Indications of PET/CT in oncology

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Case study of a famous American

18F FDG-PET and beyond
Diffusion-weighted imaging (DWI)
Dynamic contrast-enhanced MRI
Perfusion CT
Blood oxygenation level–dependent MRI (BOLD-MRI)
MR spectroscopy (MRS)
Why functional imaging?

The lesion was suspected by FDG-PET in January.

The lesion was visible on CT in April.

With current PET systems, the limit of resolution is 0.4-1.0 cm, which translates into a tumor size of 0.1-1.0 g or $10^8$-$10^9$ cells.

Cancers are usually not diagnosed until they reach a size of 10-100 g, or $10^{10}$-$10^{11}$ cells.
Metabolic changes precede structural changes
2-deoxy-D-glucose was developed as a chemotherapeutic agent

Lazlo J et al. Effects of glucose analogues (2-deoxy-D-glucose, 2-deoxy-D-galactose) on experimental tumors
J Natl Cancer Inst 1960;24:267-81
Metabolic trapping

Glucose

2-deoxy-D-glucose
18F-FDG

hexokinase

Glucose 6 Phosphate

Fructose 6 Phosphate

Pyruvate

Anaerobic resp

Citric acid cycle

18F-FDG 6 phosphate
1976 18F-FDG was developed to study cerebral glucose metabolism based on PET at Brookhaven National Laboratories.

1977 First PET brain imaging studies at UCLA.

Warburg effect in a cancer cell.
Current and future research

- **Isotopes**
  - $^{18}$F
  - $^{11}$C
  - $^{13}$N
  - $^{15}$O
  - $^{64}$Cu
  - $^{68}$Ga
  - Others
PET/CT in Western Europe 2010

Providers: 506

22 mobile centres

64% public facilities

PET/CT 87%

Source: Development of PET in Western Europe, Anthony Stevens, PhD, EANM 2011.
• Diagnosis and screening
• Staging (re-staging)
• Recurrence
• Treatment monitoring
• Treatment planning
Physiological high uptake in the brain

In the heart (variable)

Excretion into urine

The liver has inhomogenous moderately high uptake
Spleen is just visible (less activity than liver)
An abnormal FDG-PET
An abnormal FDG-PET

2 years later (after operation)

Thyroid cancer
An abnormal FDG-PET

2 years later (after operation)

Breast cancer
An abnormal FDG-PET

2 years later

Diverticulosis - colonoscopy
An abnormal FDG-PET

2 years later

Hodgkin’s lymphoma
FDG is an unspecific "all round tracer"
Diagnosis and screening

- Unknown primary
- SPN
- Unknown cancer

2-5% disease - economy – radiation exposure - ethics
Unknown primary

Known secondary (metastases)
  Lymph node (neck)
  Liver metastases
  Lung metastases

Primary is identified in app 20% of the cases
Single pulmonary nodule

Highly suspicious of malignancy
Single pulmonary nodule
Single pulmonary nodule

FDG-negative tumor

111In-octreotide positive carcinoid

Sensitivity 80%
Unknown cancer?
Unknown cancer?
Unknown cancer?
Unknown cancer?
Indications FDG-PET

- Diagnosis and screening
- Staging (re-staging)
- Recurrence
- Treatment monitoring
- Treatment planning
TNM Staging

T = tumor
N = node
M = metastase

Example:
T2N3M1
17 y male. Two months of "common cold" and pain in left ear. Now bleeding from the nose.

Cancer of the rhinopharynx

MRI has assessed the tumor to be in operable.
Tumor in rhinopharynx
Lymph nodes on both sides of the neck
M Staging

Metastases anteriorly in L4

Metastases in iliac bone
Total body examination has same radiation exposure to the patient as regional examination. Same tracer used for primary and secondaries in different organ systems.
Indications for FDG-PET

- Diagnosis and screening •√
- Staging (re-staging) •√
- Recurrence
- Treatment monitoring
- Treatment planning
Colo-rectal cancer. Increased CEA
Colo-rectal cancer. Increased CEA
Liver metastasis
The metastasis in the liver and the left lung were resected.

Check-up scanning two years later
Recurrence in the rectum (stapler line)
Collective review: The Emerging Role of 18F-Fluorodeoxyglucose Positron Emission Tomography in the Management of Primary and Recurrent Rectal Cancer


David B. Chessin MD⁎, Ravi P. Kiran MD⁎, Timothy Akhurst MD† and Jose G. Guillem

Table 1.

Comparison of Positron Emission Tomography and Computed Tomography in the Detection of Rectal Cancer Recurrence after Curative Resection

