Abstract

Conformal radiation therapy has historically used margins to account for geometrical uncertainties in the position of a target volume. The margins, in their simplest form, are simply expansions to the shape of a treatment beam, to ensure that dosimetric planning criteria are met in the presence of inter- and intra-fraction setup variations. Historically, the size of the margin in a given treatment site was difficult to determine due to the available technology and the time and effort required to obtaining accurate data. Consequently, margins were estimated to accommodate a population of patients. As new technologies have emerged, target volume position errors have become easier to measure, their accuracy has increased, and the measurements can be made much more frequently. As the quantity and quality of data has increased for patient populations, and even for individual patients, the conceptual basis of employing margins has evolved. Strategies for ensuring dosimetric coverage may now be individualized to a specific patient’s geometric uncertainty characteristics with customized margins, or they may incorporate geometric correction based on predefined action levels. Other strategies may incorporate continuous monitoring to gate or modify the beam. And finally, other strategies seek to eliminate margins by including the estimated geometrical uncertainty into the development of the dose distribution.

Educational Objectives

• To motivate the need for margins and review ICRU definitions
• To provide an educational review of the technologies and methods of measuring target volume positioning errors.
• To review methods of determining population margins from measured data.
• To review corrective and intervention strategies for patients with individualized margins.
• To briefly review planning strategies which seek to eliminate margins.

Disclaimer

The content of this presentation is for general educational purposes only.

The mention of trade names, commercial products does not imply an endorsement on the part of AAPM or the presenters.

The views, opinions and comments made in this refresher course are those of the presenters and not necessarily those of AAPM.
Conflict of Interest

DA Low:
Tomotherapy
Varian Medical Systems

DW Litzenberg:
Calypso Medical Technologies

Outline

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins

I. The Need for Margins

A. Systematic and random errors
B. Inter- and intra-fraction motion
C. Dosimetric criteria
D. Population and individualized margins
Department of Radiation Oncology • University of Michigan Health Systems
Importance of Image Guidence

N=127, patients treated to 78 Gy between 1993 and 1998
No daily image guidance
Outcomes analyzed by rectal distention at the time of simulation

What was Missing?

- Method for directly measuring prostate position
- On-board CT
  - CBCT
  - Kilovoltage or Megavoltage
  - Helical Megavoltage CT
- Markers
  - Imbedded markers
  - Planar imaging
  - On-board CT
  - Radiofrequency

Dosimetric Coverage

Population-Based Motion

Department of Radiation Oncology • University of Michigan Health Systems
1.0
0.5
0.0
-4
-2
0
2
4
Position (cm)

Patient Specific Motion

Patient Specific Margin

\[ \Sigma = 0 \]

PTV margin = Setup + Inter + Intra-fraction

\[ \Sigma = 0 \]

Estimate \( \Sigma \) And correct

\[ \text{PTV margin} = \text{Setup} + \text{Inter} + \text{Intra-fraction} \]

Why might a mm Matter?

Volume of Sphere = \( \frac{4}{3} \pi r^3 = \pi \frac{d^3}{6} \)

and \( \Delta V = (\pi \frac{d^3}{2}) \Delta d \)

then \( \Delta V/V = (\pi d^2/2) \Delta d / (\pi d^3 / 6) \)

or \( \Delta V/V = 3 \Delta d/d \)

\[ \Delta V/V = 3 \Delta d/d = 3 \times 1\text{mm} / 60\text{mm} \]

\[ = 0.10 = 10\% \]

Adding a 1 mm margin to a 6 cm target increases the volume by 10%
Outline

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins

II. Treatment Site Considerations

A. Treatment Position
B. Immobilization & Localization

Accuracy of Localization

Patient Position
Motion Management
Immobilization
Measurement
Correction
Simulation & Planning

Treatment Position

1997: No in-room soft tissue guidance available. Little to no evidence of respiratory motion.

