Dose errors and computation time

IVICFA-9 de Noviembre de 2012

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Contents:

- Monte Carlo
- Beams
- Particle Transport
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- CT
- MC and IMRT
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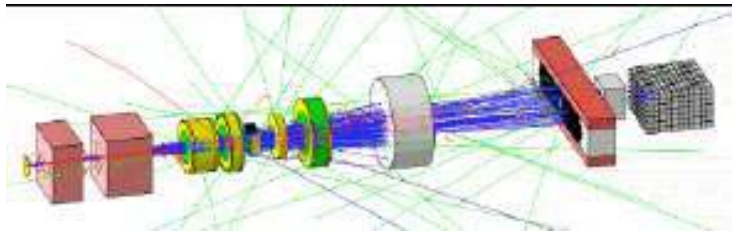
- MC efficiency and variance reduction techniques
- MC and other algorithms.
- Examples

Particle-therapy is one of the methods to treat tumour; it kills the cells releasing a large amount of energy.

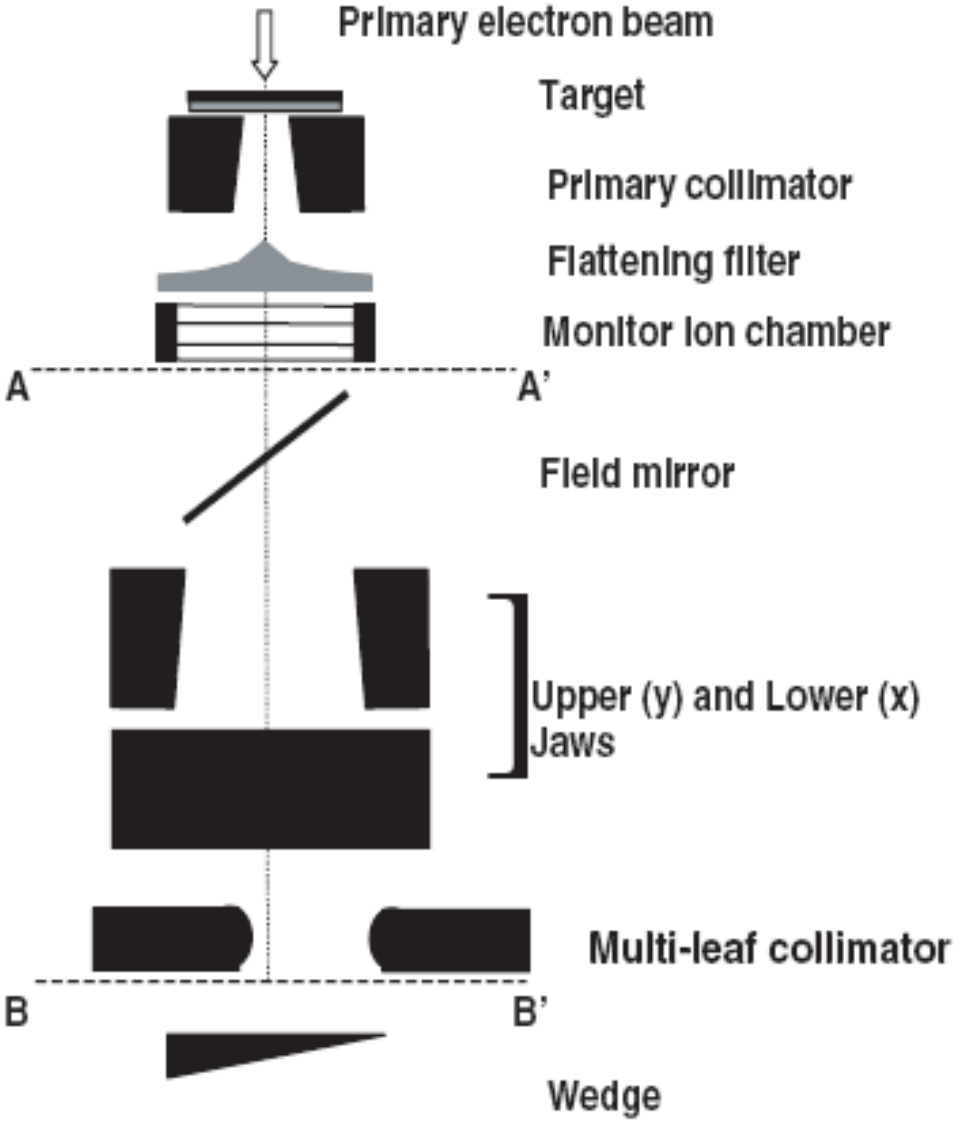
In fact is the energy/volume →Dose

It helps the fact that **healthy cells recover better** that cancer cells, but we must help tunning the place where to release the energy.

Objetive: obtain the best method to maximize the number of cancer cells killed, but with a minimum of healthy cells affected.



Variables: beam phase space, delivery time distributions, radiations, patients,…
in a ***dynamic*** context .



Beam energy:

- Photons: 4- 25 MeV
- Electrons: 4-25 MeV
- Protons: 50-250 MeV
- Heavy Ions

Figure 1. Schematic drawing of linac components modelled in Monte Carlo simulations. Different linac manufacturers place the linac components in a different order.

Why could be interesting a MC calculation?

Report of the AAPM Task Group No. 105: Issues associated with clinical implementation of Monte Carlo-based photon and electron external beam treatment planning
Chetty et al. **Med. Phys. 34, December 2007**

.- Evidence exists that dose differences on the order of 7*% are clinically detectable.*

.-5*% changes in dose* can result in 10*%–20% changes in tumor control probability* TCP or up to 20–30*% changes in normal tissue complication* probabilities NCTP if the prescribed dose falls along the steepest region of the dose-effect curves.

.-MC method consists of a straightforward **simulation of reality** and does not involve complex approximations nor models of dose deposition, but only a knowledge of the physics

.-Even without the direct use of MC simulations, the MC method already plays a significant role in radiotherapy treatment planning since the energy deposition kernels used in convolution/superposition algorithms have been calculated using MC techniques.

