Opportunities and challenges in particle radiotherapy
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Conflict of Interest
Research collaboration and two license agreements with RaySearch Laboratories AB

Conflict of Interest

Physical and biological rationale of ion beam therapy

Physical selectivity
- Depth-dose profile (Bragg-Peak)
- Lateral scattering (Z>2)

Biological Effectiveness
- Elevated local ionization density
- Influence of tumour oxygenation (OER)
- Optimal differential effect at Z ≈ 6

Is what we see what the patient receives?

Clinical rationale of ion beam therapy

RBE models in treatment planning
- Protons
  - Constant RBE = 1.1 clinically used
  - Known RBE variations with LET
  - Uncertainties of different models (typically based on LET, and α/β)
  - Unclear correlation to outcome
- Carbon ions
  - Variable RBE scheme (accounting for mixed field)
  - Different models used in the clinics (LEM, MMX) based on different underlying assumptions
  - Unclear correlation to outcome

Treatment (re)planning uncertainties

Patient model
- Metal artifacts
- Image quality (CBCT)
- HU-SPR conversion
- Tissue-dependent biological parameters

Dose calculation
- Beam model
- Tissue heterogeneities
- Biological models

Treatment (re)planning uncertainties

Nuclear Physics for Radiotherapy Report, IUPECCEC, 2014
Chordoma, \(^{12}\)C, GSI Bamstadt

Planning CT

CT after 2 w. RT

Planning CT

CT after 5 w. RT

Planning CT

Bortfeldt, AAPM 2019

Intrafractional anatomical changes

Treatment delivery uncertainties

Mitigating range uncertainties in clinical practice

Mitigating uncertainties in clinical practice

Dose and range verification

Pre-treatment range verification

Dose or range verification?

Validation of the patient-specific stopping power ratio (SPR) or probing beam range in vivo

Daily practice of compromising dose uniformity for safe delivery

Well defined relationship between range and 80% distal dose fall-off

Monitor beam range or distal dose fall-off pre-, in- and post-treatment

Dual-energy CT (DECT)

Implanted/endoscopic detectors

Range probe, ion radiography/tomography

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Pre-treatment range verification – Dual Energy Computed Tomography

Ion radiography (iRAD) / tomoscopy (ICT):
- Range probing of few selected spots (iRAD)
- Integral SPR determination (iRAD)
- 3D SPR reconstruction (ICT)

Several detector concepts under investigation worldwide

Competitive results of ICT prototype vs dual-source DECT (MAPE of 0.55% vs 0.67% at ~20 lower dose)

ICT promises SPR accuracy better than 1% at dose ≤ 1-2 mSv

Pre-treatment range verification – IRAD/ICT

In-treatment range verification – ionoacoustics

Ionoacoustics signal depends on localization of energy deposition in space (hence enhanced for PBS) and time

Sub-mm range retrieval accuracy and precision in water at few Gy dose with hydrophones at intrinsically/Artificially pulsed synchro/Isocronous cyclotrons

Expected (sub)millimeter range verification capabilities also in heterogeneous patient anatomy, but highly sensitive, broadband transducers needed

In-/post- treatment range verification – Positron Emission Tomography (PET)

Irradiation-induced $^{15}$F-activity of different signal strengths and correlation with the dose depending on
- Primary ion species
- Acquisition time (isotope half-lives: ~2-20 min)

Limited to special anatomical locations and passive delivery
In-treatment range verification – In-beam PET

First clinical experience based on instrumentation adapted from nuclear medicine
Feasibility to detect inter-fractional changes (anatomy, positioning) despite low SNR, biological washout and not yet optimal instrumentation
Next-generation dedicated detectors able of dynamic imaging just entered clinical evaluation

Prompt gamma spectroscopy
– Exploits PG energy information
– Custom-made collimated prototype close to start pilot clinical study @ MGH

Prompt gamma timing
– Exploits timing information, overcoming collimation
– Custom-made prototype under development for future clinical translation @ Dresden

Compton camera imaging
– Exploits Compton kinematics, overcoming collimation
– Commercial prototype under further development for future clinical translation @ Maryland

In-treatment range verification – Prompt gamma (PG)

Fast (sub-ns) emission eliminates issue of biological washout
Signal fall-off is closely correlated to Bragg peak position due to lower cross section thresholds than for PET
Dedicated developments for directional detection of high energy PGs (> 2.7 MeV) embedded in huge neutron background
Prototype 1D PG camera with slit collimators

Post-treatment range verification – Offline PET and MRI

Data acquisition after irradiation with offline diagnostic scanners

Conclusion & Outlook

Treatment planning strategies can account for physical and biological uncertainties, however compromising achievable dose conformity
Additional studies needed to improve biological models
In vivo dose / range verification remains unmet challenge, although many approaches are possible before, during and after treatment
Promising techniques for in vivo SPR assessment and real-time range verification are close to / just starting clinical translation & evaluation
Reduction of uncertainties at planning & delivery stage will enable more effective dose delivery and likely impact clinical outcome
Acknowledgement

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Further reading:
Medical Physics Special Issue
"Current Challenges and Prospects in Particle Therapy"
(edited by J. Farr & K. Parodi, 2018)

Thank you for your attention