Contribution of PET/CT in Radiotherapy Planning

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PET and Radiotherapy?

Why?
Development of Radiotherapy

1960 Rx
1970 CT
1980 RM
1990 PET
2000

Conformal Radiotherapy >>> IMRT
The error in target volume delineation may be the biggest error in the entire radiotherapy chain.
• geographic missing of the tumor → reduction of local control probability

• high dose irradiation of healthy tissues → increase of radio-induced damage probability
PET/CT in RTP: aim

1. Proper inclusion of the disease in the high dose volume

2. Safer OARs sparing
What the radiation oncologist needs

The radiation oncologist expects from the functional imaging important aids to evolve towards a biological dose conformation (BTV - Biological Target Volume)
Intensity Modulated Radiation Therapy

**DOSE PAINTING**

- Production of controlled inhomogeneous dose distribution
- Simultaneous irradiation of multiple targets with different dose/fraction
PET in Radiation Therapy

- PET staging
- Radiation Treatment Prescription
- CT target volume and organ localization
- Biological Target Volume (BTV)
- Treatment Planning
- Treatment Delivery
- Treatment Response Evaluation
- The radiation oncologist’s objective

The objective of the radiation oncologist is to use PET for staging, diagnosis, treatment planning, target volume and organ localization, and treatment delivery. The Biological Target Volume (BTV) is critical for delivering targeted radiation therapy.
PET and Radiation Therapy
Summary of literature
(number of articles)

- Lung
- Head & Neck
- Global PET/RT

2003
2004
2005
PET for Radiation Therapy Planning
Experience of Reggio Emilia

Cancer site

- Lung: 31%
- Head & Neck: 25%
- Others: 44%
International Meeting

Metabolic PET Imaging for a New Radiotherapy

Reggio Emilia, Italy
October 14-15 2003

Under the auspices of
AIMN - Associazione Italiana di Medicina Nucleare
AIFM - Associazione Italiana di Fisica in Medicina
AIRO - Associazione Italiana di Radioterapia Oncologica

2nd International Meeting

Metabolic PET imaging for a new Radiotherapy

October 4-5, 2005
Hotel Mercure Astoria - V.le L. Nobili, 2 - Reggio Emilia - Italy
The radiotherapist’s language

TARGET VOLUME

- **Gross Tumor Volume (GTV)**
  Volume of visible disease requiring higher dose

- **Clinical Target Volume (CTV)**
  Volume of suspected microscopic disease requiring prophylactic lower dose

- **Planning Target Volume (PTV)**
  CTV+margins to account for geometrical variation (e.g. set-up errors and internal motion)

- **Biological Target Volume (BTV)**
  Volume as defined by molecular imaging (e.g. FDG-PET)
PET and Radiotherapy

FDG-PET Problems

- Lack of anatomic detail
- Several and variable foci of physiologic FDG uptake
- Lower spatial resolution than CT and MRI
PET and Radiotherapy

FDG-PET Problems

Solution

PET/ CT?
PET
Head & Neck Cancer

PET/CT Image Fusion

68 patients (155 lesions)

Accuracy

PET
90%

PET/CT
96%

Schöder H et al Radiology, 2004
Patient positioning reproducibility: PET

CT simulation and PET imaging in the same day

Flat bed

Immobilization mask

Blotting paper

fiducial markers

About 20-25% of sub-optimal repositions

18F-FDG drop
Patient positioning reproducibility: PET/CT

CT simulation and PET imaging in the same day

Laser Positioning System

Lead markers

Immediate verification of the correct reposition during the CT acquisition by the lead markers used for CT simulation

But PET/CT allows the best reposition with the possibility of CT simulation on PET/CT in the same session
PET in Radiation Oncology
Main Applications

- Lung Cancer (NSCLC)
- Head & Neck Cancer
- Cervical Cancer

Perspectives
- Pancreas Cancer
- Prostate Cancer
- ...... and many others
Lung Cancer
FDG-PET – Lung cancer (NSCLC) Impact on the Radiation Therapy Planning

Review of literature: 1998-2005

- 459 Patients

- Changes in the Radiation Treatment Volume
  - 54% of cases
    - 33% ↑ GTV
    - 21% ↓ GTV
Head & Neck Cancer
Head & Neck Cancer

PET and Radiotherapy?

Why?

