Strategies of How and When to Adapt

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DEPT OF RADIATION ONCOLOGY

Disclosure

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- Cancer Prevention and Research Institute of Texas (CPRIT) grants
- Varian Research grants
- Elekta Research grant

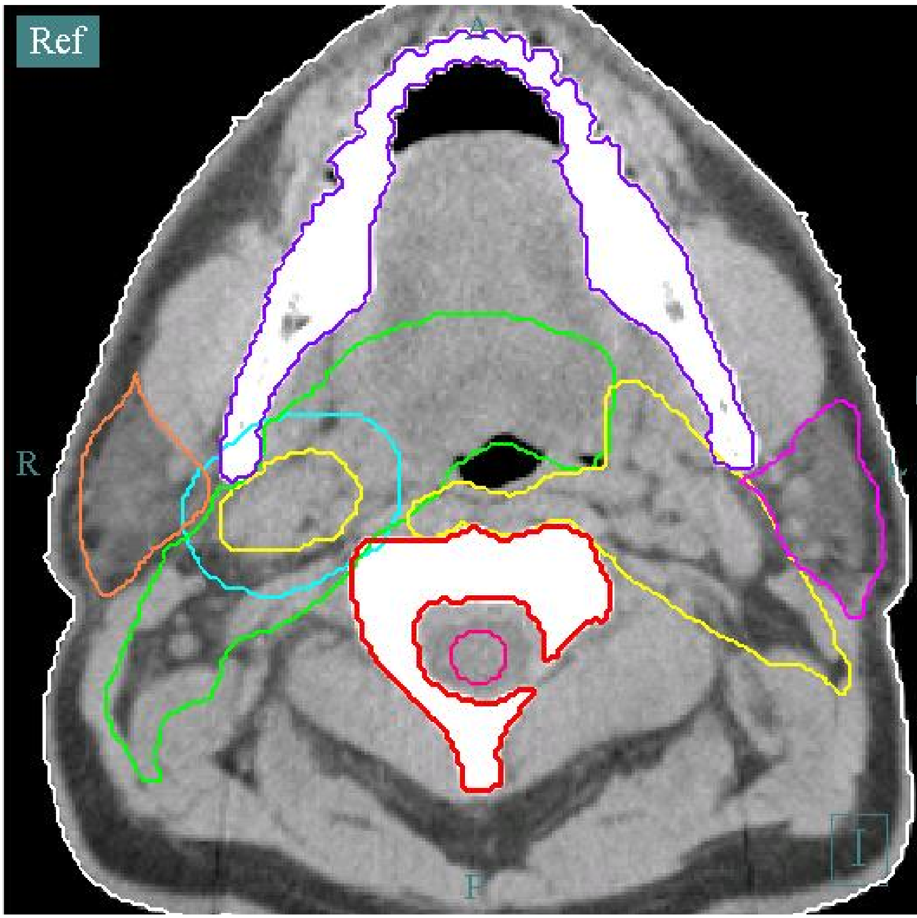
Learning Objectives

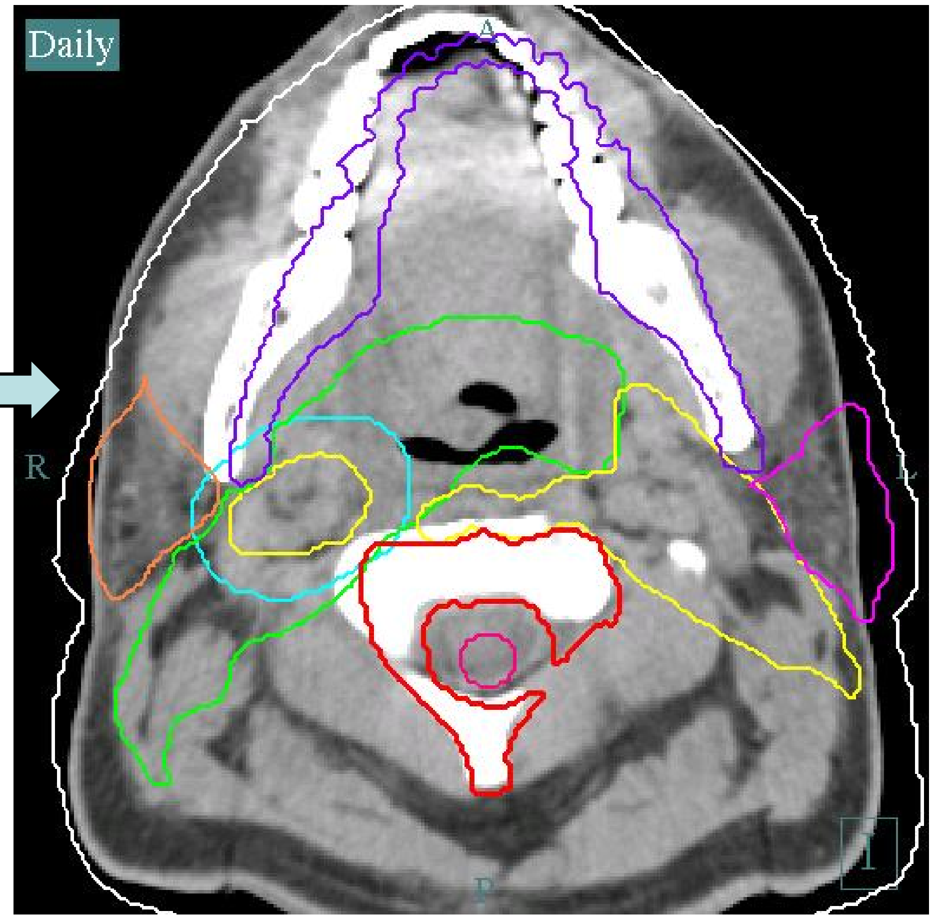
- Understand what adaptive radiation therapy can do
- Understand how and when to adapt radiation therapy

Why Adapt

- Sources of anatomic changes

Conventional





Reference Planning CT

Mask Alignment (Daily CT)

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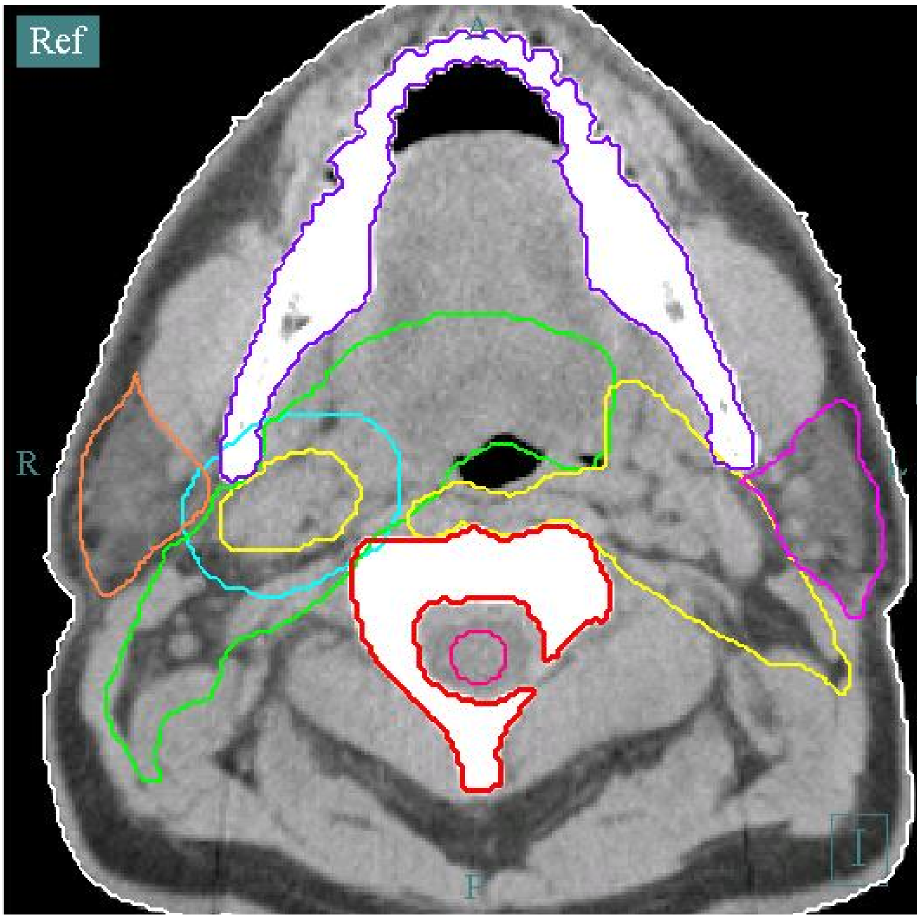
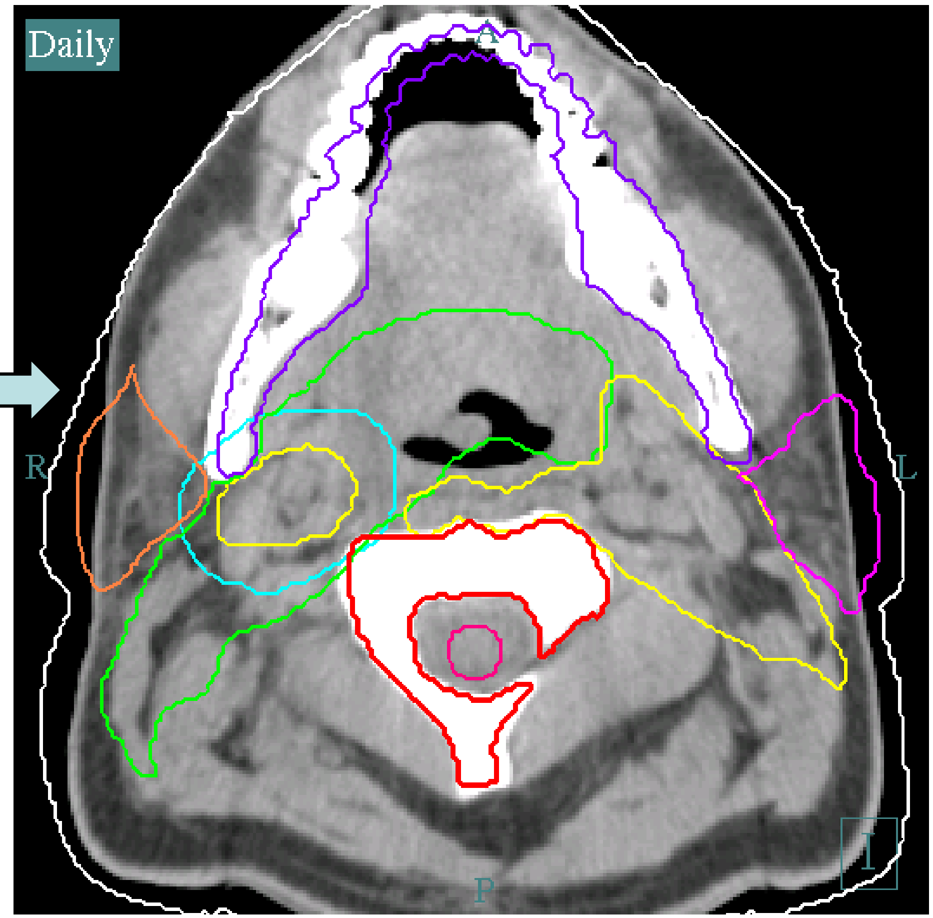
IGRT

