

## Monte Carlo-based Clinical Treatment Planning: Issues for Consideration

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## Acknowledgements

- E. Heath, G. Stroian, K. Al-Yahya, W. Parker, F. Verhaegen
- F. Deblois and A. Alexander: MMCTP GUI
- Canadian Institutes of Health Research, National Cancer Institute of Canada and Natural Sciences and Engineering Research Council for grant funding & salary support (CIHR, NCIC, NSERC)



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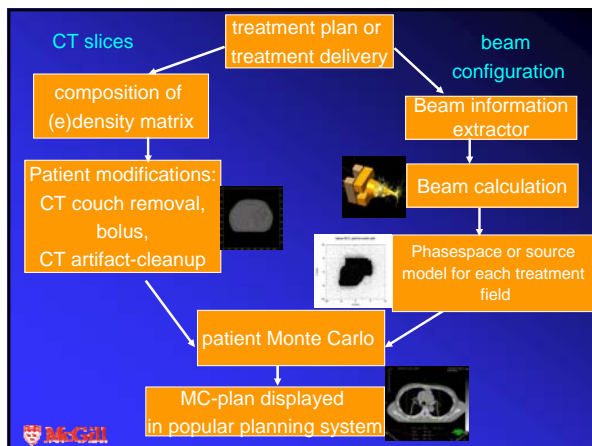
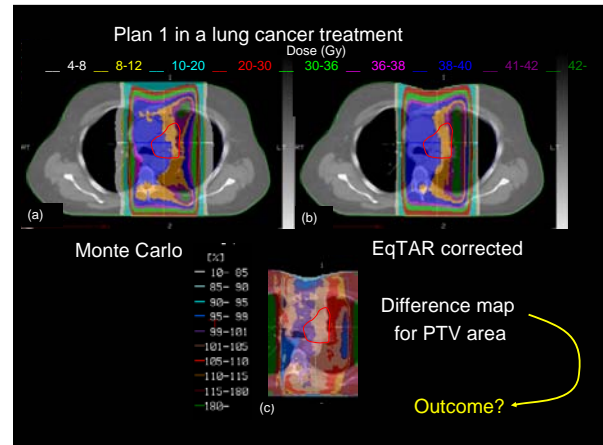
## Outline: "issues for consideration"

- Building blocks of a generic clinical MCTP system
- Verification issues in general
  - Validation of relative output
  - CT calibration & artifacts
- Dose specification
- Absolute calibration, MU calculations
- Verification issues in detail
  - Experimental verification of MC-based dose algorithms: beam modifiers (MLC)
  - Experimental verification of transport within the phantom/patient
- MC-based treatment planning: comparisons of MC versus simple (correction-based) and model-based algorithms
- Statistical Uncertainties in MC-based treatment planning
- MCTP and lung (NSCLC)
- Retrospective re-planning & outcome association
- Summary

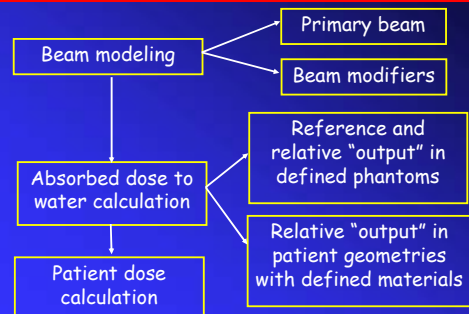


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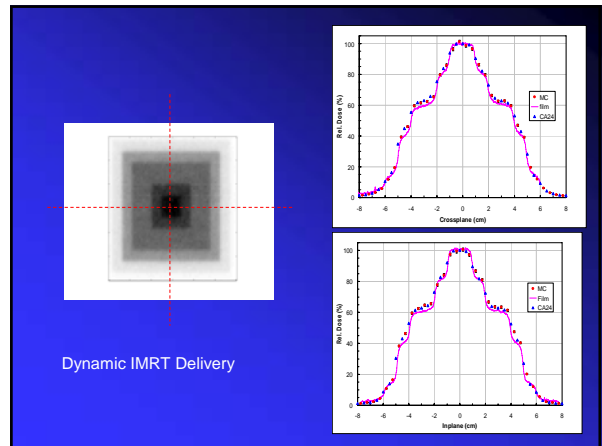
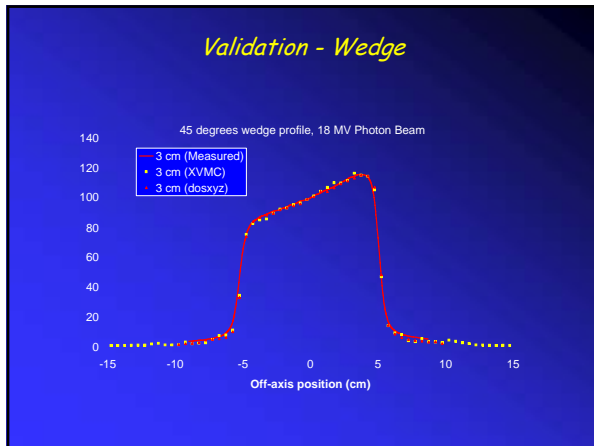


## Validation



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### Wedge factors

15x15 cm<sup>2</sup> field size

Wedge angle	15	30	45
Measurement	0.755	0.623	0.514
Simulation	0.754	0.621	0.514
Uncert. (%)	0.8	0.8	0.8
Difference (%)	-0.1	-0.2	0.0

5x5 cm<sup>2</sup> field size

Wedge angle	15	30	45	60
Measurement	0.756	0.616	0.512	0.422
Simulation	0.765	0.609	0.518	0.421
Uncert. (%)	0.7	0.9	0.7	0.7
Difference (%)	0.9	-0.7	0.6	-0.1

### Output factors

Field size	5x5	10x10	15x15	20x20
measured	0.919	1.000	1.036	1.058
simulation	0.918	1.000	1.030	1.055
difference	0.001		0.006	0.003

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### Reference dose calibration

Model-based system: fluence-based calibration

$$\frac{D_w^{ref}(10 \times 10, SSD = 100)}{U} = k \text{ [Gy / MU]}$$

U: a monitor unit (quantity with dimension MU)  
 D<sub>w</sub>: dose to water at the clinical reference point  
 k = 0.01 Gy / MU.  
 If accelerator tweaked in terms of dose to tissue:  
 then k = 0.0101 Gy / MU.

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### Reference dose calibration (cont'd)

$$\frac{D_w^{MC}(10 \times 10, SSD = 100)}{\text{particle}} = k_{MC} \text{ [Gy / particle]}$$

MC calculated reference dose to water per particle (fluence);  
 Particle fluence at an accelerator reference point (usually upstream from monitor chamber)

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## Reference dose calibration (cont'd)

$$\frac{D_{tissue}^{MC}(\vec{r})}{U} [\text{Gy/MU}] = \frac{D_{tissue}^{MC}(\vec{r})}{\text{particle}} \left( \frac{k}{k_{MC}} [\text{particle/MU}] \right)$$

MC calculated reference dose to water per particle (fluence);

Particle fluence at an accelerator reference point (usually upstream from monitor chamber)

This approach ignores backscattering of moving components into the monitor chamber!



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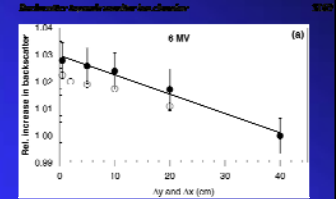
13

## Reference dose calibration (cont'd)

$$\frac{D_{tissue}^{MC}(\vec{r})}{U} [\text{Gy/MU}] = \frac{D_{tissue}^{MC}(\vec{r})}{\text{particle}} \left( \frac{k}{k_{MC}} [\text{particle/MU}] \right) B(x, y)$$

The B(x,y) factor accounts for the change in output due to monitor backscatter.

