What do we Know About Adaptive Radiotherapy?

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San Diego, California
San Diego, CA Weather Advisories, Watches & Warnings

SPECIAL WEATHER STATEMENT
in effect until Saturday, Sep 15, 7:00 PM

...HOT WEATHER CONTINUES ACROSS SOUTHWEST CALIFORNIA TODAY...
Learning Objectives

- To gain a working definition of adaptive radiotherapy (ART);
- To understand the technical and process components needed for adaptive therapy;
- To learn about different time scales (offline/online) for plan adaptation.
What is adaptive radiotherapy?
Adaptive
“Definition”

"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).
Adaptive radiotherapy requires that a new radiation plan be made for the patient, and can occur at three different timescales:

- offline between fractions;
- online immediately prior to a fraction;
- in real time during a fraction.
Conventional workflow

- Simulation
- Planning
- Treatment
Concept of Treatment Planning

Goal: To design a treatment plan based on an anticipated patient treatment

- Requirements
  - Accurate model of the patient
  - CT or 4DCT of the patient in treatment position
  - Accurate margin prediction
  - Balance of risk and benefit
  - Presentation of simulation results
  - DVHs, Isodose lines
The initial simulation CT is perhaps the most biased representation of patient’s anatomy!
Is one CT before treatment good enough for planning?
Is one DVH enough to accept the plan?
90% of daily bladder volumes are smaller than the volume at the simulation!
Bladder DVH Variations during Daily Treatment

Error bar (± 1SD) was calculated based on 24 serial CT images.
Significant Anatomic Variations

Planning CT

During Treatment

CTV is in the air!

RTOG H0022 Case
Impact of Tumor Shrinkage on Proton Dose Distribution

- Original Proton Plan
- Dose recalculated on the new anatomy

Bucci/Dong et al. ASTRO Abstract, 2007
A single plan designed before treatment is insufficient to describe the actual delivered doses, and often leads to suboptimal treatment.
What is IGRT and what can IGRT do?
Essential Components for IGRT

- Acquire an image inside a treatment room
  - Acquire the positional information of the target, target surrogates, or avoidance structures
- Obtain “target” registration error
  - Rigid image registration
  - Detect positional deviations from the original plan
- Perform an intervention
  - Move the isocenter
In-Room Imaging

**Ultrasound**
- BAT
- SonArray
- I-Beam
- Restitu

**Video-Based**
- Video Subtraction
- Photogrammetry
- AlignRT
- Real-Time Video-Guided IMRT

**Planar X-Ray**
- EPID
- CyberKnife
- Novalis
- RTRT
- Gantry-Mounted
  - Prototype
  - Tohoku, IRIS
- Commercial
  - Varian OBI
  - Elekta Synergy

**Volumetric**
- In-Room CT
- FOCAL, MSKCC
- CT-on-Rails
- Primaton
- Varian ExaCT
- Tomotherapy
- MV Cone Beam CT
  - Siemens
- kV Cone Beam CT
  - Mobile C-arm
  - Varian OBI
  - Elekta Synergy
  - Siemens In-Line

**Related Technologies**
- RPM gating/4DCT
- Optical-guided Approaches

AJ Mundt/UCSD
Alignment Process

Planning CT

Planning Contours

Planning Isocenter

Treatment CT

Treatment Image

Move Iso

Move Couch

$\Delta r$

$-\Delta r$
What IGRT can’t do well?
Change in the Neck Curvature

Planning CT

Daily Cone-beam CT with planning contour overlay
Examples of anatomy rotation between the planning CT (first row) and the daily CT (second row). The axial CT images shown on the left indicate a roll in the patient’s head; the coronal CT images on the right show yaw (rotation of the spinal column).
Setup Uncertainties In Head & Neck Treatment

Patient with Tongue Base Carcinoma
19 CT Scans over 47 Days

Lei Dong et al. (MDACC)
Setup uncertainties in sub-regions of H&N anatomy
Increased deformation with longer distances from the reference (C1-C3)
Impact of ROI Selection for Patient Setup

