Assessment and management of uncertainties in Head & Neck IMRT

Vincent GREGOIRE, M.D., Ph.D., Hon. FRCR

Head and Neck Oncology Program, Radiation Oncology Dept. & Center for Molecular Imaging and Experimental Radiotherapy, Université Catholique de Louvain, St-Luc University Hospital, Brussels, Belgium
Evidence-based management of T1N0 glottic carcinomas: level 3

Probability of loco-regional control vs. Time from diagnosis (years)

Open Surgery
Radiotherapy
Laser

p = n.s.

Rosier, R&O, 1998
IMRT in Head and Neck Tumors
IMRT in Head and Neck Tumors

Where uncertainties could come from?

• selection and delineation of TVs and OARs
• choice of the optimal imaging modality
• patient positioning
• dose optimization
• treatment adaptation
IMRT in Head and Neck Tumors

Where uncertainties could come from?

• selection and delineation of TVs and OARs
• choice of the optimal imaging modality
• patient positioning
• dose optimization
• treatment adaptation
Heterogeneity in H&N TV delineation

Harari et al., 2004
Study design

Patients with Stage III or IV SCCHN
(stratified by stage, site, hemoglobin)

Randomization

Cisplatin, RT

Tirapazamine, cisplatin, RT
Results – Final analysis by ITT

Overall Survival By Arm

- CIS
- CIS/TPZ

2P = 0.65

Estimated percentage surviving

Years following randomisation

Hazard ratio 95% CI

CIS/TPZ > CIS
Failure-free survival by deviation status

Patients who had received at least 60 Gy of RT to PTV2
Time to LRF by treatment arm in patients **without** predicted adverse impact on TCP

Patients who had received at least 60 Gy of RT to PTV2
Factors analysed for adverse impact on TCP after secondary review: Investigator factors

Number of patients enrolled

<table>
<thead>
<tr>
<th>Enrolment bracket</th>
<th>Number of patients</th>
<th>Number with major adverse impact</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4 (26 centres)</td>
<td>57</td>
<td>17</td>
<td>29.8%</td>
</tr>
<tr>
<td>5-9 (22 centres)</td>
<td>130</td>
<td>28</td>
<td>21.5%</td>
</tr>
<tr>
<td>10-19 (22 centres)</td>
<td>279</td>
<td>33</td>
<td>11.8%</td>
</tr>
<tr>
<td>≥ 20 (11 centres)</td>
<td>352</td>
<td>19</td>
<td>5.4%</td>
</tr>
</tbody>
</table>

2P<0.0001
Selection and delineation of lymph node target volumes in head and neck conformal radiotherapy. Proposal for standardizing terminology and procedure based on the surgical experience

Vincent Grégoire\textsuperscript{a,*}, Emmanuel Coche\textsuperscript{b}, Guy Cosnard\textsuperscript{b}, Marc Hamoir\textsuperscript{c}, Hervé Reychler\textsuperscript{d}

\textsuperscript{a}Department of Radiation Oncology, Université Catholique de Louvain, St-Luc University Hospital, 10 Ave. Hippocrate, 1200 Brussels, Belgium
\textsuperscript{b}Department of Radiology, Université Catholique de Louvain, St-Luc University Hospital, Brussels, Belgium
\textsuperscript{c}Department of Otolaryngology Head and Neck Surgery, Université Catholique de Louvain, St-Luc University Hospital, Brussels, Belgium
\textsuperscript{d}Department of Oral and Maxillo-facial Surgery, Université Catholique de Louvain, St-Luc University Hospital, Brussels, Belgium

Received 20 September 1999; received in revised form 28 March 2000; accepted 13 April 2000
IMRT in Head and Neck Tumors

CT-based delineation of lymph node levels and related CTVs in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines

Vincent Grégoire\textsuperscript{a,*,1}, Peter Levendag\textsuperscript{b,1}, Kian K. Ang\textsuperscript{c}, Jacques Bernier\textsuperscript{d}, Marijel Braaksma\textsuperscript{b}, Volker Budach\textsuperscript{e}, Cliff Chao\textsuperscript{c}, Emmanuel Coche\textsuperscript{f}, Jay S. Cooper\textsuperscript{c}, Guy Cosnard\textsuperscript{f}, Avraham Eisbruch\textsuperscript{c}, Samy El-Sayed\textsuperscript{g}, Bahman Emami\textsuperscript{c}, Cai Grau\textsuperscript{h}, Marc Hamoir\textsuperscript{i}, Nancy Lee\textsuperscript{c}, Philippe Maingon\textsuperscript{j}, Karin Muller\textsuperscript{b}, Hervé Reychler\textsuperscript{k}

DAHANCA: http://www.dshho.suite.dk/dahanca/guidelines.html
RTOG: http://www.rtog.org/hnatlas/main.htm
Which CTV for the node positive and the post-operative neck?

Target volume delineation

Proposal for the delineation of the nodal CTV in the node-positive and the post-operative neck

Vincent Grégoire\textsuperscript{a,}\textdagger, Avraham Eisbruch\textsuperscript{b}, Marc Hamoir\textsuperscript{c}, Peter Levendag\textsuperscript{d}

\textsuperscript{a}Department of Radiation Oncology, Head and Neck Oncology Program and Center for Molecular Imaging and Experimental Radiation Oncology, Université Catholique de Louvain, Brussels, Belgium, \textsuperscript{b}Department of Radiation Oncology, University of Michigan, Ann Arbor, MI, USA, \textsuperscript{c}Department of Head and Neck Surgery and Head and Neck Oncology Program, Université Catholique de Louvain, Brussels, Belgium, \textsuperscript{d}Department of Radiation Oncology, Rotterdam, The Netherlands
## Which CTV for the neck?

