Theragnostic Imaging and Functional
Image-Guided Head-And-Neck
Radiation Therapy

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Squamous cell carcinoma of the head and neck

<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated New Cases</th>
<th>% of all New Cancer Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>57,000</td>
<td>3.0%</td>
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<table>
<thead>
<tr>
<th>Year</th>
<th>Estimated Deaths</th>
<th>% of all Cancer Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980</td>
<td>10,690</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

From discrete volumes to 3D maps

~1980

~1990

2010+

Cu-ATSM hypoxia scan at UW
**Imaging: spatial AND biological information**

HNSCC: distant metastasis risk

- Nodal SUV_{max} vs. year distant metastasis rate [%]

**Dose painting & personalized RT prescription**

- **Personalized prescription**
  - varying the 4D dose prescription between patients according to some (imaging?) biomarker
  - Risk based (predictive)
  - Response based (adaptive)

- **Dose painting**
  - varying the 4D dose prescription within a patient (lesion-to-lesion or within-lesion) according to some (imaging?) biomarker
  - Risk based (predictive)
  - Response based (adaptive)

**FAZA PET/CT: DAHANCA 24**

- Mortensen et al. RPD 14 (2012)

- Logistic dose-response relationship with $\gamma_{50} = 1.8$
**Dose-painting by numbers**

The prescription function: \( D(I) \)

**The normalized dose-response gradient**

\[ P(D) = P(D_0) \]  
\[ \Delta P = P(D) - P(D_0) \]  
\[ \Delta D = D - D_0 \]  
\[ \Delta D / \Delta D_0 \]

**Steepness of dose-response curves for HNSCC**

- Larynx
- Head & Neck
- Supraglottic
- Pharynx
- Neck nodes

\( \gamma_57 \)
**Functional Imaging of Heterogeneity in Head and neck Tumors (FIGHHT)**

- 28 patients w. 31 lesions
- 6 random biopsies from each
- In vivo and ex vivo scans + pathology
- Large intra-tumor variability
- Significant but weak correlations between FDG and #viable tumor cells and CAIX

PI: Jacob Rasmussen, MD – UH Copenhagen

Embloc excision specimen

En bloc excision specimen FFPE tumor blocs

Specimen scan co-registered with pt. FDG

Specimen scan co-registered with pt. FDG

**Focal origin of recurrence**

HNSCC of pharynx, larynx, oral cavity

N=520

Completed definitive (chemo)IMRT

N=357

Recurred after CR

N=100

Loco-regional prog. CT scan @ rec.

N=39

Rigshospitalet, Copenhagen 2005-2009

AK Due et al. Strahlenther Onkol 188: 671 (2012)

CT at time of recurrence

PET/CT at time of primary RT planning

**Pattern of recurrence**

GTV – "PET positive"

GTV

CTV – tumor

CTV – elective

High risk

CTV – elective

Low risk

AK Due et al. AJR 161: 415 (1993)

AK Due et al. AJR 161: 415 (1993)
Recurrence density after RT for HNSCC

Data-driven dose redistribution

The CONTRAST Phase I dose-escalation trial
Particle Swarm Optimization – breast case

- CLINICAL
  - PSO – an algorithm for finding maxima on complex surfaces
  - All bioeffect models evidence-based.
  - Examples of models:
    - $\text{DFSY}_{\text{CLINICAL}} = \text{DFSY}_{\text{Algorithm}}$
    - $= 0.363^{\Psi} (1 - 0.4^{\text{PTV}})^{\text{PTV}}$

- PSO
  - $\text{Risk}_x = w_x \cdot \text{DF3} \times \text{Bravais}_{\text{P31}} \cdot \text{Bravais}_{\text{P4}} \cdot \delta_{\text{baseline}} \cdot \text{P31} \cdot \text{P4}$
Competing events in HNSCC

286 patients with locally advanced HNSCC treated with definitive chemo-RT

- 42% of cases
- 32% of cases
- 26% of cases

FFF >70% @ 2 years
40-70% FFF @ 2 years
FFF <40% @ 2 years

FFF PREDICTED AT BASELINE

Competing risks: patient level

- Individual 3-year risk estimates in 560 HNSCC pts.
- Note that a high risk of LRF is associated with a higher risk of DM

HNSCC: Increasing local therapy intensity

Selecting the highest LRF risk cases for a loco-regional therapy intensification does not yield much of a gain due to competing risk of DM
Thank you!