Treatment Position

Intrafraction Motion: Fluoroscopy

Supine Positioning Results

Department of Radiation Oncology • University of Michigan Health Systems
Supine vs Prone Treatment Position

- Respiratory motion reduced when supine
  Dawson, URROBP, 2000
  Kitamura, URROBP, 2002
- Significantly less dose to small bowel, bladder and rectum when supine
  Bayley, Radiother & Oncol, 2004
- ~ 95% treated supine
  ASTRO IGRT Symposium, 2006

Outline

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins
Simulation Imaging Modality

A. What you see
1. Computed Tomography
2. Magnetic Resonance
3. Positron-Emission Tomography

B. What you contour

Geometric Uncertainties in Planning

Target delineation
Volumes not contoured may not get treated
Increasing conformity Volumes not contoured will not get treated

Varies with imaging modality
Subject to inter-observer variability

K. Langen

PROSTATE DELINEATION:
DIAGNOSTIC KV CT vs ABSOLUTE TRUTH

A study of prostate delineation referenced against a gold standard created from the visible human data

Visible Human Project - Male
6 radiation oncologists, 120 delineations on KV CTs

Department of Radiation Oncology • University of Michigan Health Systems
Visible Human Project - Male
6 radiation oncologists, 120 delineations on KV CTs
CT volumes on average 30% larger than true volume
CT volumes encompassed, on average, 84% of the true volume.

PROSTATE DELINEATION:
DIAGNOSTIC KV CT vs ABSOLUTE TRUTH
A study of prostate delineation referenced against a gold standard created from the visible human data
33 radiation oncologists (63 individual physician working hours), 120 delineations on KV CTs
CT volumes on average 30% larger than true volume
CT volumes encompassed, on average, 84% of the true volume.

Extended too anteriorly
Missed posteriorly

Simulation Imaging Modality
A quantitative assessment of the addition of MRI to CT-based, 3-D treatment planning of brain tumors

- 15 brain cases
- 1 neuro-radiologist
- 1 radiation oncologist
- Contours on CT, MR, registered CT-MR

Simulation Imaging Modality
GTV CTV = GTV + 2 cm
14% CT only
56% Both
30% MR only


department of radiation oncology • university of michigan health systems
Outline

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins

III. Examples of Motion

A. Head and Neck
B. Lung
C. Liver
D. Pancreas
E. Prostate
Liver – Inter-Fraction Motion

- Implanted Markers (clips okay)
- Localized using OBI (orthogonal X-rays at Exhale)
- 3 mm threshold for adjustment

Intrafraction Motion and Deformation: MRI

Balter, UM

Outline

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins
IV. Treatment Planning

A. Margins
1. ICRU-29, 50, 62 – Definitions
2. Margin Recipes

B. Margin Compromises

Current ICRU Definitions of Volumes: Limitations and Future Directions

J. Purdy, 2004

ICRU 29 (1978)

- 2 years after whole-body CT scanners introduced
- Target volume:
  - contains those tissues that are to be irradiated to a specified absorbed dose according to a specified time-dose pattern
  - includes expected movements, expected variation in shape and size, variations in treatment setup
- Treated volume:
  - The volume enclosed by the isodose surface representing the minimal target dose
- Irradiated volume:
  - The volume that receives a dose considered significant in relation to normal tissue tolerance
- Hot spot:
  - Area that received a dose higher than 100% of the specified target dose, at least 2cm in a section

J. Purdy, 2004

ICRU 50 (1993)

- Gross Target Volume
  - Demonstrable extent of malignant growth
- Clinical Target Volume
  - Microscopic extension, full dose to achieve aim
- Planning Target Volume
  - CTV + uncertain margins, “dose cloud”
- Organs at Risk
  - Normal tissues that may influence plan
- ICRU Reference Point

J. Purdy, 2004
ICRU 50

Setup Margin
Uncertainties in machine-patient positioning

Internal Margin
Uncertainties in patient-CTV positioning

Internal Target Volume
CTV + internal margin

Planning Organ at Risk Volume
OAR + uncertainty margins

ICRU 62 Supplement (1999)

ICRU Definitions

Irradiated volume:
• Tissue volume that receives a dose that is considered significant in relation to normal tissue tolerance.

Treated volume:
• Tissue volume that is planned to receive at least a dose selected and specified by radiation oncology team as being appropriate to achieve the purpose of the treatment.
**ICRU Definitions**

**GTV - Gross Tumor Volume**
- Complete actual or visible/demonstrable extent and location of the malignant growth.

**CTV - Clinical Target Volume**
- A tissue volume that contains a GTV and/or subclinical microscopic malignant disease, which has to be eliminated.
- This volume has to be treated sufficiently in order to achieve the aim of the therapy: cure or palliation.

