Hybrid imaging in colorectal & esophageal cancer

Colorectal Cancer and FDG PET/CT
Clinical background

- Cancer of the colon and rectum is one of the most common (3rd) malignancy in developed countries
- **Adenocarcinoma**: this is the most common type of colorectal cancers (98%)
- The single most important **prognostic indicator** of colorectal carcinoma is the **extent of the tumor at the time of diagnosis**
- 40-50% of patients presents with liver metastasis
- The only **curative treatment** of liver metastasis is surgery

### TNM

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>T0</td>
<td>N0</td>
<td>M0</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>80-95%</td>
</tr>
<tr>
<td>II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
<td>65-75%</td>
</tr>
<tr>
<td>III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>50-60%</td>
</tr>
<tr>
<td>IV</td>
<td>T4</td>
<td>N0</td>
<td>M0</td>
<td>25-50%</td>
</tr>
</tbody>
</table>

*Note: TNM staging system for colorectal cancer. T represents tumor size and stage, N represents lymph node involvement, and M represents metastasis.*
FDG PET/CT at staging

- **Low sensitivity** (43%) of FDG PET/CT for local and loco regional evaluation (Lu et al. *Metanalysis, Nucl. Med. Comm* 2012)
- FDG-PET/CT is usually not required if conventional imaging is normal
- FDG-PET/CT is usually not required if conventional imaging has already demonstrated widespread metastatic disease and the patient would not be eligible for radical treatment

FDG PET/CT at staging with suspect metastasis

- If conventional imaging (CT/MR) detects **synchronous liver metastases** and the patient could be considered for curative liver surgery, FDG PET/CT is useful
- FDG PET should also be performed if staging CT or MRI scan detects **nodal metastases in the common iliac region** or equivocal findings such as indeterminate pulmonary, liver or bony lesions

\[\begin{align*}
\text{Niekel et al, Radiology 2010} & \quad \text{Maffione et al, EJNMMI 2015} \\
\text{Metanalysis (39 studies, 3391 patients)} & \quad \text{Metanalysis (18 studies, 1059 patients)}
\end{align*}\]

- Diagnostic of colorectal liver metastasis in patients who have not previously undergone treatment
- On a per-lesion basis the sensitivity estimates of CT, MR imaging, and FDG PET were 74.4%, 80.3%, and 81.4%, respectively
- On a per-patient basis, the sensitivities of CT, MR imaging, and FDG PET were 83.6%, 88.2%, and 94.1%, respectively
- Specificity estimates were comparable

“Aim of the review was to obtain the diagnostic performance values of 18F-FDG PET for the detection and staging of liver metastases in patients with colorectal cancer (CRC)”

- FDG PET/CT is highly accurate for the detection of liver metastases on a patient basis but less accurate on a lesion basis. Compared to MRI, PET is less sensitive but more specific and affects the management of about one-quarter of patients.
FDG PET/CT at staging with suspect metastasis

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FDG PET/CT for surgical planning

- The liver is the most common site of metastasis
- No long-term survival with untreated liver metastases; 5-year survival 30-40% with hepatectomy
- Increasing the accuracy of preoperative staging may avoid the potential morbidity of unnecessary laparotomy
- FDG PET/CT is more sensitive than CT and MRI at identifying extrahepatic disease
- FDG PET/CT leads to Upstaging
- Unnecessary surgery can be avoided in 20-40% of patients with liver metastases

Adam et al, HPB, 2013
FDG PET/CT for suspicion of recurrence

The pooled estimates of sensitivity and specificity of FDG-PET/CT in the detection of tumor recurrence in CRC patients with elevated CEA were 94.1% (95% CI, 89.4–97.1 %) and 77.2% (95% CI, 66.4–85.9%) respectively.

- 18FDG-PET/CT should be performed in patients with rising tumour markers (e.g. CEA) and/or being clinically suspicious of recurrence but with negative or equivocal findings on other imaging.
FDG PET/CT for suspicion of recurrence

