Adaptive radiotherapy in the head and neck: what is the clinical significance?

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The facts, the needs and the solutions ...

4D-IMRT

The Cathedral of Rouen
C. Monet, 1894
**Geometric 4D-IMRT**

**MVCT**

**kVCT**

**CT**

**MRI (T2)**

**FDG-PET**

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**Variation in GTVs during RT-CH (70 Gy – 3 courses on w1, w4, w7)**

- **GTV<sub>1</sub>**, **GTV<sub>2</sub>**
  - Mean slope: -2.15% / treat day (p<0.05)
  - Medial shift: 0.95mm after 25# (p<0.05)
  - Lateral shift: 1.26mm after 25# (p<0.05)

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**Variation in therapeutic CTVs during RT-CH (70 Gy – 3 courses on w1, w4, w7)**

- **CTV<sub>N</sub>**, **CTV<sub>T</sub>**
  - Mean slope: -1.46% / treat day (p<0.05)
  - Medial shift: 0.91mm after 25# (p<0.05)
  - Lateral shift: 1.52mm after 25# (p<0.05)
Variation in prophylactic tumor CTVs during RT-CH
(70 Gy – 3 courses on w1, w4, w7)

Mean slope: -0.63% / treat day (p<0.05)
No shift

Variation in prophylactic nodal CTVs during RT-CH
(70 Gy – 3 courses on w1, w4, w7)

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

Variation in parotid volumes during RT-CH
(70 Gy – 3 courses 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

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>∆COM</td>
<td>∆Volume</td>
</tr>
<tr>
<td>Barker, 2004</td>
<td>EXaCT</td>
<td>3.1 mm</td>
<td>0.6% / day</td>
</tr>
<tr>
<td>Hansen, 2006</td>
<td>kVCT</td>
<td>-</td>
<td>15.6% - 21.3% at 36 Gy</td>
</tr>
<tr>
<td>Rober, 2007</td>
<td>kVCT</td>
<td>0.8-0.9 mm / w</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>
Total Dose really received by each volume element of the patient

Impact on dose distribution

<table>
<thead>
<tr>
<th>Planning</th>
<th>V10</th>
<th>V50</th>
<th>V90</th>
<th>V95</th>
<th>V99</th>
<th>V100</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>99</td>
<td>98</td>
<td>98</td>
<td>99</td>
<td>100</td>
</tr>
<tr>
<td>Classic PET-based</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>98</td>
<td>99</td>
<td>99</td>
</tr>
<tr>
<td>Adaptive PET-based</td>
<td>99</td>
<td>100</td>
<td>98</td>
<td>98</td>
<td>99</td>
<td>99</td>
</tr>
</tbody>
</table>

P < 0.001

Dose distribution after adaptive RT-CH (n=5)

Biological heterogeneity

[18F]-FDG TEP

Registered autoradiography

SIB-IMRT

30x2.3 Gy

30x1.85 Gy

V100 V95 V90 V80 V50 V10 Planning

P < 0.001

Homo lat Parotid Dm ean (Gy)

S C D 2 (Gy)

L arynx D 5 (Gy)

Oral cavi ty Dmean (Gy)

 Mandible D 2 (Gy)

H omo lat Subm ax gl D m ean (Gy)

H etero lat Submax gl D mean (Gy)

S kin V 65Gy (cc)

V 95 % (cc)

Résolution 2.3 mm

Résolution 0.1 mm
“Dose painting” by number…

Flat dose → Non-flat dose

Survival is non-flat (higher in resistant areas)

More similar survival across entire tumor

Mean Tumor Dose = 2 Gy

Far more efficient use of dose

Adaptive radiotherapy in the head and neck: what is the clinical significance?

Tumor Control Probability (TCP)

Dose-response curve for neck nodes ≤ 3 cm

Complication probability after parotid gland irradiation

Complication = stimulated flow rate ≤ 25% of the pre-RT rate at 12 months

From Eisbruch, 1996

Braitin et al, 1982
Clinical impact of the TLD QA program of the EORTC assessed by biological modeling

65 high-energy treatment units have been checked:
- 22 underdosing
- 41 overdosing

- 3.3% loss of local control
- 7% excess mild to moderate complications

Bentzen, R & O, 48 (S1): 728, 1998

HeadSTART trial: OS (analysis by ITT)

HeadSTART trial: DFS as a function of compliance to protocol

HeadSTART trial: LR-DFS for the compliant patients
Adaptive radiotherapy in the head and neck: what is the clinical significance?

and the solutions ...

