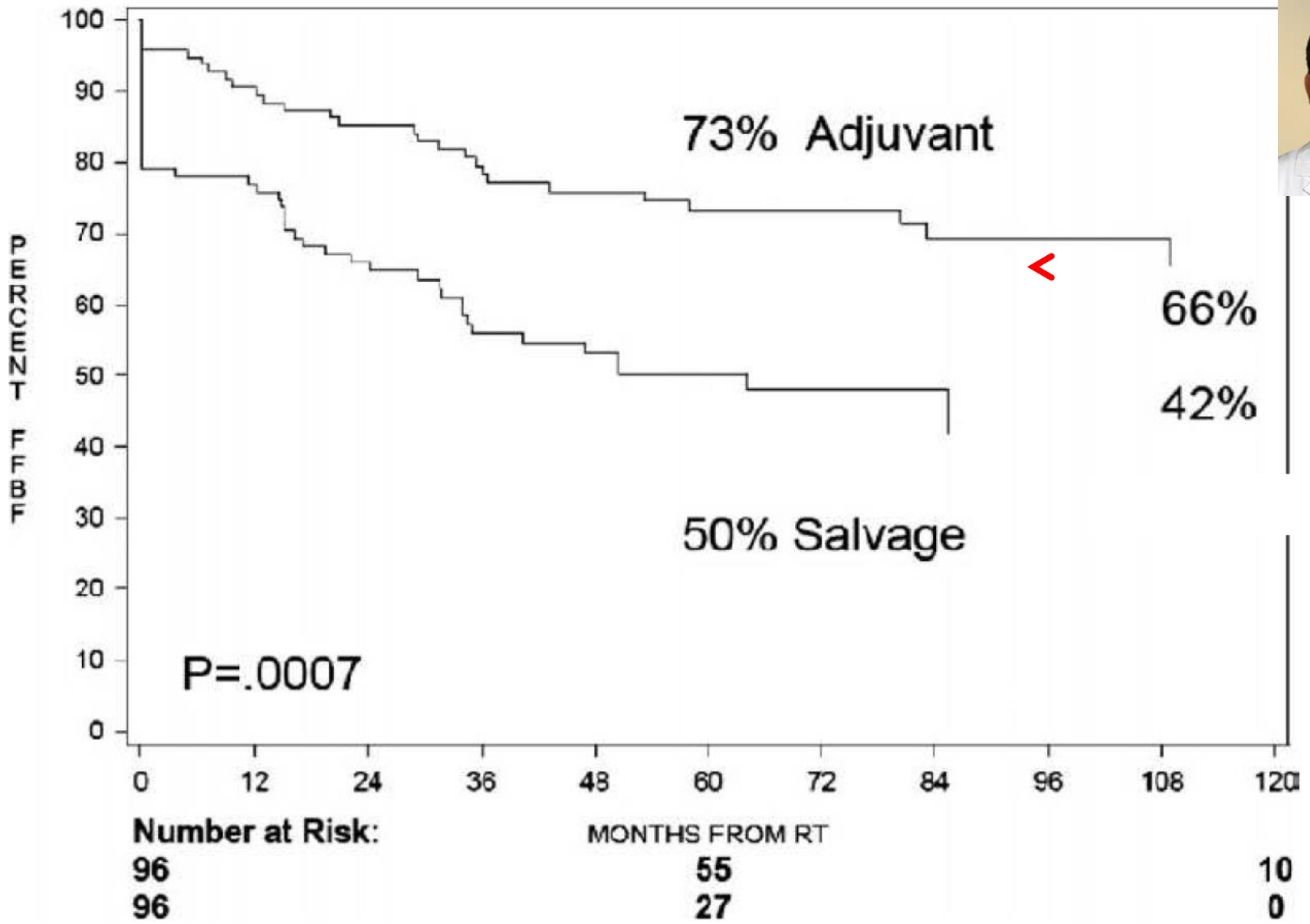




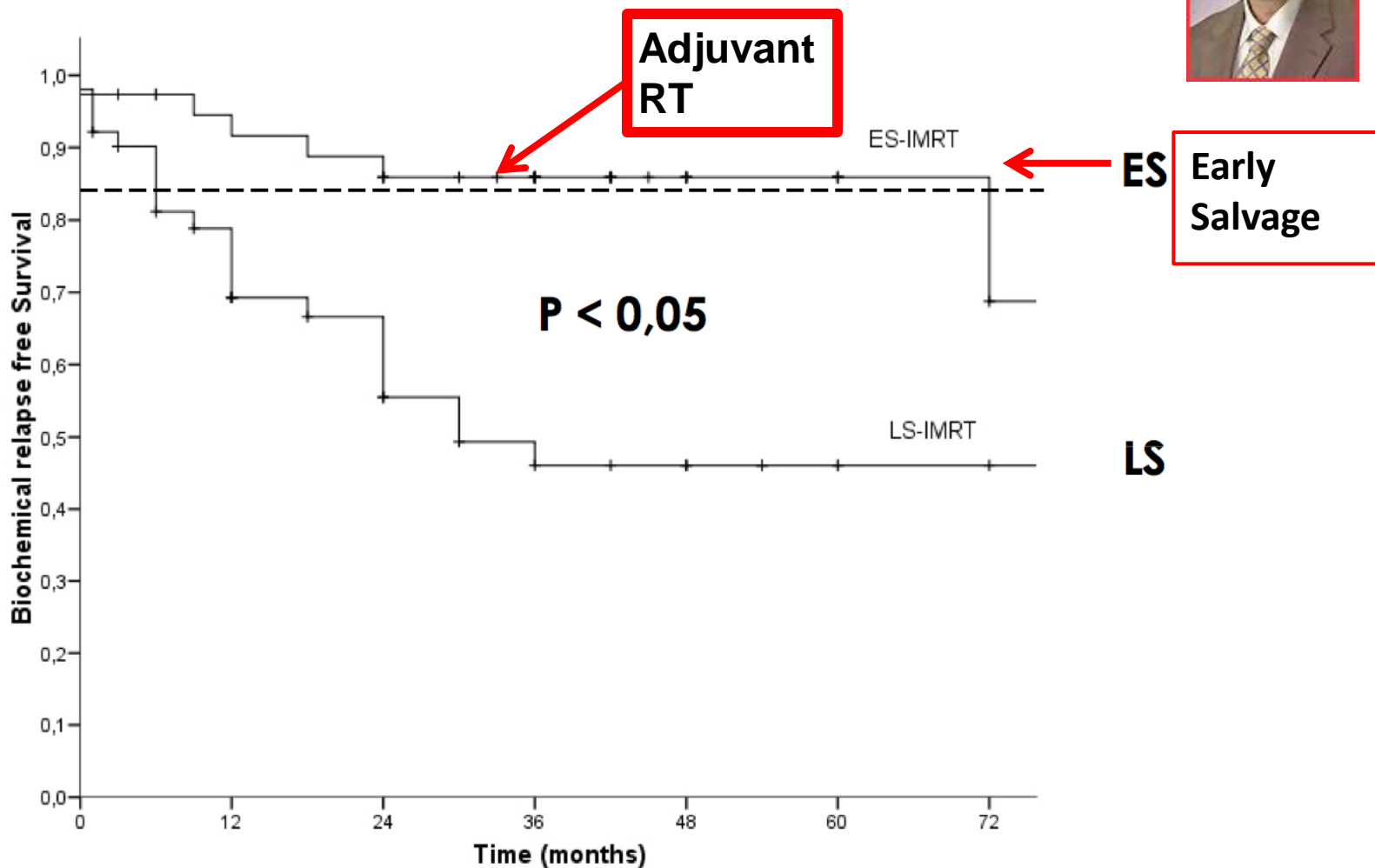
^{68}Ga -PSMA PET/CT: A NEW ERA FOR RADIATION ONCOLOGISTS and UROLOGISTS

FERNANDO MUNOZ

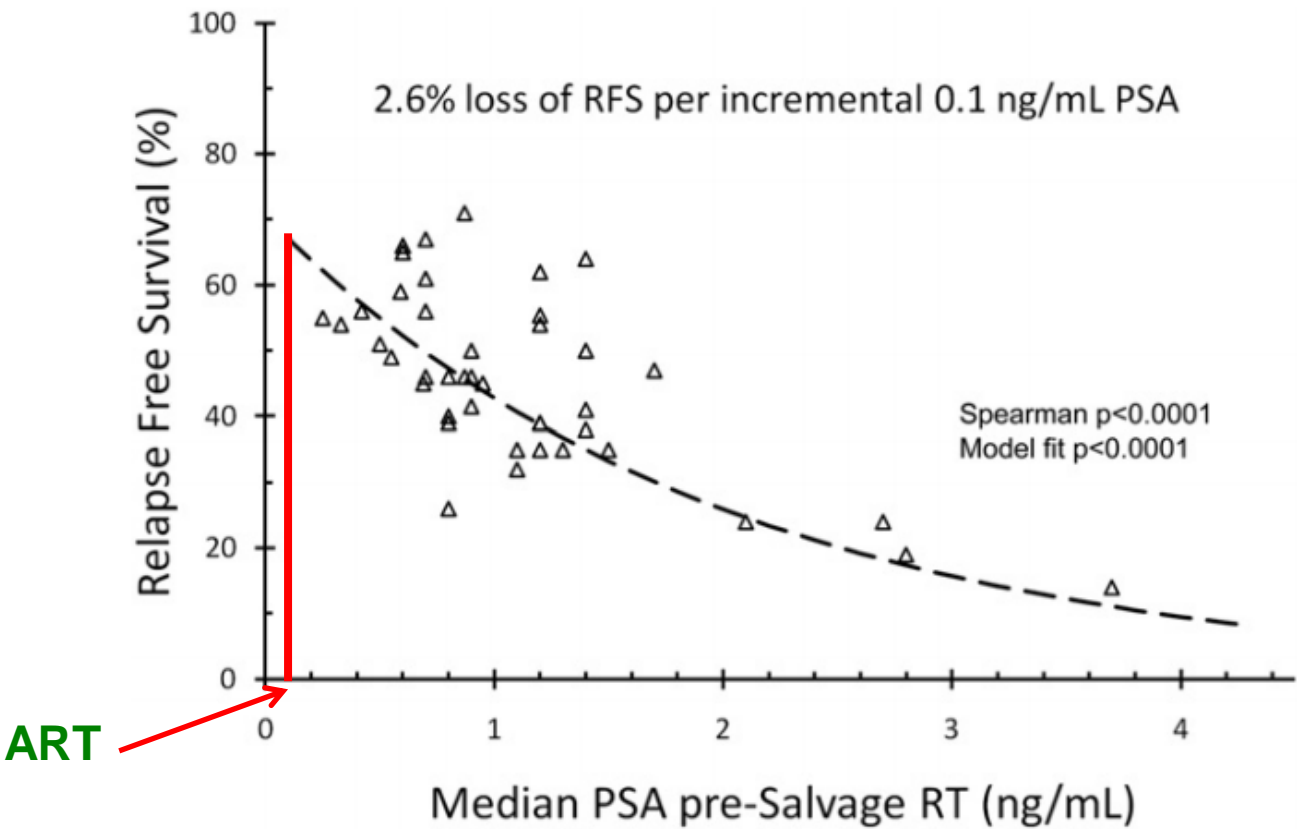
**Head of RADIATION ONCOLOGY
TomoTherapy Center
Ospedale di Aosta**



Is salvage RT as efficient as immediate adjuvant RT?

