TG-166
Outcome driven treatment planning

X. Allen Li
On behalf of AAPM TG-166

AAPM, July 19, 2010
# Evolution of biological (outcome-model) based treatment planning

<table>
<thead>
<tr>
<th>Evolution stage</th>
<th>Plan optimization strategy</th>
<th>Plan evaluation strategy</th>
<th>Representative TPS</th>
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<td>DV-based cost functions</td>
<td>DVHs</td>
<td>The majority of current TPS</td>
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<td>1</td>
<td>EUD for OARs; EUD- and DV-based cost functions for targets</td>
<td>DVHs and relative values of TCP/NTCP</td>
<td>CMS Monaco Philips Pinnacle Varian Eclipse</td>
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<td>EUD-based cost functions for all structures</td>
<td>Absolute values of TCP/NTCP</td>
<td>Future developments</td>
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<tr>
<td>3</td>
<td>Absolute values of TCP/NTCP</td>
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<td>Future developments</td>
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</table>
AAPM Task Group 166:

**The use and QA of biologically related models for treatment planning**

<table>
<thead>
<tr>
<th>X. Allen Li (Chair)</th>
<th>Markus Alber</th>
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<tr>
<td>Joseph O. Deasy</td>
<td>Andrew Jackson</td>
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<td>Kyung-Wook Ken Jee</td>
<td>Lawrence B. Marks</td>
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<td>Ellen D. Yorke</td>
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TG-166 Charges:

• To review dose-response models introduced in TPS
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• To discuss strategies, limitations, conditions and cautions for using these models and parameters in clinical treatment planning
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TG-166 Charges:

- To review dose-response models introduced in TPS
- To discuss strategies, limitations, conditions and cautions for using these models and parameters in clinical treatment planning
- To point out dosimetric differences between outcome-model based and dose-volume based plan optimization and evaluation
- To provide general guidelines and methodology for commissioning and routine QA of outcome-model based TPS
Outcome modeling for treatment planning

- Survival probability (LQ)
- Equivalent Uniform Dose (EUD/gEUD)
- TCP (Poisson model)
- NTCP (LKB, Serial, Parallel)
- Clinical Response Models (Maximum likelihood analysis)
Outcome modeling for treatment planning

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Problems:

- Largely phenomenological rather than predictive
- Unreliable model parameters, needs more clinical data (e.g., QUANTEC)
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Problems:

- Largely phenomenological rather than predictive
- Unreliable model parameters, needs more clinical data (e.g., QUANTEC)

But still useful (pushing individual DVHs towards less toxicity)!
LQ parameters:

Malignant gliomas

MG
\[\alpha = 0.06 \pm 0.05 \text{ Gy}^{-1}\]
\[\alpha/\beta = 10.0 \pm 15.1 \text{ Gy}\]

Grade 1&2
\[\alpha = 0.35 \pm 0.07 \text{ Gy}^{-1}\]
\[\alpha/\beta = 4.3 \pm 5 \text{ Gy}\]

Grade 3
\[\alpha = 0.11 \pm 0.10 \text{ Gy}^{-1}\]
\[\alpha/\beta = 5.8 \pm 11.8 \text{ Gy}\]

Grade 4
\[\alpha = 0.04 \pm 0.06 \text{ Gy}^{-1}\]
\[\alpha/\beta = 5.6 \pm 9.4 \text{ Gy}\]

Qi, Schultz, Li, IJROBP, 2006.
Dose-volume limits for >= grade 2 rectal toxicity with LQ corrected doses (\(\alpha/\beta = 3\) Gy)

- Wachter (66 Gy: 14%)
- Koper (66 Gy: 33%)
- Cozzarini (66.2-70.2 Gy: 11%)
- Jackson (75.6 Gy: 19%)
- Fiorino (70-76 Gy: 9%)
- Akimoto (69 Gy: 25% 3 Gy/frac)
- Jackson (70.2 Gy: 6%)
- Hartford (75.6 Gy: 34% Grade 1)
- Huang (74-78 Gy: 23%)

LQ equivalent dose in 2 Gy fractions (Gy)

% volume
estimates of LKB volume effect parameter $n$ for rectal complications

(Slide courtesy A. Jackson et al.)

(Note: $a = 1/n$)
Use of outcome models in computerized treatment planning

- Plan evaluation
- Plan optimization
Plan Ranking: Tomo vs IMRT
Case example: Female Anus

**Figure-of-merit**

TOMO: $f_{EUD} = 0.613$
IMRT: $f_{EUD} = 0.600$
Plan Optimization

Cost Functions: Mathematical forms of treatment goals

• Physical (dose-volume based) cost functions
  • Overdose/underdose volume constrains
  • Maximum/minimum doses

• Biological (outcome-model based) cost function.
  • Target/OAR EUDs
  • TCP/NTCP.
H&N case: Physical (XiO) vs Biological (Monaco)
Biological (solid) vs. dose-based (dashed) cost functions for OARs

Monaco
Sensitivity on model parameters: Monaco

PTV 70 cell sensitivity:
- 0.25 Gy⁻¹
- 1.0 Gy⁻¹
- 0.1 Gy⁻¹

Spinal cord PRV:
- Power law exponent:
  - 12
  - 20
  - 1

Spinal cord PRV equivalent uniform dose:
- 25 Gy
- 15 Gy
- 30 Gy

Left parotid:
- Power law exponent:
  - 3.9
  - 1.0

Left parotid reference dose:
- 26 Gy
- 15 Gy
- 35 Gy

Left parotid mean organ damage:
- 35%
- 20%
- 50%

Graphs showing volume (%) against dose (Gy) for different parameters and conditions.
Comparison: Monaco (solid), Pinnacle (dashed), Eclipse (dotted)
Why does outcome model work?
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*We know how to ask and what to ask!*
Why does outcome model work?

