Early Clinical Experience Utilizing 18F-Fluciclovine For The Detection Of Recurrent Prostate Cancer

D. Chase Rogers MD
Michel-Alexis R. Courtines MD
Daniel H. Duffy MD

Audie L. Murphy Memorial VA Hospital
**Background**

Prostate carcinoma is the most common new cancer diagnosis for men in the United States and accounts for 8% of deaths. Men have a 1 in 8 odds of being diagnosed with prostate cancer in their lifetime.

**Most common non-cutaneous cancer in men**

Definitive treatments include surgical resection and radiation therapy.

**Prostate cancer reccurs in 1 out of every 3 treated men.**

Surveillance is limited to biochemical monitoring, CT and MR anatomic imaging, bone scan, and Prostascint scan.

**Therapy for recurrent disease can be modified based on disease location.**
18F-Fluciclivone

In May 2016 the FDA approved 18F-Fluciclivone or anti-1-amino-3-18F-fluorocyclobutane-1-carboxylic acid (FACBC) for the detection of recurrent prostate cancer.

L-Leucine is an amino acid analogue that is absorbed by upregulated cells, however not utilized or incorporated into proteins resulting in increased localization.

Activly transported into both cells expressing prostate-specific membrane antigen (PSMA) and non-expressing tumor cells.

Amino acid transporters ASCT2 and LAT1
PSA levels

FACBC permits localization of disease that modifies therapy.

If the PSA is below 1.78, sensitivity decreases

First case at ALM VA Hospital

Radical prostatectomy, Gleason 7 negative nodes with extracapsular extension 9 months prior

April PSA was 0.06 with increase to 1.8 in November.

Results – No abnormal focus. NEGATIVE
Second Case

PSA 2.8
Prostatectomy with non-zero PSA nadir

Focal uptake is concerning for recurrent or residual disease. No abnormal extra-prostatic uptake.
Normal biodistribution

Most avid in the pancreas with moderate to intense uptake in the liver

Moderate salivary and pituitary uptake

Variable bowel uptake

Brain and lung have low uptake less than blood pool

Moderate bone and muscle uptake that varies with time, muscle increasing and bone decreasing.

Low renal excretion

Variable uptake in inflammatory processes and metabolically active bone lesions
Lower PSA levels

Case 18
XRT now with PSA rising to 2.4

Negative
Low PSA levels

Case 17
PSA 1.8
XRT 2 years prior

Right 11 mm external iliac node
Sensitivity

Overall positivity 85% (17/20)

100% (3/3) sensitivity for unresected biopsy proven primary disease

82% sensitivity in cases of biochemical recurrence (14/17)

Only one case was negative with PSA above 2.5, a 93% sensitivity (14/15)

Sensitivity dropped to 60% at a PSA below 2.5 (3/5)

PSA below 2 was 66% (2/3) above 88% (15/17)
Lowest PSA Tested

PSA 1.2

Left pelvic node
Just above blood pool
The original researchers report

- Efficacy of FACBC initially evaluated by Emory University
- 105 F18-FACBC PET/CT scans compared against histopathologic data
- Interpreted by 3 blinded independent readers.
- Detection rate 60% PSA for <1.78
- Detection rate 80% PSA for >1.78
- <10% extra-prostatic false positive rate

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BPH vs Prostate CA

Primary disease evaluation is limited due to benign hypertrophic disease taking up the radiotracer.
Case 5 – (Left)
PSA 11.5 biopsy proven CA, concerning nodes on CT.

demonstrated the extent of disease and helped him choose XRT over surgery.

Case 7 – (Right)
PSA 35 biopsy proven.

determined XRT and dose for local nodes instead of chemotherapy for distal nodes.
Screening with CT and Bone scan?

Reccomended screening includes:

CT to exclude abdominal mass greater than 3cm
Bone scan to detect metastatic blastic disease

In ALM VA’s 20 cases:

No masses over 3cm
Nodal disease was suspected but not defined as metastatic on 6/16 studies by CT
Bone scan detected 2/3 bony lesions found by FACBC

Prostatic bed disease in 55% (11/20)
Nodal disease in 50% (10/20)
Locoregional disease 94% (16/17)
Bony disease in 18% (3/17)

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Local recurrence after surgical resection

Signal greater than bone marrow (L3) is consistent with recurrence. If small (<1 cm) greater than blood pool is suspicious.

Case 4 – (Left)
PSA 9.9
RPR with slow rise
2.6 cm prostatic mass

Case 14 – (Right)
PRALP PSA 5.9 and rising.

Recurrent left midline mass
Recurrence after radiation therapy

If asymmetrical and greater than blood pool
If diffuse and greater than bone marrow

Case 9 – (Left)
XRT, PSA of 5.9
Mild local bed recurrence

Case 12 – (Right)
Brachytherapy, PSA 12
Asymmetric focal recurrence
Nodal disease

Midline or asymmetric nodes above blood pool
Mild and symmetric nodes may be reactive

Case 17 – (Left)
XRT, PSA 1.8

Internal iliac nodes

Case 15 – (Right)
PSA 215, biopsy proven.
Surgery vs hormone and radiation therapy.

Extensive nodal disease
Changes of therapy

Recurrent disease is treated by multidisplinary teams consisting of Surgery, Urology, Oncology, Radiation Oncology, and Radiology.

FALCON study in UK terminated early due to efficacy in determining if FACBC changed curitive/salvage therapy. Changes in 62% of patient’s therapy plan.

Salvage therapy consists of radiation, hormone, and chemotherapy.

Local disease can be treated by hormone and radiation therapy.

Localizing disease altered radiation dose and field (ie prostatic bed vs local lymph nodes).

Distant disease was chemo and hormone therapy (XRT no longer an option).

Primary disease with suspected local nodes.
Nodal disease - Lung

Case 11 – (Left) PSA 3.5 PRP, XRT
FACBC inguinal, lung nodules without avid uptake

CT chest 10 days latter

(Right) PET Avid lung and mediastinal nodules

Biopsy Prostate carcinoma
Bony Disease

Focal avidity above L3 marrow or focal visual uptake on MIP imaging

Case 16 – (Right)
PSA 70
Hormone therapy
Eval response...
Diffuse bony disease

Case 10 – (Right)
PSA 54
Negative bone scan
Left iliac nodes
Right iliac bone
Timing and Technique

Non empty bladder (if early excretion dilution will prevent false positives)

Inject while on the table, then arms up

Start CT 1-2 min after injection

Start PET scan bottom to top starting 3-5 min after injection

Decreases chance of renal excretion and muscle uptake

Avoid excessive muscle exercises 24 hours prior

Delayed imaging results in excessive muscle uptake with decreased tumor and nodal uptake.
Conclusions

- FACBC is an effective tool to visualize recurrent biochemically active recurrent prostate cancer.
- Sensitivity increases with good technique and timing
- Our initial overall positivity rate was 85%, and when PSA >2 was 88%, <2 was 66%
- FACBC changed salvage therapy plans
- Small lung nodules which are nonavid may prove to be metastatic disease
- FACBC effective at detection of bony disease that was bone scan negative
- CT screening would not have precluded any FACBC studies


