Status of ART in the Clinic

Adaptive Radiotherapy for HN Cancer: Technical Aspects

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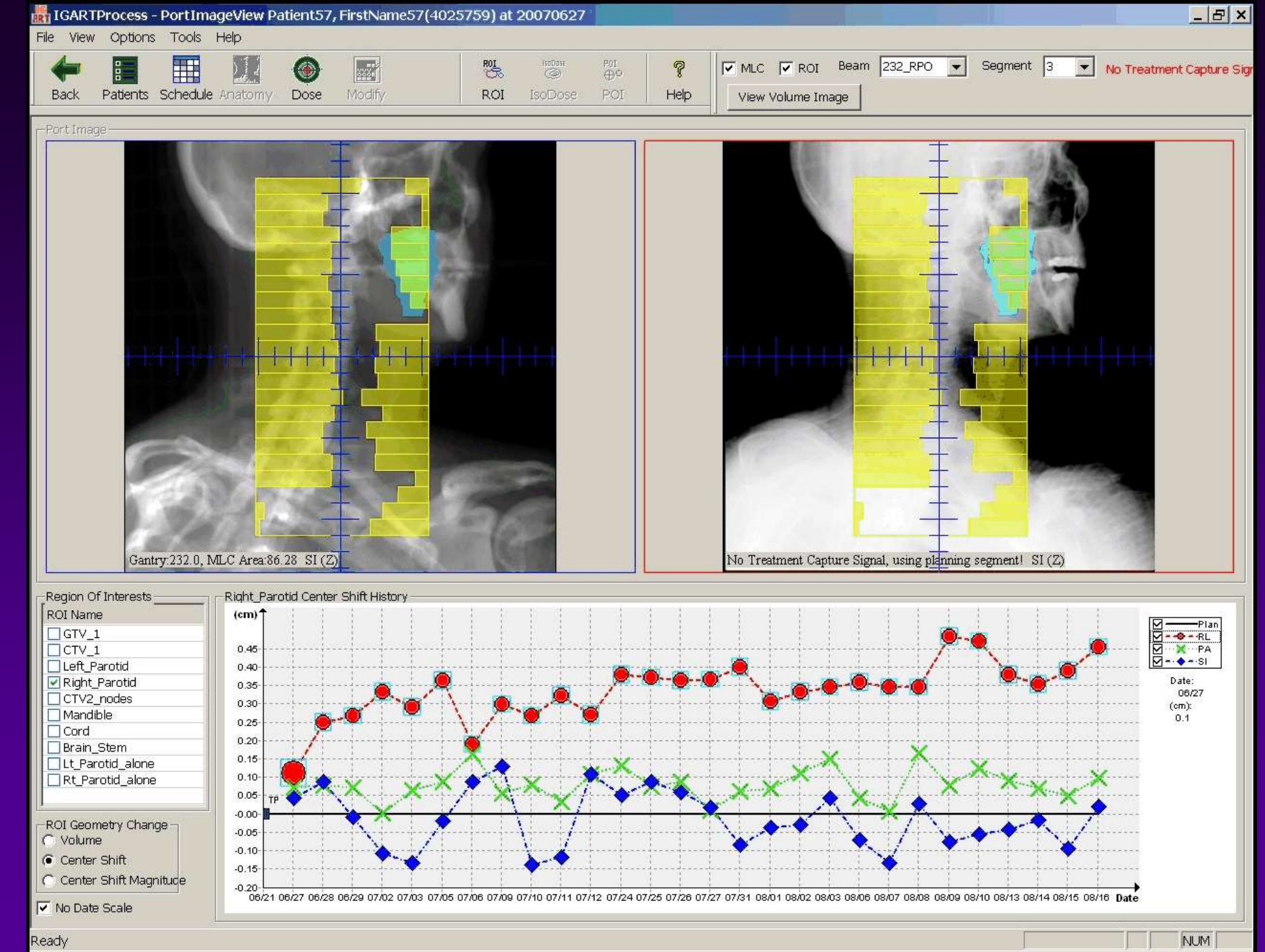
Learning Objectives

- Clinical rationales of ART for HN caner
- ART technologies & implementation in imaging, feedback & planning modification
- Practical issues of ART in clinical operation

HN Cancer ART: Clinical Rationales

- 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?



Patient/Organ Position Variation

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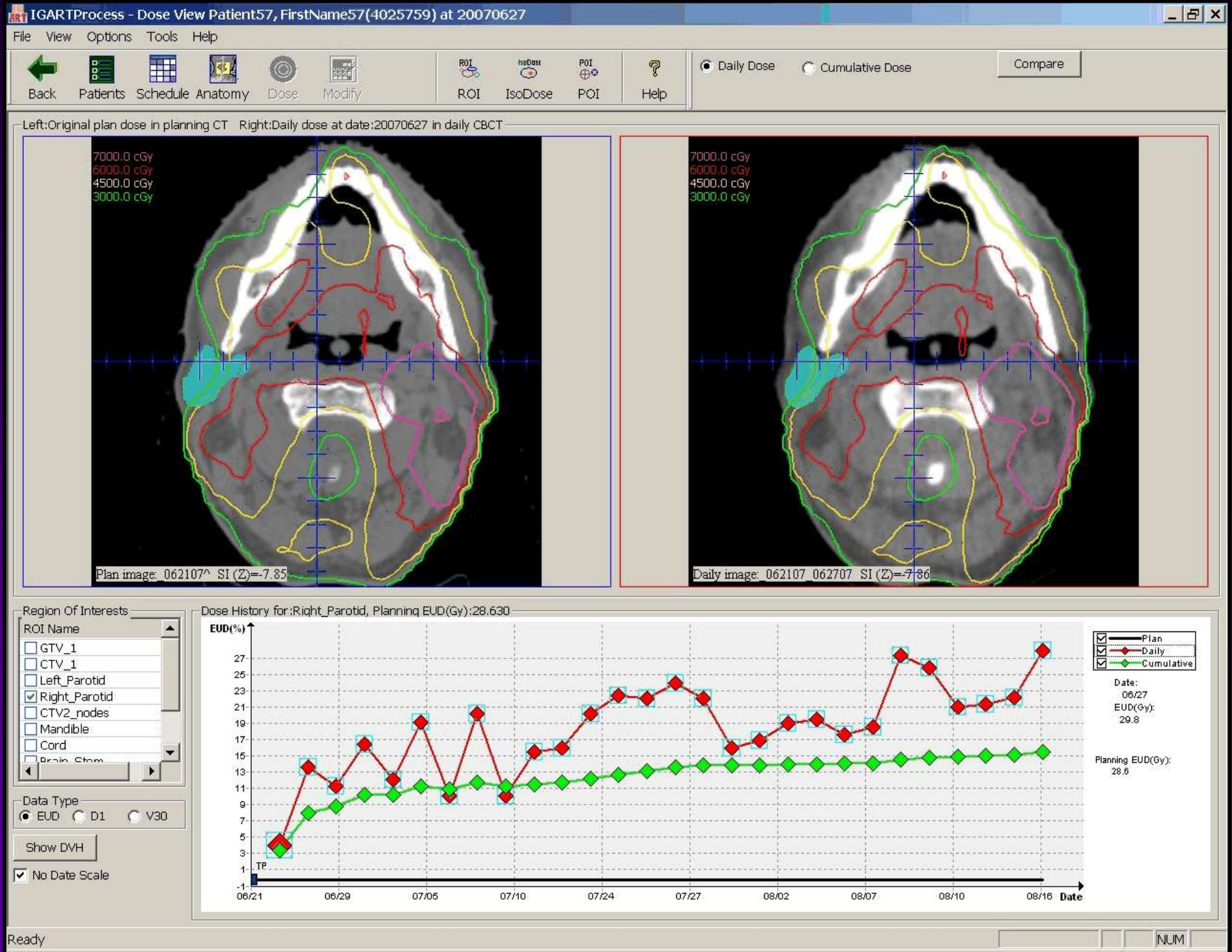
William Beaumont Hospital



