PET for HN Cancer ART: Dose Response Feedback and Adaptive DPbN

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Disclosures

No disclosures relevant to the contents of this presentation
Learning Objectives

• Metabolic imaging and dose response feedback for adaptive tumor dose painting

• Optimization of dose painting by number in target

• Clinical feasibility & workflow for adaptive DPbN
Metabolic Imaging

- **PET**: $[^{18}F, ^{11}C]$ Glucose, Glutamine, Glutamate, Lactate, Acetate, Choline
- **MRI**: Glu-CEST, Hyperpolarized $[1^{-13}C]$ Pyruvate, Lactate, Glucose
Metabolic Imaging: Application in RT

• Tumor has enhanced metabolic activity, which promotes the clinical use of metabolic imaging for target identification/delineation and post treatment response monitoring

• Metabolic image may not be a specific bio-marker to guide a targeting drug, but could be very useful for radiation treatment due to its link to all cancer hallmarks*


• Radioresistant tumor cells should maintain unaltered metabolic activity as measured using a metabolic image following fractionated radiation treatment

  — Therefore, it is possible to use Tumor Voxel Dose Response derived from temporal changes of metabolic image voxel intensity as the feedback for treatment adaptation
FDG-PET Imaging/Dose Response Feedback

FDG PET/CT image is a metabolic image, *not the best*, but very practical in clinics with relatively low cost,

I. Tumor Voxel Dose Response Matrix (DRM) from the temporal changes of image intensity obtained during the treatment course (PET/CT deformable image registration)

II. Tumor voxel Dose Prescription Function (DPF) with using the DRM and its baseline SUV\(_0\)

III. DPF is used to be the objective function for tumor DPbN planning optimization
FDG-PET Imaging: Estimate Tumor Dose Response Matrix

\[ \ln \frac{SUV(v, d)}{SUV_0(v)} = \hat{A}(v, 30\text{Gy}) \cdot d \]
SF₂ - tumor voxel survival fraction in 2Gy

$A$ linearly proportional to SF₂, i.e.

$$\hat{A}(v, \bar{d}) = k \cdot \frac{\ln SF_2(v)}{2};$$

$$SF_2(v) \sim \exp \left( \frac{2 \cdot \hat{A}(v, \bar{d})}{k} \right) = DRM(v, \bar{d})$$

$DRM_{(v,30Gy)} = \exp \left( 31.75 \times \hat{A}(v,30Gy) \right)$ Calibrated to have the numerical range of SF₂.

Bjork-Eriksson T, West C, etc. The in vitro radiosensitivity of human HN cancer. British J of Cancer. 1998;72:2371-5. Mean-$SF_2 = 0.48$
Tumor Voxel Dose Response Matrix (DRM)
Pre-tx SUV

DRM (Created in the week 4)

Local failure (3/6 months Post-Tx PET)

Overlap
Inter- & Intra-tumoral Variation in Dose Response

Controlled by ~66Gy!

Patients

HPV+

HPV-
Tumor Voxel Dose Prescription Function (DPF)

• Mathematic link between specific values of imaging intensity and the optimum clinical dose to be prescribed to the corresponding tumor voxel

• DPF can be designed to achieve a desired tumor control, while maintains the minimized integral dose

  – Is this necessary? Can we safely increase the uniform dose in target as high as needed?
Locally Controlled Tumors (35x2Gy)

$DRM \sim SF_2$ : Tumor voxel survival fraction in 2Gy

$f(SUV_0) \sim N_0$ : Tumor voxel clonogens

$TVCP(v, DRM, SUV_0, d)$
\( TVCP(SUV_0, DRM, TCD_{50}, \gamma_{50}, d) \)

determined using a likelihood of potential control and failure of tumor voxel on each weekly (SUV_0, TMR) plot

\[ \text{Max } L(TCD_{50}, \gamma_{50} \mid TVCP(d_i); i = 1, 2, \ldots, 7) \]
Dose Prescription Function (DPF): TVCP Lookup Table

SUV₀ = 4.5

SUV₀ = 8.5

SUV₀ = 12.5

SUV₀ = 16.5
## Dose Prescription Function: TVCP Lookup Table

<table>
<thead>
<tr>
<th>(TCD$<em>{50}$, $\gamma</em>{50}$)</th>
<th>SUV$_0$ = 4.5</th>
<th>SUV$_0$ = 8.5</th>
<th>SUV$_0$ = 12.5</th>
<th>SUV$_0$ = 16.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRM = 0.2</td>
<td>(3.72, 0.72)</td>
<td>(7.07, 0.63)</td>
<td>(13.62, 0.82)</td>
<td>(20.34, 0.87)</td>
</tr>
<tr>
<td>DRM = 0.3</td>
<td>(4.11, 0.66)</td>
<td>(7.79, 0.62)</td>
<td>(14.9, 0.82)</td>
<td>(22.05, 0.88)</td>
</tr>
<tr>
<td>DRM = 0.4</td>
<td>(4.6, 0.62)</td>
<td>(8.8, 0.62)</td>
<td>(17.69, 0.87)</td>
<td>(27.18, 0.97)</td>
</tr>
<tr>
<td>DRM = 0.5</td>
<td>(5.16, 0.59)</td>
<td>(10.41, 0.62)</td>
<td>(21.91, 0.87)</td>
<td>(34.01, 1.15)</td>
</tr>
<tr>
<td>DRM = 0.6</td>
<td>(5.81, 0.56)</td>
<td>(12.77, 0.58)</td>
<td>(29.71, 0.91)</td>
<td>(40.78, 1.44)</td>
</tr>
<tr>
<td>DRM = 0.7</td>
<td>(6.45, 0.52)</td>
<td>(17.44, 0.58)</td>
<td>(39.7, 1.24)</td>
<td>(47.65, 1.73)</td>
</tr>
<tr>
<td>DRM = 0.8</td>
<td>(7.46, 0.49)</td>
<td>(22.4, 0.61)</td>
<td>(46.08, 1.83)</td>
<td>(53.99, 2.42)</td>
</tr>
<tr>
<td>DRM = 0.9</td>
<td>(8.93, 0.46)</td>
<td>(28.03, 0.73)</td>
<td>(50.65, 2.42)</td>
<td>(58.92, 2.42)</td>
</tr>
<tr>
<td>DRM = 1.0</td>
<td>(10.58, 0.45)</td>
<td>(31.38, 0.91)</td>
<td>(55.51, 2.42)</td>
<td>(62.74, 2.42)</td>
</tr>
<tr>
<td>DRM = 1.1</td>
<td>(14.08, 0.47)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>DRM = 1.2</td>
<td>(15.87, 0.48)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>
Tumor Voxel DPF (TCP = 0.9) design based on (SUV₀, DRM)
Can it be managed safely by using the uniform prescription dose up to 150Gy?
9 beams IMRT:
Conventional Plan: 54Gy to CTV & 70Gy to GTV
DPbN Plan: 54Gy to CTV & Dose Painting to GTV
DPbN (solid-line) vs Standard IMRT (dash-line)
Summary

- Dose response matrix can be constructed using FDG-PET/CT images.
- Tumor DRM with its baseline $SUV_0$ provide very useful, maybe unique, information to design the optimal dose for each tumor voxel.
- DPbN is necessary and could be safely applied.
- How many images needed to implement the adaptive DPbN?

**Pre-treatment PET/CT** → **SUV_0** → **estDRM** → **Treatment PET/CT** → **Treatment PET/CT** → **DPbN Treatment** → **DPbN Planning Optimization**