Adaptive Radiotherapy in Head and Neck Cancers

Sarbani Ghosh-Laskar
Professor, Radiation Oncology
sarbanilaskar@yahoo.co.in
• IMRT – emerging standard of care in management of HN cancers

• IMRT allows the delivery of a very conformal dose to the tumour volume, with a rapid dose gradient, allowing sparing of critical structures which lie in close proximity

• Significant reduction in late toxicity
Intensity Modulated Radiotherapy

- Minor change in anatomy could result in significant dosimetric change: narrow margins
- Using a single set of planning data does not take into account anatomical changes that occur during treatment
- May lead to an increase in dose delivered to normal structures and contribute to the incidence of late toxicity (e.g. xerostomia)
Intensity Modulated Radiotherapy

- Involves narrow margins: warrants the use of imaging, for appropriate verification

- Image guided radiation therapy (IGRT)
  - On board CT imaging – CBCT
  - 3D information
  - Better resolution with Soft tissue and bone information
Why Adaptive?

- Modifications of the patient’s anatomy and positioning during the course of RT
- Decrease of tumor and nodal volumes
- Weight loss
- Decrease in post operative edema
- Alteration in muscle mass and fat distribution
- Fluid shift within the body
As patient undergoes 6-7 weeks of IMRT there are marked anatomical changes

Tumour volume on initial pCT

Tumour volume midway through treatment
What is Adaptive Radiotherapy? (ART)

“Adaptive radiotherapy" is defined as changing the radiation treatment plan delivered to a patient during a course of radiotherapy to account for

  Temporal changes in anatomy (e.g. tumor shrinkage, weight loss or internal motion)
  Changes in tumor biology/function (e.g. hypoxia)"
GTV reduction of about 10-45% by 45-46Gy
CTV reduction of 51%
PTV reduction of 18%

Changes in Critical Structures

Loss of parotid volume: 0.2cc/day
By the end of treatment: loss of parotid volume-28%
Centre of the mass shifted medially by 3mm

Schwartz D. Journal of Oncology 2011
Parotid glands reported to shrink 0.6 – 1.1%/ day
Volume reduction of 10 – 16%
Shifts: usually medially approx: 3 mm

Submandibular gland: 10 – 30% reduction in volume
Shift: 4 mm medially
Weight Loss during RT

- Seventy-two patients IMRT (median dose 70.4 Gy) with Conc CT
- All required supportive therapy by feeding tube or parenteral nutrition
- 15/72 required adaptive planning at least once
- Median weight loss: 7.8 kg
- Median volume loss: 7%.

Jenson A. IJROBP 2012
Impact on the dose distributions
Difference in planned and delivered doses

- Increased dose to the parotid glands
- Increased dose to the spinal cord
- Underdose of the target volume

Table 3: Comparison Between the Planned Doses, the Actually Delivered Doses Without Replanning, and the Actual Doses if Adaptive Plannings Were Performed

<table>
<thead>
<tr>
<th>Organs at risk</th>
<th>Planned Dose (Gy)</th>
<th>Actually Delivered Dose (Gy)</th>
<th>Re-planned Dose (Gy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parotid glands $D_{\text{mean}}$</td>
<td>17.9</td>
<td>18.7</td>
<td>18.7</td>
</tr>
<tr>
<td>Submandibular glands $D_{\text{mean}}$</td>
<td>51.9</td>
<td>52.8</td>
<td>51.7</td>
</tr>
<tr>
<td>Oral cavity $D_{\text{mean}}$</td>
<td>26.0</td>
<td>26.7</td>
<td>24.4</td>
</tr>
<tr>
<td>Spinal cord $D_2$</td>
<td>16.3</td>
<td>16.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Planning at risk volume</td>
<td>41.2</td>
<td>41.2</td>
<td>39.1</td>
</tr>
<tr>
<td>Larynx $D_5$</td>
<td>67.7</td>
<td>67.7</td>
<td>67.7</td>
</tr>
<tr>
<td>Skin $V_{60 \text{ Gy}}$</td>
<td>16.3</td>
<td>16.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Target volumes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic CTV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Therapeutic PTV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prophylactic CTV</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prophylactic PTV $D_{95}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irradiated volumes</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$V_{100%}$</td>
<td>140.4</td>
<td>150.2</td>
<td>112.1</td>
</tr>
<tr>
<td>$V_{95%}$</td>
<td>246.5</td>
<td>261.4</td>
<td>202.0</td>
</tr>
<tr>
<td>$V_{90%}$</td>
<td>274.7</td>
<td>323.1</td>
<td>261.0</td>
</tr>
</tbody>
</table>
Typical Adaptive Workflow

