PET-CT for radiotherapy planning in lung cancer: current recommendations and future directions

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Talk Outline

• Key principles underlying PET/CT acquisition
• PET/CT for staging in NSCLC
• Background of PET/CT for RTP in NSCLC
• How to acquire a PET/CT for RTP?
• Displaying a PET/CT for RTP
• Guidance on PET/CT based TVD
• 4D PET/CT
KEY PRINCIPLES OF PET
Glucose is key to PET
Positron Emission Tomography (PET)

An imaging process based on the decay of a nucleus by positron emission
Positron Emission Tomography (PET)

An imaging process based on the decay of a nucleus by positron emission

$\gamma$ (511 KeV)

Annihilation

$\gamma$ (511 KeV)

$\text{F}^{18}$
Positron Emission Tomography (PET)

An imaging process based on the decay of a nucleus by positron emission

\[ \gamma (511 \text{ KeV}) \]

Annihilation

Detector Ring

\[ \text{F}^{18} \]

Coincidence Unit
Positron Emission Tomography (PET)

An imaging process based on the decay of a nucleus by positron emission.

$\gamma$ (511 KeV)  
$e^+ + e^- \rightarrow \gamma$ (511 KeV)  
$511\text{ keV}$  
$F^{18}$
Positron Emission Tomography (PET)

An imaging process based on the decay of a nucleus by positron emission

\[ \gamma (511 \text{ KeV}) \]

\[ e^+ + e^- \rightarrow \gamma (511 \text{ KeV}) \]

\[ 511 \text{ keV} \]

\[ F^{18} \]
**Metabolic Tracers**

**Specific molecules**
- That are involved in a metabolic pathway of interest
- That accumulate in the presence of a specific disease
- That are chemically feasible for stable “labeling“
- That are applicable for human use

**Example tracers**
- Cell metabolism Glucose - F18
- DNA synthesis Thymidine - F18
- Cell membrane synthesis synthesis Choline - C11
- Octreotide receptor expression DOTA-NOC - Ga68
- Tissue hypoxia Misonidazole - F18
# Radionuclides and Radiopharmaceuticals in use

<table>
<thead>
<tr>
<th>Radionuclide</th>
<th>Half-life (min)</th>
<th>Max $\beta^+$ energy (MeV)</th>
<th>Max Range (mm)</th>
<th>Radio-pharmaceutical</th>
<th>Clinical Use</th>
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<tbody>
<tr>
<td>11 C</td>
<td>20.3</td>
<td>0.97</td>
<td>5.4</td>
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<td>18 F</td>
<td>109.6</td>
<td>0.64</td>
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<tr>
<td>Nitrogen -13</td>
<td>$^{13}$N – Ammonia</td>
<td>Blood Flow (cardiology)</td>
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<tr>
<td>Oxygen -15</td>
<td>$^{15}$O – Water</td>
<td>Blood Flow</td>
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<tr>
<td>Carbon -11</td>
<td>$^{11}$C – Methionine</td>
<td>Amino Acid Metabolism</td>
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<tr>
<td>Fluorine – 18</td>
<td>$^{18}$F – FDG Fluoro-deoxy-glucose</td>
<td>Glucose Metabolism</td>
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<tr>
<td></td>
<td>$^{18}$F – MISO Fluoro-misonidazole</td>
<td>Hypoxia</td>
<td></td>
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<tr>
<td></td>
<td>$^{18}$F FLT Fluoro-deoxy-thymidine</td>
<td>Tumour proliferation</td>
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</table>
Attenuation Correction

What scanner sees → Tissue density → Real biodistribution
PET in Oncology

• **Functional imaging technique**
  – Many tumour cells have increased glycolysis rate, leading to increased FDG uptake

• **Current and possible uses**
  – Diagnosis of primary tumours
  – Staging
  – Evaluation of response to treatment
  – Target volumes for radiotherapy
  – Evaluation of radiation damage

PET-CT images from radiotherapy planning patient
PET/CT FOR STAGING IN NSCLC
ROC Curve for LN staging in NSCLC

ROC Curve for LN staging in NSCLC

Staging modality is poor

ROC Curve for LN staging in NSCLC

Staging modality is excellent

Only 5-10% of Malignant LN are being missed by PET

PET for Patient Selection for Radical Therapy

Effect of better selection +/- better RT planning

PET/CT for RT planning in NSCLC
Why use PET/CT in RT Planning in NSCLC?

