Predicting Normal Tissue Injury in the Modern era: A Review of QUANTEC

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Disclosures

• Grants: NIH, Lance Armstrong
• Advisor: Impac (Mosaiq)
• UNC: Research grant-Siemens
• Recent:
  • Varian: grant, speaker
  • Dept of Defense: grant
Early summary table (Rubin, Cooper, Phillips)

<table>
<thead>
<tr>
<th>Organ</th>
<th>Injury</th>
<th>TD_{5/5}</th>
<th>TD_{50/5}</th>
<th>Whole or Partial Organ (Field Size or Length)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone marrow</td>
<td>Aplasia, pancytopenia</td>
<td>250</td>
<td>450</td>
<td>Whole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3,000</td>
<td>4,000</td>
<td>Segmental</td>
</tr>
<tr>
<td>Liver</td>
<td>Acute and chronic hepatitis</td>
<td>2,500</td>
<td>4,000</td>
<td>Whole</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1,500</td>
<td>2,000</td>
<td>Whole (strip)</td>
</tr>
<tr>
<td>Stomach</td>
<td>Perforation, ulcer, hemorrhage</td>
<td>4,500</td>
<td>5,500</td>
<td>100 cm</td>
</tr>
<tr>
<td>Intestine</td>
<td>Ulcer, perforation, hemorrhage</td>
<td>4,500</td>
<td>5,500</td>
<td>400 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6,000</td>
<td>6,500</td>
<td>100 cm</td>
</tr>
<tr>
<td>Brain</td>
<td>Infarction, necrosis</td>
<td>5,000</td>
<td>6,000</td>
<td>Whole</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>Infarction, necrosis</td>
<td>4,500</td>
<td>5,500</td>
<td>10 cm</td>
</tr>
<tr>
<td>Heart</td>
<td>Pericarditis, pancarditis</td>
<td>4,500</td>
<td>5,500</td>
<td>60%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>7,000</td>
<td>8,000</td>
<td>25%</td>
</tr>
<tr>
<td>Lung</td>
<td>Acute and chronic pneumonitis</td>
<td>3,000</td>
<td>3,500</td>
<td>100 cm</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1,500</td>
<td>2,500</td>
<td>Whole</td>
</tr>
<tr>
<td>Kidney</td>
<td>Acute and chronic nephrosclerosis</td>
<td>1,500</td>
<td>2,000</td>
<td>Whole (strip)</td>
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<tr>
<td></td>
<td></td>
<td>2,000</td>
<td>2,500</td>
<td>Whole</td>
</tr>
<tr>
<td>Fetus</td>
<td>Death</td>
<td>200</td>
<td>400</td>
<td>Whole</td>
</tr>
</tbody>
</table>

**TD 5/5** = Max Tolerated Dose 5% rate at within 5 years.

**TD 50/5** = Max Tolerated Dose 50% rate within in 5 years.
Task force estimated normal tissue tolerance

**TD 5/5, TD 50/5** (5% or 50% risk at 5 years)
for 1/3, 2/3 and whole organ, using

- Literature review
- Task force members’ “own experience”

... for 26 organs
**Table 1. Normal tissue tolerance to therapeutic irradiation**

