FDG-PET/CT in Colo-rectal Cancer & Gastrointestinal Cancer
(A) CT-based virtual colonoscopy showing several areas of stool that are difficult to distinguish from potential malignant polyp

(B) PET/CT virtual colonoscopy showing intense 18F-FDG uptake that highlights suspected polyp relative to surrounding stool and greatly aids in differentiation of lesion from stool.
(C and D) Retrospective review of standard 2D PET/CT tomographic slices reveals abnormal focus in colon that was missed on original interpretation (C) and would not have been detected without 3D fusion rendering (D). p = polyp; s = stool
(A) Supine PET/CT without air insufflation showing abnormal focus (arrows) in rectosigmoid colon on PET.
(B) Prone PET and CT with air insufflation providing excellent definition of same lesion shown in A on both PET and CT images.
(C) PET/CT without air insufflation illustrating good image and lesion (arrow) coregistration.
(D) 3D-rendered PET/CT colonography demonstrating lesion in its entirety
Physiological uptake/secretion of FDG in the bowel is variable and unpredictable. Usually takes the form of a diffuse or segmental pattern with *no corresponding morphological abnormality*

The mechanism unclear:
- muscular peristaltic activity
- high concentration of white blood cells in the bowel wall
- presence of lymphoid tissue in the cecum
- presence FDG-secreting cells (colostomy)

Intense colonic uptake has been reported in acute enterocolitis, pseudomembranous colitis, IBD, constipation and metformin treatment

Focal FDG uptake in the colon, is more worrisome

In patients with colorectal cancer, it has been estimated that 5% have synchronous colonic carcinomas and more than one-third have other adenomatous polyps in the colon.
Incidental focal FDG uptake

Clinical significance of incidental focal colorectal $^{18}$F-fluorodeoxyglucose uptake: our experience and a review of the literature


6000 patients
64 (1.1%) focal uptake
48 colonoscopy

Colonoscopy is recommended for further evaluation of incidental focal colorectal uptake of FDG, given the high incidence of malignant and premalignant lesions.
Incidental focal hypermetabolic colorectal lesions identified by positron emission tomography: prevalence of malignancy

Philip Shie
Diagnostic Imaging Services, Kaiser Permanente Fontana Medical Center, Fontana, CA, USA

In this article, current literature of incidental colorectal FDG uptake on PET and PET/CT were reviewed. In the studies reviewed, the incidence of unexpected colorectal FDG uptake is low at 1.6%, (95% CI: 1.4%–1.7%). However, the risk of malignancy and pre-malignancy is quite high, calculated to be 61.5% (95% CI: 55.6%–67.1%) in the group of 286 patients with further evaluation. Thus, incidental FDG lesions in the colon-rectum should warrant further evaluation when encountered on PET if the discovery of a second primary malignancy will impact patient management and survival.

Unexpected focal colorectal FDG uptake is seen in 1.6% of all patients

The risk of malignancy/pre-malignancy in these foci is 61.5%
Established roles for PET in CRC

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
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 PET in CRC:

**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
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 PET in CRC:

- **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

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

J Brush, K Boyd, F Chappell, F Crawford, M Dozier, E Fenwick, J Glanville, H McIntosh, A Renehan, D Weller and M Dunlop

September 2011
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HTA

Health Technology Assessment
NIHR HTA Programme
www.hta.ac.uk
Indication for PET:
Surgical planning:
Limited stage IV

Result:
Tumor in coecum
8-9 liver mets
Carcinosis
Bowel obstruction
44 male, months complaints of anal abscessus. Initially treated with drainage, developed pararectal fistula. Biopsy: rectal cancer (mucin producing) 
Referred for staging (long time occult disease)

T4 rectal cancer growing into the pelvis and abscessus in the right gluteal musculature. N0, M0

Metastatic disease (clinical suspicion)
The tumor extends into the mesorectal fat (left side)
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 – potentially resectable mets
- Residual disease after local ablative therapy
Evaluation of suspected disease relapse (CEA)
For therapeutic assessment in clinical protocols
The liver is the most common site of metastasis (25% at primary diagnosis)

No long-term survival with untreated liver metastases; 5-year survival 30-40% with hepatectomy

Up to 50% of patients with apparently limited metastatic disease have inoperable findings at laparotomy

Increasing the accuracy of preoperative staging may avoid the potential morbidity of unnecessary laparotomy
Conclusions:

FDG PET/CT is more sensitive than CT and MRI at identifying extrahepatic disease.