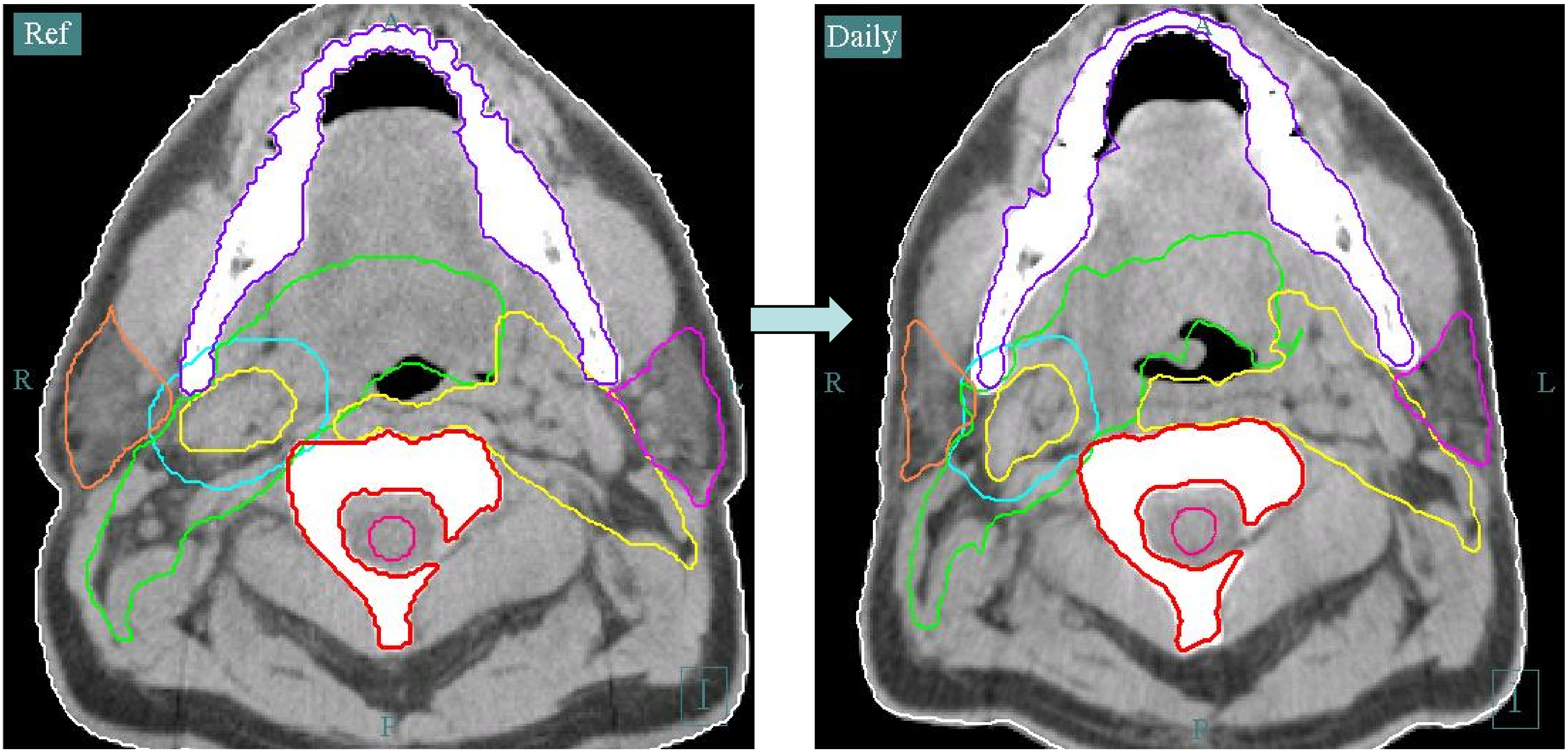


Reference Planning CT



Bone Alignment
(Daily CT)

IG-ART

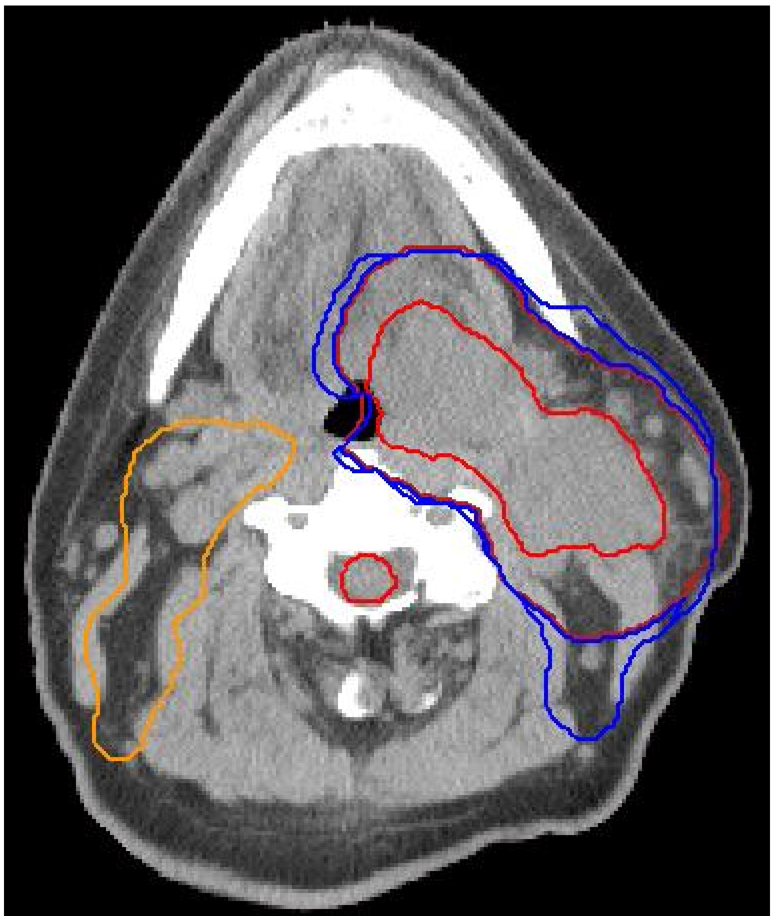


Reference Planning CT

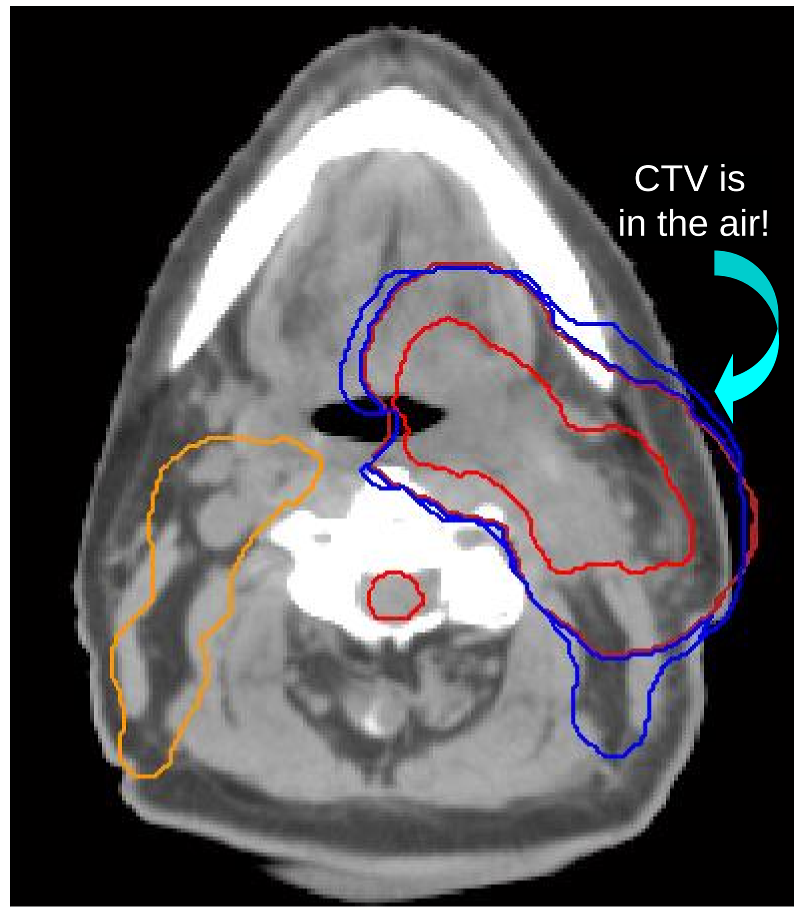
Adapt to Anatomy (Daily CT)

