**Positron Emission Tomography for Treatment Assessment**

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**Why treatment assessment?**

- Based on early treatment assessment one could modify treatment:
  - If likely not successful:
    - Escalate therapy
    - Change therapy
    - Selectively add dose (RT)
  - If likely successful:
    - Descalate therapy
    - Stop therapy early

- Enormous benefits for the patient - improved tumor control, reduced side effects, and costs

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**What is used for treatment assessment now?**

- **Histopathological evaluation:**
  - Typically by regression score (viable tumor vs. fibrosis), e.g., Salzer-Kuntschik for osteosarcomas
  - Limitations: need complete resection, problem with point biopsies because of tumor heterogeneities

- **Radiological evaluation:**
  - Defined by the therapy-induced reduction of tumor size: WHO, RECIST
  - Limitations: numerous
Anatomic response criteria

- **WHO (Miller, Cancer, 207, 1981):**
  - The size of a tumor should be estimated based on two perpendicular diameters.
  - Positive tumor response to therapy should be defined as a reduction of at least 50% in the product of these two diameters.

- **RECIST (Response Evaluation In Solid Tumors) (Therasse, JNCI, 205, 2000):**
  - The size of a tumor is estimated based on unidimensional.
  - Positive tumor response to therapy is at least 30% decrease in the largest dimension of the tumor.

**Complete Response (CR):** Disappearance of all disease compared with the baseline examination, whether it be measurable or not.

**Partial Response (PR):** A reduction in the sum of the greatest lengths of individual tumors by at least 30% compared with the baseline measurement.

**Stable Disease (SD):** This lies between the definitions for PR and PD.

**Progressive Disease (PD):** An increase in the total length of all measurable lesions of more than 20% compared with the smallest sum of lesion sizes (not the baseline values), or the appearance of unequivocal new disease.

Inherent inconsistencies in expert observers: 15-40%
Other issues...

- **Tumor shrinkage** is only the final step in a complex cascade of cellular and subcellular changes after treatment.

- **Several cycles** of therapy (radiotherapy fractions, chemotherapy) are needed before treatment response can be assessed by anatomic imaging.

- **Residual mass** is often present after treatment—it is hard to differentiate between viable tumor posttreatment changes, such as scarring and fibrosis.

Visual example

CT scan and comparable FDG-PET scan in a patient with gastrointestinal stromal tumor (GIST) with hepatic metastatic lesions

Prognostic relevance of FDG-PET

**AFTER therapy**

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Ref</th>
<th>No Pat</th>
<th>Survival response (mo)</th>
<th>Survival non-resp (mo)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head neck</td>
<td>Kunkel 2003</td>
<td>32</td>
<td>&gt;24</td>
<td>&gt;20</td>
<td>0.002</td>
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<tr>
<td>Esophagus</td>
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<td>&gt;30</td>
<td>&gt;20</td>
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<tr>
<td>Lung</td>
<td>Grigsby 2004</td>
<td>37</td>
<td>&gt;20</td>
<td>&gt;20</td>
<td>0.001</td>
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<tr>
<td>Cervix</td>
<td>Grigsby 2004</td>
<td>152</td>
<td>&gt;45</td>
<td>&gt;24</td>
<td>&lt;0.001</td>
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<tr>
<td>Lymphoma</td>
<td>Several 2001-04</td>
<td>&gt;200</td>
<td>&gt;30, &gt;60</td>
<td>&gt;30</td>
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</tr>
</tbody>
</table>

All chemoradiotherapy except lymphoma (chemo only)

**DURING therapy**

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Ref</th>
<th>No Pat</th>
<th>Cr</th>
<th>Survival response (mo)</th>
<th>Survival non-resp (mo)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head neck</td>
<td>Brunt 2002</td>
<td>47</td>
<td>50%</td>
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<td>&gt;120</td>
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<tr>
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<td>&gt;20</td>
<td>&gt;40</td>
<td>0.006</td>
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<tr>
<td>Cervix</td>
<td>Ott 2003</td>
<td>15</td>
<td>50%</td>
<td>&gt;20</td>
<td>&gt;40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Kostakoglu 2002</td>
<td>30</td>
<td>Vis</td>
<td>&gt;24</td>
<td>&gt;9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

All chemotherapy

- **Post-treatment metabolic response is highly predictive of overall survival**

- **Mid-treatment metabolic response is highly predictive of overall survival**
**FDG-PET and radiation therapy**

![Graph showing SUVmax over time with averages for metabolic responders and non-responders](image)

Baardwijk, Radiother Oncol, 82, 145 (2007)

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**Molecular imaging targets in oncology**

- Rapid cellular proliferation
- Subverted cellular regulation:
  - Intracellular signaling
  - Cell-to-cell signaling
  - Extracellular matrix signaling
- Altered tumor microenvironment:
  - Hypoxia
  - Changes in perfusion
  - Changes in diffusion
- Evading cellular death

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**Response to chemotherapy in AML**

Antracycline, cytarabine and/or etoposide

![Images of responder and non-responder](image)

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Response to targeted therapy in HNSCC

Avastin (bevacizumab) therapy

Pre-Avastin
SUVmax = 4.2
CuATSM-PET/CT
Post-Avastin
SUVmax = 7
CuATSM-PET/CT

Tumor response to radiation therapy can be very dynamic

Spatial response assessment

Pre-RT FLT-PET
Treatment plan

Spatial response assessment

Pre-RT FLT-PET
Mid-RT FLT-PET
Anatomical change more important than biological change

The problem of partial volume effects

Partial volume effects are complicated

Other challenges...
Treatment response can be extremely powerful.

Treatment response can reveal unwanted results.

Assessment of normal tissue damage.

Assessment of normal tissue damage.
**Conclusions**

- Early treatment assessment has enormous potential to change patient care
- Anatomical imaging used for treatment assessment has many limitations
- Functional/molecular imaging is more powerful and versatile in assessment of treatment response
- Tumor response kinetics can be very complex
- Need for clinical trials with extensive functional/molecular imaging component

**Thanks to:**

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