<table>
<thead>
<tr>
<th>Organ</th>
<th>TD 5/5 Volume</th>
<th>TD 50/5 Volume</th>
<th>Selected endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/3</td>
<td>2/3</td>
<td>3/3</td>
</tr>
<tr>
<td>Kidney I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney II</td>
<td>5000</td>
<td>3000*</td>
<td>2300</td>
</tr>
<tr>
<td>Bladder</td>
<td>N/A</td>
<td>8000</td>
<td>6500</td>
</tr>
<tr>
<td>Bone:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femoral Head I and II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T-M joint mandible</td>
<td>6500</td>
<td>6000</td>
<td>6000</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rib cage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10 cm²</td>
<td>30 cm²</td>
<td>100 cm²</td>
</tr>
<tr>
<td></td>
<td>7000</td>
<td>6000</td>
<td>5500</td>
</tr>
<tr>
<td>Brain</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain stem</td>
<td>6000</td>
<td>5000</td>
<td>4500</td>
</tr>
<tr>
<td>Optic nerve I &amp; II</td>
<td>No partial volume</td>
<td>5000</td>
<td>No partial volume</td>
</tr>
<tr>
<td>Chiasma</td>
<td>No partial volume</td>
<td>5000</td>
<td>No partial volume</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>5 cm</td>
<td>10 cm</td>
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<td></td>
<td>5000</td>
<td>5000</td>
<td>4700</td>
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<tr>
<td>Cauda equina</td>
<td>No volume effect</td>
<td>6000</td>
<td>No volume effect</td>
</tr>
<tr>
<td>Brachial plexus</td>
<td>6200</td>
<td>6100</td>
<td>6000</td>
</tr>
<tr>
<td>Organ</td>
<td>TD 5/5 Volume</td>
<td>TD 50/5 Volume</td>
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<tr>
<td>Kidney I</td>
<td>5000</td>
<td>3000*</td>
<td>2300</td>
</tr>
<tr>
<td>Kidney II</td>
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</tr>
<tr>
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<tr>
<td>Brain</td>
<td>6000</td>
<td>5000</td>
<td>4500</td>
</tr>
<tr>
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<td>6000</td>
<td>5300</td>
<td>5000</td>
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<td>5000</td>
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<tr>
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<td>20 cm</td>
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<tr>
<td>Cauda equina</td>
<td>No volume effect</td>
<td>6000</td>
<td>No volume effect</td>
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<td>6200</td>
<td>6100</td>
<td>6000</td>
</tr>
<tr>
<td>Eye lens I and II</td>
<td>No partial volume</td>
<td>1000</td>
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<tr>
<td>Eye retina I and II</td>
<td>No partial volume</td>
<td>4500</td>
<td></td>
</tr>
<tr>
<td>Ear mid/external</td>
<td>3000</td>
<td>3000</td>
<td>3000*</td>
</tr>
<tr>
<td>Ear mid/external</td>
<td>5500</td>
<td>5500</td>
<td>5500*</td>
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<tr>
<td>Parotid* I and II</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Larynx</td>
<td>7900*</td>
<td>7000*</td>
<td>7000*</td>
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<tr>
<td>Larynx</td>
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<td></td>
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<tr>
<td>Lung I</td>
<td>4500</td>
<td>3000</td>
<td>1750</td>
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<tr>
<td>Lung II</td>
<td>6000</td>
<td>4500</td>
<td>4000</td>
</tr>
<tr>
<td>Heart</td>
<td>6000</td>
<td>4500</td>
<td>4000</td>
</tr>
</tbody>
</table>
“3D Hope”

Dose/volume

Normal tissue

outcome
"3D Hope"

Dose/volume

Normal tissue outcome

Applicability? Evolving therapies, SRS, IMRT, Hypo fxn

"Reality"

Information overload. Which parameters? DVH limitations

Patient/tumor factors

Which endpoints?
QUANTEC: QUAntitative Normal Tissue Effects in the Clinic

Summarize Dose/Volume/Outcome data

Both AAPM and ASTRO recognized ($$

Clinical need for updated data: 3D, and IMRT treatment planning and optimization (update Emami)
History of QUANTEC

2006 AAPM Science Council: Ellen Yorke, Rock Mackie
Steering Committee: Deasy, Bentzen, Yorke, Ten-Haken, Jackson, Marks, Eisbruch, Constine, Morris

2007 1st QUANTEC meeting: Madison Wisconsin
Initial review of tolerances: physicists, statisticians and physicians.