### Oropharyngeal Carcinoma

<table>
<thead>
<tr>
<th>Nodal stage (AJCC 1997)</th>
<th>Levels to be included in the CTV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>Ipsilateral neck</strong></td>
</tr>
<tr>
<td>N0 - N1 (in level II, III or IV)</td>
<td>II-III-IV + RP(^1) for post. pharyngeal wall tumor</td>
</tr>
<tr>
<td>N2a - N2b</td>
<td>Ib, II, III, IV, V + RP</td>
</tr>
<tr>
<td>N2c</td>
<td>According to N stage on each side of the neck</td>
</tr>
<tr>
<td>N3</td>
<td>I, II, III, IV, V + RP ± adjacent structures according to clinical and radiological data</td>
</tr>
</tbody>
</table>

\(^1\)retropharyngeal nodes

Grégoire et al., 2000
CT-based delineation of lymph node levels in the neck: international consensus guidelines

Level Ia and Ib

- **Ant.** symphysis menti / platysma
- **Post.** hyoid bone / submandibular gland
- **Lat.** ant. belly of digastric m. (Ia)
  - mandible / platysma (Ib)
- **Med.** ant. belly of digastric m. (Ib)
- **Cra.** geniohyoid m./mandible (Ia)
  - mylohyoid m, submandibular gland (Ib)
- **Cau.** hyoid bone

Grégoire et al., 2003
CT-based delineation of lymph node levels in the neck: retrostyloid space

Grégoire et al., 2006
CT-based delineation of lymph node levels in the neck: subclavicular fossae
H&N IMRT practice heterogeneity among Dutch Radiation Oncologists

Rasch et al., 2007
Inter-observer variability on OAR delineation with CT-scan and MRI

Organ At Risk (OAR)

Parotid glands

Spinal cord

**Average (± sem) diameter (mm)**

<table>
<thead>
<tr>
<th></th>
<th>Obs1</th>
<th>Obs2</th>
<th>Obs3</th>
<th>Obs4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT-scan</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>MRI</td>
<td>11</td>
<td>10</td>
<td>9</td>
<td>8</td>
</tr>
</tbody>
</table>

**ANOVA: p=0.004**

**Average (± sem) volume (cc)**

<table>
<thead>
<tr>
<th></th>
<th>Obs1</th>
<th>Obs2</th>
<th>Obs3</th>
<th>Obs4</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT-scan</td>
<td>20</td>
<td>25</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>MRI</td>
<td>35</td>
<td>30</td>
<td>25</td>
<td>20</td>
</tr>
</tbody>
</table>

**ANOVA: p<0.001**

Organ At Risk (OAR) delineation with CT-scan and MRI

Geets *et al*, 2005
IMRT in Head and Neck Tumors

Where uncertainties could come from?

- selection and delineation of TVs and OARs
- choice of the optimal imaging modality
- patient positioning
- dose optimization
- treatment adaptation
Betrayal of images

This is not an apple…

R. Magritte

Target selection and delineation
Image-Guided Radiation Therapy in HNSCC

The Gross Target Volume (GTV) is the gross demonstrable extend and location of the malignant growth …
Detection of metastatic disease in the neck:
Comparison between CT, MRI and FDG-PET

- Meta-analysis: n= 1236 patients (32 studies)
- HNSCC (all sites)
- Neck dissection for all patients

Table:

<table>
<thead>
<tr>
<th>Diagnostic methods compared</th>
<th>No. of studies (references)</th>
<th>Independent estimates (95% CI)</th>
<th>Likelihood ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sensitivity</td>
<td>Specificity</td>
</tr>
<tr>
<td>CT</td>
<td>16 (20,21,23,24,26,28,31,</td>
<td>0.74 (0.61 to 0.83)</td>
<td>0.76 (0.68 to 0.83)</td>
</tr>
<tr>
<td></td>
<td>32,36,40,43–47,49,50)</td>
<td>0.82 (0.72 to 0.89)</td>
<td>0.86 (0.78 to 0.91)</td>
</tr>
<tr>
<td>18F-FDG PET</td>
<td></td>
<td>0.78 (0.54 to 0.92)</td>
<td>0.80 (0.67 to 0.88)</td>
</tr>
<tr>
<td>MRI</td>
<td>9 (20,21,24,31,40,43,</td>
<td>0.78 (0.64 to 0.87)</td>
<td>0.85 (0.79 to 0.90)</td>
</tr>
<tr>
<td></td>
<td>44,47,48,51)</td>
<td>0.78 (0.54 to 0.92)</td>
<td>0.80 (0.67 to 0.88)</td>
</tr>
<tr>
<td>CT + MRI</td>
<td>4 (19,27,34,47)</td>
<td>0.66 (0.44 to 0.82)</td>
<td>0.76 (0.53 to 0.90)</td>
</tr>
<tr>
<td>18F-FDG PET</td>
<td></td>
<td>0.73 (0.58 to 0.84)</td>
<td>0.89 (0.84 to 0.93)</td>
</tr>
<tr>
<td>USFNA</td>
<td>4 (20,21,25,39)</td>
<td>0.42 (0.01 to 0.97)</td>
<td>0.96 (0.76 to 0.99)</td>
</tr>
<tr>
<td>18F-FDG PET</td>
<td></td>
<td>0.45 (0.27 to 0.64)</td>
<td>0.88 (0.76 to 0.95)</td>
</tr>
</tbody>
</table>

* CI = confidence interval; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; CT = computed tomography; 18F-FDG PET = positron emission tomography using 18F-fluorodeoxyglucose; MRI = magnetic resonance imaging; USFNA = ultrasound-guided fine-needle aspiration.
The Gross Tumor volume (GTV)

Tumor Volume in Pharyngolaryngeal Squamous Cell Carcinoma: Comparison at CT, MR Imaging, and FDG PET and Validation with Surgical Specimen¹

Jean-François Daisne, MD
Thierry Duprez, MD
Birgit Weynand, MD
Max Lonneux, MD, PhD
Marc Hamoir, MD
Hervé Reychler, MD, DDS
Vincent Grégoire, MD, PhD

Index terms:
Head and neck neoplasms, CT,
26.1211, 27.1211
Head and neck neoplasms, MR,

Daisne et al., Radiology, 233: 93-100, 2004
How far are we from the truth?