Complex Uncertainties—Intrinsic Anatomic Changes

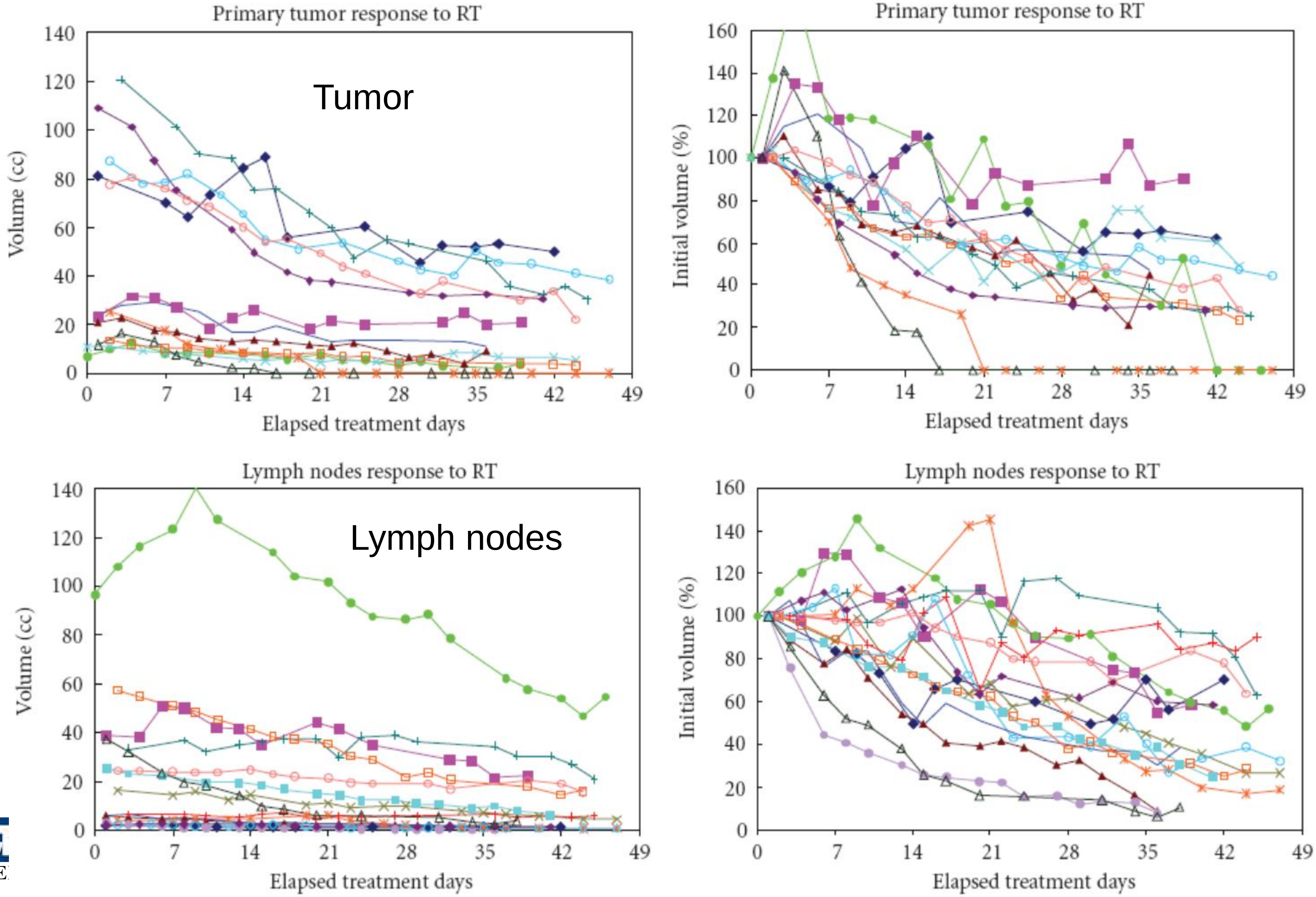
Planning CT



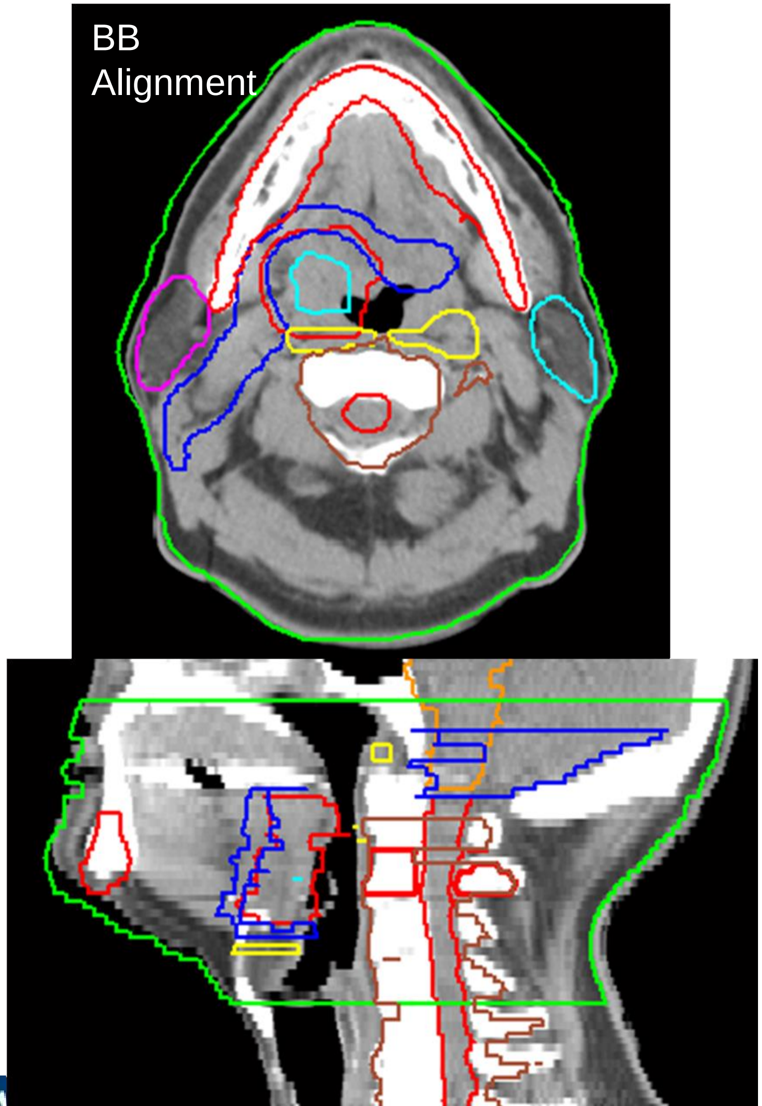
During RT Course

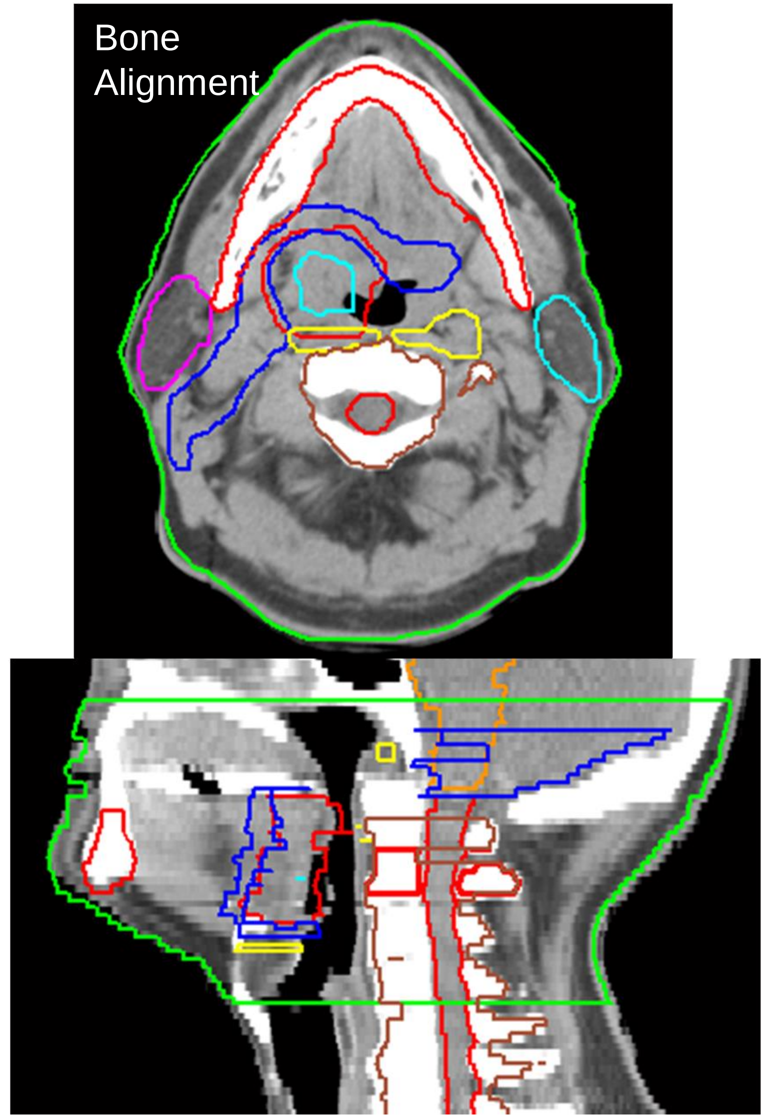


H&N Cancer Treatment Response



Initial Setup Images





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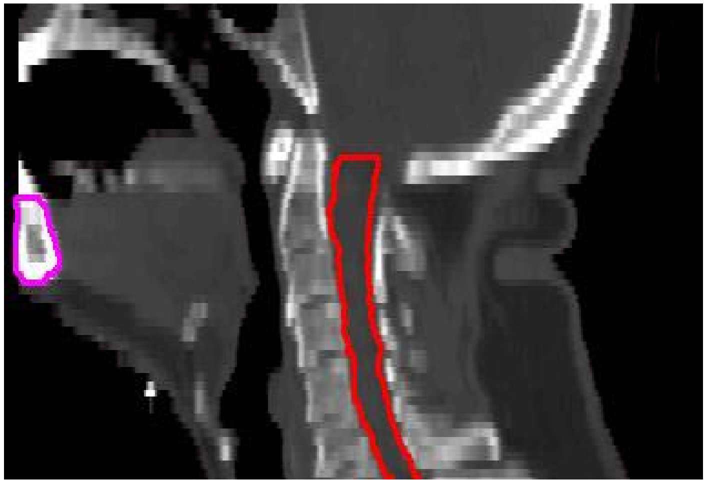
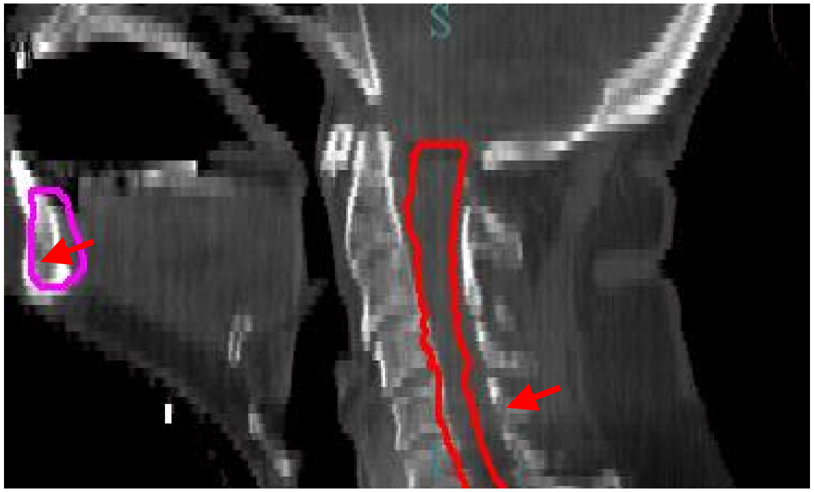
Complex Uncertainties— Neck Curvature



Planning CT



Daily Cone-Beam CT

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T3N2 BOT—
Weight Loss @ Fx#20

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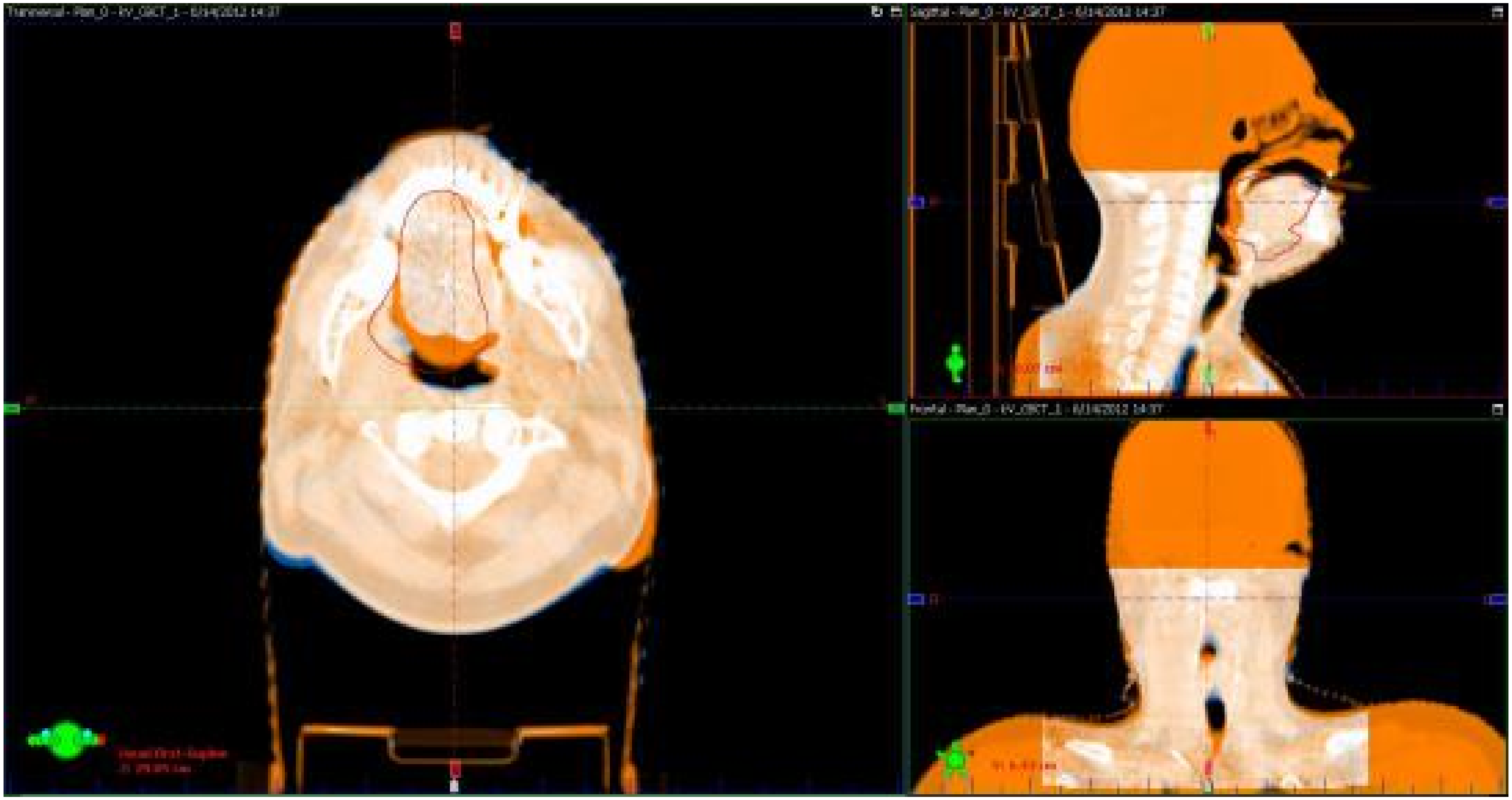
T2N1 “Young Tongue”— Resolving Oral Edema @ Fx#12



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Why Adapt

- Sources of anatomic changes
  - Tumor volume shrinkage in response to the treatment
  - Tumor shape deformation due to filling state change of neighboring organs
  - Relative position change between tumor and normal organs
- Plan and planning margins

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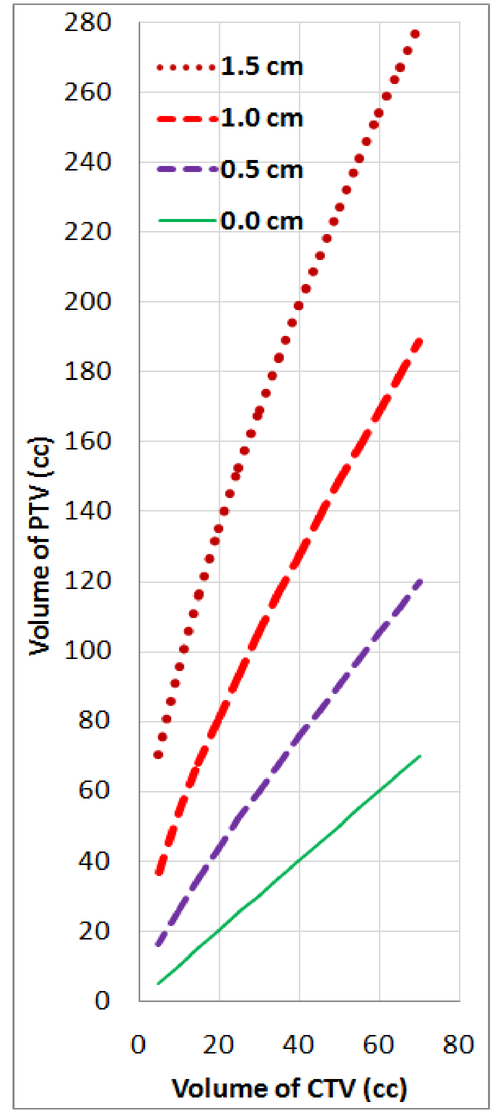
CTV-to-PTV Expansions—The Millimeters Matter

$$4/3\ \pi r^3$$



Adapted from Verellen et al *Nature Rev Cancer* 7:949-60 [2007]