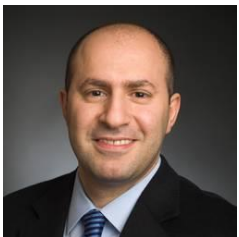


- Start of eSRT at the lowest PSA level: >0.05 ng/mL (ultrasensitive)



DETECTION OF RECURRENT DISEASE

- Detect recurrence site is important:
 - Establish correct treatment:
 - Localized vs Systemic (*clinic criteria unuseful*)
- Coventional imaging techniques (BS, CT scan, MR,US)
 - Should be able to detect the site of recurrence, but...
 - Not sensitive enough for low PSA levels
 - Show positive finding in < 10%:
 - Not recomended in Guidelines
 - Only if PSA levels are > 20 ng/ml o PSA velocity is > 2 ng/ml



Choueri et al. J Urol, 2008

DETECTION OF RECURRENT DISEASE

- Conventional imaging techniques:

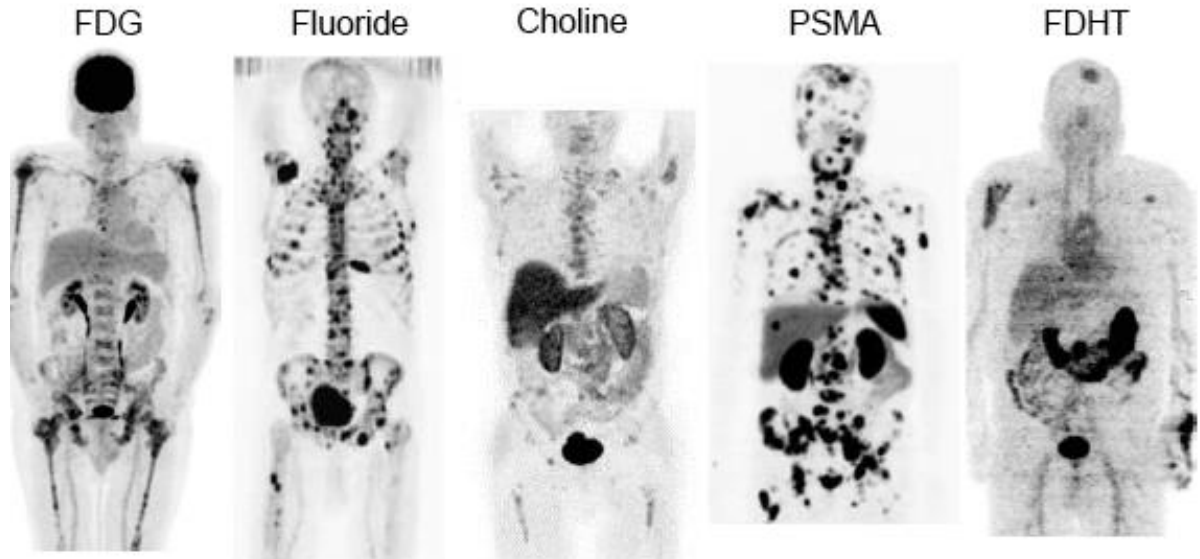
- US
- CT
- MRI
- BS



Limitation at low PSA levels and SS e SP

- PET/CT? → Molecular targets

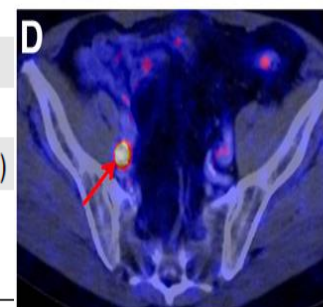
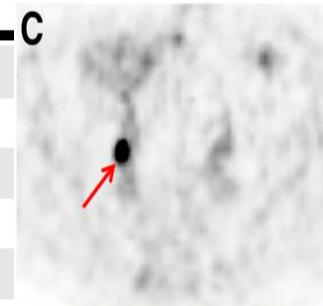
- FDG
- Choline
- Acetate
- PSMA
- ...



PSMA COMPARING CT

Region/combination of regions	No. of patients with positive findings exclusively demonstrated in ⁶⁸ Ga-PSMA		No. of patients with additional involved regions exclusively demonstrated in ⁶⁸ Ga-PSMA	
	PET	CT	PET	CT
LR only	18		11	
LN metastases only	31	1	17	2
Bone metastases only	9	1	24	7
LR + LN metastases	7		2	
LR + bone metastases	6		1	
LN + bone metastases	4		5	
LR + LN + bone metastases	1			
Other (e.g., lung, liver metastases)	5	1	1	17
Total	81 (32.7%)	3 (1.2%)	61 (24.6%)	17 (6.9%)

LR = local recurrence; LN = lymph node.





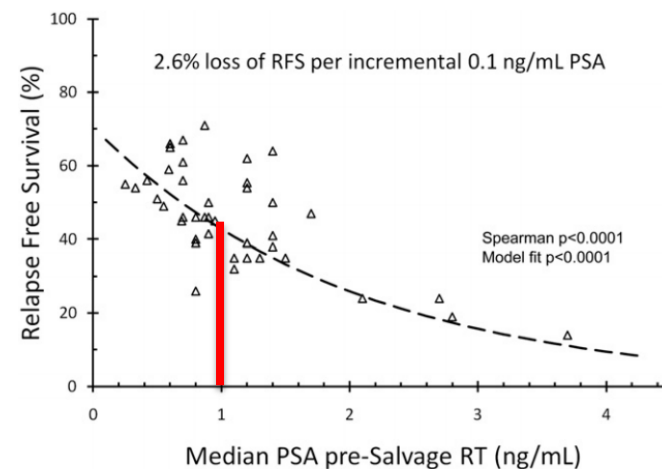
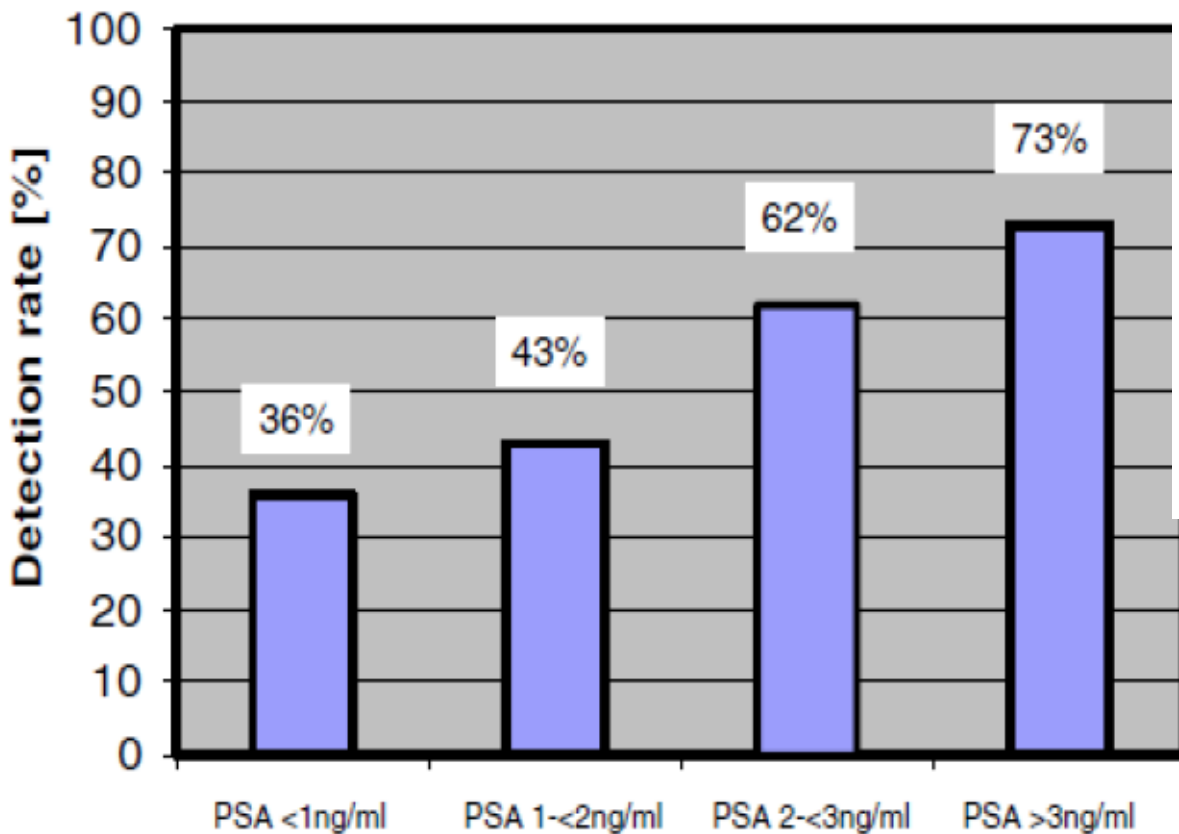
Which tracer??



