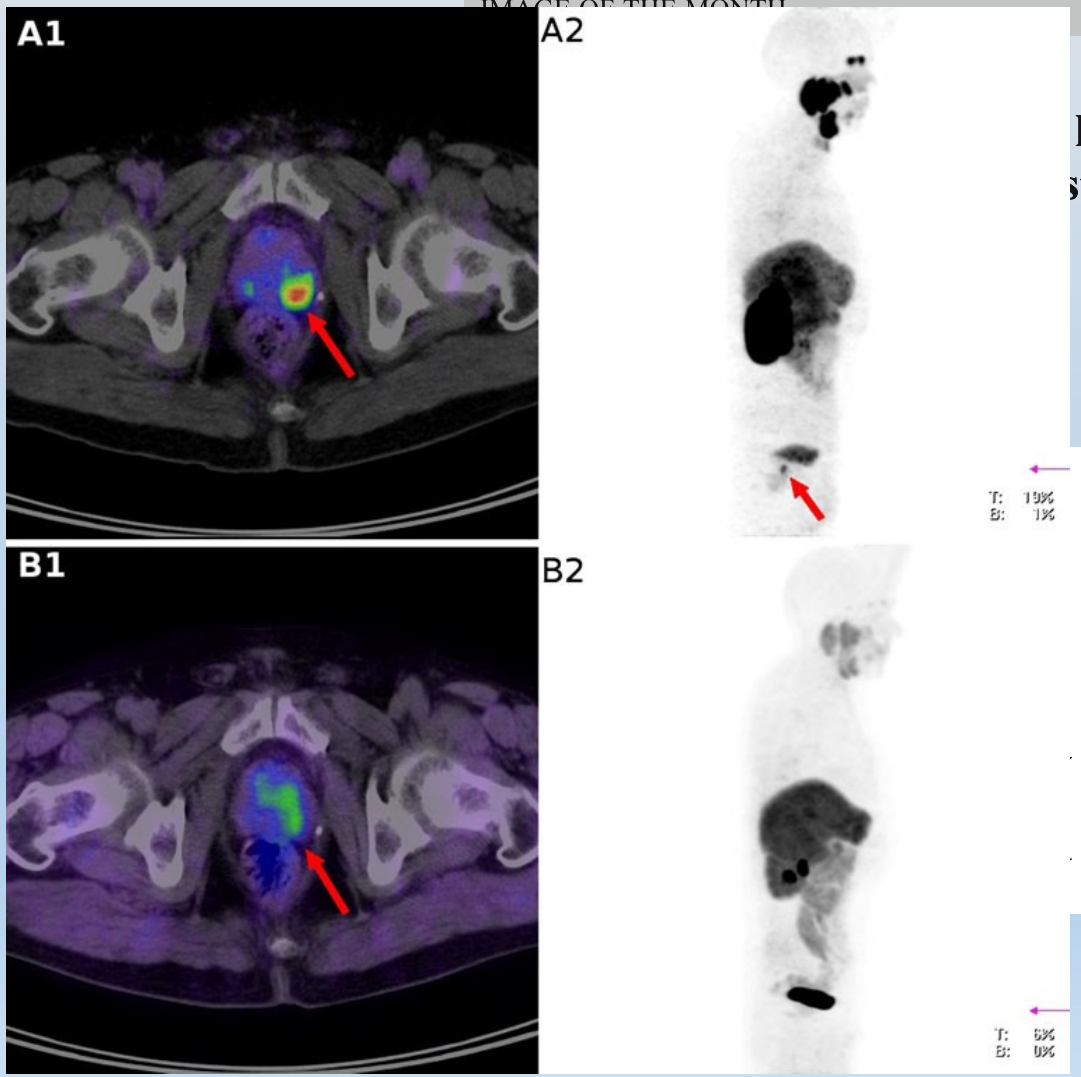
^{68}Ga-labeled RP's for PC

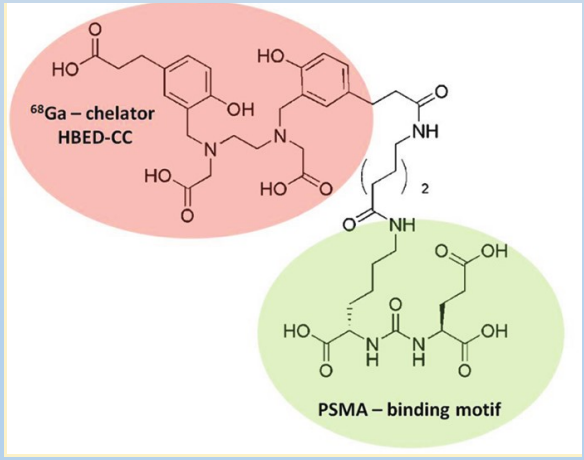
PSMA Ligands

Eur J Nucl Med Mol Imaging (2012) 39:1085–1086
DOI 10.1007/s00259-012-2069-0

IMAGE OF THE MONTH

ligand as superior PET
state cancer: comparison





New Targets

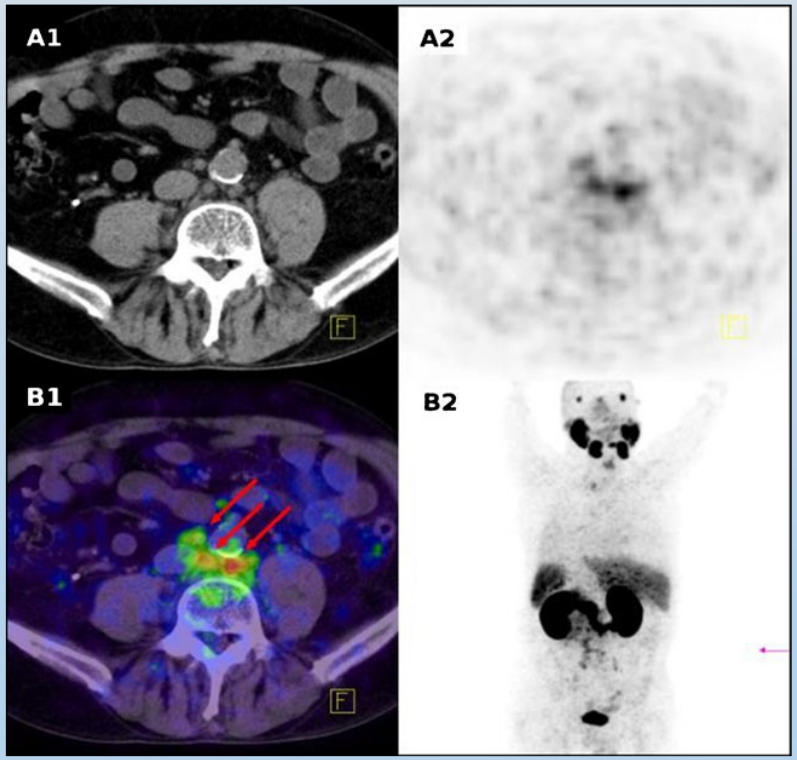
^{68}Ga-labeled RP's for PC

PSMA Ligands

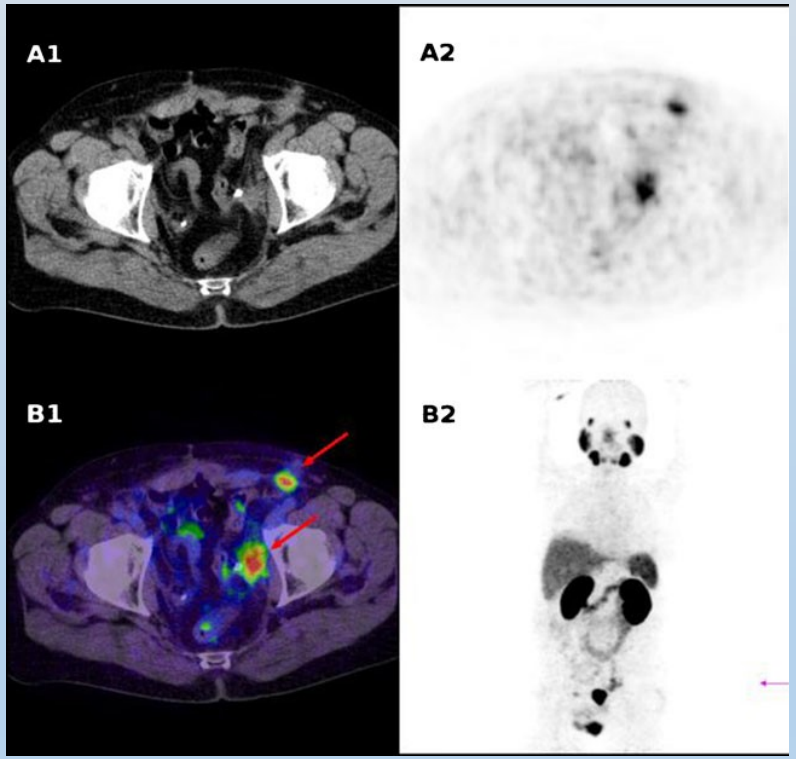
PET imaging with a [^{68}Ga]gallium-labelled PSMA ligand for the diagnosis of prostate cancer: biodistribution in humans and first evaluation of tumour lesions

A. Afshar-Oromieh · A. Malcher · M. Eder · M. Eisenhut · H. G. Linhart · B. A. Hadaschik · T. Holland-Letz · F. L. Giesel · C. Kratochwil · S. Haufe · U. Haberkorn · C. M. Zechmann

Eur J Nucl Med Mol Imaging (2013) 40:486–495



68Ga-PSMA PET/CT of patient 22 who received the lowest dose of radiotracer (52 MBq). Red arrows point to several small lymph nodes with clearly visible pathological tracer uptake.



68Ga-PSMA PET/CT of patient 21 with a minimal PSA value (0.01 ng/ml). Red arrows point to typical lymph node metastases. The combination of minimal PSA levels despite visible tumour lesions suggests a dedifferentiation of the prostate cancer.

