Choline PET/CT in Prostate Cancer Imaging

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UKRC June 2014
Aims of talk

1. To understand the role of choline PET in the multimodality pathway of prostate cancer
2. To describe the mechanism of action and technical aspects
3. To understand the main indications of choline PET in prostate cancer
4. To highlight the imaging pearls and pitfalls with case examples.
Prostate cancer

- Most commonly diagnosed cancer in men (PSA screening)
- Second cause of cancer death after lung cancer
- Diagnostic tools DRE, PSA, TRUS and perineal template biopsy
- Controversy regarding – over diagnosis, spectrum of disease, what is clinically significant etc

<table>
<thead>
<tr>
<th>Stage (DRE)</th>
<th>Low</th>
<th>Intermediate</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1-T2a</td>
<td></td>
<td>T2b</td>
<td>≥T2c</td>
</tr>
<tr>
<td>GS</td>
<td>2-6</td>
<td>7</td>
<td>8-10</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>&lt;10</td>
<td>10-20</td>
<td>&gt;20</td>
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NCCN/ NICE
Prostate cancer

- Most frequent metastases to lymph nodes (pelvic / retroperitoneal)
- Bone - 80% of the metastatic sites but only 10% have bone metastases at diagnosis
- Lung and liver (late stages)

Treatment

- LOCALISED: active surveillance, radical prostatectomy, EBRT and brachytherapy
- LOCALLY ADVANCED hormone therapy
- METASTATIC hormone therapy/ chemotherapy/ novel agent
F-18 FDG PET prostate cancer

Pitfall FDG: Limited utility due to relatively low glucose metabolism of most PC
Why Choline?

- Essential component of phospholipids and cell membrane metabolism
- Choline is incorporated into cell membrane phospholipids through phosphoryl choline synthesis

  Roivainen A et al 00

- Choline is phosphorylated by choline kinase & trapped in the cell
- Malignant tumours increased cell membrane metabolism, increased choline use and increased CK expression (enzyme which phosphorylates choline)

  Ackerstaff et al, Can Res 2001
### C-11 F-18 choline in prostate cancer

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-11 choline</td>
<td>Low urinary excretion</td>
<td>Half life 20 mins</td>
</tr>
<tr>
<td></td>
<td>Ideal choline tracer (biologically the same as natural choline)</td>
<td>On site cyclotron</td>
</tr>
<tr>
<td>F-18 fluoroethylcholine (FEC)</td>
<td>Half life 110 mins</td>
<td>Urinary excretion (FMC&lt; FEC)</td>
</tr>
<tr>
<td>F-18 fluoromethylcholine (FMC)</td>
<td></td>
<td>Limited availability in UK</td>
</tr>
</tbody>
</table>
- Patient prep- fasting 6 hours (reduced bowel uptake)
- Administered activity 330 MBq (approx 10 mSv) De Grado JNM 01
- Started with early dynamic pelvic
- Now 45-60 mins pi half body vertex to upper thighs
- Flat bed
Availability and cost

- Erigal F-18 FEC
  Tuesdays & Thursdays

- Petnet F-18 FMC
  Mondays

Cost £450 - £650
PET/CT in prostate cancer

- Diagnosis
- Localization
- Primary staging
- Biochemical relapse post radical therapy
- Radiation therapy planning
- Response assessment- salvage and systemic therapy
Multiparametric MRI (mp MRI)

NICE 2014: mpMRI
Men with negative prostate biopsy and elevated PSA
Staging if knowledge of T or N stage could affect management
Staging Prostate cancer

- mpMRI is superior for localisation and T stage
- Choline PET cannot reliably differentiate between BPH and cancer
- Not reliable for ECE and SV invasion
- CECT, Bone scintigraphy
PSA rising, repeated negative biopsies has pacemaker so can’t have mpMRI

**Pitfall:** cannot differentiate between BPH and prostate cancer- NOT for localisation/ T stage

**Pearl:** may however be useful in cases where MRI contra indicated
PET/CT in prostate cancer

- Diagnosis
- Localization
- Primary staging
- Biochemical relapse post radical therapy
- Radiation therapy planning
- Response assessment - salvage and systemic therapy