Organ Volume/Dose Variations

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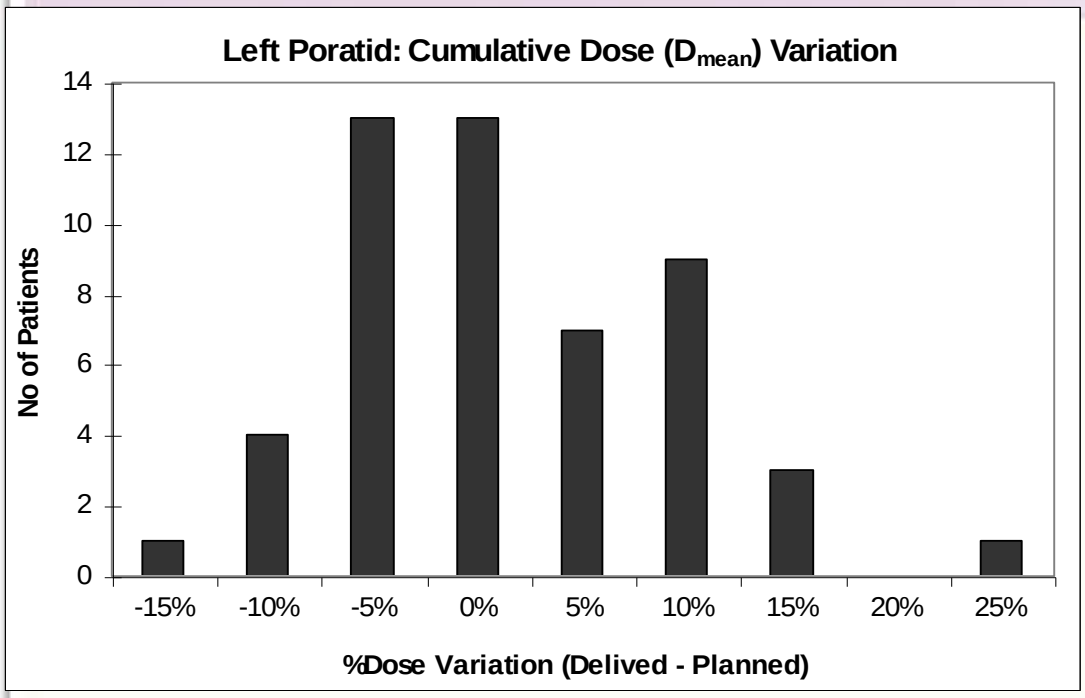
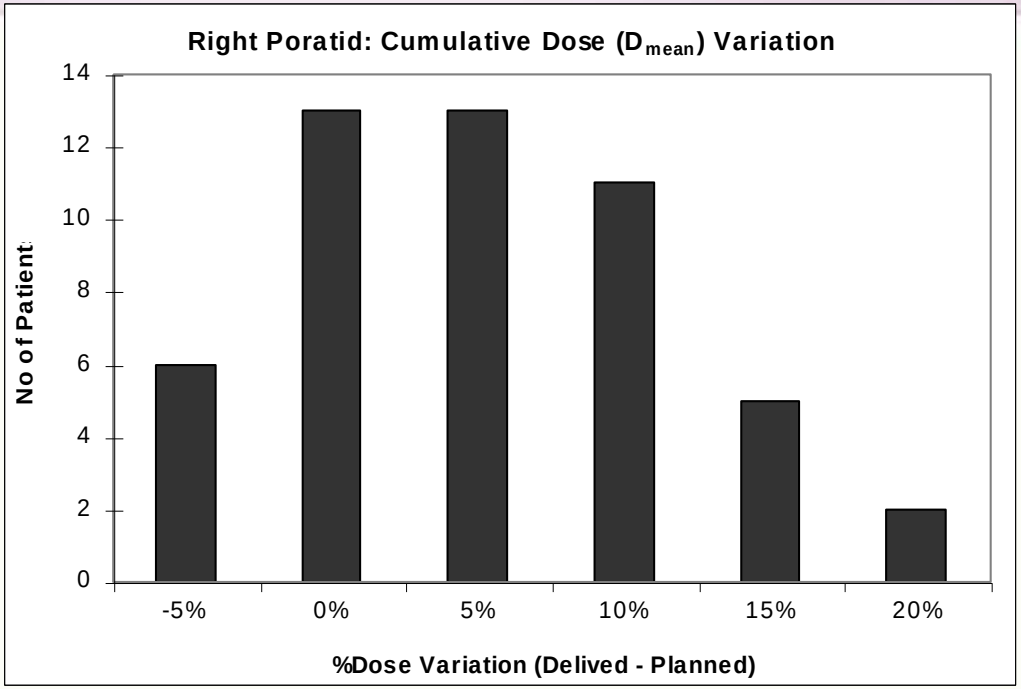
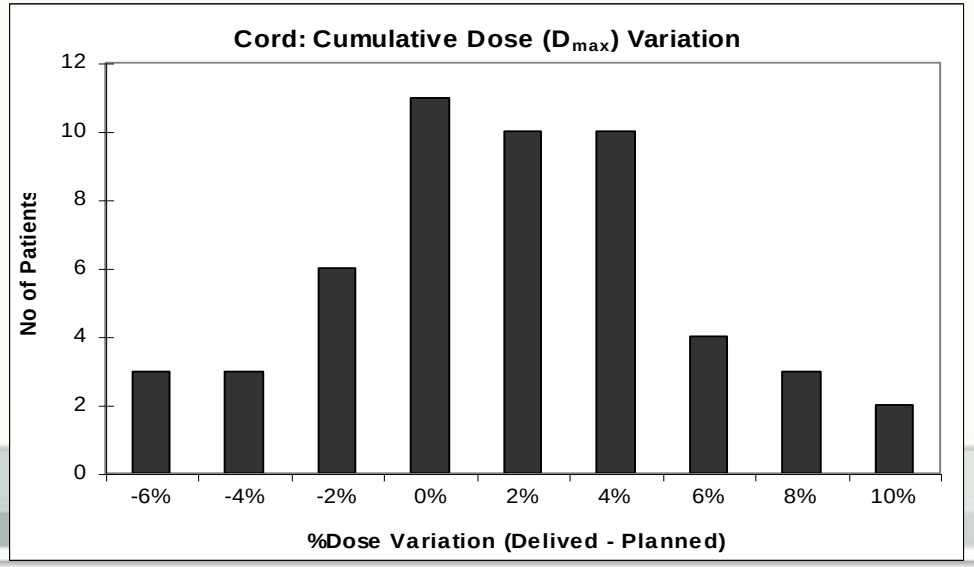
Organ Dose Variations during the Treatment







