New Concepts in PET Imaging Prostate Cancer

Leonard G. Gomella, MD
Chairman, Department of Urology
Director Sidney Kimmel Cancer Network
Sidney Kimmel Cancer Center
Thomas Jefferson University
Philadelphia, PA
Imaging Modalities Used for the Evaluation of Prostate Cancer

- Plain X-Ray
- Ultrasound modalities
- CT scan
- $^{99}$Tc Bone scan
- MRI
- **PET**: scans exploit various aspects of cancer metabolism
PET Scans

Prostate cancer avid molecule (acetate, choline, fluciclovine, fluoride, PSMA analogue)

Positron emitting tracer ($^{11}\text{C}$, $^{18}\text{F}$, $^{68}\text{Ga}$)

Fuse with CT or MRI
## PET Imaging Methods in PC

<table>
<thead>
<tr>
<th>Technique</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(^{111})In ProstaScint</strong></td>
<td>Radiolabeled murine monoclonal antibody against intracellular epitope of PSMA</td>
</tr>
<tr>
<td><strong>(^{18})F-FDG</strong></td>
<td>Positron-emitting radiopharmaceutical transported by glucose proteins</td>
</tr>
<tr>
<td><strong>(^{18})F-NaF</strong></td>
<td>Chemisorption occurs with exchange of 18F-ion for OH-ion to form fluoroapatite, which migrates into crystal matrix of bone for recognition via PET scan</td>
</tr>
<tr>
<td><strong>(^{11})C-Na acetate</strong></td>
<td>Uses carbon and acetate to recognize fatty acid synthase upregulated in PC</td>
</tr>
<tr>
<td><strong>(^{11})C-Choline</strong></td>
<td>Recognizes choline kinase overexpressed from cell proliferation in PC</td>
</tr>
<tr>
<td><strong>(^{18})F Fluciclovine</strong></td>
<td>AA based detects upregulated amino acid transport in tumors (Axumin)</td>
</tr>
<tr>
<td><strong>(^{99m})Tc MIP-1404</strong></td>
<td>Radiolabeled to target PSMA extracellular domain</td>
</tr>
<tr>
<td><strong>(^{68})Ga-HBED-CC</strong>&lt;br&gt;<strong>PSMA</strong></td>
<td>Radiolabeled to target PSMA extracellular domain</td>
</tr>
<tr>
<td><strong>(^{18})F CTT1057 PSMA inhibitor</strong></td>
<td>Irreversible binding affinity to PSMA and robust internalization (ASCO 2017)</td>
</tr>
<tr>
<td><strong>(^{64})Cu-TP3805</strong></td>
<td>Targets VPAC-1 receptor</td>
</tr>
<tr>
<td>Tracer</td>
<td>Radionuclide</td>
</tr>
<tr>
<td>------------------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>PSMA</td>
<td>18F</td>
</tr>
<tr>
<td>DCProx</td>
<td>68Ga</td>
</tr>
<tr>
<td>HBED-CC-PSMA (PSMA-11)</td>
<td>68Ga</td>
</tr>
<tr>
<td>J594</td>
<td>89Zr</td>
</tr>
<tr>
<td>IA522M</td>
<td>89Zr</td>
</tr>
<tr>
<td>P26-093</td>
<td>68Ga</td>
</tr>
</tbody>
</table>

**Lipid metabolism**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Radionuclide</th>
<th>Synthesis</th>
<th>Mechanism / Target</th>
<th>Number of not yet recruiting, recruiting, active, invited, or completed clinical trials using the tracer for PCa on clinicaltrials.gov (as of 07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Choline, Fluorocholine, Ethylcholine, Fluoroethylcholine</td>
<td>18F/11C</td>
<td>Cyclotron</td>
<td>Membrane turnover</td>
<td>35</td>
</tr>
<tr>
<td>Acetate</td>
<td>11C</td>
<td>Cyclotron</td>
<td>Lipid synthesis</td>
<td>9</td>
</tr>
</tbody>
</table>