MC tools

MC in the market:

- EGS4, EGSnrc, EDTRAN/ITS, MCNP4,PENELOPE, GEANT4,…

Physics to simulate:

- In the energy range of interest for external beam radiotherapy megavoltage range, photons interact with surrounding matter via four main processes:
  - incoherent Compton scattering with atomic electrons,
  - pair production in the nuclear or electron electromagnetic field,
  - photoelectric absorption,
  - and coherent Rayleigh scattering.
- Additionally:
  - Elastic interactions
  - Inelastic collisions with atoms and molecules→excitations and ionizations (Ionizations lead to secondary electrons, sometimes referred to as “ δ particles”)
  - Radiative interactions (bremsstrahlung and positron annihilation): coupled electron-photon showers.

Beam simulation

Knowledge of the sensitivity of MC simulation results to input parameters, such as the **position, direction, and energy of the initial** electron **beam** exiting the accelerator and to details of the **geometry of the treatment head**, is important. A sensitivity analysis is indispensable in determining which source and geometry parameters to adjust and by how much in order to improve agreement with user-specific measurements.

To provide accurate beam models verified by measurements for treatment planning purposes, it is necessary to have the correct parameters from the **vendors**.

The critical parameters for electron beam simulation are different than those for x rays. Due to the sensitivity of the beam range to the primary electron energy (a 0.2 MeV change in electron energy corresponds with a 1 mm change in beam range) the incident electron energy is the primary tuning parameter for electron beam simulations.

The insensitivity of dose calculations to the energy distribution of the primary electron beam for photon beam simulations is in stark contrast to accelerators producing electron beams where both build-up and build-down regions are highly sensitive to primary electron energy distributions.

BS2

Accurate **beam modeling** is an important prerequisite for accurate dose calculation within the patient.

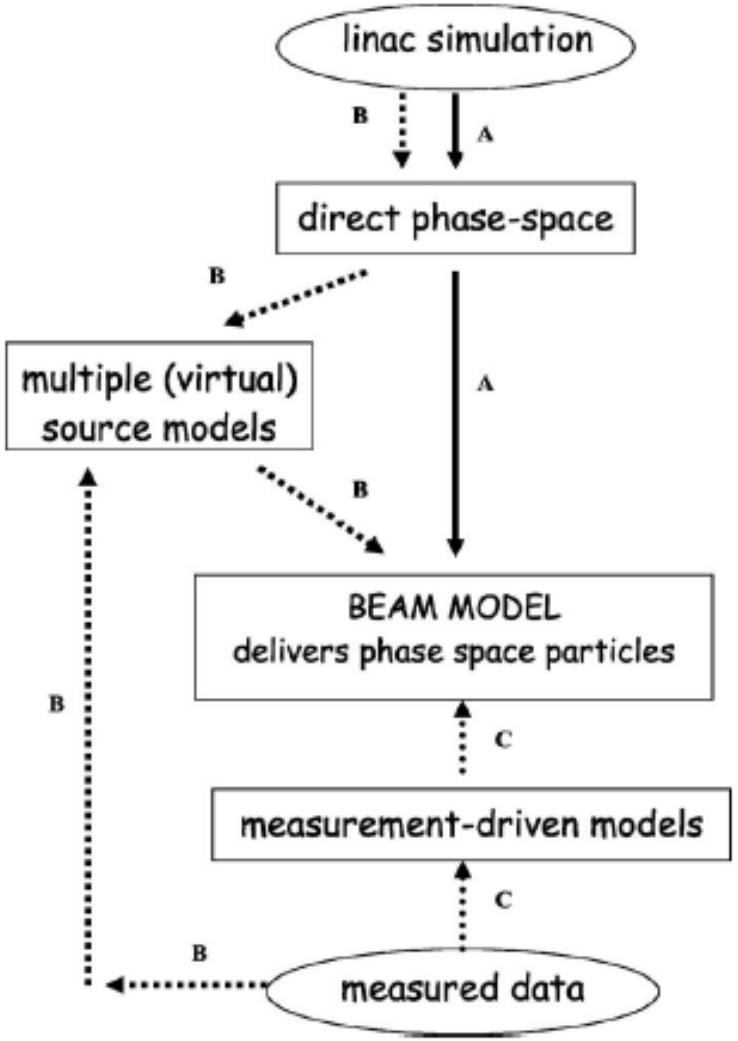


FIG. 5. The three "routes" for accelerator beam model specification: (a) solid line—direct use of phase-space information from simulation of the accelerator treatment head, (b) dashed line—multiple (virtual) source models derived from the phase-space information with or without enhancements from measured data, and (c) dotted line—development of other models derived from measurements (measurement-driven models).

BS3

(a): storage requirements are large—typical MC simulation may require up to 10^9 phase-space particles for multiple photon beams, which may amount to tens or hundreds of gigabytes of computer disk space for an accelerator with two photon energies and five electron energies with five different applicator sizes

(reading the phase-space data can be a bottleneck in the calculation)

(b): A possibly more practical approach to beam modeling involves derivation of the model parameters from a standard set of measurements. The advantage of such measurement-driven models is that they may be developed without dependence on the details of the accelerator treatment head. Fluence distributions in measurement-driven models may be developed starting with analytical models whose parameters are optimized based on minimization of the differences between calculations and measurements.