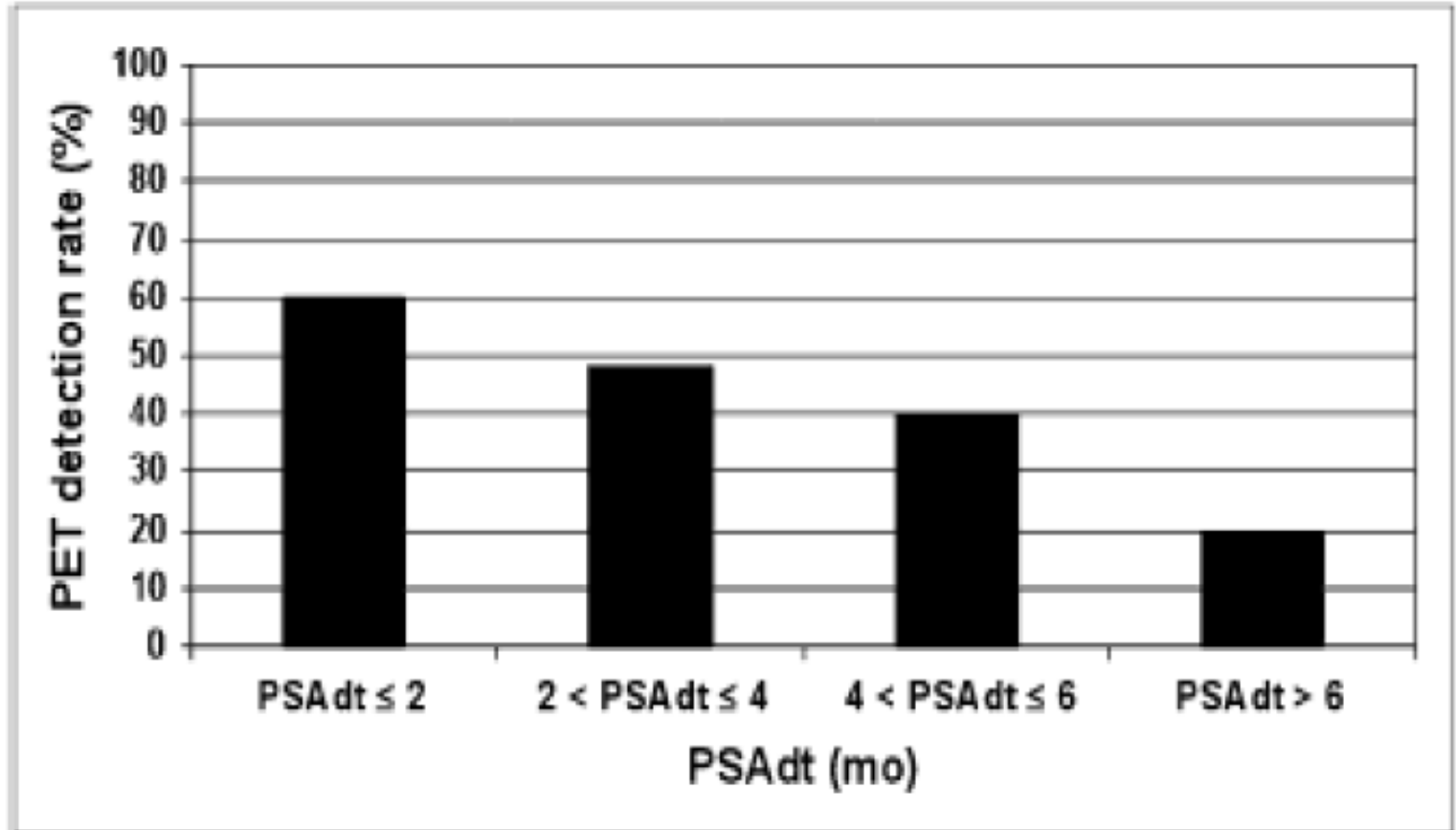
^{18}F -Choline PET

PSA and PSADT related to detection rate

DETECTION RATE OF RECURRENCE: ¹⁸F-Choline



DETECTION RATE OF RECURRENCE: ¹⁸F Choline



Castellucci et al JNM, 2011

^{18}F CHOLINE vs ^{68}Ga -PSMA

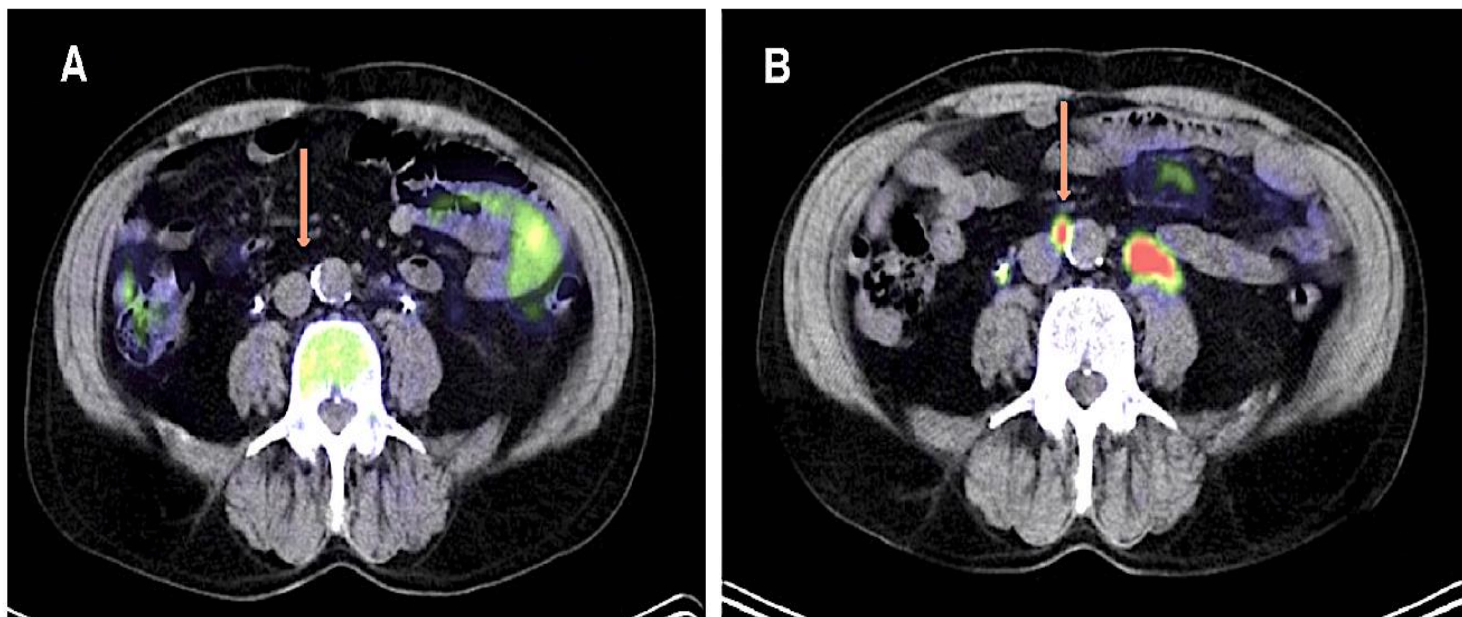


Fig. 2 – Comparison of (A) ^{18}F -fluoromethylcholine and (B) ^{68}Ga -PSMA-HBED-CC in a patient with biochemical recurrence. ^{68}Ga -PSMA-HBED-CC positron emission tomography-computed tomography shows tracer accumulation in a small aorto-caval lymph node metastasis (orange arrow), which is not seen on ^{18}F -fluoromethylcholine positron emission tomography-computed tomography.

TAKE HOME CHOLINE

- Low-moderate sensibility, specificity and detection rate
- Price and logistics concerns
- Need ciclotron
- Spatial resolution
- Dimensional limits



Prostate specific membrane antigen

^{68}Ga - PSMA

Prostate specific membrane antigen

PSMA



- Prostate-specific membrane antigen (PSMA) is a cell surface glycoprotein
 - Significantly increased overexpression in prostatic cancer cells
- NOT only in prostatic cancer :
 - PSMA overexpression in endothelial cell of tumor
 - Colon, gastric, breast, thyroid, other

^{68}Ga -PSMA: PSMA vs choline

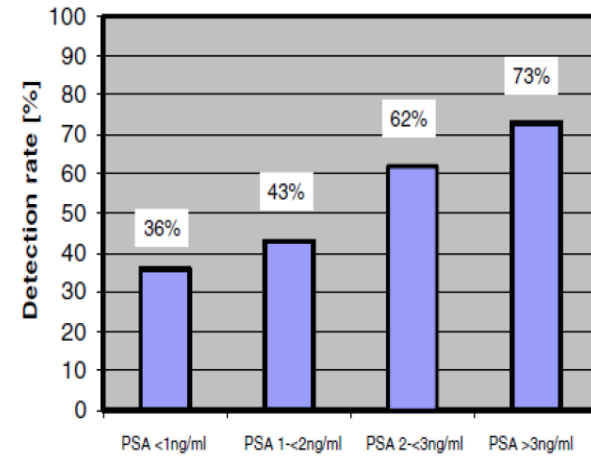
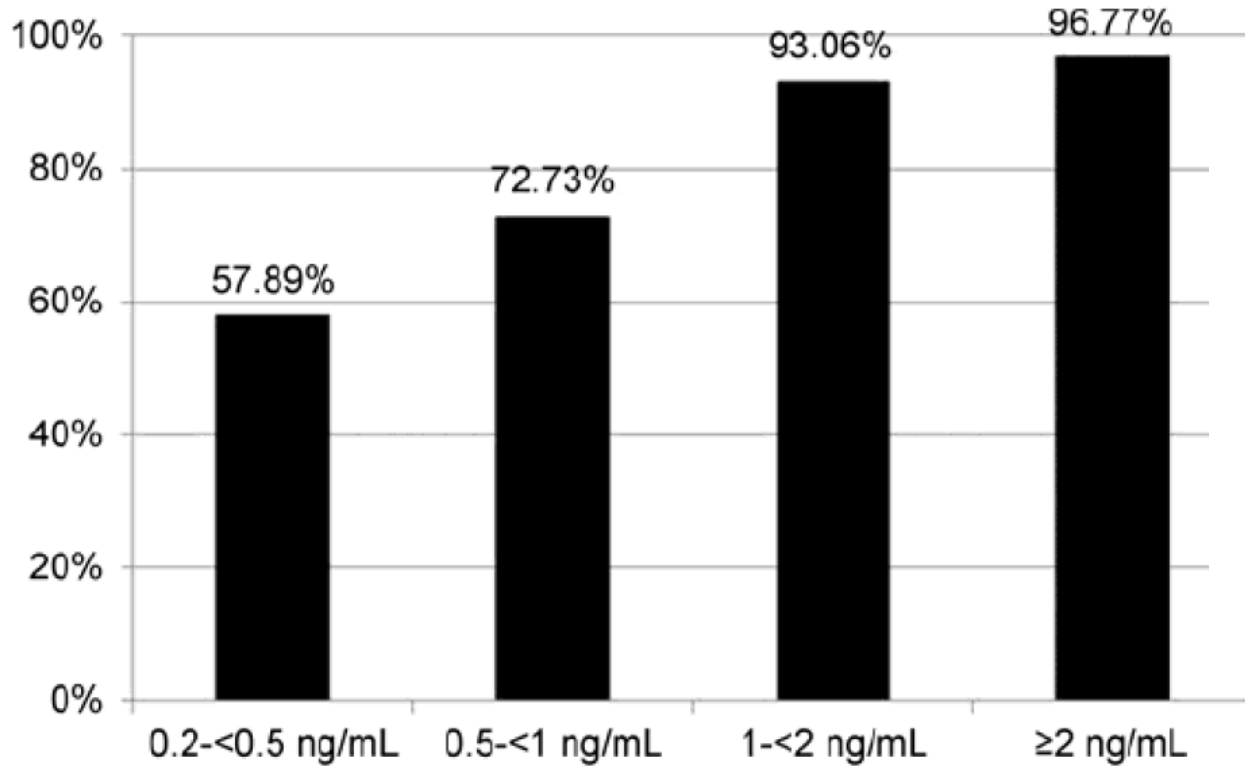


- Better detection rate compare to ^{18}F -choline
 - 86% vs 60%
- More lesions dectected with PSA < 2 ng/ml
 - 93% vs 57%
- Higher SUV max (in 80% of lesions)
- Higher tumors to background
 - LN mets (even infracentimetrics)
 - Bone marrow and liver mets