Gregoire V. Lancet 2012
# Types of ART

<table>
<thead>
<tr>
<th>TYPES OF ART</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-adaptive</td>
<td>Conformal Avoidance IMRT</td>
</tr>
<tr>
<td>Motion adaptive</td>
<td>Beaumont’s ART process, ‘Plan of the day’ IMRT</td>
</tr>
<tr>
<td>Biological adaptive</td>
<td>Theragnostic planning,</td>
</tr>
<tr>
<td>Response adaptive</td>
<td>Mid-treatment response evaluation, shrinkage of GTV &amp; OAR</td>
</tr>
<tr>
<td>Time adaptive</td>
<td>Mid-course CT and planning</td>
</tr>
</tbody>
</table>
Deformable Registration

- Non-rigid Image Registration
  - Finding the geometric correspondence of the same point in two images.
- One image is kept fixed while the other image works around to identify similar grey-scales.
Biological Adaptation and Dose Painting

- Increasing dose to the radioresistant areas and decreasing dose to the radiosensitive areas
- Aims to deliver nonhomogenous dose distribution over the target volume
- Biological properties considered for dose painting
  - Tumor proliferation
  - High metabolism
  - Tumor hypoxia
- Dose painting by volumes: target divided into subvolumes
- Dose painting by numbers: each voxel receives different dose
Dose Painting by Number/Voxel

Note: Dose painting is **within the GTV** and is not similar to SIB

Tools needed for Real-time ART

1. Pretreatment and real-time imaging

2. Deformable image registration, and

3. Fast treatment planning that facilitate image-guided adaptive radiotherapy
Is there a clinical benefit?
Head and neck cancer

Adaptive radiotherapy for head and neck cancer—Dosimetric results from a prospective clinical trial

David L. Schwartz a,b,c,*, Adam S. Garden c, Shalin J. Shah c, Gregory Chronowski c, Samir Sejpal c, David I. Rosenthal c, Yipei Chen d, Yongbin Zhang d, Lifei Zhang d, Pei-Fong Wong c, John A. Garcia c, K. Kian d

Purpose

Methods

Results:

Conclusions: This pilot trial suggests that head and neck ART dosimetrically outperforms IMRT, IGRT that leverages conventional PTV margins does not improve dosimetry. One properly timed replan delivers the majority of achievable dosimetric improvement. The clinical impact of ART must be confirmed by future trials.

- All patients required at least one replan (ART1)
- 8 patients (36%) required a second replan (ART2)
- Significant decrease in the parotid doses with ART.
- Median follow up of 30 months
- Local control 100% at 2 years
- Regional control 98% at 2 years
Adaptive Radiotherapy Using Helical Tomotherapy for Head and Neck Cancer in Definitive and Postoperative Settings: Initial Results

L. Capelle *, M. Mackenzie †, C. Field †, M. Parliament *, S. Ghosh †, R. Scrimger *

Aims: To assess whether routine mid-treatment replanning in head and neck squamous cell carcinoma patients results in meaningful improvements in target or normal tissue dosimetry and to assess which patients derive the greatest benefit.

Materials and methods: Twenty patients treated with either postoperative chemoradiotherapy or definitive chemoradiotherapy with primary or nodal disease ≥3 cm in size were included in this prospective pilot study. Seven patients received adjuvant chemoradiotherapy and 13 received definitive chemoradiotherapy.

- Helical Tomotherapy for Head Neck Cancer
- 20 patients with definitive or postoperative RT for Head neck cancer
- ART considered after 20 fractions with replanning after 15 fractions

Results in neck reduct 0.6 Gy, dose (0.6 Gy RT) with treatment adaptation with reduction in spinal cord maximum 1.2 Gy, mean parotid dose 1.2 Gy and parotid V26 6.3%. There was no significant benefit for adjuvant patients. Other factors associated with greater benefits were greater weight loss and greater reduction in neck separation and higher T stage.

