Online Adaptive Radiotherapy: Are We Ready?

Lei Dong, Ph.D.
Dept. of Radiation Physics
University of Texas MD Anderson Cancer Center, Houston, Texas

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Disclosure

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  - Philips
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- NIH/NCI Grants
  - Adaptive RT for H&N
  - Proton Therapy
- State of Texas Grant
  - Adaptive RT for Lung Cancer

Objectives

- Demonstrate advantages and limitations of adaptive radiotherapy
- Understand various forms of adaptive radiotherapy
- Discuss practical issues related to clinical implementation

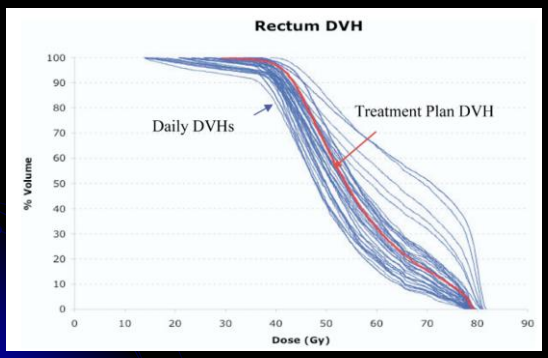
Concept of Treatment Planning

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

- **Requirements**
  - **Accurate target delineation**
    - **normal structure delineation and dose tolerance**
  - **Accurate model of the patient**
    - **CT or 4DCT of the patient in treatment position**
  - **Accurate margin prediction**
    - **Balance of risk and benefit**

The initial simulation CT is perhaps the most biased representation of patient's anatomy!

Is one DVH enough to accept the plan?

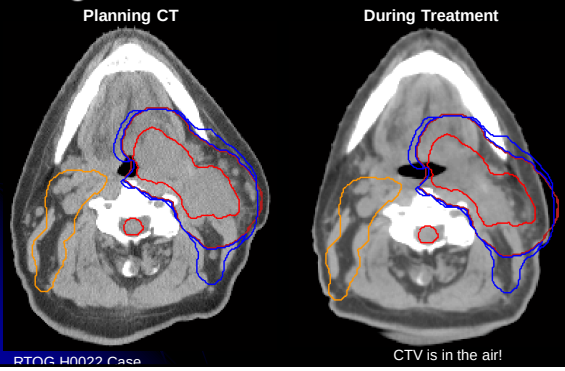


KUPELIAN et al. IJROBP vol.66, pp876 (2006)

Significant Anatomic Variations

Planning CT

During Treatment



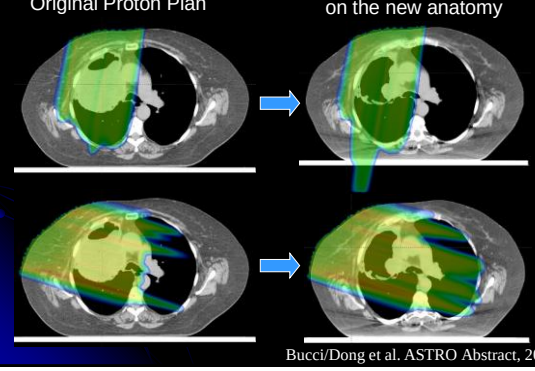
RTOG H0022 Case

CTV is in the air!

Impact of Tumor Shrinkage on Proton Dose Distribution

Original Proton Plan

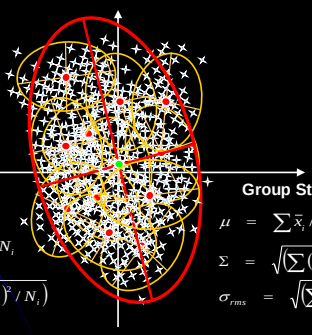
Dose recalculated on the new anatomy



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.

