Status of ART in the Clinic

Adaptive Radiotherapy for HN Cancer: Technical Aspects

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Learning Objectives

- Clinical rationales of ART for HN cancer
- ART technologies & implementation in imaging, feedback & planning modification
- Practical issues of ART in clinical operation
Significant normal tissue toxicities have been caused by the large treatment volume, and organ over dose during the treatment delivery due to:

- Patient/organ position & volume variations
- Cavity shape variation (induced hot-spot on mucosa)
- Neck and shoulder flexing in treatment setup
- Shrinkage of large tumor & edema resolving

Can online anatomical image (CBCT, CT, MRI) guided ART reduce normal tissue toxicities?
Organ Volume/Dose Variations

[Image of medical software interface showing dose variations and organ volumes]
Organ Dose Variations during the Treatment

**Left Poratid: Cumulative Dose ($D_{\text{mean}}$) Variation**

- No of Patients
- %Dose Variation (Delivered - Planned)
- No of Patients

**Right Poratid: Cumulative Dose ($D_{\text{mean}}$) Variation**

- No of Patients
- %Dose Variation (Delivered - Planned)
- No of Patients

**Cord: Cumulative Dose ($D_{\text{max}}$) Variation**

- No of Patients
- %Dose Variation (Delivered - Planned)
- No of Patients
Systematic approach to escalate or deescalate treatment dose based on spatial tumor cell bio-activities, such as

- Biological image markers to determine the most resistant tumor cells, which include
  - PET; MRI: pre-treatment image, as well as the imaging of early treatment response
  - spatial bio-parametric distribution in the planning objectives for dose painting

Can biological image guided (PET, MRI) ART be used to select patients, and improve their tumor control & long term survival?
HN Cancer ART: Clinical Implementation

- Imaging (CBCT/CT-in-room), Feedback & Adaptation

1. Pre-treatment Simulation & Planning
   - Standard CT simulation & IMRT planning
   - 0~5mm CTV-to-PTV margins & 5~7 beams
   - Planning CT image w/wo pre-selected bony structures (adjacent to the target, C₂-C₅) selected as the reference for daily treatment localization & correction
   - Segmentation (commercial tools for auto-segmentation), inverse planning, evaluation & QA: 2~4 days
2. Daily CBCT/CT-in-room Localization & Correction

- Pre-treatment CBCT/CT imaging for patient at the treatment position (~2 mins)
- Bony (C₂-C₅) registration to the reference image by using the pre-selected bony structure (2~5 mins)
- Couch translational correction (1~2 mins)
- Imaging/registration/correction (commercial tools): 5~9 mins per treatment
- Post-treatment image: once a week for QA purpose
Daily Treatment Localization
3. **Daily/Weekly Treatment Evaluation and QA**
   - Patient/organ position/volume/dose evaluation (2~4hrs per week per patient)
   - Non or few commercial tools with very limited functions at the present time can be applied for this task
   - Technologies:
     - CBCT-to-CT deformable image registration
     - Organ position & volume variation quantification
     - Daily CBCT density mapping & dose calculation
     - Daily & cumulative treatment dose construction
Daily/Weekly Treatment Evaluation/QA
4. **New CT Simulation** (after the first 10 and/or 20 treatment days)
   - New mask if necessary
   - Delineate targets and ROIs on the new CT image (auto propagation from the pre-treatment plan)
   - The new CT image will be used in the planning modification, and as the new reference image for the rest of daily image guidance
   - 1~2 working days depending on the level of automation in segmentation & planning
   - This step could be replaced using the daily CBCT directly in future
5. IMRT Re-planning or Adaptive Inverse Planning

- Re-planning on the new CT image (1~2 days)
  - on a commercial planning system
  - the initial planning objectives, constraints & weights can be used as the guidelines

- Adaptive inverse planning by including all daily CBCT images obtained during the last week,
  - organ variations in the objectives of inverse planning optimization
  - Auto-planning & evaluation (1~2 days)
Technical Issue: Deformable Image Registration

DVF

Mesh Structure
Technical Issue: Organ Variation Characterization

Patient 1

Patient 2

Patient 3

Displacement (mm)

Fraction #

Point 1

Point 2

R

L

Displacement (mm)