### Table 3

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Tumor Site</th>
<th>T Stage</th>
<th>GTV (cm³)</th>
<th>FDG PET</th>
<th>Surgical Specimen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>CT</td>
<td>MR Imaging</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>PS</td>
<td>T4</td>
<td>47.7</td>
<td>36.3</td>
<td>19.3</td>
</tr>
<tr>
<td>2</td>
<td>GL</td>
<td>T3</td>
<td>18.0</td>
<td>9.9</td>
<td>6.0</td>
</tr>
<tr>
<td>3</td>
<td>GL</td>
<td>T3</td>
<td>41.1</td>
<td>30.2</td>
<td>9.2</td>
</tr>
<tr>
<td>4</td>
<td>RC</td>
<td>T3</td>
<td>7.1</td>
<td>10.6</td>
<td>7.3</td>
</tr>
<tr>
<td>5</td>
<td>PS</td>
<td>T2</td>
<td>4.1</td>
<td>9.1</td>
<td>2.3</td>
</tr>
<tr>
<td>6</td>
<td>SGL</td>
<td>T2</td>
<td>3.7</td>
<td>1.4</td>
<td>1.2</td>
</tr>
<tr>
<td>7</td>
<td>SubGL</td>
<td>T3</td>
<td>5.8</td>
<td>7.0</td>
<td>3.2</td>
</tr>
<tr>
<td>8</td>
<td>PS</td>
<td>T3</td>
<td>17.3</td>
<td>17.6</td>
<td>12.6</td>
</tr>
<tr>
<td>9</td>
<td>PS</td>
<td>T4</td>
<td>13.1</td>
<td>30.7</td>
<td>11.4</td>
</tr>
<tr>
<td>10</td>
<td>PS</td>
<td>T4</td>
<td>55.6</td>
<td>53.4</td>
<td>34.2</td>
</tr>
<tr>
<td>11</td>
<td>SubGL</td>
<td>T2</td>
<td>1.9</td>
<td>2.4</td>
<td>3.4</td>
</tr>
<tr>
<td>12</td>
<td>GL</td>
<td>T4</td>
<td>6.2</td>
<td>9.8</td>
<td>8.5</td>
</tr>
<tr>
<td>13</td>
<td>LAR</td>
<td>T4</td>
<td>41.0</td>
<td>58.4</td>
<td>30.2</td>
</tr>
<tr>
<td>14</td>
<td>LAR</td>
<td>T4</td>
<td>11.1</td>
<td>6.6</td>
<td>8.0</td>
</tr>
<tr>
<td>15</td>
<td>LAR</td>
<td>T4</td>
<td>14.6</td>
<td>22.0</td>
<td>10.2</td>
</tr>
<tr>
<td>16</td>
<td>LAR</td>
<td>T4</td>
<td>18.4</td>
<td>22.0</td>
<td>11.4</td>
</tr>
<tr>
<td>17</td>
<td>LAR</td>
<td>T4</td>
<td>28.1</td>
<td>32.3</td>
<td>26.6</td>
</tr>
<tr>
<td>18</td>
<td>LAR</td>
<td>T4</td>
<td>25.0</td>
<td>23.5</td>
<td>20.0</td>
</tr>
<tr>
<td>19</td>
<td>LAR</td>
<td>T4</td>
<td>40.4</td>
<td>37.3</td>
<td>28.7</td>
</tr>
</tbody>
</table>

#### Mean

- **All patients** (n = 19): ······ 21.4 21.4 13.4* NA
- **Patients with specimen available** (n = 9): ······ 20.8 23.8 16.3 12.6†

Note.—GL = glottic larynx, LAR = larynx without other specification, NA = not applicable, PS = pyriform sinus, RC = retro cricoid area, SGL = supraglottic larynx, SubGL = subglottic larynx.

* In the comparison with CT and MR imaging, P < .01 (for both).

† In the comparison with CT, MR imaging, and PET, P = .003, .001, and .06, respectively.
PET image segmentation: an issue?

Volume delineation based on automatic thresholding with $^{18}\text{F}-\text{FDG}$

OSEM (unsmoothed)  
$1.1 \text{ cm}^3$

OSEM (smoothed at 6 mm)  
$1.6 \text{ cm}^3$
Image-Guided Radiation Therapy in HNSCC
The 4th dimension ...

FDG-PET

0 Gy

46 Gy
PET image segmentation during RxTh

Raw image → Image processing → Image segmentation

- SBR
- BG 6mm + deconvolution

UG 4mm
Imaging resolution and biological heterogeneity

$^{18}\text{F}$-FDG TEP

Resolved autoradiography

Resolution 2.3 mm

Resolution 0.1 mm

N. Christian, 2010
Imaging resolution and biological Heterogeneity: a scaling issue …

Dice Similarity Index (%) vs. % of Overall Tumor Volume

- FSA II (n=5)
- SCC VII (n=5)
- FSA II + RT (n=5)

N. Christian, 2007
Effect of resolution

Mouse T₀  % vol
0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1
0.0 7.0 8.7 10.0 11.0 12.1 12.7 13.1 13.9 14.5 15.0

Human T₀
0.0 13.9 17.5 20.1 22.1 23.8 25.3 26.6 27.8 28.9 30.0

Mosaic PET

FWHM  r²
1.5 mm  0.88
2.0 mm  0.84
2.5 mm  0.86
2.7 mm  0.87
3.0 mm  0.86
3.5 mm  0.84

N. Christian, 2010
Validation protocol in locally advanced HNSCC

Apport de l'imagerie fonctionnelle par Tomographie par Emission de Positrons (TEP) dans le ciblage biologique par radiothérapie de conformation (3D-CRT) et par modulation d'intensité (IMRT) de tumeurs ORL

Use of functional imaging with PET for target volume delineation in 3D-CRT/IMRT for head and neck tumors

Prof. V. Grégoire, UCL St-Luc, Brussels, Belgium
Prof. E. Lartigau, COL, Lille, France
Dr. JF Daisnes, Cliniques St-Elisabeth, Namur, Belgium
IMRT in Head and Neck Tumors

Where uncertainties could come from?