1. Relatively small effect (<1% for 10x10 and smaller)
2. Effect reduces for higher energies.
3. Effect is smaller for electrons.
4. Varian series only.

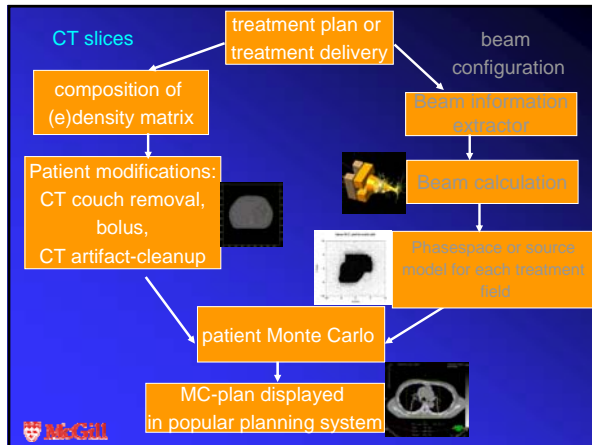


Verhaegen et al 2000, Phys Med Biol 45, 3159 - 70



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Photon beams: 6 MV, 15 MV, 250 kVp  
Electron beam: 18 MeV  
No contaminant particles

Material	HU interval	$\rho$ interval
Air	[-1000 : -950]	[0.001 : 0.004]
Lung	[-950 : -700]	[0.004 : 0.302]
ICRU tissue	[-700 : 125]	[0.302 : 1.101]
ICRP cortical bone	[125 : 2000]	[1.101 : 2.088]

CT scan

Exact geometry

Dose calculation:  
DOSXYZnrc

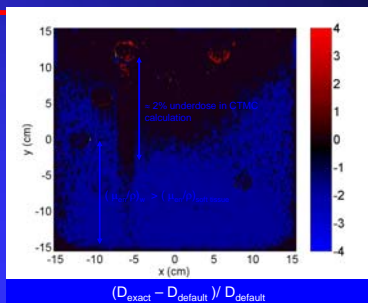


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Courtesy: Frank Verhaegen

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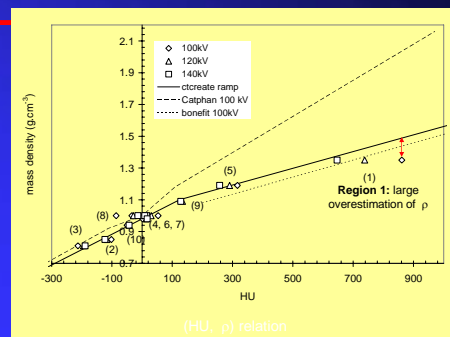
## 6 MV photons



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Courtesy: Frank Verhaegen

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Courtesy: Frank Verhaegen

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**Conclusion:**

mis-assignment of media and  $\rho$  can cause significant dose errors

**Question:**

Does using only water with  $\rho$  derived from (HU, $\rho$ ) worse than risking mis-assignment of media?

	6 MV			15 MV			250 kVp			18 MeVc		
	default	water only	Catphan*	default	water only	Catphan*	default	water only	Catphan*	default	water only	Catphan*
$k$ (%)	0.61	0.30	0.77	0.59	0.25	0.73	0.64	0.75	0.66	0.58	0.17	0.79
$\sigma$ (%)	0.26	0.36	0.32	0.30	0.33	0.33	0.95	2.0	0.91	0.72	0.92	0.99
Min (%)	-8.5	-7.9	-9.0	-8.2	-6.0	-9.6	-45	-5.2	-45	-12	-10	-12
Max (%)	+10	+5.9	+10	+8.3	+6.6	+10	+9	+78	+47	+9.7	+6.0	+34

Not assigning media (other than water) is sometimes preferable over mis-assigning media!

- > be critical about your CT calibration!
- > be careful with how a manufacturer handles (HU - interaction coefficient)



## CT artifacts, editing

- artifacts (dental fillings, etc)
- couch issues (CT vs. treatment)
- bolus or shielding editing onto CT data



## Dose specification

- Assuming proper material specification MC dose calculations will provide absorbed dose specified to tissue,  $D_{\text{tissue}}$

In TP, do we really want the dose specified in terms of  $D_{\text{tissue}}$ ?



## The debate...

- $D_{\text{tissue}}$  is the real quantity needed!
- Reply: Yes, but life is not perfect!
  - material specification is far from perfect
  - CT voxels are too large
  - soft tissues within bony matrix
- Reply: Former algo's are not accurate so they represent anything but  $D_w$
- Converting back to  $D_w$  is adding complexity
- $D_w$  is what is being used in former algo's.
- Reply: The incremental complexity is not really worthwhile talking about.



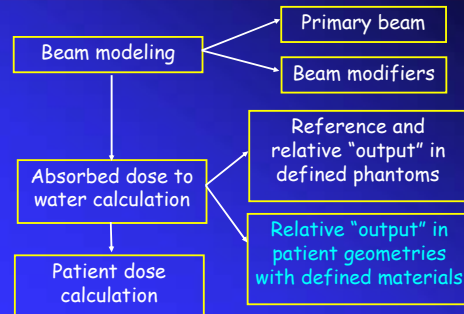
Table 2. Average water-to-medium stopping power ratios calculated for the variety of conditions and phantom setups. The incident beam was  $10 \times 10 \text{ cm}^2$  at the phantom surface. The in-field results evaluate the dose ratio within the central  $4 \times 4 \text{ cm}^2$  area of this field while the outside-field results evaluate the ratio outside a  $12 \times 12 \text{ cm}^2$  area. The in-field and outside-field results are calculated at a depth of 10 cm depth, while the others are at the depth of the interface.

Location	Air	Lung	ICRU tissue	Soft bone	Cortical bone
<b>6 MV</b>					
In field (water)	1.117	0.999	1.010	1.035	1.116
In field (bone)	1.117	1.000	1.010	1.035	1.117
Lung bone	1.120	1.000	1.010	1.035	1.117
Bone-bone	1.118	1.001	1.010	1.035	1.116
Cortical field	1.132	1.006	1.010	1.035	1.127
<b>18 MV</b>					
In field (water)	1.085	0.985	1.010	1.035	1.116
In field (bone)	1.086	0.986	1.010	1.035	1.111
Lung-bone	1.092	0.989	1.010	1.035	1.111
Bone-bone	1.086	0.987	1.010	1.035	1.116
Cortical field	1.117	0.999	1.010	1.035	1.112

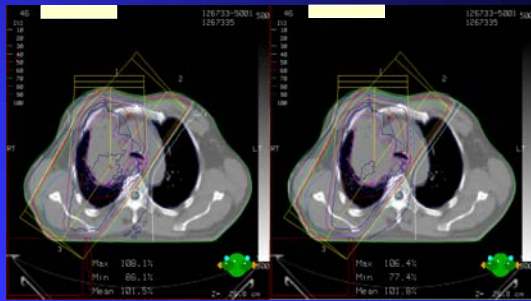
Siebers et al 2000  
PMB 45, 983



## Validation



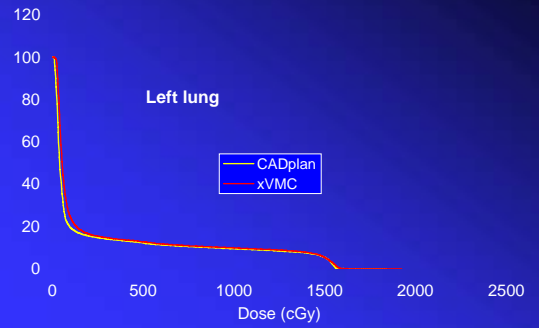
*Internal consistency*



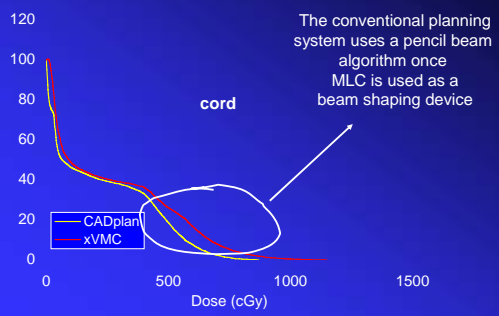
Monte Carlo - all tissues to water

CADplan

*All tissues to water, plan 2*



*All tissues to water, plan 2*



AAPM Summer School 2006, Windsor, Canada

## Monte Carlo-based Clinical Treatment Planning: Issues for Consideration

Indrin J. Chetty and Jan Seuntjens

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and McGill University, Montreal QC