Ashfar-Oromieh et al, EJMN 2013



⁶⁸Ga-PSMA



¹⁸F choline

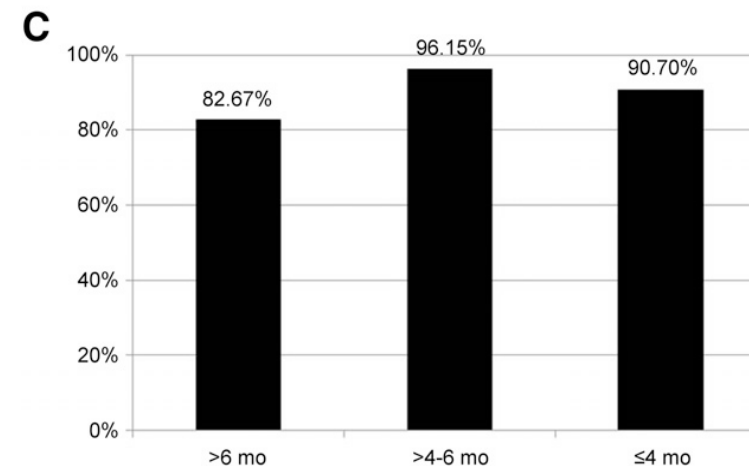
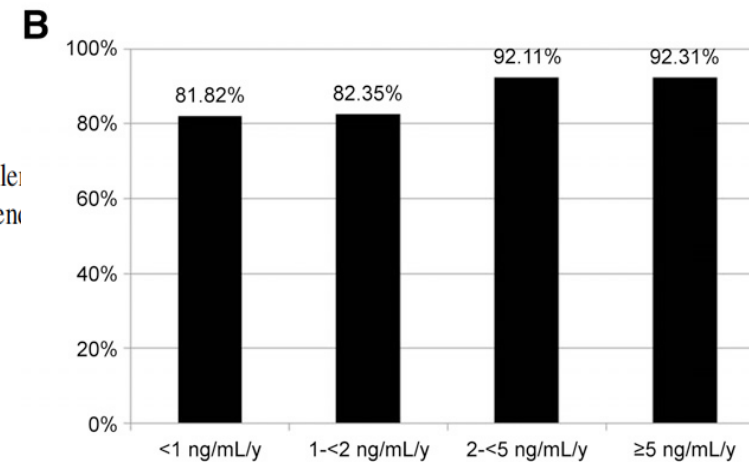
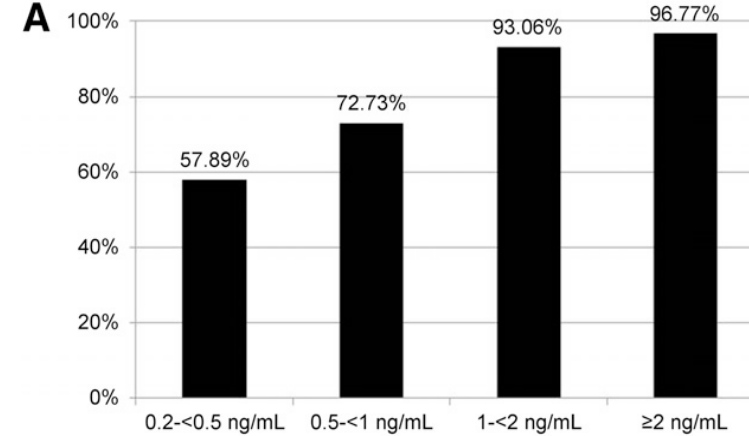


Eiber et al, JNM 2015

⁶⁸Ga-PSMA: CLINICAL EXPERIENCE

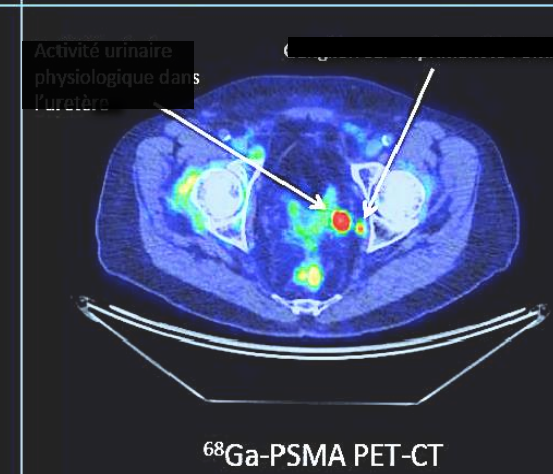
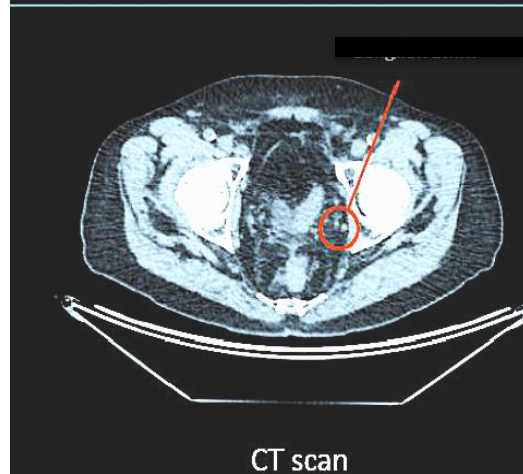
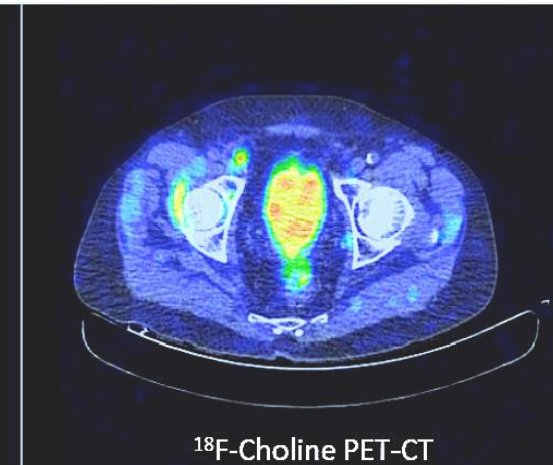
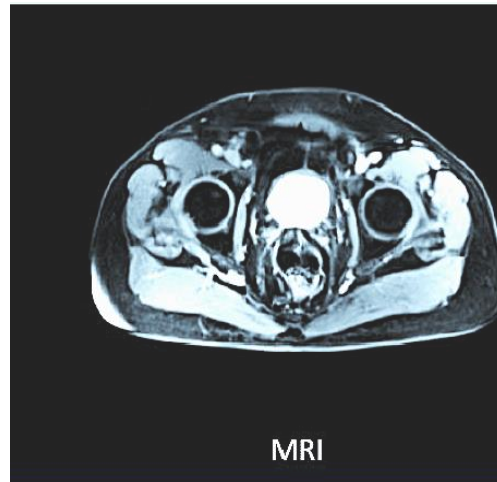
Evaluation of Hybrid ⁶⁸Ga-PSMA Ligand PET/CT in 248 Patients with Biochemical Recurrence After Radical Prostatectomy

Matthias Eiber^{*1,2}, Tobias Maurer^{*3}, Michael Souvatzoglou¹, Ambros J. Beer^{1,4}, Alexander Ruffani¹, Bernhard Halle, Frank-Philipp Graner¹, Hubert Kübler³, Uwe Haberhom⁶, Michael Eisenhut⁶, Hans-Jürgen Wester⁷, Jürgen E. Gschwend and Markus Schwaiger¹



^{68}Ga -PSMA

- pT2bN0, GS 4+3
- Biochemical relapse
(PSA 0.8 ng/ml, DT > 6
month)
After RP+PLN and SRT
~~(loggia)~~
- Negative imaging to:
BS, MRI and choline-PET

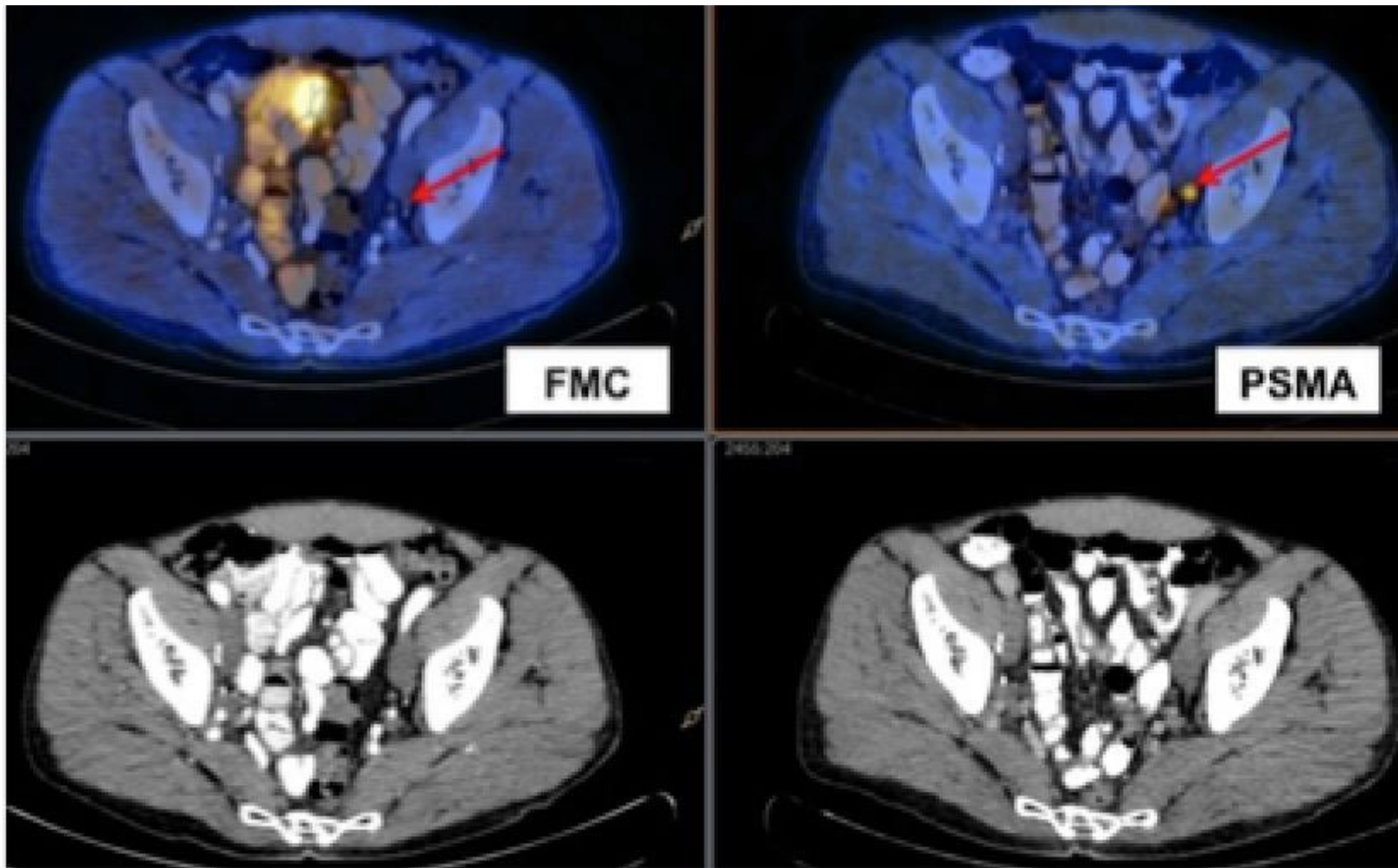


KEY POINTS PSMA



- ^{68}Ga PSMA PET/CT is demonstrating promising results in pCa pt, especially for detection of biochemical recurrence after primary treatment and prior to active therapies (price)
- PSMA PET/CT have a higher detection rate than choline PET/CT.
- The role of **PSMA PET/MRI** remains to be elucidated further, especially for guiding biopsies and delivery of focal therapy.