- 3% of all cancers
- Radiation Therapy is part of the treatment in the majority of cases
- Local control is the big challenge (recurrence >50% of the treated pts)
Selection of the patients to treat

CT: Cancer of the base of the tongue with right latero-cervical metastasis

PET/CT for RT planning but... lumbar spine metastasis
FDG-PET for H&N-I MRT
Reggio Emilia Hospital (from 2/03 to 4/06)

52 patients
Changes in 23/52 (44%)
Clinical outcome: preliminary results

Patients with FU ≥ 6 months (29)

<table>
<thead>
<tr>
<th>n</th>
<th>status</th>
</tr>
</thead>
<tbody>
<tr>
<td>21</td>
<td>Disease free</td>
</tr>
<tr>
<td>1</td>
<td>Distant metastases</td>
</tr>
<tr>
<td>5</td>
<td>Local failure * (high dose volume)</td>
</tr>
<tr>
<td>1</td>
<td>Dead</td>
</tr>
<tr>
<td>1</td>
<td>Lost at FU</td>
</tr>
</tbody>
</table>

* 1 pt with distant metastases

- No patient had failure in regions excluded from the high dose because of PET negativity.
- No patient had parotid glands toxicity more than grade 2 (ROTG scale).
# Head & Neck Cancer Impact of PET/CT in radiotherapy treatment planning

<table>
<thead>
<tr>
<th>Patients</th>
<th>Stage</th>
<th>Treatment Volume</th>
<th>Treatment Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>13 (36%)</td>
<td>5 (14%)</td>
<td>4 (11%)</td>
</tr>
</tbody>
</table>

Koshy M et al Head Neck, 2005
Laryngeal cancer
Nasopharyngs Carcinoma
Cervical Cancer
L.L., 65 anni - Ca Cervice uterina: follow up
Metastasi supraclavolinee dx e mediastinica
Cervical cancer
FDG-PET and Radiotherapy planning

PET-guided IMRT allows a dose-escalation treatment in patients with positive paraaortic lymph nodes.

Perspectives

Pancreatic cancer
Pancreatic Cancer
PET and Radiotherapy?

Why?

2005 - Cancer Mortality in USA: estimated values

<table>
<thead>
<tr>
<th>Site</th>
<th>Deaths</th>
<th>5-year survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>163.510</td>
<td>15%</td>
</tr>
<tr>
<td>Colon</td>
<td>56.910</td>
<td>61%</td>
</tr>
<tr>
<td>Breast</td>
<td>40.870</td>
<td>86%</td>
</tr>
<tr>
<td>Prostate</td>
<td>30.350</td>
<td>96%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>31.800</td>
<td>4%</td>
</tr>
</tbody>
</table>

... further progress in the treatment of pancreatic cancer can only be achieved by an interdisciplinary management of this disease

Heinrich S et al  Schweiz Rundsch Med Prax. 2005
Pancreatic Carcinoma

Summary of the FDG-PET Literature
(1999-June 2000; 419 articles and abstracts)

**Diagnosis**
- Sensitivity: **94%** (n=293)
- Specificity: **90%** (n=281)
- Change in management: **50%** (n=26)

**Staging**
- Sensitivity: **70%** (n=182)
- Specificity: **93%** (n=182)
- Change in management: **53%** (n=33)

**Monitoring therapy**
- Change in management: **16%** (n=19)

_Gambhir SS et al J Nucl Med 2001_
Radiation Therapy in Pancreatic cancer

Problems

- Movement of organs and lesions
- Difficulty in target defining by CT
- Close organs at risk

R Freelove, AD Walling, Am Fam Physicians 2006
Pancreas

contrast enhanced CT (arterial phase)

contrast enhanced CT (venous phase)

PET

CT (basal)

By courtesy of N. Di Muzio
HSR - Milan
- pancreas adenocarcinoma T4N0
- 5 FU c.i.
- Radical Tomotherapy: 60 Gy, 2 Gy/f on PTV

By courtesy of N. Di Muzio
HSR - Milan
Perspectives

Prostate Carcinoma
Recurrence of prostate cancer

Pre-Radiotherapy

Di Muzio N. “PET and Radiation Therapy” Reggio Emilia October 2005
FDG-PET
Evaluation of the response to Radiation Therapy

Morphologic Response =
- Mass reduction
  but
- Rarely the mass disappears
- Often residual tissue
  - scar
  - tumor