BS4

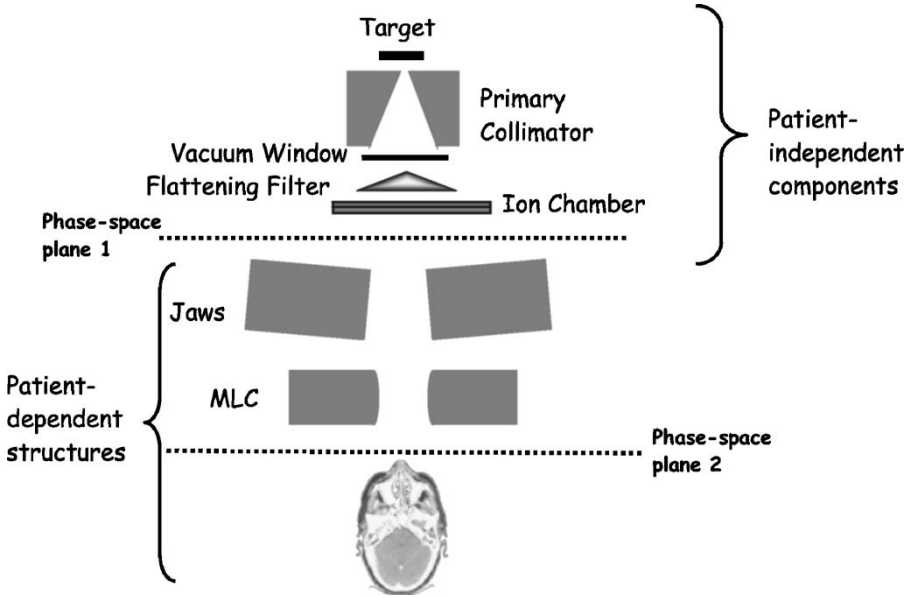


FIG. 2. Illustration of the components of a typical Varian linear accelerator treatment head in photon beam mode. Phase space planes for simulating patient-dependent and patient-independent structures are also represented. For other manufacturers, component structures such as the jaws, MLC, etc. may be in different locations, thereby potentially requiring a change in the placement of the phase space scoring planes.

The advantage of this approach is that this part of the calculation can be reused as often as necessary. Particles are then transported through the patient specific collimation system and are either stored in another phase-space file at the base of the accelerator see phase-space plane 2 in Fig. 2 or tracked through the patient in the same simulation. Storing a second phase-space may be more efficient when open fields e.g., 10x10 cm2 fields are used for treatment, however, more commonly, when MLCs are used for beam shaping, the latter approach is likely to be more efficient.

Source models

Its strength lies in the fact that the requirements on data storage are greatly reduced with respect to a full phase space approach; *because* of the reduced hard-disk traffic and because source models inherently involve some degree of *fluence smoothing*, the calculation time required to achieve a certain specified statistical variation in a dose calculation, is also reduced.

TS1

*The **transport of a particle**:*

(a) calculate **every single interaction** point: everything is simulated until the energy is below a predetermined low-energy cutoff. After that is deposited at the voxel. Typically used for the transport of neutral particles.

(b) **condensed history** simulations: many “small-effect” interactions can be grouped into relatively few condensed history “steps” and their cumulative effect taken into account by sampling energy, direction, and position changes from appropriate distributions of grouped single interactions All general purpose MC codes employ condensed history schemes for charged particle transport. (The higher the value of the cutoff, the faster the calculation but stopping at too high a cutoff energy can distort the dose distribution since the “stopped” charged particle might have deposited energy some distance from where its trajectory was terminated.)

There is a mixed condensed method, where the interaction is explicitly calculated over some energy; below this energy the condensed method is used.

Remarks:

.- With MC one can calculate both observable measurable quantities, such as dose or a particle spectrum, and quantities that cannot easily be measured such as the fraction of particles originating from a certain component of the treatment head, the dose fraction due to scattered photons, etc.

.- As the voxel size is increased, for a given statistical uncertainty the total calculation time will decrease, but the spatial resolution is reduced.

.- The presence of statistical uncertainties due to the statistical nature of the method

With charged particle transport one stops tracking the particle's movement at some **low-energy cutoff** and the choice of the cutoff can affect the calculation in two important ways. The **higher the value of the cutoff, the faster the calculation**; this can improve the calculation speed significantly. On the other hand, unless great care is taken, stopping at **too high a cutoff energy can distort the dose distribution** since the "stopped" charged particle might have deposited energy some distance from where its trajectory was terminated. Thus care must be taken in selecting an energy cutoff.

Due to significant improvements in the efficiency of photon beam treatment head simulations, the speed of the complete simulation is such that it is feasible to consider performing the entire calculation for each patient.

Dose errors

DE1

By invoking the central limit theorem, one can show that the statistical uncertainty in dose is proportional to 1/ √*N, in the limit of infinite large N (* number of independent simulated histories)

There are generally two sources of statistical uncertainty in MC calculations of patient dose:

.-those resulting from **the simulation of the accelerator treatment head**

and

.-those arising from fluctuations in the **phantom/patient** dose calculation.

the statistical uncertainty in the dose calculated in a phantom by reusing the particles from the phase space file will approach the finite, latent variance associated with the phase space data, regardless of the number of times the phase space is reused.

In estimating the statistical uncertainty in the patient dose calculation, it is necessary to account for the latent variance from the phase-space calculation as well as the random uncertainty from the patient calculation.

DE2

Calculating statistical uncertainties:

.- ***the batch method*** : the estimate of uncertainty
(standard error of the mean, *s) of a scored quantity X, is*

$$s_{\bar{x}} = \sqrt{\frac{\sum_{i=1}^{n} (X_i - \bar{X})^2}{n(n-1)}},$$

n:the number of independent batches,
X_i*: the* scored quantity (such as dose) in batch *i,*
X: the mean value of *X over all the batches.*

As *n is usually small on the order of ten or less there is statistical* fluctuation in the uncertainty itself.

.-***history-by-history method***: X_i *represents the scored quantity* in history *i rather than batch i so that the standard error of* the mean can be recast in

$$s_{\bar{x}} = \sqrt{\frac{1}{N-1}\left(\frac{\sum_{i=1}^{N} X_i^2}{N} - \left(\frac{\sum_{i=1}^{N} X_i}{N}\right)^2\right)},$$

N : the number of primary independent histories,
Xi: the contribution to the scored quantity by independent history, i.

Remarks:

.-Take into account the correlation between a primary particle and all its secondaries, especially in the case of bremsstrahlung splitting where a large number of photons may all come from a single electron. Thus, to be strictly correct, these secondaries must be treated as part of the same history. If this correlation is not taken into account one can underestimate the uncertainty in a dose calculation, as the secondaries will be treated as independent particles, reducing the uncertainty erroneously.