- CT current gold standard for GTV definition in the radical treatment of NSCLC with radiotherapy.
- Despite technical improvements in RT delivery, increased use of systemic therapies and more accurate staging, survival remains poor.
- > 50% local failure despite radical local therapy
- PET/CT is more accurate than CT alone in the staging of NSCLC.
Problems with using CT alone for GTV Definition

Intra-observer Variability
Ciernik et al, Red 2003
Intra-observer Variability
Ciernik et al, Red 2003

Upstaging with PET
Bradley et al Red 2004
PET/CT in RTP – Atelectasis

• Significant potential benefit by reducing RT volumes

• However:
  – False positive uptake in post-obstructive inflammation
  – Histological correlation of PET findings with pathology are lacking
PET/CT in RTP – Atelectasis

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  – Histological correlation of PET findings with pathology are lacking

HOW TO ACQUIRE A PET/CT FOR RTP
PET acquisition for RTP - Options

1. **Staging PET/CT**
   - **A. Visually correlated** with the RTP CT scan: used only as a diagnostic aid to identify areas of disease location during treatment planning session (visual correlation)
   - **B. Registered to a RTP CT scan** (Registration and Patient Positioning Issues)

1. **Dedicated RTP PET/CT**
   - **A. Combined RTP / staging** with whole body PET/CT scan as single scan
   - **B. Dedicated RTP scan** after a staging PET/CT
Recommendations about registering a PET/CT to a RTP CT

- PET/CT images should be registered using a rigid registration (for 4DCT – register to the average intensity projection (Ave-IP) scan)

- Registration should focus on bony anatomy which is not affected by respiratory motion (e.g. spinal column)

- It is advised that this approach should not be used routinely for gated treatments
Lung board set-up for RTP PET/CT

Requirements
- Flat bed couch insert
- Laser lights alignment system
- QA of image registration
- Fixed slots on the scanner
- Appropriate staff
  i. Nuclear medicine technical officer
  ii. Therapy radiographer
  iii. Medical Physics staff

- Arms positioned above the head, T-bar grip and arm supports.
- Small bore - restricts the positioning of the arms and prevents tilting of the lung board
Patient set-up on RTP PET/CT
Protocol for RTP PET Scan

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

- **Hot session** (post injection and 45 minute uptake period)
  - re-position patient, attach radio-opaque markers
  - Images acquired using routine diagnostic PET/CT scan protocol

- **Permanent marks made on patient** (post scan)

PET/CT BASED TARGET VOLUME DELINEATION
IAEA consensus report

PET/CT imaging for target volume delineation in curative intent radiotherapy of non-small cell lung cancer: IAEA consensus report 2014

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DISPLAYING A PET/CT FOR RTP
Setting the PET display for contouring

Avoid using multi-coloured PET displays
Setting the PET display for contouring

Thresholding is key to PET based TVD
Setting the PET display for contouring

Need to use a standardized SUV level intensity using the liver as a reference

Liver should have heterogeneous grainy display
Setting the PET display for contouring

- Use a standardised display
- Use no more than two colours in any colour wash display
- Navigate to the liver
- Adjust the brightness and contrast levels in the PET window in a way that you can still see the shape of anatomical structures e.g. the skin,
- The liver should contain almost no white pixels
WHAT TO DELINEATE?
Reproducibility of Tumour contouring in NSCLC

• Several studies have shown that tumour contouring by “expert” physicians on CT is not reproducible
• Physician variability is the biggest pitfall
• Peter Mac study showed that use of a rigorous protocol improved reproducibility
• Reproducibility is better for PET/CT but inter and intra clinician variability still exists
Image processing and display

- **Image Processing** - Most centres use similar image processing protocols for a diagnostic/staging PET/CT as for a RTP PET/CT (attenuation correction, image reconstruction etc…)

