Proton and helium beams: the present and the future of light ion beam therapy

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Rationale for proton and ion beam therapy
Inverted dose profile

Bragg peak

Lateral scattering

RBE (relative biological effectiveness):

\[ \text{RBE} = \frac{D_{\text{photon}}}{D_{\text{hadron}}} \]

for the same biological effect

The RBE depends on:
- particle type (p, \(^{12}\text{C}, \ldots\)), LET / local energy spectrum, dose
- tissue type, biological endpoint

In clinic: p RBE = 1.1

\(^{12}\text{C} RBE\) models
How do we bring particle beams to clinics?
Heidelberg Ion Beam Therapy Center (HIT)

Synchrotron-based facility
Active beam scanning delivery

$^1$H and $^{12}$C beams in clinics
$^4$He and $^{16}$O beams for research

Active Beam Scanning delivery with Synchrotron

Key: accurate dosimetric characterization of the pencil beams

$^{1,2}$Haberer et al. Radiother Oncol. 2004, 73, 186-190, NIM A 1993, 330, 296-305
Depth-dose distributions results for protons, helium, carbon and oxygen ions, respectively, from the top to the bottom panels. In the left panels the ddds of the ions in water, in the right panels, the dependence of $R_{80}$ as a function of the ion energy.

Depth-dose distributions results for protons, helium, carbon and oxygen ions, respectively, from the top to the bottom panels. In the left panels the dddds of the ions in water, in the right panels, the dependence of $R_{80}$ as a function of the ion energy.
Lateral dose distributions in water at HIT

Lateral dose distribution: Protons are represented with squares, helium ions with circles, carbon ions with triangles and oxygen ions with diamonds. In solid line, the double Gaussian (DG) fits are shown, and in dashed line the simple Gaussian (SG) fits.
Treatment planning system (TPS)

- Acquisition of imaging data (CT, MRI)
- Delineation of regions of interest
- Selection of proton/ion beam directions
- Design of each beam
- Optimization of the plan

main input for dose calculation:

dosimetric description of the interaction of the beam in water
Advanced calculation approaches
The Monte Carlo (MC) method

Invented by John von Neumann, Stanislaw Ulam and Nicholas Metropolis (who gave it its name), and independently by Enrico Fermi
Advantages/disadvantages of MC simulations for particle therapy

+ Detailed description of particle transport and interactions
+ Patients density and elemental composition in account
+ Flexibility

- Long computational time
- Programming skills needed
- Dedicated hardware
...back to clinics
Input dosimetric data for clinical treatment planning

Depth-dose distributions for p (left panel) and carbon ions (right panel)

Input dosimetric data for clinical treatment planning

Lateral dose distributions for p (upper panels) and carbon ions (lower panels)

F. Sommerer, A. Mairani, K. Parodi, Radiation Research, 2013, 54, i91–i96
Input dosimetric data for clinical treatment planning: proton database HIT vs CNAO

Fig. 6. Comparison of the HIT basic data input in both the HIT and CNAO TPS, with respect to the parameters deduced using the same fitting procedure described in this work, however applied to FLUKA MC simulations of lateral beam broadening in water using a detailed modelling of the CNAO beamline for proton beams [11]. Two similar energies of approximately 60 MeV/u (left) and 221 MeV/u (right) were considered. While the sigma parameters match fairly well, some discrepancies are observed in the weight factor $w$ directly related to the broad Gaussian component, especially for low-energy proton beams. This is likely ascribed to less large-angle scattering material in the CNAO beamline. 

F. Sommerer, A. Mairani, K. Parodi, Radiation Research, 2013, 54, i91–i96
Current clinical applications of MC
Dosimetric comparisons
Proton extended fields in water: MC vs TPS vs experimental data

1) 5 mm side cube at 5 mm depth
2) 20 mm side cube at 30 mm depth

Dosimetric accuracy as a function of the target size

G. Magro, S. Molinelli, A. Mairani, et al
Physics in Medicine Biology, 2015, 60, 6865
Patient Plan Verification

Molinelli, Mairani et al PMB 58 2013
Re-calculations of patient dose distributions

Deep-seated sacral tumor irradiated with p
Biological calculations in carbon ion therapy