**PTV - Planning Target Volume**
- Defined by specifying the margins that must be added around the CTV to compensate for the variations of organ, tumor and patient movements, inaccuracies in beam and patient setup, and any other uncertainties.
- A static geometrical concept, can be considered a 3D envelope in which the tumor and any microscopic extensions reside and move (Dose cloud).

**Organs at risk:**
- Normal tissues (eg, spinal cord) whose radiation sensitivity may significantly influence treatment planning and/or prescribed dose.

**ICRU Reference point:**
- The system for reporting doses is based on the selection of a point within the PTV, which is referred to as the ICRU Reference point
  - The dose at the point should be clinically relevant.
  - The point should be easy to define in clear and unambiguous way.
  - The point should be selected so that the dose can be accurately determined.
  - The point should in a region where there is no steep dose gradient.
ICRU Definitions

**Setup margin (SM):**
- Uncertainties in patient-beam positioning in reference to the treatment machine coordinate system.
- Related to technical factors.
- Can be reduced by
  - Accurate setup and immobilization of the patient
  - Improved mechanical stability of the machine.

**Internal margin (IM):**
- Variations in size, shape, and position of the CTV in reference to the patient’s coordinate system using anatomic reference points.
- Caused by physiologic variations
- Difficult to control from a practical viewpoint.
- The volume formed by the CTV and the IM called internal target volume (ITV).

**Planning organ at risk volume (PRV):**
- A margin is added around the organ at risk to compensate for that organ’s geometric uncertainties.
- Analogous to the PTV margin around the CTV.

**Margins Around Organs at Risk**

**Considerations**
- Systematic errors
  - Sensitive to shifts in a particular direction
- Random errors
  - Impact of dose blurring
- Serial organs at risk
  - Sensitive to hot spots
- Parallel organs at risk
  - Some tolerance to limited hot spots
Challenges of Implementing ICRU 50 & 62

A. Delineating Volumes
B. New Technologies
C. Adding Errors

Delineating the GTV

• Based mostly on clinical judgment
• Depends significantly on the imaging modality (CT, MRI, PET, Registration)
• CT is still the principal source of imaging data used for defining the GTV for 3DCRT and IMRT
• Window and level settings are critical

Delineating the CTV

• More of an art than a science because current imaging techniques are not capable of detecting subclinical tumor involvement directly.

GTV to CTV Margins


J Purdy, 2004
Delineating the PTV

The following should be taken into account:
- Data from published literature
- Any uncertainty studies performed in the clinic
- The presence of nearby organs at risk.
- The asymmetrical nature of the GTV/CTV geometric uncertainties.

Compromises Between Volumes

- PTV and PRV may overlap
- Conflict in optimization criteria
- Judgment required in resolving volume conflicts

Challenges with New Technologies

IMRT
- Sharp beam gradients
- More conformal
- More sensitive to geometric uncertainties
- Time-dependant delivery
- Motion interplay may lead to hot/cold spots

4D CT and Cone Beam CT
- Protocols for defining volumes
- Variations in motion after simulation
- Changes in volumes during therapy
Adding systematic and random errors

Systematic errors, $\Sigma$
- treatment preparation errors
- influence all fractions

Random errors, $\sigma$
- treatment execution errors
- influence each fraction individually

ICRU 62 – Combining Errors

Add systematic and random errors quadratically, with equal weighting

$$SD_{\text{tot}} = \Sigma^2 + \sigma^2$$

Combining Errors

Systematic errors are much more important in determining margins than random errors

PTV Margin Recipe

$$m_{\text{PTV}} = \alpha \Sigma + \gamma \sigma'$$

$\alpha \sim 2 – 2.5$
$\gamma \sim 0.7$

$\Sigma$ - combined standard deviation of systematic errors ($\Sigma^2 = \Sigma_m^2 + \Sigma_s^2 + \Sigma_d^2$)

$\sigma'$ - combined standard deviation of random errors ($\sigma'^2 = \sigma_m^2 + \sigma_s^2$)
Margins for geometric uncertainty around organs at risk in radiotherapy

The DVH of the Planning Risk Volume should not underestimate the contribution of the high-dose components to the Organ at Risk, in 90% of the cases.

Dan Low takes over!