<table>
<thead>
<tr>
<th>First author (y)</th>
<th>n</th>
<th>PET-sensitivity, %</th>
<th>CT-sensitivity, %</th>
<th>PET-specificity, %</th>
<th>CT-specificity, %</th>
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<tbody>
<tr>
<td>Schiepers (1995)</td>
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<td>93 (local)</td>
<td>60 (local)</td>
<td>97 (local)</td>
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<td></td>
<td></td>
<td>94 (liver)</td>
<td>85 (liver)</td>
<td>100 (liver)</td>
<td></td>
</tr>
<tr>
<td>Lai (1996)</td>
<td>34</td>
<td>100</td>
<td>100 (liver)</td>
<td>100 (liver)</td>
<td>100 (liver)</td>
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<tr>
<td></td>
<td></td>
<td>93 (liver)</td>
<td></td>
<td></td>
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<tr>
<td>Vitola (1996)</td>
<td>24</td>
<td>90</td>
<td>86</td>
<td>100</td>
<td>100</td>
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<td>Delbeke (1997)</td>
<td>52</td>
<td>91</td>
<td>81</td>
<td>96</td>
<td>60</td>
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<tr>
<td>Ogunbiyi (1997)</td>
<td>40</td>
<td>91 (local)</td>
<td>52 (local)</td>
<td>100 (local)</td>
<td>80 (local)</td>
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<tr>
<td></td>
<td></td>
<td>95 (liver)</td>
<td>74 (liver)</td>
<td>100 (liver)</td>
<td>85 (liver)</td>
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<td>Valk (1999)</td>
<td>115</td>
<td>93</td>
<td>69</td>
<td>99</td>
<td>96</td>
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<td>Arulampalam (2001)</td>
<td>42</td>
<td>93</td>
<td>73</td>
<td>58</td>
<td>75</td>
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<tr>
<td>Even-Sapir (2002)</td>
<td>62</td>
<td>88</td>
<td>63</td>
<td>80</td>
<td>10</td>
</tr>
</tbody>
</table>
Colo-rectal cancer. Increased CEA

Benign uptake due to operation

The former lung metastases
First scan: 
Liver and lung metastasis

Second scan: 
Local recurrence
PET has high sensitivity and specificity in many common cancers incl metastasis and relapse
Indications for FDG-PET

- Diagnosis and screening •✓
- Staging (re-staging) •✓
- Recurrence •✓
- Treatment monitoring
- Treatment planning
76 y male, large cell B cell lymphoma
Learning point

Morphologic lesions can be FDG-positive or FDG-negative
PET in early response evaluation

**A**

**FDG-PET after two cycles**

- FDG-PET negative
  - 61 Patients, prog=3
  - 2-year PFS 96%

- FDG-PET positive
  - 16 Patients, prog=11
  - 2-year PFS 0%

\[ P < .001 \]

**B**

**CT after two cycles**

- Unsatisfactory remission
  - 2 Patients, prog=0
  - 2-year PFS 100%

- Satisfactory remission
  - 62 Patients, prog=11
  - 2-year PFS 82%

\[ P = .554 \]
Change in FDG-metabolism can predict treatment response/survival.
• Diagnosis and screening •√
• Staging (re-staging) •√
• Recurrence •√
• Treatment monitoring •√
• Treatment planning
74 y male with lung cancer. RTP
Change of GTV

tumor

actelasis

necrosis
Indications for FDG-PET

- Diagnosis and screening ✓
- Staging (re-staging) ✓
- Recurrence ✓
- Treatment monitoring ✓
- Treatment planning ✓
Other tracers than FDG

Prostate cancer
Bone PET
Hypoxia
Other tracers than FDG

99mTc HDP planar bone scan
Acetate is activated to acetyl-CoA which is oxidized to $\text{CO}_2$ and $\text{H}_2\text{O}$ in normal cells.
Axial-fused PET/CT images demonstrate pathological 18F-choline uptake
(a) in the prostate
(b) in three pelvic lymph nodes
(c) in bones
18F NaF is chemisorbed onto bone surface by exchanging with OH-groups in hydroxapatite crystal of bone to form fluoroapatite. Same uptake mechanism as 99mTc-MDP
### Examination time:

<table>
<thead>
<tr>
<th>Imaging Type</th>
<th>Adult (70 kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{99m}$Tc-MDP*</td>
<td></td>
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<tr>
<td>Administered activity (MBq)</td>
<td>518</td>
</tr>
<tr>
<td>Effective dose in mSv/MBq (mSv)</td>
<td>0.0057 (3.0)</td>
</tr>
<tr>
<td>Bladder wall in mGy/MBq (mGy)</td>
<td>0.048 (24.9)</td>
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<tr>
<td>Bone surfaces (mGy)</td>
<td>0.063 (32.6)</td>
</tr>
<tr>
<td>Red marrow (mGy)</td>
<td>0.0092 (4.8)</td>
</tr>
<tr>
<td>$^{18}$F-labeled NaF†</td>
<td></td>
</tr>
<tr>
<td>Administered activity (MBq)</td>
<td>148</td>
</tr>
<tr>
<td>Effective dose in mSv/MBq (mSv)</td>
<td>0.027 (4.0)</td>
</tr>
<tr>
<td>Bladder wall in mGy/MBq (mGy)</td>
<td>0.22 (32.6)</td>
</tr>
<tr>
<td>Bone surfaces in mGy/MBq (mGy)</td>
<td>0.040 (5.9)</td>
</tr>
<tr>
<td>Red marrow in mGy/MBq (mGy)</td>
<td>0.040 (5.9)</td>
</tr>
</tbody>
</table>

**Examination time:** 3-4 h vs 30 – 60 min
Hypoxia is a key factor in
- Tumour aggression/progression
- Resistance to therapy

Independent negative predictive factor
Dose escalation map superimposed on CT with Planning Target Volume (red). Isodose lines show conformality to hypoxic lymph node with a maximum dose increase by 20%.

The 18FDG-PET image: Increased uptake in both the oropharyngeal tumour (arrow) and in the left neck nodal metastasis (asterix).

The 18F-MISO images:
- The left neck nodal metastasis is shown to be hypoxic.
Neuroendocrine tumors

111In Octreotide

68Ga Octreotide
High affinity (SSTR2)
Generator product
Simple labelling

L-Tyrosine

18F-DOPA

11C-HTP*
*Hydroxy tryptophan

L-DOPA
Dopamine
Norepinephrine
Epinephrine
GLUT

NET

Loss of NET or VMAT in tumor cell dedifferentiation

18F-FDG

18F DOPA