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Dilemma

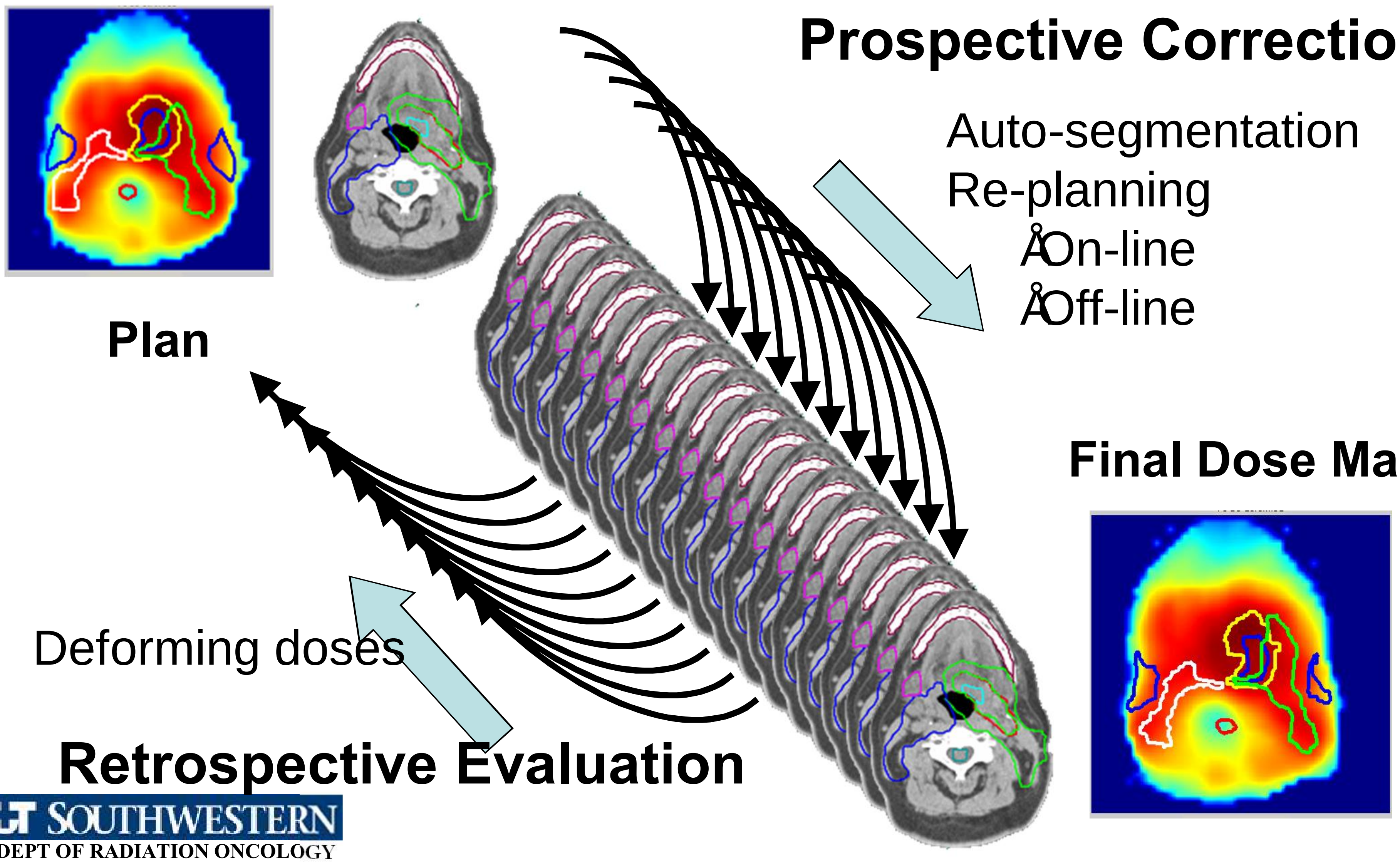
Small margins → Accuracy and safety

Large margins → Compensate uncertainties

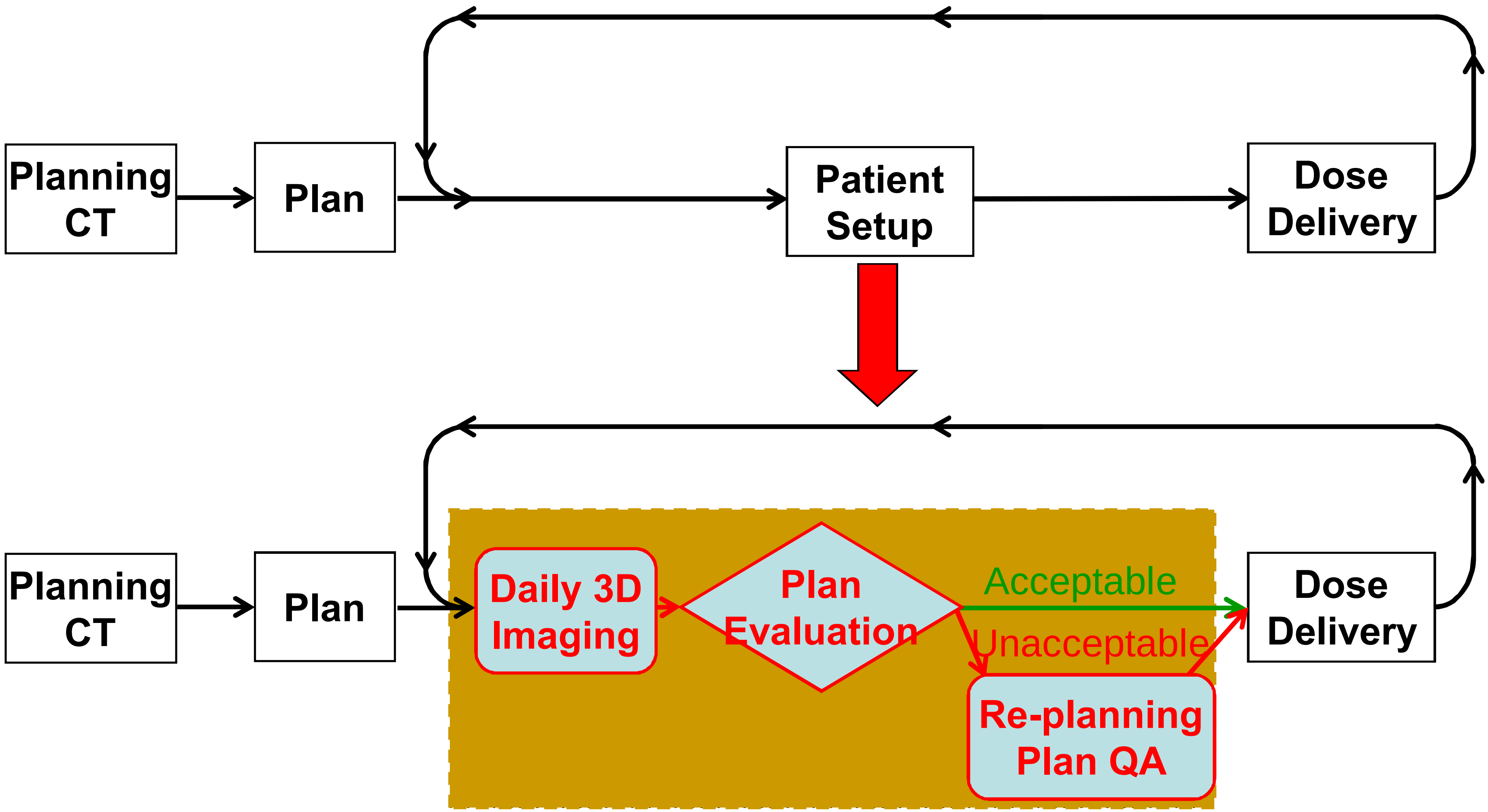
One size fits all?

One plan wonÕt work well.

ART—An Iterative Process



Flowchart of Adaptive Radiotherapy



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cone-down boost ? = adaptive radiation therapy

Reduce PTV during a course of treatment.

Normally based on the same original CT scan.

Strategies of Adaptive RT

- Off-line
  - With current treatment planning system

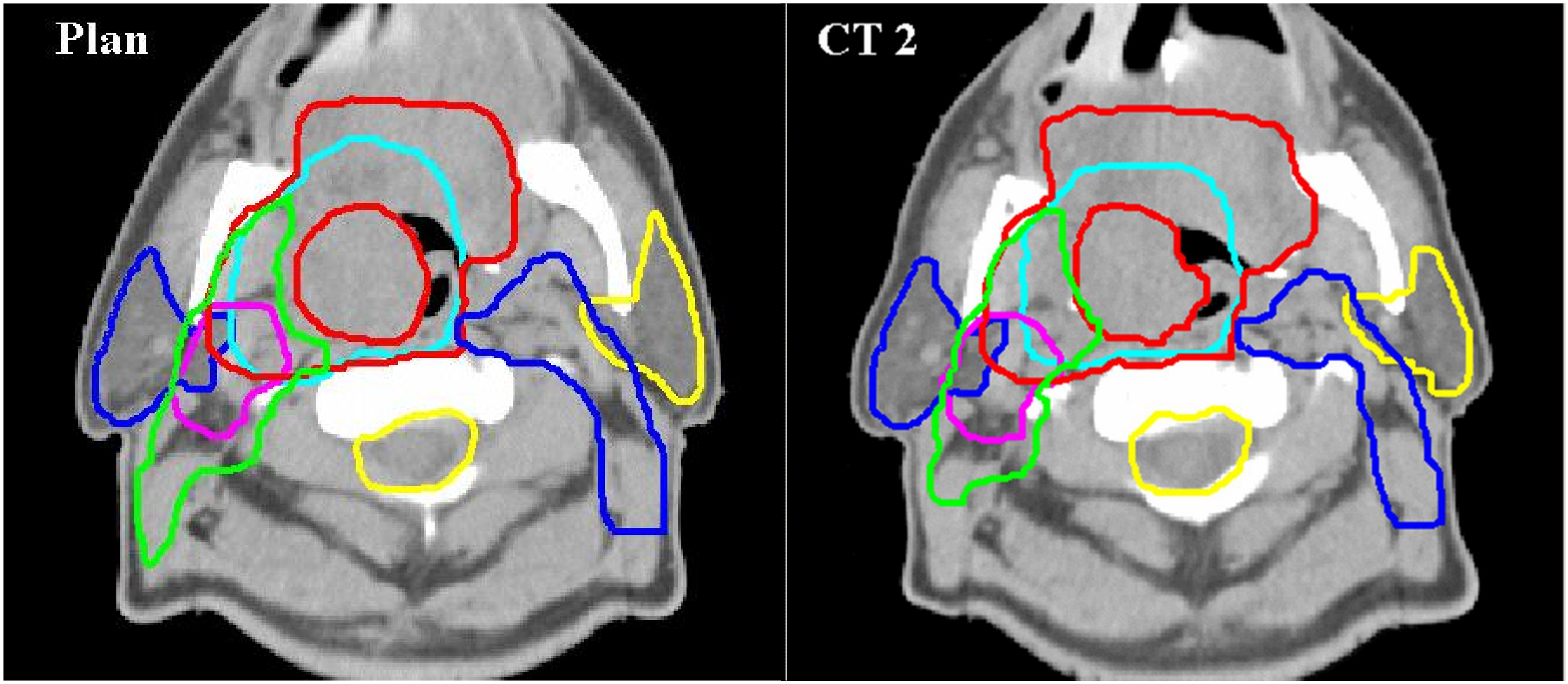
MDACC – H&N Replanning Procedure

- Standard baseline IMRT planning
  - 3mm PTVs
- ART re-plans use no PTV expansions
- Daily CT-guided setup
- Weekly deformable contour mapping to each Thursday's CT
- Offline ART evaluation and planning
  - Re-calc and re-plan