DE4

For radiation therapy dose distributions,

$sDi \propto \sqrt{D_i}$,

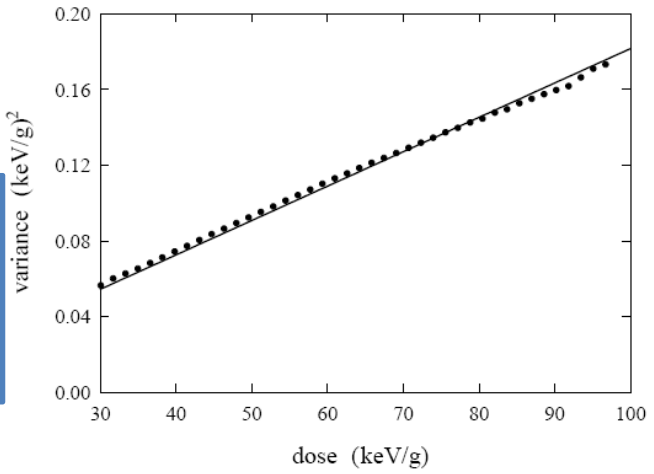
sDi:estimate of the standard error of the mean of the dose in voxel i
Di: the dose in that voxel.

x: the quotient between the MC simulated energy deposition per history and the voxel mass

$$\sigma^2(\bar{x}) = x\frac{C}{N}$$

The estimate of the variance in dose in a voxel is appr[illegible] tional to the dose itself, inversely proportional to the number of histories and *inversely proportional to the voxel surface.* From the central limit theorem when the number of simulated histories is large enough, ***x has a Gaussian distribution***

$$\sigma^2 \simeq \frac{1}{N}\left[\frac{\sum_{i=1}^{N} x_i^2}{N} - \left(\frac{\sum_{i=1}^{N} x_i}{N}\right)^2\right]$$

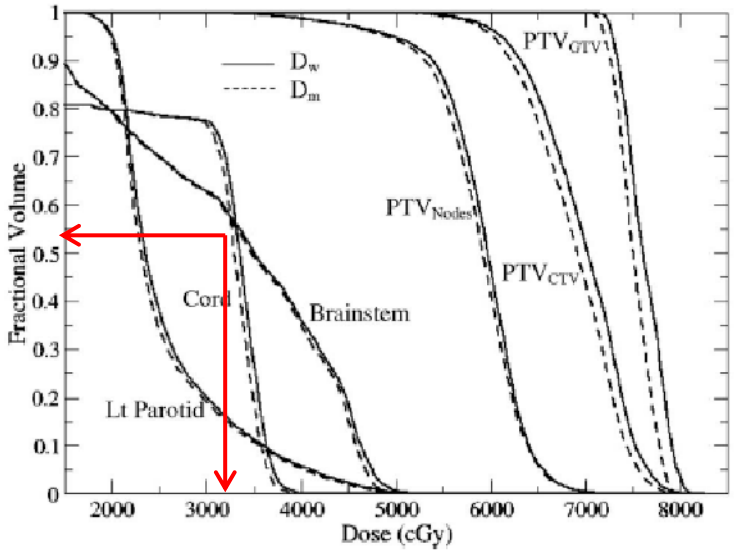


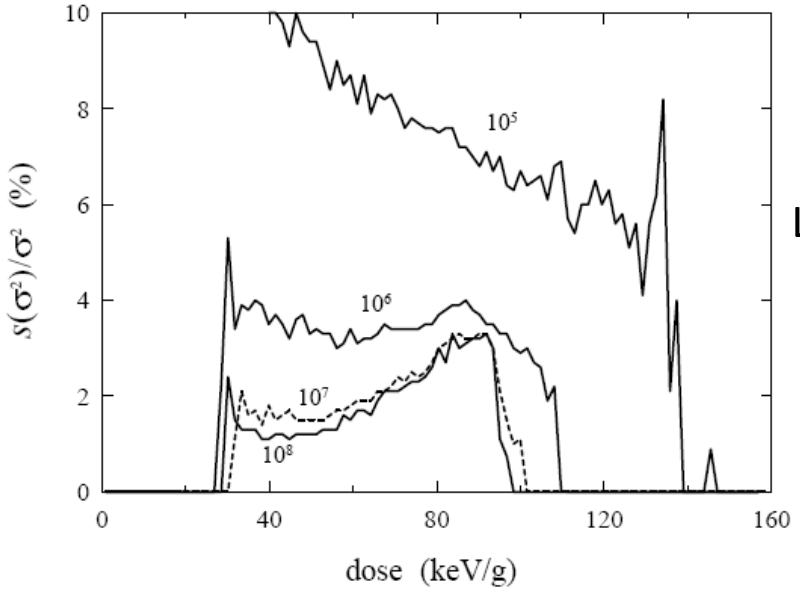
Dots represent 'experimental' MC data and the full line is a linear fit of the type $\sigma^2 = x\,C/N$. *The value of the fitting parameter C and the correlation coefficient are 181.6 MeV* g^{-1} *and r =0.9998.*

J Sempau and A F Bielajew , Phys. Med. Biol. 45 (2000) 131–157

DE5

number/% of voxels with same dose





Looks there is some convergence

Figure 5. Relative dispersion of the variance for different number of histories, N.

J Sempau and A F Bielajew , Phys. Med. Biol. 45 (2000) 131–157

DE6

Then

.- uncertainty is roughly proportional to 1/ √*N*.
.- *the simulation time T α N,*

absolute precision (s_D=*0) with MC* simulation requires an infinite calculation time.

Fortunately, absolute precision is not required in dose calculation results.

We can specified the statistical uncertainty:

.- for a single voxel, or

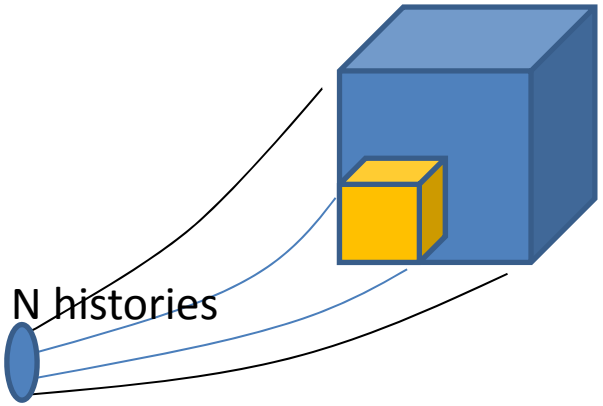
.-the statistical uncertainty over some volume, such as a planning target volume or some dose volume, such as the volume receiving greater than *X% of the* treatment dose, can be computed from the square root of the average variance of each constituent voxel. For example, the fractional uncertainty in the average dose for voxels with dose values greater than 50% of the maximum dose,

$$\bar{F}_{D>0.5D_{\max}} = \sqrt{\frac{1}{K_{D>0.5D_{\max}}} \sum_{D>0.5D_{\max}} \left(\frac{\overline{s_{D_i}}}{D_i}\right)^2},$$