HN Cancer ART: Clinical Rationales

- 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**

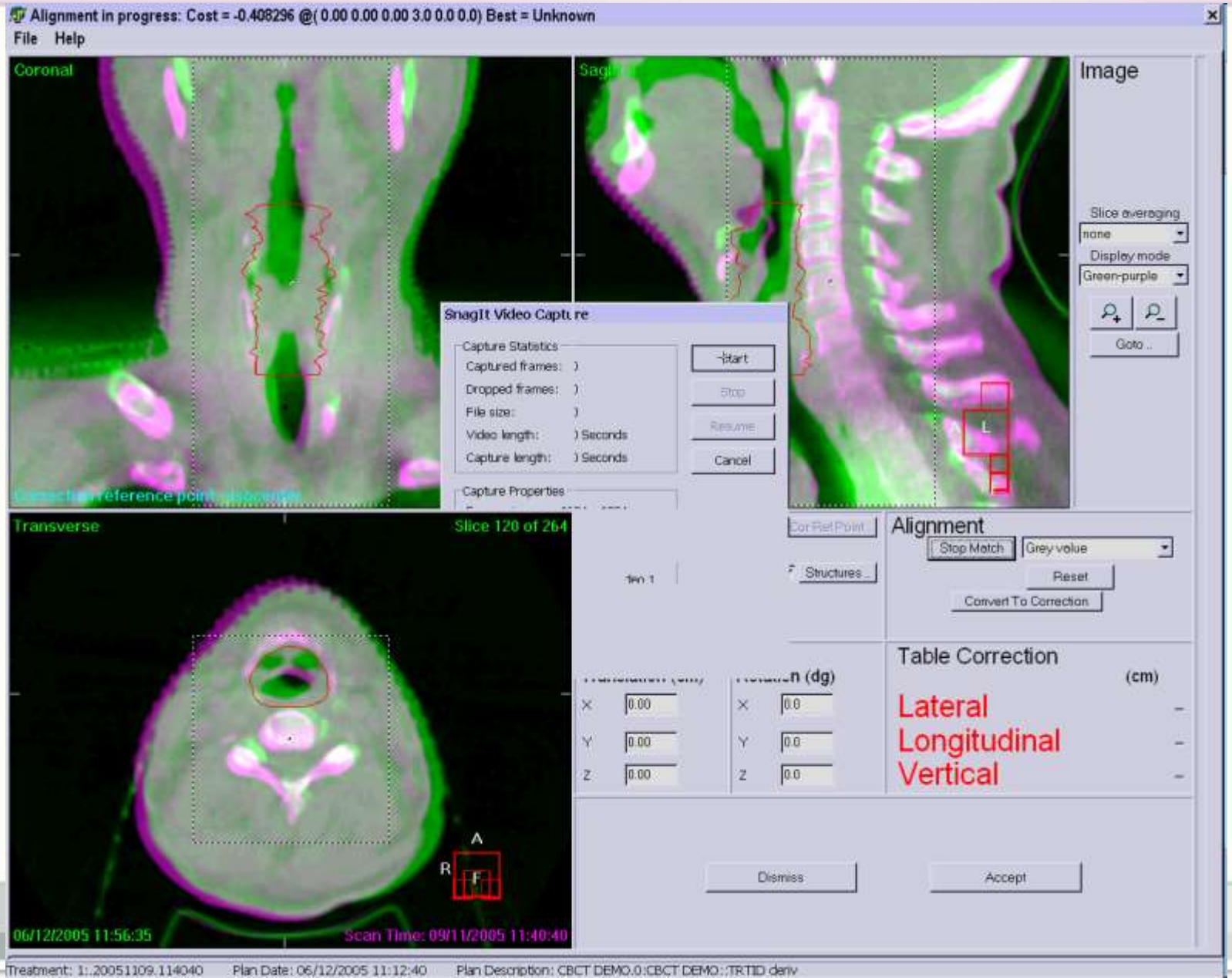
1. **Pre-treatment Simulation & Planning**
   - Standard CT simulation & IMRT planning
   - 0~5mm CTV-to-PTV margins & 5~7 beams
   - Planning CT image w/wo pre-selected bony structures (adjacent to the target, C_2-C_5) selected as the reference for daily treatment localization & correction
   - Segmentation (commercial tools for auto-segmentation), inverse planning, evaluation & QA: 2~4 days