Margins are based on random and systematic uncertainties of population



Individual Patient Statistics

$$\bar{x}_i = \sum (x - x_{ref}) / N_i$$

$$\sigma_i = \sqrt{\left(\sum (x - x_{ref})^2 / N_i\right)}$$

Group Statistics

$$\mu = \sum \bar{x}_i / N$$

$$\Sigma = \sqrt{\left(\sum (\bar{x}_i - \mu)^2 / N\right)}$$

$$\sigma_{rms} = \sqrt{\left(\sum (\sigma_i)^2 / N\right)}$$

Population margin is too big for highly conformal therapy

"Definition"

"Online Adaptive radiotherapy" is defined as changing the radiation treatment plan delivered to a patient during a treatment session to account for temporal changes in anatomy (e.g. tumor shrinkage, weight loss or internal motion) or changes in tumor biology/function (e.g. hypoxia).

"Definition"

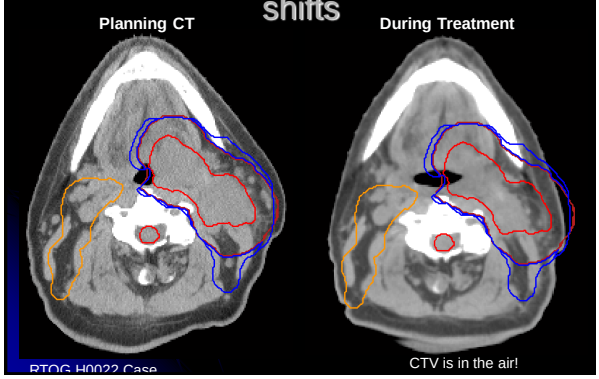
Online Adaptive Radiotherapy:

- online "near real-time" prior to a fraction
- In real time during a fraction

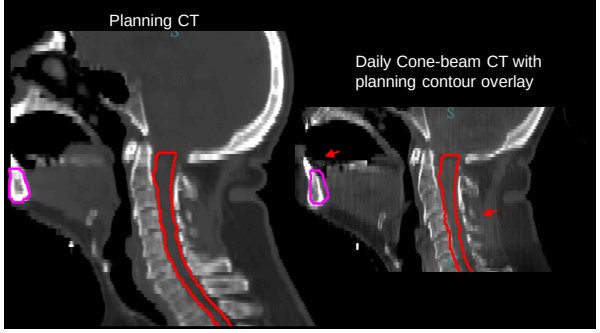
Image Guidance vs. Adaptive RT

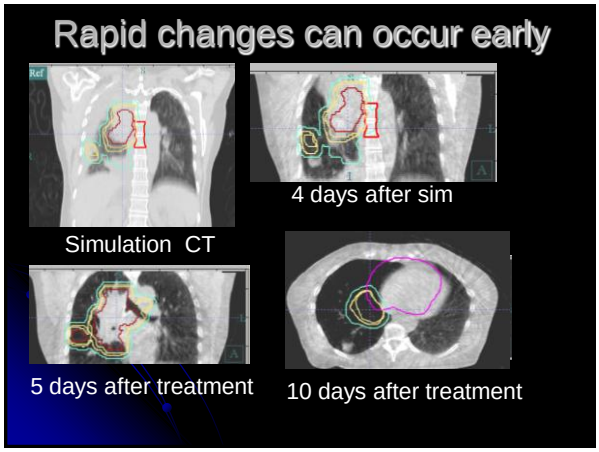
- "Image Guidance" is commonly referred to a process to re-position the patient without modifying the initial treatment plan
- Adaptive RT involves the modification of the initial plan, including

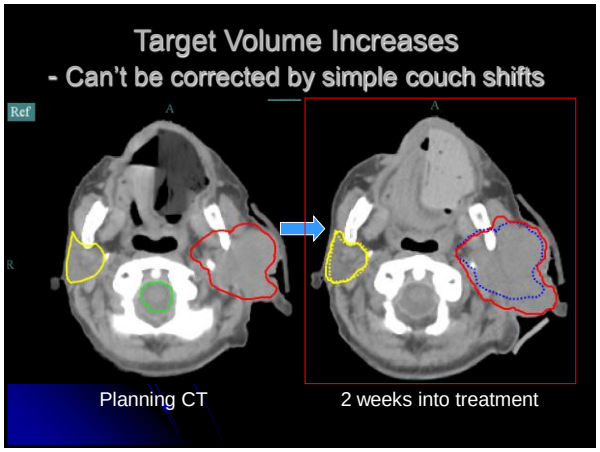
Can't be corrected by simple couch shifts