Comparison of PET imaging with a ^{68}Ga-labelled PSMA ligand and ^{18}F-choline-based PET/CT for the diagnosis of recurrent prostate cancer

Eur J Nucl Med Mol Imaging (2014) 41:11–20
DOI 10.1007/s00259-013-2525-5

Ali Afshar-Oromieh · Christian M. Zechmann · Anna Malcher · Matthias Eder · Michael Eisenhut · Heinz G. Linhart · Tim Holland-Letz · Boris A. Hadaschik · Frederik L. Giesel · Jürgen Debus · Uwe Haberkorn

^{68}Ga-labeled RP's for PC

PSMA Ligands

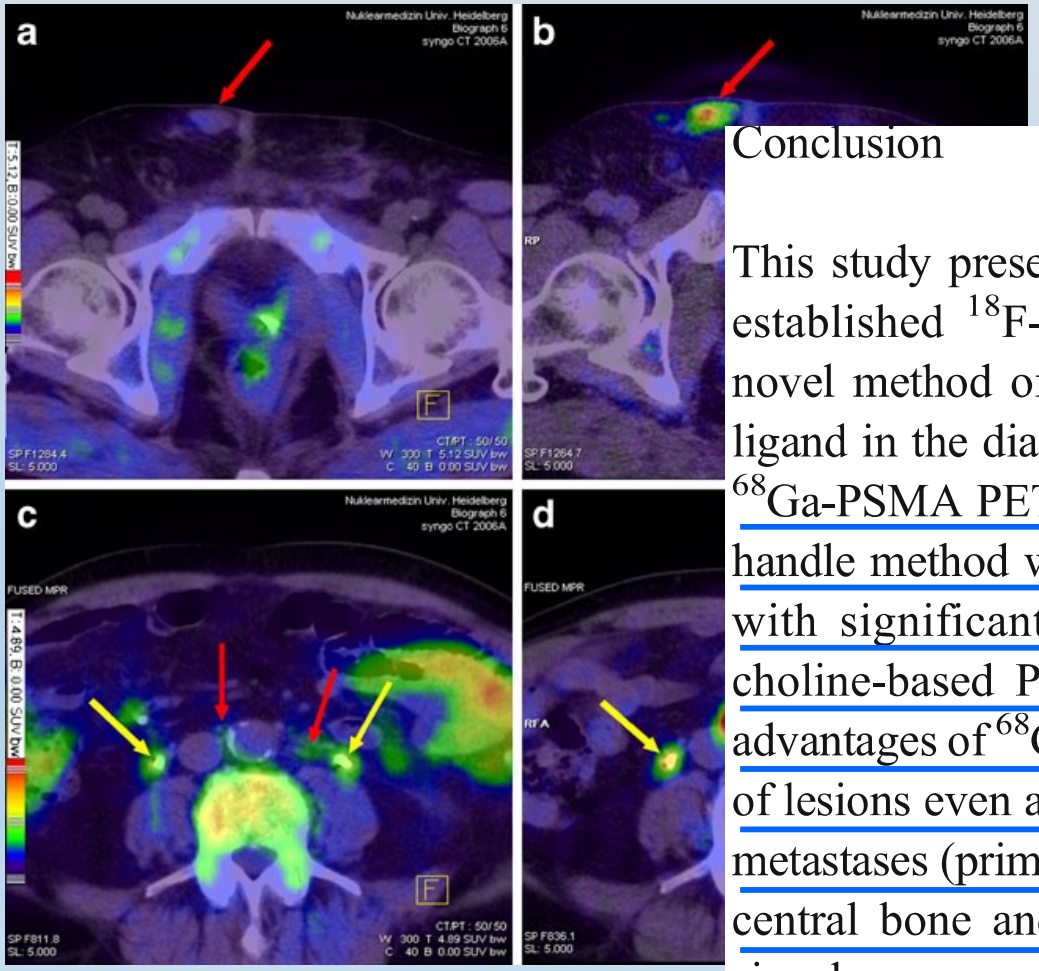


Fig. 2 Patient 12 (**a**, **b**) and patient 18 (**c**, **d**). *Red arrows* point to a nodular pelvic wall metastasis

Conclusion

This study presents a retrospective comparison between the established ^{18}F-fluoromethylcholine-based PET/CT and a novel method of PET imaging with a ^{68}Ga-labelled PSMA ligand in the diagnosis of recurrent PC. Our experience with ^{68}Ga-PSMA PET/CT strongly suggests that this is an easy to handle method which can detect PC relapses and metastases with significantly improved contrast when compared to choline-based PET/CT. Nevertheless, the most significant advantages of ^{68}Ga-PSMA PET/CT are the sensitive detection of lesions even at low PSA levels, of even small lymph node metastases (primarily due to a high radiotracer uptake) and of central bone and liver metastases due to low background signal.

Eur J Nucl Med Mol Imaging (2015) 42:197–209
DOI 10.1007/s00259-014-2949-6

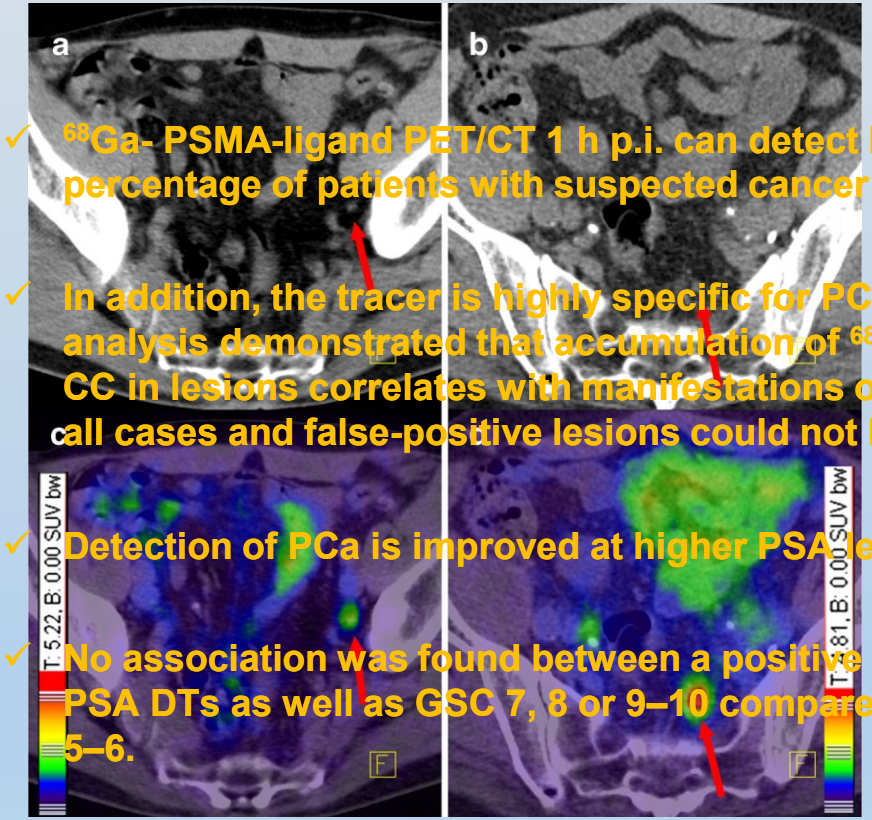
ORIGINAL ARTICLE

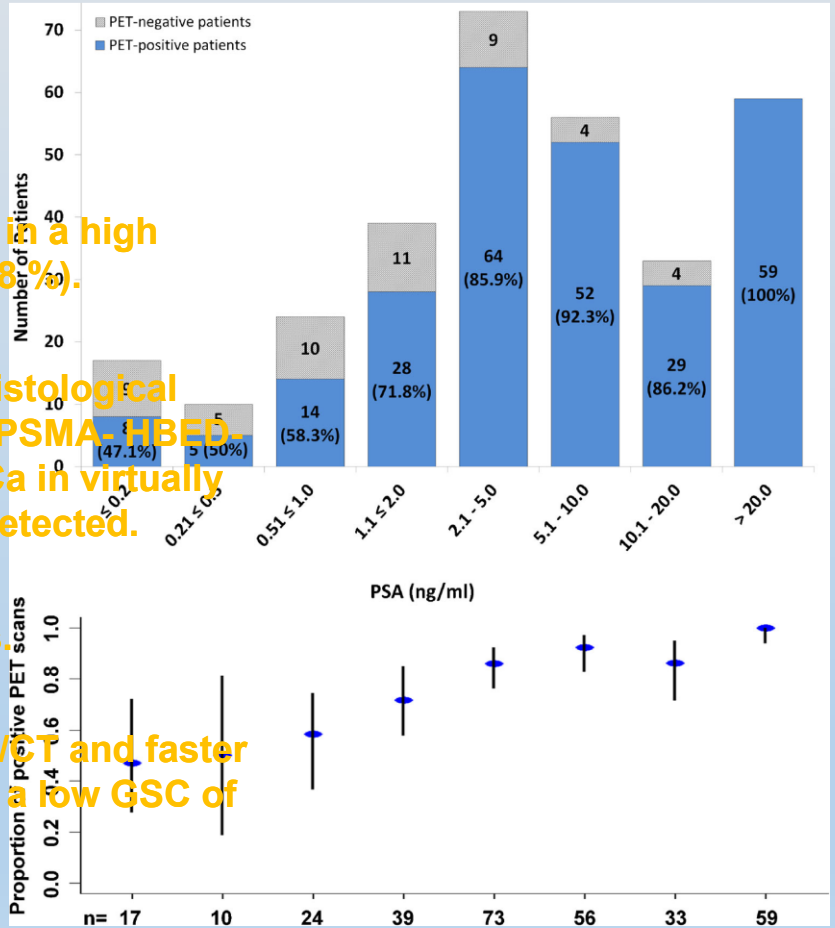
The diagnostic value of PET/CT imaging with the ^{68}Ga-labelled PSMA ligand HBED-CC in the diagnosis of recurrent prostate cancer

Ali Afshar-Oromieh · Eleni Avtzi · Frederik L. Giesel · Tim Holland-Letz · Heinz G. Linhart · Matthias Eder · Michael Eisenhut · Silvan Boxler · Boris A. Hadaschik · Clemens Kratochwil · Wilko Weichert · Klaus Kopka · Jürgen Debus · Uwe Haberkorn

