The PreciseART™ Approach to Adaptive Radiotherapy with the RADIXACT® System

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Head and Neck Radiotherapy

- Constant increase of curative exclusive radio-chemotherapy
- IMRT, VMAT, helical IMRT
  Steep dose gradients
- Pertreatment targets and OAR modifications
Primary Tumor and Lymph Nodes Modifications


Castadot et al, Rad Oncol 2011

Fig. 1. Correlation between the slope of the absolute GTV shrinkage and the variation in $O_{\text{mean}}$ of the ipsilateral parotid gland when using an adaptive planning (delivered dose minus adaptive dose).
Salivary Glands Shrink and Shift

Parotids shrink and shift medially toward high dose region
Submandibular glands shrink and shift superiorly

Figure 4: A case example of changes in parotid gland volume during a 33-fraction IMRT treatment course. (a) shows the percent of volume change for each parotid as a function of treatment fraction. The (b) and (c) shows an axial CT slice of the parotid before radiotherapy (b) and after 33 fractions of radiotherapy (c).

Schwartz et al, Journal Oncol 2011
Head and Neck Radiotherapy

- Constant increase of curative exclusive radio-chemotherapy
- IMRT, VMAT, helical IMRT
  Steep dose gradients
- Pertreatment targets and OAR modifications

Risk of
Underdosage to target volumes,
Overdosage to organs at risks

Significant impact on dose, outcome and Quality of life?
Meta-analysis on Adaptive Radiotherapy

- 24 papers reported on dosimetric changes of Parotid Glands (PG)
  - Mean dose increase with 2.2+/−2.6 Gy
  - In nasopharyngeal mean dose 10 Gy
  - Strongest association found between PG dose and PG volume loss
- 12 studies correlated OAR modifications and complications /quality of life

Brouwer et al, RadOnc2015
ADAPTIVE RADIOTHERAPY

WHO?

WHEN?

HOW?
WHO?
## Adaptive RT: Who?

- Unresected tumors
- Small parotid volume

### Trials

<table>
<thead>
<tr>
<th>Trials</th>
<th>Number patients</th>
<th>Type</th>
<th>Method</th>
<th>Endpoints</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NCT00490282</strong>&lt;br&gt;MDAnderson</td>
<td>25</td>
<td>Unresected</td>
<td>Dosimetric evaluation W1 vs W7</td>
<td>Target coverage</td>
</tr>
<tr>
<td><strong>NCT02545322</strong>&lt;br&gt;Graz</td>
<td>18</td>
<td>Unresected</td>
<td>Deformable registration W3 &amp; 5</td>
<td>PTV D98%</td>
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<tr>
<td><strong>NCT 03215719</strong>,&lt;br&gt;New York UM</td>
<td>25</td>
<td>Unresected HPV+</td>
<td>Deescalation at week 4 if &gt;40% nodal shrinkage</td>
<td>2 years progression free survival</td>
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<tr>
<td><strong>NCT03096808</strong>&lt;br&gt;MSKCCC</td>
<td>65</td>
<td>Unresected SCCHNC</td>
<td></td>
<td>Locoregional event free survival</td>
</tr>
<tr>
<td><strong>NCT01874587</strong>&lt;br&gt;Rennes cancer center France ARTIX</td>
<td>174</td>
<td>Unresected Oropharyngeal</td>
<td>Weekly replanning</td>
<td>Increase in salivary flow 25% &amp; Non inferiority in EFS</td>
</tr>
</tbody>
</table>

*Brouwer et al, RadOnc2016<br>Mahmoud et al, Tec Cancer Res 2017*
WHEN?
Adaptive RT: When?

- 38 papers evaluating volumes variations during RT
- Various methods: one to 7 rescanning;

- Examples on Parotid Glands shrinkage:
  - Studies on every day or every week rescanning
    - DeBrouwer et al, Rad Oncol 2016
  - Weekly CT of 85 patients: Parotid Glands shrinkage is not linear: mostly during first half of treatment.
    - Sanguineti et al, Br J Radiol 2013
HOW?
Adaptive RT: How ? Gaining Time
Radixact® System Example

- Radixact® System
  - Fast Dosimetric Validation
  - Fast in room imaging
  - Fast treatment delivery

- PreciseART™ Rapid co-registration with RegRefine
  - Everyday deformable registration of MVCT with planning CT.
    Everyday contours deformation on MVCT.
    - Branchini et al, Int Journal Med Phys 2017
  - « Dose of the day » evaluation of targets and OARs

- PreciseRTX™ if replanning is needed,
  - Immediate deformable co-registration of both planning CTs and contours
Dose of the Day » Delivered to Deformed Contours

Right parotid
MVCT Deformable Registration and Contouring
Dose of the Day » Evaluation to Deformed Contours

Left eye
If Replanning is Decided: Automatic Deformation of Contours on the New Planning CT: PreciseRTX™
Does Automatic Deformable Recontouring on MVCT Answer the When and How question?

Prospective GIRAFE ART Trial

- Open-label, controlled, monocentric phase II study
- 53 patients with locally advanced non-resected HNSCC in first line treatment.
- At least N1

- Simultaneous integrated boost helicoidal intensity modulated RT will be delivered
  - 70 Gy / 2 Gy fractions to the tumor and macroscopic node
  - 56 Gy/1,6 Gy to both cervical nodal regions
GIRAFE ART Trial

Initial contours on Planning CT

Daily MVCT
- Radixact® deformed contours

Weekly planning CT
- PreciseRTX™ deformed contours

Manual recontouring

DICE similarity coefficient indexes analysis
Conclusion: Head and Neck Adaptive RT

Who?
Unresected tumors/nodes
Small parotid volumes

When?
MVCT/CBCT recontouring and dose of the day evaluation

How?
Automatic deformable contours

Upcoming trial to validate contours and dose evaluation on MVCT and define the clinical ART routine