HN Cancer ART: Clinical Implementation

2. Daily CBCT/CT-in-room Localization & Correction

- Pre-treatment CBCT/CT imaging for patient at the treatment position (~2 mins)
- Bony (C_2-C_5) 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

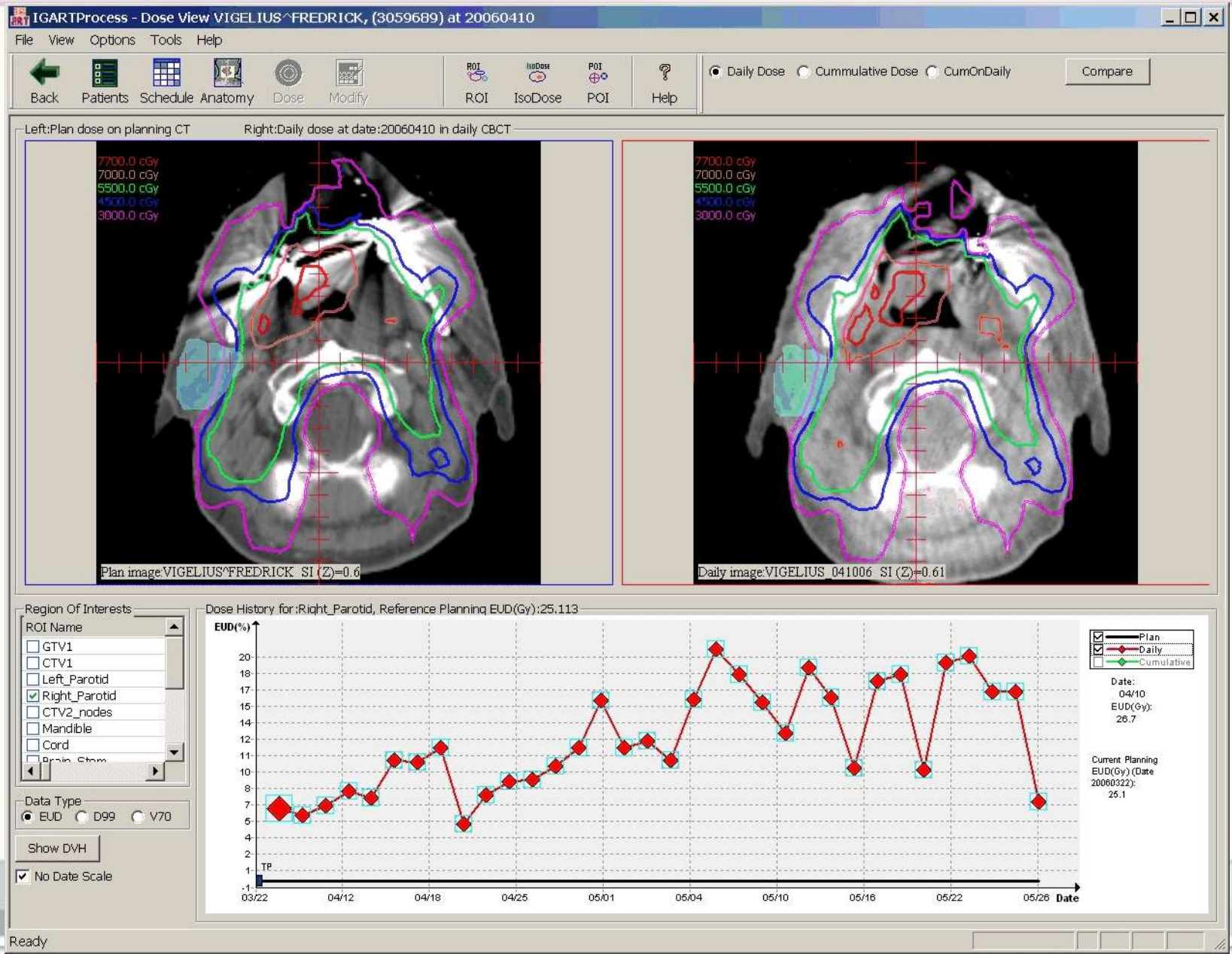
Daily Treatment Localization



HN Cancer ART: Clinical Implementation

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



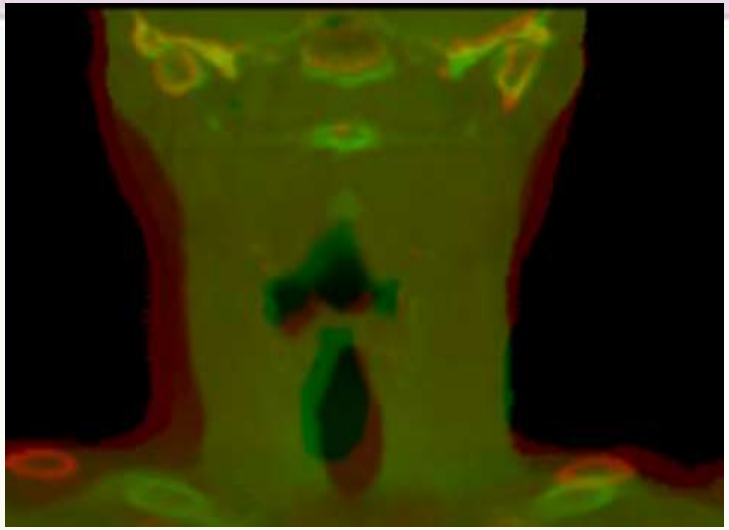
HN Cancer ART: Clinical Implementation

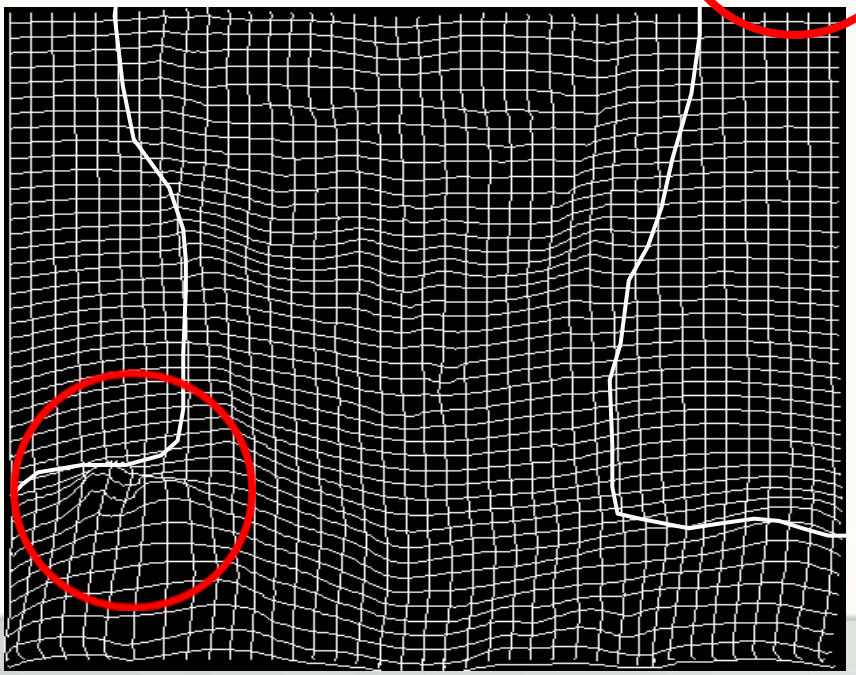
4. **New CT Simulation** (after the first 10 and/or 20 treatment days)
   - New mask if necessary
   - Delineate targets and ROIs on the new CT image (auto propagation from the pre-treatment plan)