2010 Special Issue of Red Journal
Organs Included

- Brain: Yaakov Lawrence
- Brainstem: Charles Mayo
- Optic Nerve: Charles Mayo
- Ear: Niranjan Bhandare
- Cord: John Kirkpatrick
- Salivary Glands: Joe Deasy
- Larynx/Pharynx: Avi Eisbruch
- Lung: Larry Marks
- Heart: Giovanna Gagliardi
- Esophagus: Maria Werner-Wasik
- Liver: Charlie Pan
- Kidney: Laura Dawson
- Bowel: Charlie Pan
- Rectum: Jeff Michalski
- Bladder: Akila Viswanathan
- Penile Bulb: Mack Roach
Organ specific QUANTEC articles

- Significance
- Clinically relevant endpoints
- Anatomic definitions
  - Segmentation challenges
- Systematic review of literature
dose/volume/outcome
- Patient-related risk factors
- Data modeling
- Model caveats
- Recommended Dose-volume constraints and models
- Future studies
- Recommended toxicity scoring system

Objective: MDs, physicists, statistician
Clinically relevant: pneumonitis vs CT or PFT
### Comparison of Emami vs QUANTEC

<table>
<thead>
<tr>
<th></th>
<th>Emami et al</th>
<th>QUANTEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of organs</td>
<td>26</td>
<td>16</td>
</tr>
<tr>
<td>3D data available</td>
<td>Minimal</td>
<td>More/Moderate (18 year interval)</td>
</tr>
<tr>
<td>Format dose/volume limits</td>
<td>Uniform TD 5/5, 50/5 for 1/3, 2/3, 3/3</td>
<td>Non-uniform</td>
</tr>
<tr>
<td>Endpoints</td>
<td>Specific</td>
<td>Specific</td>
</tr>
<tr>
<td>Expert Opinion</td>
<td>Moderate</td>
<td>Less</td>
</tr>
</tbody>
</table>
Examples from Quantec
Mean dose response of pneumonitis

(Andy Jackson and others)

- Patients treated for NSCLC
  - Data from 9 institutions, 10 separate studies
- 1,167 patients with 222 cases of pneumonitis
- ≥ Grade 3 RTOG ~ ≥ Grade 2 SWOG
  - (requiring steroids)
  - accepted ≥ grade 1 definition if few grade 1 cases
Pneumonitis, mean dose response - whole lung

Objective data review: Jackson, Deasy, Martel, Bentzen
1,167 pts NSCLCa, 9 centers
Quanteq Lung: Figure by Jessica Hubbs
Single Fraction Radiosurgery

Brain (1)

Yaakov Lawrence
**Brain (2)**

Long Term Side Effects

Standard fractionation (qd, d<2.5Gy)

- n<60
- n=160-120
- n>120

\[ \alpha/\beta = 3\text{Gy} \]
Brain (2)

Long Term Side Effects

Standard fractionation (qd, d<2.5Gy)

- n<60
- n=160-120
- n>120

~36 x 2Gy qd

\(\alpha/\beta = 3\text{Gy}\)
Brain (3)
Big fractions (d>=2.5Gy)

- n<60
- n=160-120
- n>120

Long Term Side Effects

Yaakov Lawrence
Brain (4)

BID (twice daily fractions)

Long Term Side Effects

Yaakov Lawrence
Brain (4)

Long Term Side Effects

BID (twice daily fractions)

α/β = 3Gy

\[ \text{BED} \approx 50 \times 1.25\text{Gy bid} \]
Radiation Induced Optic Neuropathy in Selected Studies (1.8-2.0 Gy/fx)

Author and (incidence) are shown next to points. Bars show dose range in each group.

- Martel (1/4)
- Martel (2/10)
- Pigeaud-Klessens (6/56)
- Flickinger (2/21)
- Parsons (6/73)
- Weber (0/29)
- Martel (0/2)
- Parsons (1/16)
- Parsons (1/15)
- Hoppe (0/85)
- Daly (0/36)
- Martel (0/2)

Max Dose to Optic Nerve (Gy)

Mayo et al, Optic Nerve
Mean dose response for SNHL at 4 kHz

Chen et al.
Oh et al.
Honore et al.
Pan et al.
Kwong et al.
Salivary Glands

TD50 (Gy) vs. Follow-up Duration (Months)

Deasy et al, Parotid

Münter-CRT (2007, 33)
Münter-IMRT (2007, 19)
Roesink (2004, 96)
Münter (2004, 18)
Rudat (2008, 65)
Braam(I) (2005, 52)
Blanco(W) (2005, 65)
Bussel (2004, 16)
Roesink(I) (2001, 93)
Eisbruch(I) (1999, 88)
Buus (2006, 12)
Probability Aspiration = $f$ (mean dose Glottis and Supra-Glottic Larynx)

