FDG-PET/CT in Colo-rectal Cancer & Upper Gastrointestinal Cancer
Health Technology Assessment
Multi-disciplinary field of policy analysis; medical, economic, social, ethical implications of the incremental value of medical technology

Conclusions:
There is insufficient evidence to support the routine use of FDG PET/CT in primary CRC: FDG PET/CT changes management in 10-15% of cases

The value of FDG positron emission tomography/computerised tomography (PET/CT) in pre-operative staging of colorectal cancer: a systematic review and economic evaluation

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NIHR HTA programme
www.hta.ac.uk
Conclusions:

The economic evaluations conclude that FDG PET/CT as an add-on imaging device is cost-effective in the pre-operative staging of recurrent colon, recurrent rectal and metastatic disease.

ESTABLISHED ROLES

For surgical planning

**metastatic disease (clinical suspicion)** before metastasectomy to detect **occult lesions**

**Residual disease** after local ablative therapy

Evaluation of suspected disease **relapse (CEA)**

For therapeutic assessment in clinical protocols
Clinical example – primary staging

Indication for PET:
Surgical planning:
Limited stage IV

Result:
Tumor in coecum
8-9 liver mets
carcinosis
subilus
The tumor extends into the mesorectal fat (left side)

Enlarged and normal sized paraaortal FDG-positive nodes
Clinical example - staging
Clinical example - relapse
Clinical example - recurrence

Rectal cancer 2 y ago.  
Nodal and pulmonary mets  
Pelvic pain without any explanation
**Residual disease after local ablative therapy**

FDG-PET has great potential for identifying residual tumor very early after local ablative therapy

### TABLE 2. Response Monitoring After Local Ablative Therapy for Treatment of Colorectal Cancer Liver Metastases

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Reference</th>
<th>No. of patients</th>
<th>Therapy</th>
<th>Timing of PET evaluation</th>
<th>PET response criteria</th>
<th>Outcome measures</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Langenhoff et al.</td>
<td>2002</td>
<td>26</td>
<td>22</td>
<td>CSA and RFA</td>
<td>&lt;3 wk</td>
<td>Negative results</td>
<td>Recurrence</td>
<td>NPV 100%; PPV 80%</td>
</tr>
<tr>
<td>Donckier et al.</td>
<td>2003</td>
<td>28</td>
<td>17</td>
<td>RFA</td>
<td>1 wk, 4 wk</td>
<td>Negative results</td>
<td>Residual tumor</td>
<td>NPV 100%; PPV 80%</td>
</tr>
<tr>
<td>Joosten et al.</td>
<td>2005</td>
<td>27</td>
<td>43</td>
<td>CSA and RFA</td>
<td>&lt;3 wk</td>
<td>Negative results</td>
<td>Recurrence</td>
<td>NPV 97%; PPV 88%</td>
</tr>
<tr>
<td>Veit et al.</td>
<td>2006</td>
<td>30</td>
<td>11</td>
<td>RFA</td>
<td>&lt;2 d</td>
<td>Negative results</td>
<td>Recurrence</td>
<td>Accuracy 68%</td>
</tr>
<tr>
<td>Denecke et al.</td>
<td>2007</td>
<td>20</td>
<td>21</td>
<td>LITT</td>
<td>1-3 d, 1-6 mo, &gt;6 mo</td>
<td>Negative results</td>
<td>Residual tumor or recurrence</td>
<td>NPV 96%; PPV 97%</td>
</tr>
</tbody>
</table>

CSA = cryosurgical ablation; RFA = radiofrequency ablation; NPV = negative predictive value; PPV = positive predictive value; LITT = laser-induced thermotherapy.

De Geis-Oei et al JNM 2009
Residual disease after local ablative therapy

CT and MRI
- Difficult to distinguish between residual tumour and haemorrhage
- Altered anatomy

PET
- Ablated liver cells are not able to take up FDG
- Possible inflammation is uncommon

FDG PET/CT is the preferred technique following hepatic metastectomy or ablation
Clinical example

FDG-positive metastases

FDG-negative RFA cavities
3 weeks after ablation:
NPV: 97-100%
PPV: 80-86%
n = 81 patients with 237 lesions

Early negative PET (after 1 week) is less suitable

Early and late positive PET: 100% PPV
Clinical example

70 year female check up after resection of lung metastases from colon cancer

6th January 2012

10th April 2012
Suspected disease relapse

Substantial evidence (meta-analysis) PET/ceCT is first line diagnostic imaging technique with increasing CEA.
Changes management in 37,5-82%