Outline

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins
Target Volume Localization

A. Skin marks
B. Anatomical Landmarks and Surrogates
   Bones
   Implanted markers
   Soft tissues
C. MV Portal Imaging
D. kV Imaging
E. Ultrasound
F. CBCT
G. MVCT
H. Electromagnetic
I. Surface mapping

Image Guidance: Positional Variations
Early days

N=10 Weekly Images
4-8 films per patient

Chamber matching of bony anatomy on digitized port films
Balter, LJRBP, 31, 113, 1995

Table 3. Images needed for 5% geometric coverage of the prostate

<table>
<thead>
<tr>
<th>Direction</th>
<th>Repositioning by body anatomy</th>
<th>Repositioning by prostate markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP</td>
<td>5 mm</td>
<td>3 mm</td>
</tr>
<tr>
<td>LR</td>
<td>5 mm</td>
<td>3 mm</td>
</tr>
<tr>
<td>IS</td>
<td>4 mm</td>
<td>3 mm</td>
</tr>
</tbody>
</table>

AP = anterior-posterior
LR = left-right
IS = inferior-superior

Department of Radiation Oncology • University of Michigan Health Systems
TRANSABDOMINAL ULTRASOUND

First widely used targeting technique
Started era of image guidance for routine clinical use (1998)
Introduced DAILY imaging

Transabdominal Ultrasound: Comparison with Implanted Markers

US (BAT) vs Markers (Linac)
Difference: Average ± SD (mm)

<table>
<thead>
<tr>
<th></th>
<th>Ant / Post</th>
<th>Sup / Inf</th>
<th>Lateral</th>
</tr>
</thead>
<tbody>
<tr>
<td>BAT</td>
<td>0.7 ± 5.2</td>
<td>2.7 ± 4.5</td>
<td>1.8 ± 3.9</td>
</tr>
</tbody>
</table>

Langen et al., IROBP, 2003

US (Sonaray vs Markers (Exactra)
Frequency of misalignments

- 0-5 mm: 26%
- 5-10 mm: 48%
- 10-15 mm: 17%
- 15-20 mm: 5%
- >20 mm: 4%

Transabdominal US: Comparison with CT

Dong et al. (MDACC), ASTRO 2004: BAT vs In-Room CT

N=15 patients, 3 CTs per week.
N=342 CT/US pairs, Average 23 scans/patient
Physician contours on each CT → Prostate center of volume

BAT vs CT differences (Mean ± SD):

- Lateral: 0.5 ± 3.6 mm
- Ant / Post: 0.7 ± 4.5 mm
- Sup / Inf: 0.4 ± 3.9 mm

“…the overall performance … seems unsatisfactory.”

Dong et al., IROBP, 60S, p. S332, 2004

KV CT on Rails

Diagnostic CT quality images
Full body field of view

Limitations:
Room size
Integration
Separate imaging and treatment isocenters

Scobie et al., IROBP, 2006
Cone Beam KV CT
- Elekta Synergy
- Varian Trilogy
Same Gantry
Coupled to delivery device
Volume acquisition

Sample CBCT Images: Good for H&N
Images Courtesy of Duke Univ Hosp, Durham
Courtesy Varian

Sample CBCT Images: Worse for Pelvis
CT scan acquisition & reconstruction time ≈ 2 minutes
Elekta Synergy®
Images Courtesy of Floris Pos – Netherlands Cancer Institute

Sample CBCT Images – Motion Artifacts
Images Courtesy of Floris Pos – Netherlands Cancer Institute

Department of Radiation Oncology • University of Michigan Health Systems
Sample CBCT – Breathing Motion Artifacts

Sample CBCT – Respiratory Synchronized CBCT

Liu et al, IJROBP, 2007

Li et al, IJROBP, 66; 581-91, 2007
Institutional variations in patient position, immobilization, localization technique, inter- and intra-fraction motion measurements should also be taken into account when developing margins.