PSMA- targeted imaging: **THE BEST IS YET TO COME...**



⁶⁸GA-PSMA



WHAT TO DO?

1. THERANOSTICS

- ¹⁷⁷Lu

2. TARGETING RT vs SURGERY

3. MODIFY DECISION MAKING

4. FUTURE (*GUIDED SURGERY?*)

- ^{99m}Tc-PSMA, ¹¹¹In-PSMA

Theranostics

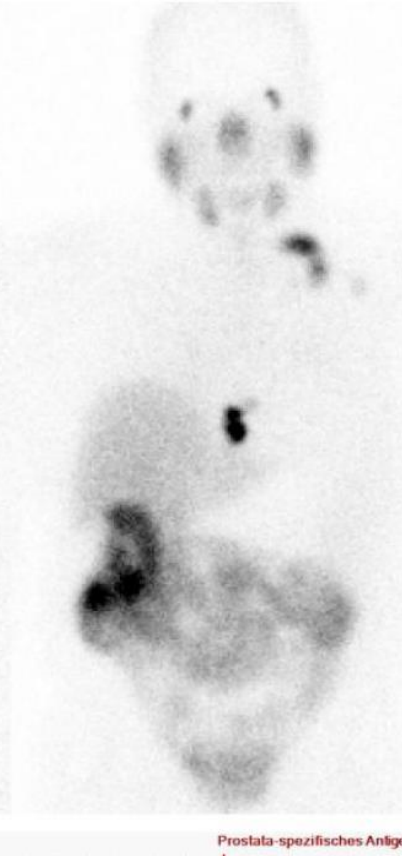
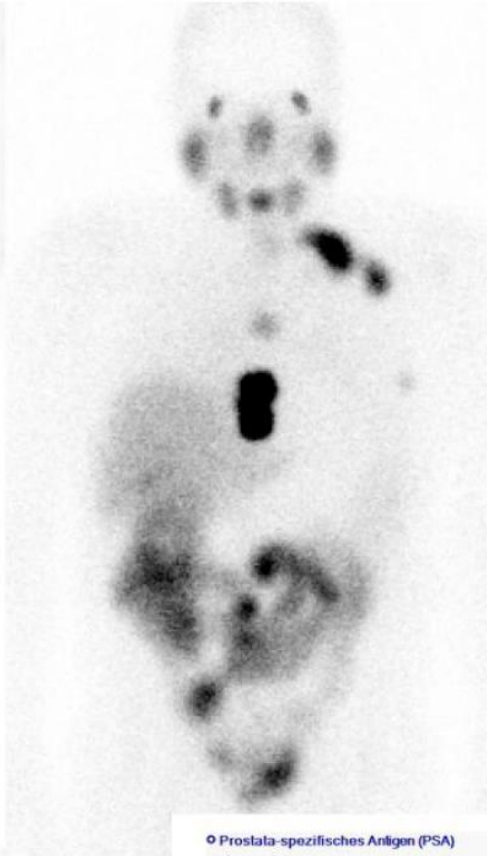
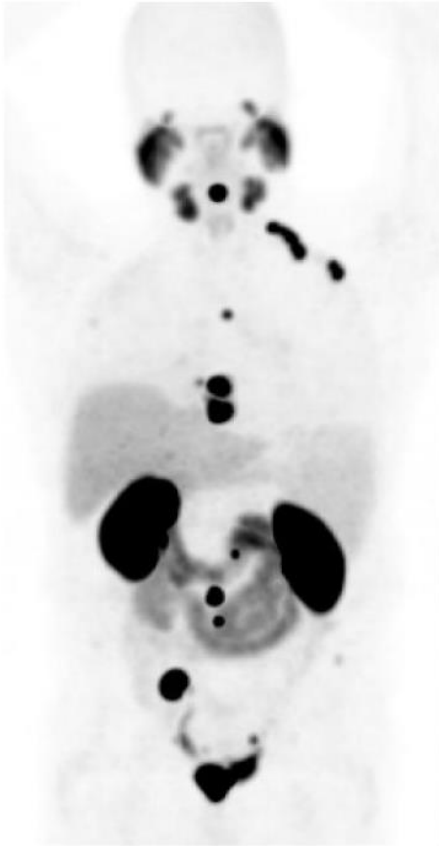
- Diagnostic procedure determines therapy
- Diagnostic imaging procedure is different from therapeutic procedure (chemo-, immuno-, radiation therapy, surgery)
- A very similar or the identical molecule is used for both, diagnosis and therapy

^{68}Ga -HBED-CC
03.12.13

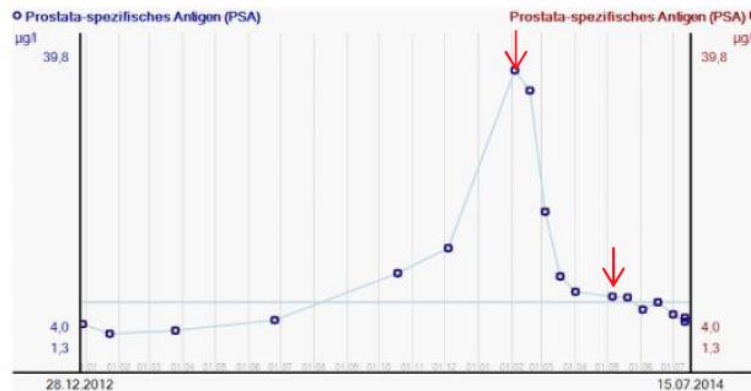
3,3 GBq ^{177}Lu -
PSMA617 03.02.14

4,0 GBq ^{177}Lu -
PSMA617 5.05.14

^{68}Ga -HBED-CC
14.7.14



Uwe Haberkorn, HEIDELBERG



⁶⁸GA-PSMA



- **WHAT TO DO?**

1. THERANOSTICS

2. **TARGETING RT vs SURGERY**

3. MODIFY DECISION MAKING

4. FUTURE (GUIDED SURGERY?)

- ^{99m}Tc-PSMA, ¹¹¹In-PSMA

TARGETING RT in recurrence patients



**TOMOTHERAPY
SC Radioterapia
Aosta**



WHY TREATING A METASTATIC PATIENT IN CURATIVE WAY?

STEREOTATIC RADIOTHERAPY (SBRT) in OLIGOMETASTATIC PATIENTS

- Oligometastatic state in cancer, first proposed in 1995 by Hellman and Weichselbaum
- Concept has been demonstrated by multiple studies with long-term survival rates in a subset of patients when treated with aggressive local therapy, including surgery and radiotherapy
- Use of high doses of single-session *stereotactic radiosurgery* or more lesions (1 to 4) *stereotactic body RT*



STEREOTATIC RADIOTHERAPY (SBRT)



- Using Stereotactic RT (1-4 fractions)
- Until 3-4 lesions

Study	No. of Lesions	Dose	Rate of Local Control	Rate of Toxicity
Herfarth ²⁸	60	14–26 Gy in 1 fraction	81% at 18 mo	No major adverse events reported
Hoyer ²⁹	44	45 Gy in 3 fractions	86% at 2 y	1 death from hepatic failure Grade 4 (1) Grade 3 (2)
Lee ³⁰	68	Median 41.8 Gy in 6 fractions	71% at 12 mo	Grade 3 (6) Grade 4 (1)
Rusthoven ²⁷	63	60 Gy in 3 fractions	92% at 2 y	No grade 4/5
Scorsetti ³¹	76	Majority 75 Gy in 3 fractions	94% at 12 mo	No grade \geq 3

⁶⁸GA-PSMA



- WHAT TO DO?