Automated Segmentation

Original Treatment Plan

Anatomy During Treatment



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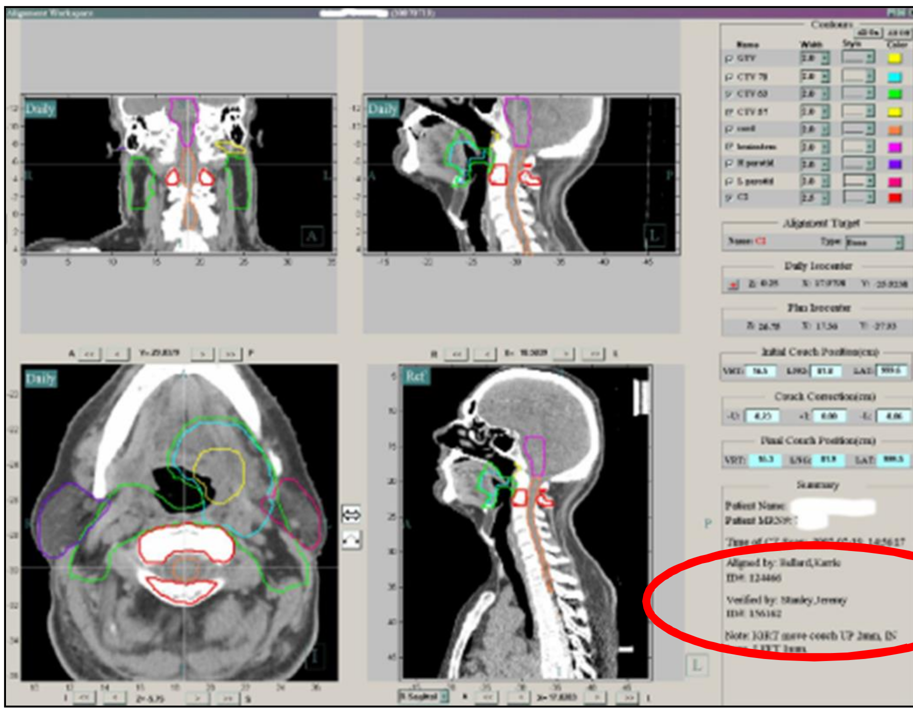
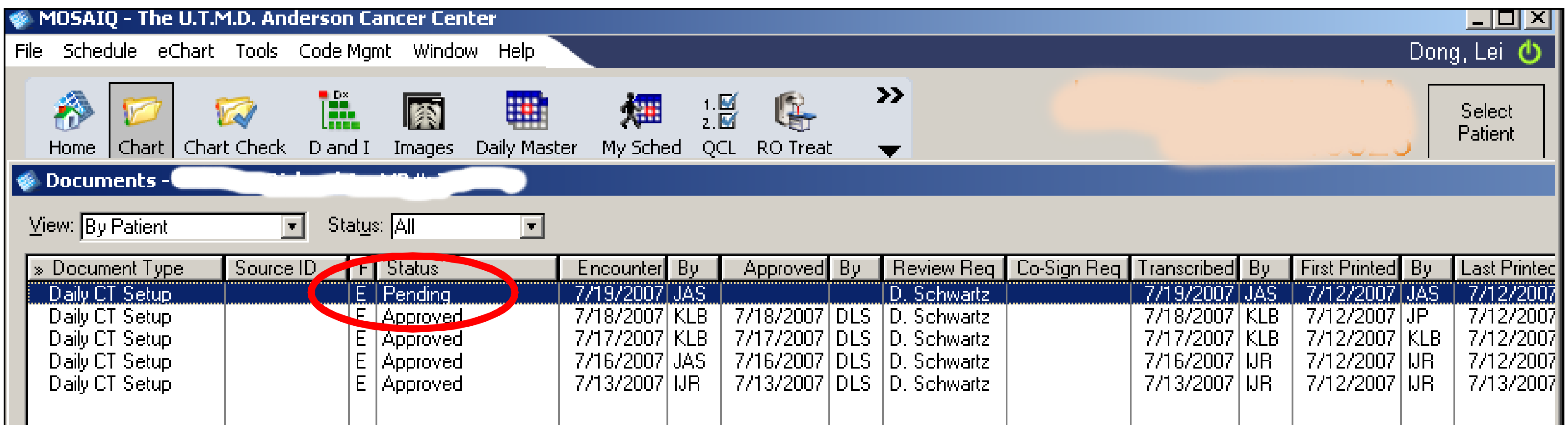
ART Clinical Workflow

- Standard baseline contouring/planning
- Day 1—Manual IGRT isocenter confirmation
  - Physics/CAT software on daily in-room imaging



ART Clinical Workflow

- Insurance approval
  - Boilerplate MD letter via Business Office before start
- Standard baseline contouring/planning
- Day 1—Manual IGRT isocenter confirmation
  - Physics/CAT software on daily in-room imaging
- Daily—MD signs IGRT image on EMR



Document Type	Source ID	F	Status	Encounter	By	Approved	By	Review Req	Co-Sign Req	Transcribed	By	First Printed	By	Last Printec
Daily CT Setup		E	Pending	7/19/2007	JAS			D. Schwartz		7/19/2007	JAS	7/12/2007	JAS	7/12/2007
Daily CT Setup		E	Approved	7/18/2007	KLB	7/18/2007	DLS	D. Schwartz		7/18/2007	KLB	7/12/2007	JP	7/12/2007
Daily CT Setup		E	Approved	7/17/2007	KLB	7/17/2007	DLS	D. Schwartz		7/17/2007	KLB	7/12/2007	KLB	7/12/2007
Daily CT Setup		E	Approved	7/16/2007	JAS	7/16/2007	DLS	D. Schwartz		7/16/2007	IJR	7/12/2007	IJR	7/12/2007
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  - Physics/CAT software on daily in-room imaging
- Daily—MD signs IGRT image on EMR
- Weekly—MD evaluation of daily in-room imaging
- Replanning—Largest resource burden
  - Dosimetry/Physics
  - MD dictates sim note to document billing
  - 1-2 replans

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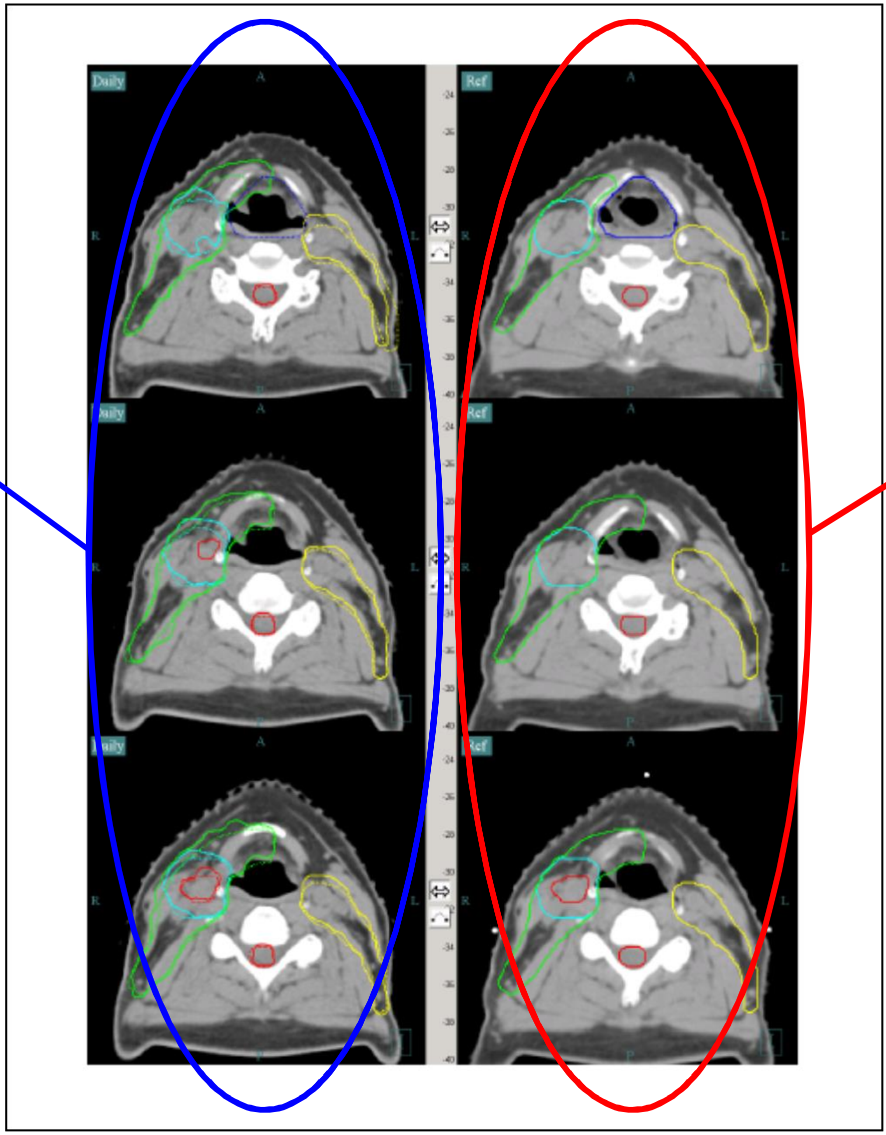
Weekly Contour Evaluation for ART

