



LOMA LINDA UNIVERSITY  
MEDICAL CENTER

# Prostate Cancer Biochemical Recurrence: Role of PET/CT

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# Objectives

- Quiz
- Overview of prostate cancer BCR
- PET/CT Radiotracers review for prostate cancer
  - PSMA, Fluciclovine, Choline
- Focus on Fluciclovine vs Choline
  - PSA <2 ng/ml
- Quiz answers

# Quiz

Prostate cancer biochemical recurrence occur in up to what % of patients after definitive therapy?

- A. 10%
- B. 20%
- C. 30%
- D. 40%

# Quiz

Which of the following imaging is considered “usually appropriate” per ACR for detection of prostate cancer biochemical recurrence?

- a. FDG PET/CT
- b. Fluciclovine PET/CT
- c. CT abdomen and pelvis
- d. Bone scan

# Quiz

What is the mechanism of PSMA-ligand?

- a. Synthetic amino acid for peptide transporters
- b. Precursor to phospholipid component of cell membrane
- c. Small molecular inhibitor with subsequent cellular internalization
- d. Molecular that binds to GLUT-1 transporter

# Quiz

Which of the following PET/CT radiotracers have reported higher detection rate in very low post-treatment PSA cohort (PSA <0.5 ng/ml)?

- a. Fluciclovine
- b. Choline
- c. PSMA
- d. FDG

What PET/CT radioligand?

- A. FDG
- B. Fluciclovine
- C. PSMA
- D. Don't know





# Introduction

- BCR occurs in up to 40% of pts
- Conventional imaging (CT/MR) is not sensitive
  - 88% of positive lymph nodes <8 mm (short axis) by PSMA
- PET/CT provides higher sensitivity for oligometastatic disease
- Two current FDA approved PET/CT agents for BCR:
  - F-18 Fluciclovine
  - C-11 Choline

National Comprehensive Cancer Network® ("NCCN") Clinical Practice Guidelines in Oncology for Prostate Cancer (Version 3.2018)

F. L. Giesel et al., Biochemical Recurrence of Prostate Cancer: Initial Results with [J Nucl Med 59, 632-635 (2018).

H. D. Zacho et al., Prospective comparison of. Eur J Nucl Med Mol Imaging, (2018).



# 2018 ACR Appropriateness Criteria

**Variant 1.** Prostate cancer follow-up. Status post radical prostatectomy. Clinical concern for residual or recurrent disease.

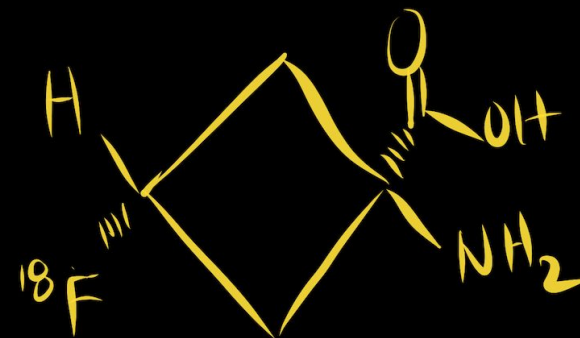
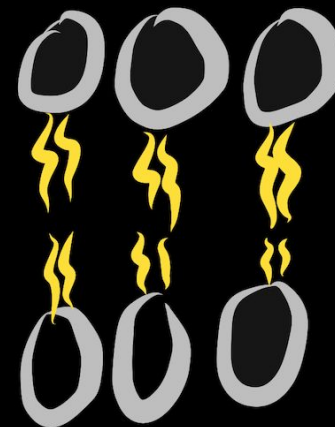
Procedure	Appropriateness Category	Relative Radiation Level
C-11 choline PET/CT skull base to mid-thigh	Usually Appropriate	⊕⊕⊕
MRI pelvis without and with IV contrast	Usually Appropriate	0
F-18 fluciclovine PET/CT skull base to mid-thigh	Usually Appropriate	⊕⊕⊕⊕
CT abdomen and pelvis with IV contrast	May Be Appropriate	⊕⊕⊕⊕
MRI-targeted biopsy prostate	May Be Appropriate	0
Tc-99m bone scan whole body	May Be Appropriate	⊕⊕⊕
TRUS guided biopsy prostate	May Be Appropriate	0
MRI abdomen and pelvis without and with IV contrast	May Be Appropriate (Disagreement)	0