DE7

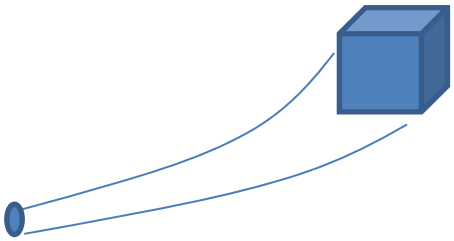
For a constant number of source particles, the statistical uncertainty also depends upon the **<u>size</u>** of the **dose voxel**.

To have the same statistical precision with a reduced volume of the voxel, it may require increasing the number of particles simulated .



$$S_{Di} \propto \sqrt{D_i},$$

$$\sigma^2(\bar{x}) = x\frac{C}{N}$$



N - n histories

Consequences:

If someone desires a region of uniform dose, that dose will not be uniform using a MC-based calculation,

due to statistical fluctuations between adjacent dose voxels.

The reported minimum and maximum dose voxels will differ from the mean of the idealized dose distribution by up to several standard deviations if many voxels are present in the distribution.

For example,

in a uniform dose distribution with 15625 voxels computed with MC algorithms, due to statistical fluctuations, there is a 63% *probability that the* dose in at least one voxel differs from the mean by more than four standard deviations.

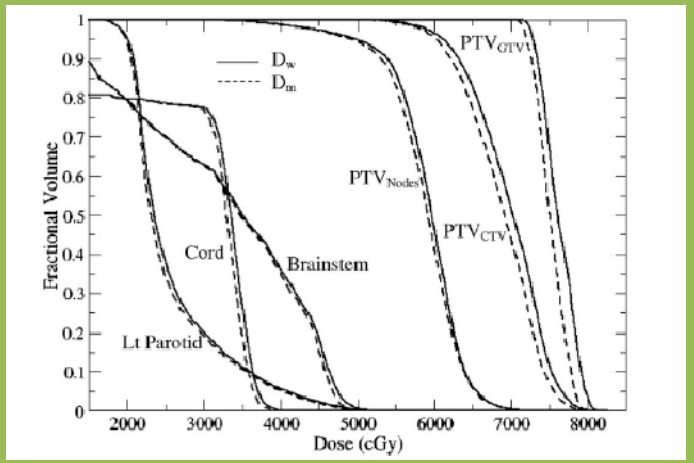
Then

DE9

the specification of the maximum dose to a single voxel when there is a desired volume of uniform dose e.g., the PTV, *will result in an underdosage to this volume.* Similarly, *dose prescription to the minimum dose voxel will result in an overdose to the relevant volume.*

"*there is uncertainty in the actual location of an isodose surface even when dose is computed with non-MC algorithms.* From this point of view, the planning team can use MC isodose jitter as a mechanism to open the dialog on realistic dose uncertainty in actual treatment delivery."

Integrated dose quantities, such as dose volume histograms DVHs are less sensitive to statistical uncertainty.



The stochastic nature of the MC method raises questions for prescribing dose. It is common clinical practice to prescribe dose to a single voxel or to base the dose prescription on the maximum or minimum dose voxels. Standard treatment planning analysis methods using isodose distributions and dose-volume histograms rely on dose averaged over a volume. It is logical to extend this practice to the prescription of dose, thereby avoiding precision issues in doses calculated in small volumes.

The dose at the calibration point may be calculated to high precision by averaging over a large number of voxels in a uniform dose region.

CT

CT2

Conventional algorithms, electron densities extracted from the CT image are used to scale the influence of primary and, ideally, also secondary radiation interactions.

MC particle transport uses the **material density and the material atomic composition**

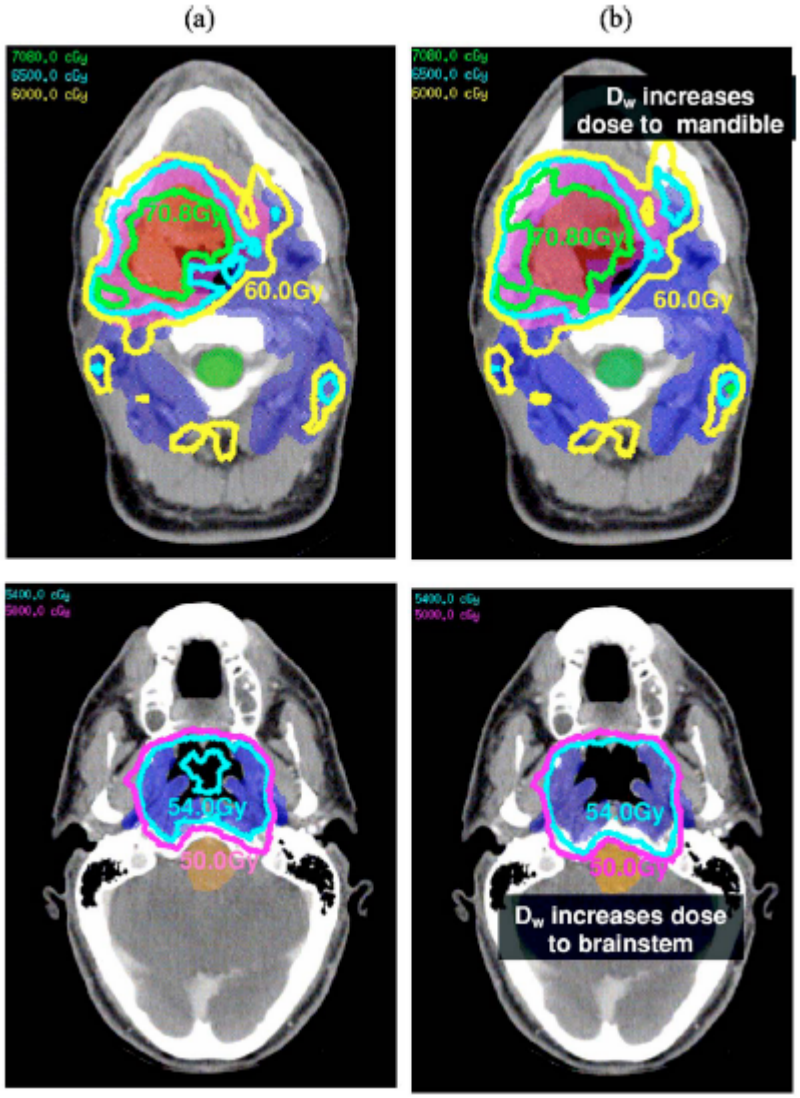
For some MC codes the material specification is obtained **relating the CT Hounsfield HU numbers to material interaction** coefficients,based upon parameterization of materials representative of the patient. for example those tabulated in ICRU Report No. 46.