### Outline

- A. Experimental verification of MC-based dose algorithms: beam modifiers (MLC) and transport within the phantom/patient
- B. Clinical treatment planning examples: MC vs. EPL and CS
- C. Statistical Uncertainties in MC-based treatment planning
- D. Conclusions

### AAPM TG 105 report

Many of the findings and recommendations presented here are reported in the **AAPM Task Group No. 105 report**: "Issues associated with clinical implementation of Monte Carlo-based treatment planning" submitted to Med Phys

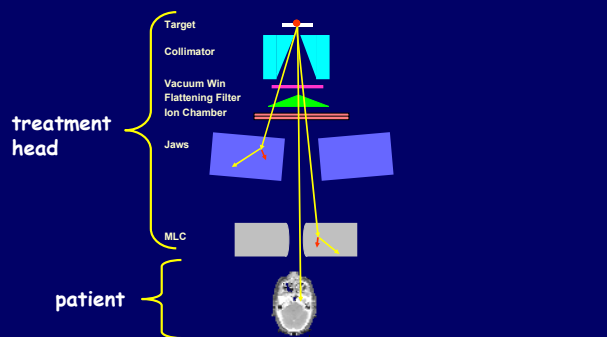
IJ Chetty, B Curran, J Cygler, J DeMarco, G Ezzell, B Faddegon, I Kawrakow, P Keall, H Liu, C-M Ma, DWO Rogers, D Sheikh-Bagheri, J Seuntjens, JV Siebers

### A. Experimental verification of MC-based dose algorithms

A Monte Carlo-based treatment planning system is just another treatment planning system and as such should be subjected to the same testing and verification requirements as any other planning system (such as provided in AAPM TG-53 - Fraass *et al.*)

MC is known to be more accurate under non-CPE conditions, and should be verified under such situations

### How should verification be performed for MC ?



### MC modeling of beam modifying devices

The BEAMnrc code system (NRCC) was developed for transport through detailed MLC geometries: component module developed by Heath and Seuntjens (PMB 48: 4045-64(2003)) for the Varian Millennium 120-leaf MLC

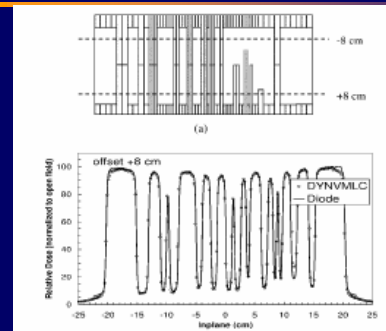
The BEAMnrc code system is not fast enough for routine clinical treatment planning (patient-dependent calculations on the order of minutes)

### MC modeling of beam modifying devices

To improve the efficiency of simulation through beam modifiers, investigators have developed other approaches:

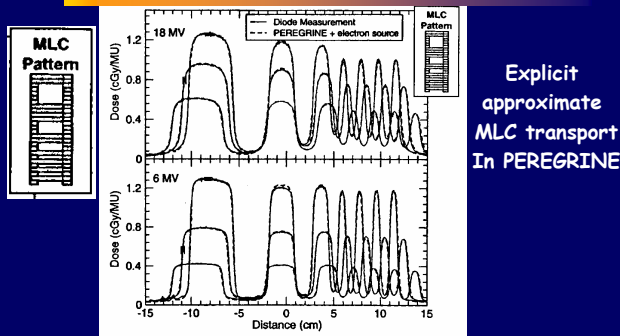
- (a) Modified transport methods: first Compton scatter or multiple order scatter, ignoring Compton electrons
- (b) Multiple source models parameterized for simulating square shapes defined by the jaws; requires explicit or empirically-based model for transport through the MLC

### Explicit MLC transport: BEAMnrc module



Heath and Seuntjens (PMB 48: 4045-64, 2003)

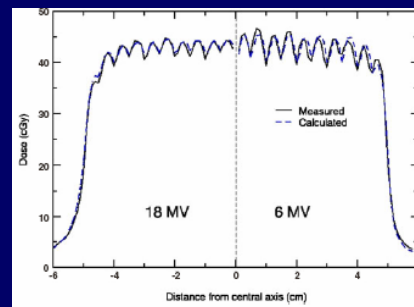
### Explicit "approximate" MLC transport



Hartmann Siantar *et al.* Med. Phys. 28 (2001)

Explicit approximate MLC transport in PEREGRINE

### First Compton transport approximation

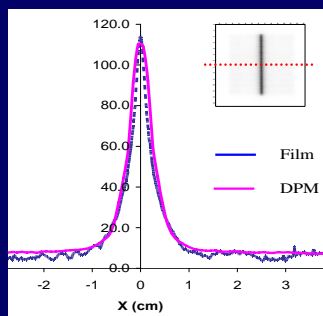


Tongue-and-groove effect maximized:

Delivered with even/odd leaves closed half the time, resp.

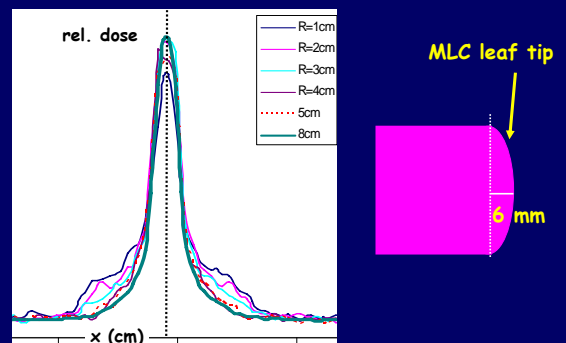
Siebers *et al.* (PMB 47:3225-49, 2002)

### Multiple order Compton scatter approx.



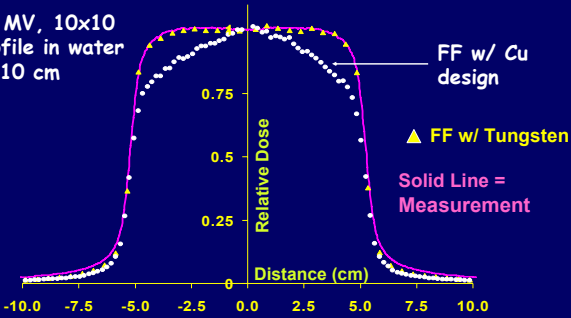
Tyagi *et al.* (Submitted to Medical Physics)