Cumulative score of mean setup error vector length (38 patients)

cumulative occurrence (in %) →

mean setup error vector length (mm) →

-5 mm setup error

Kranen et al., IJROBP, V73, pp1566 (2009)
Target Volume Increases
- Can’t be corrected by simple couch shifts
**Physics Contribution**

**Assessment of Parotid Gland Dose Changes During Head and Neck Cancer Radiotherapy Using Daily Megavoltage Computed Tomography and Deformable Image Registration**

_Coonik Lee, Ph.D.,* Katja M. Langen, Ph.D.,* Weiguo Lu, Ph.D., ‡ Jason Haimerl, M.S., ‡ Eric Schnarr, Ph.D., ‡ Kenneth J. Ruchala, Ph.D., ‡ Gustavo H. Olivera, Ph.D., ‡ Sanford L. Meeks, Ph.D.,* Patrick A. Kupelian, M.D.,* Thomas D. Shellenberger, M.D., D.M.D., ‡§ and Rafael R. Mañon, M.D.*

Departments of *Radiation Oncology and ‡Head and Neck Surgery, M. D. Anderson Cancer Center Orlando, Orlando, FL; ‡TomoTherapy, Inc., Madison, WI; and ‡§Department of Head and Neck Surgery, The University of Texas M. D. Anderson Cancer Center, Houston, TX

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week-by-week bony alignment

Ref: 2010-06-30

Daily: 2010-07-12

Daily: 2010-07-19

Daily: 2010-07-26

Daily: 2010-08-02

Daily: 2010-08-11
Image guidance (to move isocenter) can’t not fully correct for non-rigid changes
Image Guidance vs. Adaptive RT

- “Image Guidance” is commonly referred to a process to re-position the patient without modifying the initial treatment plan.
- Adaptive RT involves the modification of the initial plan, including:
  - Changing beam apertures or intensity patterns.
- Image-guidance and adaptive RT are commonly used together.
ART and delivered dose evaluation

**Prospective Correction**
- Cumulating doses
- Auto-segmentation via non-rigid image registration
- Online/offline replanning

**Retrospective Evaluation**
- Isodose line deformation
- Cumulative calculation of true doses

**Final Dose**

**Daily Dose**
What is deformable (non-rigid) registration?
Deformable image registration is a voxel mapping process
What is deformable image registration?

- Non-rigid Image Registration
  - Finding the geometric correspondence of the same point in two images.

- Approaches
  - Feature-based (control points, thin-plate spline etc.)
  - Model-based (finite element method etc.)
  - Image-intensity based (optical flow, diffusion method, free-form etc.)
A Pictorial Tour of Deformable Image Registration

Radhe Mohan, Ph.D.
Chairman of Radiation Physics

Bill Gates
Chairman of Microsoft
Deformable image registration + Image fusion
Deformable image registration is an ill-defined problem

- There is no unique solution (degeneracy)
  - Similar voxels can be grouped differently based on different rules.

- There is only one truth
  - Usually we don’t know the ground-truth!
Specifications for DIR

- Accurate (close to “real”)
  - Topology reserved
    - Neighborhood relationship (connectivity, orientability etc.)

- Robust (tolerance to variations)
  - inconsistency in voxel intensities
    - Example: CT vs. CBCT
    - Example: rectal gas

- Fast (automated)
Prostate Radiotherapy

Planning contours mapped to 24 in-room CTs

Planning contours were automatically transformed to subsequent 15 (daily) CT images.
4D CT Contour Propagation

Transverse

Sagittal

Coronal

Dong et al.
A workflow diagram for in-room CT-guided adaptive radiotherapy.
Study Goals

- Develop a practical procedure for IGART
- Evaluate the dosimetric benefits of a hybrid (on-line image guidance + off-line adaptive) approach for head & neck radiotherapy
- Evaluate clinical workflow and practical aspects of ART in a prospective trial
- Evaluate the improvement in outcome
Methods

- 22 patients treated according to IRB-approved, NCI-supported clinical trial.
- Stage III-IVa oropharyngeal SCCA.
  - Functional QOL outcome measures
- Baseline standard IMRT (3-mm PTV margins)
  - 66Gy/30 (-CTX) or 70Gy/33 (+CTX); CTV1/2/3
- Daily in-room CT-on-Rail imaging with IGRT
- Weekly off-line plan re-evaluation
- One (ART1) or two (ART2) adaptive replans
  - 0-mm PTV margins
Daily CT-guided C2-bone Setup

