# Practical issues for biologically based treatment planning

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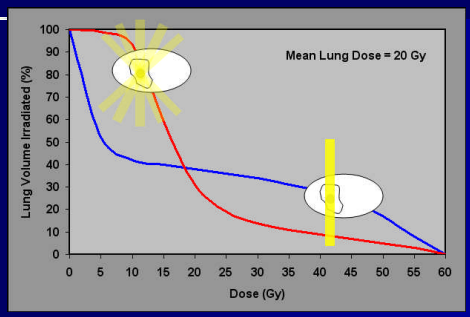
## *Limitations of dose-volume based treatment planning*

- **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.

## Evolution of biological (outcome-model) based treatment planning

| Evolution stage | Plan optimization strategy | Plan evaluation strategy | Representative TPS |
|---|---|---|---|
| 0 | DV-based cost functions | DVHs | The majority of current TPS |
| 1 | EUD for OARs; EUD- and DV-based cost functions for targets | DVHs and relative values of TCP/NTCP | Elekta Monaco Philips Pinnacle Varian Eclipse |
| 2 | EUD-based cost functions for all structures | Absolute values of TCP/NTCP | Future developments |
| 3 | Absolute values of TCP/NTCP | Absolute values of TCP/NTCP | Future developments |

## 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

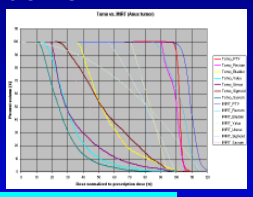
- Plan evaluation
- Plan optimization

## 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

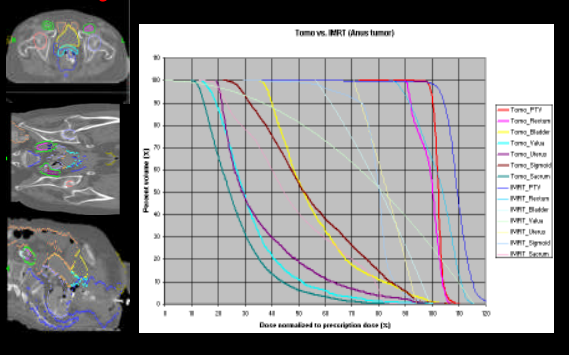
- Complicated anatomy, multiple OARs
- Complicated/crossing DVHs
- Difficult for visual inspection
- Plan merit not quantified
- DVH failure for spatial tumor heterogeneity



**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

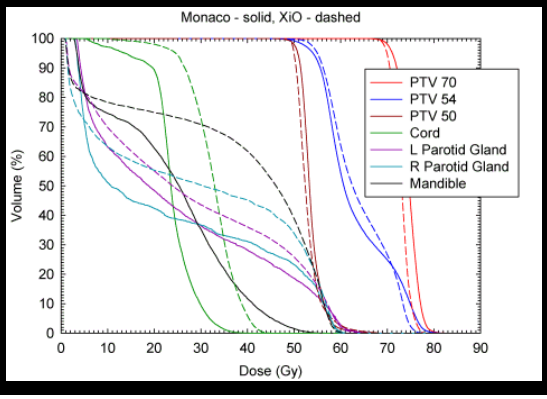



## Plan Optimization

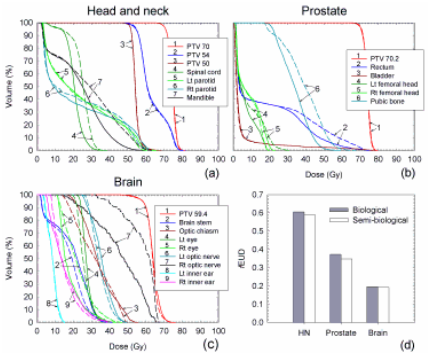
Cost Functions: Mathematical forms of treatment goals

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

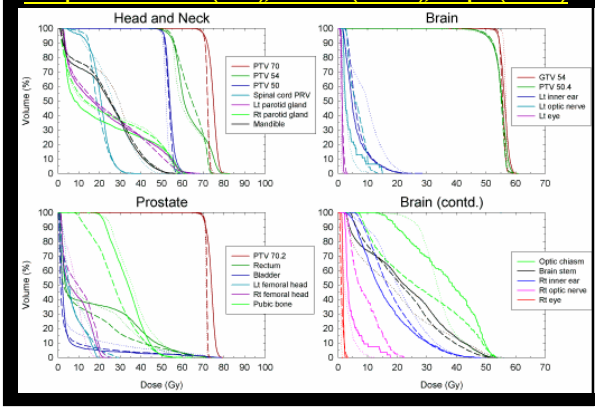
## H&N case: Physical (XiO) vs Biological (Monaco)



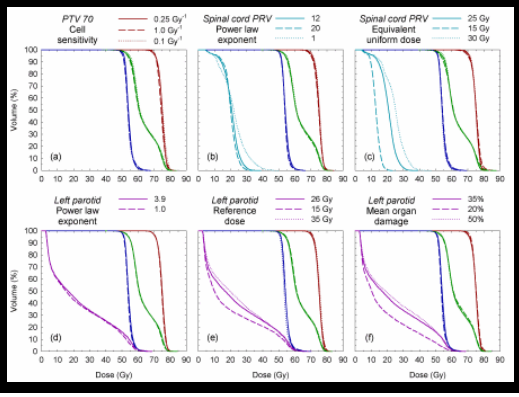
Biological (solid) vs. dose-based (dashed) cost functions for OARs
Monaco