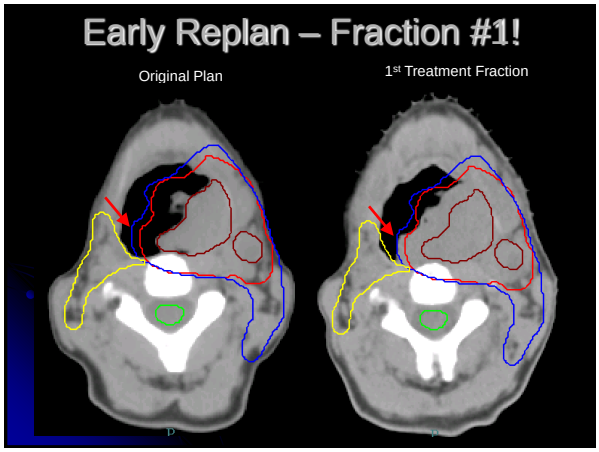


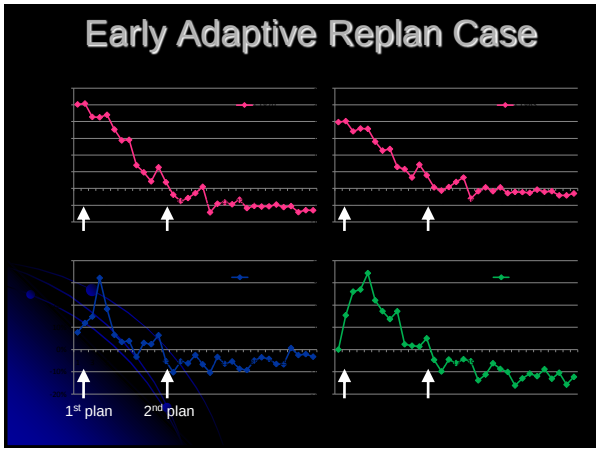
Non-rigid bony structure changes - Can't be corrected by simple couch



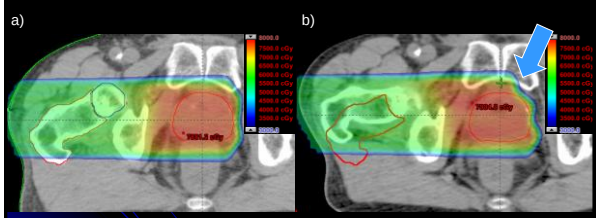

Rapid changes can occur early
Simulation CT
4 days after sim
5 days after treatment
10 days after treatment


Target Volume Increases
- Can't be corrected by simple couch shifts
Ref
Planning CT
2 weeks into treatment


Early Replan – Fraction #1!
Original Plan
1st Treatment Fraction


Early Adaptive Replan Case
1st plan
2nd plan

Anatomy Changes Along Beam Path in Proton Therapy

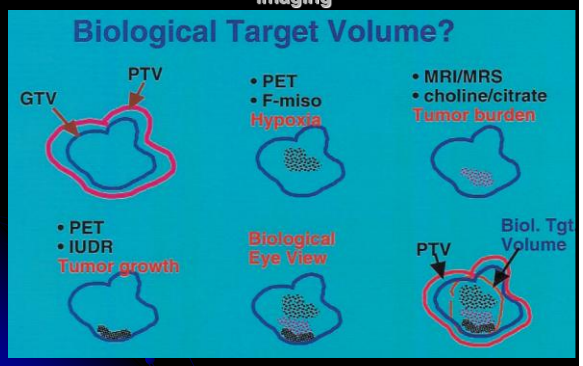


Original Plan Daily CT

Benefits of Online Anatomy-based 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