- C-11 choline, MRI pelvis and FACBC appropriate in BCR



# Localization of BCR sites: PET/CT agents

- Choline (both  $^{11}\text{C}$ - and  $^{18}\text{F}$ -choline).
  - Choline  $\rightarrow$  precursor of phospholipid lipid component of cell membrane  $\rightarrow$  Ca  $\uparrow\uparrow$  cell membrane synthesis
  - Detect in pts w/ post-tx PSA  $>2$
  - $^{11}\text{C}$ -Choline FDA approved 2012; NCCN 2014
  
- Fluciclovine
  - Synthetic amino acid  $\rightarrow$  Ca  $\uparrow\uparrow$  peptide transporters
  - More sensitive than choline for PSA  $< 1$
  - $^{18}\text{F}$ -Fluciclovine FDA approved 2016; NCCN + ACR 2018



# C-11 choline and F-18 Fluciclovine

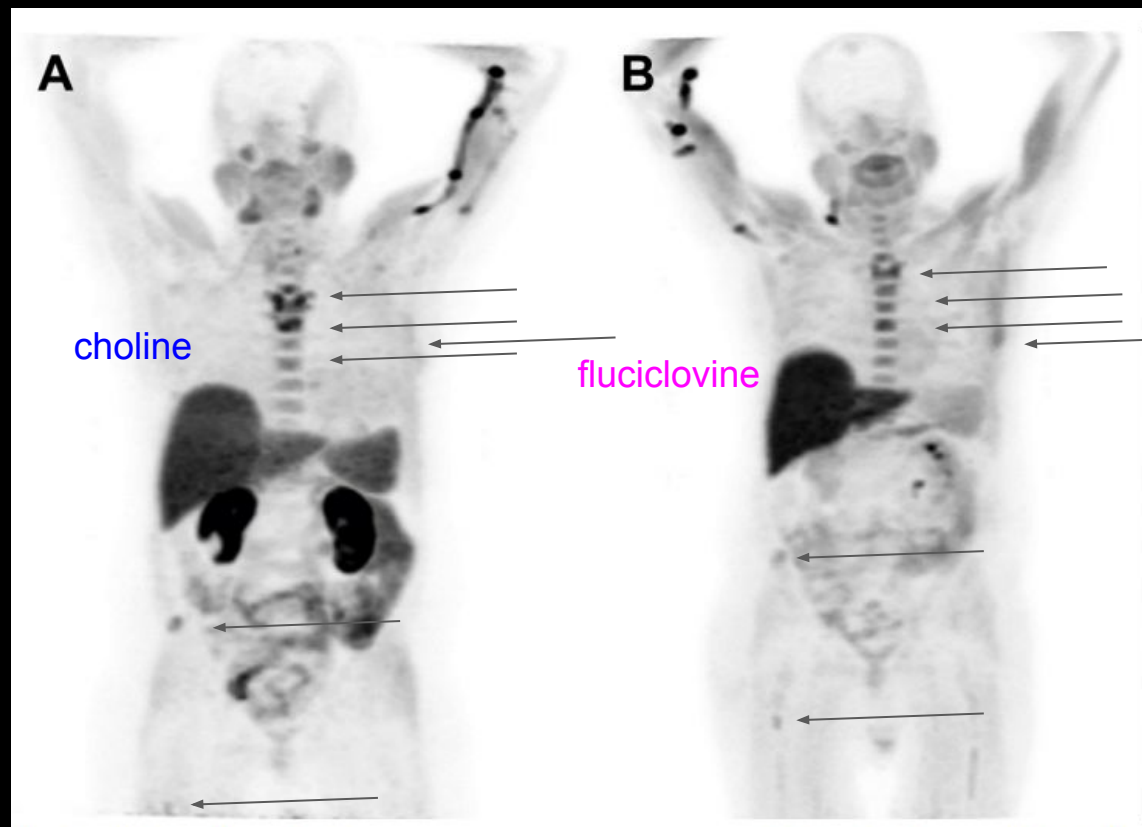
Post-prostatectomy,  
biochemical recurrence  
PSA 15