### Sensitivity of closed leaf profile to the rounded leaf tip (from Tyagi et al)



### The importance of accurate vendor information !

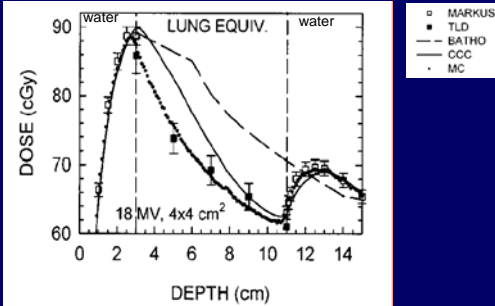
15 MV, 10x10 profile in water at 10 cm



### Patient Transport

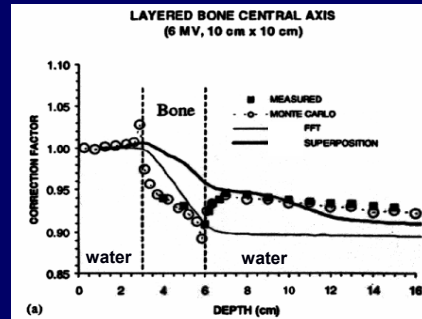
Experimental verification in phantom geometries

### Experimental verification in heterogeneous geometries



Arnfield et al. (MCV), Med. Phys, 27 (6) 2000

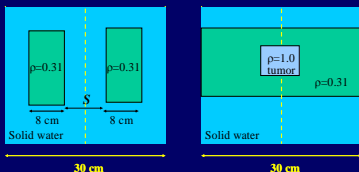
### Verification - high density inhomogeneities



Ma et al. Med. Phys. 26 (1999)

### Verification - Other geometries

- As we move MC closer to the clinic, we need more clinically realistic patient geometries



Rice et al, IJROP, 15, (1988)  
Wang et al Med. Phys., 26 (1999)

- Accurate measurements are difficult !!!

### MC-based beam modifier transport: Summary

In summary, regardless of the methods used in modeling beam modifiers, appropriate experimental verification is necessary

Experimental testing should include complex configurations designed to verify the improved accuracy expected with the use of the Monte Carlo method

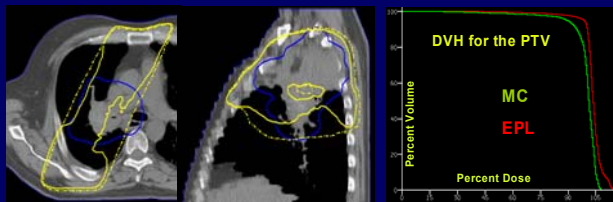
## B. Monte Carlo-based treatment planning

Comparison of MC vs. simple (EPL) and sophisticated heterogeneity correction methods (CS) in lung, head and neck cancer planning, and other treatment sites

### Treatment Planning: The main dosimetric issue

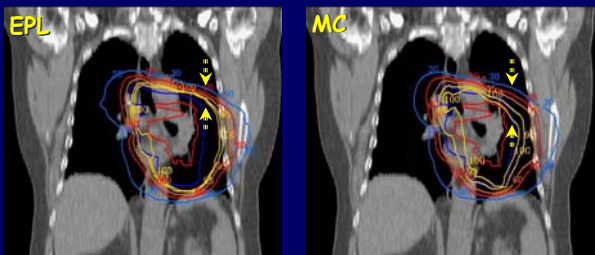
Solid = MC, 100%      6 MV oblique fields  
 Dashed = EPL, 100%  
 Blue = PTV

#### Underdosage of the PTV



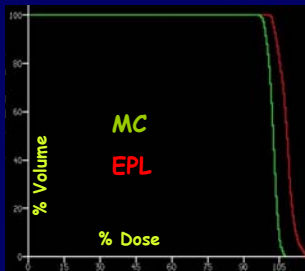
### 15 MV conformal lung plan

Note the differences in the spatial dose and dose gradient due to penumbral broadening

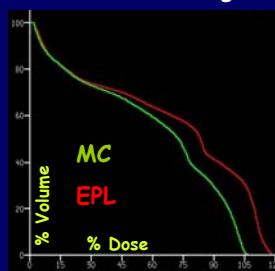


### 15 MV conformal lung plan

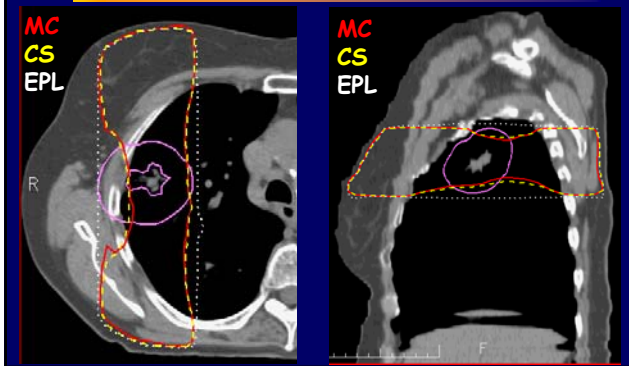
#### DVH - CTV



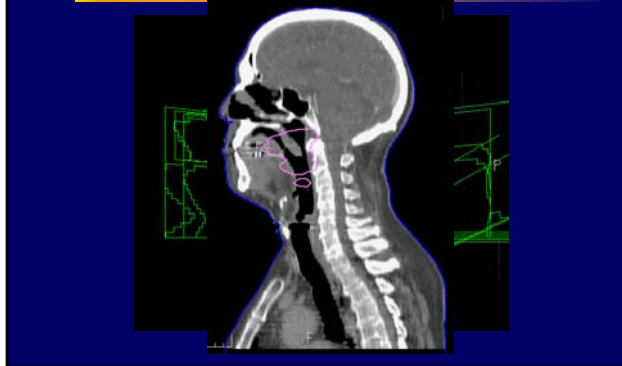
#### DVH - left lung



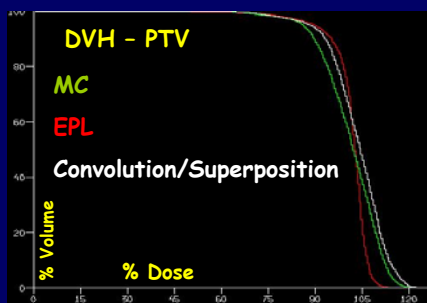
### 6 MV AP/PA lung plan: 95% IDL coverage



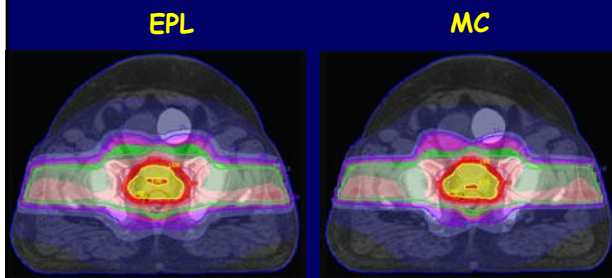
### 19 field (parotid sparing) head/neck forward plan



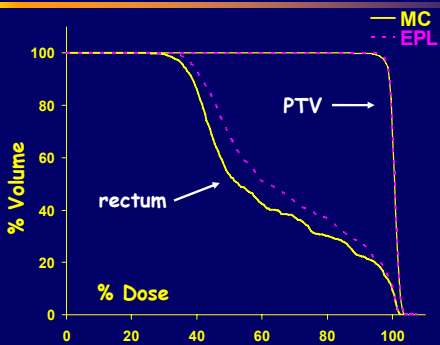
19 field (parotid sparing) head/neck forward plan



Prostate (4 fields + 3 segments)

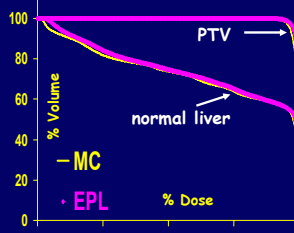
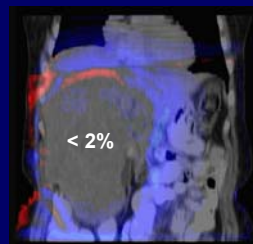