**Nutrient Transport**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Radionuclide</th>
<th>Synthesis</th>
<th>Mechanism / Target</th>
<th>Number of not yet recruiting, recruiting, active, invited, or completed clinical trials using the tracer for PCa on clinicaltrials.gov (as of 07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDG</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Glucose transport</td>
<td>25</td>
</tr>
<tr>
<td>Flucloxacine (FACBC, axumin)</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Amino Acid Transport</td>
<td>13</td>
</tr>
<tr>
<td>MPA/B</td>
<td>11C</td>
<td>Cyclotron</td>
<td>Amino Acid Transport</td>
<td>1</td>
</tr>
<tr>
<td>Methionine</td>
<td>11C</td>
<td>Cyclotron</td>
<td>Amino Acid Transport</td>
<td>1</td>
</tr>
<tr>
<td>Sarcosine</td>
<td>11C</td>
<td>Cyclotron</td>
<td>Amino Acid Transport</td>
<td>1</td>
</tr>
</tbody>
</table>

**GRPR Targeting**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Radionuclide</th>
<th>Synthesis</th>
<th>Mechanism / Target</th>
<th>Number of not yet recruiting, recruiting, active, invited, or completed clinical trials using the tracer for PCa on clinicaltrials.gov (as of 07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RM2</td>
<td>68Ga</td>
<td>Generator</td>
<td>Gastrin Releasing Peptide Receptor (GRPR) antagonist</td>
<td>4</td>
</tr>
<tr>
<td>MJ9</td>
<td>68Ga</td>
<td>Generator</td>
<td>Gastrin Releasing Peptide Receptor (GRPR) antagonist</td>
<td>1</td>
</tr>
<tr>
<td>RM26</td>
<td>68Ga</td>
<td>Generator</td>
<td>Gastrin Releasing Peptide Receptor (GRPR) antagonist</td>
<td>1</td>
</tr>
<tr>
<td>MATB8N</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Gastrin Releasing Peptide Receptor (GRPR) antagonist</td>
<td>1</td>
</tr>
<tr>
<td>BBN-RGO</td>
<td>68Ga</td>
<td>Generator</td>
<td>Gastrin Releasing Peptide Receptor (GRPR) and avB3 integrin</td>
<td>1</td>
</tr>
</tbody>
</table>

**Hypoxia**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Radionuclide</th>
<th>Synthesis</th>
<th>Mechanism / Target</th>
<th>Number of not yet recruiting, recruiting, active, invited, or completed clinical trials using the tracer for PCa on clinicaltrials.gov (as of 07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMISO</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Hypoxia</td>
<td>1</td>
</tr>
<tr>
<td>HK4</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Hypoxia</td>
<td>1</td>
</tr>
<tr>
<td>FAZA</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Hypoxia</td>
<td>1</td>
</tr>
</tbody>
</table>

**Bone Targeting**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Radionuclide</th>
<th>Synthesis</th>
<th>Mechanism / Target</th>
<th>Number of not yet recruiting, recruiting, active, invited, or completed clinical trials using the tracer for PCa on clinicaltrials.gov (as of 07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaF</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Osteoblast activity</td>
<td>14</td>
</tr>
<tr>
<td>PI5-041</td>
<td>68Ga</td>
<td>Generator</td>
<td>Bone</td>
<td>1</td>
</tr>
</tbody>
</table>

**DNA Synthesis**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Radionuclide</th>
<th>Synthesis</th>
<th>Mechanism / Target</th>
<th>Number of not yet recruiting, recruiting, active, invited, or completed clinical trials using the tracer for PCa on clinicaltrials.gov (as of 07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMAU</td>
<td>18F</td>
<td>Cyclotron</td>
<td>DNA synthesis</td>
<td>3</td>
</tr>
<tr>
<td>FLT</td>
<td>18F</td>
<td>Cyclotron</td>
<td>DNA synthesis</td>
<td>4</td>
</tr>
</tbody>
</table>

**Miscellaneous**

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Radionuclide</th>
<th>Synthesis</th>
<th>Mechanism / Target</th>
<th>Number of not yet recruiting, recruiting, active, invited, or completed clinical trials using the tracer for PCa on clinicaltrials.gov (as of 07/17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FDHT, FMODHT</td>
<td>18F</td>
<td>Cyclotron</td>
<td>Androgen Receptor</td>
<td>4</td>
</tr>
<tr>
<td>AE105</td>
<td>68Ga/64Cu</td>
<td>Generator/Cyclotron</td>
<td>Urokinase Plasminogen Activator Receptor (uPAR)</td>
<td>3</td>
</tr>
<tr>
<td>TP50805</td>
<td>64Cu</td>
<td>Cyclotron</td>
<td>VPAC1</td>
<td>2</td>
</tr>
<tr>
<td>Gallium citrate</td>
<td>68Ga</td>
<td>Generator</td>
<td>Multiple mechanisms</td>
<td>1</td>
</tr>
<tr>
<td>MSTP2108A</td>
<td>89Zr</td>
<td>Cyclotron</td>
<td>STEAP1 (immunoPET)</td>
<td>1</td>
</tr>
</tbody>
</table>

