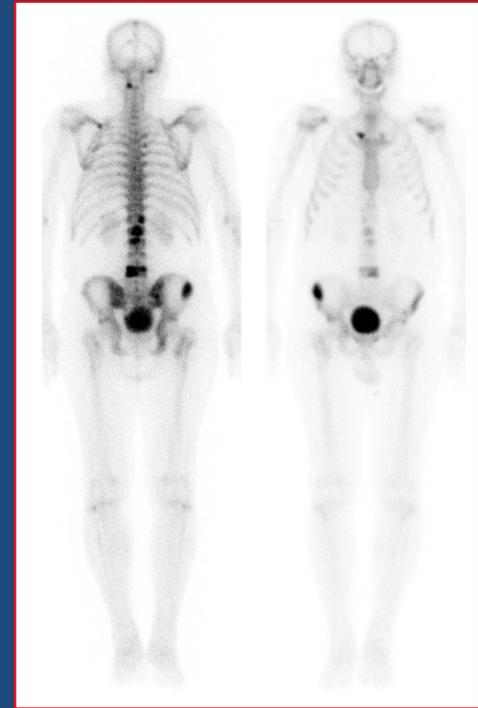


# Prostate cancer: Radioisotope diagnostic/ therapeutic methods

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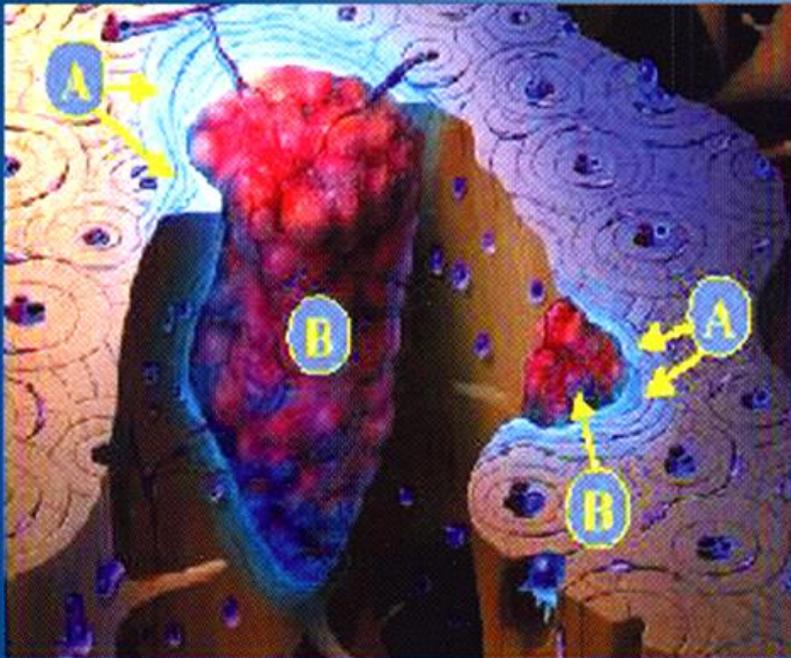
# Hormone therapy refractory PCa

- Therapy of prostate cancer starts with precision (robot assisted) surgery, then with radiation therapy and androgen deprivation. The prognosis is good.
- When the patient becomes refractory to hormone therapy, the prognosis worsens
- Two kinds of refractory patients: with bone metastases and with bone + lymph node metastases

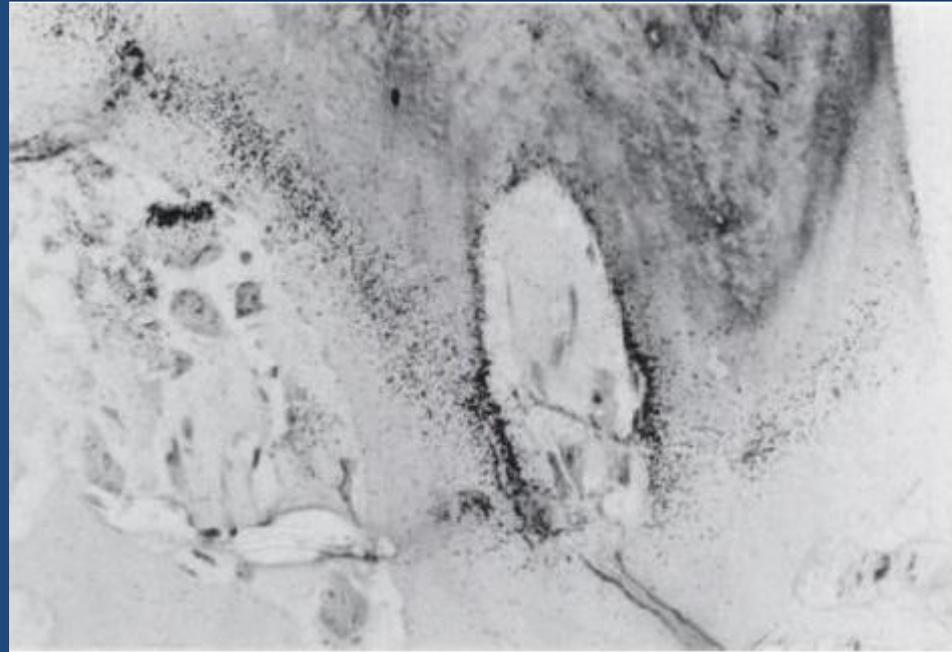


Bone scan: Bone met.no info on nodes

## $^{153}\text{SmEDTMP}$ Antalgic therapy



**Livello cellulare: l'illustrazione rappresenta la captazione di Samario 153 EDTM in un nuovo strato osseo (A) formatosi in prossimità di tumori metablastici (B)**