Original Contours and Deformed Contours on Current CT



Original Contours on Original CT

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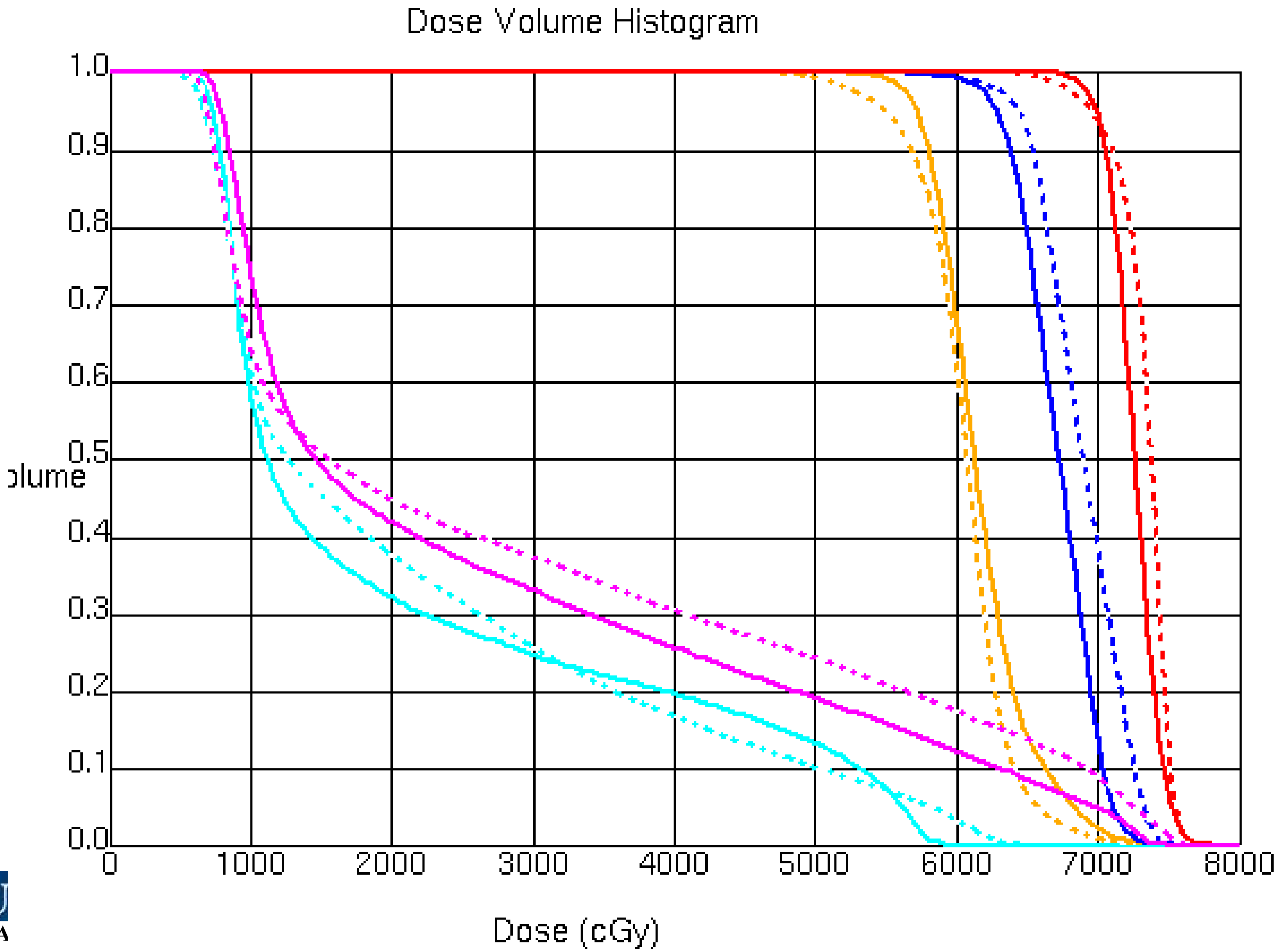
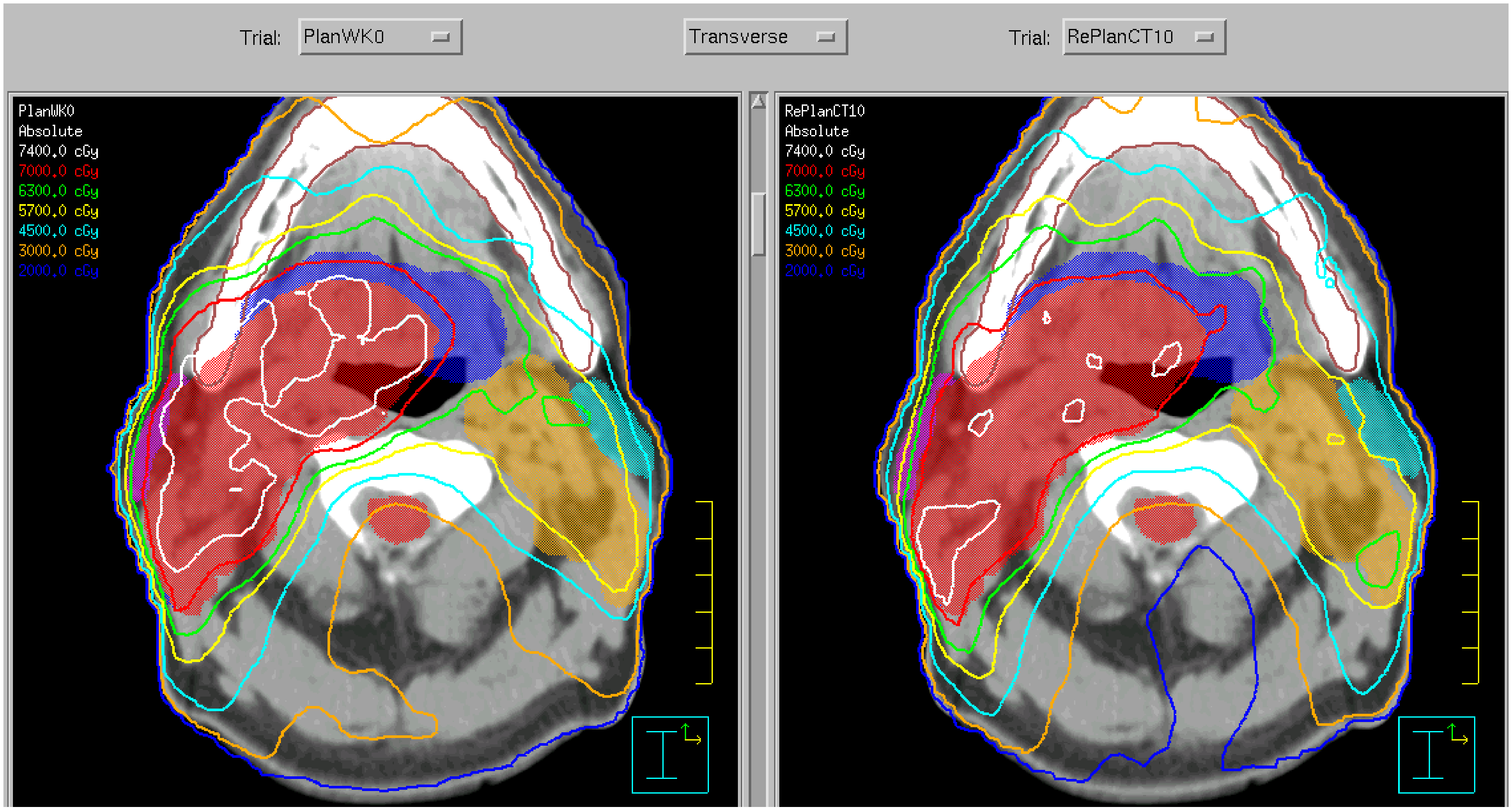
ART Replan DVH Evaluation



ART Replan Evaluation



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Operational Issues

- R & V upload time
- Plan documentation time
- QA time
- Billing dept. time & reimbursement risk
- With MDACC off-line platform, there is at least a "weekend-assisted" 1.7 fraction delay between in-room CT and delivery of ART

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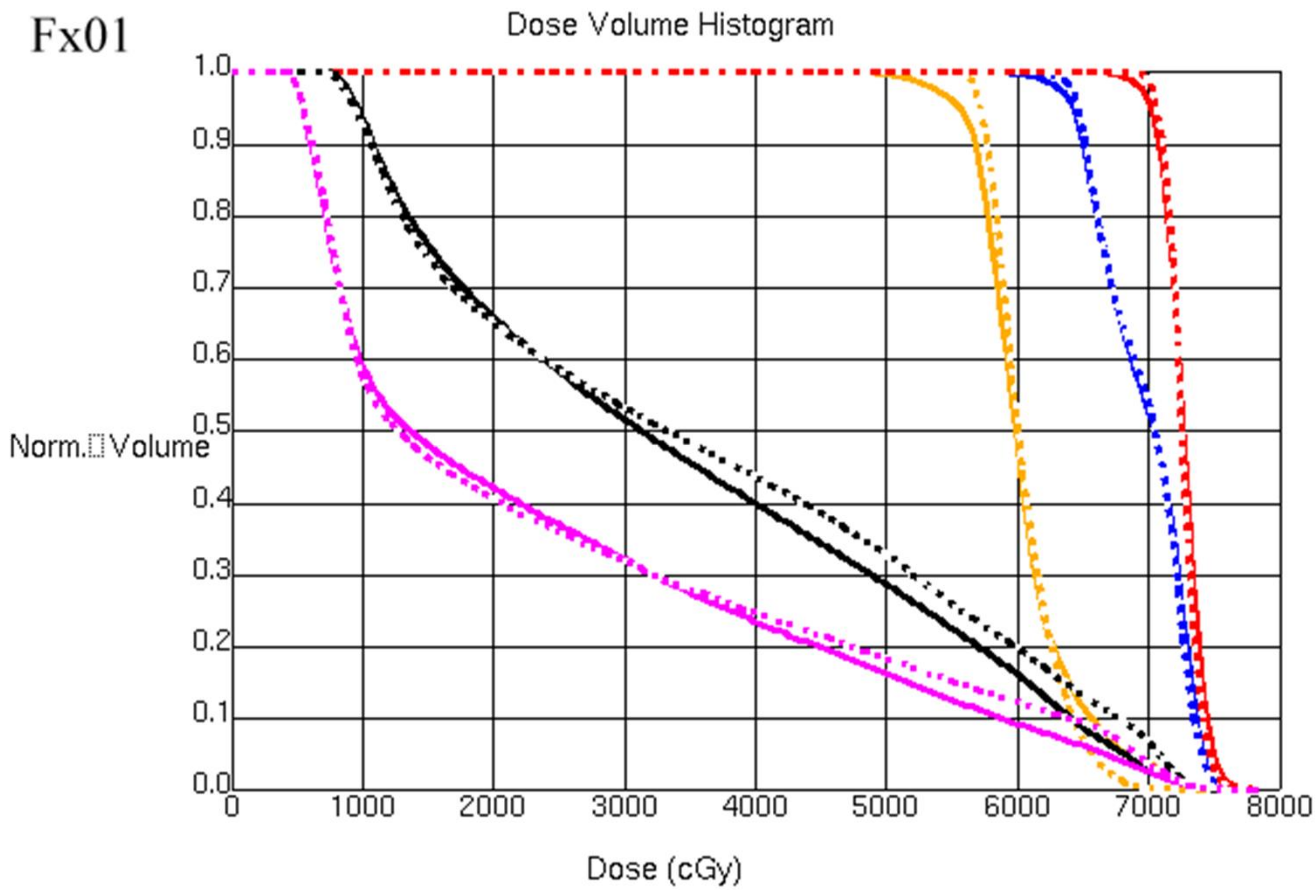
Practical Issues in Adaptive RT

What is the trigger point for replanning?

Fx01



Practical Issues in Adaptive RT

What should trigger replanning?

- ƴ Underdosing to target volumes
- ƴ Overdosing to organs at risk
- ƴ Elimination of hot spots
- ƴ Qualitative anatomic changes

Pilot Dosimetry Results

- *n* = 22 pts
- Stage III-IVa oropharyngeal SCCA
- Standard baseline IMRT
- Daily in-room CT-on-Rail imaging
- Weekly off-line plan re-evaluation
- One (ART1) or two (ART2) adaptive replans
  - <u>0-mm PTV marginS</u>

Schwartz, DL et al *Radiotherapy & Oncology* 106:80-4 [2013]

Pilot Dosimetry Results

Cumulative dosimetry from daily images calculated retrospectively for 4 planning scenarios:

(1) Pt aligned to isocenter skin markings (BB-IMRT)

(2) Pt aligned to bony anatomy (IGRT)

(3) IGRT and one adaptive replan (ART1)

(4) Actual treatment received (IGRT and 1 or 2 adaptive replans, ART2)

Schwartz, DL et al *Radiotherapy & Oncology* 106:80-4 [2013]

Plan Comparisons
Normal Tissue Sparing

- IGRT increased parotid doses vs. IMRT
- ART1 reduced IMRT parotid doses in 14/17 cases (p=0.014)
  - Contralateral parotid: -0.6 Gy (p=0.003)
  - Ipsilateral parotid : -1.3 Gy (p=0.002)
- ART2 yielded marginal parotid sparing vs. ART1
  - Contralateral parotid: 0.1 Gy (p=0.8)
  - Ipsilateral parotid: 0.8 Gy (p=0.044)

Schwartz et al *Radiotherapy & Oncology* 106:80-4 [2013]

Plan Comparisons
Normal Tissue Sparing

- ART1 reduced IGRT integral body V60Gy and V40Gy by >40 cc ($p<0.007$)

- Additional replanning (ART2) did not further reduce integral dose ($p>0.3$)

 Schwartz et al *Radiotherapy & Oncology* 106:80-4 [2013]

Clinical Outcomes

- Median follow-up: 31 months (range: 13-45)
- No primary disease site failure and 1 nodal relapse, which was surgically salvaged
- 100% local and 95% regional 2 yr disease control
- Acute toxicity comparable to conventional IMRT
- Long term outcomes continue to improve after 1 yr

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Schwartz DL, et al *IJROBP* 83:986-93 [2012]

MDACC experiences

- IGRT provide no dosimetric benefit with conventional PTV margins
- One properly timed ART replan provides majority of dosimetric improvement
- Preliminary outcomes suggest functional recovery & preservation of disease control

Strategies of Adaptive RT

- Off-line
  - With current treatment planning system
- On-line
  - Normally need some special software/tools