*Joseph Ippolito, M.D., Ph.D., ver 07/24/2017*
Common PET Scan Molecules Applicable in Prostate Cancer

- FDG (Fludeoxyglucose)- FDA approved in cancer (F-18 general PET)
- Sodium Fluoride (NaF) - FDA approved
- Choline C-11 PET - FDA approved
- Fluciclovine/FACBC (Auximin)- FDA approved

- Acetate - not FDA approved
- PSMA Ligand - PSMA-HBED-CC - not FDA approved
- DHT/AR - not FDA approved
- VPAC-1 – not FDA approved
# PET-SCAN RADIOACTIVE TRACERS

**11C Carbon vs 18F Fluorine vs 68Ga Gallium**

<table>
<thead>
<tr>
<th></th>
<th>11C</th>
<th>18F</th>
<th>68Ga</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Half-life</strong></td>
<td>20 min</td>
<td>110 min</td>
<td>68 min</td>
</tr>
<tr>
<td><strong>Excretion</strong></td>
<td>Hepatobiliary</td>
<td>Urinary</td>
<td>Urinary</td>
</tr>
<tr>
<td><strong>Decay Energy</strong></td>
<td>&gt; 99% Positrons</td>
<td>97% Positrons</td>
<td>&gt;95% Positrons</td>
</tr>
<tr>
<td><strong>Source</strong></td>
<td>Cyclotron</td>
<td>Cyclotron</td>
<td>Generator</td>
</tr>
</tbody>
</table>

J Nucl Med May 1, 2017 vol. 58 no. 5 687-688
$^{18}$F-FDG PET

(flourodeoxyglucose-”Every day PET”)

Limited utility

Relatively low glucose metabolism of most hormone sensitive PC

Performs slightly better in CRPC
Sodium Fluoride (\(^{18}\text{F-NaF PET/CT}\))

- Fluoride tracer uptake is a biomarker for bone metabolism.
- \(^{18}\text{F-NaF}\) has been evaluated in men with biochemical relapse of PC after prior local therapy.
- The positive detection rate by \(^{18}\text{F-NaF}\) of bone metastases not seen on CT and BS was 16.2%.
- Drawback is low specificity with false positives.

Tc-99 bone scan

F-18 NaF scan in the same patient
Choline and Acetate Tracers

• Choline kinase is over expressed in prostate cancer cells

• Choline is used to synthesize phosphatidylcholine – integral component of cell membranes

• Acetate also fatty acid membrane associated (C^{11} Na Acetate)
**11C-choline PET/CT**
(Carbon 11)

Detection rate for recurrent PC*:

- PSA <1  - 36%
- PSA 1-2  - 43%
- PSA 2-3  - 62%
- PSA >3  - 73%

Limitations:

- Performance at clinically relevant PSA levels for salvage RT is modest
- Appears slightly inferior in detection of bone mets than MRI
- Very limited access because of 20 min half-life of C\(^{11}\) (Cyclotron)

$^{11}$C-choline PET/CT
Detection of Retroperitoneal LN in a Patient with PSA Recurrent PC
18 F Fluciclovine (FACBC) (Axumin)

18F-Fluciclovine is an artificial amino acid PET imaging agent labelled with 18F.

Recognized and taken up by amino acid transporters\(^1\) that are upregulated in many cancer cells, including prostate cancer.

FDA-approved in May of 2016, Axumin

- Indicated PET imaging in men with suspected prostate cancer recurrence based on elevated blood PSA levels following prior treatment
- Axumin enables detection and localization of prostate cancer
- Recurrent tumors <1 cm in diameter
- Overall detection rate of recurrent prostate cancer 68% (403 of 595 scans), including positive findings in:
  - Prostate/prostate bed (39%)
  - Pelvic lymph nodes (33%)
  - Metastatic sites outside the pelvis (26%)
  - Including skeletal sites (9%)

Fluciclovine (Axumin) Case Study

- Post-radical prostatectomy, negative lymphadenectomy
- Rising PSA to 0.73 ng/mL
- Negative MR for malignancy
- Negative skeletal screening
- Imaging result: left pre-sacral node