CT1

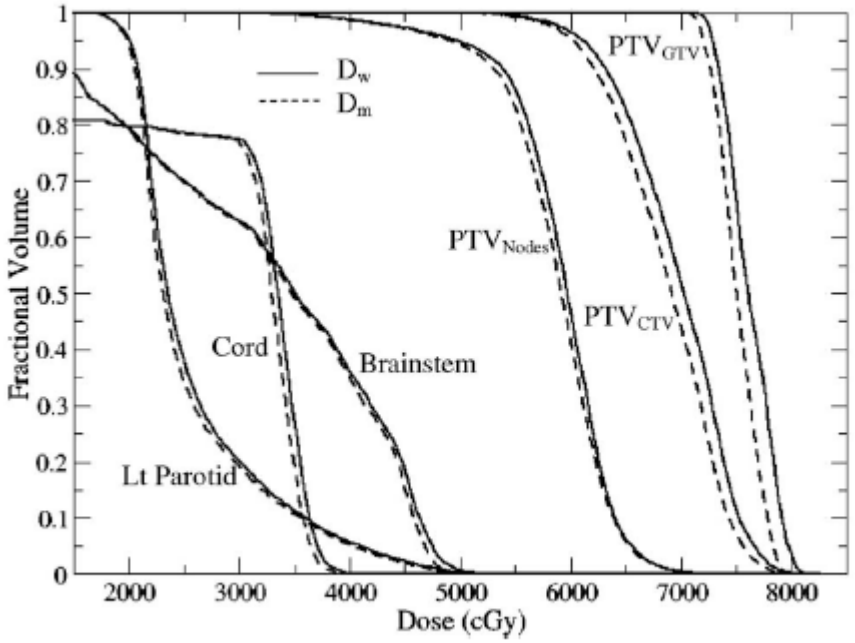
A recent evaluation of the **influence of material compositions** on dose distributions showed **dose errors of up to 10%** *for 6 and 15 MV photons,* **and 30%** ***for 18 MeV electrons*** *due to media and/or mass* density misassignment, when comparing dose distributions between a known phantom and a CT-imaged phantom with compositions and densities assigned by a conversion process.

Conversion techniques based purely on mass density (water with varying density), **is discouraged with MC simulation** because most of these methods ignore dependencies of particle interactions on the materials, which can lead to notable discrepancies in high atomic number materials.

CT number artifacts are of relevance to both MC- and non-MC-based algorithms and will need to be taken into consideration in order to perform accurate dose calculations in the dose buildup region.



CT3



Dose and DVH differences between plans calculated with D_w *and* D_m *for a typical head* and neck IMRT treatment plan

To ***compare*** D_m *with historical* D_w *results, requires* a conversion of D_m *to* D_w

MC and IMRT

IMRT often involves large intensity gradients and is usually delivered using a sequence of small static or dynamically shaped MLC segments. Under these circumstances, **the assumptions used in conventional algorithms regarding scatter equilibrium and output ratio variation with field size often break down.** Additionally, in IMRT a significant fraction of dose to structures of interest particularly dose limiting critical structures is due to radiation scattered from or transmitted through the MLC.

MC simulation avoids these limitations since it makes no assumptions regarding radiation equilibrium and can transport particles through the detailed MLC leaf geometry.

However,

MC-based IMRT plan optimization is limited by the clinical availability of MC calculation as a whole and *the large calculation time* required to perform the multiple IMRT dose calculations required for optimization.

Size of the voxel

VX1

Calculated dose is affected by the size of the scoring voxel.
Several factor for choosing the size:

Field size: for MC calculations, typical values:

- ❑ 2–5 mm for field sizes greater than 3x3 cm2
- ❑ 1–2 mm for field sizes less than 3x3 cm2.

The included **geometry:**

For calculations where geometric details of the MLC are included in the modeling, scoring voxel sizes no larger than 1–2 mm will be necessary to diminish volume averaging of dose from inter- and intraleaf leakage.

The **region**:

As with conventional algorithms, MC-based IMRT calculations should be performed using voxel sizes of 2–3 mm or less in the high gradient regions.