Choline (A)

Fluciclovine (B)

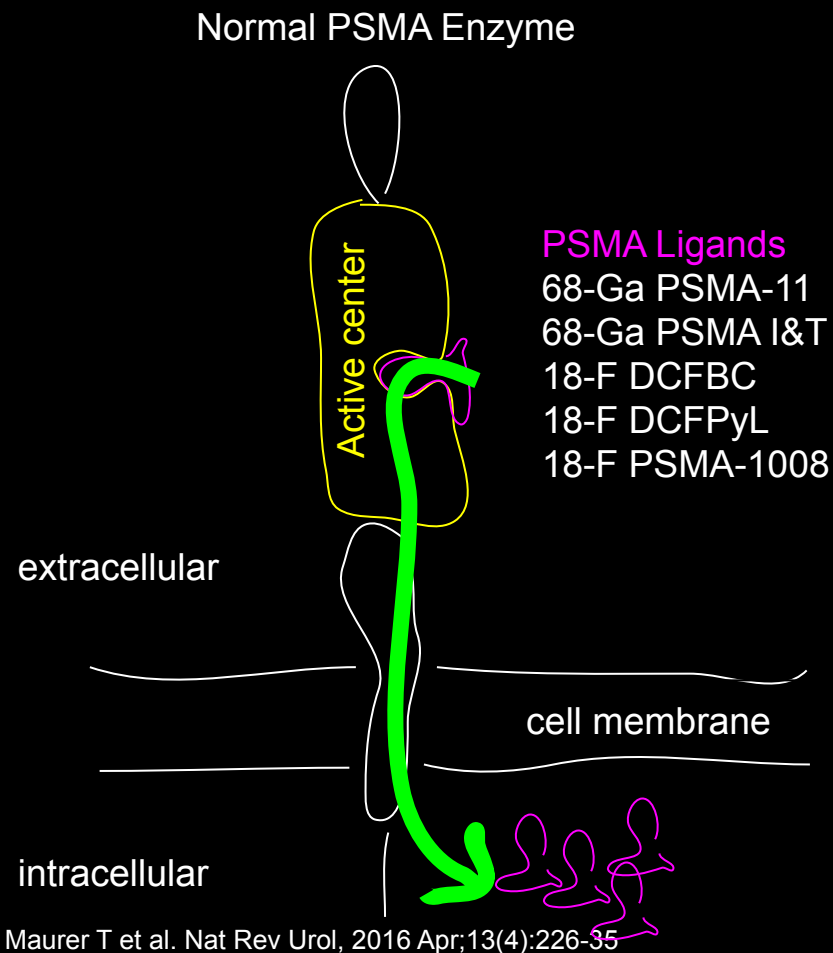
Same focal uptake in  
mets

Different distribution



# PSMA Ligands PET/CT

- **PSMA-targeted radioligands** are **small-molecular inhibitors**
- Compared to antibodies, these have rapid binding with **internalization** and rapid plasma clearance resulting in **high tumour-to-background contrast**
- PSMA ligands can be labelled either positron emitter radioisotopes Ga-68 or F-18