*in vitro data* predictions

A. Mairani, et al Physics in Medicine and Biology 2010, 55, 4273–4289

MC + LEM model

MC + NIRS approach

G. Magro,…,A. Mairani Physics in Medicine and Biology 2017, 56, 3814–3827
Future clinical applications: overcoming TPS limitations
Monte Carlo-based Treatment Planning Tool

Beyond the TPS: variable RBE in proton therapy

Beyond the TPS: variable RBE in proton therapy

Dosimetric and *in vitro* cell stack experiment: model vs data

Calculation of patient plans with variable RBE (varRBE) models

Dose difference:

\[ D\text{_{varRBE}} - D\text{_{RBE=1.1}} \]
Beyond RBE 1.1 in proton therapy: LET distributions in clinical-like scenario
$D_{RBE}$ distributions in clinical-like scenario with $(\alpha/\beta)_\text{ph} = 2$ Gy

G. Giovannini,...A. Mairani, K. Parodi
Radiation Oncology (2016) 11:68
Beyond the TPS: variable RBE in proton (and He) therapy tuning MKM input parameters

\[
\text{RBE}_\alpha = \frac{\alpha_{\text{ion}}}{\alpha_{\text{ph}}} = 1 + \left(\frac{\alpha}{\beta}\right)_{\text{ph}}^{-1} \cdot z_{1D}^*,
\]

\[
R_\beta = \frac{\beta_{\text{ion}}}{\beta_{\text{ph}}} = 1.
\]

Figure 1. Experimental RBE$_\alpha - 1$ (points with error bars) as a function of $z_{1D}^* \cdot (\alpha/\beta)_{ph}^{-1}$. $z_{1D}^*$ values have been calculated using the best fit parameters $R_d = 0.3 \ \mu m$ and $R_n = 3.6 \ \mu m$. The slope of the dashed line graphically displays a 1:1 dependence.

Mairani et al PMB (2017) 62: N244
Beyond the TPS: variable RBE in proton (and He) therapy tuning MKM input parameters

Mairani et al PMB (2017) 62: N244
Novel ions at HIT: 

$^4$He ion beams
Dosimetric comparisons

\(^4\)He as a good candidate for further particle therapy improvements:

- Favorable physical characteristics
- Smaller lateral scattering than p, Fall-off distal / lateral
- Very low tail-to-peak ratio compared to \(^{12}\)C or \(^{16}\)O

• Comparisons **MC-FLUKA\(^{6,7,8}\)** / dosimetric measurements
  → Beam Modelling (DDD + Lateral profile + SOBP)

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\(^6\) Böhlen et al. (2014)
\(^7\) Ferrari et al. (2005)
\(^8\) Battistoni et al. (2016)
MC - Beam Modelling

Depth Dose Distribution

Measurements

- **10 energies** (56.44-220.51 MeV/u, ~2.5-31 cm)
- **PeakFinder** (PTW) water column
- Delivery of a quasi-**monoenergetic** pencil-like beam in the central axis
- Step size in the peak region ~ 50µm
- w/wo Ripple Filter (RiFi)

*PeakFinder Water column*
MC - Beam Modelling

Depth Dose Distribution

Simulations

- Detailed model of the HIT beamline
- Binning of 25µm (radius=4.08cm)
- $10^6$ primary histories

- Density?
- Ionization Potential?
- Momentum spread?
**MC - Beam Modelling**

**Depth Dose Distribution**

**Simulations**

- Detailed model of the HIT beamline
- Binning of 25µm (radius=4.08cm) + WATER
- $10^6$ primary histories

![Diagram of beam propagation and scoring radius]

- Density $\rightarrow 0.998$ g.cm$^{-3}$ (Exp. Conditions)
- Ionization Potential $\rightarrow$ Trial and errors: Range comparisons
- Momentum spread $\rightarrow$ Trial and errors: Bragg Curve similitude ($\chi^2$ red.)
MC - Beam Modelling

Depth Dose Distribution

Simulations

- Detailed model of the HIT beamline
- Binning of 25µm (radius=4.08cm) + WATER
- $10^6$ primary histories