   - The new CT image will be used in the planning modification, and as the new reference image for the 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

HN Cancer ART: Clinical Implementation

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

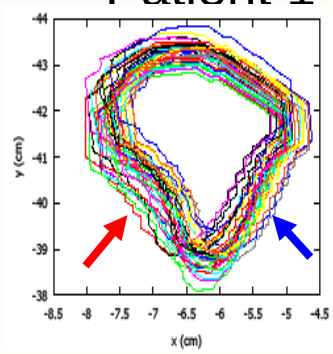




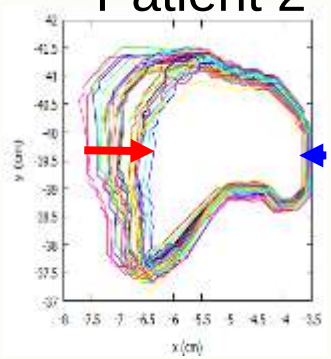
DVF
Mesh Structure

Technical Issue: Organ Variation Characterization

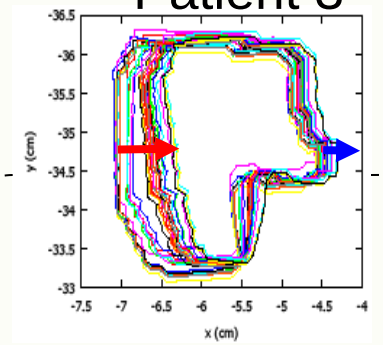
Patient 1



Patient 2



Patient 3



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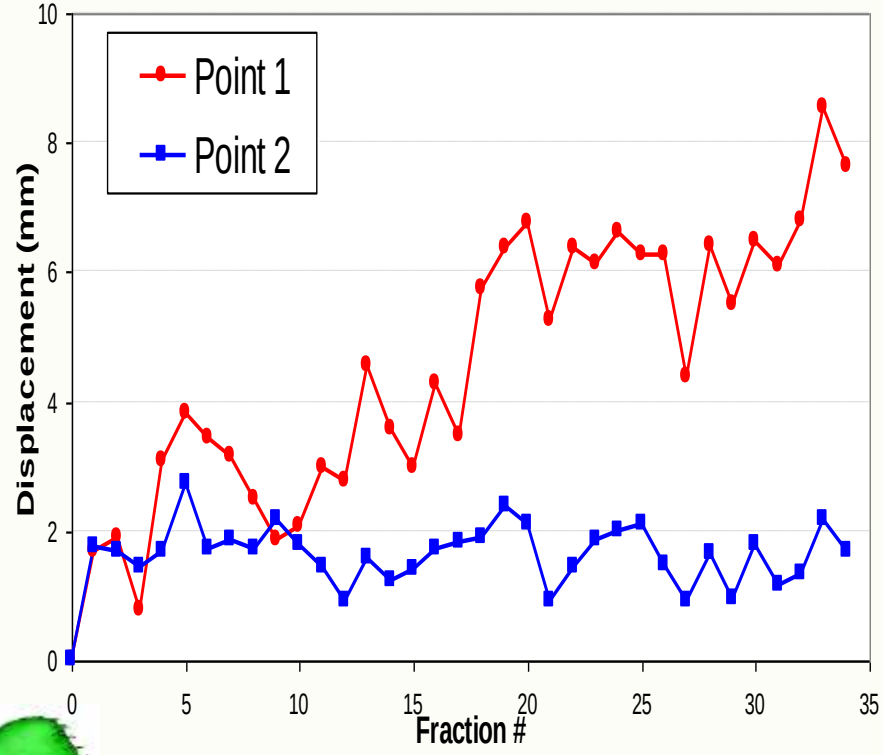
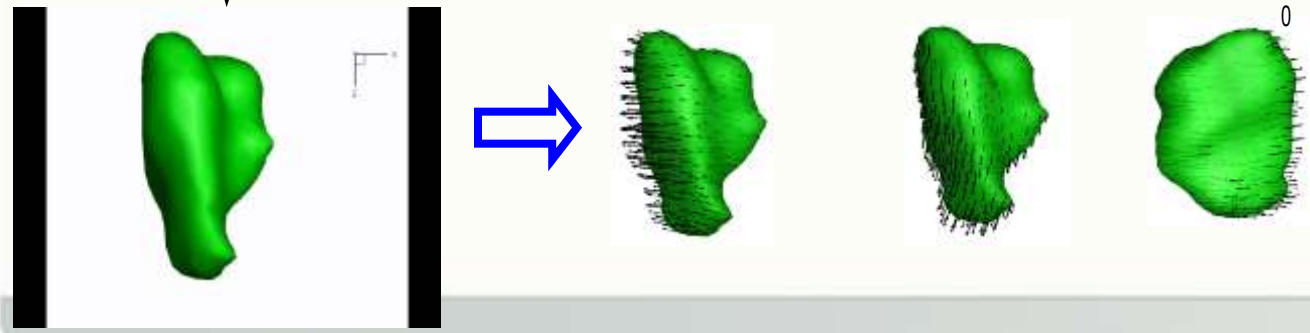
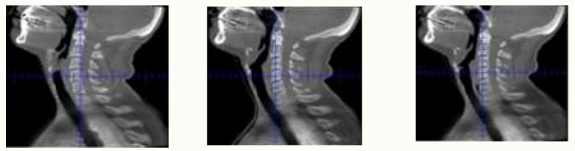
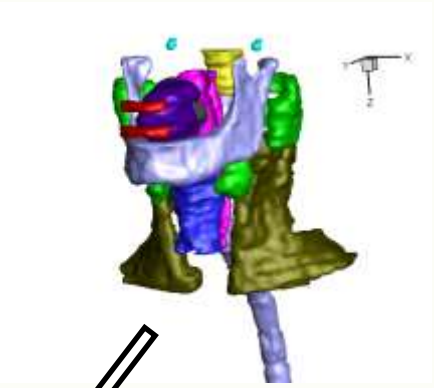




