A Monte Carlo-based treatment planning tool for proton therapy

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Hadron Therapy with active scanning

Example:
- Depth 5 cm:
  - Proton 80 MeV
  - Carbon 150 MeV/u
- Depth 25 cm:
  - Proton 195 MeV
  - Carbon 380 MeV/u
The concept of Treatment Planning (in a 1D-approx.)

Size of the tumor region

PTV = Planned Treatment Volume

This plot is in physical dose for a constant biological effectiveness
• Currently treatment planning for hadron therapy are commonly based on fast analytic dose engines using Pencil Beam algorithms.

• MC calculation of doses and fluences are superior in accuracy because they take into account heterogeneities, large densities, geometry details. They can predict secondary particle production. *However they require much longer execution times*…
Present application of MC calculations in hadron therapy

• Calculation of input physics databases (for example: the case of TPS developed within the INFN-IBA collaboration)
• Validation of TP calculation (in Water/CT systems)
• Forward (re)check of TP predictions (and possibly provide corrections)
• Calculation of secondary particle production
• Data analysis in dosimetry experiments
• Commissioning of infrastructures
• In all cases there is the question of the proper RBE to be used. MC coupled to proper radiobiological models can account better for mixed field situations (ion therapy).

• In proton therapy a constant value of 1.1 is often used (in accordance to ICRU 2007), but there are data showing that a variation occurs in the last few mm.

• Use of MC to recheck and correct standard TPS calculations has been discussed several times in literature.
Can we build a TPS using the accuracy achievable by a detailed MC calculation?

An integrated MC+optimization tool:

- to explore the possibility of a treatment planning which overcomes the “water-equivalent” approach
- to take into account all details about geometry and materials
- which can be applied to realistic treatment conditions with acceptable CPU time
- That can be applied in planning for ions with $1<Z<8$: today’s talk will be focused on protons only
Goals

• A tool which not only allows to recheck a given plan, but which also suggest a better solution

• To be used stand-alone (using some pre-processing code, see later) or as post re-optimization of plans obtained from commercial TPS (as applied at CNAO)

• To be used in research:
  o New ions and combined ion fields
  o testing of new bio-models and algorithms
  o to predict secondary fluxes: $b^+$ emitters, prompt $g$, etc.
Choice of the MC code

**FLUKA** (INFN-CERN property) is the baseline choice for this project

(http://www.fluka.org)

- Presently used in hadron therapy context
- Includes sound physical models
- Capability of being coupled to CT scans to import geometry, to import volume/organ definitions
- Possibility to be coupled to a Radiobiological model
Use of FLUKA @CNAO to provide input databases

Beam delivery

Scanning with active energy variation

Required parameters

- 147 Energy steps (30-320 mm)
- 1 Focus size @ ISO

FLUKA calculated FWHM at the isocentre as function of the proton beam energy
FLUKA calculated depth-dose distribution in water
Both the experimental data and the MC results are renormalized to the maximum at each depth.
FLUKA recalculation of a patient PLAN

- Capability to import a CT scan to build 3D voxel geometry
- Capability to assign materials and composition according to HU numbers from CT scan
- **Capability of coupling to radiobiological models based on Dual Radiation Approach Theory ➔ Calculation of RBE-weighted dose ($D_{RBE}$)**
Basic principles

**Multistep procedure:**

1. Start from a given set of PBs $P_1(N_1)$ with pre-optimized initial particle numbers $N_1$.

2. This set can be obtained from a pre-selection and pre-optimization of available PBs deliverable by the “accelerator beam library”: $P_0$ for a given treatment and beam port:
   - Two alternatives: - an already available certified TPS
   - a fast simulator

3. Starting from $P_1(N_1)$ the MC (FLUKA) allows to calculate a Dose Kernel ($D_{MC}$) using the fully detailed case geometry, composition and machine setting.

4. An optimization code will derive iteratively from $D_{MC}$ the optimized solution $P_2(N_2)$.
Components and program flow

Input
- Beam model
- CT information
- PTVs, OARs, Opt. Goals
- Radiobiological input tables

Initial guess
- $P_0(N_0)$
- Commercial TPS or Fast MC

Solution
- $P_2(N_2)$

Phase spaces of all possible pencil beams

Legend
- $P_i(N_i)$: set of pencil beams with particle numbers $N_i$
- $D_{MC}$: MC dose kernel

FLUKA input & user routines

Optimizer

$P_1(N_1)$

$D_{MC}$
Optimization procedure

Absorbed dose in voxel j from PBs (running on i index)

\[ D_j(N) = \sum_{i \in PB} d_{i,j} \cdot N_i \]