### Surveillance

**NCCN Guidelines Version 2.2017 Colon Cancer**

<table>
<thead>
<tr>
<th>PATOLOGIC STAGE</th>
<th>SURVEILLANCE</th>
</tr>
</thead>
</table>
| Stage I        | Colonoscopy at 1 y  
- If advanced adenoma, repeat in 1 y  
- If no advanced adenoma, repeat in 3 y, then every 5 y if  
  - History and physical every 3-6 mo for 2 y, then every 6 mo for a total of 3 y  
  - CEA every 3-6 mo for 2 y, then every 6 mo for a total of 3 y  
  - Chest/abdominal/pelvic CT scan every 5-12 mo (category 2b) for frequency <3 y and 1 y, then every 6-12 mo for a total of 5 y  
  - Colonoscopy* in 1 y except if no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3-6 mo  
  - If advanced adenoma, repeat in 1 y  
- PET/CT scan is not recommended  
- See Principles of Surveillance (COL-G1) |
| Stage II, III   | Colonoscopy at 1 y  
- If advanced adenoma, repeat in 1 y  
- If no advanced adenoma, repeat in 3 y, then every 5 y if  
  - History and physical every 3-6 mo for 2 y, then every 6 mo for a total of 3 y  
  - CEA every 3-6 mo for 2 y, then every 6 mo for a total of 3 y  
  - Chest/abdominal/pelvic CT scan every 5-12 mo (category 2b) for frequency <3 y and 1 y, then every 6-12 mo for a total of 5 y  
  - Colonoscopy* in 1 y except if no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3-6 mo  
  - If advanced adenoma, repeat in 1 y  
  - If no advanced adenoma, repeat in 3 y, then every 5 y if  
  - See Principles of Surveillance (COL-G1) |
| Stage IV        | Colonoscopy at 1 y  
- If advanced adenoma, repeat in 1 y  
- If no advanced adenoma, repeat in 3 y, then every 5 y if  
  - History and physical every 3-6 mo for 2 y, then every 6 mo for a total of 3 y  
  - CEA every 3-6 mo for 2 y, then every 6 mo for a total of 3 y  
  - Chest/abdominal/pelvic CT scan every 5-12 mo (category 2b) for frequency <3 y and 1 y, then every 6-12 mo for a total of 5 y  
  - Colonoscopy* in 1 y except if no preoperative colonoscopy due to obstructing lesion, colonoscopy in 3-6 mo  
  - If advanced adenoma, repeat in 1 y  
  - If no advanced adenoma, repeat in 3 y, then every 5 y if  
  - See Principles of Surveillance (COL-G1) |

*PET/CT scan is not recommended.*
Treatment monitoring with FDG PET/CT

- Not to be considered out of a clinical trial
- But more and more studies...

- de Geus-Oei LF, J Nucl Med. 2009
- Engels B, Ann Oncol. 2011
- de Geus-Oei LF, Ann Oncol. 2008
- Skougaard, J Nucl Med 2013

Treatment monitoring: impact on long term outcomes

- 18F-FDG PET/CT-based treatment response evaluation in locally advanced rectal cancer: a prospective validation of long-term outcomes

  Locally advanced rectal cancer (cT3-4 ou cN+)
  FDG PET 5 weeks after end of RT

  - Prediction of histological response
  - Significant differences in OS and DFS between PET responders and non responders
  - Delta SUV cut-off 65 %

Incidental focal colonic FDG uptake

- Incidence of unexpected colorectal FDG uptake of 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, refer patient to colonoscopy

64yo man restaging laryngeal carcinoma. Incidental uptake confirmed to be rectal adenocarcinoma

Pitfalls & artefacts

Misregistration

A. Sasikumar, 2017
Pitfalls & artefacts

Metformin

A. Sasikumar, 2017

Pitfalls & artefacts

4D respiratory gating
99mTc-mebrofenin SPECT/CT for liver function assessment before large hepatectomy in patients with liver metastasis from CCR

- Dynamic acquisition (anterior view) started immediately after injection of 99mTc-mebrofenin. Images over 6 minutes.

- Homogenous uptake of radiotracer on the whole liver

- Increase of uptake in contralateral liver (blue arrow)

- Whole liver clearance: 14.5 %/min
- Remnant liver (seg. II & III) clearance: 3.5 %/min

- Whole liver clearance: 11.6 %/min
- Remnant liver (seg. II & III) clearance: 6.1 %/min

- High increase of remnant liver function (+74%)
- Slight decrease of the whole liver function (-21%)
Extended liver venous deprivation before major hepatectomy induces marked and very rapid increase in future liver remnant function

Esophageal Cancer and FDG PET/CT
Anatomy

TNM

T, N, and M status and histologic grade definitions for esophagus and esophagogastric junction cancer in the 8th edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual
• Are considered as **regional lymph nodes** any paraesophageal lymph node, including cervical or celiac node
• Only sus-clavicular and lomboaortic nodes are M1

*T: N, and M status and histologic grade definitions for esophagus and esophagogastric junction cancer in the 8th edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual*