Prostate DVH's



Liver

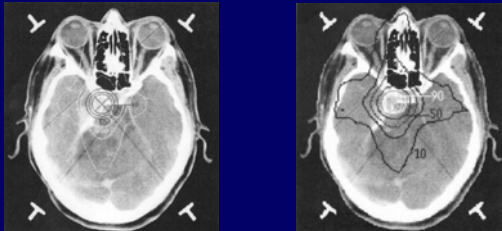
Difference map (MC-EPL) DVH's for the PTV and normal liver



Blue/red colorwash < 5% beam penumbra effects

radiosurgery

Conventional (1 cm collimation) MC (1 cm collimation)

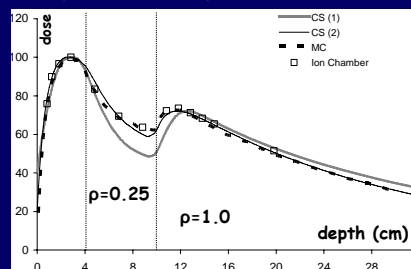


Solberg *et. al.* Radiother. Oncol. 49 (1998)

Electron disequilibrium always exists whenever the field size is smaller than the range of the secondary electrons

Comparison of "model-based" algorithms

The agreement between the MC and other model-based methods (e.g. CS) will strongly depend on the particular implementation of the algorithm



CS (1): 2 rep. component energies  
CS (2): 1 rep. energy averaged over spectrum  
Both CS (1) and (2) agree in water-based tests

## Summary

The differences found in comparing the MC method with other algorithms will be highly dependent on the beam arrangements, field sizes, beam energies, and tumor size and location

Situations where there is a lack of CPE (small field sizes, high energies, low density tissues) may pose a challenge even for CS algorithms because these algorithms do not explicitly transport electrons

## It's not just the technology



## It's how you drive it !



## Implementation is critical !

Courtesy: Solberg (UNMC)

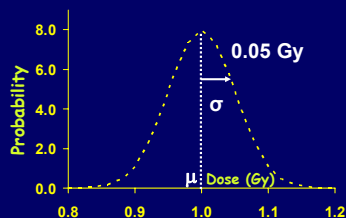
## C. Statistical uncertainties in MC-based treatment planning

"The only certainty is that nothing is certain"

Pliny the Elder  
Roman scholar & scientist (23 AD - 79 AD)

## Statistical uncertainties

"Jittery" isodose lines due to the stochastic nature of the MC method are quite different from dose distributions computed with conventional (deterministic) algorithms



$\sigma \sim 1/\sqrt{N}$ ,  
N= total no. of particles simulated

In tx planning,  
Relative uncertainty  
 $= \sigma / \mu \sim 1/\sqrt{\text{dose}}$

## Statistical uncertainties

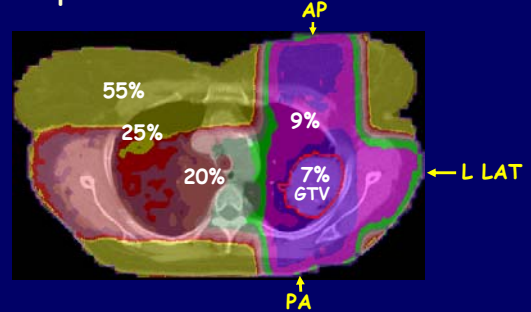
- Two sources of uncertainty: treatment head simulation (latent uncertainty - term coined by Sempau) and the patient simulation
- Latent uncertainty in the phase space is systematic in nature, while the uncertainty in the phantom dose is random
- The statistical uncertainty in calculated dose will approach (as a function of  $1/\sqrt{N}$ , where  $N$  is the number of simulated particles), the finite, latent uncertainty associated with the phase space, regardless of the number of times the phase space is sampled

### Statistical uncertainties: previous work

- Several investigators have published on statistical uncertainties in Monte Carlo dose calculation (see the chapter for references)
- Clinical planning studies show that a statistical uncertainty of 2% or less does not significantly affect isodose lines, DVHs, or biological indices

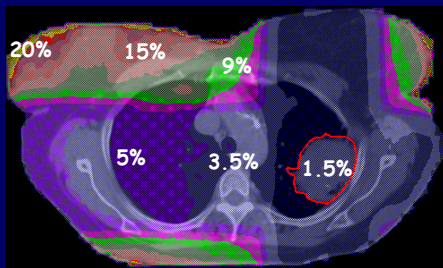
### 3F lung plan (RT\_DPM): relative uncert.

10 million particles  $\text{rel. uncert.} = (1\sigma/\mu) \times 100 \%$



### Clinical plan: one sigma % uncertainty

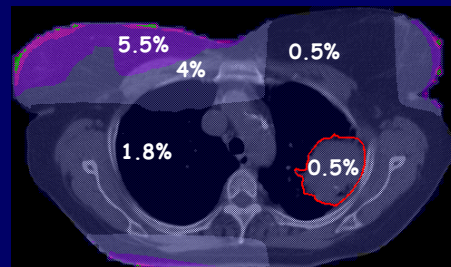
150 million particles



$\text{rel. uncert.} = (1\sigma/\mu) \times 100 \%$

### Clinical plan: one sigma % uncertainty

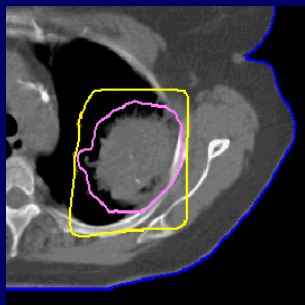
1.5 billion particles



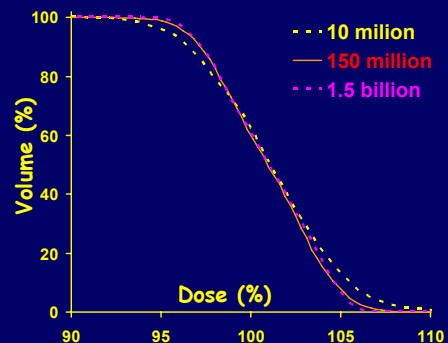
$\text{rel. uncert.} = (1\sigma/\mu) \times 100 \%$

### Effect of uncertainties on the 95% IDL

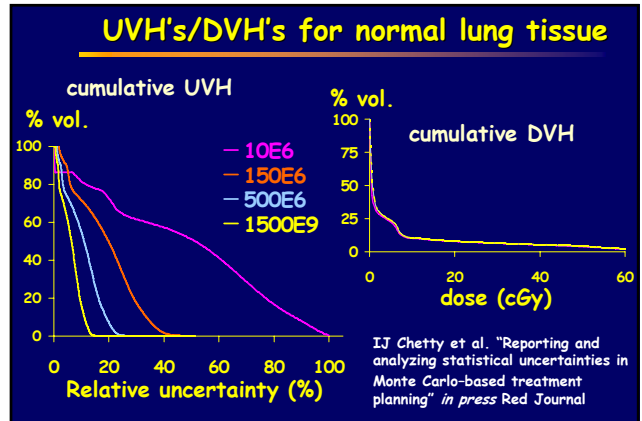
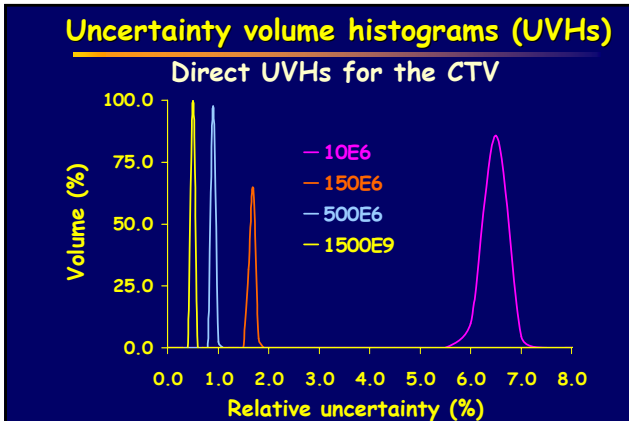
1.5 billion