Bone Alignment

Patient #2
Methods—IGRT vs. ART

Reference Planning CT

Bone Rigidly Aligned Daily CT

Deformed Contours to Match with the Daily CT
Methods

• Compared 4 planning scenarios
  • (1) the original IMRT plan aligned to the marked isocenter (BB)
  • (2) the original plan aligned according to daily bone alignment (IGRT)
  • (3) IGRT with one adaptive replan (ART1)
  • (4) actual treatment received (IGRT with one or two adaptive replans, ART2).

• Cumulative dosimetry was calculated by deformably mapping daily doses retrospectively back onto original plans.
Adaptive Replanning

• All cases underwent ART1
• Elapsed time CT to ART: 1.7 days
• Median 1\textsuperscript{st} replan: 16th fraction
• Mean parotid volume change at ART1: -16%
• Mean CTV change at 1\textsuperscript{st} replan: -5%
• 8 (36\%) cases underwent ART2
  • Median start for the 2\textsuperscript{nd} plan: 22\textsuperscript{nd} fraction
  • Mean parotid volume change: -24%
  • Mean CTV change: -14%
  • Median start for the 1\textsuperscript{st} plan: 11\textsuperscript{st} fraction
Timing of ART

![Histogram showing frequency of first and second replanning fractions.](image-url)
Early Adaptation – Fraction #1!

Original Plan 1st Treatment Fraction

Pat No.L
Early Replan – Fraction #1!

Original Plan

1st Treatment Fraction
An Example

-40%  -30%  -20%  -10%  0%  10%  20%  30%  40%

CTV70 % Change
CTV63 % Change
CTV57 % Change
Left Parotid % Change
Right Parotid % Change

Re-Plan1
Re-Plan2
Cumulative DVH after 33 fractions

Patient #1

Solid – daily treatment
Dash – Original Plan
BB Alignment

Dotted – Org Plan

Patient #4
Bone Alignment

Dotted – Org Plan
Re-plan Once

Dotted – Org Plan
Re-plan Twice

Dotted – Org Plan

Dose Volume Histogram

Fx33

Norm. Volume

Dose (cGy)

Patient #4
Early Conclusions

• IG-ART is feasible for H&N
• IGRT alone does not provide meaningful dosimetric benefit if conventional PTV margins are used.
• One properly timed adaptive replan (ART1) provided all relevant dosimetric improvements in this study.
• Clinical outcomes continue to be collected.
Is IG-ART ready for prime time?
Practical Issues in Adaptive RT

- Where do you find a physician to review your plan?
Practical Issues in Adaptive RT

- Record & Verification system slows the replanning process
- Documentation requirements for new plan
- Billing?
Other forms of adaptive RT

- **Anatomic = morphological**
  - the form and structure of organisms and their gross structural features
  - CT, T1-MRI?

- **Physiological = functional**
  - How organs or cell systems carry out the chemical or physical functions in a living system
  - PET, T2-MRI, DCE MRI…
ART – Modifying original prescription based on up-to-date biological information of the target
Emerging Biological/functional imaging for ART

Biological Target Volume?

GTV → PTV

- PET
- F-miso
- Hypoxia

- MRI/MRS
- choline/citrate
- Tumor burden

- PET
- IUoDR
- Tumor growth

Eye View

PTV

Biol. Tgt. Volume

C. Ling et al. IJROBP Vol. 47 No. 3 p551, 2000
Role of Functional Imaging
EARLY PREDICTION OF OUTCOME IN ADVANCED HEAD-AND-NECK CANCER BASED ON TUMOR BLOOD VOLUME ALTERATIONS DURING THERAPY

Blood volume maps (DCE-MRI) after 2 weeks of RT

Gained local control

Failed local control

Dose Painting By Numbers
(More accurate imaging and targeting are required for non-uniform dose prescriptions)