^{68}Ga-RP's

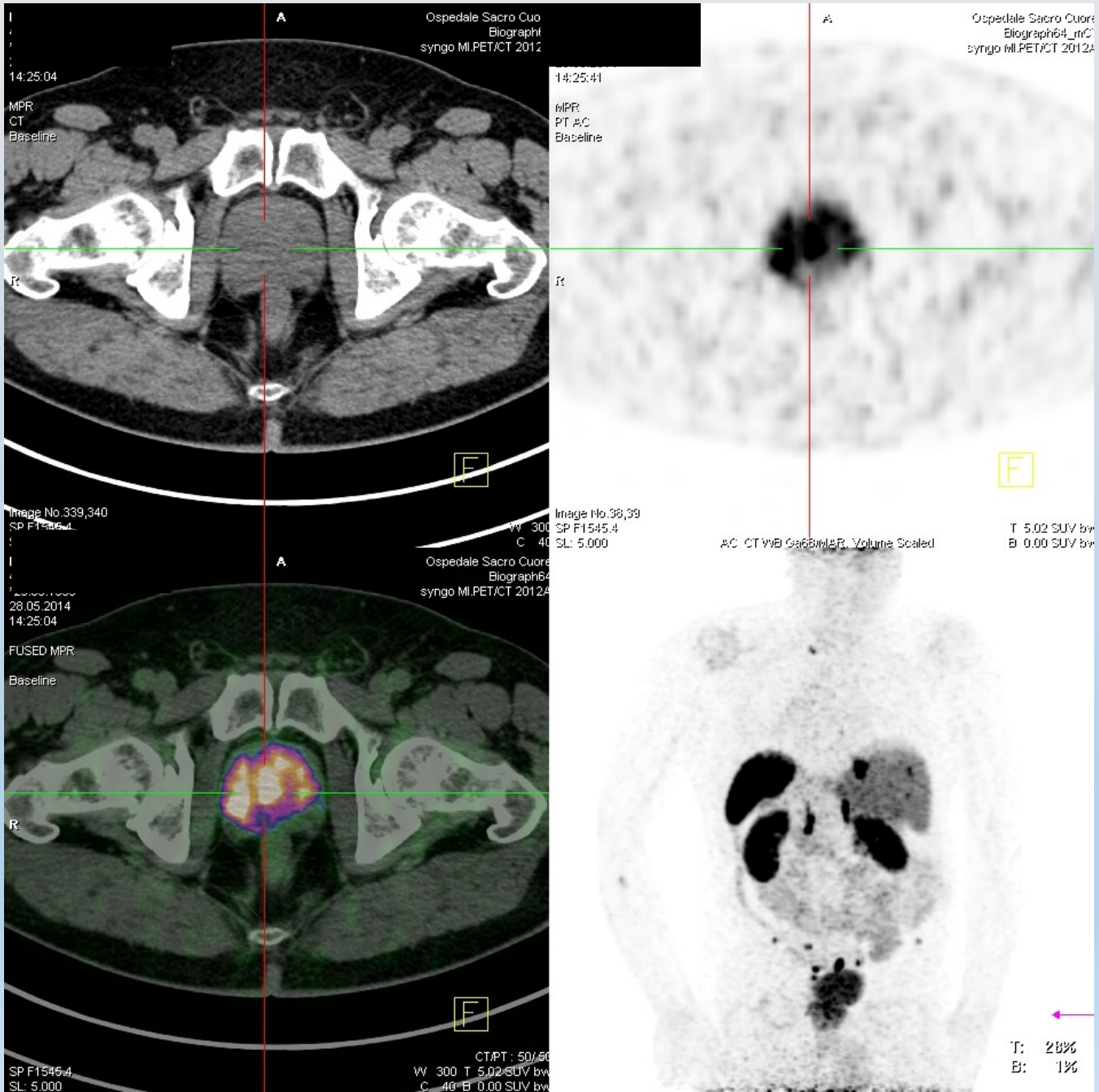
PSMA Ligands





- ✓ ^{68}Ga- PSMA-ligand PET/CT 1 h p.i. can detect PCa in a high percentage of patients with suspected cancer (82.8%).
- ✓ In addition, the tracer is highly specific for PCa: histological analysis demonstrated that accumulation of ^{68}Ga-PSMA- HBED-CC in lesions correlates with manifestations of PCa in virtually all cases and false-positive lesions could not be detected.
- ✓ Detection of PCa is improved at higher PSA levels.
- ✓ No association was found between a positive PET/CT and faster PSA DTs as well as GSC 7, 8 or 9–10 compared to a low GSC of 5–6.
- ✓ ^{68}Ga-PSMA-ligand PET/CT can help delay systemic therapy of PCa.

Ga



Ga68- Dotatoc

Tracciante in farmacopea per le neoplasie neuroendocrine

Ga68- Dotatoc

Permette di identificare caratteristiche biologiche recettoriali utili nella programmazione terapeutica

FACBC

Ga-PSMA

CHOLINE

Eur J Nucl Med Mol Imaging. 2014 Jan;41(1):11-20. Comparison of PET imaging with a (68)Ga-labelled PSMA ligand and (18)F-choline-based PET/CT for the diagnosis of recurrent prostate cancer.
Afshar-Oromieh A, Zechmann CM, Malcher A, Eder M, Eisenhut M, Linhart HG, Holland-Letz T, Hadaschik BA, Giesel FL, Debus J, Haberkorn Y

^{68}Ga-labeled RP's for PC

PSMA Ligands

PSMA as a target for radiolabelled small molecules

Matthias Eder · Michael Eisenhut · John Babich · Uwe Haberkorn

Eur J Nucl Med Mol Imaging (2013) 40:819–823

^{68}Ga-Labeled Inhibitors of Prostate-Specific Membrane antigen (PSMA) for Imaging Prostate Cancer

Sangeeta Ray Banerjee, Mrudula Pullambhatla, Youngjoo Byun, Sridhar Nimmagadda,

Synthesis, Radiolabelling and *In Vitro* Characterization of the Gallium-68-, Yttrium-90- and Lutetium-177-Labelled PSMA Ligand, CHX-A''-DTPA-DUPA-Pep

Benjamin Baur [1,†,*], Christoph Solbach [1,†], Elena Andreolli [1,2], Gordon Winter [1], gler,[§] Hans-Jürgen Machulla [1] and Sven N. Reske [1]

Pharmaceuticals **2014**, *7*, 517-529; doi:10.3390/ph7050517

urea-based inhibit
prostate-specific membrane an

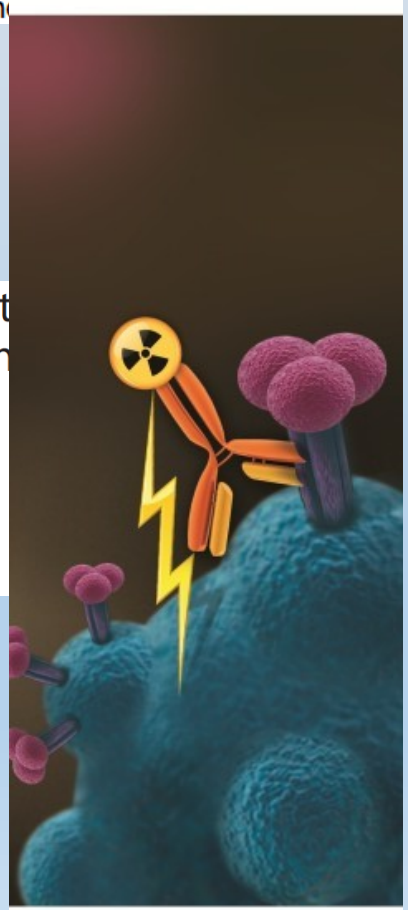
Radiation dosimetry and first therapy results with a ^{124}I/^{131}I-labeled small molecule (MIP-1095) targeting PSMA for prostate cancer therapy

Christian M. Zechmann · Ali Afshar-Oromieh · Tom Armor · James B. Stubbs · Walter Mier · Boris Hadaschik · John Joyal · Klaus Kopka · Jürgen Debus · John W. Babich · Uwe Haberkorn

Eur J Nucl Med Mol Imaging (2014) 41:1280–1292

t [1], Yvonne Remde [1], Martin Schäfer [1], Ute Hennrich [1,*], Michael Eisenhut [1], Ali Afshar-Oromieh [3], Uwe Haberkorn [3] and Klaus Kopka [1,2]

Pharmaceuticals **2014**, *7*, 779-796;



^{68}Ga-labeled RP's for PC

PSMA Ligands

Novel Preclinical and Radiopharmaceutical Aspects of [^{68}Ga]Ga-PSMA-HBED-CC: A New PET Tracer for Imaging of Prostate Cancer

Matthias Eder [1,2,†,*], Oliver Neels [1,2,†], Miriam Müller [1], Ulrike Bauder-Wüst [1], Yvonne Remde [1], Martin Schäfer [1], Ute Hennrich [1,2], Michael Eisenhut [1], Ali Afshar-Oromieh [3], Uwe Haberkorn [3] and Klaus Kopka [1,2]

Pharmaceuticals **2014**, *7*, 779-796

Table 1. Defined product specification of the final preparation of [^{68}Ga]Ga-PSMA-HBED-CC

Appearance	Clear and Colourless
pH	4–8
Radioactivity concentration	10–200 MBq/mL
Radiochemical purity (HPLC)	≥95%
Chemical impurities (HPLC)	≤5 µg/mL PSMA-HBED-CC
Concentration ethanol (GC)	<10% v/v
Approximate half-life	68 ± 6 min
Bacterial endotoxins	<17.5 IU/mL
Filter integrity (bubble-point test)	>3.5 bar
Radionuclidic purity (γ-spectrometry)	^{68}Ga > 99.9% (γ-lines at 0.511 MeV and 1.077 MeV) ^{68}Ge: ≤0.001%
Sterility	Sterile

- ✓ Fully automated synthesis
- ✓ Aceton-free cationic post processing
- ✓ Acetate buffer
- ✓ % Yield (DC) = 80±5

COLINA--> metabolismo fosfolipidico di membrana

Linee guida AIOM:

non esistono attualmente evidenze scientifiche che ne giustifichino l'utilizzo nella **stadiazione** iniziale della malattia linfonodale e a distanza nei pz con Ca prostatico.

Due metanalisi --> Se e Sp globali per la valutazione della malattia linfonodale pari a:
49,5% e 95% in 441 pz [Evangelista 2013 Eur Urol]
62% e 92% in 609 pz [von Eyben 2015 Nucl Med Commun]

Potrebbe essere indicata per il completamento stadiativo in pz a rischio alto o molto alto. In tale scenario, sembrerebbe più Se e Sp della scintigrafia ossea e della TC, ma ad oggi le limitate evidenze scientifiche non ne giustificano l'uso sistematico.