- selection and delineation of TVs and OARs
- choice of the optimal imaging modality
- patient positioning
- dose optimization
- treatment adaptation
The Cathedral of Rouen

4D-IMRT

C. Monet, 1894
Geometric 4D-IMRT

MVCT

kVCT
Geometric 4D-IMRT

Alternate week MVCTs: CTV-PTV margins

- 75 patients
- total of 1481 MVCT
- CTV-PTV: \((2\Sigma + 0.7\sigma)\)

CTV to PTV margin

Cranio-caudal direction

Medio-lateral direction

Antero-posterior direction

Vaandering, 2009
IMRT in Head and Neck Tumors

Where uncertainties could come from?

- selection and delineation of TVs and OARs
- choice of the optimal imaging modality
- patient positioning
- dose optimization
- treatment adaptation
IMRT in Head and Neck Tumors: conformal avoidance or anatomy-based IMRT

doi:10.1016/j.ijrobp.2009.09.062

PHYSICS CONTRIBUTION

EMPHASIZING CONFORMAL AVOIDANCE VERSUS TARGET DEFINITION FOR IMRT PLANNING IN HEAD-AND-NECK CANCER

PAUL M. HARARI, M.D.,* SHIYU SONG, M.D., PH.D., † AND WOLFGANG A. TOMÉ, PH.D.* †

Departments of *Human Oncology and †Medical Physics, University of Wisconsin Medical School, Madison, WI; †Department of Radiation Oncology, Medical College of Virginia, Richmond, VA

AAPM
Aug. 2011

Harari et al., 2010
IMRT in Head and Neck Tumors: conformal avoidance or anatomy-based IMRT

a) DVH comparison for GTV and CTV using TD-IMRT and CA-IMRT methods

b) DVH comparison for the Spinal Cord

c) DVH comparison for the spared parotid gland

AAPM Aug. 2011

Harari et al., 2010
# IMRT in Head and Neck Tumors: D/V constraints

<table>
<thead>
<tr>
<th>PTV / PRV</th>
<th>$D_{95}^a$</th>
<th>$D_{99}$</th>
<th>$D_5$</th>
<th>$D_2$</th>
<th>Mean dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Therapeutic PTV</td>
<td>$\geq 95%$ of prescribed dose</td>
<td>$\geq 90%$ of prescribed dose</td>
<td>$\geq 107$ of prescribed dose</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Prophylactic PTV</td>
<td>$\geq 95%$ of prescribed dose</td>
<td>$\geq 90%$ of prescribed dose</td>
<td>$?$</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PRV spinal cord</td>
<td>-</td>
<td>-</td>
<td>$\geq 50$ Gy</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$\geq 48$ Gy</td>
<td>-</td>
</tr>
<tr>
<td>Contralateral parotid</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$&lt; 20$ Gy</td>
</tr>
<tr>
<td>I ipsilateral parotid</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$&lt; 25$ Gy</td>
</tr>
<tr>
<td>Larynx$^b$</td>
<td>-</td>
<td>-</td>
<td>$\geq 45$ Gy</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Oral cavity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>$&lt; 30$ Gy</td>
</tr>
<tr>
<td>Phar constrictor m.</td>
<td></td>
<td></td>
<td>$&lt; 45$ Gy</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$Dx: dose in x% of the volume

$^b$ for oropharyngeal primary only

AAPM
Aug. 2011
IMRT for Head and Neck Tumors

Oropharyngeal SCC
T2-N0-M0
SIB-IMRT: 30x2.3 Gy
30x1.85 Gy
IMRT in Head and Neck Tumors

Where uncertainties could come from?

- selection and delineation of TVs and OARs
- choice of the optimal imaging modality
- patient positioning
- dose optimization
- treatment adaptation
CT MRI (T2) FDG-PET

PRE-R/
(Week 2)
WEEK 3
(Week 4)
WEEK 5

AAPM Aug. 2011
Variation in CT Target volumes during RT-CH
(70 Gy – 3 courses chemo on w1, w4, w7)

Mean slope: -3.18% / treat day (p<0.05)
Lateral shift: 1.26mm after 25# (p<0.05)

Mean slope: -2.55% / treat day (p<0.05)
Lateral shift: 1.52mm after 25# (p<0.05)
Variation in nodal Target Volumes during RT-CH (70 Gy – 3 courses chemo on w1, w4, w7)

Mean slope: -2.15% / treat day (p<0.05)
Medial shift: 0.95mm after 25# (p<0.05)

Mean slope: -1.46% / treat day (p<0.05)
Medial shift: 0.91mm after 25# (p<0.05)

Castadot & Lee, 2010
Variation in prophylactic CTVs during RT-CH… (70 Gy – 3 courses chemo on w1, w4, w7)

Mean slope: -0.47% / treat day (p<0.05)
No shift

Mean slope: -0.41% / treat day (p<0.05)
Medial shift: 1.76mm after 25# (p<0.05)

Castadot & Lee, 2010
Variation in parotid volumes during RT-CH…
(70 Gy – 3 courses chemo on w1, w4, w7)