FDG-PET?
## FDG-PET – Evaluation of the response to Radiotherapy

<table>
<thead>
<tr>
<th>Authors</th>
<th>Neoplasm</th>
<th>Sens %</th>
<th>Spec %</th>
<th>PPV %</th>
<th>NPV %</th>
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<tbody>
<tr>
<td>Jerusalem G et al EJ C - 2003</td>
<td>Lymphoma</td>
<td></td>
<td></td>
<td>100</td>
<td>83</td>
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<tr>
<td>Kelly RF et al – Chest - 2004</td>
<td>Lung</td>
<td></td>
<td></td>
<td>89</td>
<td>92</td>
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<tr>
<td>Conessa C et al Ann Otol Rhinol Laryngol, 2004</td>
<td>Head &amp; Neck</td>
<td>100</td>
<td>81</td>
<td>46</td>
<td>100</td>
</tr>
<tr>
<td>Scarfone C et al – JNM - 2004</td>
<td>Head &amp; Neck</td>
<td>84</td>
<td>95</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
FDG-PET – Evaluation of the response to Radiotherapy

When?

- Most Authors agree that 3 months after Radiotherapy is a correct timing
FDG-PET and NSCLC: Evaluation during Radiation Therapy

Interesting objectives

- Define early response (PET changes may predict RT response)


- Adaptive Radiation Therapy (define new target volumes and doses according to the changes during treatment)
PET/CT evaluation during RT (lung cancer)

- Basal (25/05/04)
  - SUV\textsubscript{max}: 15

- 50 Gy (19/07/04)
  - Δ SUV: -49%

- 3 months post RT (26/10/04)
  - Δ SUV: -61%

By courtesy of N. Di Muzio  HSR - Milan
PET and Radiotherapy
Open Problems

- Tumor Hypoxia

- Respiratory Movement
Tumor Hypoxia

Tumor hypoxia is considered a predictor of poor prognosis.

- Increased likelihood of local recurrence and metastases
- Resistance to radiation therapy
Tumor hypoxia
PET radiopharmaceuticals

- $^{18}$F-fluoromisonidazole ($^{18}$F-MISO)
- $^{64}$Cu-diacetyl-bis(N(4)-methylthiosemicarbazone ($^{64}$Cu-ATSM)
- $^{18}$F-Fluoroazomycin Arabinoside ($^{18}$F-FAZA)

**Mechanism of uptake**
- ischemic tissue: bioreduction and deposition
- well-oxigenated tissue: rapid removal
NSCLC
Survival according to $^{60}$Cu-ATSM uptake
(8 Responders, 6 Nonresponders, Stage IA - IV)

Dehdashti et al., Eur J Nucl Med Mol Imag 2003;
30:844-850
PET and cervical cancer
Tumor Hypoxia

\(^{60}\text{Cu-ATSM-PET}\)

High uptake
Recurrence at 6 months

Low uptake
Free of disease at 23 months

Dehdashti F et al., Int J Radiation Oncology Biol Phys, 2003
Respiratory Movement

STATIC TARGET

MOVING TARGET
4D-PET/CT Respiratory Gating

Pan et al. Med Phys 2004
Radiotherapy
Gated Treatment

Moving Tumor Gating

4D Delivery: RT Gated Treatment
RT Gated Treatment
RT Gated Treatment

© Steve B. Jiang
FDG-PET
Impact on Radiation Treatment Planning
Summary

Review of literature: 1998-2005

- 628 Patients (lung, head&neck, lymphoma, haesophagus)

- Changes in Radiation Treatment Volume
  - 59% of cases
    - 31% GTV
    - 28% GTV
FDG-PET/CT: Lung cancer Impact on Radiation Treatment Planning

19 Patients

- Changes in Radiation Treatment Volume
  52% of cases

- Interobserver GTV variability
  Concordance (difference from mean of GTVs < 10%)
  - CT: 37%
  - PET/CT: 84%

Don’t forget!!!!!!

Interdisciplinary Discussion

An interdisciplinary discussion of the cases, particularly in head and neck cancer, is indispensable.
PET/CT imaging helps

- **To select more correctly the patients** for radiation therapy
- **To identify the right target**, avoiding irradiation of non-neoplastic areas and, at the same time, preventing the omission of active tumor tissue from the radiation field
- **To evolve towards a biological dose conformation**
  (BTV - Biological Target Volume)
Thank you for your attention and... see you at 3rd International Meeting

Metabolic PET Imaging for a New Radiotherapy
Reggio Emilia, Italy
October 1-3, 2007

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