Technical Issue: Treatment Dose Construction



Organ Sample Generator



$$\left\langle D_N(v) \mid \Phi_{K+1} \right\rangle = D_K(v) + \left\langle d(\vec{x}_j(v), \hat{\Theta}_j, \Phi_{K+1}) \mid (\vec{x}_j(v), \hat{\Theta}_j) \right\rangle$$

Delivered dose

Estimated dose

Expected Treatment Dose

Technical Issue: Adaptive Inverse Planning

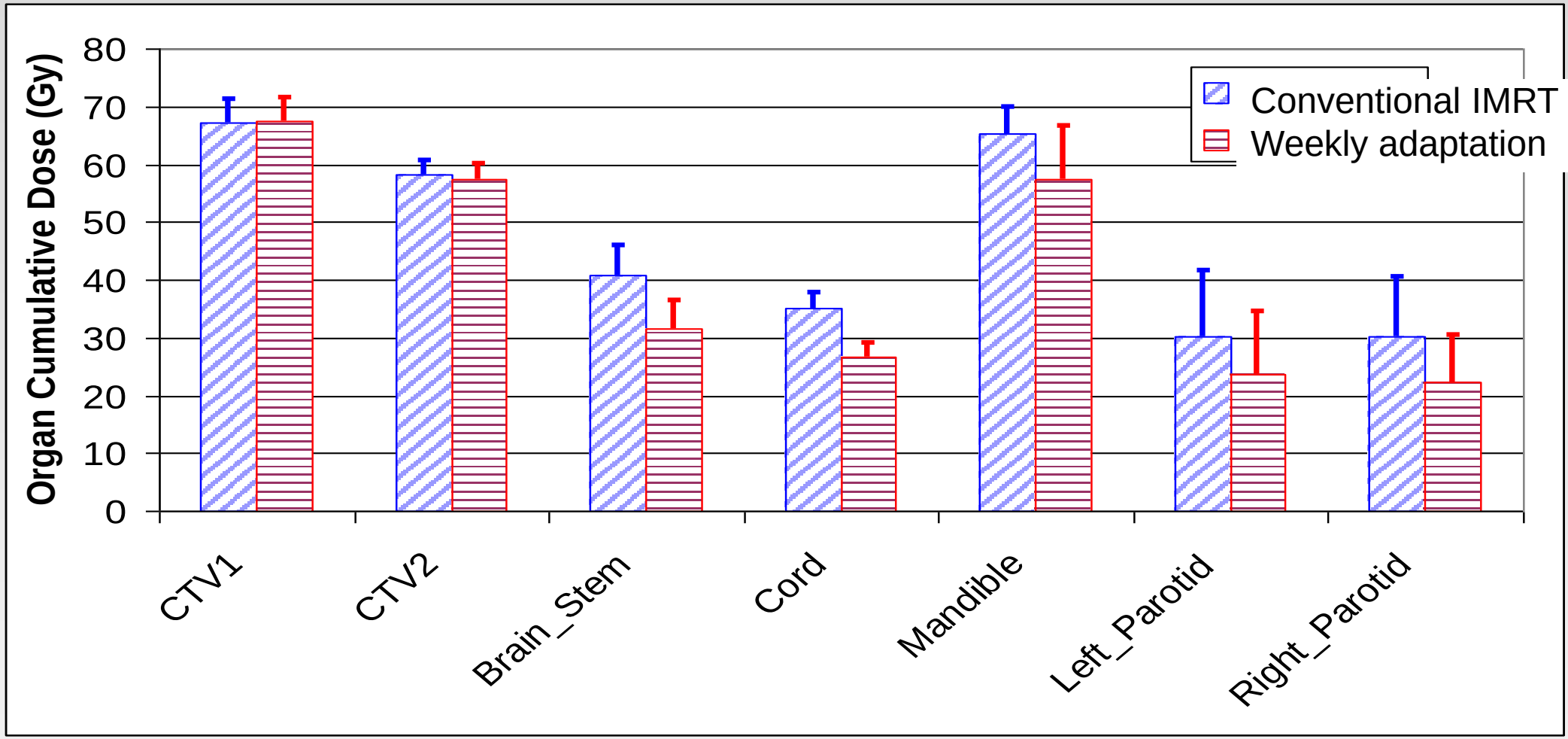
$$\underset{\Phi_{k+1}}{Max} \quad F\left(\left\langle D_N \mid \Phi_{k+1} \right\rangle\right)$$

$$G\left(\left\langle D_N \mid \Phi_{k+1} \right\rangle\right) \leq G\left(\left\langle D_N \mid \hat{\Phi}_k \right\rangle\right) - \Delta$$