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**Staging**

• **18F-FDG PET** does not clearly offers a significant benefit in nodal staging over EUS and CT (a pooled sensitivity and specificity with PET of 51% and 84%, respectively in a meta-analysis: van Westreenen HL, JCO, 2004)

• Significant FDG uptake in the primary lesion may obscure increased uptake in loco regional nodes

• FDG PET is particularly useful as a complementary imaging tool for **detecting distant metastases**, which are quite common in patients with esophageal cancer.
  • A meta-analysis showed that the sensitivity and specificity for detecting distant metastases were 71% and 93%, respectively, for 18F-FDG PET and 52% and 91%, respectively, for CT (van Vliet EP, Br J Cancer, 2008)
Staging

Thomas W. Barber, JNM, 2012

Staging

NCCN Guidelines Version 4.2017
Esophageal and Esophagogastric Junction Cancers

WORKUP

- H&P
- Upper GI endoscopy and biopsy
- Chest/abdominal CT with oral and IV contrast
- PET/CT evaluation if no evidence of N1 disease
- PET/CT with oral and IV contrast
- Endoscopic ultrasound (EUS), if no evidence of N1 unresectable disease
- Endoscopic resection (ER) is essential for the accurate staging of early-stage cancers (T1a or T1b)
- Biopsy of metastatic disease as clinically indicated
- MSI/HMS/MR testing if metastatic disease is documented/unknown
- Her2 and PD-L1 testing if metastatic adenocarcinoma is documented/unknown
- Bronchoscopy, if tumor is at or above the carina with no evidence of N1 disease
- Assign Swartz category
- Nutritional assessment and counseling
- Smoking cessation advice, counseling, and pharmacotherapy as indicated
- Screen for family history

CLINICAL STAGE

- Squamous cell carcinoma
  - See ESOPH-2
- Adenocarcinoma
  - See ESOPH-11
- Squamous cell carcinoma
  - See ESOPH-10
- Adenocarcinoma
  - See ESOPH-19

HISTOLOGIC CLASSIFICATION

Steps I-III (locoregional disease)

Steps IV (metastatic disease)
FDG PET/CT has an impact on clinical management

This multicenter prospective cohort study of 491 patients showed that PET/CT led to clinically significant changes in stage for 24% of patients.

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PET/CT changed management in 47 of 139 patients (34%).

Initial FDG PET/CT has a prognostic impact

**Suzuki A, Cancer, 2011**

- High FDG Uptake ($SUV_{max}$ and MTV) has been described as pejoratively correlated to disease free and overall survival.

**Bütof R, JNucl Med 2015**

FDG PET/CT for treatment response assessment

**Suzuki A, Cancer 2011**

- Modifications of quantitative FDG PET parameters after completion of radiochemotherapy is correlated to histological response or may allow to detect recurrent disease.
FDG PET/CT for treatment response assessment

Early assessment after neoadjuvant therapy

- The MUNICON Study

- 119 patients with locally advanced adenocarcinoma of the oesophagogastric junction

Impact in OS and EFS

Lordick, Lancet Oncol 2007
Detection of recurrence

Diagnostic Performance of $^{18}$F-FDG PET and PET/CT for the Detection of Recurrent Esophageal Cancer After Treatment with Curative Intent: A Systematic Review and Meta-Analysis

Lucas Greiner$^{1,2}$, Peter N.V. van Rooijen$^{3,4}$, Johannes B. Richter$^{5}$, Marini G.E.H. Land$^{1}$, Gert J. Mijnheer$^{1}$, Marco van Welken$^{1}$, Jelle F. Reuten$^{6}$, and Richard van Hillegersberg$^{1}$

- FDG PET and PET/CT are reliable imaging modalities, with a high sensitivity and moderate specificity for detecting recurrent esophageal cancer.
- The use of $^{18}$F-FDG PET or PET/CT particularly allows for a minimal false negative rate.
- However, histopathologic confirmation of PET/CT suspected lesions remains required, because a considerable false positive rate is noticed.
Radiotherapy Planning

- Impact on GTV delineation
- However, needs further investigations

Comparison of Tumor Glucose Metabolism Before and After Artificial Nutrition (PETANC) in patients with esophageal cancer

NCT02382237

Preliminary results: no impact of nutrition on tumor glucose metabolism
Summary

Colorectal Cancer and FDG PET/CT

- Surgical planning of metastasis
- Detection of recurrences
- Focal incidental uptake

Esophageal Cancer and FDG PET/CT

- Initial Staging
- Treatment response assessment

THANK YOU FOR YOUR ATTENTION