**Comparison: Monaco (solid), Pinnacle (dashed), Eclipse (dotted)**




**Sensitivity on model parameters: Monaco**



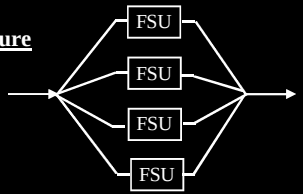

## Why do outcome models work?

***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

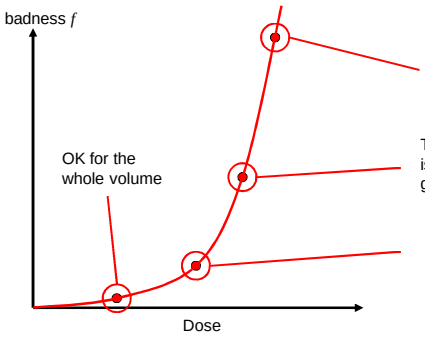
**Serial structure (spinal cord, rectum)**


**Parallel structure**



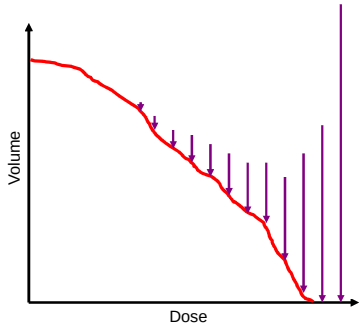

**lung, liver**

*How to make a biological cost function: serial models*




Courtesy M. Alber
Bloemfontein 2006

## 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

Courtesy M. Alber
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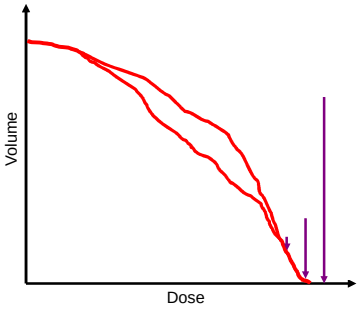
## In contrast, a quadratic penalty:




DVH control only for doses greater than threshold

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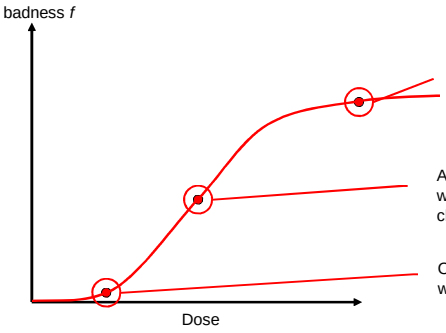
## Not all organs are serial: parallel complication models




Here, the tissue has lost function

At this dose, we begin to see changes

OK for the whole volume

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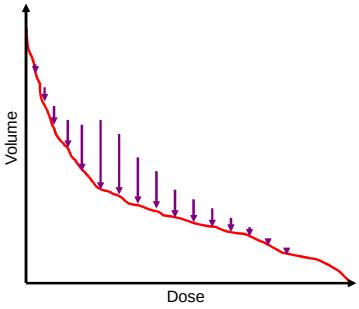
## How does a parallel complication model control the DVH ?




The length of the weight arrow grows as

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

or similar functions

Courtesy M. Alber
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## In contrast, a DVH constraint :


The constraint controls only a single point

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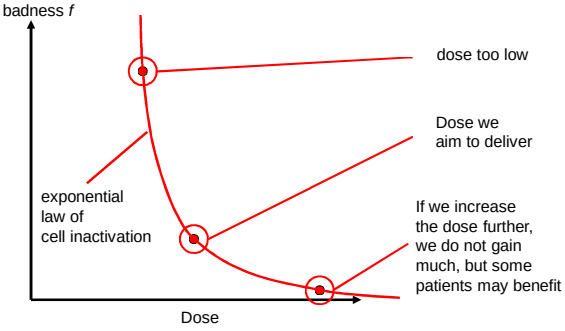
## targets




Courtesy M. Alber
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**AAPM Task Group 166:**

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


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Andrew Jackson — Kyung-Wook Ken Jee
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Charles Mayo — Vitali Moiseenko
Alan E. Nahum — Andrzej Niemierko
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TG166 Report Summary: MP, 39 (3), 2012


## TG-166 General Recommendations

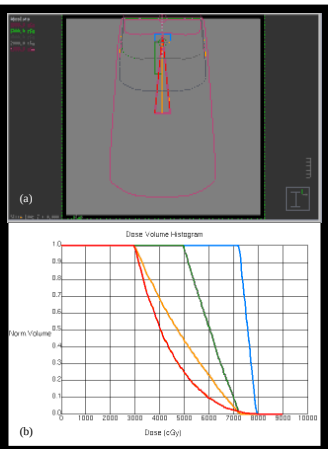
- **Outcome-model based cost functions for OARs can be *more effective* towards OAR sparing**
- **Outcome-model based TPS could generate highly non-uniform dose distributions.** Unless for deliberate and tested situations, such highly non-uniformity should be avoided by using min and/or max dose constraints.
- **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

| Structure | PTV Rectangle | Rectangle 1 | PTV Rectangle | Rectangle 1 | Rectangle 2 | Triangle 1 |
|---|---|---|---|---|---|---|
| D50 (Gy) | 63.3 | 44.2 | 80 | 75.1 | 55.3 | 46 |
| γ | 5 | 1.6 | 3 | 2.8 | 3.1 | 1.8 |
| α/β (Gy) | 10 | 10 | 3 | 3 | 3 | 3 |
| Seriality | N/A | N/A | 0.18 | 8.4 | 0.69 | 1 |
| Function | TCP | TCP | NTCP | NTCP | NTCP | NTCP |
| Value (%) | 94.1 | 80.3 | 26.6 | 18.1 | 23.5 | 29.5 |

## 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

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