Choline PET/CT indications:
1. Rising PSA post radical therapy
2. High risk staging - equivocal finding on CWU
Nodal staging in Prostate cancer

- LN metastases are seen in 25-30% of pts
- LN involvement reduces disease free survival from 85% to 50%
- Pelvic LND – gold standard
  - Invasive
  - 4-5% morbidity
  - Expensive, needs hospitalization
  - May not be able to sample all potential nodal areas
- Standard anatomic imaging has limited diagnostic accuracy
  - Pooled sensitivity – 39%
  - Pooled specificity – 82%

Hovels et al, Clin Radiol 2008
Use of $[^{11}C]Choline$ PET-CT as a Noninvasive Method for Detecting Pelvic Lymph Node Status from Prostate Cancer and Relationship with Choline Kinase Expression

Kaiyumars Contractor$^1$, Amarnath Challapalli$^1$, Tara Barwick$^2$, Mathias Winkler$^1$, Giles Hellawell$^1$, Steve Hazell$^3$, Giampaolo Tomasi$^1$, Adil Al-Nahhas$^2$, Paola Mapelli$^1$, Laura M. Kenny$^1$, Paul Tadrous$^4$, R. Charles Coombes$^1$, Eric O. Aboagye$^1$, and Stephen Mangar$^1$

- 406 LN in 26 pts lymphadeneectomy
- 27/406 LN positive- 17/27 <1cm size
- MRI Per nodal Sens 18.5% Spec 98.7%
  - Per patient Sens 50% Spec 72.2%
- PET/CT Per nodal Sens 51.9 % Spec 98.4%
  - Per patient Sens 77.8% Spec 82.4%
Heterogenous sensitivity
Patient selection
Inhomogenous-risk
Surgical technique
## M stage- bone metastases

<table>
<thead>
<tr>
<th>Modality</th>
<th>Advantages</th>
<th>Disadvantages</th>
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</thead>
<tbody>
<tr>
<td>99mTc MDP Planar bone scan</td>
<td>Widely available</td>
<td>Non specific marker of osteoblastic activity</td>
</tr>
<tr>
<td></td>
<td>Cheap</td>
<td>Reflects osteoblastic in response in cortex – will miss early marrow disease</td>
</tr>
<tr>
<td>Planar plus SPECT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>Early marrow</td>
<td>Not good for ribs</td>
</tr>
<tr>
<td></td>
<td>High spatial and contrast resolution</td>
<td>Availability / cost</td>
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<tr>
<td></td>
<td>Neural compromise</td>
<td></td>
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<tr>
<td></td>
<td>No Radiation</td>
<td></td>
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<tr>
<td>WB- MRI</td>
<td>Visceral and bony disease</td>
<td>?specificity</td>
</tr>
<tr>
<td></td>
<td>No Radiation</td>
<td>Body coils</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Availability / cost</td>
</tr>
<tr>
<td>Choline PET/CT</td>
<td>Visceral and bony disease</td>
<td>PET- spatial resolution</td>
</tr>
<tr>
<td>Choline PET/ MR</td>
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</table>
Choline PET/CT highest specificity
MRI higher sensitivity

Good study comparing FCH and WB MRI lacking
Pearl: Bone metastases often not sclerotic
Staging PSA 55 Gleason 4 +5

- Tc99m MDP
- F-18 FCH

Retroperitoneal LN mets: below size criteria
High risk staging: Gleason 4 + 5, sclerotic lesion L5 on staging MRI

**Pearl:** may detect disease in non enlarged nodes

**Pearl:** May detect early bone/marrow involvement
Rising PSA post radical treatment

- 15-40% men biochemical relapse within 10 years of post radical Rx (RT or prostatectomy)
- Recurrence-
  - 15-25% local
  - 20-25% metastatic only
  - 45-55% both local and metastatic