Nella fase di **ristadiazione:** indicata nel Ca della prostata dopo prostatectomia radicale (+/- linfadenectomia) o dopo RT con intento radicale, in caso di elevazione del PSA.
La capacità di identificare la sede di ripresa della malattia dipende da caratteristiche cliniche del tumore (es GS) e biochimiche (es livelli e cinetica del PSA).
Indicata in ristadiazione in presenza di:
PSA > o uguale a 1 ng/ml
PSA doubling time (PSAdt) <6 mesi
PSA velocity (PSAvel) >1 ng/ml/anno

PET-TC con **PSMA:** attualmente considerata indagine sperimentale.
Tropismo recettoriale, lega proteina moderatamente espressa nel tessuto prostatico sano e overespressa nel tessuto prostatico patologico.
Numerose evidenze scientifiche hanno dimostrato la sua superiorità diagnostica rispetto alla colina nell'identificare la sede di ripresa di malattia [Schwenck 2016 Eur J Nucl Med Mol Imaging; De Visschere 2019 EUO].
Recente metanalisi --> maggiore detection rate rispetto alla colina in pz con ripresa biochimica per valori di PSA < 1 ng/ml [Treglia 2019 Am J Nucl Med Mol Imaging].
Alcune evidenze suggeriscono un ruolo aggiuntivo nella stadiazione iniziale rispetto all'imaging convenzionale (es Tc e bone scan) nei pz a rischio alto e molto alto.
Potenziale impiego terapeutico (mediante marcatura con isotopi alfa o beta emittenti)-→ attualmente tracciante più promettente nel pz con Ca prostatico.
Fino al 5-7% delle neoplasie prostatiche non iperesprime PSMA.

FACBC: tracciante aminoacidico con tropismo per Ca prostatico.
Recentemente introdotto in Italia. Indicato nella ripresa biochimica dopo trattamento primario. Studi comparativi hanno dimostrato una maggiore detection rate della FACBC rispetto alla Colina [Nanni 2016 Eur J Nucl Med Mol Imaging] ed una simile detection rate rispetto al Ga-PSMA per le metastasi a distanza, sebbene superiore per quelle in loggia prostatica [Pernthaler 2019 Clin Nucl Med]

European Association of Urology guidelines 2019

N-staging prechirurgico

PET-TC con Colina

Bassa Sensibilità → non raggiunge accuratezza diagnostica clinicamente accettabile per la stadiazione della malattia linfonodale

EAU guidelines 2019

- **PSA dosabile dopo prostatectomia radicale**

6.2.6.6 Recommendations for the management of persistent PSA after radical prostatectomy

Recommendations	Strength rating
Offer a prostate-specific membrane antigen positron emission tomography (PSMA PET) scan to men with a persistent PSA > 0.2 ng/mL to exclude metastatic disease.	Weak
Treat men with no evidence of metastatic disease with salvage radiotherapy and additional hormonal therapy.	Weak

EAU guidelines 2019

Ripresa biochimica di malattia

6.3.4.4 Guidelines for imaging in patients with biochemical recurrence

Prostate-specific antigen (PSA) recurrence after radical prostatectomy	LE	Strength rating
Perform PSMA PET/CT if the PSA level is > 0.2 ng/mL and if the results will influence subsequent treatment decisions.	2b	Weak
In case PSMA PET/CT is not available, and the PSA level is ≥ 1 ng/mL, perform Fluciclovine PET/CT or Choline PET/CT imaging if the results will influence subsequent treatment decisions.		Weak
PSA recurrence after radiotherapy		
Perform prostate multiparametric magnetic resonance imaging to localise abnormal areas and guide biopsies in patients fit for local salvage therapy.	3	Strong
Perform PSMA PET/CT (if available) or fluciclovine PET/CT or choline PET/CT in patients fit for curative salvage treatment.	2b	Strong

Take home message

PSMA PET-TC:

- promettente e specifica per l'imaging del Ca prostatico
- come esame preliminare alla MRI multiparametrica per biopsia target in pz con precedenti biopsie negative
- ruolo potenziale in stadiazione nel Ca prostatico ad alto rischio (Se e Sp superiori rispetto all'imaging standard es CT, MRI e bone scan)
- detection rate elevata anche con bassi valori di PSA nella ripresa biochimica di malattia e per lesioni di piccole dimensioni
- possibilità di terapia mirata (theragnostic)

Diagnostic Accuracy of ^{68}Ga-PSMA-11 PET/MRI Compared with Multiparametric MRI in the Detection of Prostate Cancer

Robert M. Hicks, MD • Jeffry P. Simko, MD • Antonio C. Westphalen, MD, PhD • Hao G. Nguyen, MD, PhD • Kirsten L. Greene, MD, MS • Li Zhang, PhD • Peter R. Carroll, MD, MPH • Thomas A. Hope, MD

From the Department of Radiology and Biomedical Imaging (R.M.H., A.C.W., T.A.H.), Department of Anatomic Pathology (J.P.S.), Department of Urology (J.P.S., A.C.W., H.G.N., K.L.G., P.R.C.), and UCSF Helen Diller Family Comprehensive Cancer Center (A.C.W., L.Z., P.R.C., T.A.H.), University of California, San Francisco, 505 Parnassus Ave, M-391, San Francisco, CA 94143-0628. Received April 4, 2018; revision requested May 15; final revision received July 21; accepted July 31. **Address correspondence to** T.A.H. (e-mail: *thomas.hope@ucsf.edu*).

T.A.H. was supported by the Prostate Cancer Foundation (2017 Jonathan Kovler Young Investigator Award), the National Institutes of Health (grant R01CA212148), and GE Healthcare (research grant).

Conflicts of interest are listed at the end of this article.

See also the editorial by Civelek in this issue.

Radiology 2018; 289:730–737 • https://doi.org/10.1148/radiol.2018180788 • Content codes: GU MI

Purpose: To compare the diagnostic accuracy of gallium 68 (^{68}Ga)–labeled prostate-specific membrane antigen (PSMA)–11 PET/MRI with that of multiparametric MRI in the detection of prostate cancer.

Materials and Methods: The authors performed a retrospective study of men with biopsy-proven prostate cancer who underwent simultaneous ^{68}Ga-PSMA-11 PET/MRI before radical prostatectomy between December 2015 and June 2017. The reference standard was whole-mount pathologic examination. Readers were blinded to radiologic and pathologic findings. Tumor localization was based on 30 anatomic regions. Region-specific sensitivity and specificity were calculated for PET/MRI and multiparametric MRI by using raw stringent and alternative neighboring approaches. Maximum standardized uptake value (SUV_{max}) in the tumor and Prostate Imaging Reporting and Data System (PI-RADS) version 2 grade were compared with tumor Gleason score. Generalized estimating equations were used to estimate population-averaged sensitivity and specificity and to determine the association between tumor characteristics and SUV_{max} or PI-RADS score.

Results: Thirty-two men (median age, 68 years; interquartile range: 62–71 years) were imaged. The region-specific sensitivities of PET/MRI and multiparametric MRI were 74% (95% confidence interval [CI]: 70%, 77%) and 50% (95% CI: 45%, 0.54%), respectively, with the alternative neighboring approach ($P < .001$ for both) and 73% (95% CI: 68%, 79%) and 69% (95% CI: 62%, 75%), respectively, with the population-averaged generalized estimating equation ($P = .04$). Region-specific specificity of PET/MRI was similar to that of multiparametric MRI with the alternative neighboring approach (88% [95% CI: 85%, 91%] vs 90% [95% CI: 87%, 92%], $P = .99$) and in population-averaged estimates (70% [95% CI: 64%, 76%] vs 70% [95% CI: 64%, 75%], $P = .99$). SUV_{max} was associated with a Gleason score of 7 and higher (odds ratio: 1.71 [95% CI: 1.27, 2.31], $P < .001$).

Conclusion: The sensitivity of gallium 68–labeled prostate-specific membrane antigen–11 PET/MRI in the detection of prostate cancer is better than that of multiparametric MRI.

Table 3: Diagnostic Accuracy of ^{68}Ga-PSMA-11 PET and Multiparametric MRI

Parameter	^{68}Ga-PSMA-11 PET/MRI	MRI	*P* Value
Sensitivity (%)			
Raw stringent approach	67 (62, 71)	42 (37, 47)	<.001
Neighboring approach	74 (70, 77)	50 (45, 54)	<.001
GEE (population-averaged)	73 (68, 79)	69 (62, 75)	.04
Specificity (%)			
Raw stringent approach	71 (67, 75)	79 (76, 83)	<.001
Neighboring approach	88 (85, 91)	90 (87, 92)	.99
GEE (population-averaged)	70 (64, 76)	70 (64, 75)	.99
AUC at region level	0.94	0.81	.005
AUC based on GEE	0.78	0.76	.04

Note.—Numbers in parentheses are 95% confidence intervals. AUC = area under the receiver operating characteristic curve, ^{68}Ga = gallium 68, GEE = generalized estimating equation, PSMA = prostate-specific membrane antigen.

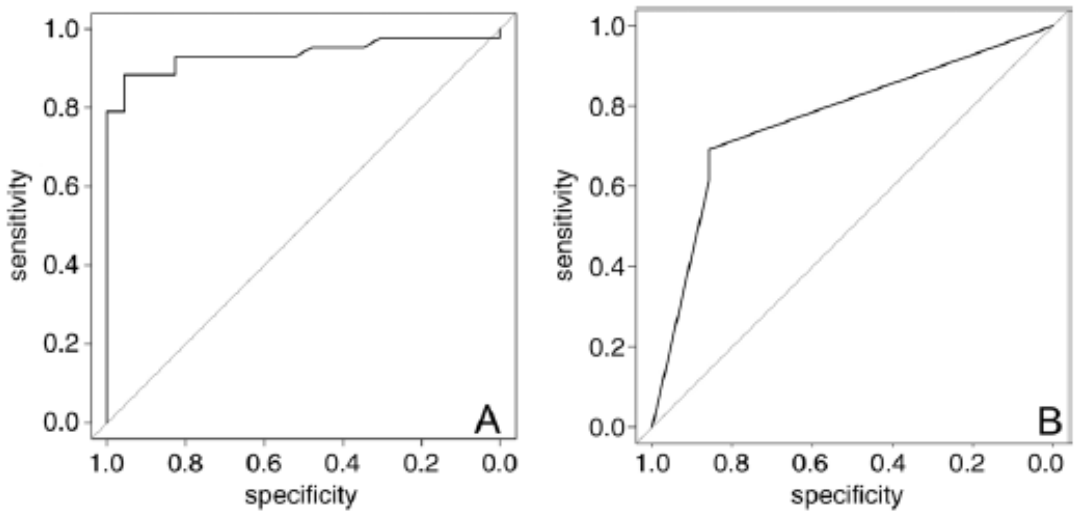


Figure 4: Receiver operating characteristic curves generated with generalized linear models of maximum standardized uptake value for, *A*, gallium 68–labeled prostate-specific membrane antigen PET/MRI and, *B*, Prostate Imaging Reporting and Data System score with multiparametric MRI. With generalized linear model estimate, the area under the receiver operating characteristic curve for PET/MRI was higher than that for multiparametric MRI ($P = .04$).

