Monte Carlo-based applications in conformal, IMRT and 4D clinical treatment planning: Pitfalls and Triumphs

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Outline

(1) Methods for “patient-dependent” simulation and verification of these methods
(2) The impact of statistical uncertainties on dose distributions and dose planning metrics
(3) Variance reduction techniques and other methods used to improve calculation efficiency
(4) Clinical implications: dose prescription issues and outcome studies
(5) Timing of MC-based calculations in Tx planning
Many of the findings and recommendations reported here come from the AAPM Task Group No. 105: “Guidance report on clinical implementation of the Monte Carlo method in external beam radiation therapy treatment planning”

IJ Chetty, B Curran, J Cygler, J DeMarco, B Faddegon, H Liu, C-M Ma, DWO Rogers, D Sheikh-Bagheri, JV Siebers

Consultants: G Ezzell, I Kawrakow, PJ Keall, J Seuntjens

Monte Carlo simulation in radiotherapy planning

Courtesy of J Siebers, P Keall, MCV
MC modeling of beam modifying devices

The BEAM 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 Millenium 120-leaf MLC.

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

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
Verification of MC-based models

It is important that experiments be designed to test the improved transport accuracy (afforded by the MC method) through detailed component geometries, such as the MLC.

Several previous studies have included sophisticated experimental verification of transport through the MLC.

Explicit MLC transport: BEAMnrc module

Heath and Seuntjens (PMB 48: 4045-64, 2003)
Explicit "approximate" MLC transport


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)
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.
Statistical uncertainties

“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

\[ \sigma \sim \frac{1}{\sqrt{N}}, \]

\[ N = \text{total no. of particles simulated} \]

In tx planning, Relative uncertainty = \( \frac{\sigma}{\mu} \)
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 can be thought of as a systematic error in the calculation, while the uncertainty in the phantom dose is more random in nature
• The statistical uncertainty in calculated dose will approach (as a function of $\frac{1}{\sqrt{N}}$, 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:

  1. Sempau and Bielajew: PMB, 45:131-57 (00')
  2. Keall, Siebers, Jeraj and Mohan: Med Phys, 27:478-84 (00')
  3. Buffa and Nahum: PMB, 45:3009-22 (00')
  4. Walters, Kawrakow and Rogers: Med Phys, 29:2745-52 (02')
  5. Kawrakow: PMB, 49:1549-56 (04')
  6. Ma, Li, Jiang et al: PMB, 50:891-907 (05')

• Clinical planning studies among the above listed 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

rel. uncert. = \(\frac{1}{\mu}\times100\%\)

Clinical plan: one sigma % uncertainty

150 million particles

rel. uncert. = \(\frac{1}{\mu}\times100\%\)
Clinical plan: one sigma % uncertainty

1.5 billion particles

rel. uncert. = (1σ/µ)×100 %

Effect of uncertainties on the 95% IDL

10 million

50 million

150 million

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.

Uncertainty volume histograms (UVHs)

Direct UVHs for the CTV
UVH's/DVH's for normal lung tissue

Effect of uncert.: parallel organs (lung)

<table>
<thead>
<tr>
<th>No. of histories</th>
<th>% σ/µ (min.)</th>
<th>% σ/µ (max.)</th>
<th>% σ/µ (mean dose)</th>
<th>MLD (Gy)</th>
<th>% NTCP 66 Gy</th>
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</thead>
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<tr>
<td>10E6</td>
<td>6.5</td>
<td>100.0</td>
<td>46.0</td>
<td>6.5</td>
<td>0.51</td>
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<tr>
<td>150E6</td>
<td>1.7</td>
<td>41.0</td>
<td>18.9</td>
<td>6.8</td>
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</tr>
<tr>
<td>500E6</td>
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<td>10.5</td>
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<td>0.55</td>
</tr>
<tr>
<td>1500E9</td>
<td>0.5</td>
<td>17.9</td>
<td>6.1</td>
<td>6.8</td>
<td>0.55</td>
</tr>
</tbody>
</table>
### Effect of uncert.: serial organs (cord)

<table>
<thead>
<tr>
<th>No. of histories</th>
<th>% σ/μ (min.)</th>
<th>% σ/μ (max.)</th>
<th>% σ/μ (mean dose)</th>
<th>% σ/μ (D&gt;0.5 Dmax)</th>
</tr>
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<tbody>
<tr>
<td>10E6</td>
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<td>97.3 (0.1)</td>
<td>42.2</td>
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<tr>
<td>150E6</td>
<td>3.3 (11.3)</td>
<td>28.0 (0.1)</td>
<td>12.9</td>
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<td>15.2 (0.1)</td>
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<td>2.0</td>
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<tr>
<td>1500E6</td>
<td>1.0 (11.4)</td>
<td>8.8 (0.1)</td>
<td>4.2</td>
<td>1.2</td>
</tr>
</tbody>
</table>

### Statistical uncertainties: 4D planning

**Deformable organ dosimetry**

Exhale

Intermediate states

Inhale

\[
\text{Dose}_{\text{voxel}} = w_E D_E + w_{\text{int}} D_{\text{int}} + w_I D_I
\]


**Statistical uncertainties: 4D planning**

Exhale

- 5.5% 4%
- 1.8% 0.5%

Inhale (mapped onto exhale CT)

- 6% 0.6%
- 2% 0.5%

Cumulative (exh+inh)

- 3.5% 0.45%
- 1.4% 0.4%

**Uncert. diff. map**

(Inh.- Exh.)

