PET/CT in Prostate Cancer

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Prostate Cancer

- In Europe 2.6 million prostate cancer cases are diagnosed each year, with a mortality rate of 30.6 per 100,000 per year.

- Is the second most common cause of cancer death, in men older than 50 years (in Europe).

- Relapse after primary therapy, occurs (within 10 years) in 20%-30% of patients who have undergone prostatectomy, and in up to 53% (within 5 years) if treated with RT.
Estimated Prostate Cancer Incidence Worldwide – 2012 (Globocan)

Estimated age-standardised rates (World) per 100,000
Limitations of Conventional Imaging in Prostate Cancer

78 year old man with prostate cancer (Gleason score 5+4), initially treated in 1999 with radical prostatectomy. The surgical lymphadenectomy - at the time - does not find any involved lymph node. The patient was staged as pT3-4N0M0. Subsequently, he was managed with LHRH analogs, and antiandrogen medication, which he has maintained until today.

Currently he has a progressive elevation of the PSA (in January 2010 was 1.57 ng/ml).

Recent CT scan of the abdomen with contrast was reported as “...stable inguinal adenopathy. In the theoretical location of the seminal vesicle, there is a questionable nodularity slightly hyperdense, measuring 13 mm, appearing to be slightly bigger than on the prior study. Review of bone windows demonstrates degenerative changes.....”
Bone Scan
CT bone window
Fluorocholine PET/CT
Fluorocholine  PET/CT

<table>
<thead>
<tr>
<th>Time (minutes)</th>
<th>SUV 15</th>
<th>SUV 30</th>
<th>SUV 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>5.4</td>
<td>5.9</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td></td>
<td></td>
<td>7.3</td>
</tr>
<tr>
<td>60 minutes</td>
<td></td>
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</tbody>
</table>
Tracers for PET imaging in Prostate Cancer

- $^{18}$F-FDG
- $^{18}$F-Sodium Fluoride
- $^{11}$C-Choline
- $^{11}$C-Acetate
- $^{11}$C-Methionine
- $^{18}$F-Fluorodihydrotestosterone (FDHT)
- Anti-$^{18}$F-FACBC
- $^{86}$Ga-PSMA ligan
- $^{18}$F-Fluorocholine
18F-Choline vs. 11C-Choline

11C-Choline
Negligible activity in the bladder

18F-Choline
Some activity in the bladder
18 Fluorocholine

- 18 Fluoro-methyl-choline
- Quaternary Ammonium.
- First, synthesized by Grado in 2001.
- Seems to be superior to 18Fluro-ethyl-choline in prostate cancer.
- Has also been used -little- in other tumors (glyomas and HCC).
Prospective study, comparing the diagnostic performance of Fluorocholine vs. FDG PET/CT, for the detection and staging of HCC.

81 patients, with chronic liver disease and liver nodules.

Sensibility: 88% for Fluorocholine and 68% for FDG.

In well differentiated tumors the sensitivity for FCH when up to 94% while for FDG was only 59%.

Talbot JN et al. JNM 2010; 51:1699-1706
18 Fluorocholine

- Is a precursor in the biosynthesis of phospholipids.
- Enters in the cell through 3 different membrane transporters.
- Inside the cell is phosphorilated to Phosphatidylcholine, by the enzyme Cholinekinase (which is overexpressed in tumor cells).
- Phosphatidylcholine is an essential component of cell membranes.
- *Does chemotherapy and antihormonal therapy affect the uptake of Choline?*
[11C]choline fused PET/CT images in two patients (a and b, respectively) of group B studied before and after bicalutamide therapy (150 mg/day). Despite a substantial difference in [11C]choline SUVmax values before therapy (SUVmax=4.5 and 11.9 for a and b, respectively), a considerable reduction in [11C]choline uptake is evident in both patients after treatment (SUVmax=1.8 and 4.1 for a and b, respectively).
# 18 Fluorocholine - Biodistribution

## Human Radiation Dose Estimates for FCH

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Dose (mSv/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>0.0124</td>
</tr>
<tr>
<td>Brain</td>
<td>0.0019</td>
</tr>
<tr>
<td>Lung</td>
<td>0.0116</td>
</tr>
<tr>
<td>Liver</td>
<td>0.081</td>
</tr>
<tr>
<td>Kidney</td>
<td>0.219</td>
</tr>
<tr>
<td>Bone</td>
<td>0.0103</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.0086</td>
</tr>
<tr>
<td>Red marrow</td>
<td>0.0116</td>
</tr>
<tr>
<td>Testes</td>
<td>0.0076</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.0105</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>0.0132</td>
</tr>
</tbody>
</table>
18 Fluorocholine – Biodistribution (SUV)

