Practical issues for biologically based treatment planning

X. Allen Li
Medical College of Wisconsin

AAPM Educational Course, Aug. 1st, 2012

Limitations of dose-volume based treatment planning
- DV metrics are merely surrogate measures of radiation response
- Commonly used DV constraints (e.g., V20 for lung)
  - More than one point correlates outcome (MLD, V5, V15,…)
  - Specific to treatment techniques (3DCRT, static or rotational IMRT…)
  - Plan optimization with multiple DV points is indirect, depending on planner’s skill.
  - Computerized optimization with multiple DV indices can be complex and can be trapped in a local minimum.

A Little to a Lot or a Lot to a Little?

Biologically based treatment planning
Feedback from biological response (outcome) models during the treatment planning process

Feedback may be either passive/automated in the case of inverse treatment planning, or with active participation from the planner in the case of forward treatment planning.

Why use outcome models?
- To fully describe responses as a function of any dose to any volume
- To predict responses based historical data
- To supplement or replace dose-volume criteria for plan optimization and evaluation.
Biologically based treatment planning

- Plan evaluation
- Plan optimization

Three commercial treatment planning systems with tools for biologically based plan evaluation and optimization

Elekta Monaco
Phillips Pinnacle
Varian Eclipse

Problems to evaluate complex plans with DVH

- Complicated anatomy, multiple OARs
- Complicated/crossing DVHs
- Difficult for visual inspection
- Plan merit not quantified
- DVH failure for spatial tumor heterogeneity

Quantitative evaluation and comparison of complicated plans based on biological effectiveness are desirable.

Plan Ranking: Tomo vs IMRT
Case example: Female Anus

Figure of merit
TOMO: fEUD = 0.613
IMRT: fEUD = 0.600

Plan Optimization

Cost Functions: Mathematical forms of treatment goals

- Physical (dose-volume based) cost functions
  - Overdose/underdose volume constraints
  - Maximum/minimum doses
- Biological (outcome-model based) cost function
  - Target/OAR EUDs
  - TCP/NTCP

H&N case: Physical (XiO) vs Biological (Monaco)
Why do outcome models work?

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

- Since, by definition, there are an infinite # of DVHs that lead 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.
How does a serial complication model control the DVH?

The length of the weight arrow grows as

$$D^{1-\alpha} \cdot \exp(\alpha D)$$
or similar functions.

In contrast, a quadratic penalty:

DVH control only for doses greater than threshold.

Not all organs are serial: parallel complication models

Here, the tissue has lost function.

At this dose, we begin to see changes.

OK for the whole volume.

How does a parallel complication model control the DVH?

The length of the weight arrow grows as

$$\frac{\exp(-\alpha D)}{(1-\exp(-\alpha D))^f}$$
or similar functions.

In contrast, a DVH constraint:

The constraint controls only a single point.

Targets:

dose too low

Dose we aim to deliver

If we increase the dose further, we do not gain much, but some patients may benefit.
AAPM Task Group 166:
The use and QA of biologically related models for treatment planning
X. Allen Li (Chair)
Markus Alber
Andrew Jackson
Lawrence B. Marks
Charles Mayo
Alan E. Nahum
Vladimir Semenenko

Joseph O. Deasy
Kyung-Wook Ken Jee
Mary K. Martel
Vitali Monseenko
Andrzej Niemierko
Ellen D. Yorke

TG-166 Report Summary: MP, 39 (3), 2012

TG-166 General Recommendations

• Outcome-model based cost functions for OARs can be 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.

Cautions for using outcome-model based TPS

• Cold and hot spots

• Sensitivity of model parameters

• Extrapolation/interpolation between fractionations (EUD, DVH)

Commissioning of biologically based TPS

• Verification of model calculations (EUD/TCP/NTCP)
  – Benchmark phantom (suggested by TG-166)

TCP/NTCP calculated for benchmark phantom

<table>
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<th>Structure</th>
<th>PTV Rectangle</th>
<th>Rectangle 1 PTV Rectangle</th>
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<td>80.3</td>
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</table>
Commissioning of biologically based TPS

- Verification of model calculations
  - EUD/TCP/NTCP
  - Benchmark phantom (suggested by TG-166)
  - Test cases (head & neck, prostate and brain cases available from TG-166 site)
  - Independent software tools (e.g., CERR (http://radium.wustl.edu/CERR/about.php), BioPlan (Sanchez-Nieto and Nahum), BioSuite (Uzan and Nahum)).
- 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
- 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 on BBTP:

Outcome-model based treatment planning

- Can be more effective to optimize plan towards normal tissue sparing.
- Needs to be implemented with caution.
- Requires commissioning and routine QA.

Acknowledgement

Members of AAPM TG-166

(V. Semenenko, C. Mayo, V. Moiseenko, …)

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

Funding support: NIH, MCW