Homolateral parotid

Mean slope: -0.93% / treat day (p<0.05)
Medial shift: 3.21mm after 25# (p<0.05)

Heterolateral parotid

Mean slope: -1.03% / treat day (p<0.05)
No shift

Castadot & Lee, 2010
## Variation in parotid and TV during RT

<table>
<thead>
<tr>
<th>Authors</th>
<th>Imaging</th>
<th>Parotid Gland</th>
<th>Target Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Δ COM</td>
<td>Δ Volume</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Δ Volume</td>
<td>Δ COM</td>
</tr>
<tr>
<td>Barker, 2004</td>
<td>EXaCT</td>
<td>3.1 mm medial</td>
<td>0.6% / day</td>
</tr>
<tr>
<td>Hansen, 2006</td>
<td>kVCT</td>
<td>-</td>
<td>15.6% - 21.5% at 36 Gy</td>
</tr>
<tr>
<td>Robar, 2007</td>
<td>kVCT</td>
<td>0.8-0.9 mm / week</td>
<td>4.9% / week</td>
</tr>
<tr>
<td>Han, 2008</td>
<td>MVCT</td>
<td>-</td>
<td>1.1% / day</td>
</tr>
<tr>
<td>Vasquez-Osorio, 2008</td>
<td>kVCT</td>
<td>3 mm medial</td>
<td>17% loss at 46 Gy</td>
</tr>
</tbody>
</table>
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

<table>
<thead>
<tr>
<th>Before R/</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
<th>Week 6</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Daily MVCT</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* R/ start</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em><em>kVCT and FDG-PET</em> Images acquisitions</em>*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- 25 patients with stage III-IV pharyngolaryngeal SCC treated by CT-RT
- MVCT images acquired daily
- kVCT and FDG-PET* images acquired before R/ and during RT after means doses of 10*, 24*, 34*, 50 and 60 Gy

Carruthers, 2010
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Carruthers, 2011
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Median Dose to PTV T (phase I)

Mean $\Sigma$ median dose = 49.9 Gy

Mean $\Sigma$ median dose = 48.9 Gy
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Mean Deviation (%) from PTV Planned dose (50 Gy)

<table>
<thead>
<tr>
<th>Dose</th>
<th>PTV T</th>
<th>Ipsilateral Nodal PTV</th>
<th>Contralateral Nodal PTV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Near Max (2%)</td>
<td>1.25% (±0.28*)</td>
<td>1.78% (±0.36*)</td>
<td>0.79% (±0.32*)</td>
</tr>
<tr>
<td>Median (50%)</td>
<td>0.39% (±0.28*)</td>
<td>0.15% (±0.28*)</td>
<td>0.06% (±0.22*)</td>
</tr>
<tr>
<td>95%</td>
<td>-1.52% (±0.43*)</td>
<td>-2.45% (±0.54*)</td>
<td>-3.35% (±0.38*)</td>
</tr>
<tr>
<td>Near Min (98%)</td>
<td>-3.32% (±0.60*)</td>
<td>-4.38% (±0.62*)</td>
<td>-4.96% (±0.60*)</td>
</tr>
<tr>
<td>Mean</td>
<td>0.37% (±0.43*)</td>
<td>-0.20% (±0.25*)</td>
<td>0.70% (±0.39*)</td>
</tr>
</tbody>
</table>

*Standard Error of Mean
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Median Dose to CTV T (phase I)

Mean Σ median dose = 49.4 Gy
Mean Σ median dose = 48.9 Gy
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Mean Deviation (%) from CTV Planned dose (50 Gy)

<table>
<thead>
<tr>
<th>Dose</th>
<th>CTV T</th>
<th>Ipsilateral Nodal CTV</th>
<th>Contralateral Nodal CTV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Near Max (2%)</td>
<td>1.26% (±0.31*)</td>
<td>1.18% (±0.25*)</td>
<td>0.96% (±0.34*)</td>
</tr>
<tr>
<td>Median (50%)</td>
<td>0.93% (±0.25*)</td>
<td>0.51% (±0.24*)</td>
<td>0.33% (±0.21*)</td>
</tr>
<tr>
<td>95%</td>
<td>-0.19% (±0.37*)</td>
<td>-1.00% (±0.54*)</td>
<td>-0.80% (±0.26*)</td>
</tr>
<tr>
<td>Near Min (98%)</td>
<td>-1.33% (±0.69*)</td>
<td>-1.12% (±0.26*)</td>
<td>-1.95% (±0.37*)</td>
</tr>
<tr>
<td>Mean</td>
<td>0.77% (±0.24*)</td>
<td>0.37% (±0.21*)</td>
<td>0.15% (±0.20*)</td>
</tr>
</tbody>
</table>

*Standard Error of Mean
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Ipsilateral Parotid Mean Dose (phase I)

\[ \Sigma \text{mean dose} = 23.66 \text{Gy} \]

\[ \Sigma \text{mean dose} = 21.23 \text{Gy} \]
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Mean Deviation(%) from OAR Planned dose (50 Gy)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Ipsilateral Parotid</th>
<th>Contralateral Parotid</th>
<th>Oral Cavity</th>
<th>PRV SC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>16.09% (±1.79*)</td>
<td>10.55% (±2.46*)</td>
<td>4.38% (±1.15*)</td>
<td>-</td>
</tr>
<tr>
<td>Near Max (2%)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4.39% (±1.12*)</td>
</tr>
</tbody>
</table>

*Standard Error of Mean
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Total Ipsilateral Parotid Shift

Latero-medial shift (mm)

Fraction#

Average/fx = 0.13mm

Σ mean movement = 4.36mm

Carruthers, 2011
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Total Ipsilateral Parotid Shrinkage

