New Advances in Prostate Cancer Radionuclide Imaging

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University of Iowa

Conflicts

- Consultant to:
  - Siemens
  - Advanced Accelerator Applications
  - Blue Earth Diagnostics
  - Jubilant DraxImage

Indications for Radiotracer Imaging of Prostate Cancer

- Screening
- Diagnosis
- Initial Staging
- Re-staging Recurrence
- Response to therapy
Prostate Cancer Imaging

- Current
  - CT
  - MRI
  - Bone scans
  - $^{18}$F NaF
  - $^{111}$In Capromab
  - $^{11}$C Choline

- Future
  - $^{11}$C Acetate
  - $^{18}$F Fluorocholine
  - $^{111}$In J591
  - $^{18}$F FACBC
  - $^{68}$Ga, $^{18}$F, $^{99m}$Tc PSMA
  - $^{68}$Ga Bombesin

Radiotracers for Prostate Cancer

Dates are first reports of imaging in humans

- Bone Scan (Sr-85) 1964
- Bone Scan (Tc-99m) 1970
- Bone Scan (F-18) NaF 1999
- Ga-68 Bombesin 2013
- In-111 J591 2003
- C-11 Choline 1998
- C-11 Acetate 2002
- PSMA small molecules 2012
- $^{18}$F FDG 1995
- $^{18}$F Fluorocholine 2000
- $^{18}$F FACBC 2007
- F-18 FDG 2004

Low sensitivity High specificity for lymph nodes


CT scanning can detect bone metastases, particularly those that are osteoblastic.

Because lymph node size is not sensitive or specific for metastasis in patients with prostate carcinoma, there is no one size criterion that is highly accurate. A commonly used criterion is a pelvic lymph node larger in size than 10 mm. Using this criterion with contemporary scanners, one study found a sensitivity of 34% and a specificity of 97% for detection of lymph node metastases.
### Prostate Cancer Imaging

#### Magnetic Resonance Imaging

**Multiparametric MRI Compared to Radical Prostatectomy**

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<tbody>
<tr>
<td>Retrospective Prospective</td>
<td>63</td>
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<tr>
<td>Age (y)</td>
<td>73</td>
<td>74</td>
<td>75</td>
<td>76</td>
<td>77</td>
<td>78</td>
<td>79</td>
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<tr>
<td>Prostate specific origin</td>
<td>N/A, N/A</td>
<td>N/A, N/A</td>
<td>N/A, N/A</td>
<td>N/A, N/A</td>
<td>N/A, N/A</td>
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<tr>
<td>Sensitivity (%)</td>
<td>88</td>
<td>96</td>
<td>95</td>
<td>95</td>
<td>97</td>
<td>96</td>
<td>77</td>
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<tr>
<td>Specificity (%)</td>
<td>44</td>
<td>64</td>
<td>64</td>
<td>64</td>
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</table>

**Evaluation for location in prostate in subjects with known disease**

- Variable sensitivity and specificity in prostate bed.


### Prostate Cancer Imaging

#### Magnetic Resonance Imaging

**Table 5**

Diagnostic performance of patient based analysis and lymph node anatomic region analysis.

<table>
<thead>
<tr>
<th>No. of true positive cases</th>
<th>11</th>
<th>15</th>
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<tbody>
<tr>
<td>No. of false negative cases</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>No. of false positive cases</td>
<td>5</td>
<td>4</td>
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<tr>
<td>Sensitivity (%)</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>85</td>
<td>85</td>
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<tr>
<td>NPV (%)</td>
<td>67</td>
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</table>

**Evaluation for regional lymph node metastases**

- Low sensitivity, high specificity for lymph nodes.


### 85Sr Bone Scan

**Charles & Sklaroff**

Earl Diagnosis of Metastatic Bone Cancer By Photocanning With Strontium 85


18F NaF and 99mTc Polyphosphate


99mTc Bone Scans

Modern 99mTc MDP Bone Scan

63 year old with Gleason 8 prostate cancer. 3 years after treatment with radiation and chemotherapy.
Question of lesion at base of skull.

Modern 99mTc MDP Bone Scan & SPECT-CT

Tc-99m Bone Scan with SPECT-CT

Tc-99m Bone Scan with SPECT-CT
Tc-99m Bone Scan with SPECT-CT

Tc-99m Bone Scan with SPECT-CT

Tc-99m Bone Scan with SPECT-CT

Tc-99m Bone Scan with SPECT-CT
Prostate Cancer Imaging

- Current
  - 111In Capromab
  - 11C Choline

- Future
  - 11C Acetate
  - 18F Fluorocholine
  - 111In J591
  - 18F FACBC
  - 68Ga, 18F, 99mTc PSMA
  - 68Ga Bombesin

111In capromab pendetide (Prostascint®)

- Low Sensitivity
- Low Specificity

68 yo m 2 y s/p prostatectomy, now with rising PSA

\[
\begin{align*}
\text{\textsuperscript{11}C-Acetate} & \hspace{1cm} \text{\textsuperscript{11}In-Prostascint}
\end{align*}
\]
Tracers in Development

- $^{11}$C Acetate
- $^{18}$F Fluorocholine
- $^{18}$F FACBC
- $^{68}$Ga, $^{18}$F, $^{99m}$Tc PSMA
- $^{68}$Ga Bombesin