### Effect of uncertainties on DVHs



DVH for a plan w/given uncertainty is derived by convolving the DVH for the "0%" uncert. plan with the given random uncertainty distribution

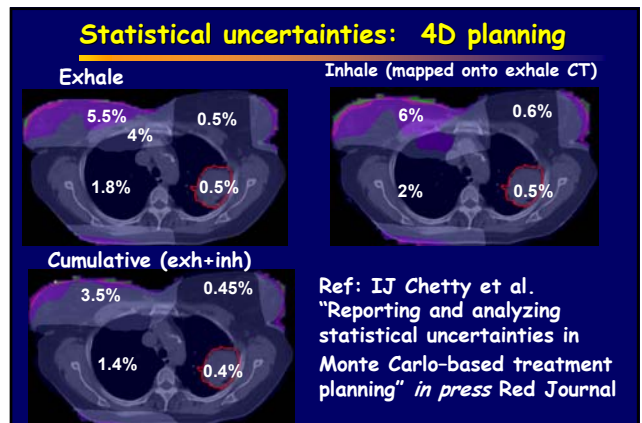
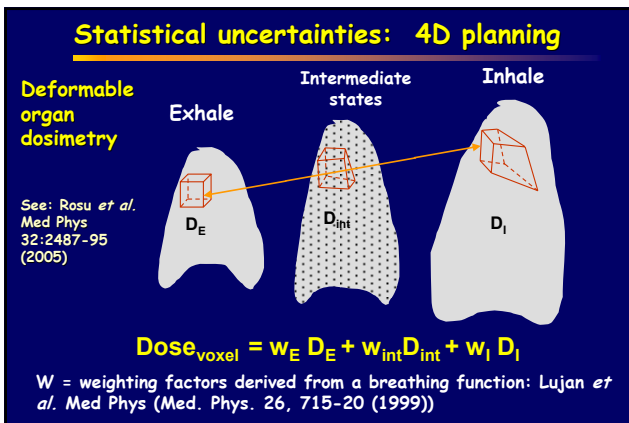


### Effect of uncert.: parallel organs (lung)

No. of histories	% $\sigma/\mu$ (min.)	% $\sigma/\mu$ (max.)	% $\sigma/\mu$ (mean dose)	MLD (Gy)	% NTCP 66 Gy
10E6	6.5	100.0	46.0	6.5	0.51
150E6	1.7	41.0	18.9	6.8	0.55
500E6	0.9	23.8	10.5	6.8	0.55
1500E9	0.5	17.9	6.1	6.8	0.55

### Effect of uncert.: serial organs (cord)

No. of histories	% $\sigma/\mu$ (min.)	% $\sigma/\mu$ (max.)	% $\sigma/\mu$ (mean dose)	% $\sigma/\mu$ ( $D > 0.5 D_{max}$ )
10E6	12.6	97.3	42.2	14.3
150E6	3.3	28.0	12.9	3.7
500E6	1.8	15.2	7.1	2.0
1500E6	1.0	8.8	4.2	1.2



### Statistical uncertainties - Summary

- AAPM TG-105 report recommendations: Report uncertainties to volumes rather than individual points, i.e.  $\sigma_{D>0.5D_{max}}$ ,  $\sigma_{PTV}$ , or  $\sigma_{PRV}$
- Point doses (ex.  $D_{max}$  points) are subject to large statistical fluctuation (See Kawrakow and Fippel, PMB: 45, 2163-83(2000))
- Point (individual voxel) dose uncertainties may be a concern for serial organs and requires further investigation
- Prescribing doses to a line may obviate the statistical issues with point doses

### D. Conclusion

- A properly commissioned MC-based dose algorithm will improve dose calculation accuracy in 3D-CRT and IMRT treatment planning and is likely to improve dose-effect correlations
- Clinical implementation of MC-based systems must be performed thoughtfully and physicists must understand the differences between MC-based and conventional dose algorithms
- Successful implementation of clinical MC algorithms will require strong clinician support and an understanding of the paradigm shift with MC algorithms

### Acknowledgements

Neelam Tyagi  
Mihaela Rosu  
Eduardo Acosta  
Martha Coselmon  
Jean Moran  
Dale Litzenberg  
Daniel McShan  
Randall Ten Haken  
Bruce Curran  
Alex Bielajew  
Feng Ming (Spring) Kong  
Benedick Fraass

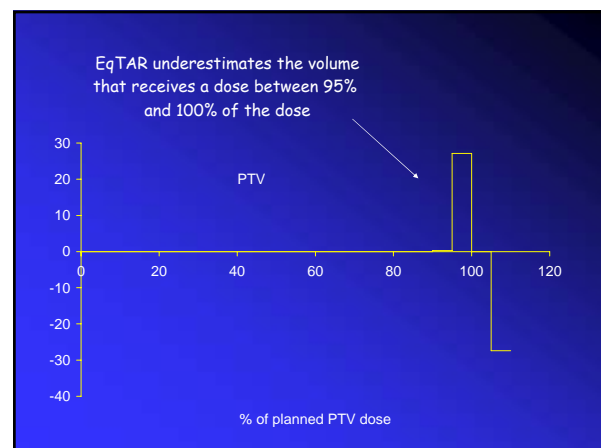
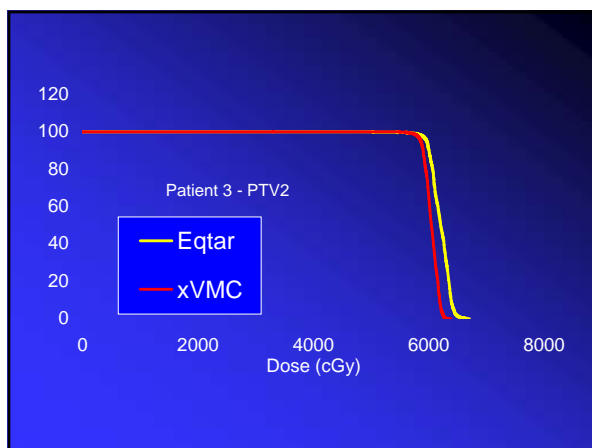
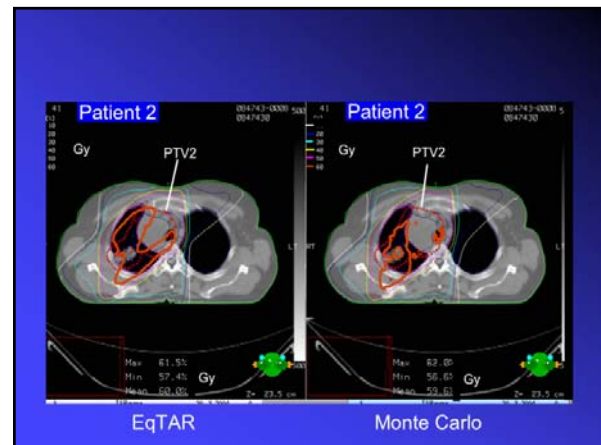
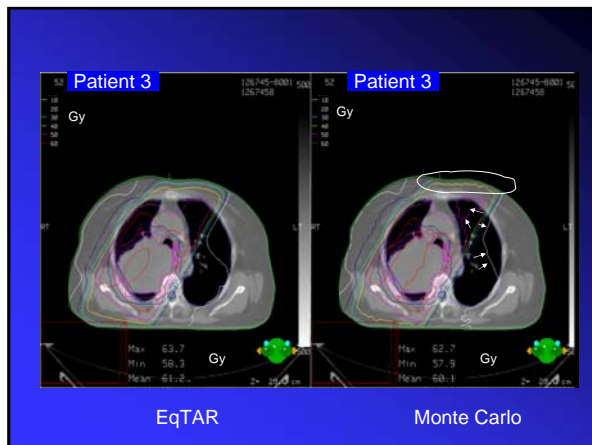
Grant Support: NIH P01-CA-59827 and R01 CA106770  
AAPM-TG 105 co-authors