Average/fraction # = 0.56%

Σ mean shrinkage = 19.03%
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Ipsilateral Parotid Shift vs Dose (PT8)
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Contralateral Parotid Shift vs Dose (PT2)
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

<table>
<thead>
<tr>
<th>Irradiated volume</th>
<th>Planned dose distribution</th>
<th>95% CI</th>
<th>Delivered dose distribution</th>
<th>95% CI</th>
<th>Adaptive dose distribution</th>
<th>95% CI</th>
<th>p-value (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$V_{100%}$ (cc)</td>
<td>140.4</td>
<td>[66.4 ; 214.4]</td>
<td>150.2</td>
<td>[69.3 ; 231.0]</td>
<td>112.1</td>
<td>[50.9 ; 173.3]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>$V_{95%}$ (cc)</td>
<td>246.5</td>
<td>[137.6 ; 355.4]</td>
<td>261.4</td>
<td>[144.7 ; 378.1]</td>
<td>202.0</td>
<td>[111.5 ; 292.5]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>$V_{90%}$ (cc)</td>
<td>274.7</td>
<td>[186.1 ; 363.3]</td>
<td>323.1</td>
<td>[189.5 ; 456.7]</td>
<td>262</td>
<td>[154.2 ; 369.7]</td>
<td>0.05</td>
</tr>
<tr>
<td>$V_{80%}$ (cc)</td>
<td>681.3</td>
<td>[533.0 ; 829.7]</td>
<td>667.5</td>
<td>[499.1 ; 835.9]</td>
<td>678.4</td>
<td>[535.9 ; 820.8]</td>
<td>0.73</td>
</tr>
<tr>
<td>$V_{70%}$ (cc)</td>
<td>1126.6</td>
<td>[921.4 ; 1331.9]</td>
<td>1142.3</td>
<td>[918.6 ; 1366.0]</td>
<td>1124.0</td>
<td>[901.4 ; 1346.7]</td>
<td>0.49</td>
</tr>
<tr>
<td>$V_{60%}$ (cc)</td>
<td>1485.4</td>
<td>[1232.8 ; 1738.0]</td>
<td>1503.4</td>
<td>[1230.7 ; 1776.1]</td>
<td>1497.9</td>
<td>[1219.0 ; 1776.8]</td>
<td>0.55</td>
</tr>
<tr>
<td>$V_{50%}$ (cc)</td>
<td>1822.5</td>
<td>[1540.5 ; 2104.4]</td>
<td>1845.2</td>
<td>[1539.1 ; 2151.2]</td>
<td>1848.3</td>
<td>[1525.1 ; 2171.5]</td>
<td>0.39</td>
</tr>
</tbody>
</table>
## Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

### Organs at Risk

<table>
<thead>
<tr>
<th>Organ</th>
<th>Planned dose distribution</th>
<th>Delivered dose distribution</th>
<th>Adaptive dose distribution</th>
<th>p-value (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid glands</td>
<td>$D_{\text{mean}}$ (Gy)</td>
<td>17.89</td>
<td>18.68</td>
<td>18.67</td>
</tr>
<tr>
<td>Submandibular glands</td>
<td>$D_{\text{mean}}$ (Gy)</td>
<td>51.90</td>
<td>52.78</td>
<td>51.73</td>
</tr>
<tr>
<td>Oral Cavity</td>
<td>$D_{\text{mean}}$ (Gy)</td>
<td>26.03</td>
<td>26.74</td>
<td>24.36</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>$D_{2%}$ (Gy)</td>
<td>40.12</td>
<td>40.95</td>
<td>39.42</td>
</tr>
<tr>
<td>PRV spinal cord</td>
<td>$D_{2%}$ (Gy)</td>
<td>42.31</td>
<td>44.22</td>
<td>41.23</td>
</tr>
<tr>
<td>Larynx</td>
<td>$D_{5%}$ (Gy)</td>
<td>67.94</td>
<td>67.74</td>
<td>67.65</td>
</tr>
<tr>
<td>Mandible</td>
<td>$D_{2%}$ (Gy)</td>
<td>56.87</td>
<td>56.19</td>
<td>54.74</td>
</tr>
<tr>
<td>Mandible</td>
<td>$V_{50\text{Gy}}$ (%)</td>
<td>9.73</td>
<td>9.05</td>
<td>10.21</td>
</tr>
</tbody>
</table>
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Adaptive approach and ipsilateral parotid irradiation

\[ R^2 = 0.65 \ (p<0.05) \]
Impact on dose distribution

Classic CT-based planning  Adaptive PET-based planning

<table>
<thead>
<tr>
<th>Planning</th>
<th>V_{10}</th>
<th>V_{50}</th>
<th>V_{80}</th>
<th>V_{90}</th>
<th>V_{95}</th>
<th>V_{100}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Classic CT-based</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Adaptive CT-based</td>
<td>99%</td>
<td>100%</td>
<td>100%</td>
<td>85%</td>
<td>80%</td>
<td>66%</td>
</tr>
<tr>
<td>Classic PET-based</td>
<td>99%</td>
<td>99%</td>
<td>98%</td>
<td>83%</td>
<td>82%</td>
<td>81%</td>
</tr>
<tr>
<td>Adaptive PET-based</td>
<td>99%</td>
<td>100%</td>
<td>98%</td>
<td>73%</td>
<td>67%</td>
<td>58%</td>
</tr>
</tbody>
</table>

SIB-IMRT
30x2.3 Gy
30x1.85 Gy

P<0.001

AAPM
Aug. 2011

Geets, 2007
IMRT in Head and Neck Tumors
WYSINWYG… !!!
Parotid gland sparing in IMRT for HNSCC

RTOG Subjective Salivary Gland toxicity ≥G2*

Nutting et al. JCO 2009:27 (18s);799s (LBA6006)

*Moderate or complete dryness of mouth poor or no response on stimulation

Nutting, 2009
Chemotherapy: Induction or Concomitant?