Table 1 $^{18}$F-FCH SUV$_{\text{max}}$ in various organs

<table>
<thead>
<tr>
<th>Organ</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>11.77</td>
<td>2.42</td>
<td>8.7–15</td>
</tr>
<tr>
<td>Pancreas</td>
<td>7.85</td>
<td>1.5</td>
<td>5.6–9.8</td>
</tr>
<tr>
<td>Salivary glands</td>
<td>4.9</td>
<td>1.1</td>
<td>3.6–6.9</td>
</tr>
<tr>
<td>Lacrimal glands</td>
<td>2.0</td>
<td>0.5</td>
<td>1–3.19</td>
</tr>
<tr>
<td>Spleen</td>
<td>3.41</td>
<td>0.72</td>
<td>2.3–4.4</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>2.88</td>
<td>0.67</td>
<td>1.7–3.6</td>
</tr>
<tr>
<td>Kidneys</td>
<td>8.51</td>
<td>1.05</td>
<td>6.8–10.1</td>
</tr>
</tbody>
</table>

$^{18}$F-FCH, $^{18}$F-choline; SD, standard deviation; SUV$_{\text{max}}$, maximum standardized uptake value.

Table 2 $^{18}$F-FCH mean SUV values in various organs

<table>
<thead>
<tr>
<th>Organ</th>
<th>Mean</th>
<th>SD</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver</td>
<td>10.48</td>
<td>2.29</td>
<td>8–14</td>
</tr>
<tr>
<td>Pancreas</td>
<td>6.68</td>
<td>1.4</td>
<td>4.6–9.2</td>
</tr>
<tr>
<td>Salivary glands</td>
<td>4.2</td>
<td>1.09</td>
<td>2.7–6</td>
</tr>
<tr>
<td>Lacrimal glands</td>
<td>1.6</td>
<td>0.38</td>
<td>0.9–2.3</td>
</tr>
<tr>
<td>Spleen</td>
<td>2.79</td>
<td>0.85</td>
<td>1.1–3.9</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>2.53</td>
<td>0.61</td>
<td>1.4–3.2</td>
</tr>
<tr>
<td>Kidneys</td>
<td>6.89</td>
<td>1</td>
<td>5.8–8.8</td>
</tr>
</tbody>
</table>

$^{18}$F-FCH, $^{18}$F-choline; SD, standard deviation; SUV, standardized uptake value.
18 Fluorocholine

Time-activity curve
18 Fluorocholine

FDG-PET

FCH-PET

Metastatic Breast Cancer
18 Fluorocholine PET/CT - Imaging Protocol (in evolution)

- Fasting for 6 hours.
- Injection of 0.10 mCi/kg of 18Fluorocholine while on the PET/CT couch.
- Dynamic PET/CT (1 frame/mn), starting at 1 mn and continuing for 8mn.
- Two bed positions of the pelvis at 15 mn pi. (4 mn emission scans)
- WB scan at 30 mn pi.
- At the end, consideration given for a “late” 60 mn p.i, scan of the pelvis.
18 Fluorocholine PET/CT Dynamic Study

1 minute pi

5 minutes pi
18 Fluorocholine PET/CT Dynamic Study

Minutes

1     2     3     4    5     6     7    8

Inferior

Superior
18 Fluorocholine PET/CT Dynamic Study

Minutes

1  2  3  4  5  6  7  8

Inferior
18 Fluorocholine PET/CT Indications

**ESTABLISHED**
- Assessment of extent of disease -regional and/or distant-, or with doughfull findings on conventional imaging.
- **Early assessment of recurrence of disease in patients with biochemical relapse.**

**FUTURE OR IN EVOLUTION**
- For aiding/guiding in the initial diagnosis of prostate cancer in challenging cases (e.g. multiple, repeated, negative biopsies).
- **To confirm localized disease (in “bordeline” high risk patients) before radical surgery or RT.**
- Assess response to therapy.
- Before, **RT planning** or pelvic lymphadenectomy.
59 year old man with prostate cancer, initially treated with radical prostatectomy in March 2008. Currently, has biochemical relapse with a PSA of 1.7 ng/ml and an inconclusive MRI.

18Fluorocholine PET/CT - Coronal views at 30 mn pi
74 year old man, with recently diagnosed with prostate cancer and progressive elevation of the PSA. Having a value of 5.26 ng/ml in July 2009. The PET/CT scan was done at the end of 2009, to evaluate extent of disease.