Images courtesy of Blue Earth Diagnostics, Ltd
LOCATE Trial 2018 SNMMI

• 213 with BCR had 18F-fluciclovine PET/CT after negative imaging (median PSA 1.0)
• 122 patients positive scans: 52% prostate/ bed; 50% nodes; 19% bone; 4% soft tissue
• 59% (126/213) changed management
• 78% (98/126) cited a “major change” in treatment

Positive scan w/PSA:
– PSA < 0.5 31% (25/81)
– PSA > 10 for to 95% (18/19)

[68]Ga-αPSMA

- Small molecule with favorable clearance
- Ga-68 short half-life decreases patient radiation exposure
- Same day imaging
- Extra- and osseous disease

Freitag, EJNMMI 2015
Imaging phenotype – PSMA - IgG

• Prostascint® with In-111 FDA-approved, not widely accepted

• HuJ591 against external domain of PSMA – greater potential
  • Long half-life
  • Theranostic (Th-227)

Osborne, Urol Oncol 2013
$^{68}$Ga-PSMA-PET vs $^{99}$Tc Bone Scan
Prostate Cancer Bone Metastases

Next development:
• PSMA Therapy
• “Theranostic”
“Theranostic”

- Next PET development:
  - Peptide Receptor Radionuclide Therapy (PRRT)
  - PSMA Ligand Therapy
- $^{177}$Lutetium- PSMA Therapy
- $^{225}$Actinium-PSMA Therapy
- $^{213}$Bismuth-PSMA Therapy
- Xerostomia is common and debilitating
VPAC in GU Malignancy: Applications for PET Imaging

• VPAC receptors bind Vasoactive Intestinal Peptide (VIP) and Pituitary Adenylate Cyclase Activating Peptide (PACAP)
• VPAC-1 receptors
  • exist on normal cells
  • 100% of prostate and bladder cancer overexpress VPAC1
  • high (10^4/cell) receptor density on PCa cells
• Many tumors types overexpress VPAC-1
• **Overexpression of VPAC-1 receptor an early event before histologic changes**
• Activates various growth factors

*Curr Pharm Des. 2007;13(11):1099-104*
25 men going for RALP were imaged preoperatively
PET/CT images compared with whole mount prostatectomy specimens
Digital autoradiography performed on whole mount sections
Autoradiography and optical imaging of prostate cancer tissue

Digital Autoradiography (DAR)

Histology prostate cancer tissue

Optical image prostate cancer tissue
Metastatic Prostate Cancer VPAC Imaging

70 year old male after Cu-64-TP3805 PET imaging. Images showed multiple bone lesions secondary to his PCa. Histological examination of the bone biopsy confirmed metastatic prostate cancer.
PC PET SCAN SUMMARY

- PET more sensitive in visualizing PC (primary and recurrent) than CT and bone scan
  - Do any improve clinical outcomes?
  - Feed debate on early treatment of mCRPC
  - Impact on approval of apalutamide for MO CRPC?
  - Best target and tracer combo?
- FDA approval means the test can be performed reproducibly/safely; w/no verdict on clinical utility
- Which modality is the most useful at this point?
  - Practical: \(^{18}\text{F-fluciclovine PET/CT (Axumin)}\)
  - PSMA-based PET promising but US access is limited.
- Trials to assess salvage therapy (efficacy, costs) are needed
Pigeons, the next great cancer detector?

By Jen Christensen, CNN

Updated 10:12 AM ET, Fri November 20, 2015
BACK UP Slides
<table>
<thead>
<tr>
<th>Prostate Cancer Characteristic</th>
<th>Imaging Modality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low water content</td>
<td>T2 weighted MRI</td>
</tr>
<tr>
<td>Restricted water diffusion</td>
<td>Diffusion weighted images MRI</td>
</tr>
<tr>
<td>Increased vascularity</td>
<td>Dynamic contrast enhanced MRI</td>
</tr>
<tr>
<td></td>
<td>Doppler US</td>
</tr>
<tr>
<td></td>
<td>Contrast enhanced Ultrasound</td>
</tr>
<tr>
<td>Increased glucose metabolism</td>
<td>FDG PET</td>
</tr>
<tr>
<td>Increased cellular proliferation, cell membrane synthesis</td>
<td>Choline, Acetate PET</td>
</tr>
<tr>
<td>Amino-acid transport</td>
<td>Fluciclovine-PET</td>
</tr>
<tr>
<td>PSMA expression</td>
<td>PSMA PET</td>
</tr>
<tr>
<td>AR expression</td>
<td>FDHT PET</td>
</tr>
<tr>
<td>Proclivity for bone metastases</td>
<td>NaF PET, Tc99 bone scan</td>
</tr>
</tbody>
</table>
Fluciclovine F18: Dosing, administration & image acquisition