(T. Rancati, M. Schwartz, A. Allen, F. Feng, A. Popovtzer, B. Mittal, and A. Eisbruch)
Charlie Pan et al, Liver
high risk of grade 3 or worse acute toxicity

low risk of grade 3 or worse acute toxicity
Bilateral Partial Kidney RT

Percent Volume

Dose, Gy, over 5 weeks

minimal risk
low risk
moderate-high risk
high risk
undefined

estimated threshold for injury
peptic ulcer
gastric cancer
seminoma
lymphoma

gastric cancer
lymphoma
gynecological cancer

Laura Dawson
Bladder: Yorkee and Viswanathan
Dose-volume limits with LQ corrected doses (a/b = 3 Gy)

Threshold DVHs

Andy Jackson  LQ equivalent dose in 2 Gy fractions (Gy)

Jackson 70.2  Jackson 75.6  Akimoto  Wachter  Koper  Cozarrino  Zapatero
70-75.6 Gy: 7%  75.6 Gy: 34%  Grade 1

Huang  Hartford
75.6 Gy: 19%  Grade 3

66 Gy: 33%  70-76 Gy: 9%
66 Gy: 14%  70-76 Gy: 9%
66.2-70.2 Gy: 11%

69 Gy: 25%  70-78 Gy: 3% Grade 3
3 Gy/fr
70.2 Gy: 6%

74-78 Gy: 23%
Dose-volume limits with LQ corrected doses (a/b = 3 Gy)

Threshold DVHs

Thicker Lines Higher Complication Rates

Jackson 70.2
Jackson 75.6
Akimoto
Wachter
Koper
Koper
Cozarrino
Zapatero
70-75.6 Gy: 7%
Huang
Hartford
75.6 Gy: 34%
Grade 1
Fiorino
Boersma
66 Gy: 33%
70-76 Gy: 9%
74-78 Gy: 23%

Andy Jackson
LQ equivalent dose in 2 Gy fractions (Gy)
Dose-volume limits with LQ corrected doses (a/b = 3 Gy)

Rectum Threshold DVHs

Thicker Lines Higher Complication Rates

Color:
Prescription Doses

Jackson 70.2
Jackson 75.6
Akimoto
Wachter
Koper
Koper
Cozarrino
Zapatero
Huang
Hartford
Fiorino
Boersma

70-75.6 Gy: 7%
75.6 Gy: 34%
66 Gy: 33%
66 Gy: 14%
66.2-70.2 Gy: 11%
69 Gy: 25%
75.6 Gy: 19%
70-76 Gy: 9%
70-76 Gy: 3%
Grade 3
70-76 Gy: 9%
70-78 Gy: 3%
Grade 3
74-78 Gy: 23%
74-78 Gy: 23%

Andy Jackson
LQ equivalent dose in 2 Gy fractions (Gy)
Dose-volume limits with LQ corrected doses (a/b = 3 Gy)

Thicker Lines Higher Complication Rates

Color: Prescription Doses

70.2 Gy: 6%
69 Gy: 25%
66 Gy: 14%
66.2-70.2 Gy: 11%
75.6 Gy: 19%
75.6 Gy: 19%
70-78 Gy: 3% Grade 3

Converge: High Dose Range

70-80 Gy: 3%
70-78 Gy: 3%
70-76 Gy: 9%
70-75.6 Gy: 7%
75.6 Gy: 34%
Huang 75.6 Gy: 34%
Grade 1

Andy Jackson  LQ equivalent dose in 2 Gy fractions (Gy)
# Tolerance of normal tissue

