Prostate Cancer Imaging with F-18 Fluciclovine (Axumin)

SWC – SNMMI 2019 – Arlington, TX

Daniella F. Pinho, M.D.
Assistant Professor
Abdominal Imaging and Nuclear Medicine Divisions
UT Southwestern Medical Center, Dallas, TX
- Nothing to disclosure
Educational Objectives

1. Discuss the indications of 18F-Fluciclovine PET/CT and why it is useful in prostate cancer

2. Study interpretation, physiologic uptake, pitfalls and overall performance

3. Present the most useful report to the requesting physician
Overview of Prostate Cancer
Prostate cancer

- Most common malignancy in men
  - US - 2018
    - ~ 165,000 new cases
    - ~ 29,000 deaths

“benign” microscopic, well-differentiated

invasive cancer - metastases, morbidity, and death

Prostate cancer

Initial treatment

- Patient’s medical condition
- Anatomic extension
- Histologic grade
- Serum PSA
- Potential complications with treatment
- Estimated outcome
Prostate cancer - treatment

- Observation
- Active surveillance
- Radical prostatectomy
- Radiation Therapy
  - Brachytherapy
  - External beam – photons / protons
- Cryotherapy
- HIFU
- Androgen deprivation therapy
- Multimodality therapy
Biochemical recurrence
Prostate cancer – biochemical recurrence

- NCCN guidelines – PSA q 6/12 months (5 years), yearly

- Biochemical recurrence:
  - Radical prostatectomy
    - PSA ≥0.2 ng/mL (x 2)
  - Radiation therapy (Decline in PSA → nadir 18 months)
    - PSA ↑ 2 ng/mL or more above nadir

Cookson MS et al. J Urol. 2007;177(2):540
Prostate cancer – recurrence evaluation

- Site and extent of recurrent disease

Local recurrence/pelvic lymph nodes

Distant metastasis

Systemic therapy (androgen deprivation therapy)

Observation

↑ morbidity

Salvage local treatment
Prostate cancer – recurrence evaluation

- Bone scan
  - If PSA < 10 ng/mL – positivity rate of 4%

- CT
  - Positive bone scan in 14% patients (higher PSA and doubling time)

- MRI
  - No established role for local recurrence detection

Kane CJ et al. Urology 2003; 61(3):607

Image c/o Dr. Daniel Costa
18F-Fluciclovine

- 18F-fluciclovine (anti-1-amino-3-F-18-flurocyclobutane-1-carboxylic acid - FACBC)
  - Non-naturally occurring amino acid analogue
  - ASCT2 and LAT1
  - Influx and efflux of amino acid – peak tumor uptake: 5 to 20 min
- Initial studies for cerebral glioma
- Incidental finding of avid retroperitoneal lymphadenopathy in patient with prostate cancer

FDA approval May 2016 – suspected prostate cancer recurrence in patients with elevated PSA following treatment
Question #1

18F-Fluciclovine PET/CT is indicated:

A. For all patients with biopsy proven prostate cancer.
B. After definitive treatment for prostate cancer with undetectable PSA levels.
C. For biochemical recurrence (serum PSA > 10 ng/mL, two measurements) after radiation therapy.
D. For biochemical recurrence (serum PSA > 0.2 ng/mL, two measurements) after prostatectomy.

18F-Fluciclovine PET/CT is indicated:
A. For all patients with biopsy proven prostate cancer.
B. After definitive treatment for prostate cancer with undetectable PSA levels.
C. For biochemical recurrence (serum PSA > 10 ng/mL, two measurements) after radiation therapy.
D. For biochemical recurrence (serum PSA > 0.2 ng/mL, two measurements) after prostatectomy.