$^{11}$C Acetate and $^{11}$C Choline
(essentially equivalent)

Patient with widespread prostate cancer

$^{11}$C-Choline, $^{18}$F-Choline and $^{11}$C-Acetate
for staging of recurrent PCa

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Sens</th>
<th>Spec</th>
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<tr>
<td>$^{11}$C-Acetate</td>
<td>192</td>
<td>83</td>
<td></td>
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<tr>
<td>$^{11}$C-Choline</td>
<td>1583</td>
<td>83</td>
<td>83</td>
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<tr>
<td>$^{18}$F-Choline</td>
<td>841</td>
<td>82</td>
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</table>

Brogsitter C, Zöphel K, Kotzerke J.
$^{18}$F-Choline, $^{11}$C-Choline and $^{11}$C-Acetate PET/CT:
Comparative analysis for imaging prostate cancer patients.
**J-591**

- First studies in 2003 (not FDA approved)
- Humanized antibody directed at PSMA
- Images are done at 5-7 days
- Better sensitivity and specificity


**F-18 FACBC**

anti-1-amino-3-[18F]fluorocyclobutane-1-carboxylic acid

- Patented by Mark Goodman, Emory University
- Patent expired in 2015
- An "un-natural" amino acid; marker of protein synthesis

Plan A: DoD funding with 3 sites (grant was not approved)
Plan B: Movember funding with 9 sites
Plan C: Movember/GE funding with 9 sites
Plan D: Phase 3: BED funding with 9+ sites
Small molecules targeting PSMA

Labels: Tc-99m, F-18, Ga-68

John Babich
Molecular Insight
(Progenics)
now at Cornell

Martin Pomper
Johns Hopkins

Advantages: rapid uptake, high specificity

Ga-68 PSMA

F-18 Fluoroethyl-choline

Biodistribution, tumor detection, and radiation dosimetry of \(^{18}\)F-DCFBC, a low-molecular-weight inhibitor of PSMA, in patients with metastatic prostate cancer.


Fig. 1 \(^{124}\)I-MIP-1095 PET images (maximal intensity projection) of patient 01


Fig. 3 whole body scintigrams of \(^{131}\)I-MIP-1095 in patient 01 at 7, 10 and 17 days

Of men with bone pain, 84.6% showed complete or moderate reduction in pain. Hematological toxicities were mild. Of men treated, 25% had a transient slight to moderate dry mouth. No adverse effects on renal function were observed. Involved lymph node and bone metastases were exposed to estimated absorbed doses upwards of 300 Gy.
75-y-old m/p RP (Gleason score, 5; pT3b, pN1), Rad Rx, rising PSA of 1.09. Negative CT images (A), but with a 5-mm lymph node behind right external iliac vein.

PET (C) and fused PET/CT images (D) show intense uptake. Whole-body MIP (B) displays this lymph node and no other suggestive lesion.

Selective lymph node resection was performed. PSA value dropped below detection limit (0.07 ng/mL) without anti-hormonal treatment.

Detection rate of \textsuperscript{68}Ga-PSMA ligand PET/CT in relation to PSA level

Eiber et al. Evaluation of Hybrid \textsuperscript{68}Ga-PSMA ligand PET/CT in 248 Patients with Biochemical Recurrence After Radical Prostatectomy J Nucl Med 2015; 56:668–674

U.S. Sites Starting with \textsuperscript{68}Ga-PSMA

- Stanford
- UCSF
- Wisconsin
- Iowa
- Vanguard
- Washington University
- UCLA
- Indiana

Goals
1. Development of common, consistent methodology and protocols
2. Collaborative effort leading to an NDA

\textsuperscript{68}Ga-PSMA Likely indications

- Preoperative staging
- Evaluation of pts s/p definitive Rx w rising PSA
- Evaluation of pts for therapy w \textsuperscript{177}Lu PSMA
**177Lu-DOTAGA PSMA**


\[ ^{177}\text{Lu} T_{1/2} = 6.7 \text{ d} \]
\[ \gamma = 113 \& 210 \text{ keV} \]
\[ \beta_{\text{max}} = 149 \text{ keV} \]

**177Lu-DOTAGA PSMA**

N=25

(88Ga-PSMA cycles)

<table>
<thead>
<tr>
<th>PSA change (%)</th>
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<tbody>
<tr>
<td>Percent (%)</td>
</tr>
<tr>
<td>No. of patients</td>
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N=25


**68Ga-Bombesin**

Bombesin targets gastrin-releasing peptide (GRP)

Tumors: Prostate, Breast, Lung cancers


Clinical Trials

- FACBC: Multi-site international trial will start within 1 year
- FDHT: Three-site trial will start within 1 year
- Fluorocholine: Phase 1 & 2 starting
- C-11 Acetate: Phase 2 studies underway
- PSMA agents: Phase 1-2 studies underway, Phase 3 starting
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• Future
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  – $^{18}$F Fluorocholine
  – $^{111}$In JS91
  – $^{18}$F FACBC
  – $^{68}$Ga PSMA
  – $^{18}$F PSMA
  – $^{99m}$Tc PSMA
  – $^{68}$Ga Bombesin

Therapy with $^{131}$I and $^{177}$Lu PSMA

The End