Original article

Nuclear Medicine Communications

Can SUVmax values of Ga-68-PSMA PET/CT scan predict the clinically significant prostate cancer?

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Purpose The intensity of prostate-specific membrane antigen (PSMA) expression increases as the tumor grade increases and the uptake of Ga-68-PSMA is higher in high-grade tumors. The aim of the present study was to evaluate the correlation of preoperative tracer uptake of primary tumor to Gleason Score in patients who underwent prostatectomy.

Patients and methods We retrospectively evaluated 141 patients who had Ga-68-PSMA positron emission tomography/computed tomography (PET/CT) imaging and who underwent prostatectomy. All patients had a diagnosis of prostate cancer on the basis of 10–24 cores transrectal ultrasound-guided biopsy (TRUS-Bx). Histological assessment was performed according to the New Contemporary Prostate Cancer Grading System. All patients had a prostate-specific antigen (PSA) level measurement within maximum of 28 days before Ga-68-PSMA PET/CT. Region of interests were drawn manually around the prostate gland, avoiding the bladder activity, to calculate the maximum standardized uptake values (SUVmax) values.

Results The median PSA values for all patients were 10.0 ng/ml. PSA values for low-risk patients were significantly lower than those of high-risk patients ($P < 0.001$). There were 41.1% upgrades and 7.8% downgrades following prostatectomy in terms of Grade Groups. According to the final pathology reports, 21% ($n = 16$) of patients moved from a low-risk level (grade groups 1 + 2) to a high-risk level (grade groups 3 + 4 + 5). The median SUVmax value was 8.8, ranging from 2.1 to 62.4. There was a strong correlation between SUVmax values and grade groups (Pearson $\rho = 0.66$) ($P < 0.001$). The mean SUVmax values of high-risk patients were significantly higher than those of low-risk patients (18.9 ± 12.1 vs. 7.16 ± 6.2, respectively) ($P < 0.001$). Receiver operation characteristic curve analysis of SUVmax at the cut-off value of 9.1 showed a high sensitivity (78%) and specificity (81%) for detection of high risk disease.

Conclusion SUVmax values correlate significantly with the grade groups of the primary tumor. The intraprostatic accumulation sites may predict clinically significant cancer and potentially serve as a target for biopsy sampling in conjunction with mpMRI in selected patients. *Nucl Med Commun* 40:86–91

Nuclear Medicine Communications 2019, 40:86–91

Keywords: Gallium-68, Gleason scoring system, guided prostate biopsy, prostate cancer, Prostate Cancer Grading System, prostate-specific membrane antigen, Positron emission tomography/computed tomography

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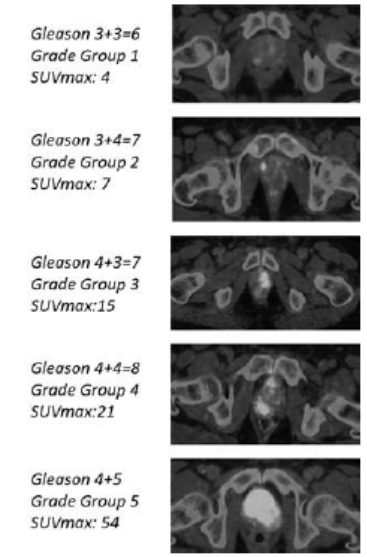
Received 16 May 2018 **Revised** 19 November 2018
Accepted 17 October 2018

Table 1 Patient data of age, prostate-specific antigen level, and SUVmax values according to grade groups obtained from biopsy results and definitive pathology results after prostatectomy

	Biopsy				Definitive pathology				
	n	Age	PSA	SUVmax	*n*	PSA	SUVmax	Upgrade [*n* (%)]	Downgrade [*n* (%)]
GG 1	37	65	8.4	6.46	10	9.0	4.77	28 (75.7)	0
GG 2	41	64	8.3	6.02	58	7.2	5.79	11 (26.8)	1 (2.4)
GG 3	31	64	16.0	15.58	28	11.5	10.84	10 (32.3)	5 (16.1)
GG 4	19	64	9.4	14.20	18	15.8	11.10	9 (47.4)	2 (10.5)
GG 5	13	67	13.0	20.48	27	13.1	20.48	0	3 (23)
Total	141	65	10.0	8.81				58 (41.1)	11 (7.8)

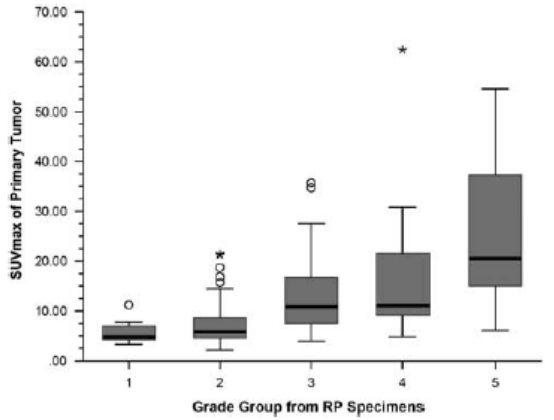
Age (years), PSA (prostate-specific antigen) levels (in ng/ml), and SUVmax (maximum standardized uptake values) are expressed as median values.
Grade group (GG) 1 = Gleason score less than or equal to 6, grade group 2 = Gleason score 3 + 4 = 7, grade group 3 = Gleason score 4 + 3 = 7, grade group 4 = Gleason score 8, grade group 5 = Gleason scores 9 and 10.

Fig. 1



Representative Ga-68-PSMA PET/CT fusion images for each grade group. Maximum standardized uptake values (SUVmax). PSMA PET/CT, prostate-specific membrane antigen positron emission tomography/computed tomography.

Fig. 2



Box plot display of SUVmax values according to grade groups obtained from pathology reports after radical prostatectomy (RP). Pearson Pearson ρ 0.66 ($P < 0.001$).

groups, which was significant ($P < 0.001$). There were 1 level upgrade of grade groups in 43 patients, 2 level upgrade in 12 patients, 3 level upgrade in two patients, and 4 level

Clin Nucl Med. 2019 Jun;44(6):431-438.

Pretherapeutic 68Ga-PSMA-617 PET May Indicate the Dosimetry of 177Lu-PSMA-617 and 177Lu-EB-PSMA-617 in Main Organs and Tumor Lesions.

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AIM:
Combined Ga-PSMA-617 PET imaging and Lu-PSMA-617 therapy is a precise targeted theranostic approach for patients with metastatic castration-resistant prostate cancer (mCRPC). The purpose of this study was to determine whether pretherapeutic standard uptake value (SUV) in Ga-PSMA-617 PET could indicate the effective dose in the main organs and absorbed dose in tumor lesions.

METHODS:
After institutional review board approval and informed consent, 9 patients with mCRPC were recruited and underwent Ga-PSMA-617 PET/CT scans. Five patients received Lu-PSMA-617 (1.30-1.42 GBq, 35-38.4 mCi) and then underwent serial whole-body planar imaging and SPECT/CT imaging of both thoracic and abdominal regions at 0.5-, 2-, 24-, 48-, and 72-hour time points. The other 4 patients received Lu-EB-PSMA-617 (0.80-1.1 GBq, 21.5-30 mCi) and then underwent the same imaging procedures at 2-, 24-, 72-, 120-, and 168-hour time points. The effective dose in the main organs and the absorbed dose in tumor lesions were calculated. Detailed correlations between the pretherapeutic SUV in Ga-PSMA-617 PET and effective dose in the main organs as well as absorbed dose in the tumor lesions were analyzed.

RESULTS:
SUV of Ga-PSMA-617 PET was moderately correlated with effective dose in main organs ($r = 0.610$ for Lu-PSMA-617, $r = 0.743$ for Lu-EB-PSMA-617, both $P < 0.001$). SUV of tumor lesions in Ga-PSMA-617 PET had high correlation with those in Lu-PSMA-617 ($r = 0.915$, $P < 0.001$) and moderate correlation with those in Lu-EB-PSMA-617 ($r = 0.611$, $P = 0.002$).

CONCLUSIONS:
Pretherapeutic Ga-PSMA-617 PET may indicate the dosimetry of Lu-PSMA-617 and Lu-EB-PSMA-617. Both the effective dose in main organs and absorbed dose in tumor lesions correlate with SUV of Ga-PSMA-617 PET. This relationship may help select appropriate candidates for peptide receptor radionuclide therapy. Further investigations of larger cohorts are needed to confirm these initial findings.

JAMA Oncology | Original Investigation

Assessment of ^{68}Ga-PSMA-11 PET Accuracy in Localizing Recurrent Prostate Cancer

A Prospective Single-Arm Clinical Trial

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JAMA Oncol. 2019;5(6):856-863. doi:10.1001/jamaoncol.2019.0096
Published online March 28, 2019.

Supplemental content

IMPORTANCE In retrospective studies, ^{68}Ga-PSMA-11 positron emission tomographic (PET) imaging improves detection of biochemically recurrent prostate cancer compared with conventional imaging.

OBJECTIVE To assess ^{68}Ga-PSMA-11 PET accuracy in a prospective multicenter trial.

DESIGN, SETTING, AND PARTICIPANTS In this single-arm prospective trial conducted at University of California, San Francisco and University of California, Los Angeles, 635 patients with biochemically recurrent prostate cancer after prostatectomy (n = 262, 41%), radiation therapy (n = 169, 27%), or both (n = 204, 32%) underwent ^{68}Ga-PSMA-11 PET. Presence of prostate cancer was recorded by 3 blinded readers on a per-patient and per-region base. Lesions were validated by histopathologic analysis and a composite reference standard.

MAIN OUTCOMES AND MEASURES Endpoints were positive predictive value (PPV), detection rate, interreader reproducibility, and safety.

RESULTS A total of 635 men were enrolled with a median age of 69 years (range, 44-95 years). On a per-patient basis, PPV was 0.84 (95% CI, 0.75-0.90) by histopathologic validation (primary endpoint, n = 87) and 0.92 (95% CI, 0.88-0.95) by the composite reference standard (n = 217). ^{68}Ga-PSMA-11 PET localized recurrent prostate cancer in 475 of 635 (75%) patients; detection rates significantly increased with prostate-specific antigen (PSA): 38% for <0.5 ng/mL (n = 136), 57% for 0.5 to <1.0 ng/mL (n = 79), 84% for 1.0 to <2.0 ng/mL (n = 89), 86% for 2.0 to <5.0 ng/mL (n = 158), and 97% for ≥5.0 ng/mL (n = 173, $P < .001$). Interreader reproducibility was substantial (Fleiss κ, 0.65-0.78). There were no serious adverse events associated with ^{68}Ga-PSMA-11 administration. PET-directed focal therapy alone led to a PSA drop of 50% or more in 31 of 39 (80%) patients.

