Treatment Planning: Current Challenges & Research in Progress in Lyon

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PART I: Challenges in Ion Beam Therapy Treatment Planning
1. Dose calculation accuracy
2. From passive to active treatment delivery
3. Biological dose
4. Organ motion
5. Imaging in treatment planning
1. Dose calculation accuracy

Sources of uncertainties:

- Beam description
- Cross sections (fragmentation)
- Stoichiometric calibration
- CT artefacts (metal implants)

CT scan of a pelvic phantom with steel insert
[Jäkel and Reiss, PMB, 2007]
Sources of uncertainties (continued):

- Variability of tissue composition and $I$-value

SHIELD-HIT simulation
300 MeV/u carbon ions
[Andreo, PMB, 2009]

Reconsider the range precision achievable in clinical practice. Sub-centimetre precision is questionable.
Sources of uncertainties (continued):

- Patient heterogeneities / approximations in calculations
- Patient positioning → in situ CBCT
- Anatomical changes → re-planning with new CT

Overlay of two CTs in the case of a weight gain
[Albertini, Rad. Onc., 2008]
Dose calculation accuracy: what should be done?

- Assessment of available physical models
- Cross section measurement programme
- Multiple modalities (PET, MRI)
- Multi-energy CT (dual, MV+kV)
- Dosimetric validations
  - dose measurements in phantoms and in vivo
    [Lu, PMB, 2008]

- In vivo treatment monitoring → ENVISION
- Increase margins from CTV to PTV?
- Individualized determination of tissue composition?
2. From passive to active delivery

Passive scattering: **forward planning**

![Diagram](attachment:image.png)
Active delivery: spot scanning → more conformational

**Inverse planning**
Optimization of several $10^4$ spots with fast iterative analytical algorithm. Verification with MC simulation
See e.g. [Krämer, Paganetti, Newhauser, Schaffner, Bourhaleb]
3. Biological dose

Prescription in terms of biological dose

\[ \text{Biol. dose (GyE) = phys. dose (Gy) \times RBE} \]

The RBE depends on “radiation quality”

**NIRS:**

\[ \text{RBE = f(average local LET)} \quad [\text{Kase, PMB, 2006}] \]

**GSI/Heidelberg:** Local Effect Model

\[ \text{RBE = f(partic., } E, \text{ dose, cell line)} \quad [\text{Jäkel, JRR, 2007}] \]

**Validations:**

- radiation quality investigations (partic. spectra, LET)
- biological dose: cell survival experiments
4. Organ motion

Inter-fraction motion
Image-guiding for online positioning: cone beam CT → adaptive radiation therapy

Intra-fraction motion
Lung cancer treatment: margins, breath-hold, gating
Specificity of active treatment: the interplay effect

4D treatment planning:
- 4D CT → contouring, adapted margins
- 4D dose calculation (deformable image registration)
Example: Geant4/GATE simulation
5. Imaging in treatment planning

TPS presently plan dose delivery

In the future they will plan imaging too

- in-beam TOF-PET
- prompt-γ imaging
- interaction vertex imaging

Feedback from on-line imaging to TPS

→ Include in the TPS the generation and detection of secondary radiation: $\beta^+$, γ, fragments (ENVISION)

Still large discrepancies between simulation and measurements [Le Foulher et al., IEEE ANIMMA 2009]
PART II: on-going research
Participants

- Université de Lyon
- Research laboratories CREATIS, CNDRI, IPNL
- Léon Bérard cancer center
- Rhone-Alpes Research Program in Hadrontherapy (PRRH)
- ANR
Outline

- Main goals
- Ex n° 1: Monte Carlo simulations
- Ex n° 2: Radiochromic films
- Ex n° 3: Hybrid simulations
### Dose calculation engine (DCE)

<table>
<thead>
<tr>
<th>Method</th>
<th>Time</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fast analytical</td>
<td>&lt; second</td>
<td>Optimization</td>
</tr>
<tr>
<td>Analytical</td>
<td>~ minute</td>
<td>Plan comparison</td>
</tr>
<tr>
<td>Hybrid</td>
<td><em>in between?</em></td>
<td><em>Inhomogeneities, ...</em></td>
</tr>
<tr>
<td>Monte Carlo</td>
<td>hours</td>
<td>Kernel, dose, RBE, imaging, ...</td>
</tr>
</tbody>
</table>

