Advice Statement 004/17

What is the most clinically effective and cost effective non-FDG tracer for use in PET-CT for staging and assessment of patients with suspected recurrent prostate cancer?

This advice has been produced following completion of evidence note 67 by Healthcare Improvement Scotland, in response to an enquiry from the Scottish PET-CT Working Group.

Background
Prostate cancer is the most common cancer among males in the UK, accounting for 26% of all male cancer diagnoses. In 2014 there were 3,202 new cases of prostate cancer in Scotland, over half occurring in men aged 70 years or older.

Prostate cancer recurs in up to one in three men who have undergone treatment with curative intent for localised disease. Biochemical recurrence is initially demonstrated by a rise in total serum PSA, often despite normal findings with conventional imaging. Early detection and precise localisation of the site of recurrence is critical in informing further treatment decisions.

Functional imaging with PET-CT has primarily used $^{18}$F-2-fluoro-2-deoxy-D-glucose (FDG) as a radiolabelled tracer for oncological indications. For cancers, such as prostate cancer, where glucose metabolism is low, several non-FDG tracers have been developed. In Scotland choline tracers are currently used in PET-CT restaging of patients with suspected recurrent prostate cancer and there is growing interest in using anti-$^{18}$F-FACBC or $^{68}$Ga-PSMA.

Clinical effectiveness
- In a single meta-analysis of pooled data from twelve studies $^{18}$F-choline was more sensitive than $^{11}$C-choline (91.8% vs 81.8%) in detecting recurrent prostate cancer.
- In a systematic review of two studies on $^{68}$Ga-PSMA and four studies on choline tracers, $^{68}$Ga-PSMA had higher median detection rates for recurrent disease in restaging prostate cancer, particularly at low PSA levels:

<table>
<thead>
<tr>
<th>PSA level (choline)</th>
<th>Median detection rate: Choline</th>
<th>PSA level ($^{68}$Ga-PSMA)</th>
<th>Median detection rate: $^{68}$Ga-PSMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1ng/ml</td>
<td>20%</td>
<td>&lt;0.5ng/ml</td>
<td>49%</td>
</tr>
<tr>
<td>1-2ng/ml</td>
<td>46%</td>
<td>0.5-2ng/ml</td>
<td>68%</td>
</tr>
<tr>
<td>&gt;2ng/ml</td>
<td>80%</td>
<td>&gt;2ng/ml</td>
<td>90%</td>
</tr>
</tbody>
</table>

- A systematic review comparing cholines, $^{68}$Ga-PSMA and anti-$^{18}$F-FACBC for restaging in patients with suspected prostate cancer recurrence reported that only $^{68}$Ga-PSMA had superior detection rates for any recurrence:
  - $^{68}$Ga-PSMA vs. choline: odds ratio 3.6, 95% CI 1.3 to 10.2, p=0.014
Anti-\(^{18}\)F-FACBC vs. choline: odds ratio 1.8, 95% CI 0.79 to 3.9, p=0.16
- Evidence for anti-\(^{18}\)F-FACBC and \(^{68}\)Ga-PSMA was limited to a few small studies.

### Safety
- No adverse events relating to the use of \(^{11}\)C-choline, \(^{18}\)F-choline, anti-\(^{18}\)F-FACBC or \(^{68}\)Ga-PSMA tracers in PET-CT restaging of recurrent prostate cancer were reported.

### Cost effectiveness
- No cost effectiveness studies on the use of non-FDG PET-CT in recurrent prostate cancer were identified.

### Context/Organisational issues
- Cyclotrons for producing cholines and anti-\(^{18}\)F-FACBC are available at a limited number of NHSScotland sites. Generators for producing \(^{68}\)Ga-PSMA are not currently present on NHSScotland premises.
- Transfer of non-FDG tracers between hospitals is limited by the half-life of the molecules. In particular the 20 minute half-life of \(^{11}\)C-choline restricts its use to within a single facility. Other tracers can be transported between sites within the range of their half-life.
- Producing \(^{68}\)Ga-PSMA requires specially trained staff and is covered by regulations on good manufacturing practice in the UK. A \(^{68}\)Ga-PSMA PET-CT service may require up-skilling existing staff and/or recruitment of a small number of new staff.
- Volume of patients requiring annual \(^{68}\)Ga-PSMA PET-CT for prostate cancer restaging is likely to be comparable to current use of choline based PET-CT in this population.

Approximate costs for non-FDG PET-CT tracers are included below for information:
- One cyclotron run produces a single dose of \(^{11}\)C-choline at a cost of approximately £3,000, or four doses of \(^{18}\)F-choline at a cost of £500 per dose.
- Anti-\(^{18}\)F-FACBC is marketed as Axumin in the USA by Blue Earth Diagnostics at $3,675 per unit dose (approximately £3,000). Anti-\(^{18}\)F-FACBC can be produced in existing cyclotrons.
- A \(^{68}\)Ga-PSMA generator produces two to four doses per cycle at a cost of £500-£1,000 per dose.
- Estimated capital costs for \(^{68}\)Ga-PSMA production equipment are £117,000. The annual cost of providing a \(^{68}\)Ga-PSMA PET-CT service in NHS Lothian is estimated at £175,000 or £117,000 per annum after savings from stopping other non-FDG tracer use.

### Conclusion
- Implementing non-FDG PET-CT in Scotland for restaging patients with suspected prostate cancer recurrence has potential cost and infrastructure implications. All the evidence identified on non-FDG PET-CT restaging in prostate cancer patients addressed diagnostic accuracy, therefore no conclusions can be drawn about the effect on treatment decisions or patient outcomes in this population.
- A small number of studies suggest \(^{68}\)Ga-PSMA is more accurate in detecting recurrent disease compared with cholines.
- Large, prospective, multicentre studies are necessary to evaluate the cost effectiveness, diagnostic performance, impact on patient management and place in the patient care pathway of new non-FDG tracers (\(^{18}\)F-FACBC or \(^{68}\)Ga-PSMA) in PET-CT restaging of patients with suspected prostate cancer recurrence.
Advice context:
The status of SHTG Advice Statements is advisory.

No part of this advice may be used without the whole of the advice being quoted in full. This advice represents the view of the SHTG at the date noted.

It is provided to inform NHS boards in Scotland when determining the place of health technologies for local use. The content of this Advice Statement was based upon the evidence and factors available at the time of publication. An international evidence base is reviewed and thus its generalisability to NHSScotland should be considered by those using this advice to plan services. It is acknowledged that the evidence constitutes only one of the sources needed for decision making and planning in NHSScotland. Readers are asked to consider that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. SHTG Advice Statements will be considered for review on a 2-yearly basis. The evidence will be updated if requested by the clinical community, dependent on new published reports. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

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Chair
Scottish Health Technologies Group