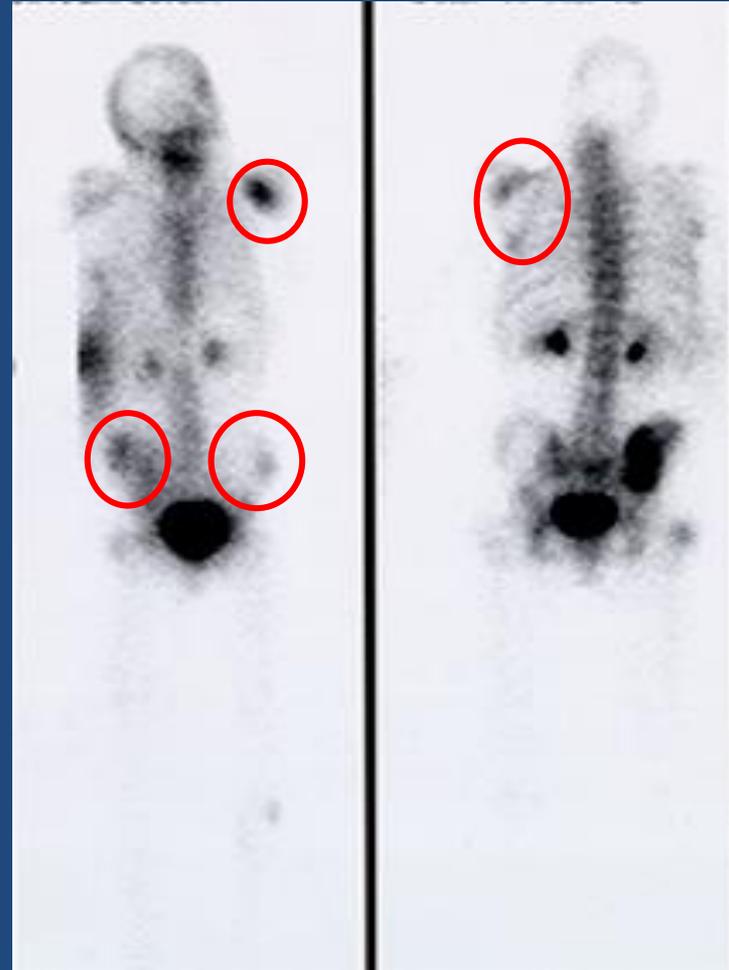


**Autoradiography  
Sm -153 EDTM**

# $^{153}\text{Sm}$ EDTMP

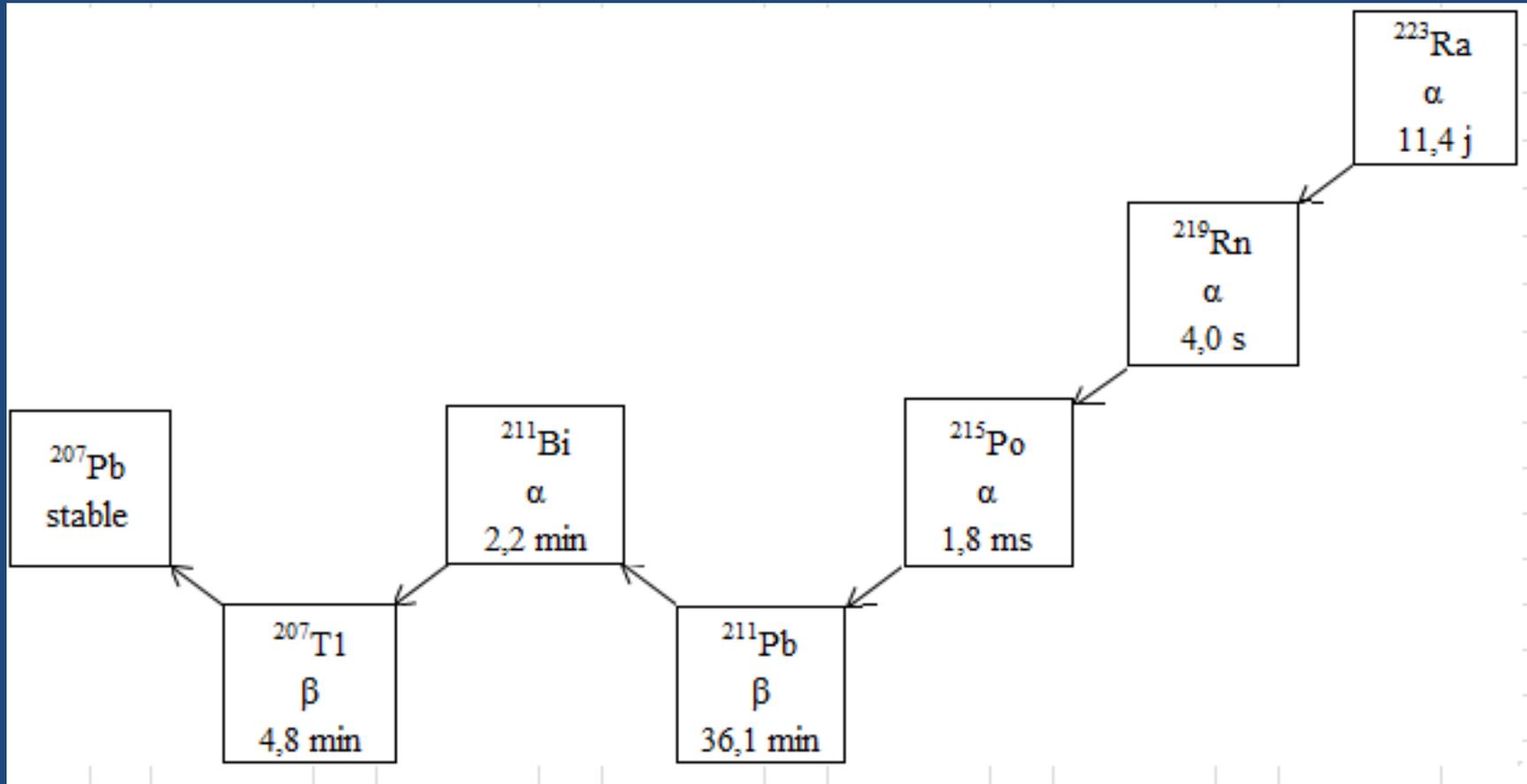


$^{99\text{m}}\text{Tc}$  Pre-therapy bone scan



$^{153}\text{Sm}$  post-therapy bone scan

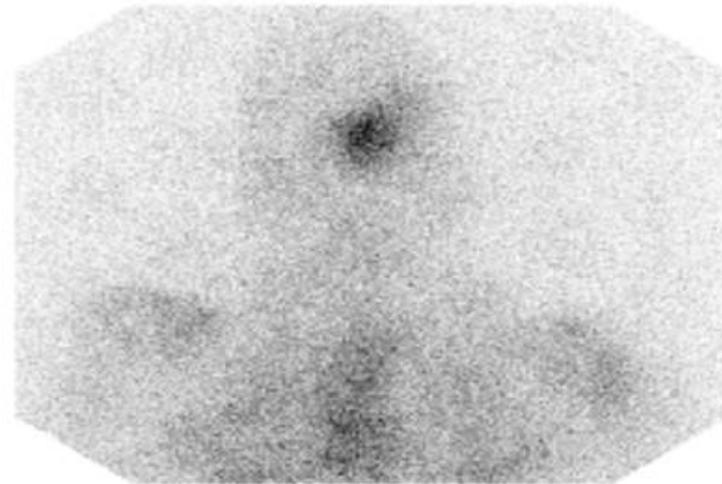
# $^{223}\text{Ra}$ : $\alpha$ emitter; antalgic therapy, improvement of prognosis