Adaptive Radiotherapy with Emerging Biological/functional imaging

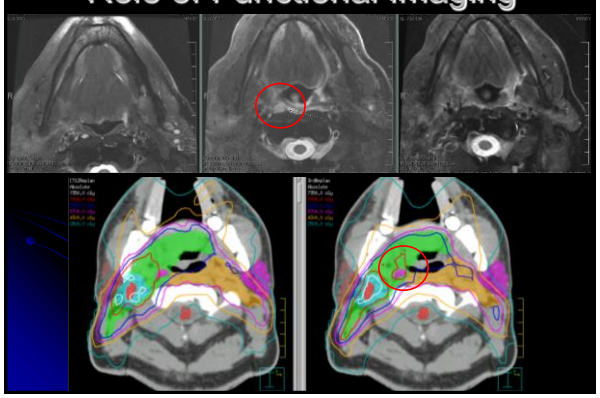


C. Ling et al. IJROBP Vol. 47 No. 3 p551, 2000

Adaptive Boost Treatment of Biological Target Volume

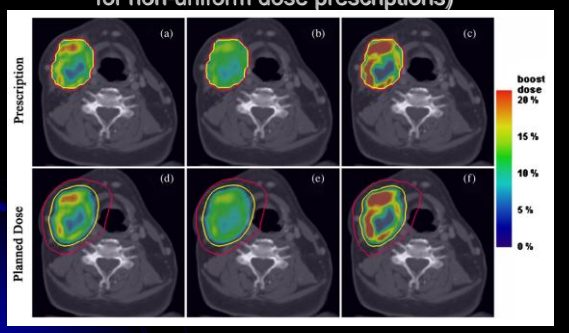
- Bentzen (Lancet Oncol 2005)
  - A partial GTV boost may be even more appealing if we can determine the parts of the GTV at the highest risk of failure because of high clonogen density, proliferation rate, hypoxic content, or low cellular radiosensitivity.
- Geets et al. (Radiother Oncol 85 (2007))
  - FDG-PET-based and adaptive IMRT planning reduced the irradiated volumes by 15–40% compared to pretreatment CT planning.

Role of Functional Imaging



Dose Painting By Numbers

(More accurate imaging and targeting are required for non-uniform dose prescriptions)



Brown SR et al. PMB 54 (2009) 1483–1501

Biologically targeted adaptive therapy

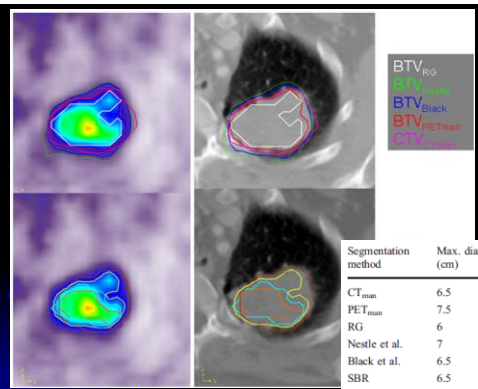
- Up-to-date treatment response information
- Further reduction in target volume

Limitations of Functional Imaging

Table 1 Summary of main pros/cons of the various categories of PET image segmentation techniques

Category	Characteristics	Limitations
Manual techniques	Visual interpretation and manual delineation of contours. Very simple to use. Tools to transfer RT objects to treatment planning systems available from most vendors	Time consuming. Susceptibility to window level settin Suffer from intra- and inter-observer variability. Con reading by nuclear medicine physician and radiation oncologist hardly practical in busy clinical departme
Thresholding techniques	Most frequently used due to their simple implementation and high efficiency	Hard decision making. Too sensitive to PVE, tumour heterogeneity and motion artefacts. Some methods f volume, others focus on intensity differences. Comb of both seems to provide best results [95]
Variational approaches	Subpixel accuracy, boundary continuity and relatively efficient. They are mathematically well developed and allow for incorporation of priors such as shape	Sensitive to image noise. As a PDE, stability and con could be subject to numerical fluctuations, especially parameters are not properly selected
Learning methods	Utilize pattern recognition power. Two main types: supervised (classification) and unsupervised (clustering)	Computational complexity especially in supervised m which require time-consuming training. Feature sele besides commonly used intensity is a flexibility but a challenge
Stochastic models	Exploit statistical differences between tumour uptake and surrounding tissues. Most natural to deal with the noisy nature of PET	Effect of initialization and convergence to local optim solutions are concerns, especially when compromise to improve efficiency

