Volume Effects and Reporting Standards for SBRT

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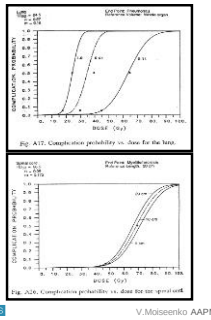
RETHINKING MEDICAL PHYSICS

Outline

- Volume effects
- Design of clinical trials based on dose-volume consideration
  - Use of Vx constraints
  - Use of effective volume approach
- Reporting standards
- Data archiving

Volume effects

- Volume effects
  - What governs normal tissue response
    - Mean dose (but there are other possibilities) vs hot spots
  - Parallel model vs serial model
    - Lung – strong volume effect
    - Spinal cord – weak volume effect



Emami et al 1991 & Burman et al 1991

Dose-volume-response: Outcomes data analysis → planning guidelines

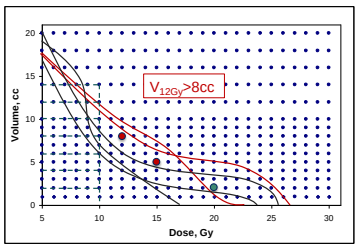
- Establish what is safe
- Provide planning guidelines
- Suggest studies to refine/update or develop guidelines
- Pitfalls

Dose-volume-response: what is reported

- Dose-volume cut-offs
  - Often reported
  - Demonstrate statistical significance but not full dose-volume response
- Response as a function of a dose-volume cut-off
  - Sometimes reported
  - Demonstrates incidence-cut-off relationship to decide what is safe
- Full dose-volume-response model
  - Rarely reported
  - Requires variability in dose-volume
  - Requires a substantial number of complications (10 per parameter)
  - Can be used to decide what is safe for dose-volume combinations

V_x (or D_x) cut-off approach

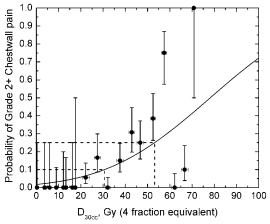
- Does median V_x separate patients into groups different in incidence?
- Can we find a V_x which separates patients into likely and unlikely to develop complications with the most predictive power?
- This separates patients into groups, does not always tell us if risk is acceptable
- Need incidence-V_x data



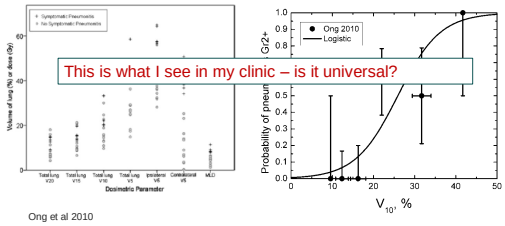
V_x – incidence approach

- Logistic or probit
  - Level of acceptable risk can be set
  - Recommendations for dose-volume constraints can be made

Kimsey et al 2016



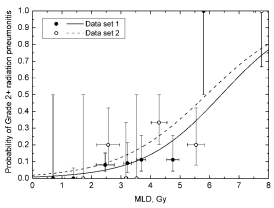
V_x – incidence approach



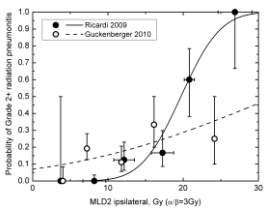
This is what I see in my clinic – is it universal?

Ong et al 2010

Are guidelines transferrable?



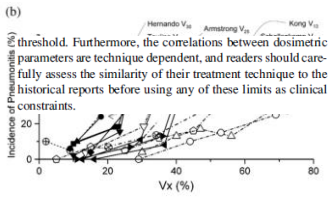
Yamashita et al 2007
Okubo et al 2017



Kong et al (in preparation)

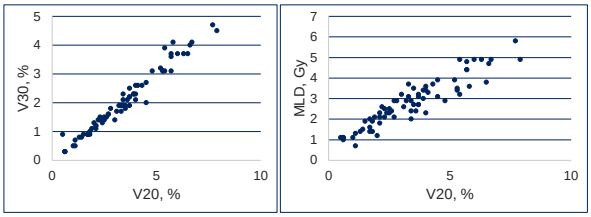
V_x – does the choice of X matter?