# PSMA



Lacrimal

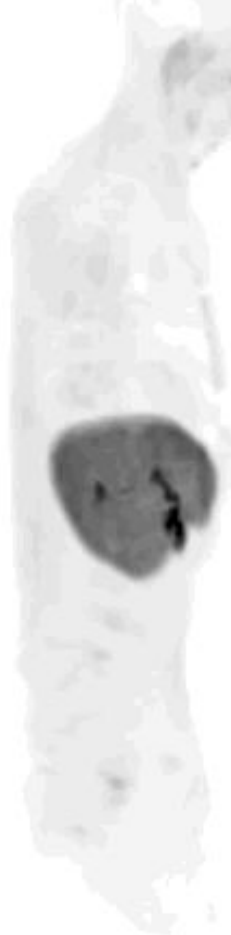
Parotid/ submandibular  
gland

Renal uptake

Small  
intestines/duodenum

Rectum

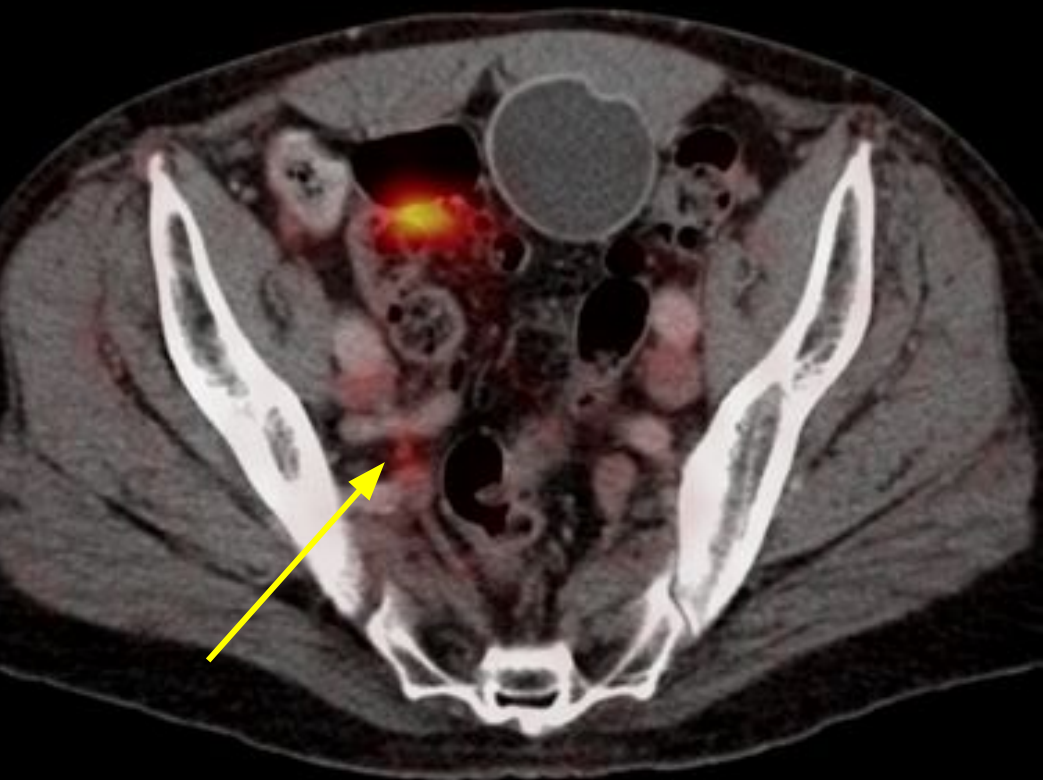
# Fluciclovine



Liver

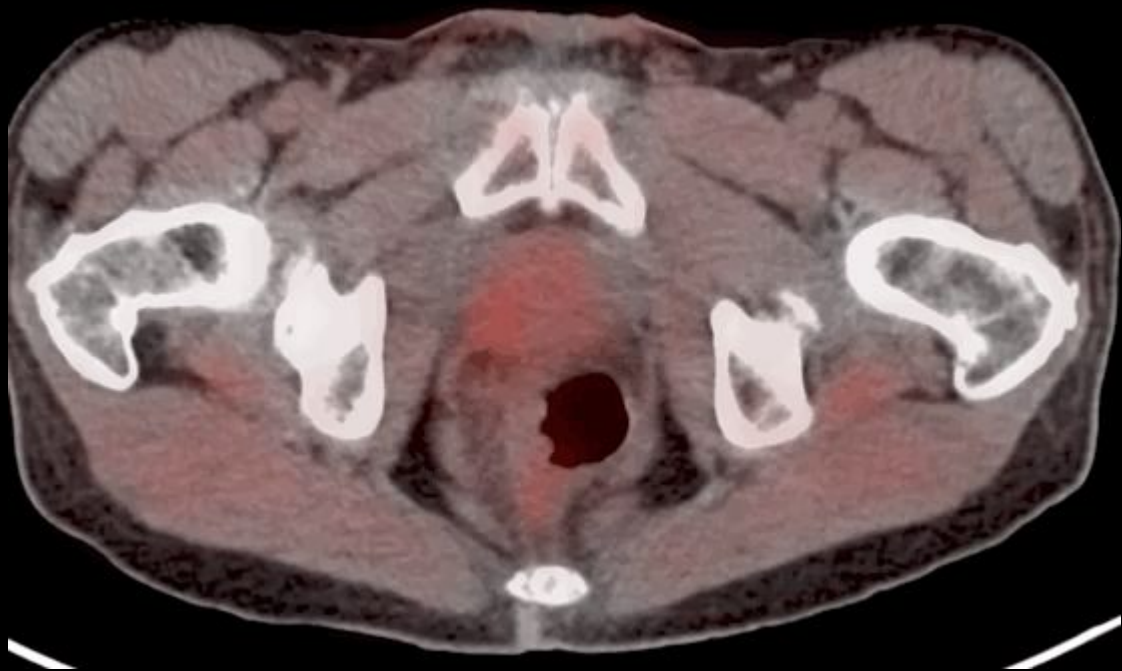
Pancreas

PMSA post-RP PSA 0.2 ng/ml



Right 3 mm internal iliac  
lymph node (sub-threshold  
by CT)