**Data to help PTV margin determination**

<table>
<thead>
<tr>
<th>Name</th>
<th>Year</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li et al.</td>
<td>2007</td>
<td>IJROBP, 68; 581-91</td>
</tr>
<tr>
<td>Kang et al.</td>
<td>2008</td>
<td>IJROBP, 71(3), 801-812</td>
</tr>
<tr>
<td>Langen et al.</td>
<td>2008</td>
<td>IJROBP, 71, 1084-1090</td>
</tr>
<tr>
<td>Pierburg et al</td>
<td>2008</td>
<td>IJROBP, 69, S23-S24</td>
</tr>
<tr>
<td>Rajendran et al</td>
<td>2009</td>
<td>IJROBP, In Press</td>
</tr>
</tbody>
</table>

**GEOGRAPHIC MISSES VERSUS DOSIMETRIC MISSES**

**Impact of real time motion on dosimetry:**
Prostate (Calypso tracks)


Rajendran et al: Daily isocenter correction with electromagnetic based localization improves target coverage and rectal sparing during prostate radiotherapy. IJROBP, In Press, 2009
**WHY NOT IMAGE EVERYDAY?**

**IMAGING DOSE: MVCT vs KV CBCT**

**MVCT:**
- 1 - 2 cGy per image*
- Relatively uniform dose
- 40 - 80 cGy per entire course
- Can limit length of scan

---

**KV CBCT:**
- 1 - 5 cGy per image**, depending on site
- Heterogeneous throughout scan volume
- 40 - 200 cGy per entire course
- Cannot limit length of scan

---

* Shah et al., BRDIP. 2007; 69(3): S193-196. ASTRO 07; ABSTRACT 1100

**ASTRO 07; ABSTRACT 1100**

---

**In-Room Guidance:**

*Inter-Fraction
Motion Management Example*

**Implanted Markers**

---

**Advantages of Markers**

- Accuracy
- Measured in treatment position
- Semi- to fully automated
- User independent
- No contouring
- Real-time position possible
- Beam gating

---

**Marker Visualization & Extraction**

- 3 – 4 markers
- Centroid of visible markers
  \[ \sigma_{\text{CM}} < 1 \text{ mm} \]
  Pouliot, IJROBP, 2003
- 99.6% visualization of 3 markers
  18 MV (1x3 mm)
  Herman, IJROBP, 2003
- Automated marker extraction
  \[ 93\% \text{ per marker, } 85\% \text{ for 3 markers} \]
  Aubin, MedPhys, 2003
  \[ 90\% - 100\% \text{ based on ROI (MVCT)} \]
  Chen, AAPM, 2005
Marker Migration & Stability

- 1.3 (0.44 – 3.04) mm (Pouliot, IJROBP, 2003)
- 1.2 +/- 0.2 mm (Kitamura, Radiother Oncol, 2002)
- 0.7 – 1.7 mm (Litzenberg, IJROBP, 2002)
- 1.01 +/- 1.03 mm (Kupelian, IJROBP, 2005)
- 0.8 mm with Beacons (Willoughby, IJROBP, 2006)

Area of marker triangle proportional to CT volume of prostate (Moseley, AAPM, 2005)

Frequency & Time for Adjustment

- 5 mm action threshold with skin mark setup
  - 53% of fractions realigned pre-treatment
  - 1.5 minute mean increase in treatment time
  - Herman, IJROBP, 2003

- 2 mm action threshold
  - 74% of fractions realigned
  - < 5 minute increase in treatment time
  - Beaulieu, Radiother & Oncol, 2004

Need for implanted fiducials with CT scans

kV cone beam CT
MV cone beam CT
Helical MV CT

Prostate alignment study
MVCT scans

Radiation Therapist vs Physician

Alignment methods:
- Marker
- Anatomy
- Contours

3 patients, 112 scans

Langen et al., IJROBP, 62, 1517, 2005
Therapist vs Physician registration

Difference ≥ 5 mm

<table>
<thead>
<tr>
<th>Marker</th>
<th>Anatomy</th>
<th>Contour</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/P: 1%</td>
<td>A/P: 5%</td>
<td>A/P: 17%</td>
</tr>
<tr>
<td>S/I: 2%</td>
<td>S/I: 10%</td>
<td>S/I: 31%</td>
</tr>
<tr>
<td>Lat: 1%</td>
<td>Lat: 0%</td>
<td>Lat: 3%</td>
</tr>
</tbody>
</table>

Langen et al., IJROBP, 62, 1517, 2005

Cone Beam KV CT Alignment techniques
Fiducials vs Soft Tissues
Moseley et al., IJROBP, 67(3), 942–953, 2007

Princess Margaret Hospital: 15 patients, 256 CT sets
Fiducial vs Soft tissues on cone-beam CT
PTV margins: 10 mm except 7 mm posteriorly