\( N \) has to be determined by minimizing the following cost function:

\[ \chi^2(N) = \sum_{j \in PTV} \frac{w_j (\hat{D}_j - D_j)^2}{\hat{D}_j^2} + \sum_{j \in OAR} \frac{w_j (\hat{D}_j - D_j)^2}{\hat{D}_j^2} \Theta(\hat{D}_j - D_j) \]

Prescribed dose in dose grid voxel

Weight associated to grid voxel j based on planner’s prescription

Two optimization methods tested:
1) Gradient-Based optimization ("Steepest Descent")
Dose-to-medium vs Dose-to-water

• In order to compare to standard TP calculation Dose has to be expressed as Dose-To-Water (MC calculated directly Dose-To-Medium)

• TP rescale depth-dose profiles in water using Water Equivalent Path Length (WEPL) approximantion

• in our approach we get Dw by scoring in MC Fluence x LET in Water (from MC model)
Calculating RBE-weighted doses

- **RBE**: ratio of the dose from a reference radiation ($D_{RX}$) and the dose for the actual radiation ($D_r$) needed to achieve the same biological effect under consideration.

$$R.B.E. = \left( \frac{D_{RX}}{D_r} \right)_{SF=SF_0}$$

- for a given radiation field, RBE is not a univoque quantity
- ... it depends on:
  - The definition used in the calculus;
  - The considered biological effect (survival, induction of mutations etc.)
  - The cell type
  - The considered “Level of expression” for a given biological effect
RBE defined using Survival Fraction

\[ SF = \exp(-\alpha D - \beta D^2) \]

\[ SF = \exp(-\alpha D) \]
Radiobiological Model

• Values of non-constant RBE are obtained by a re-implementation of the “local effect model” (LEM, version IV) developed in Heidelberg.


  Warning: using for the moment a reference cellular line (non-human) typical in radiobiology studies…

• Radiobiological input tables computerd with LEM are interfaced with FLUKA to calculate RBE-weighted doses $D_{RBE}$
Coupling to radiobiological model

• LEM predicts $a_{ion}$ and $b_{ion}$ for single ion at a given energy.
• In a real case this condition is never met: energy straggling, scattering and nuclear fragmentation, mixed radiation field contribute to the same given voxel with fluences of different particle species of different energies.
• Common approach: by MC calculation we derive dose-weighted averages for $a$ and $b$ in voxel $j$:

$$\bar{\alpha}_j = \frac{\sum_i \Delta d_{ij} \cdot \alpha_{ij}}{\sum_i \Delta d_{ij}}$$

$$\sqrt{\beta}_j = \frac{\sum_i \Delta d_{ij} \cdot \sqrt{\beta_{ij}}}{\sum_i \Delta d_{ij}}$$
Optimization of $D_{RBE}$

- $D_{RBE,j}$ replaces $D_j$
- In gradient based optimization, the case of constant RBE weight (e.g. RBE=1.1 for protons) is trivial
- for varying RBE values one has to consider the following gradient:

$$\nabla D_{RBE,j} = W_{RBE,j} \nabla D_j + D_j \nabla W_{RBE,j}$$

However, at typical target dose levels, RBE is a slowly varying function of Ni as compared to Dose. This allows us to neglect the second term and approximate $W_{RBE}$ as a stepwise constant. Similar arguments apply to DDO approach.
Verification of MCTPS Plans

• Cases:
  o single field irradiation of homogeneous 3D dose distribution of 2 Gy in a cubic shale (3x3x3 cm\(^3\)) in water phantom
  o Patient cases with 2 or 3 beam ports. \(D_{RBE} = 2\) Gy for PTV either with fixed RBE=1.1 or variable RBE as predicted by LEM. PTVs of 32.5 ml and 103.5 ml

• For Patient Cases: TP at CNAO is Syngo RT Planning by Siemens AG (Version VB10A). This is used for pre-optimization phase.

• Input to Syngo and to our Fast MC are: acc. beam energies, FWHM of lateral profiles at isocenter, CT or contoured phantom, optimization goals and radiobiological tables (only for fast MC)
MC Set-up

• Simulation set up includes CNAO Nozzle so to generate “PB” with actual phase space distribution: lateral FWHM ~ 1.0 cm at isocenter, lateral spacing of 3 mm. Spacing between Bragg peak position of 2 neighbouring beam energies 2 mm.