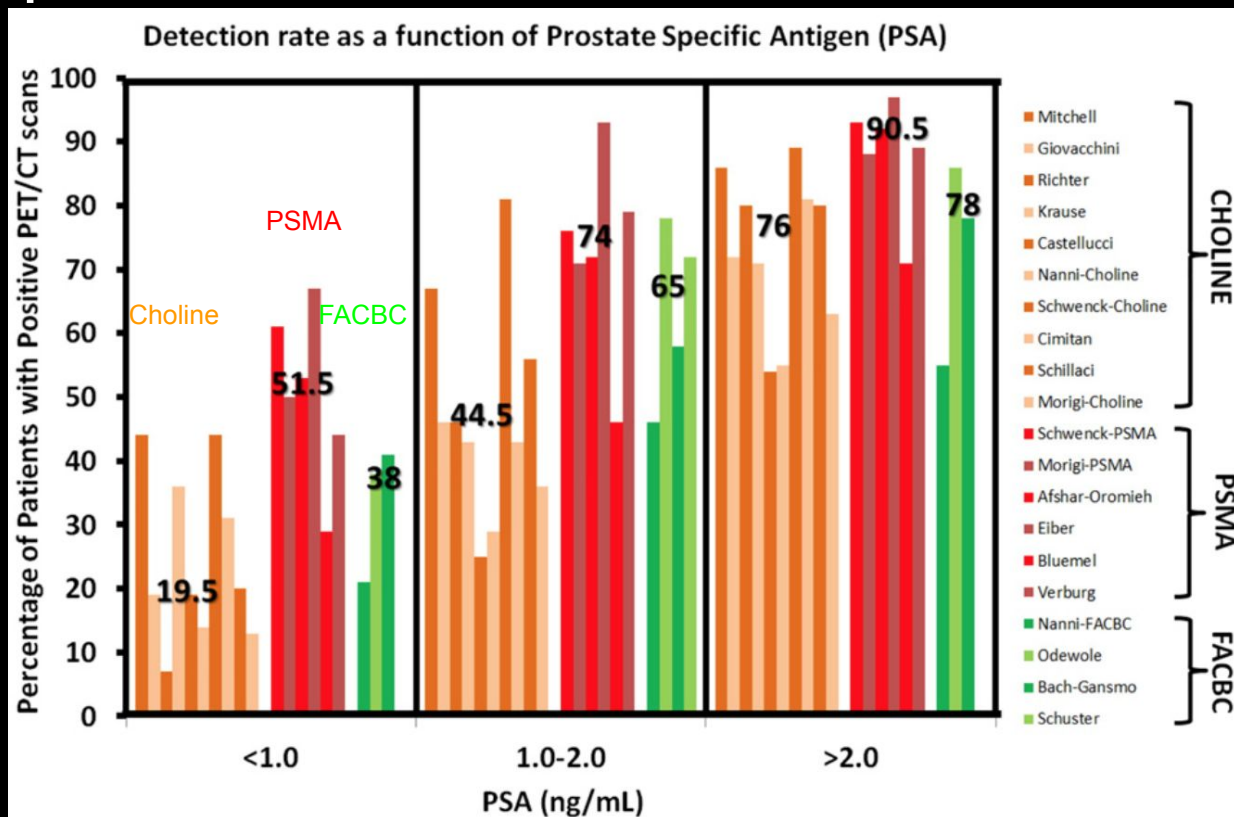
Post-XRT. PSA 1.8 ng/ml



- Recurrence in prostate

# BCR Detection vs post-treatment PSA levels

- **Green:** FACBC
- **Red:** PSMA
- **Orange :** Choline
- PSA <1.0
  - **PSMA > FACBC > Choline**
- PSA 1-2
  - **PSMA ~ FACBC > Choline**
- PSA >2
  - **PSMA > FACBC > Choline**
- No data for <0.5

