Cost-effectiveness of $^{18}$F-FDG PET/CT for screening distant metastasis in stage II/III breast cancer patients

- from a UK, US and Dutch perspective-

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Introduction: DM screening in stage II-III BC

PST (=NACT) an emerging treatment approach in breast cancer

↑ QoL¹ (↑ rates of breast conserving surgery)
↑ Survival² (allows monitoring and adapt treatment based on response)

PST in stage II-III requires prior distant metastasis screening

Guideline recommendation in

Conventional imaging (CI)

Bone scan (bone) + abdomen US (liver) + chest X-ray (lung)ú
+ chest /abdomen CT (liver and lung)

Introduction: Added value of PET/CT

$^{18}$F-FDG PET/CT (PET/CT) is more accurate than CI$^{1-3}$

Sensitivity 97-100% vs 60-85%  Specificity 91-98% vs 67-83%

PET/CT is more expensive than CI

Additional costs/ patient:  £1531  $342  €710

Research question

What is the added value of PET/CT vs CI in screening for DM in stage II-III breast cancer patients?

In  & four subtypes (by ER (+/-) and HER2 (+/-))

$^1$Niikura, Oncologist 2011; $^2$Fuster, JCO 2008, $^3$Koolen, BCRT 2012
Methods: PSA and outcomes

Probabilistic sensitivity analysis (PSA)

Markov model (Excel)

Compared cost and effects of DM screening with PET/CT vs CI

Stage II-III breast cancer women, 50 years old

Cycle length 1 year/ Time horizon 5 years / 10,000 simulations

Health care system perspective (Direct medical costs)

Outcomes (PET/CT vs CI)

Incremental effects

# of false- and false+ prevented

# of true- and true+, life years (LY) and quality-adjusted-LY (QALYs) gained

Incremental costs (€ 2013)

Incremental cost-effectiveness (net monetary benefit, iNMB)
Methods: Decision tree & Markov model

DM → Biopsy

True +

1 DM → PBC\(_{tx}\) → L\(_{tx}\)

≥2 DM → Palliative\(_{tx}\)

False + → PBC\(_{tx}\)

imaging

with US\(_{liver}\) + MRI\(_{bone}\) + CT\(_{chest}\)
with PET/CT\(_{whole\ body}\)

Single DM

Non BC death

Terminal

DM ≥2 DM

1 DM

≥2 DM

Stable

Single DM

Multiple DM

Stable

Multiple DM

No DM

PBC\(_{tx}\) → FU

Biopsy & imaging

True –

False –

with Cl (depending on DM site)
with PET/CT\(_{whole\ body}\)

Stable

Stable

Single DM

Multiple DM

Tx: treatment, PBC-tx: PST, breast surgery +/- radiotherapy, adjuvant chemotherapy, L: local, S: systemic mo: months, FU: follow-up
### Methods: Survival, costs & QoL of true/false +/-

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>++</td>
<td>DM (early)</td>
<td>++</td>
<td>Presence DM Pall_{tx}</td>
<td>+++</td>
<td>Biopsy L_{tx} DM Pall_{tx} DM</td>
</tr>
<tr>
<td>False +</td>
<td>+++++</td>
<td>No DM</td>
<td>+++</td>
<td>PBC_{tx}</td>
<td>++</td>
<td>Biopsy Imaging</td>
</tr>
<tr>
<td>True -</td>
<td>+++</td>
<td>No DM</td>
<td>+++</td>
<td>PBC_{tx}</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>False -</td>
<td>+</td>
<td>DM (late)</td>
<td>+</td>
<td>Painful DM Pall_{tx}</td>
<td>++++</td>
<td>Imaging Biopsy L_{tx} DM Pall_{tx} DM</td>
</tr>
</tbody>
</table>

QoL: quality of life, tx: treatment, L: local, Pall: palliative, PBC: primary breast cancer treatment
Methods: Input data for the model

**NKI – AVL database** (n=544)

- Imaging performance
- Primary breast cancer treatment, per subtype (2013 treated patients)