Unnecessary surgery can be avoided in 20-40% of patients with liver metastases.
Two recent meta-analysis supports the use of MRI for detection of CRC liver metastases

MRI with a liver-specific contrast agent is recommended for the preoperative evaluation before liver surgery for liver metastases because of high sensitivity and better discrimination between small metastases and cysts compared to MDCT


Potentially resectable liver metastases

Planning liver resection and RFA of liver metastasis. Enlarged node on the CT-scan.
Potentially resectable liver metastases

71 y female with rectal cancer

Liver metastasis (US)
Referred before decision on local treatment

FDG PET/CT: liver and lung metastasis
Potentially resectable adrenal metastases

T4N1M0 colon cancer 12 mo ago. Referred with metastases in right adrenal gland before adrenal ectomy

FDG-positive nodes above the kidney vein
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 PET in CRC

**ESTABLISHED ROLES**

For surgical planning:

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

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

For therapeutic assessment in clinical protocols.

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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Health Technology Assessment NIHR HTA programme
www.hta.ac.uk
CT and MRI
   Difficult to distinguish between residual tumour and haemorrhage
   Altered anatomy

PET
   Ablated liver cells are not FDG avid
   Possible inflammation is uncommon

FDG PET/CT is the preferred technique following hepatic metastectomy or ablation
Residual disease after local ablative therapy

FDG-positive metastases

FDG-negative RFA cavities
**Residual disease after local ablative therapy**

Data from literature

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
Residual disease after local ablative therapy

70 y female check up after Resection of lung metastases from colon cancer

6th January 2012

10th April 2012
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 100%</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.
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

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

J Brush, K Boyd, F Chappell, F Crawford, M Dozier, E Fenwick, J Glanville, H McIntosh, A Renehan, D Weller and M Dunlop
Use of FDG-PET or PET/CT to detect recurrent colorectal cancer in patients with elevated CEA: a systematic review and meta-analysis

Yu-Yu Lu • Jin-Hua Chen • Chun-Ru Chien • William Tzu-Liang Chen • Shih-Chuan Tsai • Wan-Yu Lin • Chia-Hung Kao

30% of patients (first 2 years of surgery)
CEA is the earliest indicator of recurrence in 60%
Precede clinical symptoms (4.5–8 months)

In patients with raised CEA and negative or equivocal conventional imaging, FDG PET/CT sensitivity/specificity 90.3%/80.0%
FDG PET/CT has a very high negative predictive value of 95–100%
Evaluation of suspected disease relapse
Evaluation of suspected disease relapse
Evaluation of suspected disease relapse

Rectal cancer (T3N0M0) 3 month ago
Operation complicated with fistula and abscess – FDG-positive inflammation

Increased CEA – recurrence?

Adenocarcinoma
Evaluation of suspected disease **relapse**
72 y male T4N2M0 rectal cancer at diagnosis. Operation and adjuvant chemotherapy. Now increasing CEA
Evaluation of suspected disease relapse

Rectal cancer 2 y ago.
Nodal and pulmonary mets
Pelvic pain without any explanation

Nodal and pulmonary lesions
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%.
Assessment of Tumor Recurrence in Patients With Colorectal Cancer and Elevated Carcinoembryonic Antigen Level: FDG PET/CT Versus Contrast-Enhanced 64-MDCT of the Chest and Abdomen

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.

N=50
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 metastasctomi 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.
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 PET in CRC

**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*
Monitoring and Predicting Response to Therapy with $^{18}$F-FDG PET in Colorectal Cancer: A Systematic Review

Lioe-Fee de Geus-Oei$^1$, Dennis Vriens$^1$, Hanneke W.M. van Laarhoven$^2$, Winette T.A. van der Graaf$^2$, and Wim J.G. Oyen$^1$

$^1$Department of Nuclear Medicine, Radboud University, Nijmegen Medical Centre, Nijmegen, The Netherlands; and $^2$Department of Medical Oncology, Radboud University, Nijmegen Medical Centre, Nijmegen, The Netherlands

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 approximately 5%, and 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).
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
Conclusion: Response evaluation with EORTC criteria and PERCIST gave similar responses and OS outcomes with good agreement on BOmR and similar significant differences in median OS between response groups.
**Anal cancer** (squamous cell carcinoma) is a distinct entity from CRC. Staging, clinical progression, and treatment are all different. FDG-PET/CT is used in staging of selected patients considered for radical treatment with equivocal imaging and for recurrence.

Physiological FDG-uptake may be seen in the anal sphincter; should be circumferential, uniform, and without mass/soft tissue irregularity.
Clinical example – primary staging (anal cancer)

**Anal cancer** FDG-PET/CT is used in staging of selected patients considered for radical treatment with equivocal imaging.