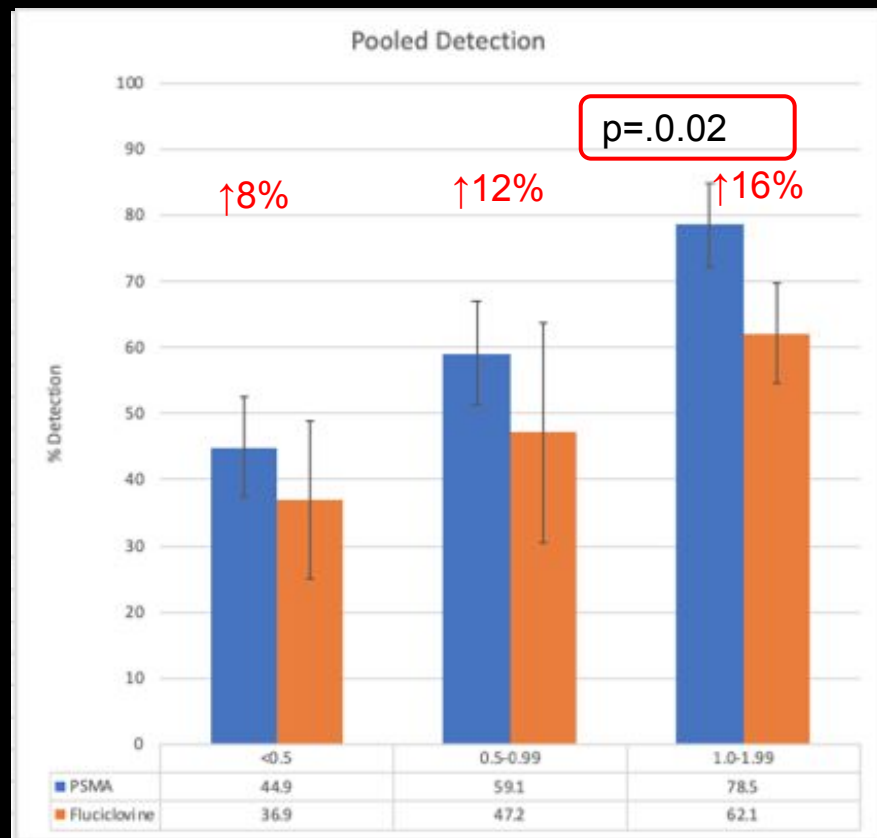






# PSMA vs Fluciclovine: post-treatment PSA < 2

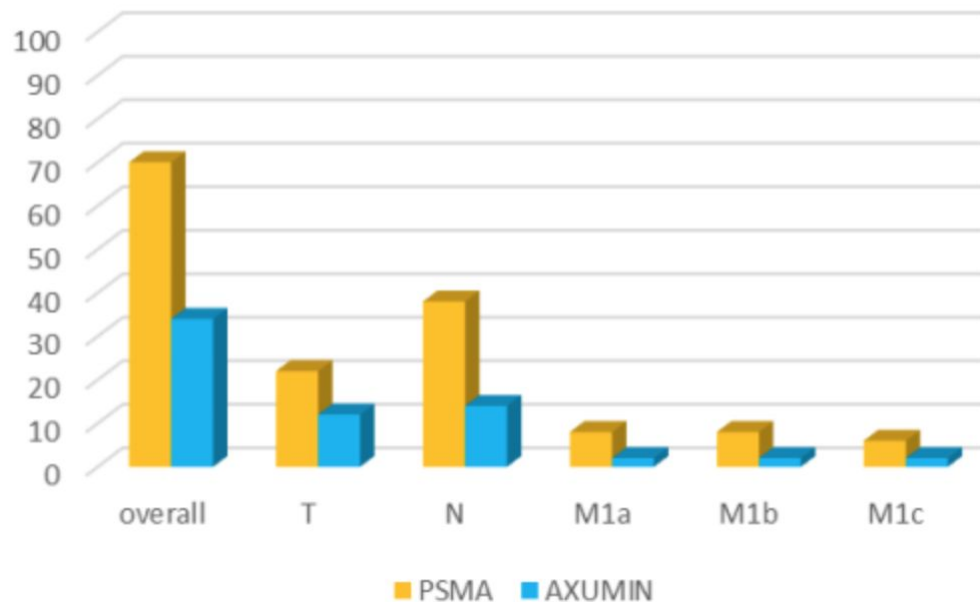
- *Meta-analysis per-patient* detection
  - n=30 PSMA, n=5 FACBC
- Meaningful but not significant per-pt detection btw PSMA & Fluciclovine due to limited data in latter
  - PSA <0.5: 45 vs 37% (8% ↑ PSMA)
  - PSA 0.5-1: 59 vs 47% (12% ↑PSMA)
- Significant difference in detection for PSA