Fraction #
\[ \langle D_N(v) | \Phi_{K+1} \rangle = D_K(v) + \langle d(\bar{x}_j(v), \Theta_j, \Phi_{K+1}) | (\bar{x}_j(v), \Theta_j) \rangle \]

Delivered dose

Estimated dose

Expected Treatment Dose
Technical Issue: Adaptive Inverse Planning

\[
\begin{align*}
Max_{\Phi_{k+1}} & \quad F\left(\langle D_N \mid \Phi_{k+1} \rangle\right) \\
G\left(\langle D_N \mid \Phi_{k+1} \rangle\right) & \leq G\left(\langle D_N \mid \hat{\Phi}_k \rangle\right) - \Delta
\end{align*}
\]

“Expected Treatment Dose” in the objective & constraints to determine the new or modified plan

* \(\Delta\): Expected improvement from the previous treatment is used to determine if “accepting the plan modification”
ART vs Conventional IMRT (5mm Target Margin)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Conventional IMRT</th>
<th>Weekly adaptation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTV1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CTV2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain Stem</td>
<td>70±0</td>
<td>80±0</td>
</tr>
<tr>
<td>Cord</td>
<td>70±0</td>
<td>80±0</td>
</tr>
<tr>
<td>Mandible</td>
<td>60±0</td>
<td>70±0</td>
</tr>
<tr>
<td>Left Parotid</td>
<td>60±0</td>
<td>70±0</td>
</tr>
<tr>
<td>Right Parotid</td>
<td>60±0</td>
<td>70±0</td>
</tr>
</tbody>
</table>

**Improvement in Gy:**
- **Dmax:** 9.5±6
- **Dmax:** 7.2±2
- **Dmax:** 6.5±10
- **Dmean:** 6.7±10
- **Dmean:** 7.8±3
Improvement of ART vs Clinical Efforts

% of reduction wrt the Pre-Tx Cum. Dose

- Brain_Stem
- Cord
- Mandible
- LP
- RP

1 Adaptive Modification
2 Adaptive Modifications
3 Adaptive Modifications
4 Adaptive Modifications
5 Adaptive Modifications
All treatment organ doses are normalized to the baseline IMRT plan with 0 target margin.

T1: Daily IGRT with 0 target margin

T2: Daily IGRT + two weekly replanning

T3: Daily IGRT + two adaptive planning

*Dose heterogeneity in targets could be a major concern*
‘Daily IGRT’ vs ‘Hybrid ART’

[Chart with data points for different regions and T1, T2, T3 categories]
Segmentation: 2~3 CTs and/or daily CBCTs
  - Manual: ~5 hrs per image
  - Auto + manual editing: 10 mins ~ 3 hrs per image
Planning: 2~3 times
  - Manual: 6 hrs per plan
  - Auto + manual modification: 30 mins ~ 4 hrs
Daily treatment position localization/correction
  - 5~10 mins per fraction
Weekly volume/dose evaluation
  - 2~5 hrs per week per patient
  - Who should do it in long term, Physicist or RTT?
Practical Issues

- Decision of Modification: Cut-off value based on
  - Change of patient/organ volume?
  - Shrinkage of the target?
  - Patient weight loss?
  - Overdosing to a critical organ?
  - Hot-spots on oral mucosa?
  - Underdosing in targets?
  - OR
  - “Expected Improvement” of organ dose-volume obtained from the adaptive plan candidate
Practical Issues

- Treatment QA
  - Manual target delineated on the new CT could be quite different than the auto-one. How to add dose in the target?
  - Missing daily CBCT image
  - Increased clinical QA activity & error report
  - Workflow management: procedure tracking & notification
  - Proper documentation for billing
Adaptive radiotherapy of HN cancer with daily image feedback & adaptive planning modification is feasible in the routine clinic.

Significant improvement in normal tissue dose could be achieved by multiple weekly replanning, or optimized by adaptive inverse planning;

- Average 10% ~ 18% improvement can be achieved for most of normal organs using a single adaptive modification
- Average 15% ~ 29% improvement can be achieved using the weekly adaptive modifications

The main challenge in clinical implementation is now the lack of necessary software tools, and clinical workflow support.

Summary
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