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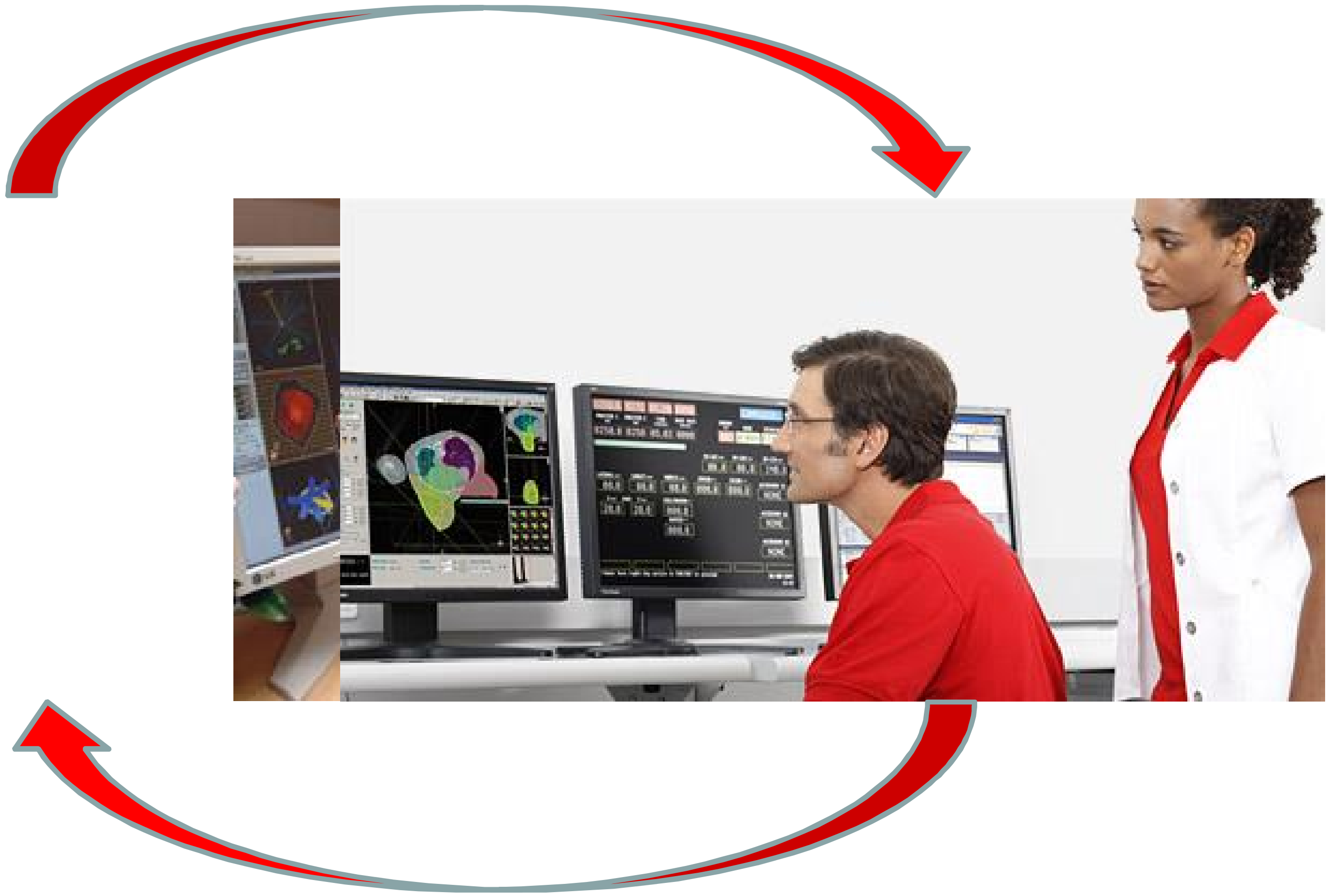
Problems with Current Planning - Low Efficiency



The whole process may take a week !

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MCW - Pancreatic cases

Liu et al, Int J Rad Onc Biol Phys 2012, e423-e429

- Daily imaging - CT on rail
- Contouring - Atlas-based Autosegmentation [ABAS], (Elekta CMS software)
- Re-planning - RealART (Panther version 4.71, Prowess Inc)

More efforts of physicists and physicians.

Medical College of Wisconsin - Pancreatic cases

Liu et al, Int J Rad Onc Biol Phys 2012, e423-e429

Table Dose-volume quantities for adaptive plans

Quantity	Adaptive (3 mm)	Repositioning (10 mm)	Repositioning (3 mm)	p value (10 mm)	p value (3 mm)
CTV V_{100} (%)	99.1 ± 0.6	99.7 ± 0.8	97.8 ± 3.7	<0.0001	0.0004
CTV mean dose (Gy)	52.7 ± 0.7	53.2 ± 0.8	52.8 ± 1.0	<0.0001	0.40
CTV maximum dose (Gy)	54.4 ± 1.2	55.3 ± 1.4	54.8 ± 1.3	<0.0001	0.02
PTV V_{100} (%)	96.0 ± 1.6	93.0 ± 5.0	93.5 ± 6.0	<0.0001	<0.0001
Duodenum $V_{50.4}$ (%)	15.6 ± 6.7	43.4 ± 17.8	23.0 ± 12.0	<0.0001	<0.0001
Stomach V_{45} (%)	1.4 ± 1.2	6.4 ± 3.7	2.3 ± 1.6	<0.0001	<0.0001
Large bowel V_{45} (%)	0.9 ± 1.4	4.7 ± 5.8	1.4 ± 2.6	<0.0001	0.08
Small bowel V_{45} (%)	0.5 ± 0.9	2.4 ± 2.6	0.8 ± 1.9	<0.0001	0.14
Liver $V_{30\ Gy}$ (%)	2.2 ± 2.8	8.8 ± 10.0	3.2 ± 4.1	<0.0001	0.04
Right kidney V_{15} (%)	12.9 ± 9.3	22.4 ± 13.8	13.1 ± 9.5	<0.0001	0.88
Left kidney V_{15} (%)	11.5 ± 5.7	12.1 ± 6.0	9.0 ± 5.4	0.45	0.0012

Table data are mean ± SD values of various dose-volume quantities for the adaptive plans using a 3-mm margin and repositioning plans using 10 mm (default; see text) and 3-mm margins for all selected daily CT sets of 10 patients. p values of an unpaired two-tailed t-test of the two repositioning plans with respect to the adaptive plans are given.

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MCW - Pancreatic cases

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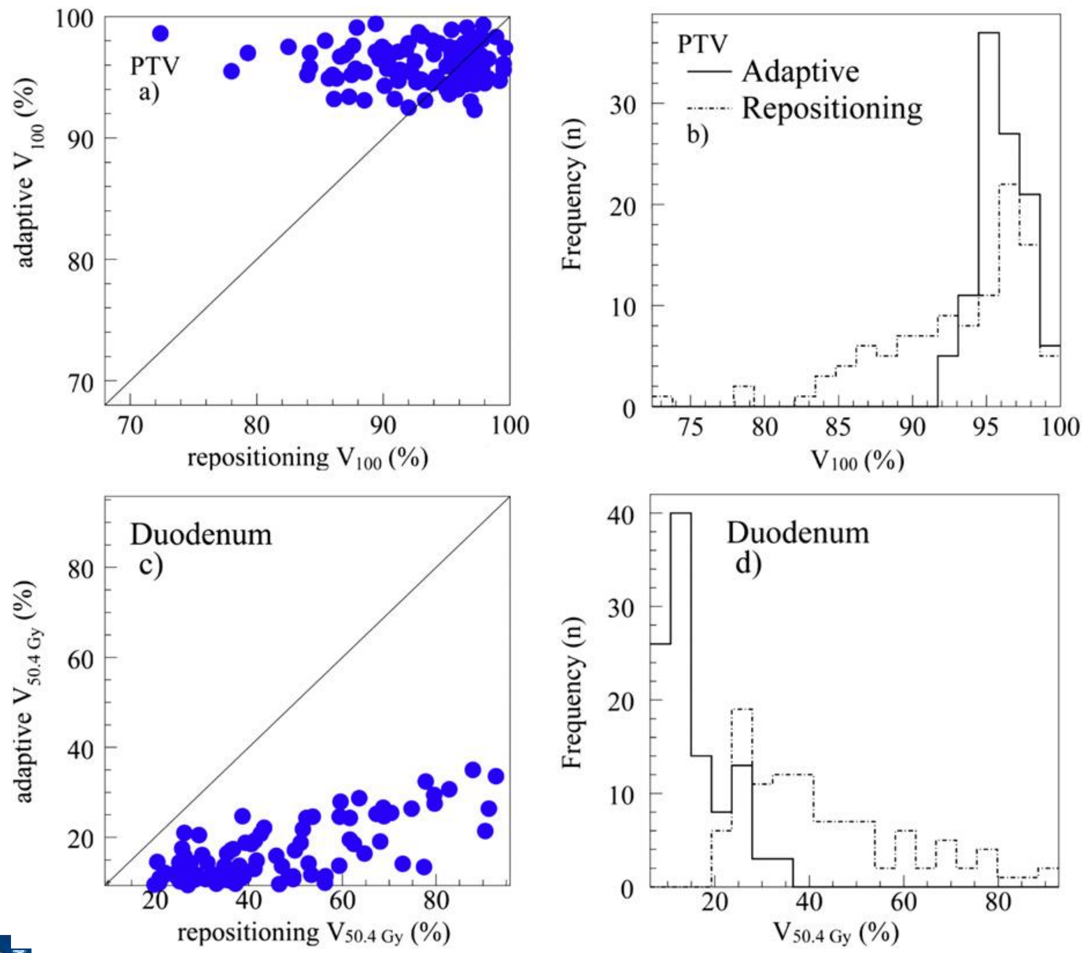

Strategies of Adaptive RT

- Off-line
  - With current treatment planning system
- On-line
  - Normally need some special software/tools
  - Use of GPU cards
    - Improve efficiency for some computational tasks in radiotherapy
    - More importantly, change the way we treat patients

GPU-based Interactive Tuning

Plan review/revision:
days → minutes

Dose Engine #1: GPU-based FSPB model

- ❑ Version 1
  - ð Gu et al *Phys Med Biol.* 54(20):6287-6297, 2009
  - ð Conventional FSPB model
- ❑ Version 2
  - ð Gu et al *Phys Med Biol.* 56(11): 3337-3350, 2011
  - ð With 3D density correction
  - ð Accuracy greatly improved
  - ð Still extremely efficient: <1 s for IMRT, ~15 s for VMAT

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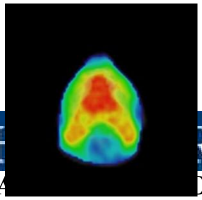
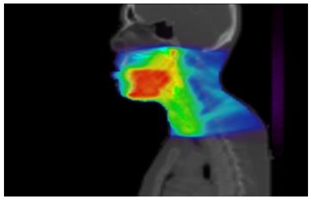
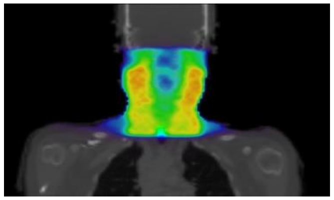
Dose Engine #2: GPU version of DPM MC code

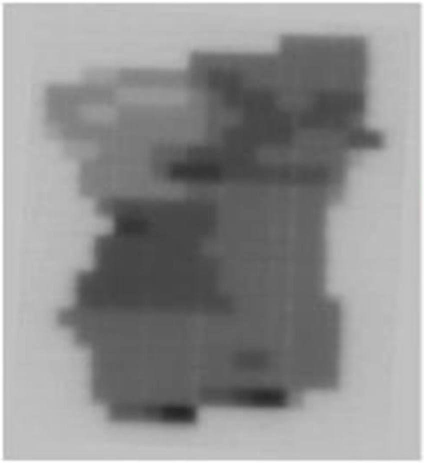
- Version 1
  - Jia et al *Phys Med Biol.* 55(11): 3077–3086, 2010
  - A straightforward implementation
- Version 2
  - Jia et al *Phys Med Biol.* 56(22):7017-7031, 2011
  - More GPU friendly
  - < 30 s for IMRT and VMAT
- Version 3
  - Townson et al *Phys Med Biol.* 58(12):4341-4356, 2013
  - Tian et. al., Phys. Med. Biol. 59, 6467 (2014)
  - Phase space files and commissioning procedure





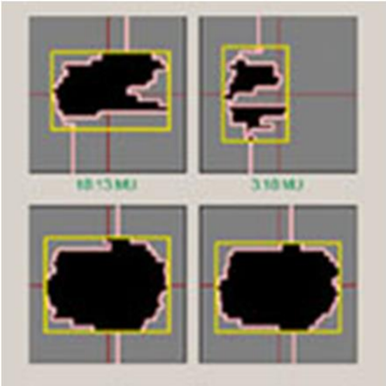


Three GPU-based Optimization Models



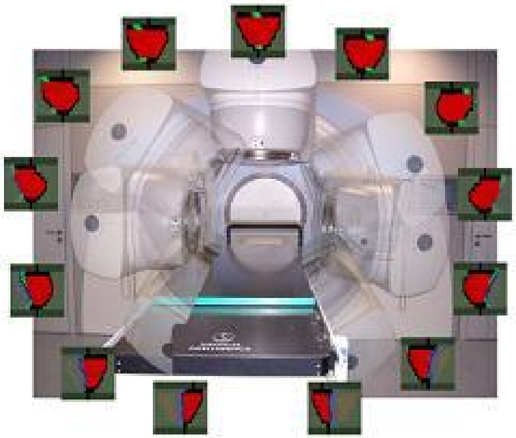
Men et al *Phys Med Biol.* 54(21):6565-6573, 2009

< 1 second



Men et al *Phys Med Biol.* 55(15):4309-4319, 2010

~ 2 seconds



Men et al *Med Phys* 37(11): 5787-5791, 2010

Peng et al *Phys Med Biol.* 57(14):4569-88, 2012

~ 20-60 seconds

Deformable Image Registration (DIR)