The only current FDA approved indication for 18F-Fluciclovine PET/CT is biochemical recurrence:
- After radical prostatectomy - PSA level of at least 0.2 ng/mL, followed by a confirmatory PSA level of at least 0.2 ng/mL
- After radiation therapy - rise in PSA levels of 2 ng/mL or more above the nadir, regardless of the type of radiation therapy

Properties and kinetics
18F-Fluciclovine - kinetics

Imaging protocol
Patient preparation / Imaging Protocol

- 4h fasting / avoid heavy exercise
- Gastrointestinal contrast (450 mL of Barium)
- Void 15-30 minutes before scanning
- Dose 10 mCi/370 MBq IV bolus + 20-30 mL saline flush
- Right arm (avoid stasis in the left axillary vein)
Physiologic distribution
Physiologic distribution

- **Intense uptake:**
  - Pancreas (↑↑↑), Liver (↑↑)

- **Mild to moderate:**
  - Salivary glands and pituitary

- **Mild to moderate, variable:**
  - Bowel and bone marrow

- **Muscle - no significant uptake early, increase uptake with time**

- **Minimal renal excretion, small activity in the bladder can be seen (5-10% of patients)**
Muscular uptake

Normal distribution
Venous uptake
Question #2

In regards to the physiologic distribution and imaging acquisition of 18F-Fluciclovine

A. Moderate to high uptake is seen in the brain.
B. Commonly seen renal excretion with radiotracer accumulation in the bladder limits evaluation of the pelvic region.
C. Most intense uptake is seen in the pancreas followed by the liver.
D. Images are acquired after a standard uptake time of 60 - 90 minutes after radiotracer injection.

In regards to the physiologic distribution and imaging acquisition of 18F-Fluciclovine:

A. Moderate to high uptake is seen in the brain.
   Incorrect. There is no significant accumulation of 18F-Fluciclovine in the brain.

B. Early renal excretion with radiotracer accumulation in the bladder limits evaluation of the pelvic region.
   Incorrect. There is minimal renal excretion, in a degree that usually does not interfere with interpretation.

C. Most intense uptake is seen in the pancreas followed by the liver.
   Correct.

D. Images are acquired after a standard uptake time of 60 - 90 minutes after radiotracer injection.
   Incorrect. Uptake time is between 3-5 min (acquisition is immediately after injection).

Interpretation Criteria
Interpretation criteria

- Prostate / Prostate bed / lymph nodes (typical sites)
  - Focal uptake, visually = or > bone marrow (L3)

57 y/o prostatectomy (2010), salvage radiation (2013), ↑ PSA (5.85)
Interpretation criteria

- Prostate sparing therapies - limited evaluation of local recurrence:
  - Post treatment related uptake – usually lower, more diffuse
  - Local recurrence – usually higher, more focal uptake

- Better performance after prostatectomy
Interpretation criteria

Post treatment related

UPTAKE:
Low Diffuse

Recurrence

UPTAKE:
High Focal
73 y/o, prostatectomy, PSA 1.0

Recurrence at the prostatectomy bed
Interpretation criteria

- Focus <1 cm - suspicious if visually > blood pool

PSA 0.46

6 months later - PSA 7.94
Interpretation criteria

- Lymph nodes – atypical sites (inguinal, distal external iliac, hilar and axillary nodes)
  - Mild, symmetric uptake = physiologic
  - if + other clear malignant disease = suspicious

Physiologic uptake inguinal nodes
Interpretation criteria

- **Bone**
  - Focal uptake MIP / PET-only images = suspicious for cancer.
  - Bone abnormality visualized on CT (dense sclerosis without uptake):
    - Does NOT exclude metastasis
    - Additional imaging - MR, NaF PET-CT, bone scan (SPECT-CT)
Metastatic bone lesion
Question #3

For the interpretation criteria of 18F-fluciclovine studies:

A. Sclerotic bone lesions with no 18F-fluciclovine uptake are definitely benign.

B. For the lesions smaller than 1 cm, SUV max should be higher than 3 to be considered a suspicious lesion.

C. Uptake in the inguinal lymph nodes is always suspicious for metastasis.

D. Focal uptake, visually equal to or greater than bone marrow (L3), in sites typical for prostate cancer recurrence are suspicious for cancer.

For the interpretation criteria of 18F-fluciclovine studies:

A. Sclerotic bone lesions with no 18F-fluciclovine uptake are definitely benign.
   Incorrect. 18F-fluciclovine uptake in metastatic sclerotic bone lesion is usually low.