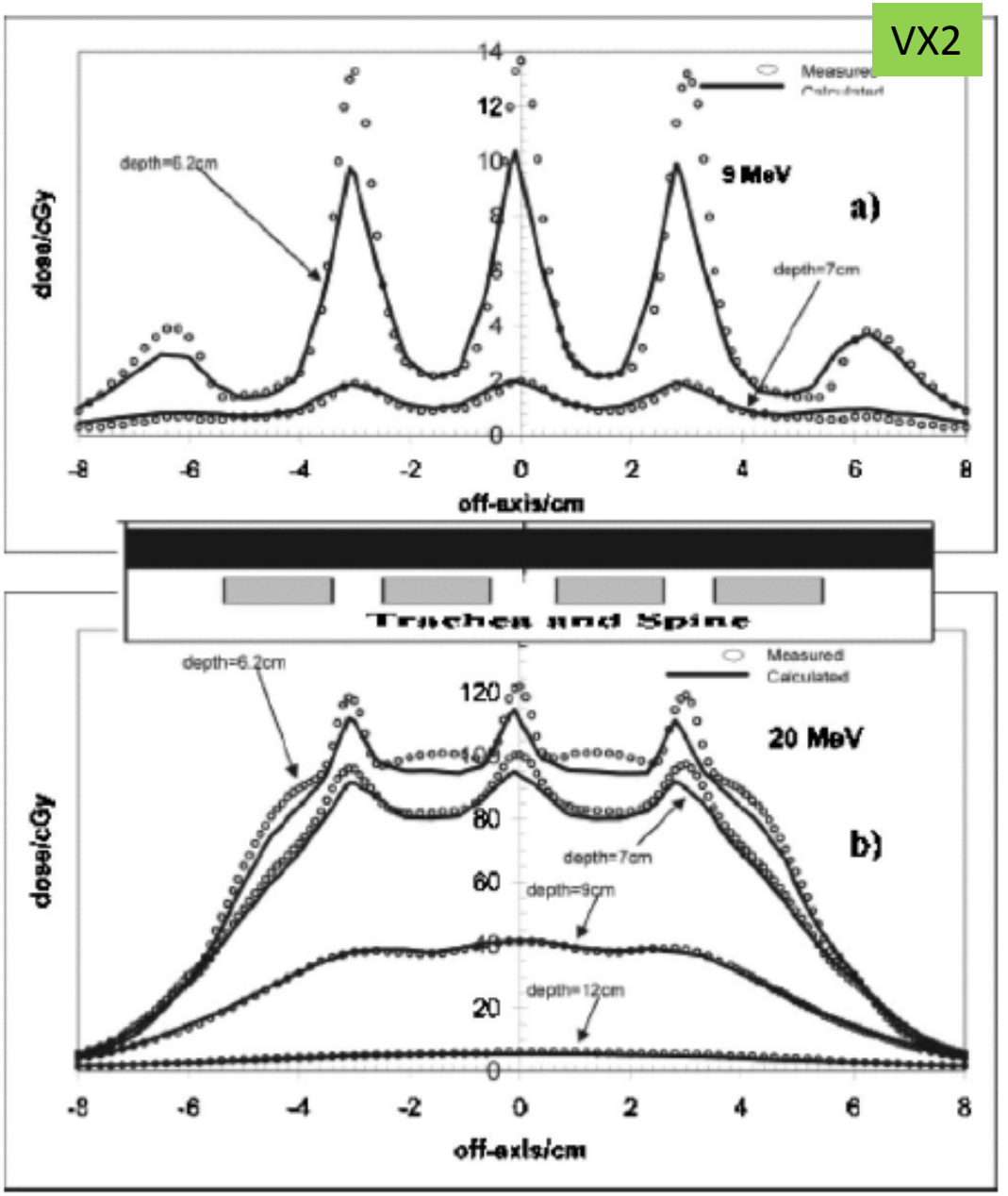
Reducing the voxel size will increase the relative uncertainty for a fixed number of source particles because fewer particles deposit dose in the smaller volume.

Increasing the voxel size will reduce the relative uncertainty but may introduce errors due to reduced spatial resolution.

The MC calculations are found to **underestimate the measurements** because the large voxel size averages the density distribution in the vicinity of the heterogeneity, **effectively reducing the calculated dose across the low-density heterogeneity**

Trachea and spine phantom:
measured and Monte Carlo Masterplan, Nucletron, based on VMC++ calculated crossplane dose profiles at various depths for: a) 9 and b) 20 MeV. SSD=100 cm, 1010 cm2 applicator. Monte Carlo simulations were performed with 50 000 histories/cm2 and a **voxel size of 0.49 cm.** 100 MU were used for the calculations. The relative uncertainty in the calculations is about 1%−1.5%. *The phantom geometry is shown in the inset.* ***Differences between*** **measurements and calculations in this example were attributed to the volume averaging effects of a large voxel size 0.5 cm**

VX2



MC efficiency: $\varepsilon = \frac{1}{s^2 T}$

s^2: *variance* of the quantity of interest
T: is the CPU time required to obtain this variance.
N: number of histories

N s^2 → Cte
T/N → Cte

→

ε → Cte

$$S_{Di} \propto \sqrt{D_i},$$

$$\sigma^2(\overline{x}) = x\frac{C}{N}$$

To improve the efficiency we need Variance reduction techniques

Variance reduction techniques: to reach the objective with less computation time

Without additional variance reduction techniques the increase in calculation time would simply be the reciprocal of the delivery efficiency.

- Transport cutoffs
- Secondary particle creation thresholds
- *Electron range rejection*
- *Bremsstrahlung splitting and Russian Roulette*
- *Interaction forcing*

The decreased efficiency of IMRT treatments (meaning more monitor units have to be delivered to reach a certain dose in the treatment target) means that many more particles have to be sampled in MC simulations. -> Variance reduction techniques

MC vs conventional algorithms

Photon beam:
Lung planning studies have shown sometimes substantial differences 10%–20% *between conventional and MC* algorithms. Depending on the location and size of the tumor, and the beam energy, underdosage of the PTV in lung planning may be significant.

Electron beam:
Electron MC calculations require fewer primary histories to achieve a given uncertainty on the dose being calculated because electrons deposit their energy in a more continuous manner, in a smaller volume . This timing advantage has allowed the development of commercial electron beam MC algorithms which are time efficient taking on the order of minutes per plan even on a single processor.

What is the effect of more accurate MC dose distributions on patient clinical outcome?