- Demons on GPU
  - Gu et al *Phys Med Biol* 55(1): 207-219, 2010
- Contour-guided DIR
  - Gu et al *Phys Med Biol* 58(6):1889-1901, 2013
- CT/CBCT DIR with intensity correction
  - Zhen et al *Phys Med Biol* 57: 6807-6826, 2012

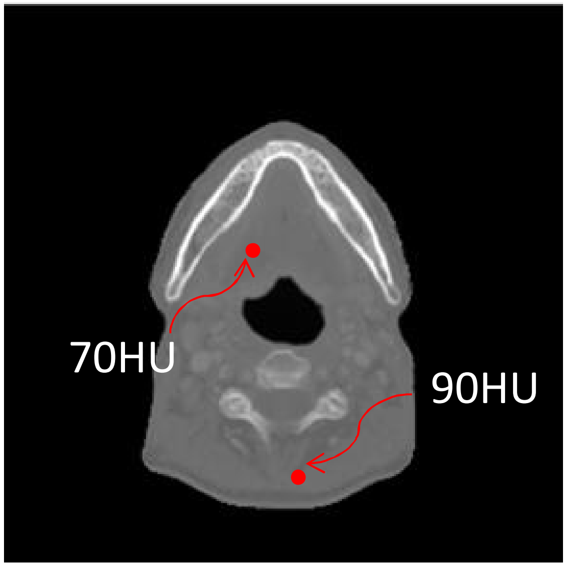
Contour-guided Demons DIR

- After DIR contour propagation, manual inspection and revision (if needed)
- DVF updating for accurate dose accumulation and consistency between DVH and accumulative dose distribution

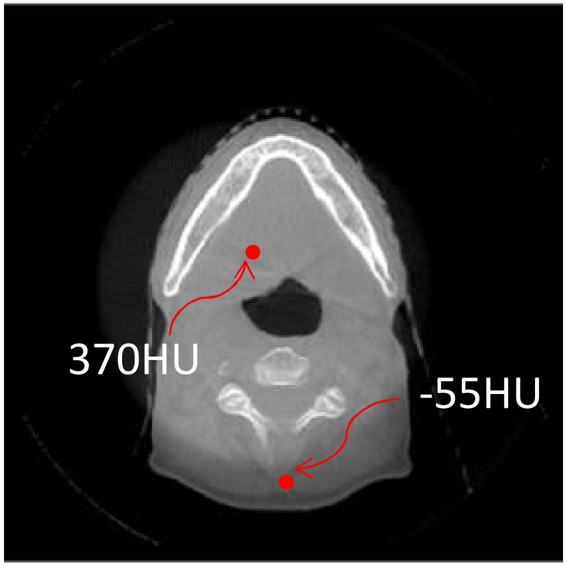
Gu et al, *Phys Med Biol.* 58(6):1889-1901, 2013.

Intensity Inconsistency between CT and CBCT

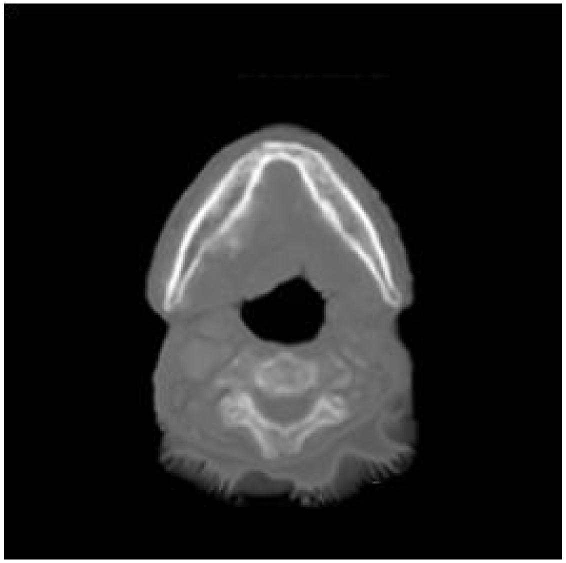
- Scatter artifacts in CBCT
- Bowtie filter artifact
- Different scan geometry
- Different level of noise, beam hardening, etc



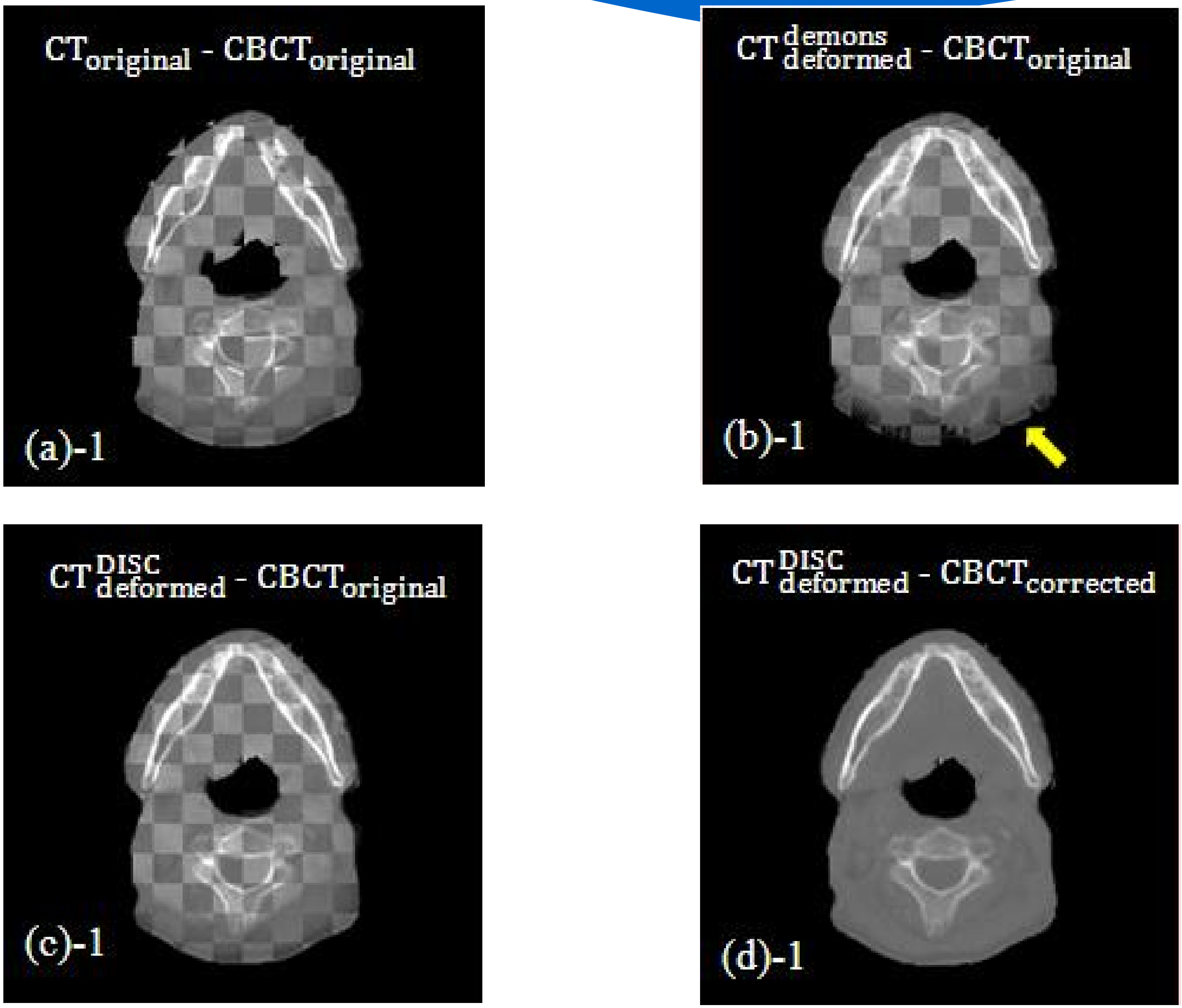
CT



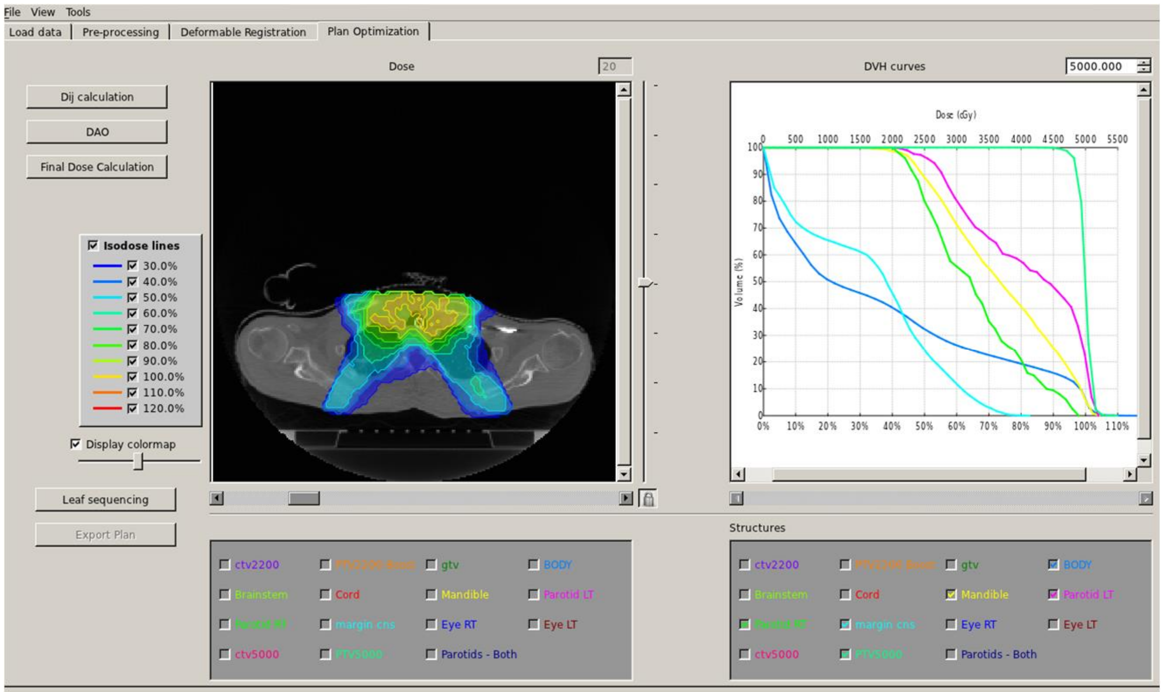
CBCT



Demons: Deformed CT


$CT_{original} - CBCT_{original}$
(a)-1
$CT^{demons}_{deformed} - CBCT_{original}$
(b)-1
$CT^{DISC}_{deformed} - CBCT_{original}$
(c)-1
$CT^{DISC}_{deformed} - CBCT_{corrected}$
(d)-1

SCORE → Supercomputing On-line Re-planning Environment



A GPU-based real-time automatic re-planning system

A research platform for online and offline ART

Clinical studies: H/N, pancreas, GYN, prostate, lung, *etc*

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Online Re-planning - A Paradigm Shift

- Past and current: <u>plan-centered</u>
  - A snapshot of patient anatomy before treatment
  - A treatment plan based on this snapshot
  - Try to match this plan with the patient anatomy throughout the whole treatment course
- Future: <u>patient-centered</u>
  - Automatic plan re-optimization on CBCT every day
  - Setup errors and anatomical variations are considered in the new plan
  - Much smaller PTV margin and faster patient setup

Conclusion

- Adaptive Radiation Therapy should be triggered by dosimetric assessment due to anatomic changes. It will be different due to disease sites.
- Both offline and online adaptive radiation therapy will help improve dose coverage on tumors and sparing normal tissues.

Acknowledgement

- Drs. Steve Jiang and David Schwartz
- Other colleagues at UT Southwestern

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How to decide whether to adapt a treatment

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0% 2. Physicistô s preference

0% 3. Progress of the treatment course

0% 4. Daily imaging

0% 5. Daily dosimetric assessment

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Schwartz, DL et al *Radiotherapy & Oncology* 106:80-4 [2013]

What's the main purpose of adaptive radiation therapy in addition to IGRT

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0%	2. Increase dose to tumor
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0%	4. Increase dose to normal tissues
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What's the major drawback of adaptive radiation therapy in clinical practice

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Liu et al, Int J Rad Onc Biol Phys 83: e423-e429 [2012]

Strategies of How and When to Adapt

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