CONCLUSIONS AND RELEVANCE Using blinded reads and independent lesion validation, we establish high PPV for ^{68}Ga-PSMA-11 PET, detection rate and interreader agreement for localization of recurrent prostate cancer.

RESULTS A total of 635 men were enrolled with a median age of 69 years (range, 44-95 years). On a per-patient basis, PPV was 0.84 (95% CI, 0.75-0.90) by histopathologic validation (primary endpoint, n = 87) and 0.92 (95% CI, 0.88-0.95) by the composite reference standard (n = 217). ^{68}Ga-PSMA-11 PET localized recurrent prostate cancer in 475 of 635 (75%) patients; detection rates significantly increased with prostate-specific antigen (PSA): 38% for <0.5 ng/mL (n = 136), 57% for 0.5 to <1.0 ng/mL (n = 79), 84% for 1.0 to <2.0 ng/mL (n = 89), 86% for 2.0 to <5.0 ng/mL (n = 158), and 97% for ≥5.0 ng/mL (n = 173, $P < .001$). Interreader reproducibility was substantial (Fleiss κ, 0.65-0.78). There were no serious adverse events associated with ^{68}Ga-PSMA-11 administration. PET-directed focal therapy alone led to a PSA drop of 50% or more in 31 of 39 (80%) patients.

Detection Efficacy of ^{18}F-PSMA-1007 PET/CT in 251 Patients with Biochemical Recurrence of Prostate Cancer After Radical Prostatectomy

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Prostate-specific membrane antigen (PSMA)–targeted PET imaging recently emerged as a new method for the staging and restaging of prostate cancer. Most published studies investigated the diagnostic potential of ^{68}Ga-labeled PSMA agents that are excreted renally. ^{18}F-PSMA-1007 is a novel PSMA ligand that has excellent preclinical characteristics and that is only minimally excreted by the urinary tract, a potential advantage for pelvic imaging. The aim of this study was to investigate the diagnostic efficacy of ^{18}F-PSMA-1007 for biochemical recurrence (BCR) after radical prostatectomy. **Methods:** From 3 academic centers, 251 patients with BCR after radical prostatectomy were evaluated in a retrospective analysis. Patients who had received second-line androgen deprivation therapy (ADT) or chemotherapy were excluded, but prior first-line ADT exposure was allowed. The median prostate-specific antigen (PSA) level was 1.2 ng/mL (range, 0.2–228 ng/mL). All patients underwent PSMA PET/CT at 92 ± 26 min after injection of 301 ± 46 MBq of ^{18}F-PSMA-1007. The rate of detection of presumed recurrence sites was correlated with the PSA level and original primary Gleason score. A comparison to a subset of patients treated previously with ADT was undertaken. **Results:** Of the 251 patients, 204 (81.3%) had evidence of recurrence on ^{18}F-PSMA-1007 PET/CT. The detection rates were 94.0% (79/84), 90.9% (50/55), 74.5% (35/47), and 61.5% (40/65) for PSA levels of greater than or equal to 2, 1 to less than 2, 0.5 to less than 1, and 0.2 to less than 0.5 ng/mL, respectively. ^{18}F-PSMA-1007 PET/CT revealed local recurrence in 24.7% of patients (n = 62). Lymph node metastases were present in the pelvis in 40.6% of patients (n = 102), in the retroperitoneum in 19.5% of patients (n = 49), and in supradiaphragmatic locations in 12.0% of patients (n = 30). Bone and visceral metastases were detected in 40.2% of patients (n = 101) and in 3.6% of patients (n = 9), respectively. In tumors with higher Gleason scores (≤7 vs. ≥8), detection efficacy trended higher (76.3% vs. 86.7%) but was not statistically significant (P = 0.32). However, detection efficacy was higher in patients who had received ADT (91.7% vs. 78.0%) within 6 mo before imaging (P = 0.0179). **Conclusion:** ^{18}F-PSMA-1007 PET/CT offers high detection rates for BCR after radical prostatectomy that are comparable to or better than those published for ^{68}Ga-labeled PSMA ligands.

Key Words: ^{18}F-PSMA-1007; PET/CT; hybrid imaging; prostate cancer; biochemical recurrence

J Nucl Med 2019; 60:362–368
DOI: 10.2967/jnumed.118.212233

Biochemical recurrence (BCR) represents a major concern for prostate cancer patients who have undergone primary prostatectomy. The ability to localize sites of recurrent prostate cancer is important for directing salvage therapy with curative intent. At present, only conventional imaging, such as whole-body bone scanning and cross-sectional abdominopelvic contrast-enhanced CT imaging or enhanced MRI, is recommended for detecting recurrence; however, these modalities have very limited sensitivity for recurrent disease (*1*).

The recent introduction of ^{68}Ga-PSMA-11 improved prostate cancer detection in the BCR setting. Some form of the ^{68}Ga-labeled prostate-specific membrane antigen (PSMA) ligand tracer has been used for more than 3,000 patients worldwide (*2–6*). The results have surpassed those obtained using PET/CT with ^{18}F-choline, formerly considered the best available PET agent for prostate cancer (*7,8*). Most impressive has been the ability of ^{68}Ga-PSMA PET to detect recurrent dis-

TABLE 2
^{18}F-PSMA-1007 PET/CT Detection of Different Regions Involved by Recurrent Prostate Cancer

Region	No. of patients	Percentage of patients
Local recurrence	62	24.7
Lymph node metastases		
Pelvic	102	40.6
Retroperitoneal	49	19.5
Supradiaphragmatic	30	12.0
Bone metastases	101	40.2
Other (lung, liver) metastases	9	3.6

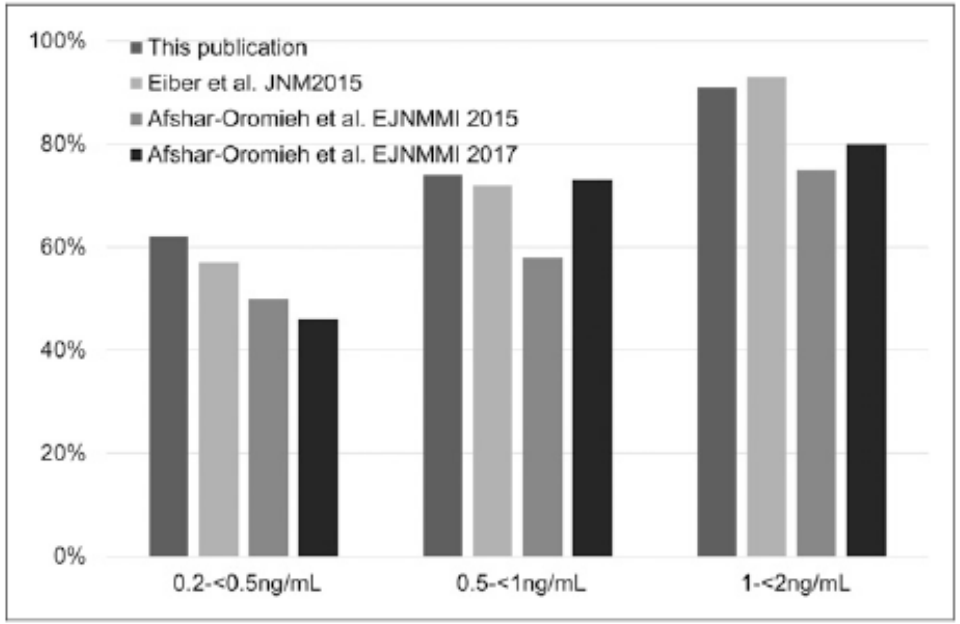

FIGURE 5. Comparison of rates of detection for ^{18}F-PSMA-1007 and ^{68}Ga-PSMA-11 derived from different studies.

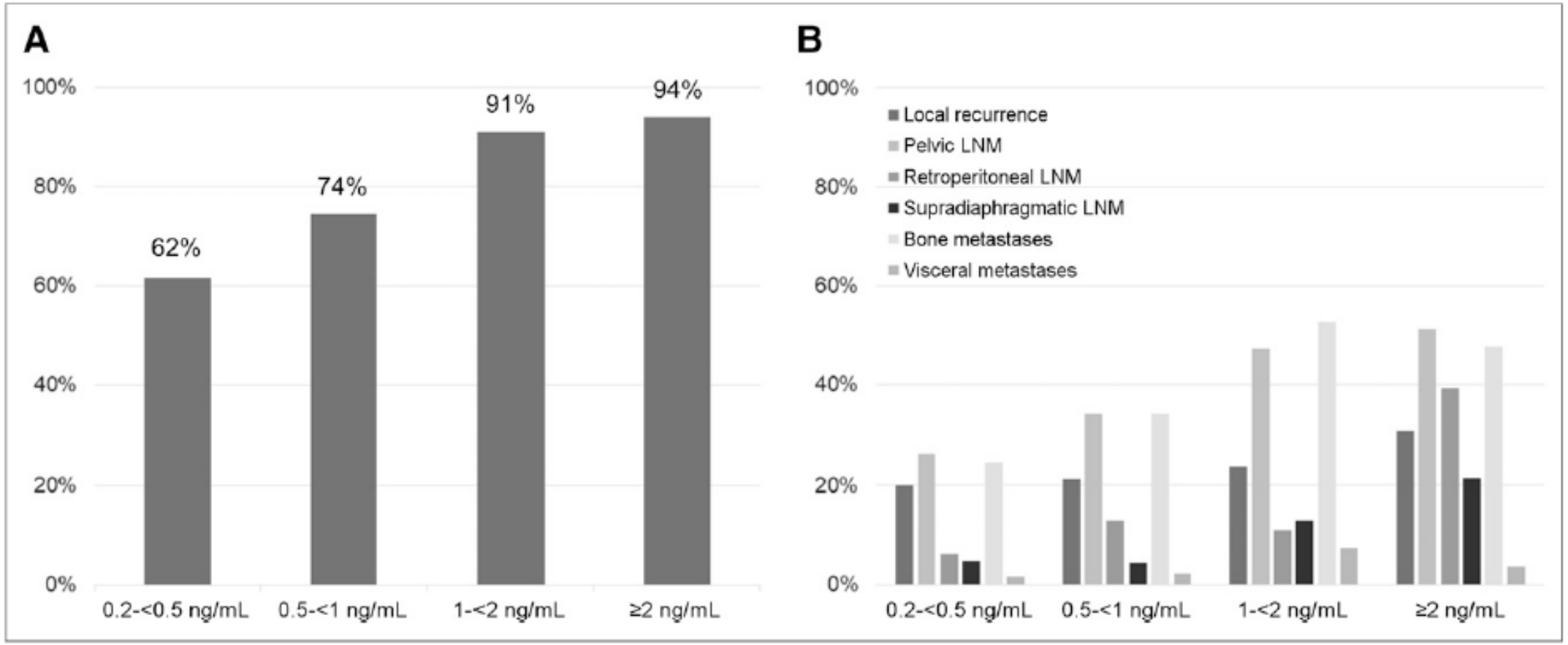

FIGURE 1. Overall rate of detection for ^{18}F-PSMA-1007 PET/CT (A) and relative number of lesions grouped by different regions (B) in relation to PSA levels. LNM = lymph node metastases.