- Density $\rightarrow$ 0.998 g.cm$^{-3}$
- Ionization Potential $\rightarrow$ 76.8 eV
- Momentum spread $\rightarrow$ $dp/p=f(E)$
Overall good agreement between simulations and measurements (w/wo RiFi)
- Range differences $< 0.10$ mm
- Dose differences from 0.5 to 6% in the high dose region
- Small differences in the tail
- Average dose-weighted dose-difference from 0.4 to 2.5%
  - Good results of the FLUKA models
  - Room for improvements (production of secondaries ?)
**MC - Beam Modelling**

**Lateral Dose Distributions**

**Measurements**

- **3 energies**
- After Vacuum Gaussian size assessment ...

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[Diagram showing beamline propagation and measurements of vertically scanned line]
MC - Beam Modelling

Lateral Dose Distributions

Simulations
- Detailed model of the HIT beamline and water
- Binning 1x1x1mm³
- 200x10⁶ primary histories
- ICs sensitive volume

Analysis
- Simple Gaussian parametrization along depth
- Triple Gaussian parametrization along depth
(ROOT – Minuit Package)
MC - Beam Modelling

Lateral Dose Distributions

Simulations
- Detailed model of the HIT beamline and water
- Binning 1x1x1mm³

Analysis
- Simple Gaussian parametrization along depth ➔ FWHM evolution
- Triple Gaussian parametrization along depth ➔ Dose contributions

(ROOT – Minuit Package)
**MC - Beam Modelling**

**Lateral Dose Distributions**

- **Results**
  - Good agreements
  - But differences for:
    - High energies
    - Large depth/Lat. position

![Graphs showing lateral dose distributions for low, medium, and high energy beams.](image)
Lateral Dose Distributions

Results

- FWHM differences < 0.5 mm at the entrance and near Bragg peak region
- Differences in the halo for high energies at large depth

→ Good results of the FLUKA models
→ Underestimation of secondary particles ? Large angles ?
Optimization with FLUKA–MCTP

- SOBP **size**: 3x3x3 and 6x6x6 cm$^3$
- **Position** (center) of SOBPs: 5, 12.5 and 20 cm
- **Dose** planned: 1 Gy (physical optimization)
- **Re-calculation** with: 1x1x1 mm$^3$ bins / 150x10$^6$ primaries

**Measurements**

- **Measurements** in the water tank
- Acquisition of **depth-dose** distributions (step size 1 mm)
- Acquisition of **lateral dose** distributions (step size 2 mm)

*Tessonnier, et al.* PMB (2017); 62(16):6579-6594
Results

MCTP Platform: He

- Overall good agreement
- Range difference < 0.5 mm
- Global dose deviation < 2.5 %
- Mean dose deviation in SOBP region < 1%
- Consistent results

→ Satisfying results from MC models, the optimizer and beam monitor calibration

Tessonnier, ..., Mairani et al. PMB (2017); 62(16):6579-6594
He RBE model development

Mairani et al 2016 PMB 61 888, Mairani et al 2016 PMB 61 4283
1 – Bio. Optimized SOBP
2 – Measurements verifications
3 – Cell Survival (A549) + RBE

→ Validated in-house model for He (5%) and H (2%)

Mairani et al 2016 PMB 61 4283
Plan Comparisons

Methods

- Meningiomas treated with proton (4 patients)
- Re-optimization with FLUKA–MCTP for helium ions AND protons
- Dose in PTV 1.8 GyRBE

- Tissue types CNS $\alpha/\beta = 2$ Gy, PTV $\alpha/\beta = 3.7$ Gy
- Protons without RiFi, variable RBE (calculated “online”)
- Helium ions with RiFi, variable RBE (calculated “online”)
- Comparisons: DVH for PTV and OAR

Tessonnier, Mairani et al 2018 Radiation Oncology 13(2)
Plan Comparisons

Results

Comparable PTV coverage
Better sparing of OAR with He
Less dose to normal tissues

Tessonnier, Mairani et al 2018 Radiation Oncology 13(2)
Higher benefits for large depth (lateral/distal fall-off)

→ Promising results from plan comparison between He and protons

Tessonniere, Mairani et al 2017 Radiation Oncology 13(2)
Thank you for Your Attention!