Functional Imaging is rarely tumor specific

- Neither FDG nor FLT are tumor specific
- Nonspecific uptake has been seen with virtually all PET tracers
- Particularly in post-radiation therapy setting, the infiltration of FDG avid macrophages, inflammation, reactive lymph nodes,…
- Image processing techniques from raw signals to biological signals
Anatomy and Physiology are tied together

- Anatomy, the study of form and structural features, and physiology, the study of function, are intrinsically tied.
- Functional images must be fused with anatomical images to provide meaningful interpretation and quality assurance.
- A treatment plan must be calculated on a CT-equivalent anatomy.
“One should still realize that no form of biological imaging is capable of showing tumor deposits that are small relative to the resolution of the scanners (which is, for instance, at best 5 mm for PET). This means that tumor deposits on a microscopical level cannot be visualized and may be missed, and moreover that dose painting based upon biological images showing radioresistant areas (i.e., hypoxia) at a low resolution may be suboptimal. In addition, the complexity of the tumor biology makes the interpretation of molecular images far from trivial”
Timing of Adaptive Radiotherapy

- **Image-guidance is a “near real-time” online isocenter correction method**

- **Offline Adaptive Radiotherapy**
  - Minimum lag time is 1 day

- **Online Adaptive Radiotherapy**
  - Replanning and use the new plan for the current treatment session
Daily IGRT is very effective in correcting target positions

Is the center of tumor more important than the edge?
Illustration of Target Registration Error
Boundary of target is more vulnerable than the center of target
Early Replan – Fraction #1!

Original Plan

1st Treatment Fraction
week-by-week bony alignment

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Requirements for Online ART

- Fast imaging
- Fast target and normal tissue delineation
- Auto-planning
- Fast QA or real-time beam verification
- Intra-fractional management
Is technology ever a bottleneck?
SCORE: A GPU-based Re-planning System for Online Adaptive Radiotherapy

Steve Jiang, Ph.D.
GPU → Graphics Processing Unit
GPU based Online ART

- Imaging and reconstruction: 1 min
- Target and normal tissue delineation: 10s
- Auto-planning: 1 min
- Fast QA or real-time verification: ?
Online Adaptive ART Available Today!

Online Adaptive Radiotherapy for Prostate Cancer: Clinical Implementation and Initial Experience

X. Allen Li
E. Ahunbay, C. Peng, G. Chen, F. Liu, C. Lawton

AAPM, 10:30AM, Ballroom A, Aug. 4, 2011
Online ART

1. Image Acquisition via CT-on-Rails
2. Contour generation (auto segmentation with manual editing) - 2-5 min
3. Segment Aperture Morphing (SAM) & Segment Weight Optimization (SWO) - 2 min
4. Dose/DVH evaluation and comparison - 1 min
5. ART plan transferring & QA verification with software - 2 min
6. Delivery and documentation

8-12 min for prostate, comparable to current repositioning !!!

Implemented in RealArt by Prowess Inc

A X. Li (MCW)
Software tools for QA prior and after delivery: verifying MU#, plan data transferring and actual delivery
Benefits of Online Adaptive Radiotherapy

- Correction for non-rigid anatomical changes beyond image guidance
- Further improvement in conformality of the delivered plan
  - Reducing margin requirements for IGRT
  - Reducing normal tissue dose
  - Dose-guided, instead of anatomy based
  - Correction for acute biological changes
<table>
<thead>
<tr>
<th>Problems</th>
<th>IGRT Offline</th>
<th>ART Online</th>
<th>ART Online</th>
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<tr>
<td>Daily target position</td>
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Summary for Applications of ART

- Correct for deficiencies in the simulation process
- Correct for non-rigid anatomical changes beyond image guidance
- Further improve the conformality of the delivered plan
- Creating better conformal treatments
  - Reduce margin requirements for IGRT
  - Reduce normal tissue dose by treating a smaller target volume
Adaptive Radiotherapy is a nature progress towards truly personalized radiation medicine.

Potential clinical gains outshine near-term difficulties.
ART and Teenage Sex

😊 It is on everybody's mind all the time,
😊 Everyone is talking about it,
😊 Everyone thinks everyone else is doing it,
😊 Almost no one is really doing it,
😊 The few who are doing it are:
   😊 Doing it poorly;
   😊 Sure it will be better next time.
Adaptive?