Conclusions: There is minimal benefit to routine adaptive replanning in unselected patients, and no benefit in adjuvantly treated patients. Patients with nasopharyngeal carcinoma or with greater weight loss or reduction in neck separation did have clinically significant benefits. These patients should be targeted for adaptive strategies.
Median patient and tumor dimensions at the time of initial (CT1) and mid-treatment (CT2) scans

<table>
<thead>
<tr>
<th></th>
<th>CT1</th>
<th>CT2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral neck separation C1 level (cm)</td>
<td>14.7</td>
<td>14.0</td>
</tr>
<tr>
<td>Lateral neck separation mid PTV60/66 level (cm)</td>
<td>12.4</td>
<td>11.8</td>
</tr>
<tr>
<td>Lateral neck separation thyroid notch level (cm)</td>
<td>12.0</td>
<td>11.3</td>
</tr>
<tr>
<td>GTV volume (cm$^3$)</td>
<td>57.5</td>
<td>50.3</td>
</tr>
<tr>
<td>CTV60 volume (cm$^3$)</td>
<td>72</td>
<td>72</td>
</tr>
<tr>
<td>PTV60/66 volume (cm$^3$)</td>
<td>168</td>
<td>147</td>
</tr>
<tr>
<td>PTV54 volume (cm$^3$)</td>
<td>1024</td>
<td>927</td>
</tr>
<tr>
<td>Right parotid volume (cm$^3$)</td>
<td>26.2</td>
<td>19.7</td>
</tr>
<tr>
<td>Left parotid volume (cm$^3$)</td>
<td>25.0</td>
<td>20.0</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>74.9</td>
<td>70.9</td>
</tr>
<tr>
<td>Parameter</td>
<td>Treatment component 1 (19 fractions)</td>
<td>Treatment component 2 (11 fractions)</td>
</tr>
<tr>
<td>-----------------------------------------------</td>
<td>--------------------------------------</td>
<td>--------------------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Non-adapted dose †</td>
</tr>
<tr>
<td>PTV60/66 D₉₅ (Gy)</td>
<td>41.6</td>
<td>23.3</td>
</tr>
<tr>
<td>PTV60/66 D₁ (Gy)</td>
<td>43</td>
<td>25.3</td>
</tr>
<tr>
<td>PTV54 D₉₅ (Gy)</td>
<td>34.6</td>
<td>19.9</td>
</tr>
<tr>
<td>PTV54 D₁ (Gy)</td>
<td>42.0</td>
<td>24.6</td>
</tr>
<tr>
<td>Spinal cord max (Gy)</td>
<td>27.2</td>
<td>16.0</td>
</tr>
<tr>
<td>Combined parotid mean (Gy)</td>
<td>20.6</td>
<td>12.3</td>
</tr>
<tr>
<td>Combined parotid V₂₆ (%) ‡,§</td>
<td>52.5</td>
<td>54.6</td>
</tr>
<tr>
<td>N tissue ≥50 Gy (cm³) ‡</td>
<td>725</td>
<td>667</td>
</tr>
<tr>
<td>Skin ≥50 Gy (cm²) ‡</td>
<td>398</td>
<td>336</td>
</tr>
</tbody>
</table>

Modest benefit in definitive patients. No benefit in postoperative patients.
Clinical Outcomes

• 317 patients with newly diagnosed squamous carcinoma of head and neck region were treated with IMRT
• 51 (16%) patients were treated with Adaptive RT
• Median dose of RT was 66Gy
• 2 year locoregional control was 88% in patients treated with adaptive and 79% for patients treated without adaptive (p=0.01)
• Median time to local recurrence was 15 months
• All the recurrences were in the high dose region.

Chen AM, Head and Neck, 2014 Nov; 36(11):1541-6
Is it safe to modify CTV??
How often?

- Shrinkage of target volumes during RT
- Recontouring may involve modification of the CTV
- Modification of CTV towards skin – acceptable
- Overall modifications in other areas (overlap with OARs) remains questionable
- No data/ guideline on CTV modification
When: Online vs Offline?

- **Online ART**
  - Modification based on day to day changes
  - Requires lot of physician, physicist and technologist time daily.

- **Offline ART**
  - More practical approach
  - In head and neck daily variations are not much
Is It Really Necessary?

- Oral cavity: RT is mainly in Postoperative setting: ART may not be useful
- Nasopharynx/ Oropharynx: Radio-responsive tumors-tumor shrinkage during RT common: ART may be considered
- Larynx/ Hypopharynx /Nasopharynx: Especially with bulky nodal disease, issues with movement
- More than 10% weight loss during RT
In Conclusion

- Image guidance is an essential component of IMRT
- ART needs to be tailored to the individual patient
- Identify patients, clinical situations that benefit most
- Evidence/guidelines lacking for extent of margin modification: CTV and OAR
- Dose escalation, biological ART are under evaluation