Therapy: 6 administrations (Cycles) in 6 months

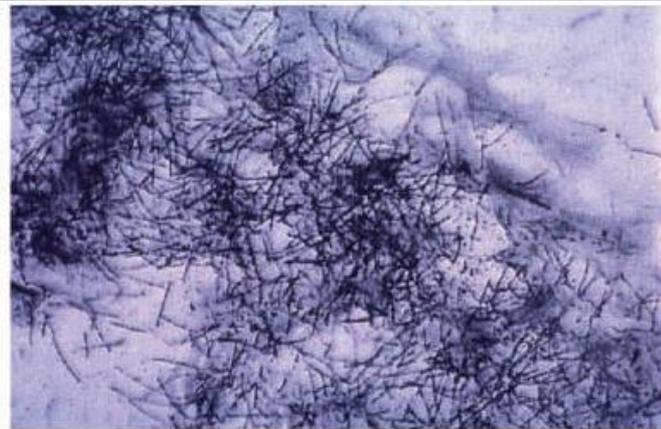
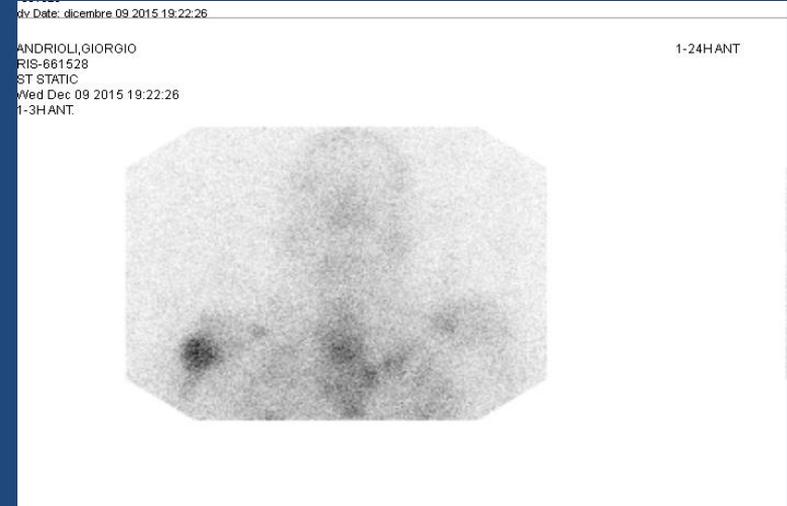
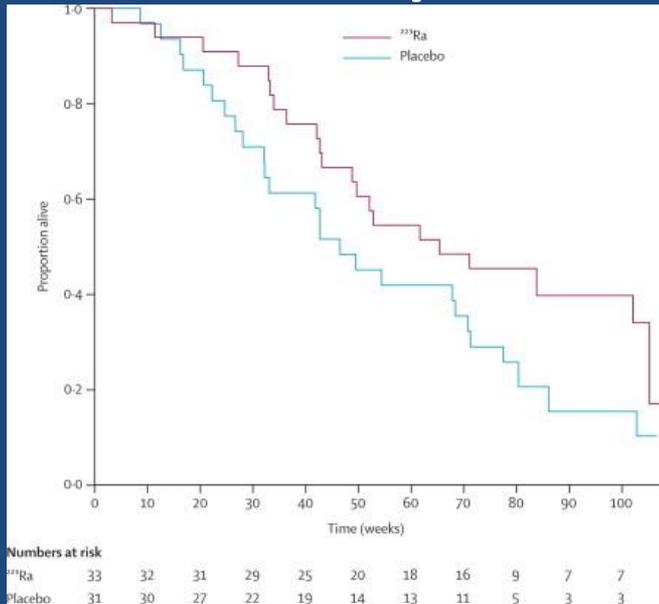
$^{223}\text{Ra}$ :  $\alpha$  emitter; analgic therapy, improvement of prognosis.  
Patients with castration resistant prostate cancer

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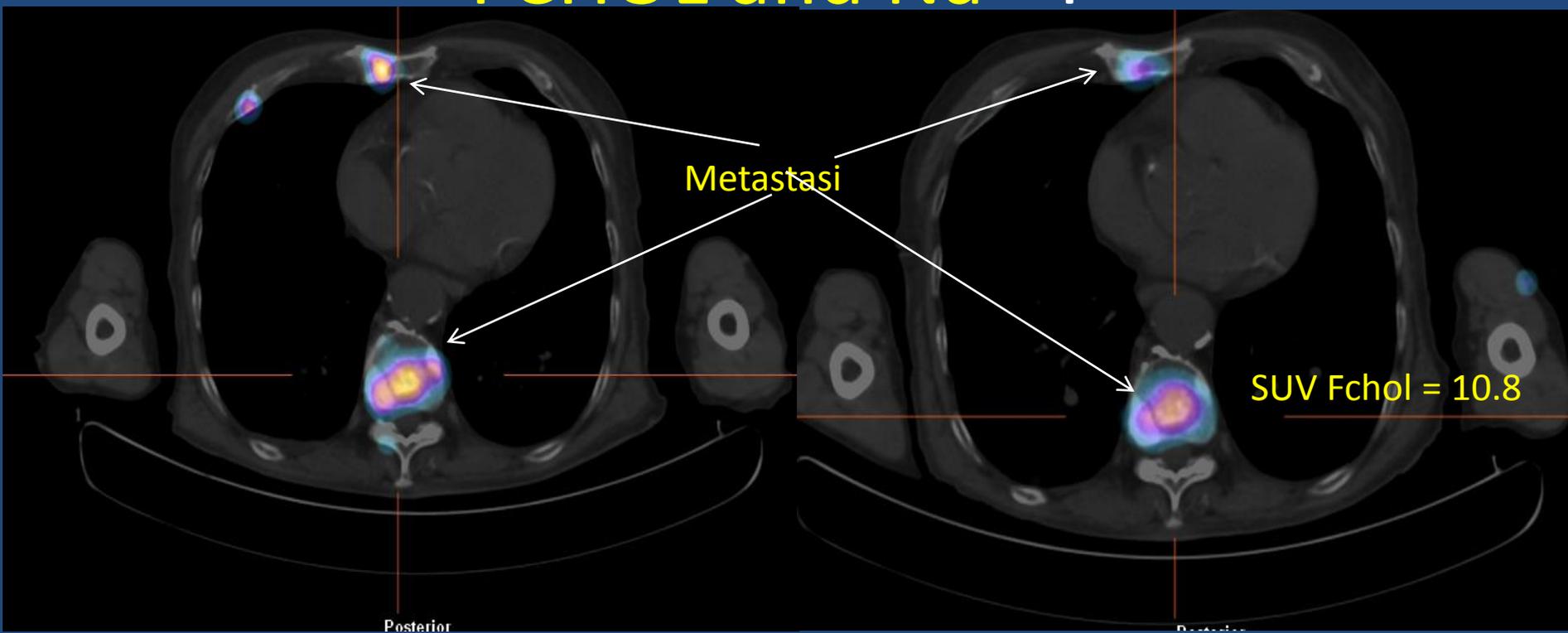
# $^{223}\text{Ra}$ : $\alpha$ emitter; antalgic therapy, improvement of prognosis