With equivocal posttreatment radiologic residual structural mass and signs pointing to recurrence FDG PET changes management in 45-66%.
CONCLUSION: FDG PET/CT has higher sensitivity than MDCT in the identification of sites of recurrent and metastatic disease in patients with colorectal cancer and an elevated CEA level. The two techniques appear to have similar specificity.
Initial results suggest that differences in accuracy for local and distant metastases detection using FDG-PET-CT and WB-MRI for integrated screening of tumour recurrence in colorectal cancer depend on the location of the malignant focus. Our results show that nodal disease is better detected using PET-CT, whereas organ disease is depicted equally well by both investigations.
18F-FDG PET plays a pivotal role in staging before surgical resection of recurrent colorectal cancer. Staging before metastasectomy, the localization of recurrence in patients with an unexplained rise in CEA, assessment of residual masses after treatment.
There is no evidence that a baseline PET can identify patients with poor prognosis or patients less likely to respond to treatment.
Monitoring and Predicting Response to Therapy with $^{18}$F-FDG PET in Colorectal Cancer: A Systematic Review

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Molecular imaging with $^{18}$F-FDG PET has been proven useful in the management of colorectal cancer. $^{18}$F-FDG PET plays a pivotal role in staging before surgical resection of recurrent colorectal cancer and metastases, in the localization of recurrence in patients with an unexplained rise in serum carcinoembryonic antigen levels, and in the assessment of residual masses after treatment. Currently, there is increasing interest in the role of $^{18}$F-FDG PET beyond staging. The technique appears to have significant potential for the characterization of tumors and for the prediction of prognosis in the context of treatment stratification and early assessment of tumor response to therapy. This systematic review provides an overview of the literature on the value of $^{18}$F-FDG PET in colorectal cancer. The current 5-y survival rate approaches 66% (1). The prognosis for patients with this disease has improved substantially, mainly because of earlier detection and the introduction of effective systemic (chemo)therapeutic agents (2-4).

Molecular imaging with $^{18}$F-FDG PET has been shown to be useful in the management of colorectal cancer. $^{18}$F-FDG PET already plays a pivotal role in staging before surgical resection of locally recurrent cancer and metastases, in the localization of recurrence in patients with an
Overall conclusions:
SUV reduction significantly greater in responders (histopathology, survival)
Predicted outcome better than ERUS, CT, MR
Clinical consequences remain unclear

Recommendations for the application of FDG PET in measuring therapeutic response in specific clinical scenarios have not yet been established. This is largely due to

- the differences in study methodology
- PET acquisition, timing, histopathologic interpretation and/or clinical endpoint
- lack of common definitions for therapeutic response
Responses seen on FDG-PET are closely related to **clinical benefit** while conventional objective response criteria (tumor size) lag weeks and months behind the FDG-PET.

The response can be seen 1 month after initiating therapy, and as early as 24 h after treatment.

**Lack of metabolic response** on FDG-PET indicates **primary resistance** to the drug. **Re-emergence** of metabolic activity within tumor sites following a period of therapeutic response indicates **secondary resistance** to the drug.
FDG-PET and correlating CT scans of a patient prior to and 1 month after imatinib therapy.
Upper gastrointestinal cancer – staging
Ultra short version

**Pancreas**
FDG PET/CT upstages 10-12% of the cases, but is not recommended as routine

**Esophagus, cardia, stomach**
FDG PET/CT is recommended for staging in patients with resectable tumors
FDG-PET/CT has higher sensitivity and specificity for N-staging than stand alone CT (51% and 84%)
FDG-PET detects occult M-stage in 5-10%
PET/MRI – cases from Herlev

Anal cancer – planning of radiotherapy (scientific purpose)
PET/MRI – cases from Herlev

Fusion of PET-CT and MRI in OTP planning system (nucletron)
Initial results suggest that differences in accuracy for local and distant metastases detection using FDG-PET-CT and WB-MRI for integrated screening of tumour recurrence in colorectal cancer depend on the location of the malignant focus. Our results show that nodal disease is better detected using PET-CT, whereas organ disease is depicted equally well by both investigations.
22 y male.
Ewing sarcoma from rib (white arrow) was resected 12 mo ago
Postoperative infection and abscess in the area.
Now lesion ventral to the spine (red arrow) slight signs of infection in blood test.
99mTc-labelled white blood cell SPECT
Ewing sarcoma.

MRI

PET

FDG PET

PET-MRI
Images after 2 series of chemotherapy. No uptake in tumor.

Metabolic active bone marrow
Due to chemotherapy.