Lymph node in relation to internal iliac vessels
Clinical example – primary staging (anal cancer)

Lymph nodes in the groin
Clinical example – primary staging (anal cancer)

Anal cancer – Common site of metastasis
Esophageal, gastric and gastroesophageal junction (GEJ) cancers
Complete resection is the only method of achieving permanent control.
Surgeries can be morbid and futile in patients who have advanced disease, making appropriate staging and characterization of disease burden of paramount importance.
Upper gastrointestinal cancer – staging

Treatment:
- surgery: 5 %
- chemotherapy and surgery: 30 %
- inoperable (stage/comorbidity): 70 %
- radiation (esophagus)

5y survival (localised disease):
- Esophagus: 40%
- GEJ cancer: 32%
- Gastric cancer: 45%

The decision not to operate is difficult in the individual patient. M staging in possible resectable tumors is very important:
1. more aggressive lymphadenectomy
2. avoidance of surgery (futile, unnecessarily morbid)
Gastric and GEJ cancers

Low FDG-uptake:
- Mucinous carcinoma
- Signet ring cell carcinoma
- Poorly differentiated adenocarcinomas

Imaging problems:
- Physiologic uptake in gastric wall
- Perigastric nodes close to tumor
- Limited spatial resolution of PET
Primary diagnosis: Endoscopy, endoscopic US, laposcopic US
N stage
PET-CT is better than CT alone: sensitivity and specificity 51% and 84%
Hepatoduodenal, retropancreatic, mesenteric, para-aortic nodes are regarded as distant metastases as they are not amendable for surgery with standard lymphadenectomy

US of the neck if lymph node metastasis is suspected
N-stage
M-stage:
FDG PET-CT is sensitive.
M-stage disease is seen in 5-10%
Summary

FDG-PET/CT is included in NCCN 2012 for staging workup
   Its role in the evaluation of the primary tumor is limited
   It shows promise in assessment of locoregional nodal disease
   It is clearly a valuable tool for distant metastases

Can avoid unnecessary surgeries

In recurrent disease FDG- PET/CT is mores sensitive and specific than conventional imaging
   (obs high rate of false positive at the site of anastomosis)
Pancreatic cancer ranks as one of the most lethal malignancies.

Only 20% are suitable for resection at presentation.

Accurate delination to tumoral extent is crucial (US, CT, EUS and MRCP)
Pancreatic cancer

Exocrine pancreas
FDG PET has high sensitivity and specificity but is not recommended as routine; upstages 10%

Recommended for
1) Staging of patients with potentially operable adenocarcinoma where cross-sectional imaging is equivocal for metastatic disease
2) Detection of recurrence in FDG-avid tumor types
Hepatocellular cancer (HCC)

HCC is the most frequent liver cancer and prognosis of untreated patients is poor.

Well differentiated HCC:
Low FDG-uptake
  Low expression of GLUT-1
  High expression of glucose-6-phosphatase
Sensitivity: 50%

FDG-uptake is related to tumor grade
Acetate and choline uptake is moderate-high

Poorly differentiated HCC
High FDG-uptake
Low acetate and choline uptake
77 y male with HCC
Focal FDG uptake in the neck, axilla, Mediastinum, and carcinosis
Moderately high focal uptake in the HCC
Hemangioma
FDG PET/CT is recommended for:
Staging of potentially operable primary HCC where cross-sectional imaging is equivocal for metastatic disease in patients fit for operation where a positive FDG PET/CT would lead to a decision not to operate

Suspected recurrence in selected patients, where other imaging is equivocal or negative, taking into consideration that up to 50% of differentiated HCC may nor be FDG avid

FDG PET may be a predictor of post operative recurrence incl post liver-transplantation risk of tumour recurrence

Restaging after ablation (TACE) or antiangiogenic drugs
Cholangiocellular carcinoma (CCC)

The second most common primary hepatic tumor
Not commonly associated with distant metastases.

The resectability rate is low because the disease is frequently beyond the limits of surgical therapy

As curative resection is the only possibility for survival.

Accurate definition of tumor extent, potential infiltration of adjacent structures, loco-regional lymph nodes, and distant metastases are mandatory.
Cholangiocellular carcinoma (CCC)

The accuracy of 18FDG PET dependent on the Anatomic location
- intrahepatic
- extrahepatic
- perihilar
- Klatskin

Growth pattern
- infiltrating (sclerosing, periductal-infiltration)
- polypoid/papillary (intraductal-growing)
- nodular (mass forming, exophytic)

Sensitivity: 85% for the nodular morphology
- 18% for infiltrating morphology
- 78% for gallbladder cancer

Advantage over CT and MRI/MRCP in recurrence after curative resection
Cholangiocellular carcinoma (CCC)

- FDG PET/CT appears to outperform CT and MRI for the detection of regional lymph node involvement, and clearly improves M-staging.
- The addition of FDG-PET/CT to the staging of CCC changes management in 30% of the patients.
Cholangiocellular carcinoma (CCC)
Cholangiocellular carcinoma (CCC)

Recurrence in the abdominal wall
Babette's Feast short story by Karen Blixen
Film by Gabriel Axel (1987)
Oscar for Best Foreign Language Film