- Is X organ response-driven or depends on treatment technique?
- Is there a correlation between V_x if patient were treated with a similar technique?
- Can we tell a true predictor if V_x of choice is a predictor because it correlates with a true predictor?



Marks et al 2010

How much correlation between V_x do we see?

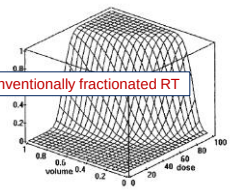


Okubo et al 2017

Volume effects

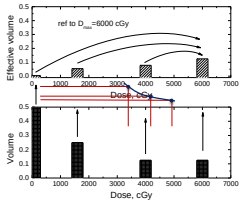
- Full dose-volume-response
  - Typically three parameters
    - D_{50} for reference (typically whole)
    - Slope parameter
    - Volume effect parameter
  - Lyman-Kutcher-Burman model is a popular choice
    - Requires uniform dose to partial volume
    - Need to reduce DVH into a single step DVH

Available for main organs at risk for conventionally fractionated RT



DVH Reduction, effective volume, V_{eff}

- Based on power law for tolerance dose
  - Need volume dependence parameter, n (a=1/n in gEUD)
  - n→1 means mean dose drives complications
  - n→0 mean maximum dose drives complications
  - For a reference dose of choice (D_{max}, prescription dose) converts DVH into a single step D_{ref} to V_{eff}

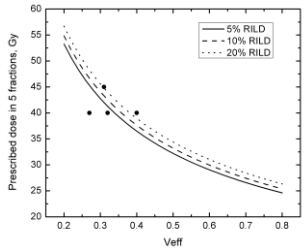


$$D_V = D_1 / V^n$$

$$V_{eff} = \sum v_i (D_i / D_{ref})^{1/n}$$

Choice of prescribed dose, V_{eff} approach

- Calculate iso-effect plots for various toxicity levels
- Set acceptable level of toxicity and use this to prescribe dose



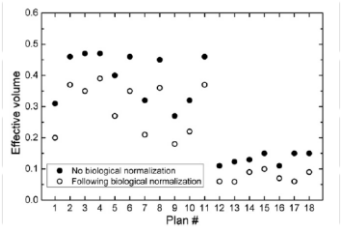
Choice of prescribed dose, V_{eff} approach

- V_{eff} is sensitive to dose distribution only
  - If all doses including the reference dose are scaled by the same factor V_{eff} does not change
  - Patients can be stratified to different prescription doses according to V_{eff}

Primary Liver Cancer: Dose per fraction (Gy)					
Level	level 1	level 2	level 3	level 4	level 5
Max dose (Gy)	9.0	9.0	9.0	9.5	10
NTCP	0.05	0.10	0.20	*0.20**	*0.20**
Veff					
<0.16	9.0	9.0	9.0	*9.5*	*10.0*
0.18	9.0	9.0	9.0	*9.5*	*10.0*
0.20	8.8	9.0	9.0	*9.5*	*9.5*
0.22	8.4	8.7	9.0	*9.0*	*9.0*
0.24	8.0	8.2	8.5	*8.5*	*8.5*
0.26	7.6	7.9	8.1	*8.1*	*8.1*
0.28	7.3	7.5	7.8	*7.8*	*7.8*
0.30	7.0	7.3	7.4	*7.4*	*7.4*
0.32	6.7	7.0	7.3	*7.3*	*7.3*
0.34	6.6	6.7	7.0	*7.0*	*7.0*
0.36	6.4	6.6	6.7	*6.7*	*6.7*
0.38	6.2	6.4	6.6	*6.6*	*6.6*
0.40	6.0	6.2	6.4	*6.4*	*6.4*