• Simulation includes voxelized water phantom or CT patient image: 2x2 mm² transaxial pixels and 2 mm slices (as for the certified default TPS at CNAO). This defines transport and scoring granularity in MC

• Materials and Composition assigned to voxels according to Schneider et al, PMB 45 (2000) 459 and Parodi et al. PMB 52 (2007) 3369

• Dose Kernel Matrix $D_{MC} \equiv (d_{j,i}; a_{j,i}; b_{j,i})$

• Total no. of PB to be simulated: 3438 for the cube-shaped PTV to 6257 and 13920 for the 2 patient cases

• $5 \times 10^3$ primary protons per PB at the given granularity $\Rightarrow$ mean statistical uncertainty on PTV $\sim$ 1% (max 2%)
CT stoichiometric calibration

CT segmentation into 27 materials of defined elemental composition (from analysis of 71 human CT scans)

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Schneider et al PMB 45, 2000
Assign to each material a “nominal mean density”, e.g. using the density at the center of each HU interval (Jiang et al, MP 2004)

But “real density” (and related physical quantities) varies continuously with HU value: a HU-dependent correction on density on each voxel is applied.
Details on dosimetric checks

• Validation of MCTPS calculations we present dosimetric verification results performed following the same procedure for patient quality assurance adopted at CNAO.

• Water phantom (MP3-P T41029, PTW) typically employed for patient plan verification.

• 3D stack of PinPoint Ionization Chambers (ICS, TM31015, PTW). Simultaneous readout of 12 IC.

• Acceptance criteria: average (m) and r.m.s (s) of \( \left[ D_{\text{meas}} - D_{\text{calc}} \right] / D_{\text{max}} \) over a data set of 12 points are within ±5% and below 5% respectively.
The Cube case

Here we also used a fast MC as pre-processor:

FRED
FRED (by A.S.)

- **Num of Fields, energy numbers, Monitors/filters**
- **Treatment Facility Specs**
- **Patient data**: CT, PTV, OAR

PB skimming: set of PB to be traced

Pre-optimization: different statistical weight for each PB

Fast-TPS: whole MC-TPS check with reduced physics model
• Light-weight C++ Monte Carlo code written for high tracing-rate performance
• Reduced physical model for capturing essential features of PB energy deposition
• Converts CT into density map and stop.pow. scale factors: goes beyond water equivalent phantom
• Multiple fields, arbitrary geometry, modular beam filter package
• Can be used to drive external/auxiliary codes in the TPS workflow
• Parallel execution: multi-core, multi-node
• Porting to GPU accelerated hardware underway
• Input: dicom files, free-form text finput file, tabulated data
• Output: ASCII files, silo format for Visit, binary maps for Matlab post-processing
The 2-port chordoma case

The Syngo TPS prescription

MC fw simutation of TPS prescription

Result of our MC Optimization
The 3-port chordoma case

The Syngo TPS prescription

MC fw simulation of TPS prescription

Result of our MC Optimization
Results of the QA tests

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<th>μ (%)</th>
<th>σ (%)</th>
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<td>Patient beam 1 position 1</td>
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<td>Patient beam 1 position 2</td>
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<td>Patient beam 2 position 1</td>
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<tr>
<td>Patient beam 2 position 2</td>
<td>0.72</td>
<td>1.93</td>
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Confirmation of:

a) dose prediction by MCTPS and also of

b) conversion of MCTPS plans to the formats needed by the machine controls and dose delivery system
The % of volume fulfilling gamma-index criterion for PTV is 91% and 81% for OAR.

The % of volume fulfilling gamma-index criterion for PTV is 72% and 90% for OAR.
RBE as predicted by LEM for abs. doses larger than 10% of prescribed dose

3-port case
Optimization of $D_{RBE}$ (with variable RBE from LEM) 3 port case
Comparing fixed vs variable RBE

Optimization using constant RBE=1.1 resulted in about 9%/4% higher total energy deposited in the patient (for 2/3 port case respectively) as compared to the case of variable RBE.

Effective Range increases (see also Paganetti, PMB 57 (2012) R99)

Warning: this is just a demonstrative effect. RBE calculated only for one cellular line! (V79)
Computing effort

Example: for the 2-port parent case:

MC calc. of RBE-weighted dose matrixes (5 k MC histories per PB) = 50 h (20 CPUs, 10 CPUs/field)
Optimization time = 2h (1 CPU)

Comparison of Optimization methods

```
Work in Progress!!
```

```
Cost

Time [min]
```

```
DDO  GBO

Comparison of Optimization methods
```
Some Conclusions about the MCTPS

• The achieved results are very promising
• Computation speed is actually acceptable only for a research tool
• Next steps:
  o Study robustness of MCTPS plans
  o Work the case of hadron therapy with $Z>1$ ions
  o Integrate the different pieces together with the Fast MC preoptimizer plus graphical tools