# Current diagnostic radiopharmaceuticals

- $^{99m}\text{Tc}$  MDP: Detects bone growing around the cancer
- $^{18}\text{F}$  NaF : a PET bone
- $^{18}\text{F}$  Choline: detects growing prostate cancer, though when it is not very aggressive
- $^{18}\text{F}$  DFG: detects prostate cancer when it becomes aggressive

# Bone metastases: Assessment with FCHOL and Na <sup>18</sup>F



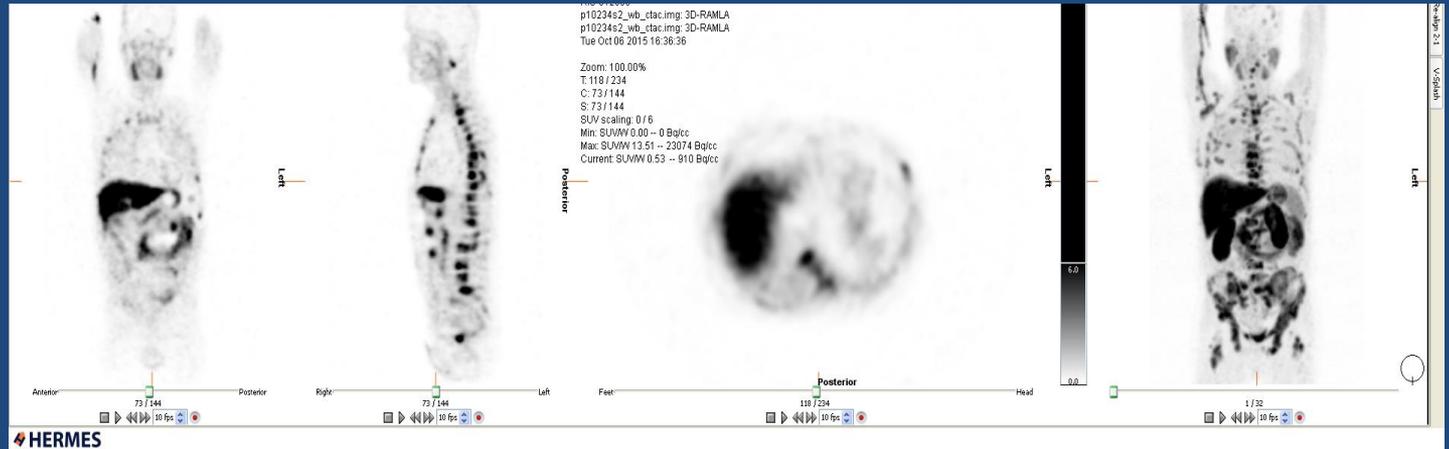
<sup>18</sup>F Na F

<sup>18</sup>F FCHOL

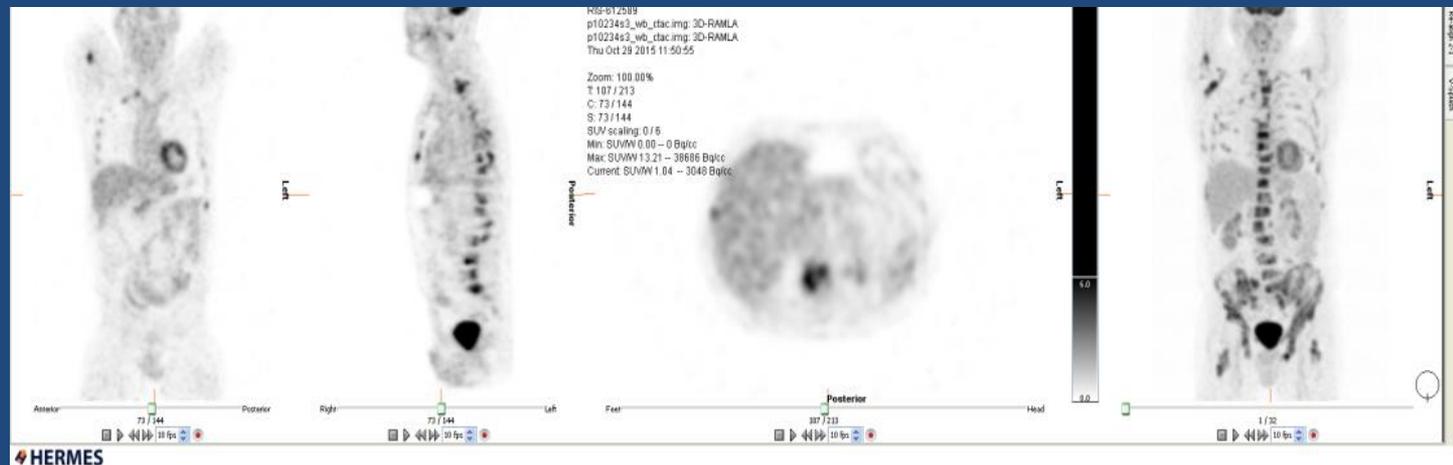


# $^{18}\text{F}$ DFG PET; aggressiveness

$^{18}\text{F}$  FCH  
( F CHOLINE)

