This house believes that the use of Functional Imaging for treatment planning of head and neck tumors needs to be carefully considered.

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This house believes that …

• RO will be (even more) multidisciplinary…
• RO is conformal (e.g. IMRT, proton, hadrons)…
• RO will be tailored (individualized) (based on imaging and molecular profiling) and adaptive …
• RO will be associated with targeted agents …

Heterogeneity in H&N TV delineation

Harari et al., 2004
Target selection and delineation

Betrayal of images
This is not an apple...
R. Magritte

Segmentation methods: one by lab...

- Manual delineation
  - Visual interpretation
  - Subjective approach

- Histogram-based
  - Fixed threshold (SUV, %)
  - Adaptive threshold (SBR)
  - Soft thresholding (probabilistic)

- Feature-based
  - (Fuzzy) clustering
  - Clustering of TAC

- Image-based
  - Probabilistic modeling
  - Gradient based

Variability in PET image segmentation for H&N tumors...

Experimental conditions
- Data sets
- Validation studies

Macroscopy
CAT Scan
18F-FDG PET
threshold?

<table>
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<tr>
<th>Patient</th>
<th>Surgical Specimens</th>
<th>40%</th>
<th>50%</th>
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<td>11.8</td>
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<td>5.6</td>
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<tr>
<td>9</td>
<td>24.3</td>
<td>39.9</td>
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<tr>
<td>mean</td>
<td>13.3</td>
<td>26.5*</td>
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Image-Guided Radiation Therapy in HNSCC
The 4th dimension …

FDG-PET

<table>
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<tr>
<th>Gy</th>
<th>Image</th>
<th>FDG-PET</th>
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<td>50</td>
<td><img src="image3.png" alt="Image" /></td>
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PET image segmentation during RxTh

PET in radiotherapy planning for NSCLC
Pathological correlation? Clinical validation?

NSCLC with atelectasis
NSCLC digital MC PET phantom
Different segmentation methods ...

PET in radiotherapy planning for NSCLC

Objective evaluation of the available segmentation methods

Statistical methods
Simulated PET images (MC)
Pathology validated patient images

Gradient detection
Reproducibility/robustness

Scanner model
3D phantom
NCAT
Zubal
3D tumor model
Clinical image used as an example
and associated segmentation
NURBS surface
Simulated 3D PET
PET imaging: a wide range of molecular probes

- Glucose metabolism
  - 18F-FDG
- Protein synthesis
  - 11C-MET
  - 18F-PET
- Proliferation
  - 18F-FLT
- Hypoxia
  - 18F-FMISO
  - 18F-FAPA
- Receptors
  - 18F-FES
  - 68GA-Trastuzumab (HER2)
  - 64Cu-DOTA-panitumumab (EGFR)

A word of caution …

Biological heterogeneity

From Kaanders., 2001

Effect of resolution

Registered autoradiography

N. Christian, 2010
**In Vivo experimental set-up**

- PET tracer, Hoechst
- Pimonidazole
- Tumor sectioning
- Micro PET
- Immuno-fluorescence microscopy (hypoxia, vessels, perfusion)
- Autoradiography (2-D distribution of FAZA)

**FAZA autoradiogram & pimonidazol**

- Busk et al. IJRBOP 2008;70:1202-12

**Scaling issue...**

- Tumor: FSA II
- Mouse no. 2, 1
- Tum Volume: 2.30 ml
- \(^{18}\)F-FDG – 300 µCi

- Volume corresponding to the highest 10 percent of activity

- AR Volume
- PET Volume
- Mismatch

**Scaling issue...**

- Dice Similarity Index (%)
- Scaling issue...

- Data Source: N. Christian, 2007
**PET imaging: a wide range of molecular probes**

- **Glucose metabolism**
  - $^{18}$F-FDG
- **Protein synthesis**
  - $^{11}$C-MET
  - $^{18}$F-PET
- **Proliferation**
  - $^{18}$F-FLT
- **Hypoxia**
  - $^{18}$F-FMISO
  - $^{18}$F-FAZA
- **Receptors**
  - $^{18}$F-FES
  - $^{68}$Ga-Trastuzumab (HER2)
  - $^{64}$Cu-DOTA-panitumumab (EGFR)

*Courtesy of Geets, 2011*

**Comparison $^{18}$F-FDG / $^{14}$C-EF3**

<table>
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<tr>
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<th>SCCVII</th>
<th>FSAII</th>
<th>SCCVII+hypoxia</th>
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<tbody>
<tr>
<td>$^{14}$C-EF3</td>
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<tr>
<td>$^{18}$F-FDG</td>
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</tbody>
</table>

**Comparison $^{18}$F-FDG / $^{14}$C-EF3**

Anova: $p = 0.19$

*Courtesy of Geets, 2011*
Survival is non-flat (higher in resistant areas)

Mean Tumor Dose = 2 Gy

More similar survival across entire tumor

Molecular imaging dose painting by number

- Tomotherapy Hi-Art
- H&N SCC: T4N2bM0
- 60 Gy + SIB of 30 Gy

Molecular imaging dose painting by number

- DPBN based on FDG-PET
  - Median dose of 80.9 Gy (n=7) or 85.9 Gy (n=14)
  - No grade 4 acute toxicity

“Dose painting” by number

Flat dose

Non-flat dose

Survival is non-flat

Mean Tumor Dose = 2 Gy

More similar survival across entire tumor

“Dose painting” : the physics issue

Courtesy of D. De Ruysscher

“Dose painting” by number

Deveau et al., 2010

DUa et al., 2010

Duprez et al., 2010
Functional imaging for H&N treatment planning

- Great potential … but …
- Don’t trust your physician …
- Rely on user’s independent methods
- Be aware of the various conceptual limitations …
- Never forget the clinical knowledge
- At the end, the proof is in the pudding