Intergroup trial R-91-11: laryngeal SCC

Laryngectomy-free survival

- Induction CT (PF)
- Concurrent (p=0.0047 vs. Induction)
- RT alone (p=0.22 vs. Induction)

Forastiere, 2001
The Human Condition.

R. Magritte, 1935
Molecular imaging dose painting by number

- Tomotherapy Hi-Art
- H&N SCC: T4N2bM0
- 60 Gy + SIB of 30 Gy
- Hypoxia (Cu-ATSM)
Molecular imaging dose painting by number

- DPBN based on FDG-PET
- Median dose of 80.9 Gy ($n=7$) and 85.9 Gy ($n=14$)
- No grade 4 acute toxicity
### Radiobiological and clinical issues in IMRT for HNSCC

Comparison between SIB and 2-phase IMRT (50 Gy + 20 Gy)

<table>
<thead>
<tr>
<th>Dose level (Gy)</th>
<th>Two-phase IMRT</th>
<th>SIB IMRT</th>
<th>% difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>2,183</td>
<td>2,169</td>
<td>0.6</td>
</tr>
<tr>
<td>20</td>
<td>1,975</td>
<td>1,941</td>
<td>1.8</td>
</tr>
<tr>
<td>30</td>
<td>1,557</td>
<td>1,459</td>
<td>6.7</td>
</tr>
<tr>
<td>40</td>
<td>1,096</td>
<td>1,016</td>
<td>7.9</td>
</tr>
<tr>
<td>50</td>
<td>732</td>
<td>604</td>
<td>21.2</td>
</tr>
<tr>
<td>60</td>
<td>388</td>
<td>238</td>
<td>63.0</td>
</tr>
<tr>
<td>70</td>
<td>83</td>
<td>62</td>
<td>34.0</td>
</tr>
</tbody>
</table>

Mohan et al., 2000
Work in progress

Reference image

Rigid registration

Non-rigid registration

Loeckx & Maes
ESAT, 2004
Work in progress

Checkerboard

Body contour

Dose distribution at $T_1$

Non-rigid checkerboard transformation

Deformed body contour

Deformed dose distribution on CT at $T_2$
Variation in therapeutic CTVs during RT-CH…
(70 Gy – 3 courses chemo on w1, w4, w7)

Mean slope: -1.46% / treat day (p<0.05)
Medial shift: 0.91mm after 25# (p<0.05)

Mean slope: -2.55% / treat day (p<0.05)
Lateral shift: 1.52mm after 25# (p<0.05)
### Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

#### Target volumes

<table>
<thead>
<tr>
<th></th>
<th>Planned dose distribution</th>
<th>95% CI</th>
<th>Delivered dose distribution</th>
<th>95% CI</th>
<th>Adaptive dose distribution</th>
<th>95% CI</th>
<th>p-value (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CTV&lt;sub&gt;ther&lt;/sub&gt;</strong></td>
<td>D&lt;sub&gt;2%&lt;/sub&gt;</td>
<td>71.02</td>
<td>[70.57 ; 71.48]</td>
<td>70.63</td>
<td>[70.36 ; 70.89]</td>
<td>70.52</td>
<td>[69.87 ; 71.17]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;50%&lt;/sub&gt;</td>
<td>69.35</td>
<td>[69.25 ; 69.45]</td>
<td>69.39</td>
<td>[69.28 ; 69.51]</td>
<td>69.13</td>
<td>[69.00 ; 69.26]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;95%&lt;/sub&gt;</td>
<td>68.38</td>
<td>[68.15 ; 68.61]</td>
<td>68.42</td>
<td>[68.21 ; 68.63]</td>
<td>65.34</td>
<td>[64.00 ; 66.68]</td>
</tr>
<tr>
<td><strong>CTV&lt;sub&gt;proph&lt;/sub&gt;</strong></td>
<td>D&lt;sub&gt;2%&lt;/sub&gt;</td>
<td>70.55</td>
<td>[70.25 ; 70.84]</td>
<td>70.36</td>
<td>[70.14 ; 70.56]</td>
<td>70.11</td>
<td>[69.61 ; 70.60]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;50%&lt;/sub&gt;</td>
<td>63.48</td>
<td>[59.74 ; 67.22]</td>
<td>63.62</td>
<td>[59.86 ; 67.38]</td>
<td>62.71</td>
<td>[59.07 ; 66.35]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;95%&lt;/sub&gt;</td>
<td>54.88</td>
<td>[54.66 ; 55.10]</td>
<td>54.85</td>
<td>[54.55 ; 55.16]</td>
<td>55.19</td>
<td>[54.96 ; 55.41]</td>
</tr>
<tr>
<td><strong>PTV&lt;sub&gt;ther&lt;/sub&gt;</strong></td>
<td>D&lt;sub&gt;2%&lt;/sub&gt;</td>
<td>71.33</td>
<td>[70.95 ; 72.52]</td>
<td>70.87</td>
<td>[70.32 ; 71.43]</td>
<td>71.02</td>
<td>[70.22 ; 71.81]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;50%&lt;/sub&gt;</td>
<td>69.15</td>
<td>[69.05 ; 69.25]</td>
<td>69.21</td>
<td>[69.06 ; 69.36]</td>
<td>68.78</td>
<td>[68.18 ; 69.39]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;95%&lt;/sub&gt;</td>
<td>68.57</td>
<td>[66.10 ; 67.04]</td>
<td>66.59</td>
<td>[65.94 ; 67.23]</td>
<td>62.02</td>
<td>[60.54 ; 63.50]</td>
</tr>
<tr>
<td><strong>PTV&lt;sub&gt;proph&lt;/sub&gt;</strong></td>
<td>D&lt;sub&gt;2%&lt;/sub&gt;</td>
<td>70.57</td>
<td>[70.12 ; 71.01]</td>
<td>70.26</td>
<td>[70.00 ; 70.51]</td>
<td>70.06</td>
<td>[69.55 ; 70.57]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;50%&lt;/sub&gt;</td>
<td>60.19</td>
<td>[57.38 ; 63.01]</td>
<td>60.64</td>
<td>[57.31 ; 63.98]</td>
<td>58.70</td>
<td>[56.97 ; 60.42]</td>
</tr>
<tr>
<td></td>
<td>D&lt;sub&gt;95%&lt;/sub&gt;</td>
<td>54.11</td>
<td>[53.94 ; 54.27]</td>
<td>53.96</td>
<td>[53.70 ; 54.22]</td>
<td>54.31</td>
<td>[54.06 ; 54.56]</td>
</tr>
</tbody>
</table>
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Non-adaptive approach and spinal cord irradiation