J Nucl Med 2019; 60:362–368

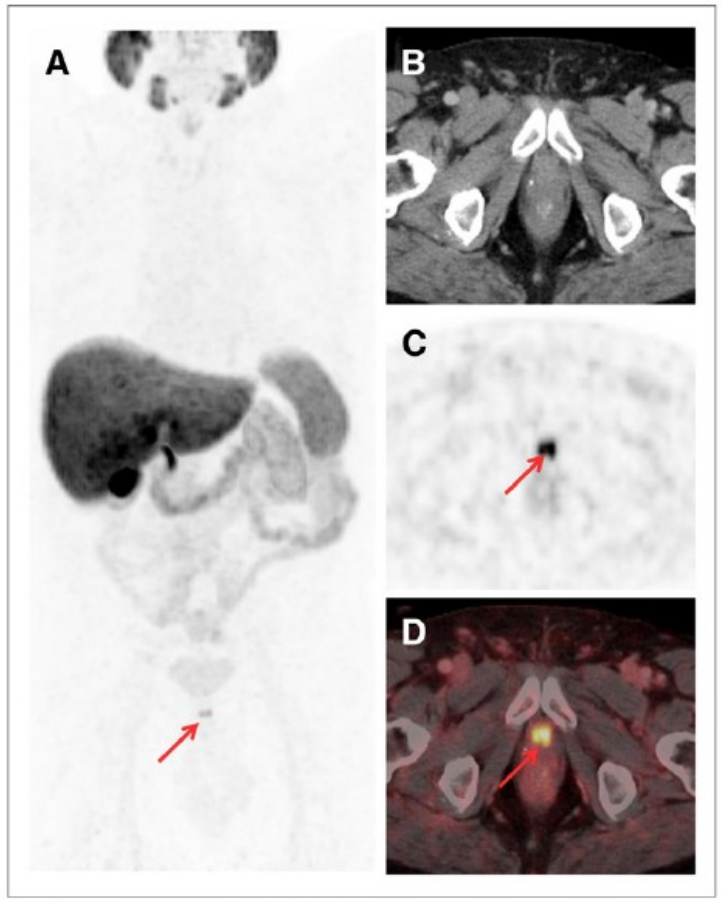

FIGURE 3. Images from 64-y-old patient after radical prostatectomy (August 2012; Gleason score of 9; pT3b; pN0) and with PSA level rising to 3.9 ng/mL (October 2017). (A) Maximum-intensity projection of ^{18}F-PSMA-1007 PET shows intense tracer-associated uptake in lesion (arrow) below bladder. (C and D) It could be localized (arrows) in region of urethral anastomosis using transaxial PET (C) and fused PET/CT (D) images. (B) Corresponding CT image. Postimaging salvage radiation to prostatic fossa was performed in combination with single injection of gonadotropin-releasing hormone analog in October 2017 and resulted in drop in PSA level to below detection threshold (<0.07 ng/mL; last measurement in February 2018).

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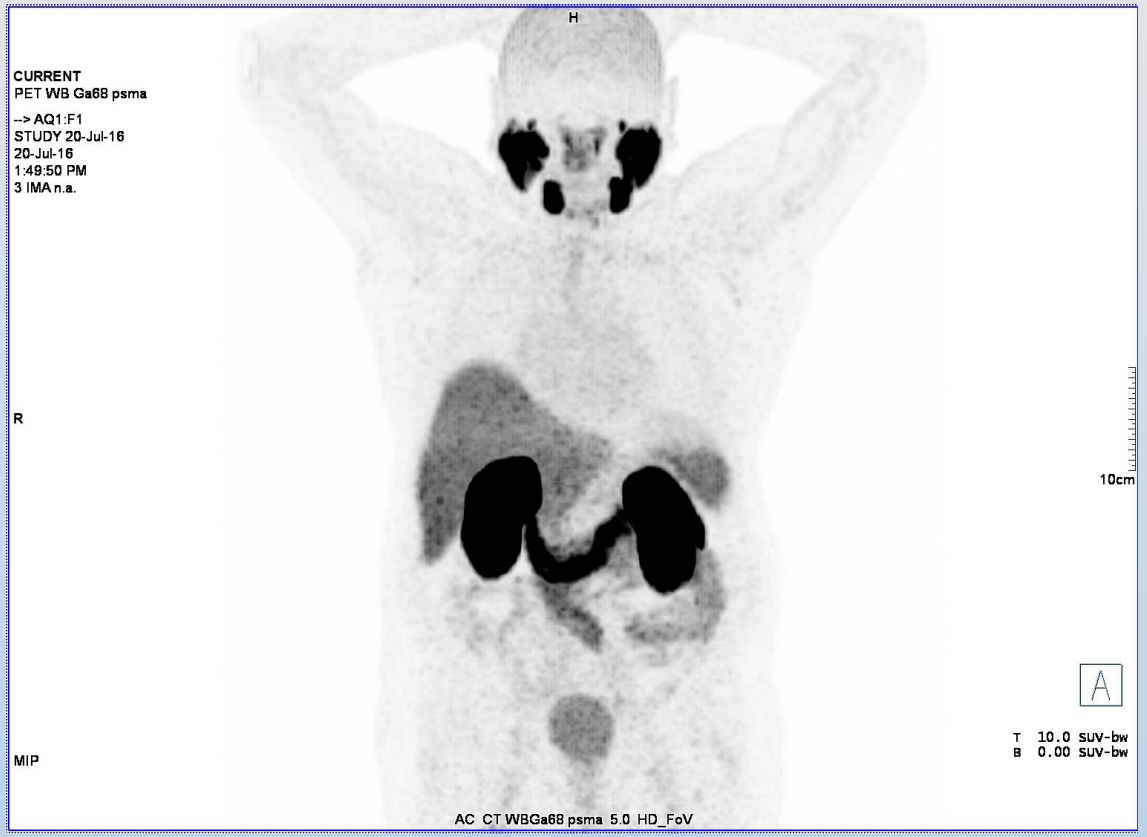


Biodistribuzione esocrina del tracciante

IRCCS Istituto di Ricovero e Cura a Carattere Scientifico
Sacro Cuore – Don Calabria
Ospedale Classificato e Presidio Ospedaliero Accreditato - Regione Veneto

Titolo dello studio:

Interventional two arms open-label study for evaluating the diagnostic performance of PET PSMA in patients affected by biochemical recurrent prostate cancer

Codice protocollo: PSMA-2018

Versione e data del protocollo: Versione n. 1.~~6~~5 del ~~16.07~~02.10.2019

Eudract number: 2018-003652-21

Sperimentatore Principale: Dr. Matteo Salgarello

Unità Operativa: Medicina Nucleare

Promotore: IRCCS Sacro Cuore Don Calabria di Negrar (VR)

Responsabile del monitoraggio: Dr.ssa Elvia Malo – Unità per la Ricerca Clinica

Supporto metodologico e statistico: Dr.ssa Elvia Malo – Unità per la Ricerca Clinica
Dr. Ronaldo Silva – Unità per la Ricerca Clinica

11.1 Subgroup A: 0.2 to 0.5 PSA ng/mL

18F-Choline	18F-PSMA (actual value)	18F-PSMA (Superiority margin)	N1=N2	N	N + dropout
.4	.8	.2	85	170	178