  - PSA 1.0-1.9=78 vs 62% (16% ↑PSMA)



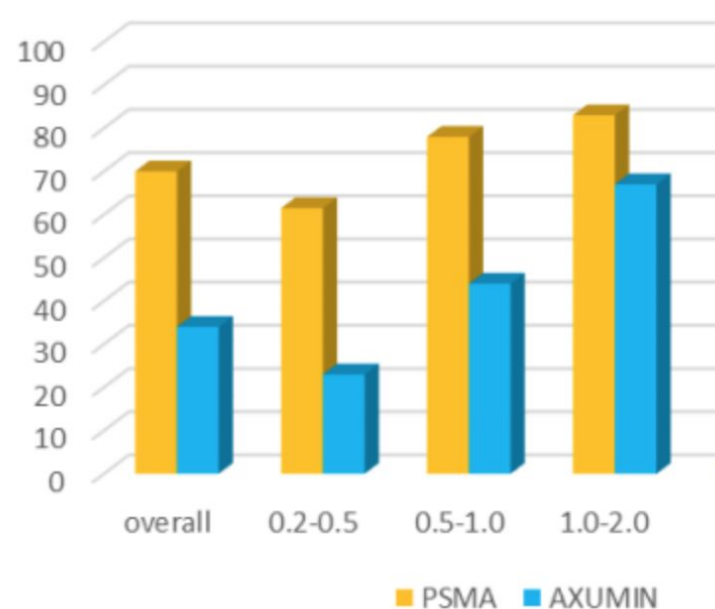


# RCT FACBC vs PSMA in Post- tx PSA<2

Detection Rate per Region (%)



Detection Rate per PSA (%)



50 pts underwent both FACBC and PSMA. **Higher per-lesion and per-patient detection across tiers**

## Quiz answer

Prostate cancer biochemical recurrence occur in up to what % of patients after definitive therapy?