- **RTP PET display** - Ensure that when images are exported to RT planning software they appear the same (need to undertake phantom studies)
Contouring methods

Human/Visual

• Subject to variability of edge definition
• Variation in interpretation
• Uses human knowledge, intelligence and experience
• Uses all available information
• Is actually the final arbiter when patients are treated

Automated

• Entirely reproducible for a given dataset and technology
• Gives widely different results depending on algorithm chosen
• Ideal algorithm does not exist
• Uses only PET information
• Not “intelligent”
PET and respiratory movement

Expiration
PET and respiratory movement

Inspiration
PET and respiratory movement

PET averaged
Using CT alone for RT Planning

Where is the Cancer?
Using PET/CT for RT Planning

Where is the edge of the Cancer?
Using PET/CT for RT Planning

Where is the edge of the Cancer?
PET/CT for delineation of atelectasis

Defining the edge of the GTV/ITV

- If CT margin extends beyond PET - contour the CT unless clearly atelectasis
- If PET extends beyond CT edge of tumour or is obscured by atelectasis - More difficult!
Defining the edge of the GTV
Peer Review
"To improve our teamwork, only three of the chutes will open."
More Contour Examples – Tumor beside the liver

More Contour Examples – CT edge versus PET edge

PET/CT RTP Margins to use...

- When delineating on PET – structure incorporates a respiratory motion
- Consensus statement refers to this as a respiratory expanded GTV (reGTV)
- Suggest reGTV $\Rightarrow$ CTV 6mm or 8mm
- Suggest CTV $\Rightarrow$ PTV at least 5mm (dependent on local set-up error)

HOW TO INCORPORATE GATING?
How to incorporate gating?

• 4DCT now standard technique to account for tumour motion

• 4DCT gives reliable information about tumour morphology and movement

• Where 4DCT acquisition is used alongside PET/CT the GTV edge should be based on the 4DCT

• The PET being used to discriminate tumor and non-tumor sites to adapt the GTV where appropriate
4D PET/CT
Phase based PET attenuation correction

CT in each Phase

PET in each Phase

Phase by Phase attenuated PET
Attenuation Correction

## 3D vs 4D PET/CT

<table>
<thead>
<tr>
<th>Disadvantages</th>
<th>3D PET/CT</th>
<th>4D PET/CT</th>
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<tbody>
<tr>
<td></td>
<td>• Respiratory Averaging</td>
<td>• Technically difficult</td>
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<td></td>
<td>• Possibly inaccurate SUV</td>
<td>• Noisy patterns</td>
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<td></td>
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<td>• Prolonged Acquisition times</td>
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<table>
<thead>
<tr>
<th>Advantages</th>
<th>3D PET/CT</th>
<th>4D PET/CT</th>
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<tbody>
<tr>
<td></td>
<td>• No Noise</td>
<td>• Accurate tumour volume definition</td>
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<td></td>
<td>• Relatively Fast Acquisition</td>
<td>• Detection of Small Lesions</td>
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<tr>
<td></td>
<td></td>
<td>• Better quantification of SUV ($SUV_{MAX}$)</td>
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<td></td>
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<td>• Dose Painting / Better characterisation of heterogeneity within tumour</td>
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Detection of Small Lesions with 4D PET/CT

Lesion detected at hilar area in 4D PET; Not visible (blurred) using 3D PET.

3DPET vs 4D PET vs 4DCT

<table>
<thead>
<tr>
<th>4D CT MIP</th>
<th>4D PET MIP</th>
<th>Free Breathing PET</th>
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<tbody>
<tr>
<td>TYPE 1</td>
<td>TYPE 2</td>
<td>TYPE 3</td>
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<td>TYPE 4</td>
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PET/CT for RTP in NSCLC

- PET/CT has established role in staging
- PET/CT must be used to inform TVD in NSCLC RTP
- A dedicated PET/CT is preferable
- QA of transfer of the PET images to the RTP system is essential
- IAEA Consensus Statement 2014 provides guidance on PET/CT delineation approach
- 4D PET/CT may be provide more accurate tracer quantification