- Recommended dose is 370 MBq (10 mCi) administered as an intravenous (IV) bolus injection, followed by IV saline flush.
- Avoid any significant exercise for at least one day prior to PET imaging.
- Fasting for at least 4 hours prior to administration.
- Inject on PET scanner table.
- Position the patient supine with arms above the head.
- Begin PET scanning 3 to 5 minutes after completion of injection.
- Start acquisition at mid-thigh and proceed to the base of the skull.
- Typical total scan time is between 20 to 30 minutes.
## SUMMARY OF MAIN PET IMAGING TECHNIQUES UTILIZED IN PROSTATE CANCER

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Half-life</th>
<th>Cyclotron</th>
<th>Mechanism of action</th>
<th>Excretion</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{11}$C-choline</td>
<td>20</td>
<td>On-site</td>
<td>Cell membrane synthesis</td>
<td>Hepatic</td>
<td>38-98</td>
<td>50-100</td>
<td>Low urine excretion</td>
<td>Short half-life</td>
</tr>
<tr>
<td>$^{11}$C-acetate</td>
<td>20</td>
<td>On-site</td>
<td>Lipid synthesis</td>
<td>Hepatic</td>
<td>42-90</td>
<td>64-96</td>
<td>Low urinary excretion</td>
<td>Moderate specificity Not FDA approved</td>
</tr>
<tr>
<td>$^{18}$F-Fluciclovine</td>
<td>110</td>
<td>Regional</td>
<td>Amino acid transport</td>
<td>Renal</td>
<td>89-100</td>
<td>67</td>
<td>Availability</td>
<td>Moderate specificity</td>
</tr>
<tr>
<td>$^{18}$F-NaF</td>
<td>110</td>
<td>Regional</td>
<td>Adsorption within bone matrix</td>
<td>Hepatic</td>
<td>87-89</td>
<td>80-91</td>
<td>Sensitivity</td>
<td>Only for bones, not specific</td>
</tr>
<tr>
<td>$^{68}$Ga-PSMA</td>
<td>68</td>
<td>Generator (no cyclotron)</td>
<td>PSMA analog</td>
<td>Renal</td>
<td>63-86</td>
<td>95-100</td>
<td>Not dependent on cyclotron</td>
<td>Moderately short half-life Not FDA approved</td>
</tr>
<tr>
<td>$^{18}$F-FDHT</td>
<td>110</td>
<td>Regional</td>
<td>AR</td>
<td>GI and renal</td>
<td>63</td>
<td>N/A</td>
<td>AR - specific</td>
<td>not effective in castrate sensitive setting, not FDA approved</td>
</tr>
</tbody>
</table>

* Interpret with caution, few studies used biopsy / surgery as gold standard
Fluciclovine Tracer (also known as FACBC)

anti\textsuperscript{1}-amino-3-18F-fluorocyclobutane-1-carboxylic acid
Fluciclovine F18: Pharmacodynamics

Imaging: begin with in 3-5 minutes; complete within 20 – 30 minutes.

All Regions - SUV (Mean)

- Prostate Tumours
- Lymph Node Lesions
- Muscles
- Marrow
- Bladder
- Vesicle lesion

SUV mean

Time (min)
FDG and Acetate Tracers

- **FDG** - Analog of glucose; reflects the increased glycolytic activity of tumors (Warburg effect); FDG is trapped in cells via GLUT transport and irreversible HK phosphorylation – **poor performance in hormone sensitive prostate cancer**

- **Acetate** - Naturally occurring metabolite; converted to acetyl-CoA and incorporated into cholesterol and fatty acids; fatty acid synthetase and acetyl-CoA carboxylase are oncogenic enzymes upregulated in prostate cancer – **not FDA approved**
Fluciclovine F18: Bio-distribution

• Amino acid (AA) transporters ubiquitous throughout body; upregulated in prostate cancer

• Distribution after IV dosing:
  • Liver: 14%*
  • Red bone marrow: 12%*
  • Lung: 7%*
  • Myocardium: 4%*
  • Pancreas: 3%*

• First 4 hrs. post-injection:
  • 3% excreted in urine*

*% of administered radioactivity

2. Fuciclovine F 18 Injection; US Prescribing Information, Blue Earth Diagnostics, Ltd; August 2016
77 yr old post RT, PSA recurrence
Comparison of choline-PET/CT, MRI, SPECT, and bone scintigraphy in the diagnosis of bone metastases in patients with prostate cancer: a meta-analysis