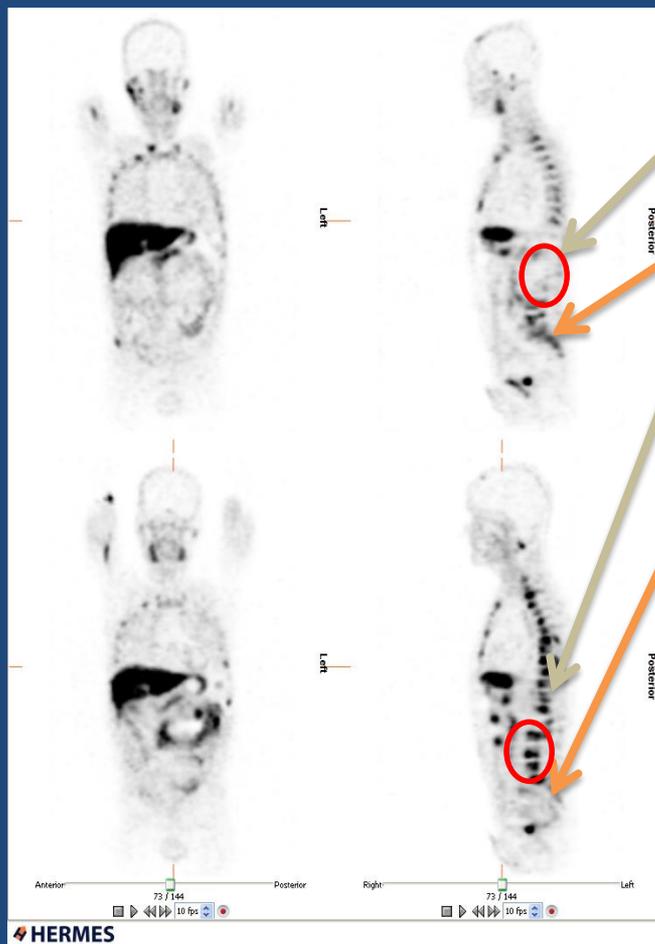


$^{18}\text{F}$  DFG



# Follow-up: $^{18}\text{F}$ choline (FCH) before $^{223}\text{Ra}$ and after 3 administrations

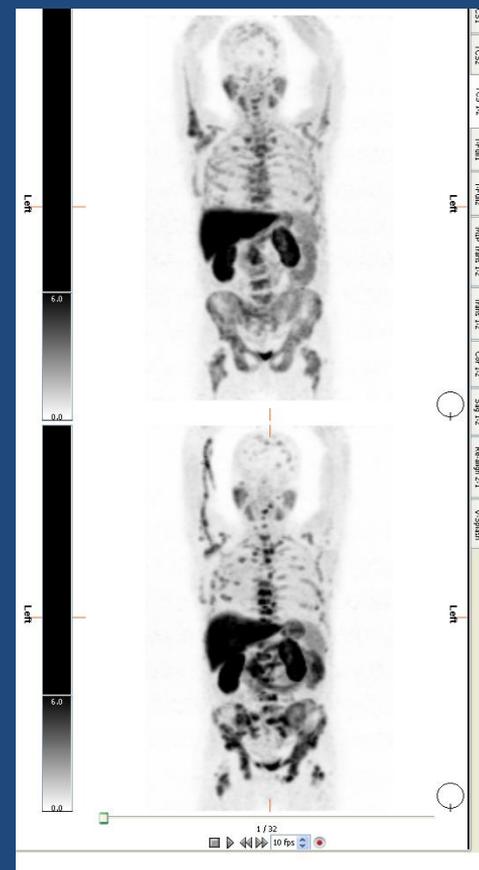
Reduction of cancer burden



FLAIRE

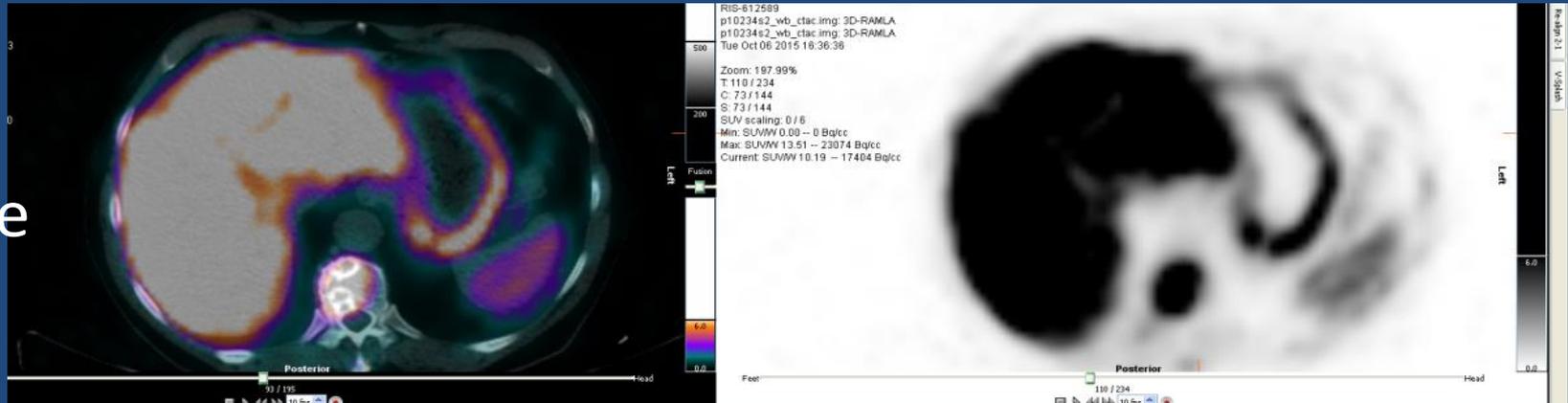