B. For the lesions smaller than 1 cm, SUV max should be higher than 3 to be considered a suspicious lesion.
   Incorrect. if a focus of uptake is small (<1 cm) it is considered suspicious if the uptake is visually greater than blood pool.

C. Uptake in the inguinal lymph nodes is always suspicious for metastasis.
   Incorrect. Mild benign symmetric uptake within the inguinal lymph nodes may be seen and should not be called positive unless “disease pattern marching out of pelvis.”

D. Focal uptake, visually equal to or greater than bone marrow (L3), in sites typical for prostate cancer recurrence suspicious for cancer recurrence.
   Correct.

Performance
Performance

- **Overall** detection rate ~ 70%
- Detection rate **PSA < 1 ng/mL** ~ 40%
  - local and pelvic LN > distant
- **Prostate / bed**
  - Great sensitivity ~ 90%
  - Moderate specificity ~40-60%
- **Overall NPV** ~ 50-70%
- **Overall PPV** ↑↑ (~90%)
  - extraprostatic > prostate/bed

Schuster DM et al. (J Urol. 2014)
England, JR et al. (Clin Nucl Med 2019)
Odewole et al. (Eur J Nucl Med Mol Imaging 2016)
England, JR et al. (Clin Nucl Med 2019)
Performance – compared to CT

- ↑↑↑ Positivity rate
  - Fluciclovine 77% x CT 19%

- ↑↑ Sensitivity
  - Prostate/bed – Fluciclovine 89% x CT 11%
  - Extraprostatic – Fluciclovine 46% x CT 11%

- ↑↑ NPV
  - Prostate/bed – Fluciclovine 69% x CT 31%
  - Extraprostatic – Fluciclovine 52% x CT 39%

Odewole et al. (Eur J Nucl Med Mol Imaging 2016)
74 y/o, prostatectomy

PSA 0.27 ng/mL

MRI prostate no evidence of disease

Salvage radiation therapy to prostatic bed

4 months later

PSA 0.48 ng/mL

Radiation to LN

PSA from 0.83 to 0.08
Performance – bone lesions

- Lack of data for bone lesions
  - Intense uptake in lytic mets
  - Moderate uptake in mixed sclerotic lesions
  - Absent uptake in dense sclerotic lesions

- Additional imaging - MR, NaF PET-CT, bone scan (SPECT-CT) is sclerotic lesions with NO uptake
70 y/o, prostatectomy, PSA 0.6 ng/mL

Metastatic prostate cancer
Question #4

In regards of detection of bone lesions by 18F-Fluciclovine PET/CT in patients with prostate cancer:

A. Has very high sensitivity but low specificity.
B. Intense uptake is seen in lytic lesions.
C. Has replaced completely dedicated bone scans due to better performance for detection of bone lesions.
D. A bone lesion with SUV max of 2.5-3 or more is suspicious for malignancy.

In regards of detection of bone lesions by 18F-Fluciclovine PET/CT in patients with prostate cancer:

A. Has very high sensitivity for bone lesion detection.
   Incorrect. The sensitivity is low for sclerotic lesions.

B. Intense uptake is seen in lytic lesions.
   Correct.

C. Has replaced completely dedicated bone scans due to better performance for detection of bone lesions.
   Incorrect. Hasn’t replaced conventional bone scan. A bone scan should be performed if there is a suspicious sclerotic lesion on CT, even if there is no 18F-Fluciclovine uptake.

D. A bone lesion with SUV max of 2.5-3 or more is suspicious for malignancy.
   Incorrect. The interpretation criteria for bone lesions is focal uptake clearly visualized on MIP of PET-only images, not based on SUVmax.