PET-guided delineation of treatment volume: a survey of image segmentation method. Zaidi et al. Eur J. Nuc Med Mol Imaging (2010) 37:2165-2187



Segmentation method	Max. diameter (cm)	Volume (cc)
CT_{man}	6.5	98
PET_{man}	7.5	80
RG	6	61
Nestle et al.	7	138
Black et al.	6.5	117
SBR	6.5	65
FCM	4.8	32
FCM-S	5.5	45
FCM-SW	6.5	76

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

Vol 453|12 June 2008|doi:10.1038/nature06976 nature

REVIEWS

What we can do and what we cannot do with fMRI

Nikos K. Logothetis[1]

Acta Oncologica, 2008; 47: 1186–1187

inform healthcare

EDITORIAL

Will IGRT live up to its promise?

MARCEL VAN HERK

The Netherlands Cancer Institute/Antoni van Leeuwenhoek Hospital, Amsterdam, the Netherlands

Marcel van Herk (2008)

- "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"

Time Requirement for Online ART

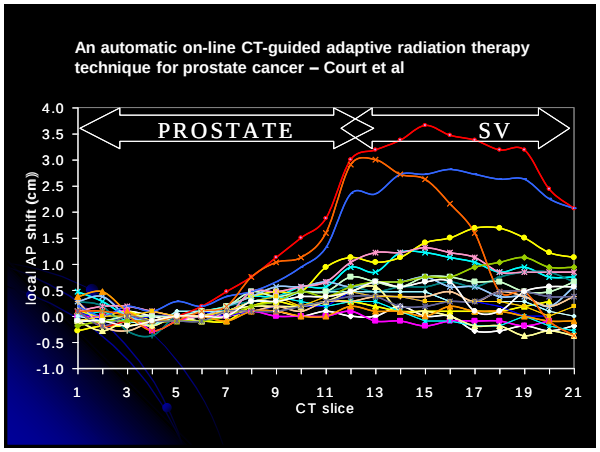
- Imaging
- Target and normal tissue delineation
- Auto-planning
- Fast QA or real-time verification
- Intra-fractional management
  - ART for beam-by-beam delivery

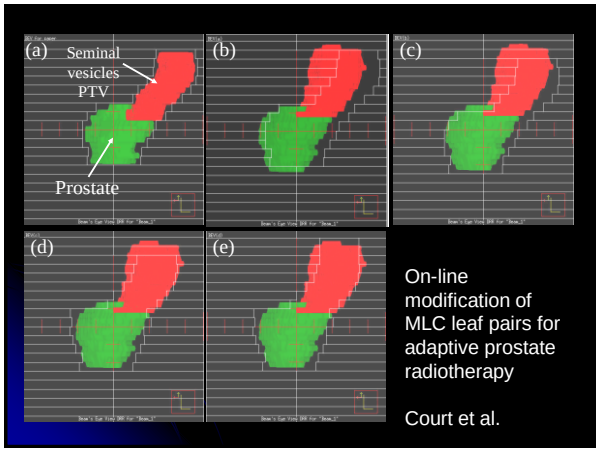
Adaptive Radiotherapy: Correction Techniques

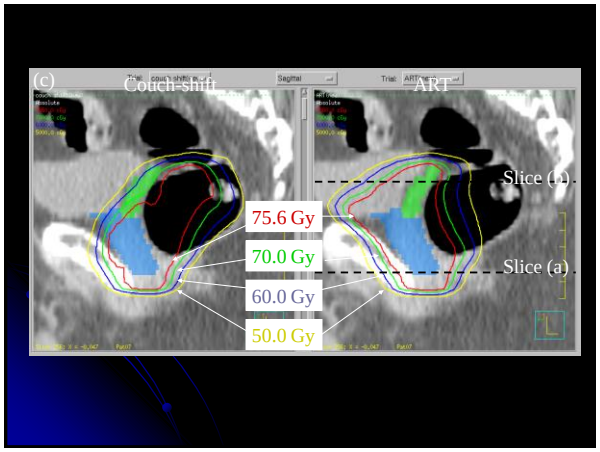
AN AUTOMATIC CT-GUIDED ADAPTIVE RADIATION THERAPY TECHNIQUE BY ON-LINE MODIFICATION OF MULTILEAF COLLIMATOR LEAF POSITIONS FOR PROSTATE CANCER