**Statistical uncertainties - Summary**

- **AAPM TG-105 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
Variance reduction and efficiency enhancing methods

Definition of Efficiency

- The efficiency, $\varepsilon$, of a Monte Carlo calculation is defined as: $\varepsilon = 1/(\sigma^2 T)$,
  $\sigma^2$ is the variance on the quantity of interest (e.g. dose) and $T$ is the CPU time required to achieve the variance.

- Two approaches to reduce $\varepsilon$:
  (a) either reduce $\sigma^2$ for a given $T$
  (b) reduce $T$ for a given $N$ (no. of histories)
VRT’s and EET’s

• AAPM TG-105 classification:
  (a) methods reducing $\sigma^2$ while producing a mathematically unbiased result are called variance reduction techniques (VRT’s) : ex. photon forcing, bremsstrahlung splitting, Russian roulette
  (b) methods which reduce $T$ for a given $N$ but are approximate (introduce bias) are termed efficiency enhancing techniques (EET’s) : ex. Range rejection and electron/photon energy cutoffs

• Both of the above methods are vital in MC-based clinical calculations

Variance reduction techniques

• Photon forcing: “Parent” photon is forced to interact with it’s weight being appropriately reduced to produced an unbiased result

• Bremsstrahlung splitting: Electron is forced to produce many brems. photons; these secondary photons have appropriately adjusted weights to conserve particle weights

• Russian roulette: Typically played with events of little interest; particles are terminated with a given probability but surviving particle weights are increased with inverse probability to render the game unbiased
Efficiency enhancing techniques

- Range rejection: Electron’s history is terminated when it’s residual range is so low that it cannot escape from the current region; note that this method ignores the possible creation of brems photons while slowing down and is therefore biased.

- Energy cutoffs: Photons and electrons are terminated if their energies fall below a low energy cutoff. This method is biased as it ignores photon and electron interactions that could take place below the energy threshold.

Influence of EET’s in treatment planning

- ECUT (10 keV) - ECUT (200 keV) +21 %

Reference:
IJ Chetty: SU-FF-T-295
VRT's and EET's: Summary

- VRT's and EET's are necessary in MC-based tx planning, and if used judiciously can significantly improve calculation speed.
- VRT's are mathematically unbiased, EET's introduce bias - improper use either of the methods can lead to highly unpredictable results.
- In clinical planning, appropriate testing of VRT's and EET's is necessary over a range of clinical cases.

Some References

Clinical treatment planning: dose prescriptions and clinical outcomes
MC-calculated doses in lung cancer planning can in some instances be significantly different (10-20%) than conventional algorithms, such as radiological path length convolution-based methods.

In light of these differences: How should dose prescriptions change with MC-based calculations?

AAPM TG 105 perspective:
Dose prescription issues are not specific to MC-based dose calculation; the MC method is just a more accurate dose algorithm.
As with other changes to the therapy treatment process, users should correlate doses and prescriptions with respect to previous clinical experience.

How do the more accurate MC-based dose distributions impact clinical outcome in terms of tumor response (control) and normal tissue effects?

- Retrospective studies investigating correlations of dose-effect for both tumor and normal tissue to help give early indication of the clinical benefit of the MC method.
- Retrospective studies may also help clinicians determine how to use MC doses in planning.
- Retrospective analyses will help guide us in using the data in prospective studies.
De Jaeger et al. Radioth. Oncol. 69 (1), 1-10 (2003), in comparing outcomes for 68 lung cancer patients showed that parameterizing the Lyman (NTCP) model using CS (vs. EPL) dose distributions, resulted in observed incidence of radiation pneumonitis occurring at a 12-14% lower dose.

It is likely that the use of MC-based dose calculation will add a much higher degree of accuracy to the dose effect relationships.

Two ongoing outcome studies involving MC-based dose calculation:


Initial results from both studies (though anecdotal at this early stage) are indicative that MC-based dose calculations are likely to impact clinical outcome with respect to both tumors and normal tissues.
Lung cancer dose-effect relationships

- The University of Michigan lung ca dose escalation trial shows the following: Lung ca 5 year overall survival increases by 1.2% per Gray (FM Kong et al. IJROBP in press, 2005)

- In 2005 about 164,000 people will die of lung ca in the US. If the dose calculation accuracy is improved by even 2% (over a standard course of 66Gy) this amounts to 2600 lives!

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

- AAPM TG-105 will provide useful guidelines on the clinical implementation of MC-based systems
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