After 3 cycles  
Flaire effect

Before therapy

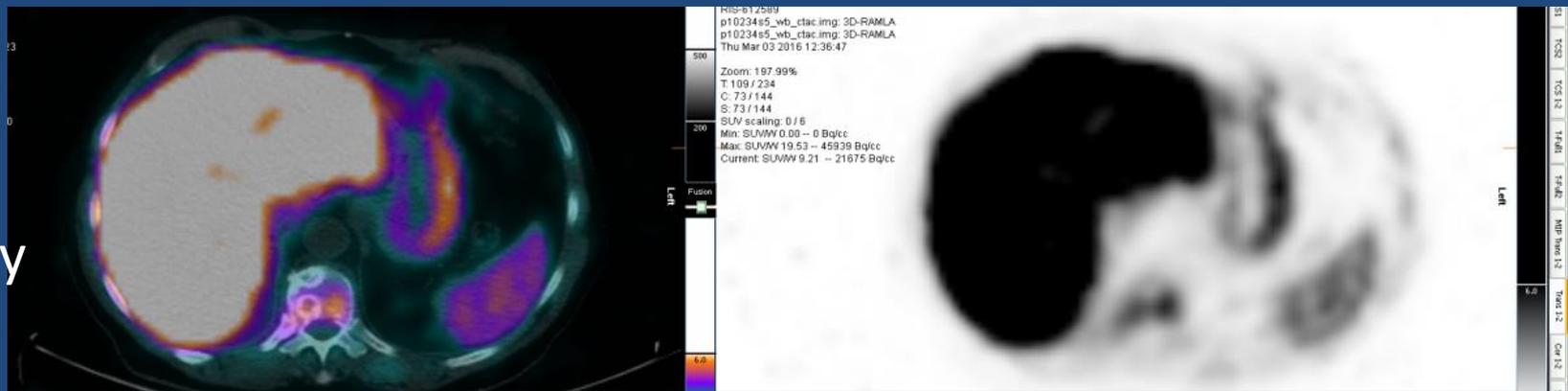


# $^{18}\text{F}$ Choline PET before and after $^{223}\text{Ra}$

Before  
 $^{223}\text{Ra}$

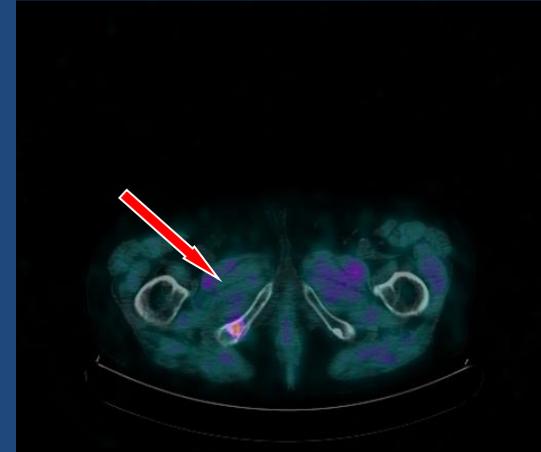
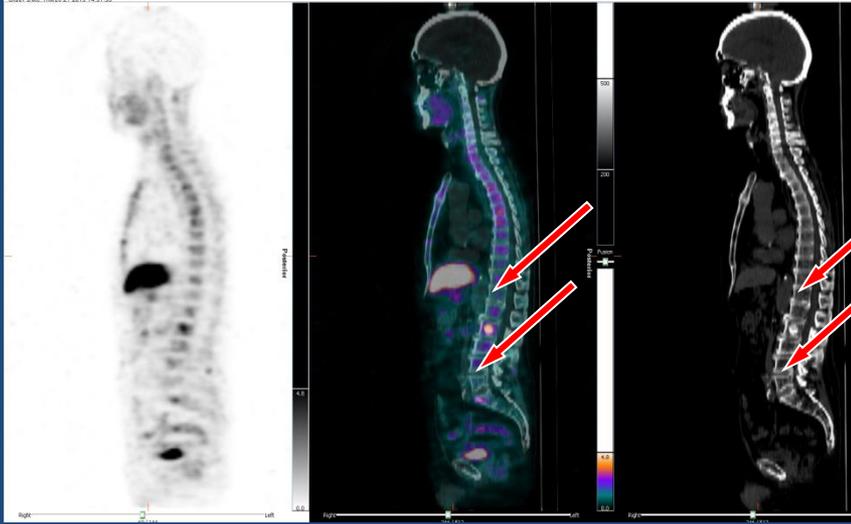