Inter-observer Variability (mm)

<table>
<thead>
<tr>
<th>Systematic Error (SD)</th>
<th>Vertical (AP)</th>
<th>Long (SI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Markers</td>
<td>0.03</td>
<td>0.15</td>
</tr>
<tr>
<td>Systematic Error (SD)</td>
<td>0.26</td>
<td>0.95</td>
</tr>
<tr>
<td>Random Error</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft tissues on CBCT</td>
<td>0.61</td>
<td>1.61</td>
</tr>
<tr>
<td>Systematic Error (SD)</td>
<td>1.50</td>
<td>2.96</td>
</tr>
<tr>
<td>Random Error</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Less inter-observer variability with markers

Moseley et al., IJROBP, 67(3), 942–953, 2007

Cone Beam KV CT Alignment techniques
Fiducials vs Soft Tissues
Moseley et al., IJROBP, 67(3), 942–953, 2007

Agreement within 3 mm Pearson’s correlations R2

<table>
<thead>
<tr>
<th>LR</th>
<th>AP</th>
<th>SI</th>
</tr>
</thead>
<tbody>
<tr>
<td>91%</td>
<td>64%</td>
<td>64%</td>
</tr>
<tr>
<td>0.90</td>
<td>0.55</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Moseley et al., IJROBP, 67(3), 942–953, 2007
In-Room Guidance:
MOTION
INTRA FRACTION

Real-Time Marker Tracking

IRIS
Dual Fluoroscopy and Flat Panels

Department of Radiation Oncology • University of Michigan Health Systems
**Marker Implantation Feasibility**

**AC Wireless Magnetic Tracking**

- Calypso System
- Measurements at 10 Hz
- Sub-mm resolution
- Real-time tracking
- Potential for fast correction

### Table 1: Measurements and Accuracy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Median</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range (mm)</td>
<td>1.4</td>
<td>2.5</td>
<td>2.05</td>
<td>0.8</td>
<td>3.8</td>
</tr>
<tr>
<td>Temporal</td>
<td>0.5</td>
<td>0.6</td>
<td>0.55</td>
<td>0.4</td>
<td>0.7</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.2</td>
<td>0.3</td>
<td>0.25</td>
<td>0.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Mouth/Maxilla</td>
<td>0.5</td>
<td>1.0</td>
<td>0.8</td>
<td>0.3</td>
<td>1.2</td>
</tr>
<tr>
<td>Nasopharynx/Oral</td>
<td>0.7</td>
<td>1.2</td>
<td>0.9</td>
<td>0.4</td>
<td>1.5</td>
</tr>
<tr>
<td>Temporal/Medulla</td>
<td>0.3</td>
<td>0.5</td>
<td>0.4</td>
<td>0.1</td>
<td>0.7</td>
</tr>
</tbody>
</table>

* Denotes values below 0.2 mm difference.
* Values with ±0.2 mm separation due to measurement of motion percentage in parentheses.

**Real Time Motion Data – Patient 1**

- IS
- AP
- LR

**Real Time Motion Data – Patient 2**

- IS
- AP
- LR
**Percentile: Regular Breather**

Regular Breather

\[ v_x = \text{Volume at which patient had } v \text{ or less volume } x\% \text{ of the time} \]

**Percentile Analysis**

Irregular Breather

**Example V_{98} (93\% \text{ of time}) vs V_{85} (80\% \text{ of time})**

<table>
<thead>
<tr>
<th>Amount of Motion We Want to Know</th>
<th>Available 3D Image Datasets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Images that cover 80% of breathing cycle show only 72% of the motion at 93% of the breathing cycle!</td>
<td></td>
</tr>
</tbody>
</table>

**In-Room Correction Strategies**

A. Action Levels

B. Gating
Variation vs Action Level

4.0  
3.5  
3.0  
2.5  
2.0  
1.5  
1.0  
0.5  
0.0  
Corrected Uncertainty, \( \sigma \) (mm)

Action Level (mm)

\[ \sigma_{\text{intra}}^2 + \sigma_{\text{pos}}^2 \]  

Lam, AAPM, 2006

Patient Specific Margin

\[ \Sigma = 0 \]