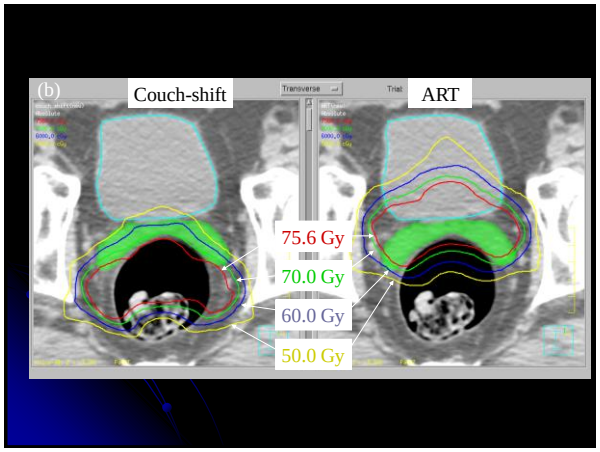
Laurence E. Court, Ph.D., Lei Dong, Ph.D., Andrew K. Lee, M.D., Rex Cheung, M.D., Mark D. Bonnen, M.D., Jennifer O'Daniel, M.S., He Wang, Ph.D., Radhe Mohan, Ph.D., and Deborah Kuban, M.D.

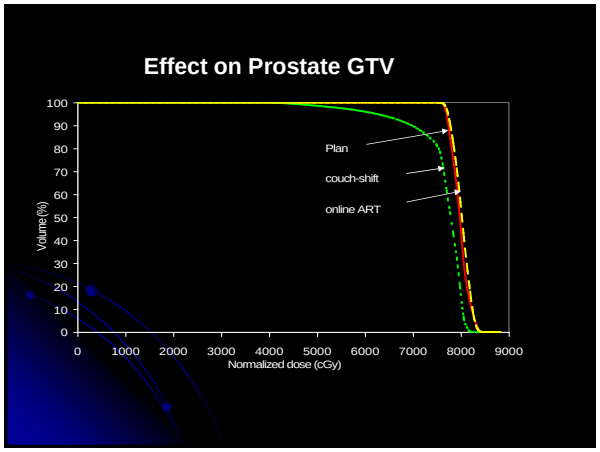
2004

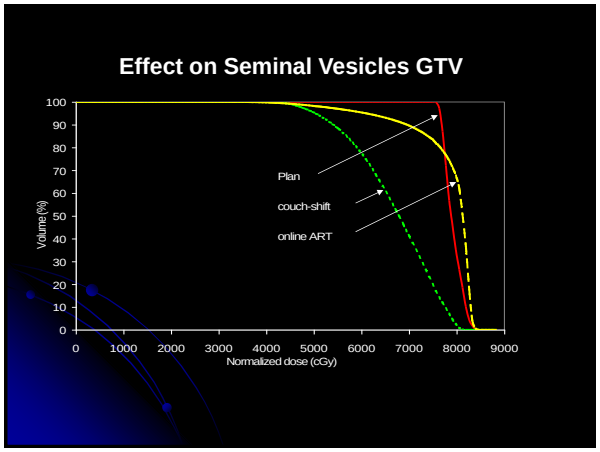

An automatic on-line CT-guided adaptive radiation therapy technique for prostate cancer – Court et al
PROSTATE
SV
local AP shift (cm)
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
1
3
5
7
9
11
13
15
17
19
21
CT slice


(a)
Seminal vesicles
PTV
Prostate
(b)
(c)
(d)
(e)
On-line modification of MLC leaf pairs for adaptive prostate radiotherapy
Court et al.