After  
Therapy

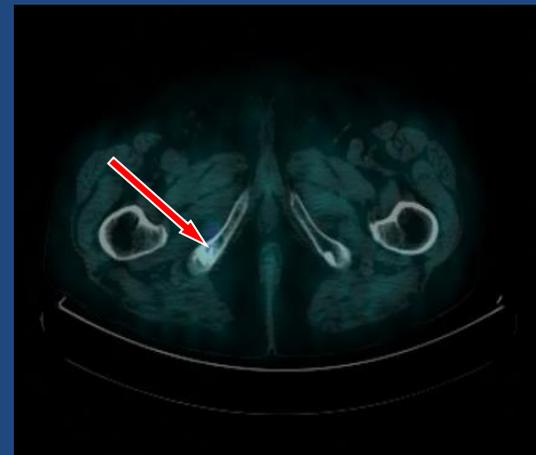


Interim PET after 3 Cycles: partial reduction of metastases

# $^{18}\text{F}$ FCH before and after therapy F: full remission of metastases



$^{18}\text{F}$  FCH PET ; **PSA 17 ng/ml**

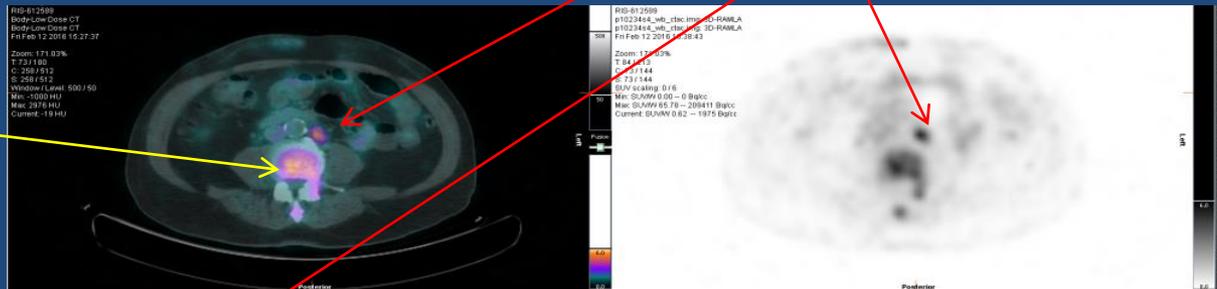


**Final  $^{18}\text{F}$  FCH PET 2 months after the end of therapy PSA 2.38 ng/ml**

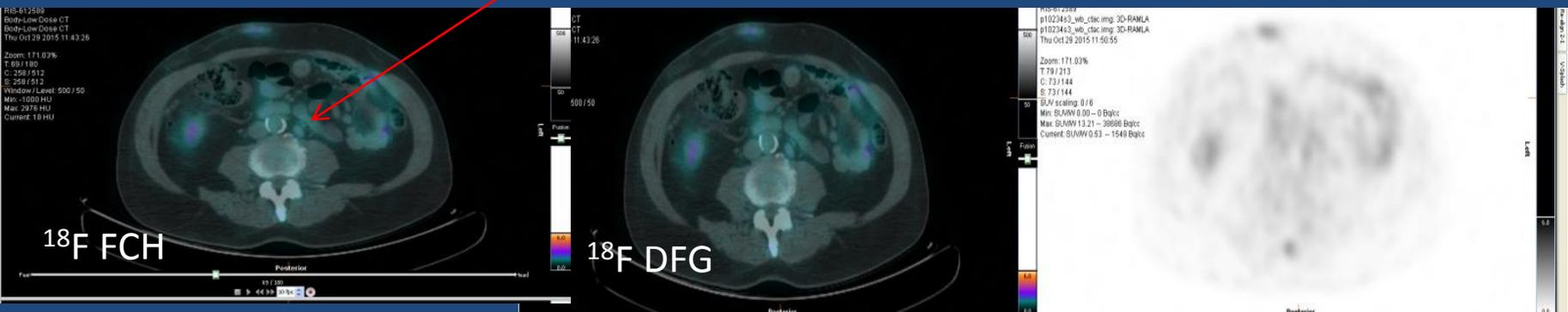
# But FCH can miss extraosseous localization: need of higher sensitivity

Interim PET. Previously not detected aggressive metastasis on a lymph node

Flaire on Bone



$^{18}\text{F}$  DFG after 3 Cycles



# More sensitive PET radiopharmaceuticals

- **$^{68}\text{Ga}$  PSMA.** The glutamate carboxypeptidase Membrane PSA is a transmembrane glycoprotein overexpressed in prostate cancer, that shows a pharmacofore pocket able to bind the **Glu- ureido Lys**, a specific inhibitor of PSMA, in its extracellular domain.  $^{68}\text{Ga}$  can label the **Glu- ureido Lys** via the chelator HBED-CC. This radiopharmaceutical can be used for diagnostic purposes, showing very high values of sensitivity and specificity
- **$^{64}\text{Cu}$  PSMA.** When labelled with  $^{64}\text{Cu}$ , the same radiopharmaceutical is useful for diagnosis and also for therapy: a true theragnostic agent
- **$^{177}\text{Lu}$  PSMA.** Trials are starting on PSMA labelled with  $^{177}\text{Lu}$  as a therapeutic radiopharmaceutical
- **$^{68}\text{Ga}$  Bombesin.** Bombesin-GRP is a 14 amino acid peptide that shows the activity of growth factor on several tumors. Prostate cancer express specific receptors for bombesin. B. can be labelled with  $^{99\text{m}}\text{Tc}$  and also  $^{68}\text{Ga}$  for diagnostic purposes.
- **$^{177}\text{Lu}$  Bombesin.** B. can be labelled with  $^{177}\text{Lu}$  for therapy.

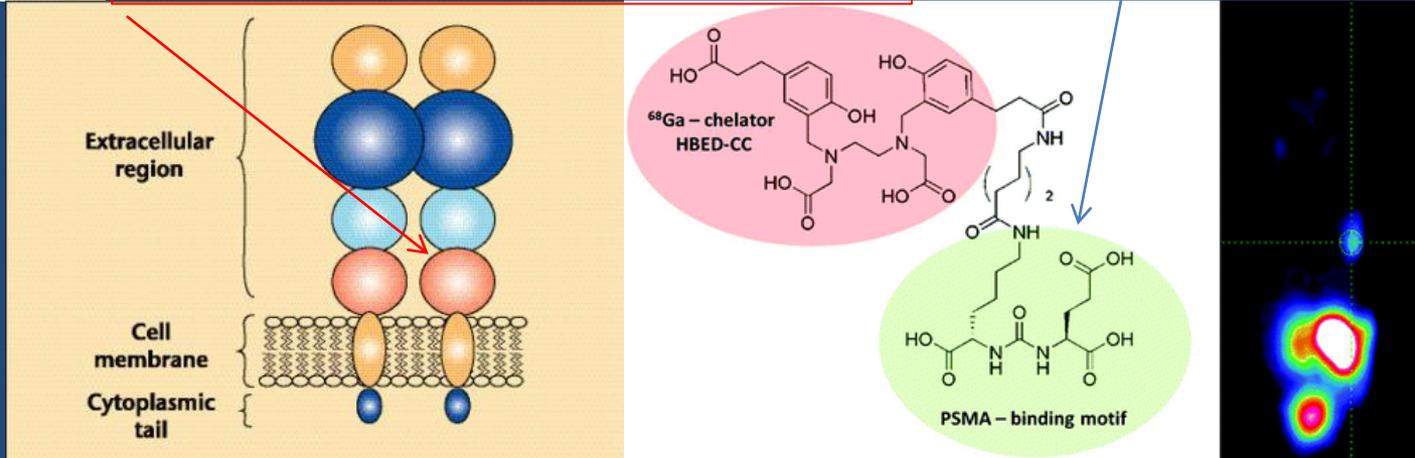
At the moment all these radiopharmaceuticals are experimental