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

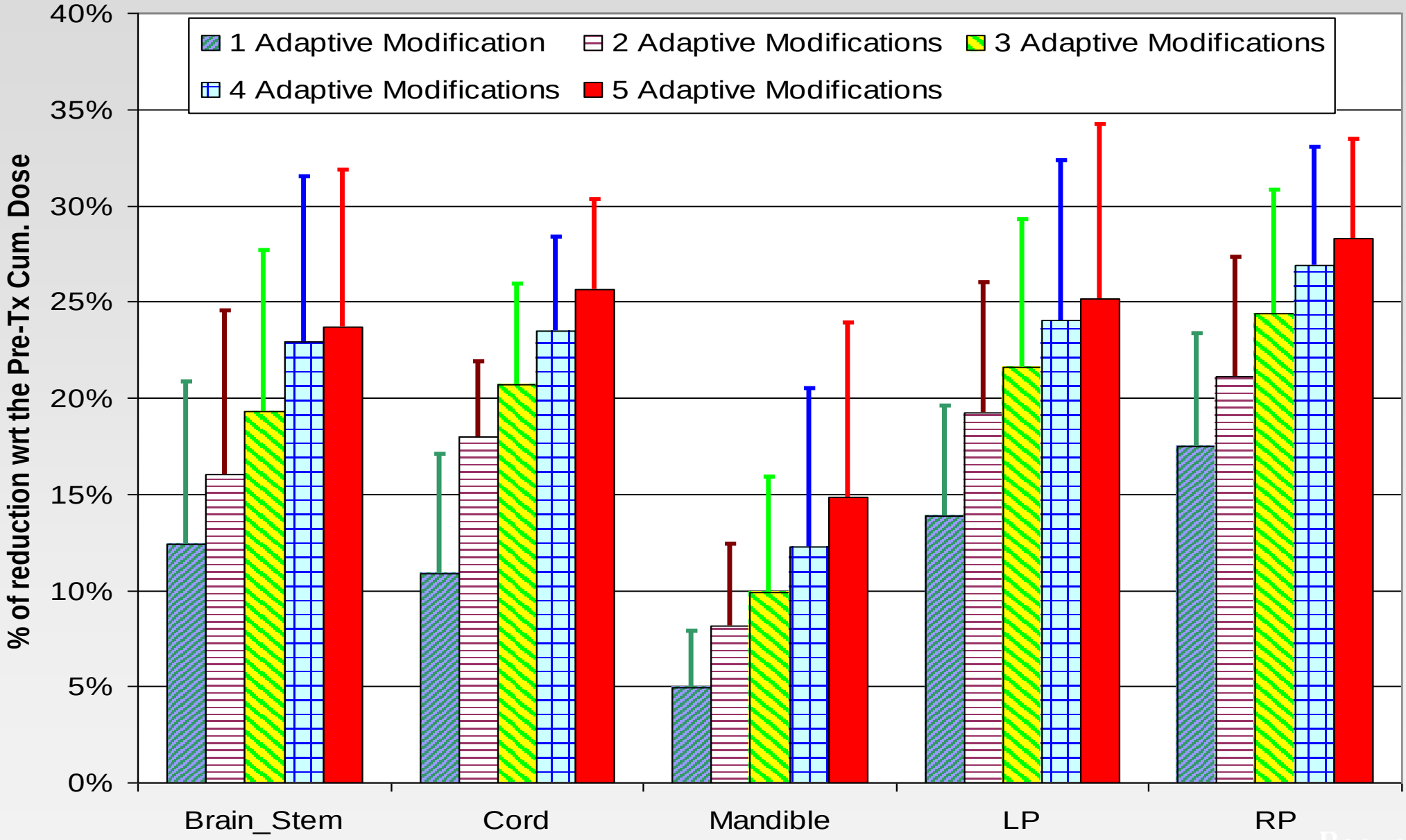
* Δ: Expected improvement from the previous treatment is used to determine if "accepting the plan modification"

ART vs Conventional IMRT (5mm Target Margin)