B. Emami et al.

## Table 1. Normal tissue tolerance to therapeutic irradiation

<table>
<thead>
<tr>
<th>Organ</th>
<th>TD 5/5 Volume</th>
<th>TD 50/5 Volume</th>
<th>Selected endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1/3</td>
<td>2/3</td>
<td>3/3</td>
</tr>
<tr>
<td>Kidney I</td>
<td>5000</td>
<td>3000*</td>
<td>2300</td>
</tr>
<tr>
<td>Kidney II</td>
<td>N/A</td>
<td>8000</td>
<td>6500</td>
</tr>
<tr>
<td>Bladder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bone:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Femoral Head I and II</td>
<td>6500</td>
<td>6000</td>
<td>6000</td>
</tr>
<tr>
<td>T-M joint mandible</td>
<td>5000</td>
<td>3000</td>
<td>5200</td>
</tr>
<tr>
<td>Rib cage</td>
<td>10 cm²</td>
<td>30 cm²</td>
<td>100 cm²</td>
</tr>
<tr>
<td>Skin</td>
<td>7000</td>
<td>6000</td>
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<td>Brain</td>
<td>6000</td>
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<td>Spinal cord</td>
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</tr>
<tr>
<td>Cauda equina</td>
<td>5000</td>
<td>5000</td>
<td>4700</td>
</tr>
</tbody>
</table>

Note: * denotes data from work by other authors.
Missing growth neurocognitive endocrine cancer induction
Data in children from Matthew Krasin, St Jude
Quantec: Mostly conventional fractionation

Some hypo-fractionation
brain
lung
liver
Context/Limitations

• Data is NOT great!!!

• Incomplete (16 vs 26 organs); e.g. small bowel

• Clinically useful, MD’s

• MD’s want it made simple

• Be careful, recognize uncertainties
Discard spatial, anatomic, physiologic data

Extract unambiguous data
  • Single Point: e.g. V20
  • Global: e.g. mean dose

Compute model-based NTCP estimates

Cumulative DVH

% Volume at ≥ Dose x

3D dose distribution

V20

20 Gy
DVH-Based Models

- Exportability
- Applicability
  - IMRT vs. 3D
  - SRS
- Model limitations
- Fractionation
- Anatomy
Exportability?
Michigan (mets) vs. Fudan/Guangxi (primary liver tumors)

See letter to editor Nov 2006 from U Mich

Xu et al. *IJROBP* 65:193, 2006; Fudan University, Shanghai, Cancer Hospital, Guangxi Medical University, Nanning, China
Pneumonitis, mean dose response - whole lung

Mean dose (Gy)

0 10 20 30

0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0

MSKCC (10/78)
Duke (39/201)
Michigan (17/109)
MD Anderson (~497/223)
NKI (17/106)
WU (52/219)
Martel et al. (9/42)
Oeztel et al. (10/66)
Rancati et al. (7/55)
Kim et al. (12/68)

logistic fit

Low Risk Group:
70% of pts. ×
15% risk RP = 10.5%

High Risk:
30% of pts. ×
40% risks = 12%
17/109 with MLD > 20
70% \times 17 = 12 \text{ patients}

92/109 with MLD < 20
10% \times 92 = 9 \text{ patients}

Kong, U Mich, IJROBP 2006
Ignores Anatomy/Physiology
Fig. 3. Schematic diagram illustrating the compression and tension stresses that exist in the normal femur (a). An anatomic gross section of the bone (b).  

Fig. 4. Diagram illustrating the vascular supply of the proximal femur. The majority of blood to the femur is delivered via the medial circumflex artery (1). This artery passes medially and posterior to the neck of the femur and supplies the neck and head. The secondary vessel is the lateral femoral circumflex arterial system (2). If radiation-induced damage to the femur occurs, the position of these vessels and their branches relative to the XRT beam is important (30).
Esophagus contours: variable area (volume)
Univariate and Multivariate Analyses

CT \rightarrow \text{esophageal contours} \rightarrow 3D metrics

Anatomic correction

“corrected” 3D metrics

\rightarrow \text{Outcome}

RTOG acute & late toxicity
### Toxicity = $f$ (Dosimetric Parameters)

<table>
<thead>
<tr>
<th></th>
<th>V 50 Uncorrected</th>
<th>V 50 Corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute ≥ grade 2</td>
<td>0.008</td>
<td>0.005</td>
</tr>
<tr>
<td>Acute ≥ grade 3</td>
<td>0.05</td>
<td>0.003</td>
</tr>
<tr>
<td>Late ≥ grade 1</td>
<td>0.14</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Adapted from Kahn et al. 2004 (Duke)
Organ interactions
Proton RT in Rats: Resp Rate = f (lung and heart RT)