\[ R^2 = 0.79 \ (p < 0.05) \]
RESULTS

95% isodose to CTV T (phase I)

Σmean dose = 48.17 Gy

Σmean dose = 48.11 Gy
RESULTS

Median Dose to Ipsilateral Nodal CTV (phase I)

- Planned Dose
- Actual Dose Delivered

Σmean dose = 49.23 Gy

Σmean dose = 48.99 Gy
RESULTS

95% isodose to Ipsilateral Nodal CTV (phase I)

Σ mean dose = 48.23 Gy

Σ mean dose = 48.05 Gy

Dose(Gy)

Fraction#
RESULTS

Median Dose to Contralateral Nodal CTV (phase I)

![Graph showing median dose to contralateral nodal CTV](image)

- Planned Dose
- Actual Dose Delivered

\[ \Sigma \text{mean dose} = 49.18 \text{Gy} \]

\[ \Sigma \text{mean dose} = 49.48 \text{Gy} \]
RESULTS

95% isodose to Contralateral Nodal CTV (phase I)

Σmean dose = 48.70 Gy

Σmean dose = 47.93 Gy
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

AAPM
Aug. 2011

Carruthers, 2011
Factors analysed for adverse impact on TCP after secondary review: Investigator fac

<table>
<thead>
<tr>
<th>Country</th>
<th>Number of patients</th>
<th>Number with major adverse impact</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>W Europe C</td>
<td>39</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Oceania A</td>
<td>154</td>
<td>8</td>
<td>5.2%</td>
</tr>
<tr>
<td>N America A</td>
<td>101</td>
<td>6</td>
<td>5.9%</td>
</tr>
<tr>
<td>E Europe A</td>
<td>48</td>
<td>5</td>
<td>10.4%</td>
</tr>
<tr>
<td>S America A</td>
<td>54</td>
<td>6</td>
<td>11.1%</td>
</tr>
<tr>
<td>W Europe B</td>
<td>67</td>
<td>8</td>
<td>11.9%</td>
</tr>
<tr>
<td>W Europe E</td>
<td>25</td>
<td>3</td>
<td>12.0%</td>
</tr>
<tr>
<td>Oceania B</td>
<td>16</td>
<td>2</td>
<td>12.5%</td>
</tr>
<tr>
<td>W Europe A</td>
<td>127</td>
<td>17</td>
<td>13.4%</td>
</tr>
<tr>
<td>S America B</td>
<td>42</td>
<td>6</td>
<td>14.3%</td>
</tr>
<tr>
<td>E Europe B</td>
<td>28</td>
<td>4</td>
<td>14.3%</td>
</tr>
<tr>
<td>N America B</td>
<td>63</td>
<td>10</td>
<td>15.9%</td>
</tr>
<tr>
<td>W Europe D</td>
<td>30</td>
<td>5</td>
<td>16.7%</td>
</tr>
<tr>
<td>W Europe F</td>
<td>6</td>
<td>2</td>
<td>33.3%</td>
</tr>
<tr>
<td>W Europe G</td>
<td>4</td>
<td>2</td>
<td>50.0%</td>
</tr>
<tr>
<td>E Europe C</td>
<td>14</td>
<td>13</td>
<td>92.9%</td>
</tr>
</tbody>
</table>
Biological adaptive IMRT

- 10 patients with stage III-IV pharyngo-laryngeal SCC treated by CT-RT
- Images acquired before R/ and during RT after means doses of 14, 25, 35 and 45 Gy

<table>
<thead>
<tr>
<th>Before R/</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
<th>Week 6</th>
<th>Week 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>R/ start</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Images acquisitions

Anatomic imaging

Dynamic FDG-PET

Geets, 2006
Adaptive Image-Guided IMRT in pharyngolaryngeal squamous cell carcinoma

Adaptive approach and spinal cord irradiation

\[ R^2 = 0.75 \ (p<0.05) \]
Adaptive Image-Guided IMRT in pharyngo-laryngeal squamous cell carcinoma

Conclusions 1

• Planned dose distribution ≠ delivered dose distribution
• Adaptive approach useful for selected patients
• GTV shrinkage as a good surrogate for plan adaptation
Inter-observer variability on target volume delineation with CT-scan and MRI

Gross Tumor volume (GTV)

<table>
<thead>
<tr>
<th></th>
<th>Oropharyngeal tumors (n= 10)</th>
<th>Hypopharyngeal/laryngeal tumors (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT-scan</strong></td>
<td>ANOVA: p=0.47</td>
<td>ANOVA: p=0.29</td>
</tr>
<tr>
<td><strong>MRI</strong></td>
<td>ANOVA: p=0.59</td>
<td>ANOVA: p=0.16</td>
</tr>
</tbody>
</table>

Geets et al, 2005
Functional imaging and automatic segmentation

Volume delineation based on automatic thresholding with $^{18}$F-FDG