- IMPORTANT TO ESTABLISH IF SUITABLE FOR LOCAL SALVAGE (Surgery or RT) OR SYSTEMIC RX
- After Radical Prostatectomy PSA >0.2 ng/ml
- After Radiation therapy PSA > 2 + nadir ng/ml
Rising PSA post radical treatment

- C11choline overall detection rate 40-71%  *Picchio et al, Krause et al, Reske et al*
- FCH overall detection rates 43-55%  *Pelosi et al, Marzola et al, Cimitan et al*
- High Specificity & PPV, less high sensitivity and NPV
- Sensitivity increases with trigger PSA value
  - PSAdt (doubling time)
  - PSAvel (velocity)
- Even if detecting disease in only 30% with PSA levels 1.5ng/ml
  1. Cure after RP with salvage RT is more successful when lower PSA-levels (<1 ng/ml)
  2. local therapy not appropriate if systemic disease present
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

Clinical Nuclear Medicine • Volume 38, Number 1, January 2013

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

**FIGURE 1.** $^{18}$F-Choline PET/CT detection rate versus trigger PSA level obtained in the whole sample of 233 patients.

Box plot of the PSA velocity (ng/mL/yr) distribution.
Rising PSA post radical prostatectomy. PSA 1.62
77 yr old post radical RT biochemical relapse PSA 6
Rising PSA post radical radiotherapy
Exploring the potential of $[^{11}C]$choline-PET/CT as a novel imaging biomarker for predicting early treatment response in prostate cancer

Amarnath Challapalli, Tara Barwick, Giampaolo Tomasi, Michael O’Doherty, Kaiyumars Contractor, Simon Stewart, Adil Al-Nahhas, Kevin Behan, Charles Coombes, Eric O. Abogaye and Stephen Mangar

Lesion at level of Prostate

Lesion at level of Seminal vesicles

ADT causes marked reduction in choline uptake
ADT - neoadjuvant, primary and adjuvant treatment

In vitro & in vivo studies report ADT to reduce choline uptake in hormone sensitive PCa \textit{De Grado, Giovacchini}

**Implications for initial staging**

Biochemical failure on ADT (hormone resistant Pca) are more likely to have a positive choline than hormone sensitive \textit{Giovacchini, Castellucci, Husarik}

\textit{‘In absence of strong evidence for an inhibitory effect of ADT in hormone resistant PCa prolonged withdrawal of ADT in patients experiencing progression of disease may be ethically questionable’}
Inguinal and mediastinal LN

**Pitfall:** Active infection/inflammation can be choline avid
Incidental findings
Incidental findings
Thyroid Lymphoma Incidentally Detected by $^{18}$F-Fluorocholine (FCH) PET/CT

Amy Eccles, MB BChir, FRCR, Amarnath Challapalli, MBBS, MD, MRCP, FRCR, Sameer Khan, MBBS, MRCP, FRCR, Tara Barwick, MB ChB, MSc, MRCP, FRCR, and Stephen Mangar, MB ChB, MRCP, MSc, FRCR, MD

Clinical Nuclear Medicine • Volume 38, Number 9, September 2013
Indications for choline PET/CT in prostate cancer:
- Rising PSA post radical therapy (PSA kinetics)
- High risk staging- equivocal finding on CWU

Thanks to Amar Challapalli, Steve Mangar, Eric Aboagye, Sameer Khan, Stefano Fanti

Thank you for your attention
M stage - bone metastases

- **BS vs Choline PET**: Relapse & Neg BS - Choline PET identified bone mets in 15% (*Fuccio* 12)

- **BS vs NaF F-18 PET**: F-18 NaF PET/CT more sensitive and specific than BS (*Even-Sapir* 06)

- **WB DW MRI vs F-18 NaF PET**: WB MRI higher specificity but lower sensitivity (*Mosavi* 12)

Choline more sensitive than bone scintigraphy

Choline PET and WB MRI complimentary-

?PET/MRI
Rising PSA post radical prostatectomy.
65 yr old. PSA 11. Staging suspicious pelvic nodes on MRI