# Need of more sensitive PET radiopharmaceuticals

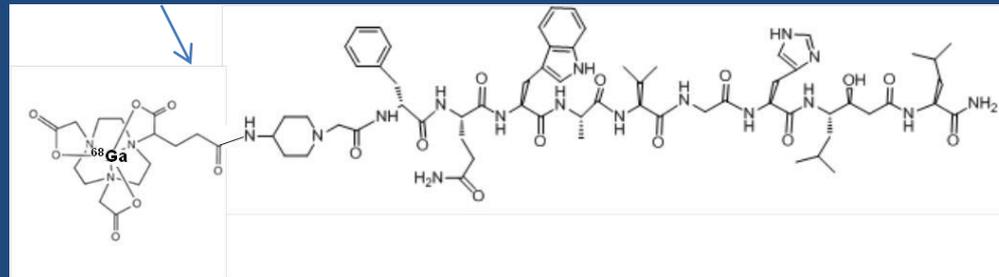


Binds to pharmacophore pocket of PSA

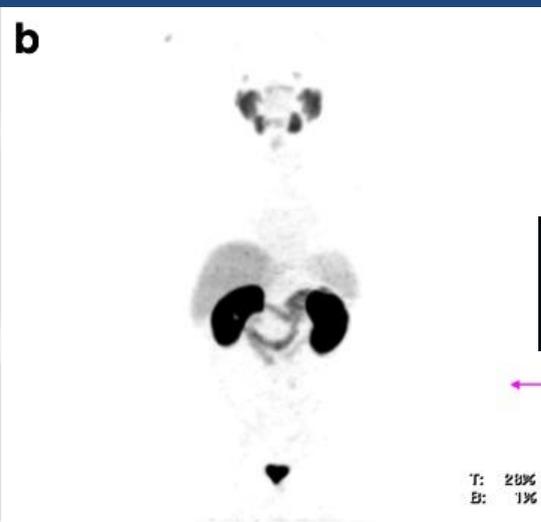
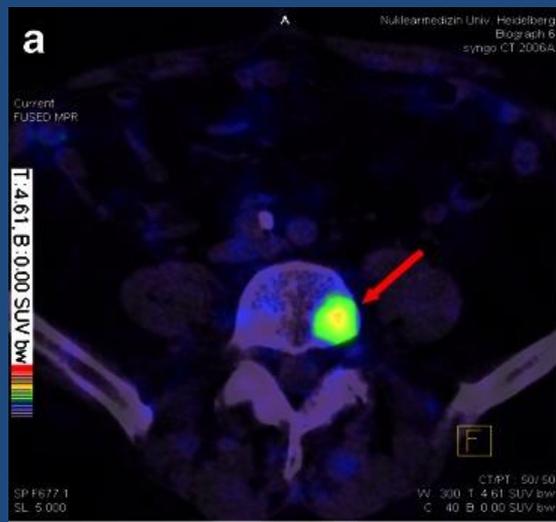
Glu-ureido-lys



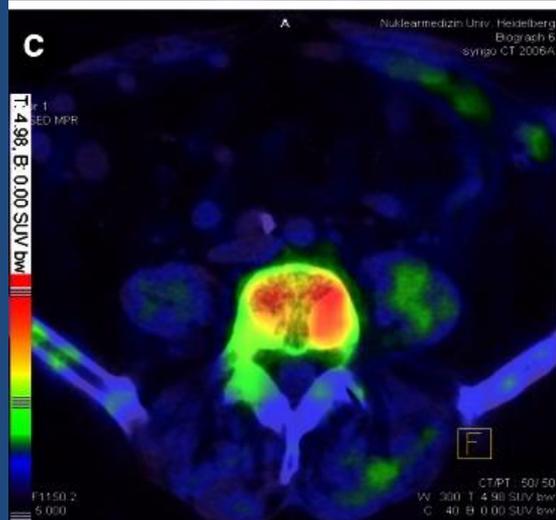
Bombesin: neuro peptide, releasing factor, growth factor.



# $^{68}\text{Ga}$ PSMA is more sensitive than Choline

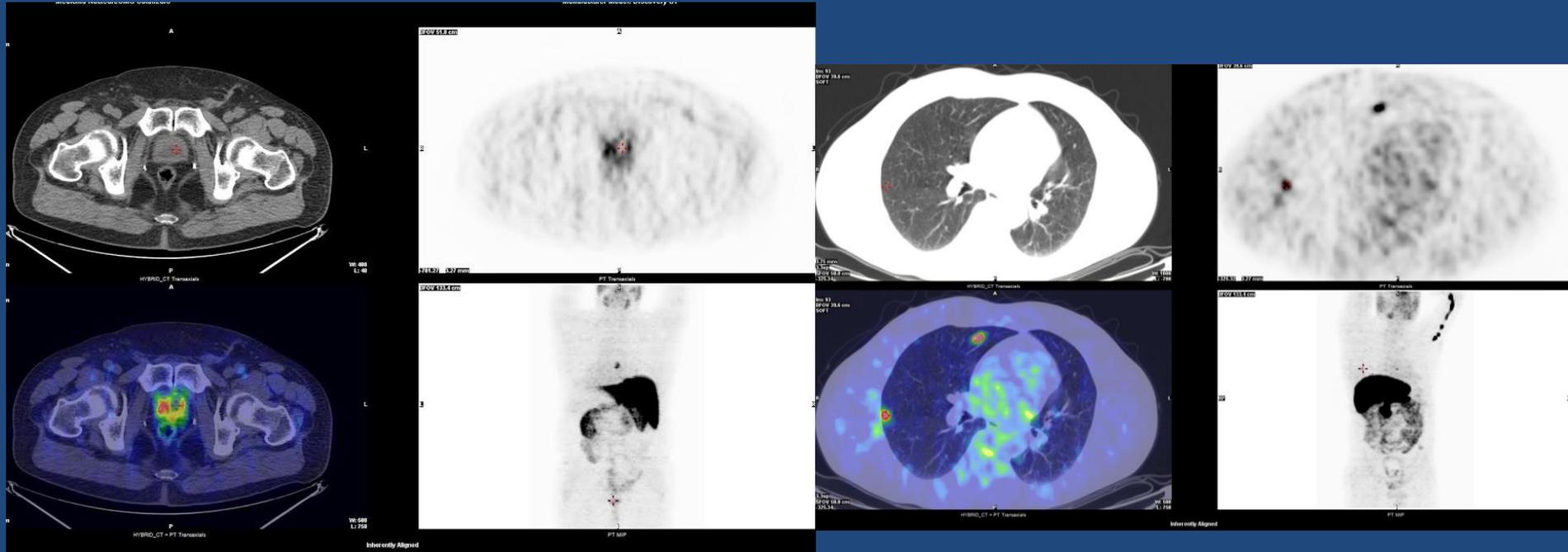


$^{18}\text{F}$  FCH



$^{68}\text{Ga}$  PSMA

# $^{64}\text{Cu}$ PSMA



**Detection and possible cure of occult early metastases missed by Choline**

# Conclusions

Since now, accurately chosen radioisotope therapy can improve the prognosis of hormone-refractory patients with multiple bone metastases

Accurate staging, namely lymph node staging, is important because to-date available radioisotope therapy are very effective, but only on bone met.

Experimental radiopharmaceuticals are very promising: clinical trials with  $^{177}\text{Lu}$ / $^{64}\text{Cu}$  PSMA are already starting .