Strategies of How and When to Adapt

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March 2015
Disclosure

Currently supported by
- 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)
IGRT

Reference Planning CT

Bone Alignment (Daily CT)
Reference Planning CT

Adapt to Anatomy (Daily CT)
Complex Uncertainties—Intrinsic Anatomic Changes

Planning CT

During RT Course

CTV is in the air!
H&N Cancer Treatment Response

Primary tumor response to RT

Tumor

Volume (cc)

Elapsed treatment days

0 7 14 21 28 35 42 49

0 20 40 60 80 100 120 140

Primary tumor response to RT

Lymph nodes response to RT

Lymph nodes

Volume (cc)

Elapsed treatment days

0 7 14 21 28 35 42 49

0 20 40 60 80 100 120 140

Initial volume (%)

Elapsed treatment days

0 7 14 21 28 35 42 49

0 20 40 60 80 100 120 140
Initial Setup Images
Complex Uncertainties—
Neck Curvature

Planning CT

Daily Cone-Beam CT
T3N2 BOT—
Weight Loss @ Fx#20
T2N1 “Young Tongue”—Resolving Oral Edema @ Fx#12
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
CTV-to-PTV Expansions—The Millimeters Matter

\[ \frac{4}{3} \pi r^3 \]

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

Small margins → Accuracy and safety

Large margins → Compensate uncertainties

One size fits all?

One plan won't work well.
ART—An Iterative Process

Prospective Correction
- Auto-segmentation
- Re-planning
  - On-line
  - Off-line

Plan

Deforming doses

Retrospective Evaluation

Final Dose Map
Flowchart of Adaptive Radiotherapy

Planning CT → Plan → Patient Setup → Dose Delivery

Dose Delivery → Planning CT → Plan → Daily 3D Imaging → Plan Evaluation

Plan Evaluation
- Acceptable
- Unacceptable → Re-planning → Plan QA
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
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
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
- Weekly—MD evaluation of daily in-room imaging
ART Clinical Workflow

- **Insurance approval**
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- **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

- **Weekly**—MD evaluation of daily in-room imaging

- **Replanning**—Largest resource burden
  - Dosimetry/Physics
  - MD dictates sim note to document billing
  - 1-2 replans
Weekly Contour Evaluation for ART

Original Contours and Deformed Contours on Current CT

Original Contours on Original CT
ART Replan DVH Evaluation
ART Replan Evaluation
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
Practical Issues in Adaptive RT

What is the trigger point for replanning?

![Dose Volume Histogram](image-url)
Practical Issues in Adaptive RT

What should trigger replanning?

- Underdosing to target volumes
- Overdosing to organs at risk
- Elimination of hot spots
- 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
  - 0-mm PTV margins

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)
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

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
Problems with Current Planning - Low Efficiency

The whole process may take a week!
MCW - Pancreatic cases


- 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


## Table: Dose-volume quantities for adaptive plans

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

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.
MCW - Pancreatic cases

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 $\rightarrow$ minutes
Dose Engine #1: GPU-based FSPB model

- **Version 1**
  - Conventional FSPB model

- **Version 2**
  - With 3D density correction
  - Accuracy greatly improved
  - Still extremely efficient: <1 s for IMRT, ~15 s for VMAT
Dose Engine #2: GPU version of DPM MC code

- **Version 1**
  - A straightforward implementation

- **Version 2**
  - More GPU friendly
  - < 30 s for IMRT and VMAT

- **Version 3**
  - Phase space files and commissioning procedure
Three GPU-based Optimization Models

< 1 second

~ 2 seconds

~ 20-60 seconds
Deformable Image Registration (DIR)

- Demons on GPU

- Contour-guided DIR

- CT/CBCT DIR with intensity correction
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

Intensity Inconsistency between CT and CBCT

- Scatter artifacts in CBCT
- Bowtie filter artifact
- Different scan geometry
- Different level of noise, beam hardening, etc
DISC i  Deformation Intensity Simultaneously Corrected
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
Online Re-planning - A Paradigm Shift

- **Past and current: plan-centered**
  - 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: patient-centered**
  - 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
How to decide whether to adapt a treatment

0% 1. Physician’s preference
0% 2. Physicist’s preference
0% 3. Progress of the treatment course
0% 4. Daily imaging
0% 5. Daily dosimetric assessment
How to decide whether to adapt a treatment

1. Physician’s preference
2. Physicist’s preference
3. Progress of the treatment course
4. Daily imaging
5. Daily dosimetric assessment

Schwartz, DL et al *Radiotherapy & Oncology* 106:80-4 [2013]
What’s the main purpose of adaptive radiation therapy in addition to IGRT

0% 1. Collect more money from patients
0% 2. Increase dose to tumor
0% 3. Reduce dose to tumor
0% 4. Increase dose to normal tissues
0% 5. Reduce dose to normal tissues
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What’s the major drawback of adaptive radiation therapy in clinical practice

0% 1. Need acquire daily imaging
0% 2. Much more efforts from physicians/physicists
0% 3. Billing code is not available
0% 4. Need perform QA of new plans
0% 5. Longer treatment time may disturb clinical treatment flow
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