- Several complementary methods
  - Tradeoff between accuracy / speed
  - Specialized / generic

Several DCE in a TPS
Goal: Hadrontherapy simulation platform

- Radiation quality
- Physical models
- TPS Validation
- DICOM RT

- Dose
- LET
- Secondary radiation

- Pencil beam
- Superposition/convolution

- Energy, intensity optimisation
- Dose constraints

Hadrontherapy simulation platform

Monte Carlo

Hybrid

Analytical

Inverse planning

Dose

RBE

Imaging
Monte Carlo module

- Geant 4
- OpenGate collaboration

OpenGateCollaboration.healthgrid.org

- GATE software
  PET, SPECT (nuclear imaging) → Radiation Therapy
  - No need to be C++ expert (at first), use macros
  - Validation
  - Collaborative development (cvs, official release)
Example with GATE

- Real-scale example
- Pencil-beam scanning
  - Carbon ion beams
  - ~250 spots per beam
  - ~15 energy layers
- Dicom CT image
  - Target = cubic 2.5 cm wide PTV
  - Stoichiometric calibration [Schneider2000]
- Rough inverse optimization
  - 1D physical dose fitting [Kramer2000]
  - WEPL: Water Equivalent Path Length

~3800 spots/field
PTV
Deposited energy (or dose) distribution
Example with GATE

- Real scale example
- In progress: DICOM RT Plan import for TPS validation

- **Computing time**
  - Full simulation, without variance reduction
  - Voxel & dosel size = $\sim 2^3 \ \text{mm}^3$
  - Statistical uncertainty $\sim 2\%$
  - $\sim 30$ hours (single CPU 2.0 GHz)
Computing with grid

- Split simulation in independent jobs
- GATE-LAB project
  [Glatard, Pop et al. EGEE 2009]

"One-click" interface to submit GATE simulation to grid, to monitor running jobs, to retrieve results.
Example of RBE model

- Method of [Kase2006] [Furusawa 2000]
- Survival curves of HSG tumour cells
- $\alpha \beta$ as a fct of LET $\rightarrow$ RBE

Monte Carlo
dose averaged LET

From [Kase2006]
Example of RBE model

Tumour (PTV)

- Physical dose
- RBE
- Biological dose

SOBP as a function of depth in water
Estimated biological dose distribution

One RBE value per voxel
GATE

• More on RBE: next talk
• Next official release by the OpenGate collaboration
Outline

- Main goals
- Ex n° 1: Monte Carlo simulations
- Ex n° 2: Radiochromic films
- Ex n° 3: Hybrid simulations
Radiochromics films

• Good properties: high resolution, self-development, tissue equivalent, water resistant ...

• Can they help for hadron dosimetry?
Radiochromics films

- Optical density does not depend only on dose, but also on radiation quality

**Bragg Peak**

**76 Mev/u Carbon beam**

- Optical density (data)
- Dose (MC simulation)
We did a lot of experiments with a lot of films ...
Radiochromics films

- Optical density can be predicted with Monte Carlo (using “local LET”)

[ Frisson et al. NIM A 2009 ]
Hybrid simulation

Goal:
- Improve precision & reduce computing time
- trade-off between MC and deterministic approaches

Idea:
- Separate calculations of $1^{\text{ary}}$ and $2^{\text{ary}}$ dose contributions
- MC-based simulation with small statistics,
- Splitting of fragmentation processes
- Deterministic dose deposition using TLE techniques
  \textit{(Track Length Estimator)}
Hybrid simulation

1: Monte Carlo (MC) simulation with small statistics

2: Primary dose deposition by deterministic ray casting (DRC)

3: Secondary dose deposition by MC frag. splitting + DRC
Hybrid simulation

- Validated for photon beam [Smekens et al. PMB 2009]
- In development for carbon beam [Le Loirec et al. Workshop Erice 2009]

$^{12}\text{C} @ 250\text{MeV/u}$

Primary dose map (deterministic)

Secondary dose map (Monte Carlo)
Conclusion

- **Challenges** in hadron TPS: dose calculation engine, IMPT, RBE, organ motion, imaging

- **Hadrontherapy simulation platform** project in Lyon
  - Multiple dose engines
  - OpenGate, Monte Carlo for: dose + RBE + imaging
  - Radiochromics films
  - Hybrid method for carbon ion

- **Bottleneck**: validation

- **Projects**: PARTNER, ULICE, ENVISION
THANKS!

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