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Physics Contribution

Mapping of RBE-Weighted Doses Between HIMAC– and LEM–Based Treatment Planning Systems for Carbon Ion Therapy

Olaf Steinsträter, Ph.D.,* Rebecca Grün, M.Sc.,*,†,‡ Uwe Scholz, M.Sc.,*,§ Thomas Friedrich, Ph.D.,* Marco Durante, Ph.D.,*,§ and Michael Scholz, Ph.D.*

**Abteilung Biophysik, GSI Helmholtzzentrum für Schwerionenforschung, Darmstadt, Germany; †Institut für Medizinische Physik und Strahlenschutz, TH-Mittelhessen, Gießen, Germany; ‡Fachbereich Medizin, Philipps-Universität Marburg, Marburg, Germany; and §Institut für Festkörperphysik, Technische Universität Darmstadt, Darmstadt, Germany*

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Summary

A method was developed to convert clinically prescribed RBE (Relative Biological Effectiveness)-weighted doses from the approach used at the Heavy-Ion Medical Accelerator facility (HIMAC; National Institute of Radiological Science, Japan) to the Local Effect Model–based approach used at GSI Helmholtzzentrum, Germany, and other centers. For interpretation and comparison of clinical trials, this conversion is of extreme importance because, given the different methods to determine the RBE-weighted dose, similar dose values might not necessarily be related to similar clinical outcomes.

Purpose: A method was developed to convert clinically prescribed RBE (Relative Biological Effectiveness)-weighted doses from the approach used at the Heavy-Ion Medical Accelerator (HIMAC) at the National Institute of Radiological Science, Chiba, Japan, to the LEM (Local Effect Model)-based TReatment planning for Particles (TRiP98) approach used in the pilot project at the GSI Helmholtzzentrum, Darmstadt, and the Heidelberg Ion-Beam Therapy Center (HIT).

Methods and Materials: The proposed conversion method is based on a simulation of the fixed spread-out Bragg peak (SOBP) depth dose profiles as used for the irradiation at HIMAC by LEM/TRiP98 and a recalculation of the resulting RBE-weighted dose distribution. We present data according to the clinical studies conducted at GSI in the past decade (LEM I), as well as data used in current studies (refined LEM version: LEM IV).

Results: We found conversion factors (RBE-weighted dose LEM/RBE-weighted dose HIMAC) reaching from 0.4 to 2.0 for prescribed carbon ion doses from 1 to 60 Gy (RBE) for SOBP extensions ranging from 20 to 120 mm according to the HIMAC approach. A conversion factor of 1.0 was found for approximately 5 Gy (RBE). The conversion factor decreases with increasing prescribed dose. Slightly smaller values for the LEM IV–based data set compared with LEM I were found. A significant dependence of the conversion factor from the SOBP width could be observed in particular for LEM IV, whereas the depth dependence was found to be small.

Conclusions: For the interpretation and comparison of clinical trials performed at HIMAC and GSI/HIT, it is of extreme importance to consider these conversion factors because according to the various methods to determine the RBE-weighted dose, similar dose values might not necessarily be related to similar clinical outcomes. © 2012 Elsevier Inc.

Keywords: Carbon ion radiotherapy, Treatment planning, RBE, HIMAC, LEM

Reprint requests to: Olaf Steinsträter, Ph.D., Abteilung Biophysik, GSI Helmholtzzentrum für Schwerionenforschung, Planckstraße 1, 64291 Darmstadt, Germany. Tel: (+49) 6159-71-1650; Fax: (+49) 6159-71-2106; E-mail: o.steinstraeter@gsi.de

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Introduction

Starting in 1994 and 1997, respectively, extensive clinical studies on carbon ion radiotherapy have been conducted at the National Institute of Radiological Science (NIRS), Chiba, Japan (1) and at the GSI Helmholtzzentrum für Schwerionenforschung, Darmstadt, Germany (2). To draw maximal benefit from these studies, a common basis for the mapping between center-related beam parameters and clinical outcomes should be established.

Although at both centers the treatment plans were based on the concept of RBE (Relative Biological Effectiveness)-weighted doses, the approaches to estimate these doses are quite different, strongly influenced by the different beam delivery systems. At HIMAC, the RBE-weighted dose is derived from an empirically established equivalence between carbon and neutron beams exploiting experiences with neutron radiation therapy at NIRS (3). For the pilot project at GSI, a radiobiological model, the Local Effect Model (LEM) (4–7) has been developed that derives RBE values from experimental data available for photons.

Because of the different methods to relate RBE-weighted and physically absorbed dose, the same clinically prescribed RBE-weighted dose will typically not result in the same depth dose distribution at the two centers. Clinical outcomes are therefore not necessarily comparable if the given RBE-weighted doses are identical.

In this study, we provide a method to convert between a prescribed RBE-weighted dose as realized at NIRS and the dose specification based on the LEM used for treatment planning at GSI and other centers (*e.g.*, Heidelberg Ion-Beam Therapy Center [HIT], Particle Therapy Marburg, NRoCK Kiel, CNAO Pavia, Shanghai Heavy Ion Therapy Center).