Guohua Shen • Houfu Deng • Shuang Hu • Zhiyun Jia

Role of $^{18}$F-Choline PET/CT in Biochemically Relapsed Prostate Cancer After Radical Prostatectomy

Correlation With Trigger PSA, PSA Velocity, PSA Doubling Time, and Metastatic Distribution

Maria Cristina Marzola, MD,* Sotirios Chondrogiannis, MD,* Alice Ferretti, MD,† Gaia Grasseto, MD,* Lucia Rampin, MD,* Arianna Massaro, CNMT,* Paolo Castellucci, MD,‡ Maria Picchio, MD,§ Adil Al-Nahhas, MD, Patrick M. Colletti, MD,¶ Adriano Marcolongo, MD,# and Domenico Rubello, MD*
Quantitative Imaging of biologic processes

- PET imaging inherently quantitative
- Metabolic
  - Warburg effect
  - Amino-acid metabolism
- Cell surface characteristics
  - PSMA
  - CA-IX
  - Varying ligands
    - Small molecules
    - Antigen-binding proteins
Other PET tracers

• Tracers that reflect metabolism (Choline, Acetate)
  Or
  Hypoxia (F-MISO)
  have not been utilized extensively.
• INCREMENTAL benefit to FDG may be minimal if any.

Shreve, J Nucl Med 1995
Utility in staging may not be better than CT alone.

For all tracers excreted through the kidneys.


[11C]Choline
Imaging metastatic CaP

• PCWG2 → 3... imaging ill-defined

• Bone scans remain mainstay
  • NaF PET/CT greater accuracy (with higher FP)
  • Utility in f/u not clear
    • Flare
    • Non-specific
Prostate cancer PET imaging issues

- Castration-sensitive rarely glucose avid.
- Castration-resistant usually glucose avid.
- Other metabolic agents employed
  - Choline
  - Fluciclovine
Radiocholine

- [11C]-choline has NDA approval
- Increasing utilization in Europe
  - [18F]-choline
- NOT incorporated as biomarker per EAU ‘13

Hernandez-Argüello, Prostate, 2015
Radiocholine for CRPC

Ceci, Clin Nucl Med 2015
Metabolic tracers

Nanni, Clin Nucl Med 2015
Metabolic tracers

• Both amino acids and choline will likely have comparable biodistribution
• [11C]- half life limits centralized production
  • Addressed by FMC/FEC
• Dextro-amino acids may represent a metabolic paradigm akin to FDG
  • May provide better signal:noise (accumulation)
• Fluciclovine is [18F]-labeled
  • FDA approved
[18F]-Fluciclovine

Fluciclovine positivity (Detection Rate)

Prostate/bed | Extra-prostatic | Whole body

PSA quartiles ng/mL

<=0.79 | 0.80-2.03 | 2.04-6.00 | >6.00

T. Bach-Gansmo. 10.1016/j.juro.2016.09.117
Phenotype - PSMA

Choline v αPSMA

Afshar-Oromieh, EJNMMI 2014
[68]Ga-αPSMA

- Small molecule with favorable clearance
- Ga-68 short half-life decreases patient radiation exposure
- Same day imaging
- Extra- and osseous disease

Freitag, EJNMMI 2015
Figure 5 | Imaging of 65-year-old patient with prostate cancer and diffuse metastases

Nature Reviews Urology April 2016
Imaging phenotype – PSMA - IgG

- Prostascint® with In-111 FDA-approved, not widely accepted

- HuJ591 against *external* domain of PSMA – greater potential
  - Long half-life
  - Theranostic (*?Th-227*)

Osborne, Urol Oncol 2013
[89Zr]-DFO-huJ591

- Slow clearance of intact IgG precludes same day imaging
- Current comparisons with sub-optimal imaging modalities (bone scans!!!)
- Theranostic potential

Pandit-Taskar, Clin Cancer Res 2015
PET in CaP

• Metabolic agents:
  • NaF sensitive, non-specific
  • FDG PET/CT may have utility in CRPC
  • [11C]-choline, FDA approved
    • [18F]-choline under development
  • [18F]-fluciclovine, FDA approved

• Phenotype characterization (PSMA$_x$)
  • Small molecules (PSMA-11)
  • Antibody (J591) and antigen-binding proteins