11.2 Subgroup ~~A~~B: 0.51 to 2 PSA ng/mL

18F-Choline	18F-PSMA	18F-PSMA	N1=N2	N	N + dropout

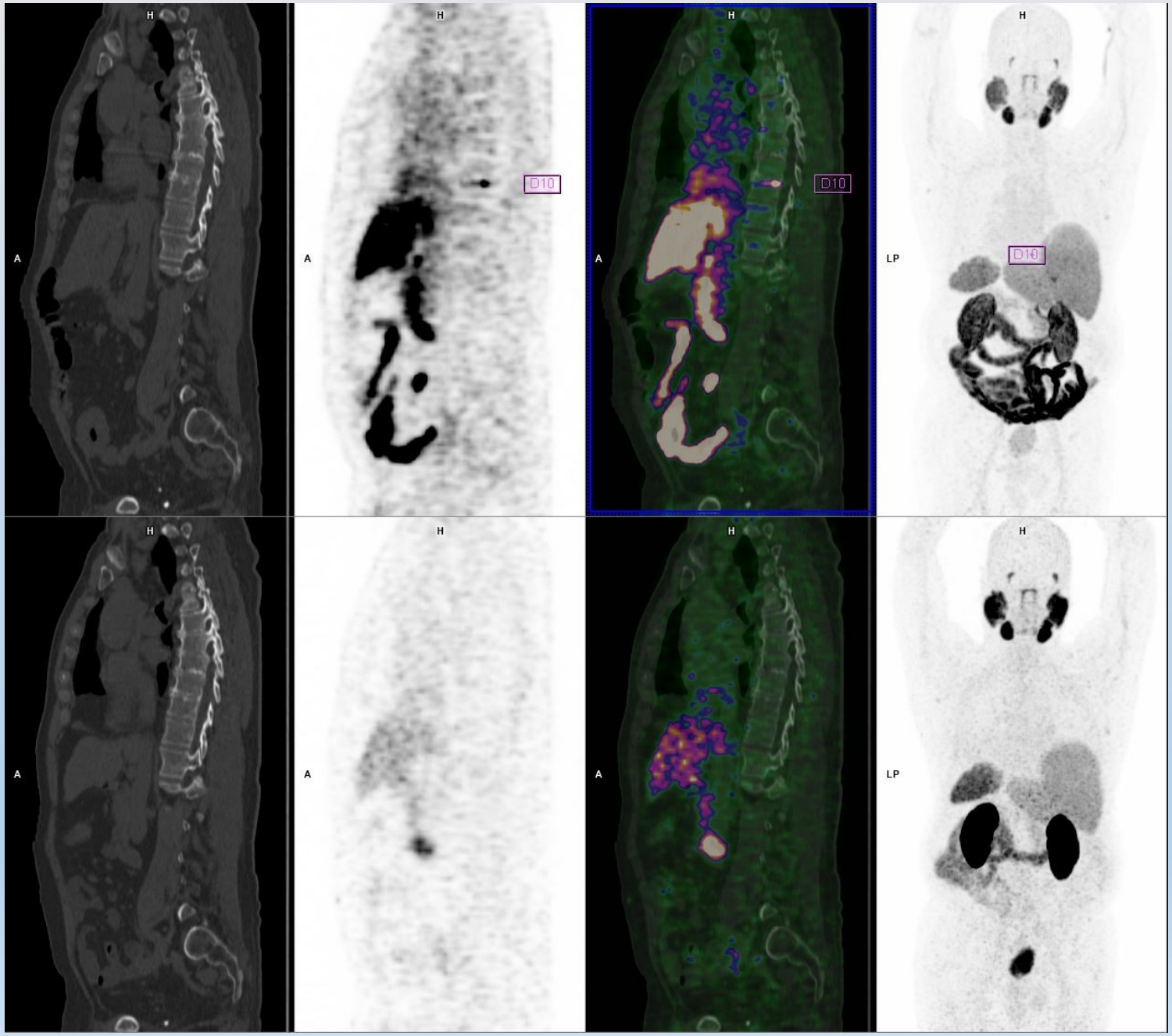
	(actual value)	(Superiority margin)			
.6	0.95	.2	99	198	208

11.3 Subgroup ~~A~~C: > 2 PSA ng/mL

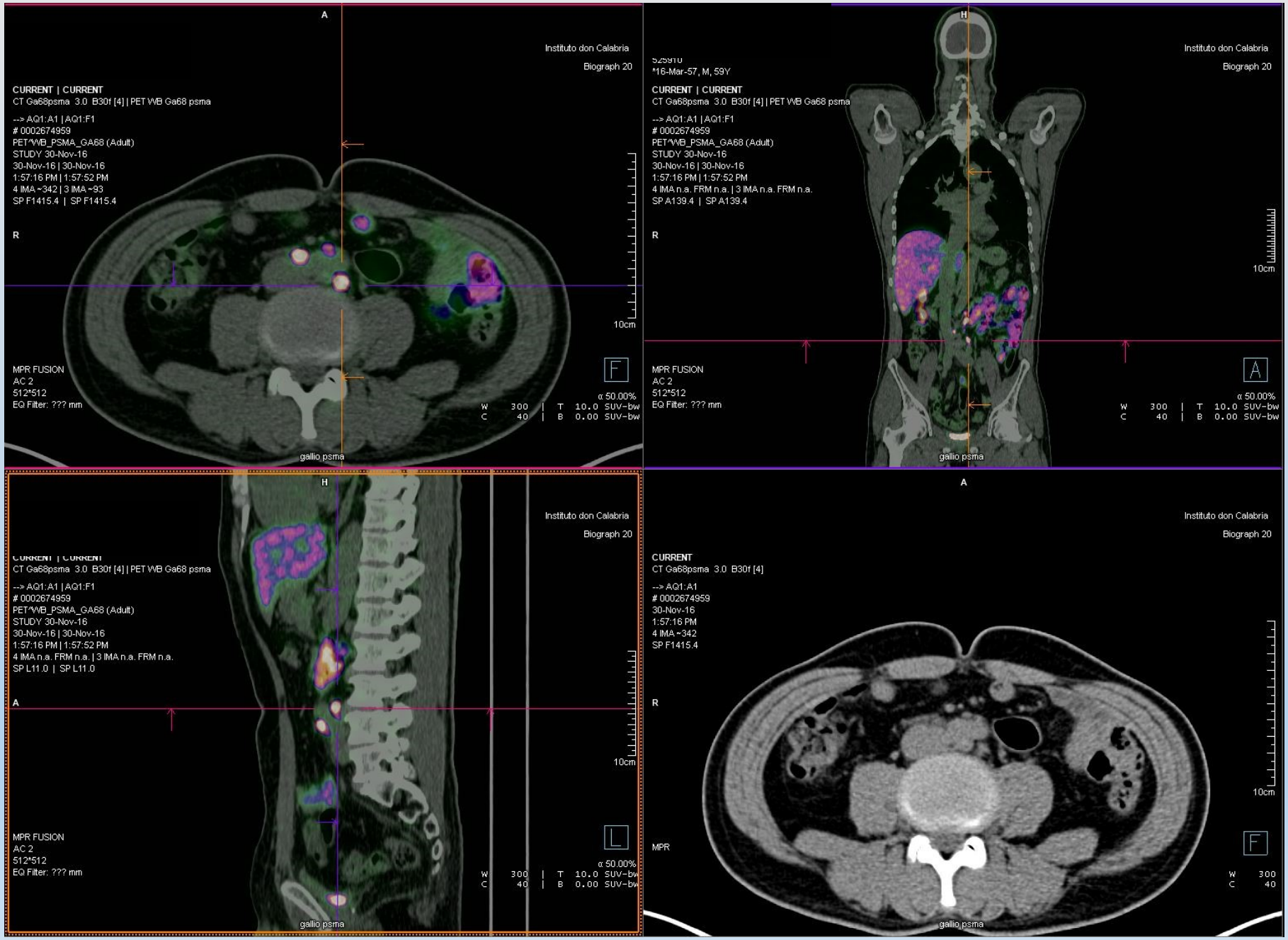
18F-Choline	18F-PSMA (actual value)	18F-PSMA (Superiority margin)	N1=N2	N	N + dropout
.75	.98	.15	241	482	508

Considering the sample size of the three subgroups under study, a total of 894 patients will be enrolled.

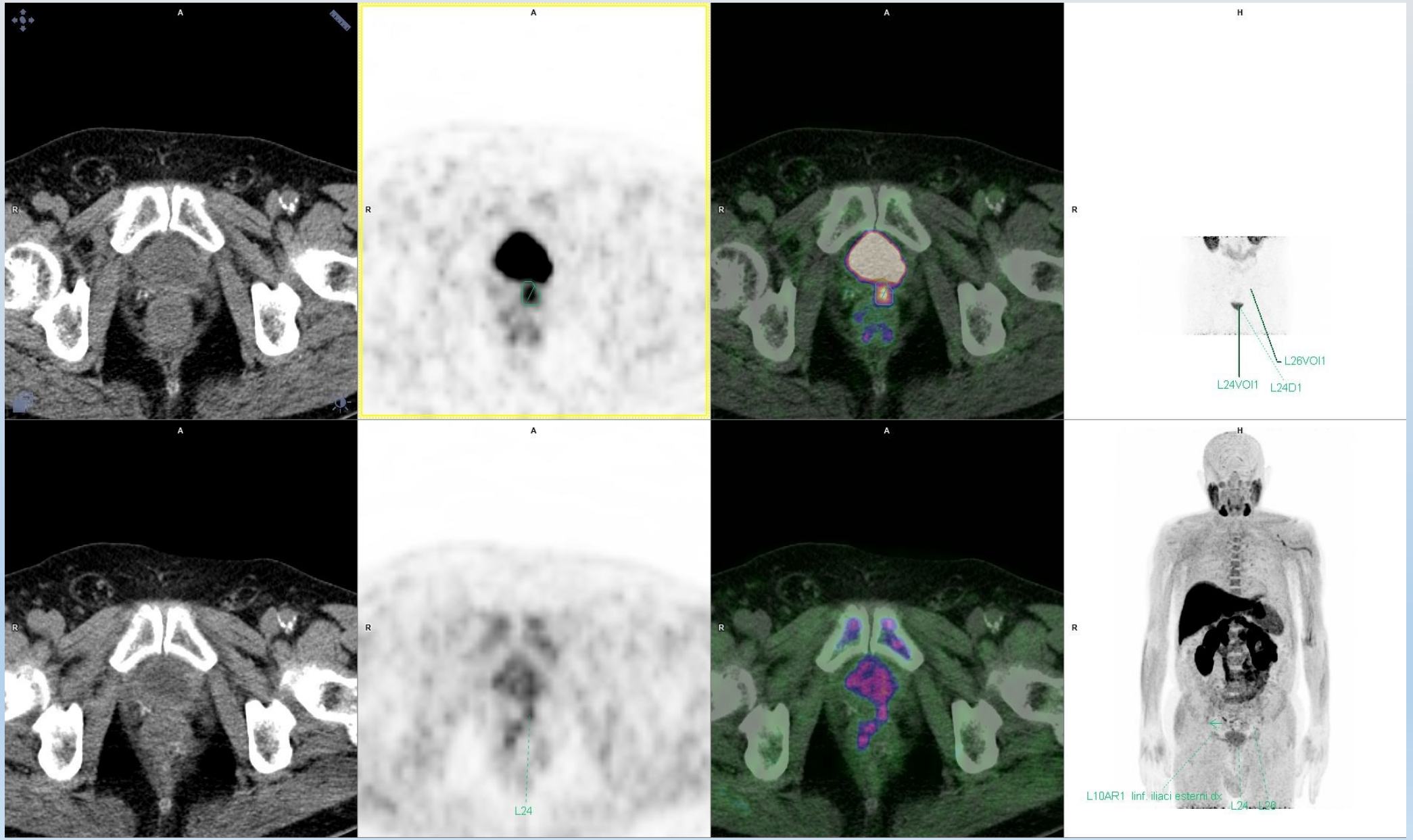
F-18 PSMA vs 68GaPSMA



F-18 PSMA linfonodi millimetrici



F-18 PSMA recidiva in loggia



Negrar Imaging/Terapia

11C-Choline 18F-Choline	Ga68-Dotatoc per lo studio della differenziazione neuroendocrina	Radio 223	18F-FACBC	F18-PSMA	Ittrio-Lutezio-PSMA terapia
SI	SI	SI per routine clinica	SI? Comitato etico GE trial farmacopea	Comitato etico (2019)	Comitato etico 2020? Fase III