PTV margin = Setup + Inter + Intra - fraction Measurement + Correction

Initial Setup Variations

Assume \( \sigma_s = 1 \) mm

Intra-Fraction Correction
Radiofrequency transponders: Prostate rotation

- Apply real rotations from tracked data to assess plan efficacy
- Real-tracking data (sampled at 10Hz) from a research version of the Calypso System
- Rotational and translational corrections were applied to the prostate contours for each patient and the amount of time the prostate was outside the PTV was determined

C. Noel, Washington University

Plan Evaluation

For 3 patients, over 122 total fractions, the percentage of time any portion of the prostate is outside of a 5mm PTV: ***

<table>
<thead>
<tr>
<th>% Time out of 5mm PTV</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>25%</td>
</tr>
<tr>
<td>Patient 2</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>Patient 3</td>
<td>51%</td>
</tr>
</tbody>
</table>

***C Noel, ASTRO 2008

...for a 3mm PTV margin:

<table>
<thead>
<tr>
<th>% Time out of 3mm PTV</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>80%</td>
</tr>
<tr>
<td>Patient 2</td>
<td>5%</td>
</tr>
<tr>
<td>Patient 3</td>
<td>93%</td>
</tr>
</tbody>
</table>

***C Noel, ASTRO 2008
Plan Evaluation

...for a 8mm PTV margin:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Time out of 8mm PTV</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>2</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>3.3%</td>
</tr>
</tbody>
</table>

C Noel, ASTRO 2008

Visualize Rotations

Contoured prostate and PTV from plan

Visualize Rotations

Tracked motion data

Visualize Rotations

Change PTV from 5mm to 3mm

Day 1: Prostate Position at Set-up: 9°
Day 2: Prostate Position at Set-up: 30°

Department of Radiation Oncology • University of Michigan Health Systems
Outline

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins

Offline Adaptive Protocols

- Adaptive Radiation Therapy – ART
  - N ~ 5 CT scans with contours
  - Union of volumes to form patient-specific PTV
- No Action Level protocol – NAL
  - N ~ 5 portal images to estimate Σ
    De Boer, et al, IJROBP, 2001
- Shrinking Action Level protocol – SAL
  - N_{max} ~ 5 portal images to estimate Σ
  - If Σ_{N} < α_{N} = α / N^{1/2}, apply offset to all fractions
  - Else apply and restart at N = 1

Confidence-Limited PTV (cl-PTV)

Initial CTV + 4 CTVs = ITV
ITV + Random Setup Error of Bones = cl-PTV
Kestin, RTOG, 2006

Adaptive Radiation Therapy - ART
**Adaptive RT Trial**

**Margin Reduction (N=600)**
- Margins stringently designed to allow <3% dose reduction within CTV with an 80% confidence.
- PTV volume reduced by mean of 34% (N=600 patients) in >30% of conventional PTV unnecessary in 75% of patients.
- Equivalent uniform margin: mean = 5.6 mm
- If planning based on single CT scan: ≈ 14 mm margin (AP) required to meet similar dosimetric criteria.
- Average IMRT dose escalation of 7.5% (86.7 Gy).


**Outline**

I. The Need for Margins
II. Treatment Site Considerations
III. Simulation Imaging Modalities
IV. Examples of Motion
V. Treatment Planning
VI. In-room Guidance and Correction Strategies
VII. Off-line Adaptive Strategies
VIII. Planning without margins

**Treatment without Margins**

- Multiple Instance Geometry Approximation (MIGA)
- Approximate positional uncertainties by a modeled sequence of positions (e.g., independent CT scans)
- Dose calculation is for weighted sum of different patient geometries
- Assuming that model is correct, dose calculation accounts for geometric uncertainty

**MIGA**

- MIGA: Multiple Instance Geometry Approximation
- Inverse plan optimization accounting for random geometric uncertainties with a multi-instance geometry approximation (MIGA).
- Requires no geometric tumor constraints.
- Setup uncertainties are approximated by a modeled sequence (e.g., independent CT scans).
- Dose calculation is for weighted sum of different patient geometries.
- Assuming that model is correct, dose calculation accounts for geometric uncertainty.
• Fluence is NOT just a blurring of the PTV-based plan!
• No PTV margin
• Simultaneous optimization of multiple instances of geometry
• Solutions maybe worse than the static geometry solution, but are much better than the static geometry solution when compromised by motion

The End!

Thanks for attending!

Up Next:
Treatment Planning of Complex Cases
M Hunt and T Nurushev