Luijk Ca Res 65:6509, 2005
Neighborhood Effects
Rat Proton Cord RT

ED 50 (Gy) to “shower”

- No bath (control): 88 (dose in peak)
- 4 Gy bath, both sides: 61
- 4 Gy bath, one side: 69
- 18 Gy bath, both sides: 31
- Wide shower, 8 mm: No bath effect

Serial vs. parallel

Less well defined
Migration of stem cells
Cytokine/neighborhood effects
Vascular

Bisl et al. IJROBP 64:1204-1210, 2006
What I really worry about

- Missing the tumor; Unrealistic fears
  - Blocking chiasm for GBM
- Large palliative fields work!! (fast, cheap)
  - Generation of fear, slaves to DVH’s
  - There was RT pre DVH’s
- Complication = death? Usually not
  - Grade 1 pneumonitis, rectal bleeding
- Don’t take data too seriously (models)
- Chemo, fraction size
Field Margins

Physically or biologically necessary margin

Certainty of Gross Anatomy

More conservative approach

Too fancy: marginal miss
### Prostate: Too Fancy?

<table>
<thead>
<tr>
<th>Method</th>
<th>Margins (mm)</th>
<th>Biochemical Disease Free Survival (5yrs)</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implanted Seeds for Localization (N = 25)</td>
<td>3-5</td>
<td>58%</td>
<td>0.02</td>
</tr>
<tr>
<td>No Implanted Seeds (N = 213)</td>
<td>6-10</td>
<td>91%</td>
<td></td>
</tr>
</tbody>
</table>

Engels, IJROBP 74:388, 2009
Too Fancy? Orbital Lymphoma

Method

GTV + Margin (12)
Whole Orbit (12)

Local Control

67%
100%

Grade ≥2 Toxicity

25%
33%

From Pfeffer et al., IJROBP 2004
Gross Tumor Volume (GTV) + Microscopic Spread + Internal Motion + Set-up Errors

Clinical Target Volume (CTV)

Internal Target Volume (ITV)

Planning Target Volume (PTV)- treated volume

Used to lump them together: 1.5-2.0 cm margins routinely
Addressing physical uncertainties unmasked biological ignorance

- Imaging: CT, PET
- Gross Tumor Volume (GTV) + Microscopic Spread + Internal Motion + Set-up Errors
- Clinical Target Volume (CTV)
- Internal Target Volume (ITV)
- Planning Target Volume (PTV)- treated volume
- Respiratory gating
- On board imaging
- biologic uncertainties

Old fashioned ways to reduce toxicity

- Positioning
  - Neck
  - Decubital
- Reducing skin folds
- Barium in bowel
- Careful team work
- Keep it simple!!, use time wisely

Applicable in Modern Era!
QUANTEC

• Each Organ-Specific Paper:
  • Needed research, challenges

• End of the issue: “Vision Papers”
  • True dose
  • Imaging
  • Biomarkers
  • Data Sharing
  • Lessons of Quantec
Summary

• Since Emami
  • More 3D dosimetry --> toxicity data
  • DVH-based predictions sub-optimal (physiology)
  • Quantec incomplete; Emami still relevant

• Is the prior data still applicable?
  • 3D beams --> IMRT
  • Chemo- moving target
  • BID RT

• Challenges for normal tissue injury studies

• Over-Reliance on technology to reduce morbidity (e.g. IMRT, OBI, CBCT)
Acknowledgments

- David Fried, Liyi Xie, Janet Bailey, Micheal Lawrence, Jessica Hubbs, Jiho Nam, Mert Saynack, John Kirkpatrick

- Quantec Steering Committee: Joe Deasy, Soren Bentzen, Randy Ten Haken, Ellen Yorke, Andy Jackson, Sandy Constine, Avi Eisbruch, David Morris

- Emami et al, Rubin, Cooper, Phillips, et al

- ASTRO, AAPM; Authors, Reviewers