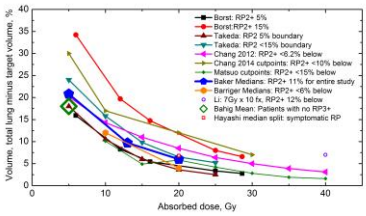
Choice of prescribed dose, V_{eff} approach

- Ideally isotoxicity curves have to be derived from SBRT data
  - What if model parameters are not available for SBRT but available for conventional fractionation
  - Account for dose-per fraction using linear-quadratic (α/β)
  - Accounting for dose-per-fraction is non-linear, V_{eff} will change



Working group challenges and solutions

- Full dose-volume response often cannot be assessed
- Enough to recommend what is safe
- Source data are presented in papers



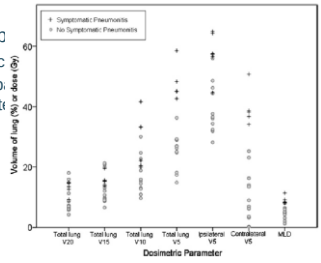
Data compiled by Ellen Yorke

Working group challenges and solutions

- Recommendations based on the balance of evidence
- Tried to explain inconsistencies
- Projections to high risk region often cannot be made, i.e., only can define what is safe
- It will be helpful if reporting standards are followed

What to report

- Has to b
  - Replic
  - Comp ata to the report



What to report

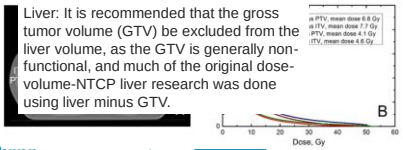
- All aspects
  - Patient eligibility, description of the cohort including underlying conditions
  - Immobilization, motion management
  - CT scanning + other imaging
  - Contouring, planning
  - QA (optional)
  - Treatment
  - Outcomes – follow-up, scoring
  - Statistical analysis

Dose-volume analysis

- Does
  - Mi
  - PT from institution to ins e not negligible

During RT planning, the total lung volume is usually defined to exclude the gross tumor volume (GTV). Excluding the planning target volume (PTV) rather than the GTV from the lung volume may reduce the apparent lung exposure (because normal lung within the PTV but outside the GTV will be excluded) and may increase interinstitutional variations (because PTV margins may vary).

Liver: It is recommended that the gross tumor volume (GTV) be excluded from the liver volume, as the GTV is generally non-functional, and much of the original dose-volume-NTCP liver research was done using liver minus GTV.



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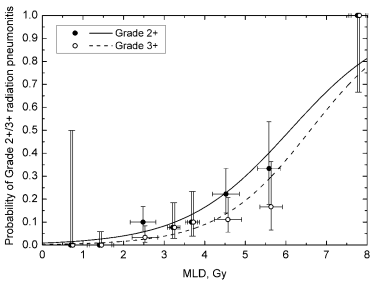

Okubo et al 2017

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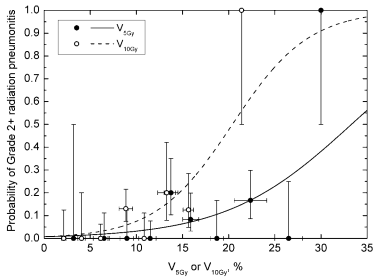

Okubo et al 2017

Data archiving/sharing

- Tools to query clinical data sets are available
- Archiving data and querying saved data has been done, tools are available
- Challenges are many
  - Test for Tx interrupts, incomplete treatments, planning on multiple CTs, naming convention
- Many journals now allow publishing supplementary material on-line

Data archiving/sharing

- Projects started in a few places
  - UMichigan
  - Various Europe-based projects
- Many journals now allow publishing supplementary material on-line
- Medical Physics now allows publishing data

Alexander Vasilyevich Sevan'kaev