(c)
Couch-shift
ART
Slice (b)
Slice (a)
75.6 Gy
70.0 Gy
60.0 Gy
50.0 Gy


(b)
Couch-shift
ART
75.6 Gy
70.0 Gy
60.0 Gy
50.0 Gy

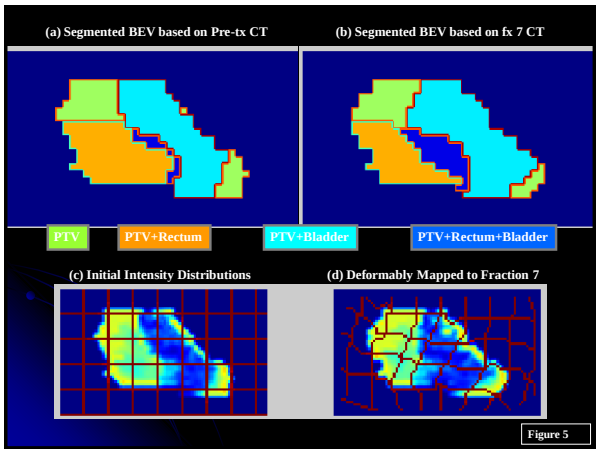




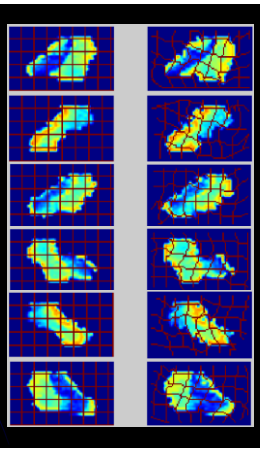
Adaptive Radiotherapy: Correction Techniques

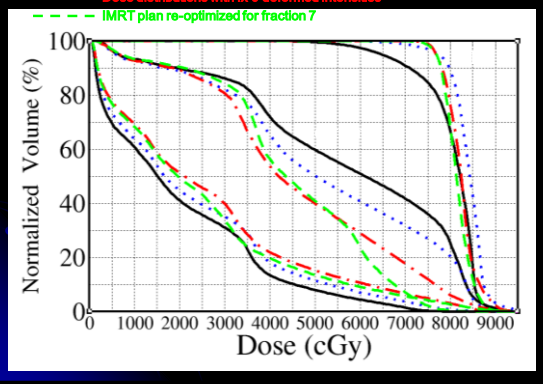
Use of Deformed Intensity Distributions for On-Line Modification of Image-Guided IMRT to Account for Inter-Fractional Anatomic Changes

Radhe Mohan, Ph.D., Xiaodong Zhang, Ph.D., He Wang, Ph.D., Yixiu Kang, Ph.D., Xiaochun Wang, Ph.D., Helen Liu, Ph.D., K. Kian Ang, MD, Debora Kuban, MD, Lei Dong, Ph.D.