## Outline: "issues for consideration"

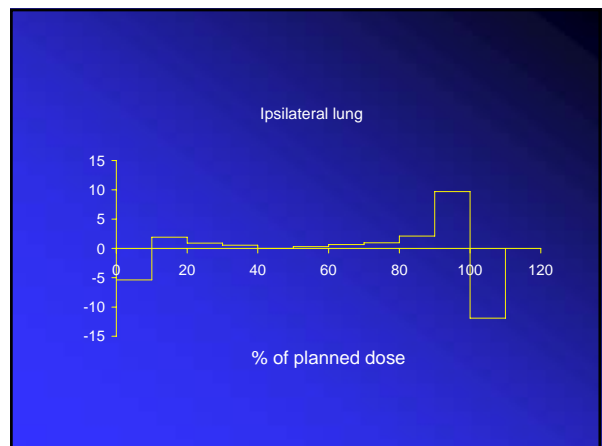
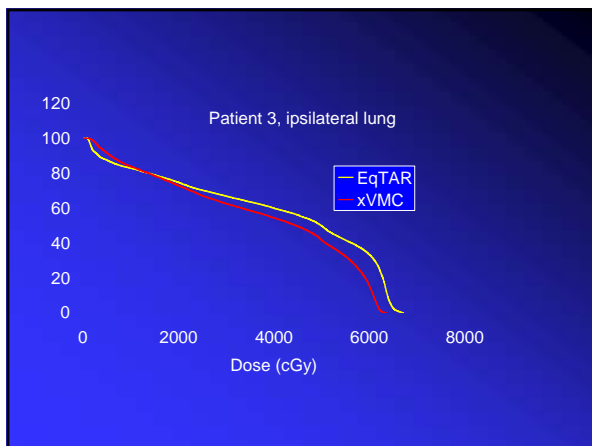
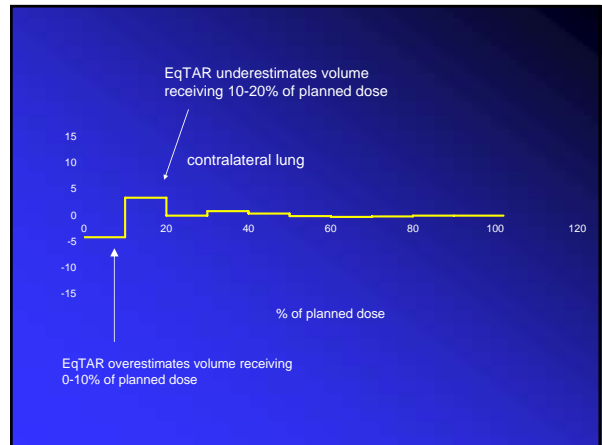
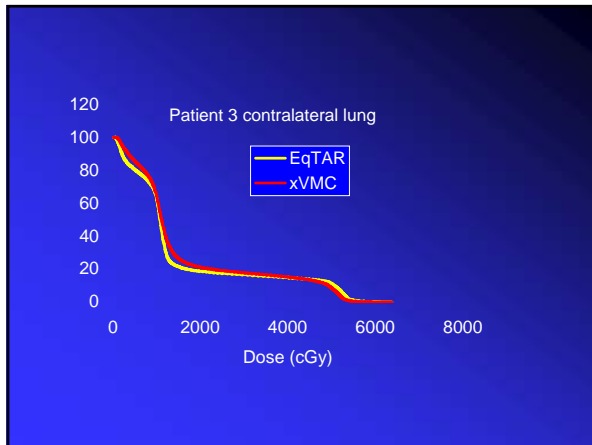
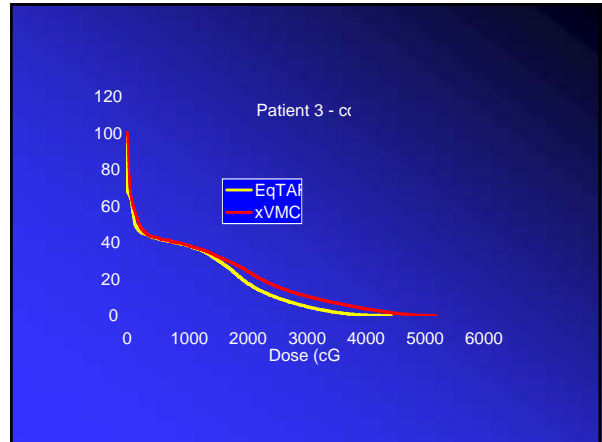
- Building blocks of a generic clinical MCTP system
- Verification issues in general
  - Validation of relative output
- CT calibration & artifacts
- Dose specification
- **Absolute calibration, MU calculations**
- Verification issues in detail
  - Experimental verification of MC-based dose algorithms: beam modifiers (MLC)
  - Experimental verification of transport within the phantom/patient
- MC-based treatment planning: comparisons of MC versus simple (correction-based) and model-based algorithms
- Statistical Uncertainties in MC-based treatment planning
- **MCTP and lung (NSCLC)**
- **Retrospective re-planning & outcome association**
- Summary

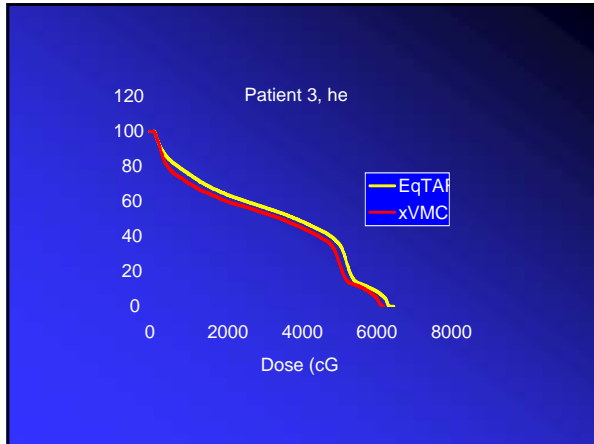
## Retrospective lung treatment planning

- Patients from a Phase I/II multicentre clinical trial (stage IIIA + B NSCLC, concomitant chemo)
- Treatment planning:
  - plan I (PTV1 dose up to 40 Gy)
  - plan II (PTV2 boost to 60 Gy)
  - Typically 3-fields per plan, MLC shaped, wedged (CADplan, no heterogeneity corrections)
- Delivered dose simulated from delivered MU's



Mean PTV Dose				Maximum PTV Dose		
Patient	EqTAR	MC	Diff	EqTAR	MC	Diff
1	62.0	60.8	-1.9%	67.9	64.8	-4.6%
2	60.8	59.9	-1.5%	63.6	62.8	-1.3%
3	61.9	60.3	-2.5%	67.0	63.7	-5.0%
4	60.1	58.6	-2.5%	62.9	62.8	-0.2%
5	60.7	60.2	-0.8%	65.5	64.7	-1.2%
6	61.3	60.8	-0.8%	66.1	64.9	-1.8%
7	61.5	59.6	-2.2%	63.5	60.9	-3.1%
8	63.1	59.3	-6.0%	67.9	63.7	-6.2%
9	60.1	57.1	-5.1%	63.3	62.1	-1.9%
10	58.9	57.2	-2.9%	63.0	61.2	-2.8%
11	60.4	61.6	2.0%	65.0	65.3	0.4%
12	60.9	59.1	-2.6%	64.2	63.1	-1.7%
Average			-2.2%			-2.5%