A clinical trial?
IMRT > geometrical adaptive IMRT?
Geometric adaptive IMRT > biological adaptive IMRT?

“My” vision of Radiation Oncology in 2009 and beyond …

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

But … still a long way to go …

Harari et al., 2005
The reality…

- Adaptive IMRT: geometrical, biological & dosimetric
  - which imaging modalities??
  - which biological pathways??
  - which volume/dose registration algorithms??
  - how frequently??

Challenges in Head & Neck loco-regional treatment

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  - Adriana PARRAGA, Eng., Benoit MACQ, Eng., Ph.D.
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“My” vision of Radiation Oncology in 2009 and beyond …

- RO will be combined (e.g., IMRT, proton, hadrons) …
- RO will be tailored (based on imaging and molecular profiling) and adaptive …
Challenges in Head & Neck loco-regional treatment

- Target selection and delineation
- Adaptive IMRT: geometrical, biological & dosimetric
- which imaging modalities?
- which biological pathways?
- which volume/dose registration algorithms?
- how frequently?
- Concomitant association with drugs and/or “small molecules”

H&N IMRT practice heterogeneity among Dutch Radiation Oncologists

effect

\[ \Delta E \]

\[ \Delta D \]

Tumor Control Probability (TCP)


total of 1481 MVCT

\[ \text{CTV-PTV: } (2^\Sigma + 0.7 \sigma) \]

Geometric 4D-IMRT

Alternate week MVCTs: CTV-PTV margins

- 75 patients
- total of 1481 MVCT
- CTV-PTV: \((2^\Sigma + 0.7 \sigma)\)
**Parotid gland sparing in IMRT for HNSCC**

**PARSPORT Trial Design**
- Head and neck cancer patients at risk of radiation induced xerostomia (oropharynx/hypopharynx)
- Randomisation 1:1
  - Conventional radiotherapy (CRT)
  - Parotid-sparing IMRT

**RTOG Subjective Salivary Gland toxicity ≥G2**
- Graph showing cumulative percentage of patients with subjective salivary gland toxicity.

**Treatment Received**

<table>
<thead>
<tr>
<th></th>
<th>CRT n=47</th>
<th>IMRT n=46</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiotherapy delivery</td>
<td>43*</td>
<td>91%</td>
</tr>
<tr>
<td>Radiotherapy given as</td>
<td>29</td>
<td>62%</td>
</tr>
<tr>
<td>Treatment</td>
<td>29</td>
<td>81%</td>
</tr>
<tr>
<td>Mean (SD) radiotherapy</td>
<td>65 Gy (6.5)</td>
<td>65 Gy (6.4)</td>
</tr>
<tr>
<td>dose PTV1</td>
<td>59 Gy (6.3)</td>
<td>45 Gy (10.4)</td>
</tr>
<tr>
<td>Ipsilateral Parotid</td>
<td>60 Gy (6.5)</td>
<td>35 Gy (6.8)</td>
</tr>
<tr>
<td>mean (SD) dose</td>
<td>15</td>
<td>32%</td>
</tr>
<tr>
<td>Radiotherapy given post-</td>
<td>64 Gy (2.3)</td>
<td>61 Gy (2.2)</td>
</tr>
<tr>
<td>operatively</td>
<td>61 Gy (5.0)</td>
<td>50 Gy (12.0)</td>
</tr>
<tr>
<td>Mean (SD) radiotherapy</td>
<td>57 Gy (10.3)</td>
<td>27 Gy (3.7)</td>
</tr>
<tr>
<td>dose PTV1</td>
<td>Received neoadjuvant chemotherapy</td>
<td>19</td>
</tr>
</tbody>
</table>

* * denotes IMRT due to lower dose; † integrals, ‡ indicated dose was used.

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