Fluciclovine for initial staging

- Not FDA approved indication
- Limited data - may have some utility as
  - adjunct to MP-MRI– high-risk patients
    - LN mets : ↑ specificity; ↓ sensitivity
    - ↑ sens primary prostate cancer combined (~82%)
- to help guide biopsy

Selnaes KM et al. Eur Radiol 2018
Türkbey, B., et al. (2014)
86 y/o, initial staging, high risk, Gleason 4+5, PSA 21.25
Impact on therapy management

  - 42 prostatectomy patients
  - Radiotherapy decisions changed in 40.5% of subjects

- LOCATE trial – Andriole GL et al (J Urol 2019)
  - 213 subjects
  - 57% detection rate
  - 59% change in management after scan
    - Salvage or non-curative to watchful waiting – 25%
    - Non-curative systemic to salvage – 24%
    - Salvage to non-curative systemic – 9%
Pitfalls
Differential diagnosis / pitfalls

- **Prostate**
  - Inflammatory changes, BPH

- **Extraprostatic**
  - Other cancers (upregulated amino acid transport)
  - Nodal inflammation (mild, symmetric, atypical locations)
  - Bone lesions (osteoid osteoma)
  - Meningioma
Meningioma
Question #5

Which of the following can have false positive uptake with 18F-fluciclovine:

A. Degenerative bone changes
B. Meningioma
C. Bone island
D. Post radiation changes in the bone marrow

Question #5

Which of the following can have false positive uptake with 18F-fluciclovine:

A. Degenerative bone changes  
B. Meningioma  
C. Bone island  
D. Post radiation changes in the bone marrow

Meningioma is the only one of this list that can have false positive uptake in 18F-fluciclovine studies.

Atypical presentations
Mediastinal lymph node
Abdominal wall lesion
Other PET tracers for prostate cancer
Other PET tracers for prostate cancer

- C-11 choline (half-life 20.4 min)
  - Fluciclovine has similar/slightly better performance
  - Also – easier production, longer half-life, lower background activity
- Ga-68 PSMA
  - Attach to the extracellular domain of PSMA transmembrane protein
  - Superior detection – lower PSA levels
How to report
Case #1

- 58 y/o, prostatectomy, ↑ PSA (6.9)

- Typical location
- Uptake >> bone marrow

- IMPRESSION: Fluciclovine avid periaortic lymph node suspicious for metastatic disease
Case #2

- 62 y/o, prostatectomy, ↑ PSA (1.2)

- Atypical location
- Uptake ≥ blood pool

- IMPRESSION: Mildly avid non-enlarged fluciclovine lymph node in the distal left external iliac chain, favors benign / reactive etiology.

Bx – negative for metastatic disease
Case #3

- 84 y/o post radiation therapy, PSA 23.41

- Atypical location
- Uptake ≥ bone marrow
- ???

IMPRESSSION: Fluciclovine avid prostatic lesion, multiple pelvic and retroperitoneal lymph nodes and left supraclavicular lymph node, consistent with malignancy.
Case #3

- 75 y/o, prostatectomy, ADT, ↑ PSA

- Very atypical location for metastasis
- Uptake ≥ bone marrow

- IMPRESSION: Diffuse uptake in the esophagus, may be related to esophagitis, recommended clinical correlation.
Case #4

- 79 y/o, prostatectomy, ↑ PSA

- Typical location (prostatectomy bed)
- Uptake ≥ bone marrow
- * NO bladder activity

- IMPRESSION: Focal increased fluciclovine uptake in the left prostatectomy bed (anastomosis), suspicious for local recurrence.
Case #5

- 80 y/o, prostatectomy, PSA 8.7

- Bone sclerosis
- Uptake ≥ bone marrow

IMPRESSSION: Sclerotic lesion in the right iliac bone with peripheral increased fluciclovine uptake, suspicious for metastatic disease
Summary – F18-Fluciclovine (Axumin)

- Suspected prostate cancer recurrence in patients with elevated PSA following treatment
- Better performance compared to conventional imaging; great impact on management
- Early acquisition (3-5 min), ↑↑ pancreas
- Qualitative evaluation, visually = or > bone marrow (L3)
  (<1 cm - suspicious if visually > blood pool)
- Sclerotic bone lesions with NO uptake – further evaluation
- Atypical findings, pitfalls
Thank you!

daniella.pinho@utsouthwestern.edu