1. THERANOSTICS

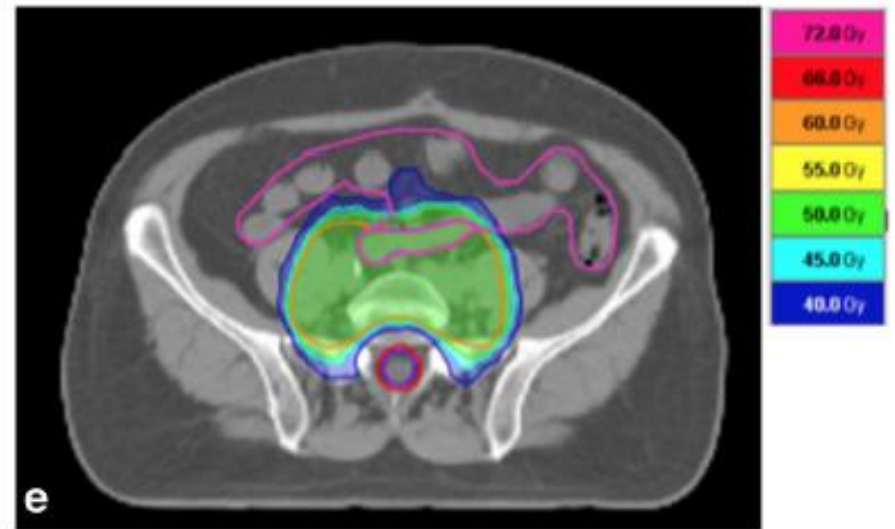
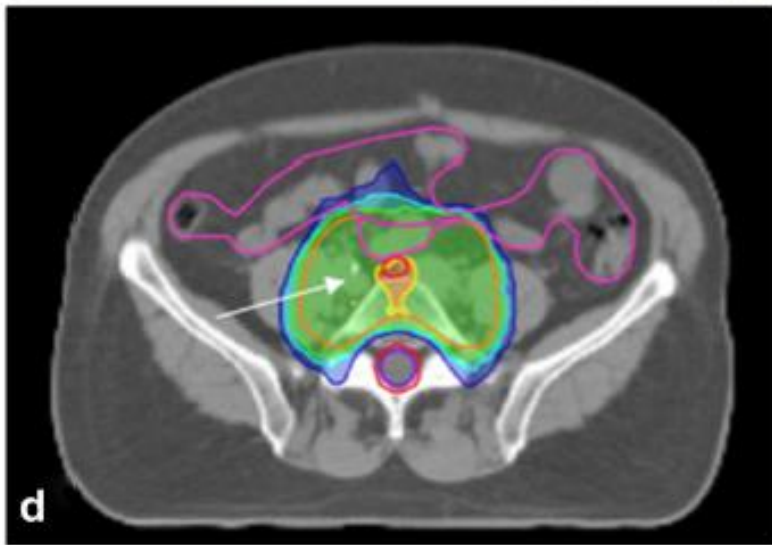
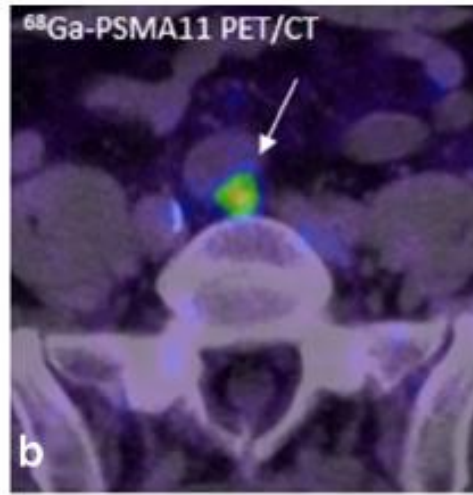
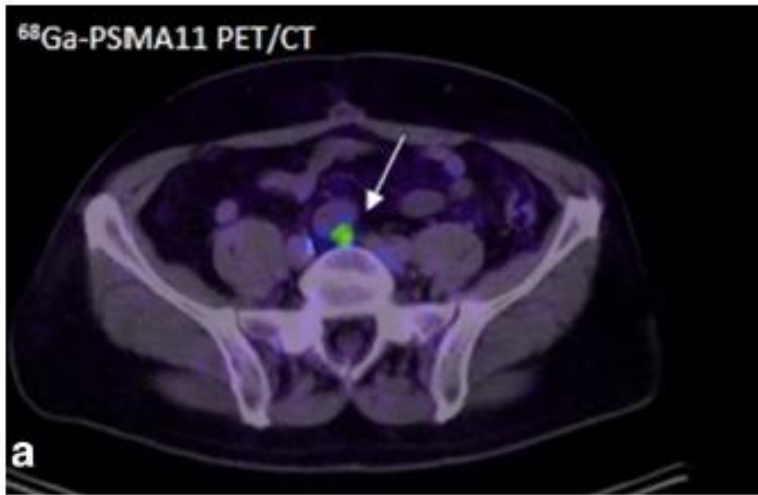
2. TARGETING RT vs SURGERY

3. MODIFY DECISION MAKING in RT

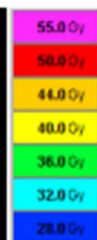
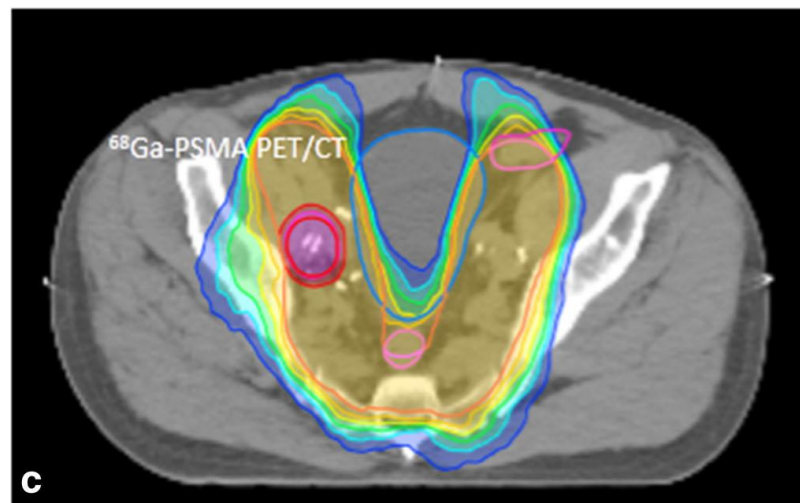
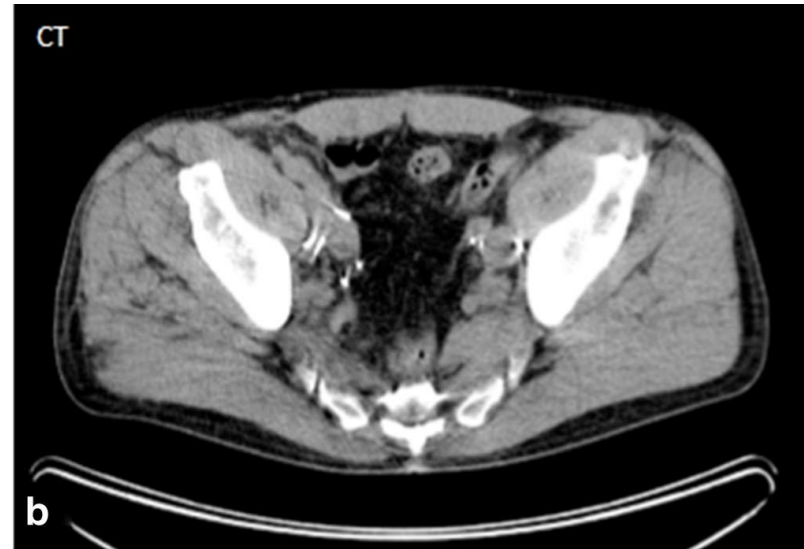
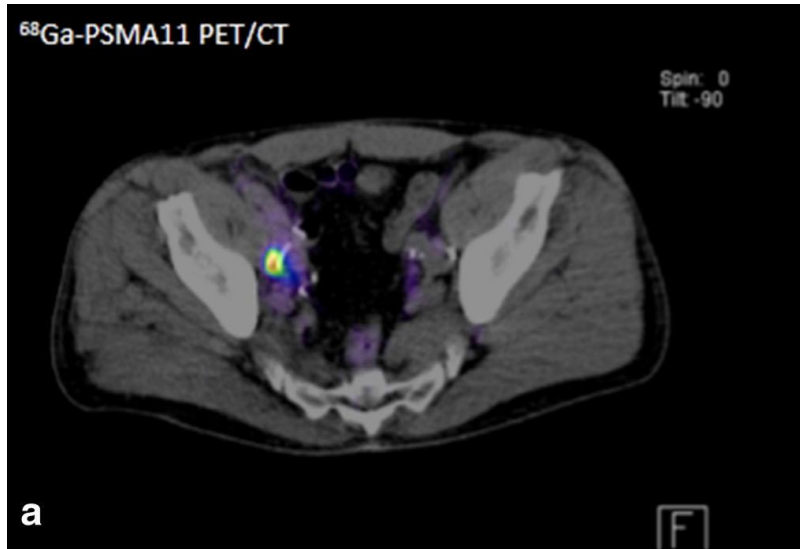
4 . FUTURE (GUIDED SURGERY?)

