The use of PET-CT in radiotherapy planning for non-small-cell lung cancer patients

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PET-CT in RTP & Belfast

- Pilot study  
  Jan ‘03 – April ‘03
  – 5 patients scanned in treatment position

- Research grant  
  Sept ‘04 – Sept ‘07
  – Radiotherapy / nuclear medicine physics programme
  – Clinical study - 30 patients recruited (NSCLC)

- Clinical research fellowship  
  Mar ‘07 – Mar ’10
Aim of radiotherapy

• To deliver a dose of radiation to a well-defined target volume which will kill the tumour cells, while sparing the surrounding normal tissue
Where is the target?

- Gross Tumour Volume (GTV)
- Clinical Target Volume (CTV)
- Planning Target Volume (PTV)
- Treated Volume (TV)
- Irradiated Volume (IV)
- Organs at Risk (OAR)
Why use PET in RTP for NSCLC?

• Poor outcomes despite:
  – technical improvements in RT delivery
  – increased systemic therapies
  – more accurate staging

• Local failure in up to 50% of patients after RT
  – improved targeting of primary disease may reduce local failure rates

• Better sensitivity and specificity of PET-CT compared to CT in NSCLC staging

• Improvement in inter-observer variability
NSCLC

• A large number of published studies have shown that inclusion of PET has significant impact in large number of patients (30-60%) – Mainly due to inclusion of additional nodal or primary disease shown on PET or better demarcation of tumour within atelectatic lung
Role of PET in Treatment Planning

• **Inform the planning process**
  – Are suspected nodes positive and should they be included in the GTV?
  – Can tumour be differentiated from normal tissue better using PET than CT e.g. atelectasis

• **Target volume delineation**
  – Where is the edge of the tumour
Inform the planning process

- Does the patient need to be scanned in the treatment position?
- Can a staging/diagnostic scan be used along with the report from the radiologist?
- Do the PET images need to registered with the planning CT scans or is the availability of hard copy images sufficient?
- Do you outline directly using the PET images?
Target volume delineation

• How should the patient be scanned?
  – Are dedicated planning PET scans required?

• When should the PET scan be undertaken?
  – Is this an additional PET scan?
  – What is the effect of induction chemotherapy on the PET image?

• What does the PET image mean and how should the data be used?
  – Should areas that are CT positive and PET negative be included? – GTV reduced
  – Should areas that are CT negative and PET positive be included? – GTV increased
Aim of the study

• To compare gross tumour volumes (GTVs) delineated using either CT alone or $^{18}$F-FDG PET-CT during radiotherapy planning for NSCLC patients
Methods (1)

- 28 NSCLC patients
  - 22 male, 6 female
  - 14 had induction chemotherapy

- Referred for radical RT
  - Have had staging diagnostic PET-CT

- Dedicated radiotherapy planning PET-CT
  - Treated based on CT plan
  - PET used for research only
Requirements for performing RTP PET-CT scans on a combined scanner

• Patient scanned in treatment position using immobilisation devices and markers
• Flat-bed couch and external lasers
• Involvement of radiotherapy staff - therapy radiographers/clinical oncologists
• Quality control of image registration and CT
• Transfer of images to planning computer
**PET-CT $^{18}$FDG Imaging Protocol**

<table>
<thead>
<tr>
<th></th>
<th>Whole body scan</th>
<th>RTP planning scan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uptake phase</td>
<td>45 minutes</td>
<td>45 minutes</td>
</tr>
<tr>
<td>CT axial scout scan</td>
<td>10 seconds</td>
<td>10 seconds</td>
</tr>
<tr>
<td>CT helical scan</td>
<td>20 seconds</td>
<td>20 seconds</td>
</tr>
<tr>
<td>Time (5 minutes per FOV – 15cm extent)</td>
<td>25-50 minutes (5-6 bed positions)</td>
<td>10-15 minutes (2-3 bed positions)</td>
</tr>
<tr>
<td>Total time in scanner</td>
<td><strong>Approx. 40 minutes</strong></td>
<td><strong>Approx. 15 minutes</strong></td>
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IV administration of 375 MBq $^{18}$FDG

Diazepam may be administered
Belfast PET-CT RTP scan protocol

• 9am appointment, 60 minute scan slot

• **Cold session** *(pre FDG injection)*
  – patient positioning, initial marking and set-up

• **Hot session** *(post FDG injection and 45 min uptake period)*
  – re-position patient, attach radio-opaque markers
  – Images acquired as for diagnostic PET-CT scans (but shorter extent)

• **Permanent marks made on patient** *(post scan)*
Methods (2)

• Gross Tumour Volume (GTV) were outlined using Oncentra® treatment planning software
  – Diagnostic and clinical information for each patient including the staging PET-CT images available to Oncologist
  – used outlining protocol

• 4 Radiation Oncologists independently delineated the GTV on:
  – CT images alone
  – Fused PET-CT images
Outlining protocol – CT alone