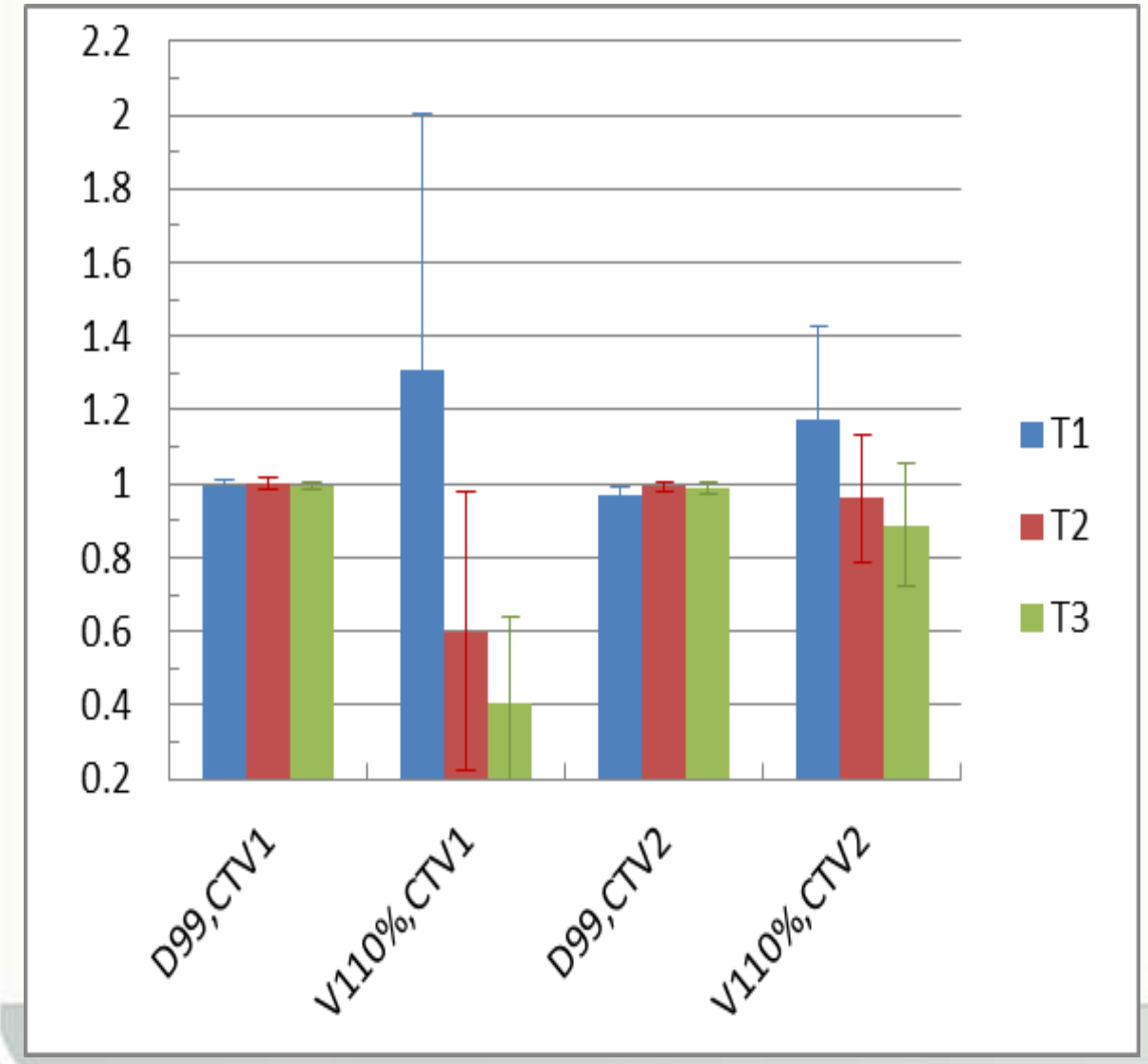


Improvement in Gy:	9.5±6 Dmax	7.2±2 Dmax	6.5+10 Dmax	6.7±10 Dmean	7.8±3 Dmean

Improvement of ART *vs* Clinical Efforts



‘Daily IGRT’ vs ‘Hybrid ART’



All treatment organ doses are normalized to the baseline IMRT plan with 0 target margin

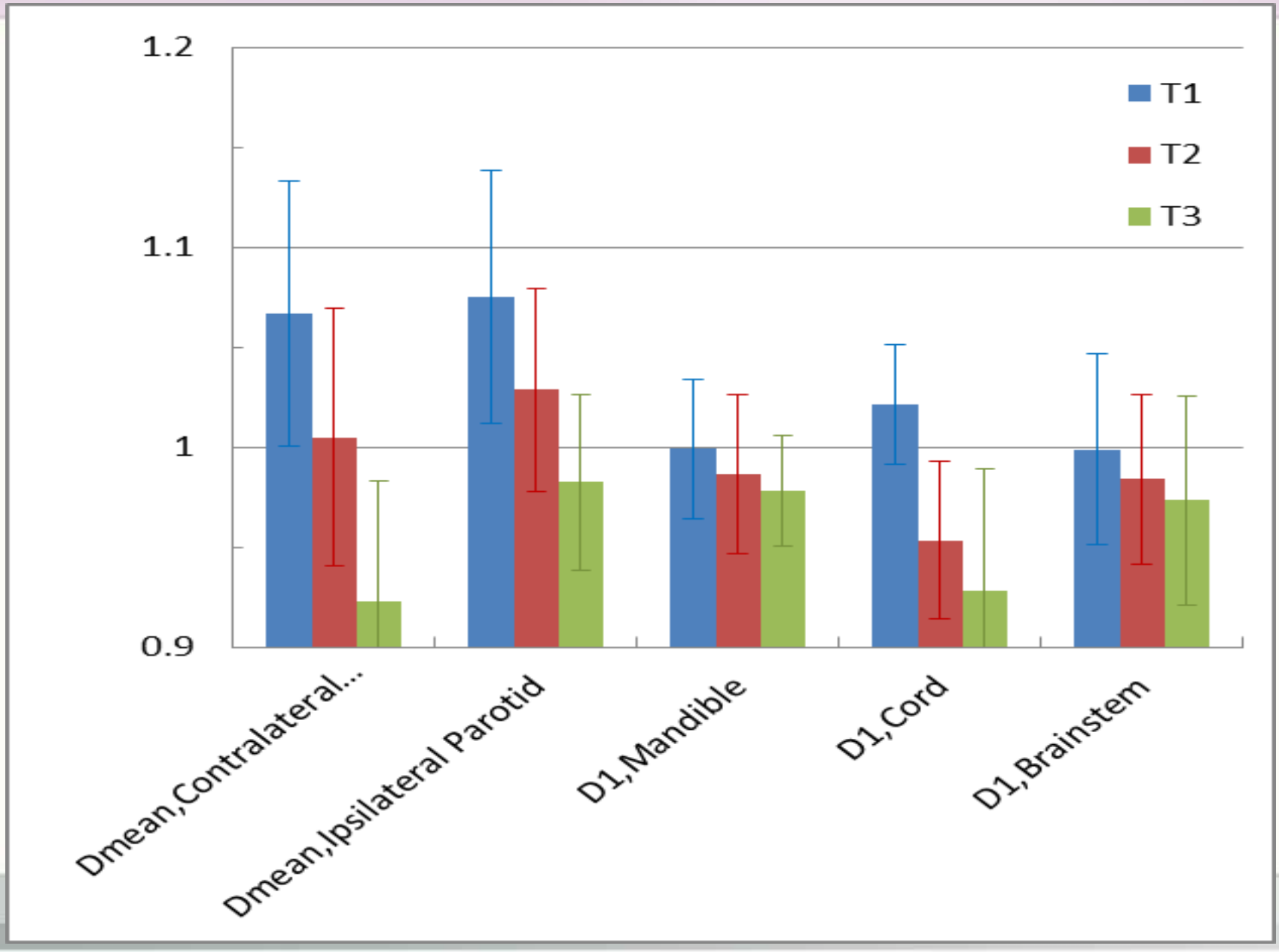
T1: Daily IGRT with 0 target margin

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’



Practical Issues (workload)

- 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

Summary

- 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

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