Methods and Materials

Methods to determine the RBE-weighted dose at NIRS and GSI

The HIMAC irradiation system uses passive beam shaping (3): starting with a fixed beam energy, shape and depth of the spread-out Bragg peak (SOBP) are adjusted by a ridge filter designed to reach a uniform survival fraction of 10% for human salivary gland tumor (HSG) cells inside its nominal SOBP width. If $D(z;10\%HSG)$ is the physical depth dose distribution of the filter design (z the water equivalent depth), the physical dose $D(z;d_{presc}^{HIMAC})$ used at HIMAC for irradiation according to the clinically prescribed RBE-weighted dose, d_{presc}^{HIMAC}, is given by

$$D\left(z;d_{presc}^{HIMAC}\right)=\lambda_{presc}^{HIMAC}D(z;10\%HSG), \quad (1)$$

with a factor λ_{presc}^{HIMAC} depending on the prescribed dose d_{presc}^{HIMAC}. The calculation of λ_{presc}^{HIMAC} is based on the neutron-equivalent depth $z_{neutron}$ inside the SOBP, where the carbon beam is biologically equivalent to the NIRS neutron beam (30 MeV deuteron projectiles on beryllium target) (3). For HSG cells at 10% survival level, $z_{neutron}$ can be identified by an RBE of 2.0 (3):

$$D(z_{neutron};10\%HSG)=\frac{D^{RBE}(10\%HSG)}{2.0}. \quad (2)$$

Here, $D^{RBE}(10\%HSG)$ = 4.0359 Gy (RBE) (according to Kanai *et al.* (8): $\alpha=0.3312$ Gy^{-1}, $\beta_{photon}=0.0593$ Gy^{-2}) is the constant RBE-weighted dose within the SOBP.

The clinically determined RBE for the therapeutic neutron beam at NIRS was determined to 3.0 (3), and for a given prescribed dose d_{presc}^{HIMAC}, this results in

$$D\left(z_{neutron};d_{presc}^{HIMAC}\right)=d_{presc}^{HIMAC}/3.0 \quad (3)$$

at the neutron-equivalent position. Combining Eqs. 1, 2, and 3 leads to

$$\lambda_{presc}^{HIMAC}=2/3\frac{d_{presc}^{HIMAC}}{D^{RBE}(10\%HSG)}. \quad (4)$$

In contrast to the passive HIMAC irradiation system, at GSI a magnetic scanning system together with active energy variation is used (9). Starting with a clinically prescribed RBE-weighted dose, d_{presc}^{LEM}, for the tumor volume, the treatment planning system TRiP98 (TReatment planning for Particles) is used to derive an individually optimized physical depth dose profile (9–11). A detailed description of the radiobiological response of the irradiated tissue is needed for this optimization and provided to TRiP98 by an externally calculated data set (we use the term "RBE table" in this article) containing RBE information for each relevant ion type (carbon and possible fragments) and energy. An RBE table is individually derived from photon response data of the irradiated tissue by means of the Local Effect Model (LEM); the TRiP98 optimization results thus strongly depend on the particular choice of this input data set. This study is mainly based on the extended LEM version recently proposed by Elsässer *et al.* (7), here termed LEM IV. In addition, because the clinical data collected at GSI in the past decade was based on a previous version (4), LEM I, we also show results based on this version.

The biological basis of LEM-based RBE tables can be characterized by three parameters: α_{photon} and β_{photon} describing the linear and quadratic part of the Linear Quadratic (LQ) model, respectively, and D_t marking the high-dose transition from linear-quadratic to purely linear dose response, in accordance with (12). A LEM calculation additionally needs the effective radius of the cell nucleus, but for all RBE tables discussed in this article, a fixed radius of 5 μm was assumed.

Conversion between RBE-weighted dose specifications used at NIRS and GSI

We based our conversion method on a reconstruction of the physical dose distributions used at NIRS by the GSI treatment planning system. Because of the different beam delivery systems, the physical composition of the beams may be different even though the physical dose is identical; however, it was shown that for comparable depth-dose profiles, the biological effects are also comparable (13).

Following the requirements used to design the ridge filters at NIRS, TRiP98 was used to optimize SOBPs from 20 mm to 120 mm (step size 20 mm) and for the three depths reported by Kanai *et al.* (3) for a survival level of 10% for HSG cells (photon parameters (7): $\alpha_{photon}=0.3130$ Gy^{-1}, $\beta_{photon}=0.0615$ Gy^{-2}, $D_t=7.5$). Although the relative shapes of the calculated depth dose profiles were found to be in good agreement with the results reported in Kanai *et al.* (3), the absolute dose values were slightly higher than the measured values. Therefore, an additional scaling factor $\mu = 0.88$, determined by a least square fit, was applied. The need for a scaling factor might be attributed to long-term variation of cellular sensitivity of the HSG cells, as also discussed by Inaniwa *et al.* (14), and the corresponding change in the photon parameters α and β. However, because the main aspect of the work