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- Since, by definition, there are an infinite number of DVHs that leads to an EUD for a given organ, outcome-model based cost functions can lead to the desired EUD directly.
Why does outcome model work?

*We know how to ask and what to ask!*

- Since, by definition, there are an infinite number of DVHs that leads to an EUD for a given organ, outcome-model based cost functions can lead to the desired EUD directly.
- Can get the best possible result (not just any acceptable result) and will get it more quickly and easily.
Serial structure (spinal cord, rectum)

Parallel structure

lung, liver
How does a serial complication model control the DVH?

The length of the weight arrow grows as

\[ D^{k-1} \exp(\alpha D) \]

or similar functions.
In contrast, a quadratic penalty:

DVH control only for doses greater than threshold

Courtesy M. Alber

Bloemfontein 2006
How does a parallel complication model control the DVH?

The length of the weight arrow grows as

\[ \frac{\exp(-\alpha D)}{(1 + \exp(-\alpha D))^2} \]

or similar functions.
In contrast, a DVH constraint:

The constraint controls only a single point.

Courtesy M. Alber

Bloemfontein 2006
Cautions for using outcome-model based TPS

- Cold and hot spots
- Sensitivity of model parameters
- Extrapolation/interpolation between fractionations (EUD, DVH)
TG-166 General Recommendations

- Outcome-model based cost functions for OARs are *more effective* towards OAR sparing
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• Outcome-model based cost functions for OARs are more effective towards OAR sparing

• Outcome-model based TPS could generate highly non-uniform dose distributions. Unless for deliberate and tested situations, such highly non-uniformity should be avoided by using min and/or max dose constraints.
TG-166 General Recommendations

- Outcome-model based cost functions for OARs are *more effective* towards OAR sparing.

- Outcome-model based TPS could generate highly non-uniform dose distributions. Unless for deliberate and tested situations, such highly non-uniformity should be avoided by using min and/or max dose constraints.

- At present, plan evaluation should base on established dose-volume criteria (3D dose distribution, DVH). Biological indices may be used to help select rival plans. Use of absolute estimates of TCP/NTCP as main indicators of plan quality is not warranted at this time.
Commissioning of biologically based TPS

- **Verification of model calculations (EUD/TCP/NTCP)**
Commissioning of biologically based TPS

• **Verification of model calculations (EUD/TCP/NTCP)**
  – Benchmark phantom (suggested by TG-166)
Benchmark Phantom for verification of EUD, TCP and NTCP calculation
## TCP/NTCP calculated for benchmark phantom

<table>
<thead>
<tr>
<th>Structure</th>
<th>PTV Rectangle</th>
<th>Rectangle 1</th>
<th>PTV Rectangle</th>
<th>Rectangle 1</th>
<th>Rectangle 2</th>
<th>Triangle 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>D50 (Gy)</td>
<td>63.3</td>
<td>44.2</td>
<td>80</td>
<td>75.1</td>
<td>55.3</td>
<td>46</td>
</tr>
<tr>
<td>$\gamma$</td>
<td>5</td>
<td>1.6</td>
<td>3</td>
<td>2.8</td>
<td>3.1</td>
<td>1.8</td>
</tr>
<tr>
<td>$\alpha/\beta$ (Gy)</td>
<td>10</td>
<td>10</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Seriality</td>
<td>N/A</td>
<td>N/A</td>
<td>0.18</td>
<td>8.4</td>
<td>0.69</td>
<td>1</td>
</tr>
<tr>
<td>Function</td>
<td>TCP</td>
<td>TCP</td>
<td>NTCP</td>
<td>NTCP</td>
<td>NTCP</td>
<td>NTCP</td>
</tr>
<tr>
<td>Value (%)</td>
<td>94.1</td>
<td>80.3</td>
<td>26.6</td>
<td>18.1</td>
<td>23.5</td>
<td>29.5</td>
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- **Verification of model calculations (EUD/TCP/NTCP)**
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  - Test cases (head & neck, prostate and brain cases available from TG-166 site)
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  - Independent software tools (e.g., CERR [http://radium.wustl.edu/CERR/about.php], BioPlan (Sanchez-Nieto and Nahum), BioSuite (Uzan and Nahum).
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- **Double planning for first several cases from each representative tumor site using the outcome-model based TPS and the standard dose-based TPS**
Routine QA for outcome-model based TPS

- Establish a sample plan with baseline data (e.g., DVH, EUD, TCP, NTCP) at commissioning
Routine QA for outcome-model based TPS

- Establish a sample plan with baseline data (e.g., DVH, EUD, TCP, NTCP) at commissioning

- Replan the sample case annually or after a major upgrade and compare to the baseline data, to ensure that models, parameters, and algorithms implemented in the TPS remain the same
Summary:

Outcome-model based treatment planning

• is more effective to optimize plan towards normal tissue sparing.
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• requires more data/work for outcome modelling
Summary:

Outcome-model based treatment planning

• is more effective to optimize plan towards normal tissue sparing.
• needs to be implemented with cautions.
• requires more data/work for outcome modelling.

• is coming into clinic and is here to stay!
Acknowledgement

Members of TG-166

(Vladimir Semenenko, Chuck Mayo....)

- An Tai, Ph.D
- Jian Wang, Ph.D
- Mariana Guerrero, Ph.D
- Rob Stewart, Ph.D
- Sharon Qi, Ph.D
- J. Frank Wilson, MD
- Chris Schultz, MD
- Beth Erickson, MD

Funding support: NIH, MCW