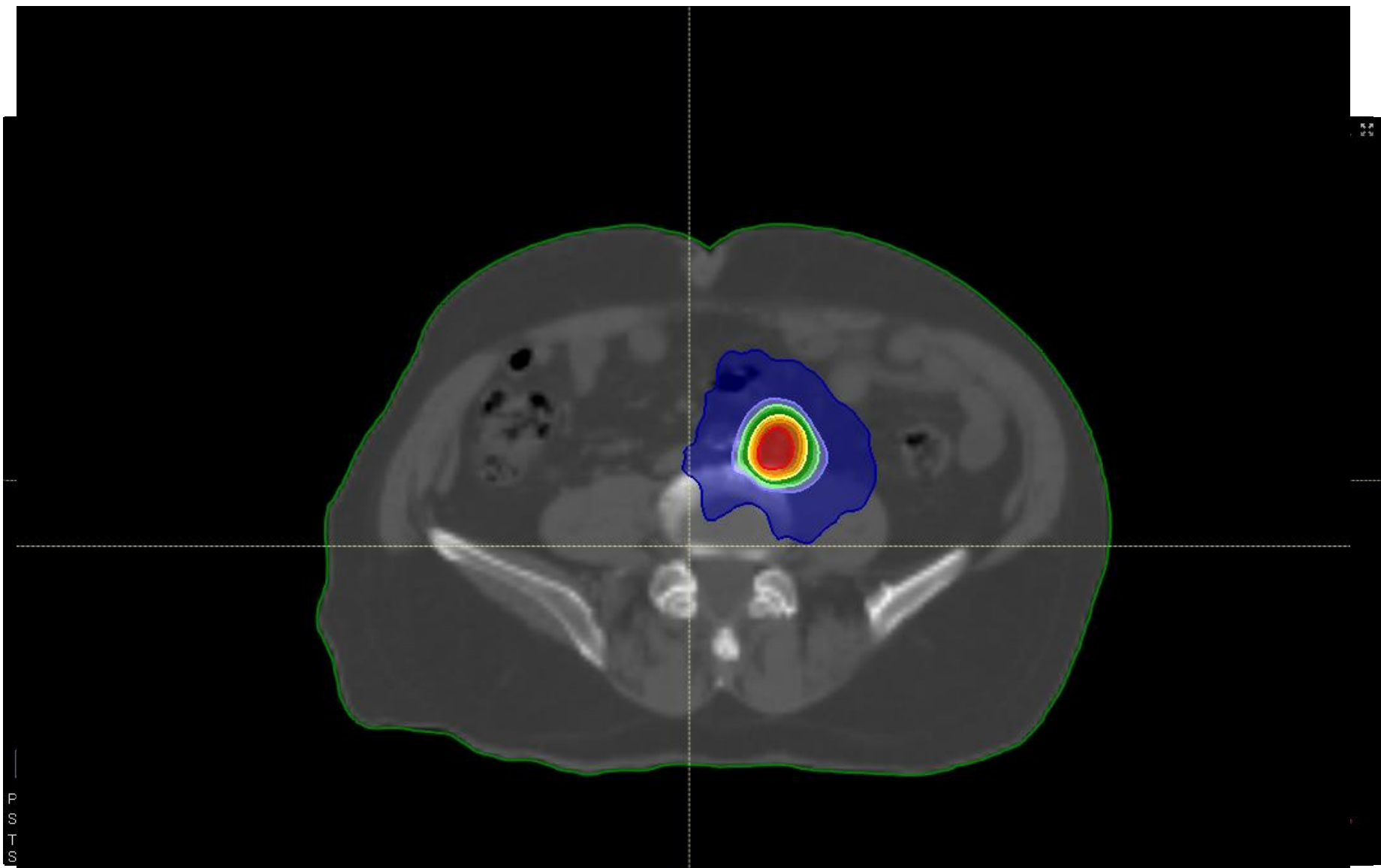
- ^{99m}Tc-PSMA, ¹¹¹In-PSMA

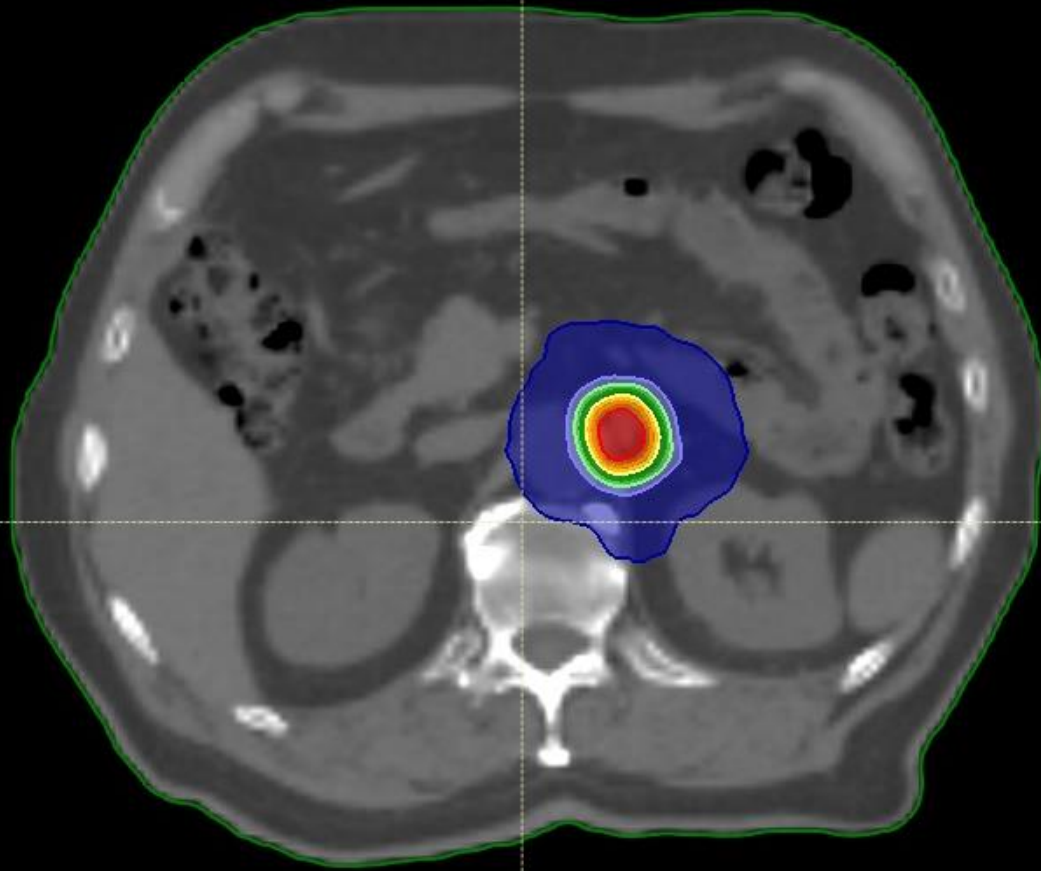
Targeting RT in “virgin patients” modifying decision making



Targeting RT in “virgin patients” modifying decision making

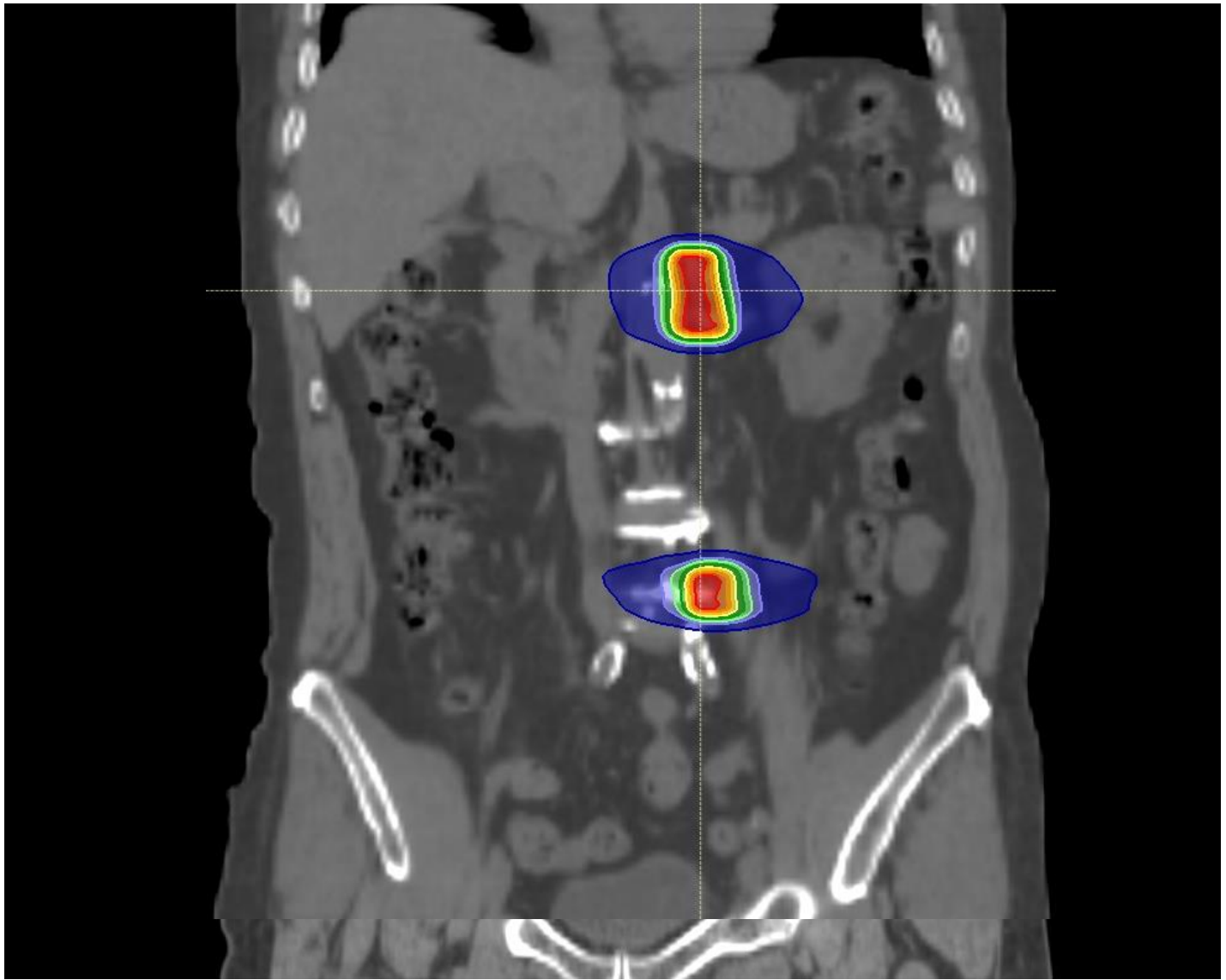


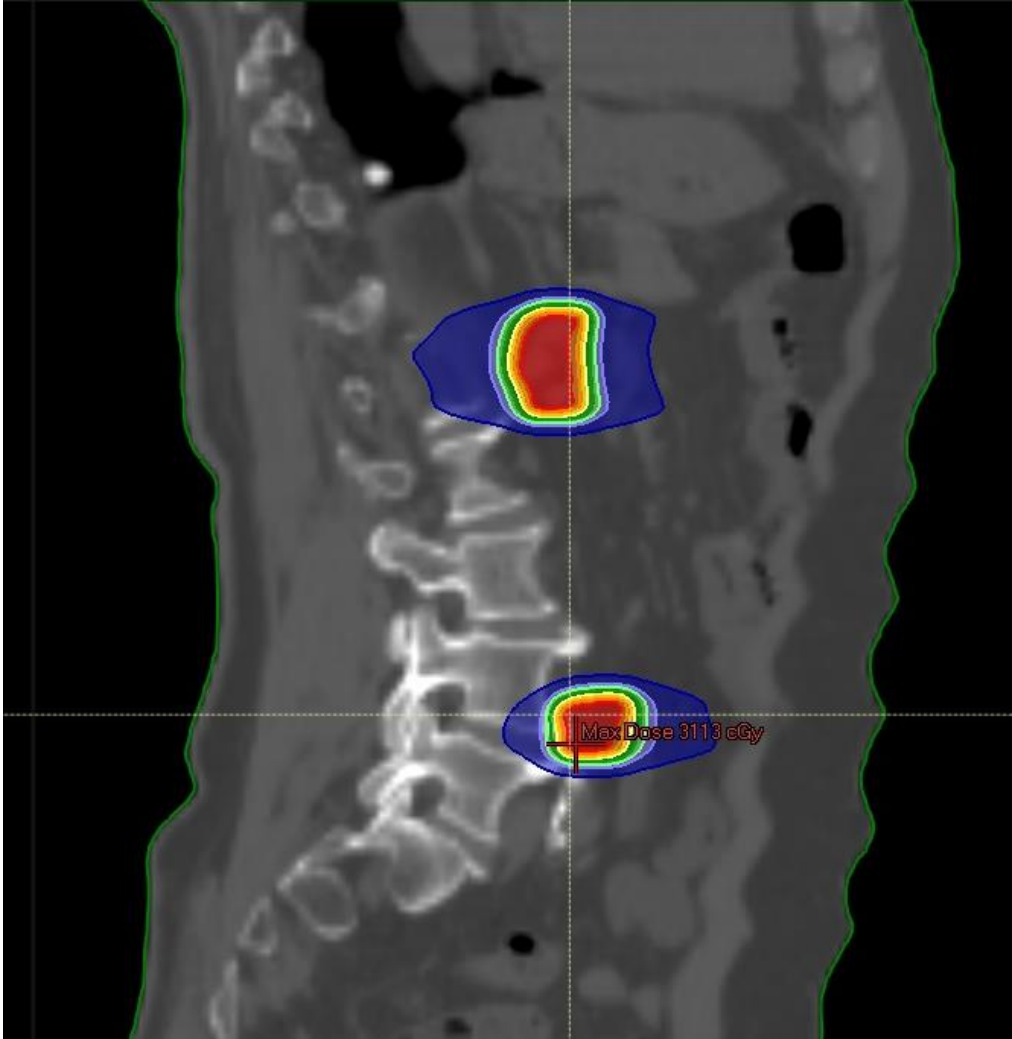




Transversal: 17.93 cm
Slice 179/225

0 1 2 3 4 5 6 cm





⁶⁸GA-PSMA

- WHAT TO DO?