18Fluorocholine PET/CT - Coronal views at 15 mn pi
18Fluorocholine PET/CT – Coronal Views at 30 mn pi
18Fluorocholine PET/CT – Coronal views at 30 mn pi

SUV = 4.3
FDG vs C-11 Choline PET/CT in Meningiomas

Clin Nucl Med 2009;34: 7–10
Detection of disease relapse according to the value of PSA. FDG vs. Choline

71 year old man colon cancer treated with right hemicolecctomy in August 2009. Currently, has an elevated PSA with positive biopsy for prostate cancer. In the CT scan, there is abdominal adenopathy. An FDG PET/CT scan was requested......

**Fluorocholine vs. FDG PET/CT**

FDG 3/23/2010

Fluorocholine 5/17/2010
71 year old man with colon cancer treated with a right hemicolecotmy in August 2009. Currently, has an elevated PSA with positive biopsy for prostate cancer. In the CT scan, there is abdominal adenopathy. An FDG PET/CT scan was requested....

**18Fluorocholine vs. FDG PET/CT**
Biochemical relapse in Prostate Cancer. Influence of PSA in the Detection Rate.

Influence of Trigger PSA and PSA Kinetics on $^{11}$C-Choline PET/CT Detection Rate in Patients with Biochemical Relapse After Radical Prostatectomy

58 year old man with prostate cancer (Gleason 3+3) initially treated with surgery in November 2006, followed by adjuvant RT and hormonal therapy for 2 years. Currently, has biochemical relapse with negative conventional imaging studies (CT, MR and BS). PSA at the time of the scan was 1 ng/ml.
58 year old man with prostate cancer, with biochemical relapse and negative conventional imaging studies (CT, MR and BS). Current PSA of 1 ng/ml.
18\textsuperscript{Fluorocholine PET/CT}

74 year old man with prostate cancer, and progressive elevation of PSA after initial treatment with RT, followed by Casodex.
Fluorocholine PET/CT

Axial Images

5 minutes p.i.  60 minutes p.i.
Comparative study in 38 patients with prostate cancer. Both studies done within 2 weeks.

321 lessons.

Sensi, specif, and accuracy with Sodium Fluoride was 81%, 93%, 86%, respectively.

With Fluorocholine was 74%, 99% y 85%, respectively. Management change in 2/38 pts.

CONCLUSION: Fluorocholine is superior for the early detection of metastatic bone disease. Sodium Fluoride was more sensitive than Fluorocholine, but the difference was not statistically significant.
Hormonal Therapy

The Use of F-18 Choline PET in the Assessment of Bone Metastases in Prostate Cancer: Correlation with Morphological Changes on CT

Mohsen Beheshti, Reza Vali, Peter Waldenberger, Friedrich Fitz, Michael Nader, Josef Hammer, Wolfgang Loidl, Christian Pirich, Ignac Fogelman, Werner Langsteger

![Graph showing correlation between HU and SUVmax](image-url)
By patient, Choline PET/CT demonstrated in these two studies a sensitivity of 60-100%, specificity of 66-98%, PPV of 90%, NPV of 87-100% and accuracy of 88-92%.

One meta-analysis from a Radiology paper concluded the sensitivity and specificity for CT was 26-56% and 80-83%, respectively. For MR it was 22-56% and 79-83%, respectively.

The maximum diameter (on average) of true positive nodes was 15 mm. versus 6.3 mm for the false negatives ones (p=0.0004).

Eur Urol 2007; 52:423–429
Eur Urol 2008; 54:392–401
Fluorocholine PET/CT for Assessment of Response to Therapy

69 year old man with prostate cancer, treated with radical prostatectomy in April 2008. Currently with biochemical relapse and a PSA of 0.31 ng/ml.

6/2/2010
PSA 0.31

LHRH analog

9/13/2010
PSA 0.070
$^{18}$Fluorocholine PET/CT
Change in Clinical Management

11C-Choline – Correlation to Patients Outcome

64 patients with a mean follow up of 50 months.
Median PSA of 1.4 ng/ml

Prognosis Related to Metastatic Burden Measured by $^{18}$F-Fluorocholine PET/CT in Castration-Resistant Prostate Cancer

Kaplan–Meier survival curves. Differences in survival were significant among patients stratified by net MATV (A), net TLA (B), and SUV$_{\text{max}}$ of most active tumor (C) and borderline among patients stratified by PSA level (D).

Kwee SA et al. JNM 2014
Future Tracers – 18F-FACBC
Future Tracers – 68Ga-PSMA ligand
Conclusions

- Fluorocholine PET/CT constitutes nowadays, despite its fairly recent development, a diagnostic tool of great value in the management of prostate cancer patients.

- There are well established indications, and others ones in “evolution”.

- Urinary excretion of Fluorocholine, using an adequate imaging protocol, does not represent a limitation for acquiring high quality clinical images.

- New radiopharmaceuticals for PET/CT and PET/MR imaging are being developed.
Thank You