$100 * (MC - EqTAR) / EqTAR$

	Cord	Tumour bearing lung	Contralateral lung	heart
Patient 1	6.2%	-4.2%	20.3%	-4.5%
Patient 2	6.3%	-2.2%	15.9%	-6.1%
Patient 3	19.1%	-7.5%	6.1%	-7.7%
Patient 4	-1.6%	2.2%	8.7%	-2.2%
Patient 5	5.3%	1.9%	15.7%	35.8%
Patient 6	6.6%	9.9%	14.4%	41.4%
Patient 7	2.6%	0.3%	2.8%	17.3%
Patient 8	0.0%	3.6%	6.7%	32.6%
Patient 9	1.7%	4.8%	11.1%	4.6%
Patient 10	2.2%	6.1%	18.4%	24.2%
Patient 11	7.4%	4.6%	8.2%	5.8%
Patient 12	7.3%	-1.0%	13.5%	11.1%
Average	5.3%	1.5%	11.8%	12.7%
St.Dev.	(5.3%)	(4.8%)	(5.4%)	(17.3%)
	Beam model		e-scatter	Beam model

How can an improved dose calculation algorithm be useful in relation to outcome?

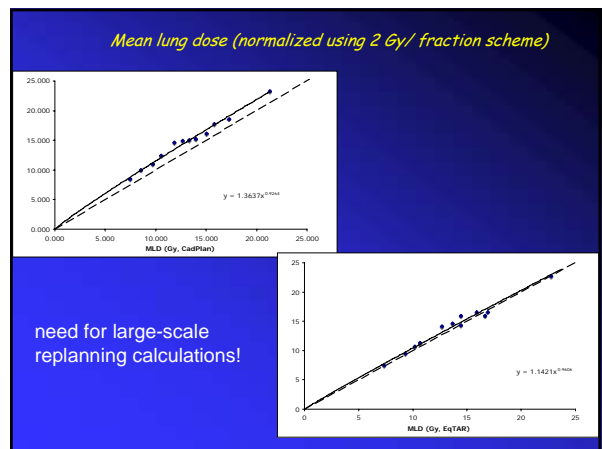
- > Revise known dose-response or dose-complication relations
- > Study associations of outcome with difference maps

*Radiation Pneumonitis*

A main complication for lung cancer radiation therapy

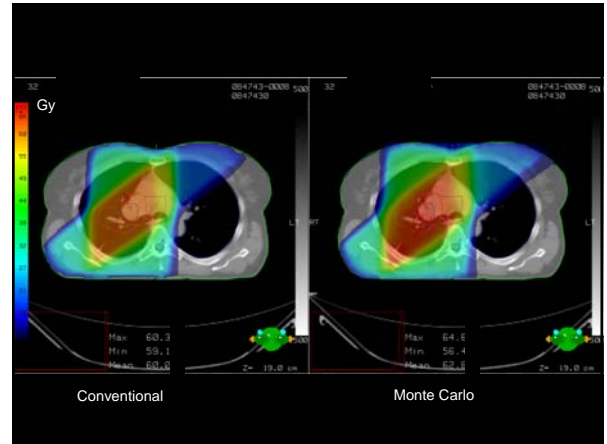
Bio-model indicators for radiation pneumonitis:

- Mean lung dose (MLD)
- $V_{dose}$  ( $V_{20}$  or  $V_{30}$ )
- NTCP

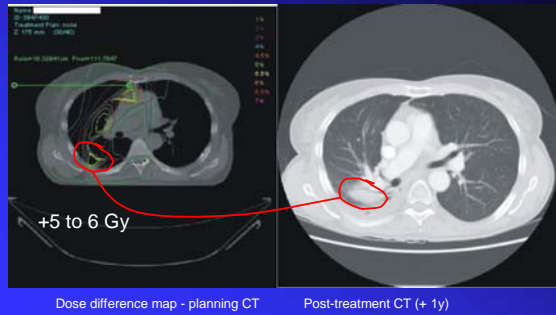


How can an improved dose calculation algorithm be useful in relation to outcome?

- > Revise known dose-response or dose-complication relations
- > Study associations of outcome with difference maps



Post-treatment complications (patient 1)



### Correlating late complications with dose

Automatic fibrosis segmentation using:

- > Automatic lung volume segmentation on planning and diagnostic CT images
- > Calculated Pre/Post RT tissue density changes corresponding to Pre RT lung volume
- > Mean tissue density changes corresponding to physician-identified radiographic fibrosis grades\*:
  - ✓ Grade 1 fibrosis: from 0.123 to 0.279 g/cc
  - ✓ Grade 2 fibrosis: from 0.279 to 0.546 g/cc
  - ✓ Grade 3 fibrosis: from 0.546 to 0.799 g/cc

I. Rosen, T. Fischer, J.A. Anatolak *et al*, Radiology, 221:614-622, 2001

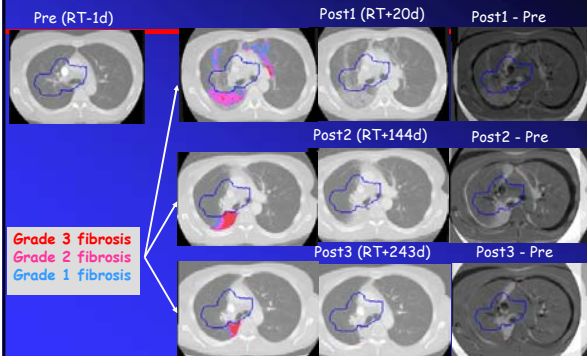


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### Fibrosis segmentation through image registration



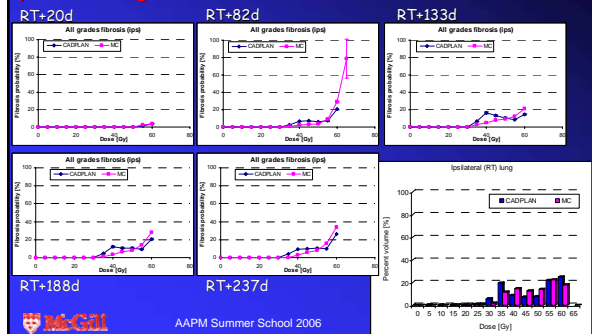
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### Dose-fibrosis correlation

Dose-response curves for the RT-induced fibrosis in the ipsilateral lung

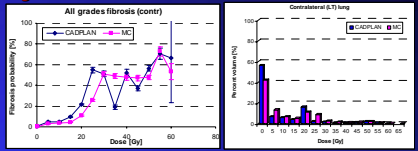


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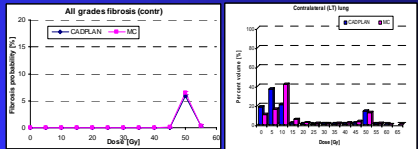
## Dose-fibrosis correlation (cont'd)

Dose-response curves for the RT-induced fibrosis in the contralateral lung

Patient #4;  
RT+82d



Patient #2;  
RT+362d



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## Conclusions

- MC planning = raising the bar
  - The devil is in the details
  - Dosimetric differences are due to two components:
    - beam model accuracy
    - heterogeneities
- MC planning presents specific clinical issues in addition to the issues one is already familiar with.
- The new dose information can be used retrospectively in two ways:
  - revise dose - response relationships
  - to correlate to complications



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