- A. 10%
- B. 20%
- C. 30%
- D. 40%**

Explanation: Biochemical recurrence of prostate cancer (PCa) after definitive therapy can occur within 10 years in up to 25-41% of patients after radical prostatectomy (RP) and in up to 20-39% of patients after definitive radiotherapy

## Quiz answer

Per 2018 ACR Appropriateness Criteria, which of the following imaging is considered “usually appropriate” for detection of prostate cancer biochemical recurrence?

- a. F-18 FDG PET/CT
- b. F-18 Fluciclovine PET/CT**
- c. CT abdomen and pelvis
- d. Bone scan

Explanation: F-19 Fluciclovine, C-11 Choline and MR pelvis are considered “usually appropriate” for the detection of prostate cancer biochemical recurrence

## Quiz answer

What is the mechanism of PSMA-ligand?

- a. Synthetic amino acid for peptide transporters
- b. Precursor to phospholipid component of cell membrane
- c. **Small molecular inhibitor with subsequent cellular internalization**
- d. Molecular that binds to GLUT-1 transporter

Explanation: PSMA-ligand is a small molecular inhibitor of PSMA active center which is subsequently internalized resulting in high tumor or background ratio. Fluciclovine is a synthetic amino acid. Choline is a precursor to phospholipid component of cell membrane. FDG is a glucose analog that binds to GLUT-1 transporter

## Quiz answer

Which of the following PET/CT radiotracers have reported detections in very low post-treatment PSA cohort (PSA <0.5 ng/ml)?

- a. Fluciclovine
- b. Choline
- c. PSMA**
- d. FDG

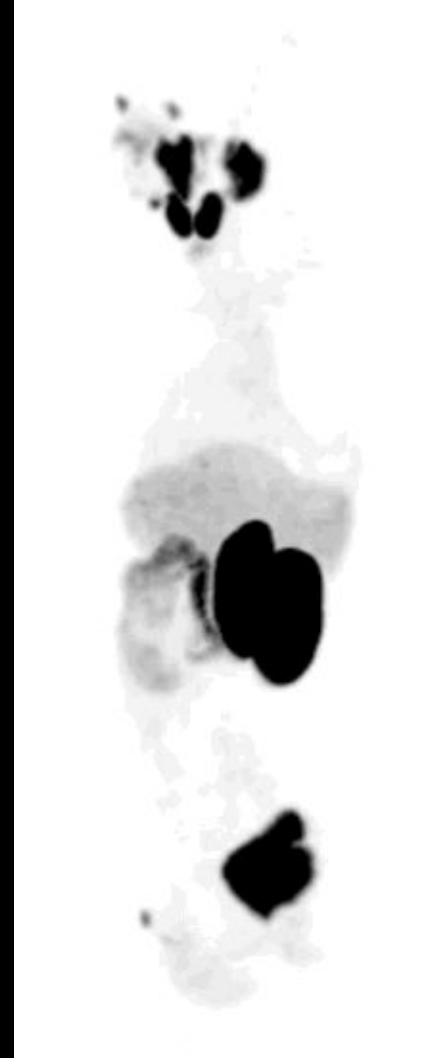
Explanation: In the available literature, PSMA radiotracer is the only agent that detect metastatic and locally recurrent prostate cancer in patients with very low PSA (<0.5 ng/ml).

# What PET/CT radioligand?

- A. FDG
- B. Fluciclovine
- C. PSMA**
- D. Don't know

Explanation:

PSMA has lacrimal, parotid and submandibular glands, renal, duodenum, rectum.



# Summary

- PET/CT in prostate cancer biochemical recurrence
- Current approved agents: FACBC, Choline
- In the pipeline: PSMA