1. THERANOSTICS

2. TARGETING RT vs SURGERY

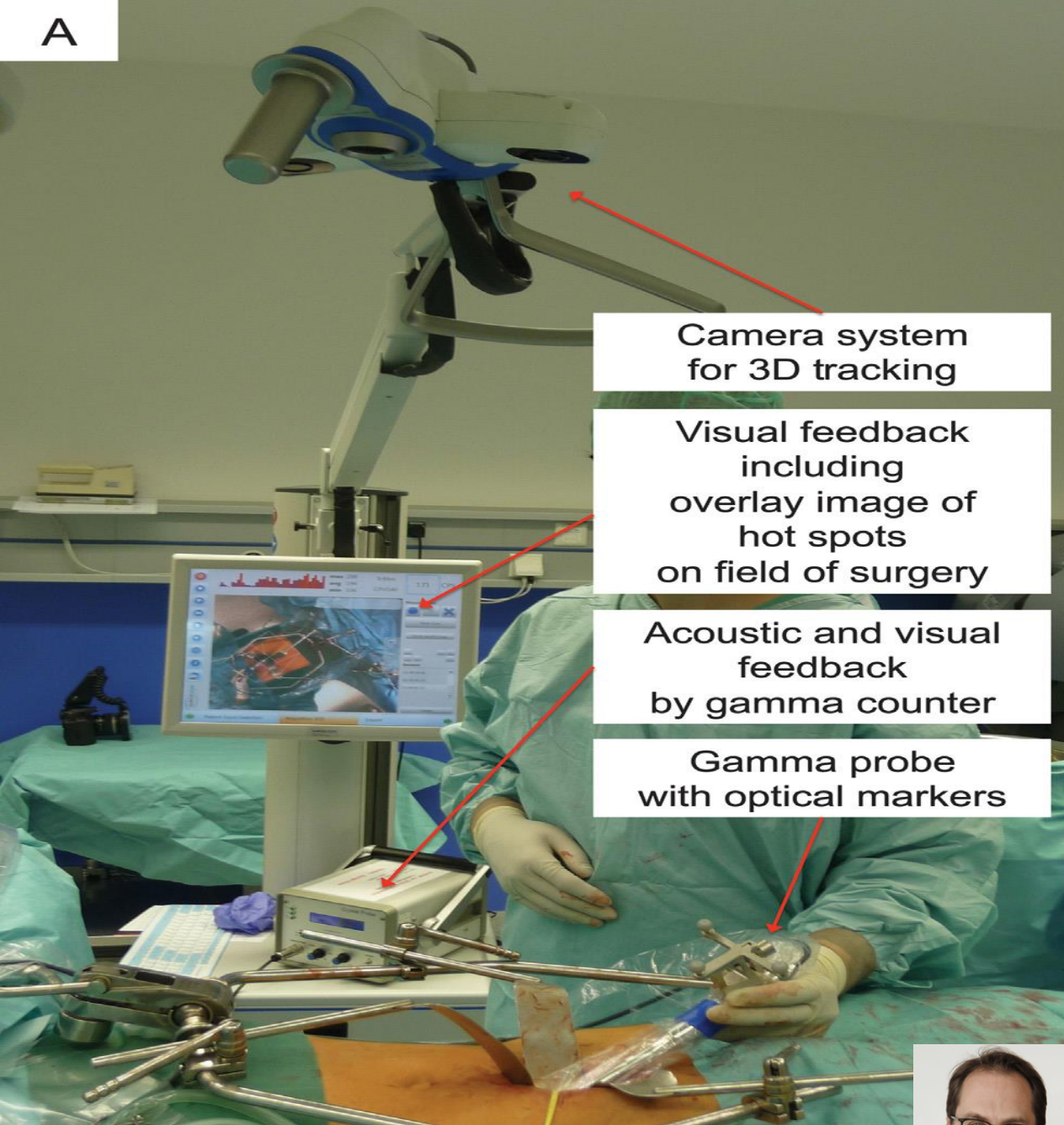
3. MODIFY DECISION MAKING in RT

4. **FUTURE (GUIDED SURGERY?)**

- ^{99m}Tc-PSMA, ¹¹¹In-PSMA



A

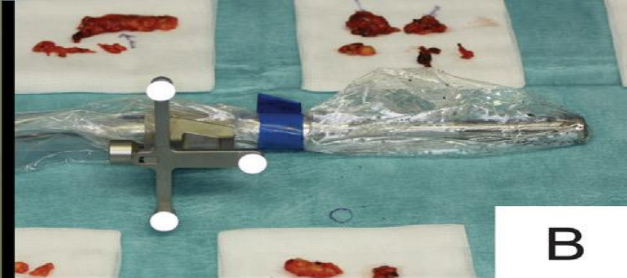


Camera system for 3D tracking

Visual feedback including overlay image of hot spots on field of surgery

Acoustic and visual feedback by gamma counter

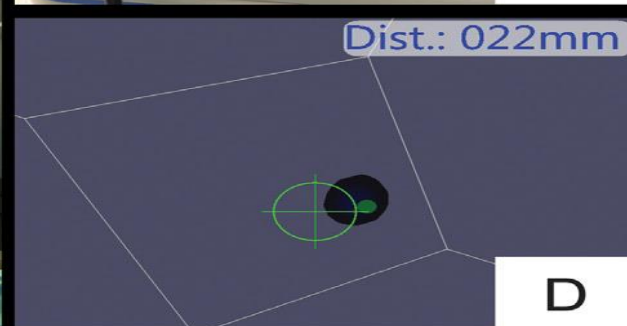
Gamma probe with optical markers



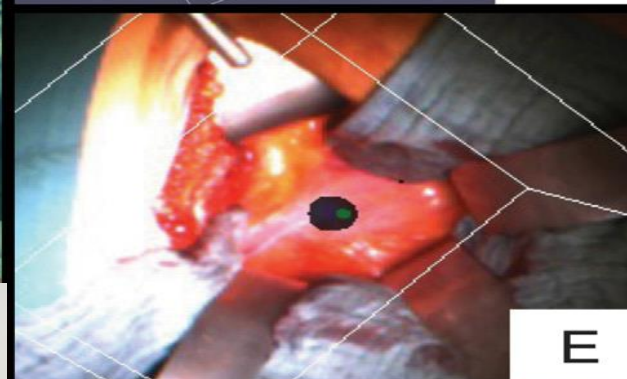
B



C



D



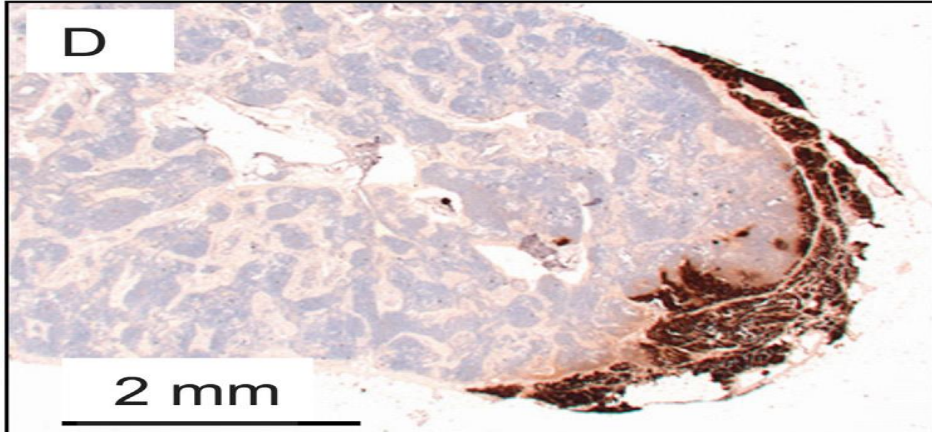
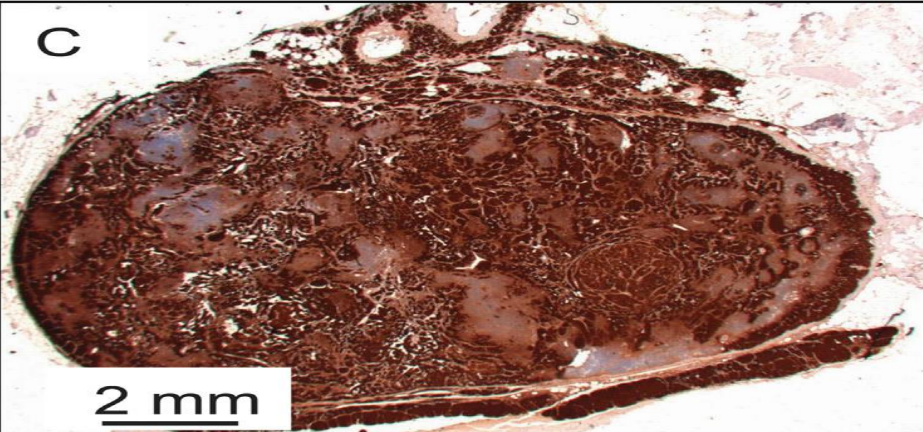
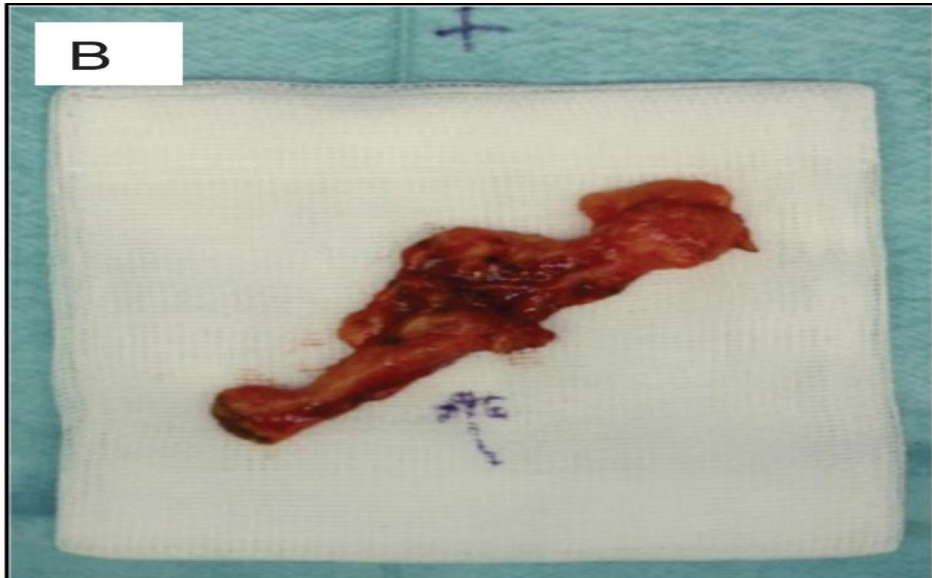
E

Courtesy: Tobias MAURER, MUNICH



Prostate-specific Membrane Antigen–radioguided Surgery for Metastatic Lymph Nodes in Prostate Cancer

Tobias Maurer^{a,*}, Gregor Weirich^b, Margret Schottelius^c, Martina Weineisen^d, Benjamin Frisch^e, Asli Okur^{d,e}, Hubert Kübler^a, Mark Thalgott^a, Nassir Navab^e, Markus Schwaiger^d, Hans-Jürgen Wester^c, Jürgen E. Gschwend^a, Matthias Eiber^d



change

is

difficult.

not

changing

is

fatal.