



Contribution ID: 83

Type: not specified

## Basic of biological models in Particle Therapy (PT) Treatment Planning

Wednesday, December 15, 2021 12:00 PM (1 hour)

### Basic of biological models in Particle Therapy (PT) Treatment Planning

One of the advantages of light ions in radiation therapy (RT) treatments is their higher relative biological effectiveness (RBE) in creating damage to tumour cells, with respect to conventional RT photons. Treatment planning systems (TPS) must account for this increased efficacy in dose calculation. RBE depends on several factors including radiation quality, linear energy transfer (LET), tissue type, dose, endpoint [1]. How this is accounted for in TPS significantly affects the dose actually delivered to the patient [2].

Protons are clinically considered to be all and everywhere 10% more effective than photons ( $RBE = 1.1$ ). This approximation is not always valid, particularly at the end-of-range LET elevation in tissues with a low  $\alpha/\beta$  [3]. Newly available commercial software, providing inhomogeneous RBE calculation according to different models, renewed the discussion on the adequacy of a constant RBE and opened new possibilities on the clinical use of more complex modelling strategies. The topic is still controversial, being all long-term clinical data based on  $RBE = 1.1$  and hardly translatable into a new language. Recent works include in the problem LET distribution and LET dependence of proton therapy efficacy and toxicity [4].

Radiobiological properties of carbon ions demand a 3D RBE modelling in tissues for clinical dose calculation and optimization. All Japanese centres adopted the same mixed-beam RBE model [5] for passive scattering and the modified microkinetic dosimetric model [6], for pencil beam scanning. Conversely, all European centres followed the German experience and implemented the local effect model version-I [7]. Each model in turn contains several parameters, fitted to reproduce in-vitro and in-vivo experimental data, which can be modified to drive the optimization in the desired direction. All models agree on the fact that carbon ions effectiveness increases in the distal part of the spread out Bragg peak (SOBP). Therefore, to obtain a homogeneous RBE-weighted dose distribution in the target, a lower physical dose should be delivered in the distal portion of the SOBP. The question is: "how much more and how much less?" and the answer strongly depends on the model used. Several groups studied dose deviations implied in the use of different RBE models to ease the comparison of clinical results between different centres [2, 8-10]. For the same nominal RBE-weighted dose value, the corresponding physical dose deviates differently along the spread-out and even more outside, in the entrance channel and lateral fall-off regions, with significant implications on clinical outcomes [11-13]. RBE modelling still represents a challenge in prescribing, recording and reporting dose for all light ions used in RT [14]. New TPS provide multi-model calculation and optimization options, which could support the process of future harmonization of PT treatments.

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## Summary

**Presenter:** MOLINELLI, silvia