**Literature**

- Epidemiological (number and sites of metastasis, per subtype)
- Survival (per site and number of metastasis)
- Costs (National official tariffs – NL, UK; Medicare - US)
- Quality of life (EQ-5D)
Results: Incremental effects

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
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<tbody>
<tr>
<td>PET/CT: 92%</td>
<td>98%</td>
</tr>
<tr>
<td></td>
<td>CI: 13%</td>
</tr>
<tr>
<td></td>
<td>94%</td>
</tr>
</tbody>
</table>

# false -/+ prevented

\[ \uparrow \text{by } 0.89x \quad \text{by } 0.65x \]

# true -/+ gained

\[ \uparrow \text{by } 1.04x \quad \text{by } 8.3x \]

# LYs gained per patient

\[ 0.007 \pm 0.0001 = 1.9 \text{ days} \]

# QALYs gained per patient

\[ 0.002 \pm 0.0001 \]
## Results: Incremental costs

<table>
<thead>
<tr>
<th>Subtype</th>
<th>NL (€)</th>
<th>UK (€)</th>
<th>US (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER+/HER2-</td>
<td>447</td>
<td>780</td>
<td>-1606</td>
</tr>
<tr>
<td>ER+/HER2+</td>
<td>1739</td>
<td>3107</td>
<td>2822</td>
</tr>
<tr>
<td>ER-HER2-</td>
<td>1050</td>
<td>1864</td>
<td>-1090</td>
</tr>
<tr>
<td>ER-/HER2+</td>
<td>582</td>
<td>936</td>
<td>146</td>
</tr>
</tbody>
</table>

≠ **between countries:**

(Mainly) DM screening costs (UK>NL>US)

(Also by) palliative treatment costs (if very expensive, as in the US)

≠ **between subtypes:**

Palliative treatment costs in true+ and false- (and their relationship)

Subtypes with costly true+ tx (vs false-), had ↑ incremental costs (ER+/HER2+)

Subtypes with costly false- tx (vs true+), had more costs savings (ER+/HER2-)
Results: Incremental cost-effectiveness

<table>
<thead>
<tr>
<th></th>
<th>NL: €80.000/QALY</th>
<th>UK: £30.000/QALY</th>
<th>US: $50.000/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>ER+/HER2-</td>
<td>-259, 25%</td>
<td>-597, 3%</td>
<td>1799, 97%</td>
</tr>
<tr>
<td>ER+/HER2+</td>
<td>-1560, 4%</td>
<td>-2932, 0%</td>
<td>-2669, 11%</td>
</tr>
<tr>
<td>ER-HER2-</td>
<td>-883, 10%</td>
<td>-1701, 5%</td>
<td>1261, 83%</td>
</tr>
<tr>
<td>ER-/HER2+</td>
<td>-384, 31%</td>
<td>-739, 22%</td>
<td>56, 48%</td>
</tr>
</tbody>
</table>

iNMB > 0 = Cost-effective; Thresholds for cost-effectiveness NL: €80.000/QALY, UK: £30.000/QALY, US: $50.000/QALY
Conclusion: Take home message

**DM screening in s. II-III BC with PET/CT (vs CI)**

Prevents false +/-, increases true +/-, yet LY and QALY benefit is low
Incremental costs driven by DM screening and palliative \( t_x \) costs
Cost-effectiveness expected in HER2- subtypes of \( \text{③} \) (high certainty)
Cost-effectiveness uncertain in the remaining subtypes/countries

**Limitations**

Follow up time in determining true/false –
Factor to lower survival in DM detected at follow up (vs at screening)

**Future plans**

Value of information analysis
Wait for further evidence
Acknowledgments

Health services research
Prof. Wim van Harten
Dr. Lotte Steuten
Dr. Valesca Retèl

Nuclear Medicine
Suzana Teixeira, MD
Dr. Renato Valdes Olmos

Surgical oncology
Prof. Emiel Rutgers

Medical oncology
Prof. Sjoerd Rodenhuis

Biometrics
Dr. Vincent van der Noort

Tumor registry
Caroline Pauwels-Heemskerk