- CT, staging PET-CT and diagnostic reports available
- No outlining for elective nodal irradiation
  - Involved node either FDG avid on staging scan or $\geq$1cm
- GTV for primary tumour and nodes to be outlined separately if appropriate, using preset CT windows
Outlining Protocol – Fused

- PET images displayed using standard intensities
- PET will be used to define disease but CT correlate will generally be used to define (anatomical) margin
Methods: Analysis

- Concordance Index (C.I) used to compare volumes. This is the ratio of intersection compared to the union of the 2 volumes under comparison (varies between 0 and 1).

\[
= \frac{(A \cap B)}{(A \cup B)}
\]

- Intra-observer variability between GTV_{CT} and GTV_{FUSED}
- Inter-observer variability for both GTV_{CT} and GTV_{FUSED}
Comparison of $\text{GTV}_{\text{CT}}$ and $\text{GTV}_{\text{FUSED}}$

Oncologist 1

Oncologist 2

Oncologist 3

Oncologist 4
Comparison of $\text{GTV}_{\text{CT}}$ and $\text{GTV}_{\text{FUSED}}$

**Volumes**

<table>
<thead>
<tr>
<th>% change</th>
<th>% of patients</th>
<th>$\text{GTV}_{\text{CT}}$ larger</th>
<th>$\text{GTV}_{\text{FUSED}}$ larger</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 20</td>
<td>20.5</td>
<td>31.2</td>
<td></td>
</tr>
<tr>
<td>&gt; 50</td>
<td>4.5</td>
<td>18.8</td>
<td></td>
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**Concordance Indices**

- 70% of all treatment plans had CIs between CT-GTV and FUSED-GTV of less than 0.75
- 46% had concordance indices of less than 0.60
- Mean CI was 0.63 (SD 0.17) for all sets.
Patient with atelectasis showing differences in $\text{GTV}_{\text{CT}}$ and $\text{GTV}_{\text{FUSED}}$

$\text{GTV}_{\text{CT}}$ shown in red
$\text{GTV}_{\text{FUSED}}$ shown in blue
Patient where PET changes inclusion of nodes in GTV
### GTV – Inter-Observer Variability

<table>
<thead>
<tr>
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<th>CT-CT</th>
<th>FUS-FUS</th>
<th>Wilcoxon Statistic</th>
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<tbody>
<tr>
<td>All Cases</td>
<td>0.55</td>
<td>0.59</td>
<td>p=0.001</td>
</tr>
<tr>
<td>Induction Chemo</td>
<td>0.44</td>
<td>0.49</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Medically Inoperable</td>
<td>0.60</td>
<td>0.63</td>
<td>p=0.18</td>
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- Improvement in CI between observers when defining the GTV using the PET-CT images, particularly for induction chemotherapy group.
Improvement in concordance index of GTVs for PET-CT images

$GTV_{CT}$

$GTV_{FUSED}$
Comparison of GTVs defined by different Oncologists

Oncologist 1

Oncologist 2

comparison
Summary of Results

• Significant alteration of GTV volumes by inclusion of PET information

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• Significant reduction in inter-observer variability when planning PET-CT RTP scan is used compared to CT alone
Observations

• Comparing GTVs requires outlining to be done consistently according to defined protocols
• Further work required to evaluate impact of change in GTV on PTV and treatment plan
• Issue of timing of RTP scan with regard to induction chemotherapy remains to be addressed
Timing of RTP PET-CT scan with regard to induction chemotherapy

- NSCLC patients often receive induction chemotherapy prior to their planning scan and RT
- Patients would not normally be PET scanned until at least 3 weeks after their last chemo cycle
Patient who received induction chemotherapy
When should the patient be scanned?

- What is the effect of induction chemotherapy on the PET (and CT) image?
Further work

• Further analysis of GTV data:
  – tumour location, histology and presence of atelectasis.

• Extend analysis to look at PTV
  – Repeat analysis as for GTVs
  – Construct RT plans based on $PTV_{CT}$ and $PTV_{FUSED}$

• Analysis of input of Nuclear Medicine Radiologist

• Outlining methods

• Compare using registered staging scan to use of planning RTP scan
Conclusions

• The use of a PET-CT RTP scan leads to changes in the GTV compared to that defined using CT alone

• Reduces inter-observer variability particularly for induction chemotherapy group

• Optimal use of PET-CT in RTP for NSCLC and its precise role require further work before introduction into routine clinical practice
• “The uncritical non-standardized use of FDG PET and/or PET-CT in radiotherapy planning of NSCLC to “tailor down” target volumes to FDG-positive areas outside of prospective studies could impair rather than improve the prognosis of our patients by missing affected or including too much unaffected tissue”
  – U. Nestle, Radiotherapy and Oncology, 2006
• “The introduction of PET images into the treatment planning procedure remains a challenging issue. ... In conclusion, before proper validation of the use of various PET tracers has been performed and all methodological aspects have been fully optimised, it is reasonable to state that the use of PET for treatment planning should not be routine but should remain in the clinical research arena”
Acknowledgements

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