Example of deformed intensity maps

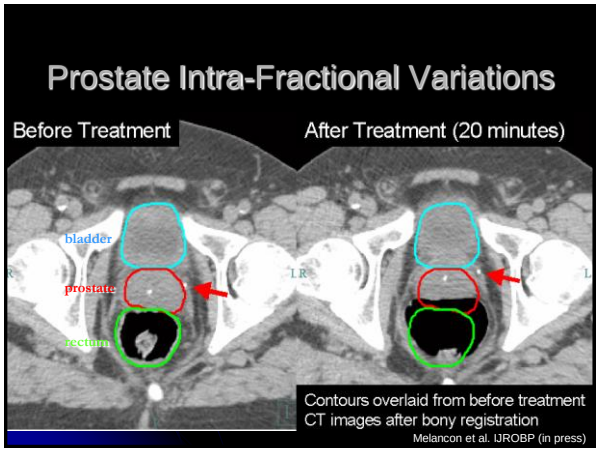


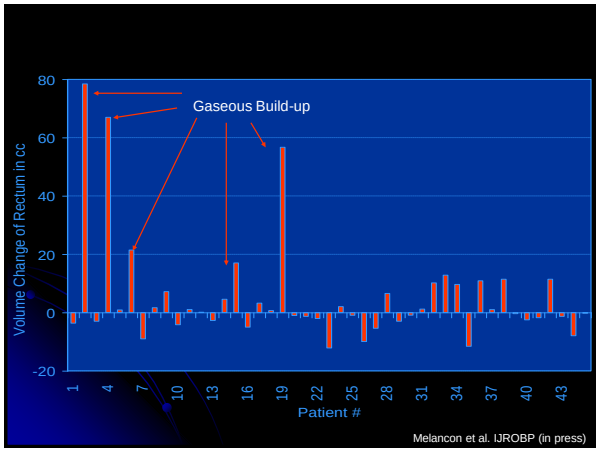


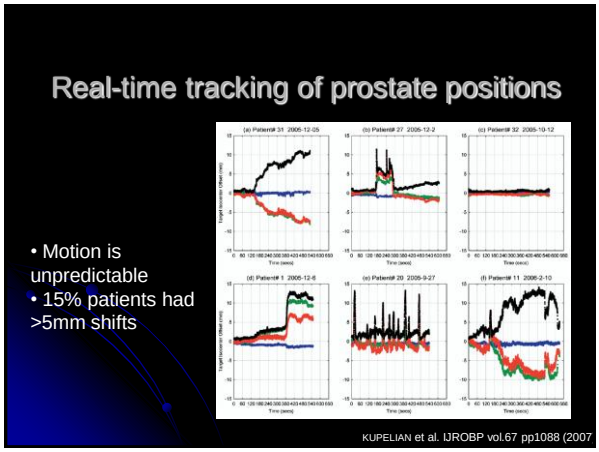
Practical Challenges

- Time for imaging
- Time in Planning
  - Auto-segmentation
  - Correction strategies
  - Efficient replanning
- Time for plan-verification (QA)
  - Approval process
  - R & V
- Adapting intra-fractional changes

How much time do you need?


Prostate Intra-Fractional Variations
Before Treatment
After Treatment (20 minutes)
bladder
prostate
rectum
Contours overlaid from before treatment CT images after bony registration
Melancon et al. IJROBP (in press)


Gaseous Build-up
Volume Change of Rectum in cc
80
60
40
20
0
-20
1
4
7
10
13
16
19
22
25
28
31
34
37
40
43
Patient #
Melancon et al. IJROBP (in press)


Real-time tracking of prostate positions
• Motion is unpredictable
• 15% patients had >5mm shifts
KUPELIAN et al. IJROBP vol.67 pp1088 (2007

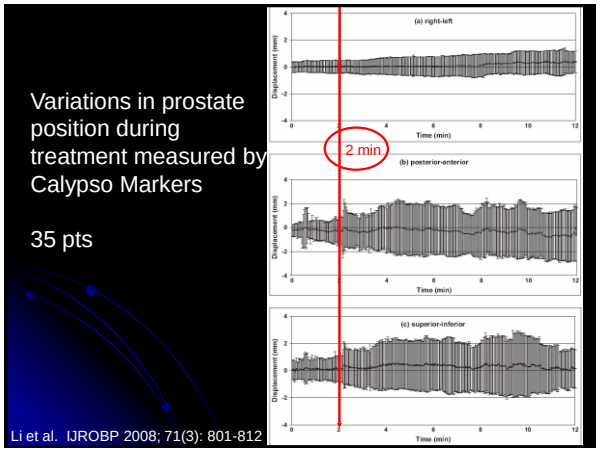

Variations in prostate position during treatment measured by Calypso Markers
35 pts
2 min
(a) right-left
(b) posterior-anterior
(c) superior-inferior
Time (min)
Displacement (mm)
Li et al. IJROBP 2008; 71(3): 801-812

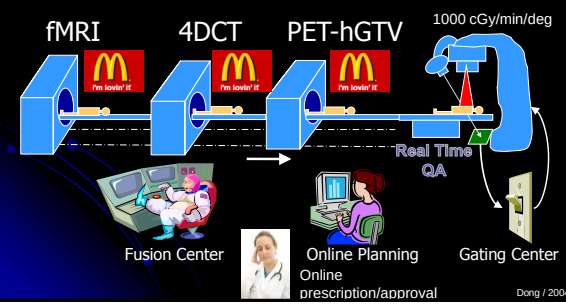
Image Quality is the Limiting Factor For IGRT

My wish list

- Magic imaging techniques that can see "CTV"

My wish

- Imaging-on-rails in treatment room



I am still waiting