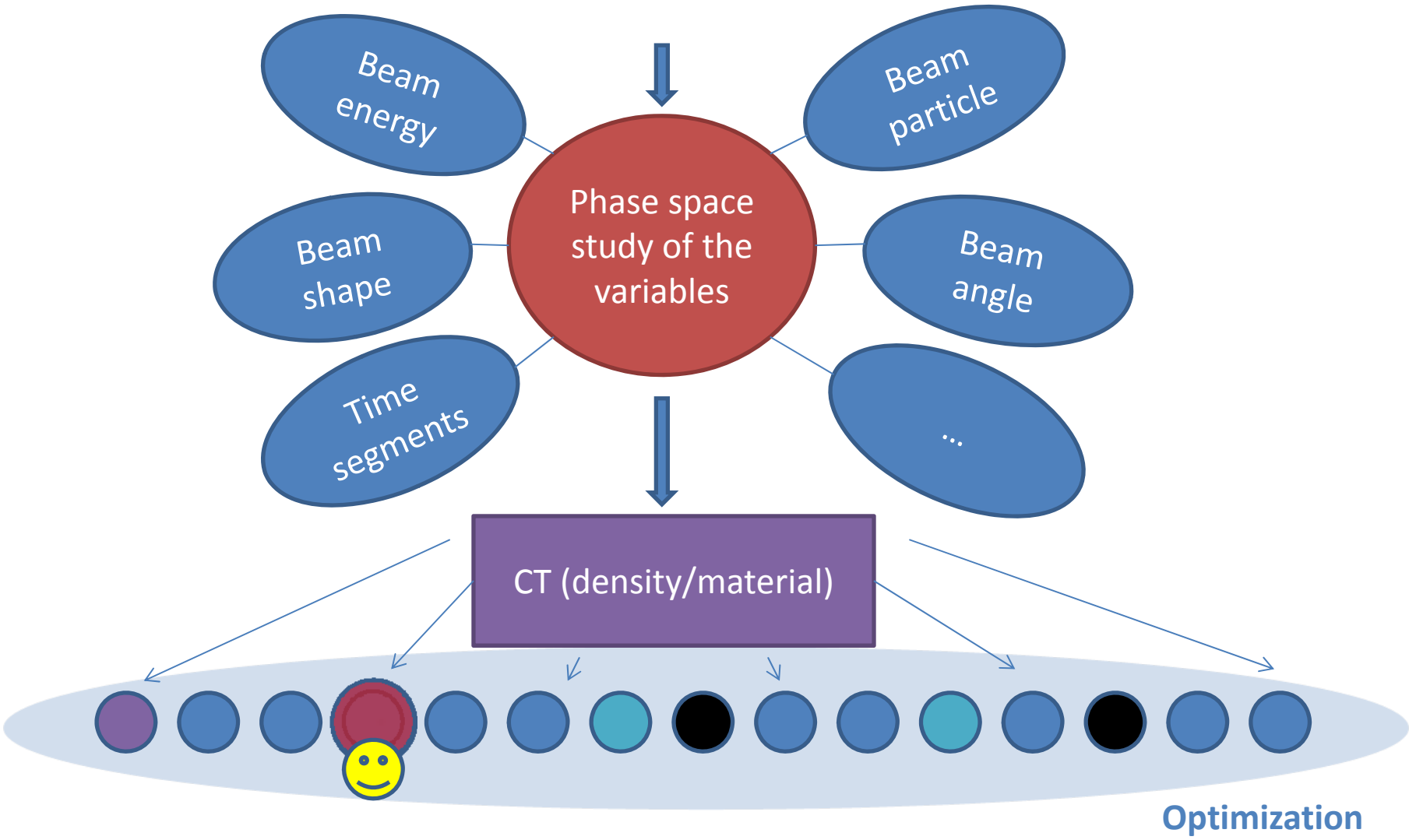
In terms of tumor control and normal tissue toxicity there is a need for more studies addressing the clinical impact of MC-calculated dose distributions.

Dose delivery based on MC treatment plans, particularly for lung cancer, have the potential to result in clinically significant changes

But, ***dose differences found between MC-based and conventional algorithms will be highly dependent on the beam arrangements, field sizes,beam energies, tumor size, and location.*** This is particularly true in anatomical sites where the target is situated near tissues with widely varying densities, such as the lung and head/neck.

- MC is the best approximation to reality
- Considerations:
  - $>10^6$ beam particles to have a “good” statistics (< 5%)
  - Voxel size enoughtly small (~ 1 mm^3 ?)
  - MC reproduce the physics processes but is time consuming
  - There are different densities and materials.
  - Fast: the context is dynamic.

There is an optimization process to select the best configuration



Examples:

(Sempau et al. Phys. Med. Biol. 45(2000)2263)

Radiotherapy: 400 MHz, 10^6 electrons histories, 128x128x128 voxels 1 mm^3

*REMARKS: with Pencil/Broad Beam, (no MC); times for **one** configuration*

Electrons beams	Time CPU (s)
Pencil beam 10 MeV in **water**	169.4
Broad beam 10 MeV in **water**	181.4
Pencil beam 5 MeV in **water**	111.2
Pencil beam 15 MeV in **water**	250.6
Pencil beam 20 MeV in **water**	327.0
Broad beam 15 MeV in ***CT***	**383.2**

Examples:

Protontherapy: 2.83 GHz, database of trayectories to calculate the dose in an heterogeneous medium, with extrapolations from water, 490680 voxels de 2.5x2.5x2.5 mm^3. Circular beams with 8 cm Ø, 200 MeV, database with 27 KB/proton.

(Phys. Med. Biol. 54(2009)2263 **)

REMARKS: ***one*** *configuration/energy, extrapolating, 2.5x2.5x2.5,* ***database***

	time/history (s)	10^6 histories (days)	Protons
GEANT4	**1.38**	**15.97**	**$5x10^6$**
MCNPX	0,58	6.71	$1x10^8$
**	**0,0028**	**47 m**	**$5x10^6$**

E3

Examples:

(Paganetti et al. Phys. Med. Biol. 53(2008)4825)

- GEANT4 (with modifications) with ***protons***.
- Cluster with 26 dedicated computers with 2 / 4 CPU/each. configured in 80 virtual slots
- 176x147x126 voxels of 0.936x0.936x2.5 mm^3 .
- 6 h with 20 slots for ***<u>one</u>*** simulation, although 90% of time for the calculation outside the patient (treatment head).
- The MC result does not affect the treatment plan decision obtained with a Pencil Beam Scanning (1h).

Conclusions:

- MC takes time and resources
- There are several variables affecting differently the time (Ex. 1)
- Databases are partial solutions(Ex. 2)
- MC is now used to validate other methods (Ex. 3). Enough?
- CPUs farms are needed. (Ex. 3)

- We need small voxel and large statistics (Ex. 1-3).

  For Proton- ICRU Report 78 (2007):

  2% accuracy and 2 mm implies tens of millions of histories (hours or even days)

  But keeping uncertainty under control and optimizing the time.