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Full Monte Carlo-based biological treatment plan optimization system for intensity modulated carbon ion therapy on GPU

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Abstract

Purpose—One of the major benefits of carbon ion therapy is enhanced biological effectiveness at the Bragg peak region. For intensity modulated carbon ion therapy (IMCT), it is desirable to employ Monte Carlo (MC) methods to compute properties of each pencil-beam spot for treatment planning, because of their accuracy in modeling physics processes and estimating biological effects. We have previously developed goCMC, a graphics processing unit (GPU)-oriented MC engine for carbon ion therapy. The purpose of this study is to build a biological treatment plan optimization system based on goCMC.

Methods and Materials—The repair-misrepair-fixation model was implemented to compute spatial distribution of linear-quadratic model parameters for each spot. A treatment plan optimization module was developed to minimize the difference between the prescribed and actual biological effect. We employed a gradient-based algorithm to solve the optimization problem. The system was embedded in the Varian Eclipse treatment planning system under a client-server architecture to achieve a user-friendly planning environment. We tested the system with a 1-dimensional homogeneous water case and 3-dimensional patient cases.

Results—Our system generated treatment plans with biological spread-out Bragg peaks covering the targeted regions, while sparing critical structures. Using four NVidia GTX 1080 GPUs, total computation time including spot simulation, optimization, and final dose calculation was 0.6 hours for the prostate case (8282 spots), 0.2 hours for the pancreas case (3795 spots), and 0.3 hours for the brain case (6724 spots). The computation time was dominated by MC spot simulation.

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Conclusions—We have built a biological treatment plan optimization system for IMCT that performs simulations by a fast MC engine, goCMC. To our knowledge, this is the first time that full MC-based IMCT inverse planning has been achieved in a clinically viable timeframe.

1. Introduction

Carbon ion therapy has been attracting increasing attention in recent years [1,2]. Compared to conventional photon and electron beams, physical dose distributions of carbon ion beams are highly conformed to tumors because of the presence of the Bragg peak. Carbon ion beams also feature a smaller lateral penumbra than the more widely used proton beams. In addition, carbon ion therapy provides enhanced relative biological effectiveness (RBE) [3] in the Bragg peak region, allowing a better focusing of biological effect to targets [1,4,5]. The therapy's effectiveness under hypoxic conditions makes it even more attractive as a treatment modality [6,7].

Recent developments in spot scanning technology have enabled intensity modulated carbon ion therapy (IMCT). By adjusting the weight of each individual pencil-beam spot, one can achieve a carefully sculpted 3-dimensional (3D) dose distribution that features increased target coverage and reduced dose to critical structures compared to passive scattering approaches [1,2]. Optimizing the biological dose distribution in treatment planning requires modeling the biological effects. This is a complex task, because RBE depends on many factors, such as dose level (biological end-point), particle type, energy, and cell type. Over the last few decades, extensive radiobiological studies have led to several radiobiological models that calculate biological effects based on the beam properties [8–13].

Currently, clinical treatment planning systems (TPS), such as TRiP98 (TReatment Planning for Particles, 1998) [14–16], use pencil-beam algorithms. These algorithms tabulate spot dose data in a homogeneous water phantom and transform them into patients with appropriate scaling by assuming water-equivalent materials. Such approaches can achieve clinically viable computation efficiency, but accuracy is limited because of the lack of detailed modeling of the physical processes, especially nuclear fragmentations. A recent study comparing dose calculations using a pencil-beam algorithm and a Monte Carlo (MC) method observed a biological dose difference of up to 10% in head-and-neck and pelvis cases [17]. This difference was ascribed to the pencil-beam algorithm's insufficient modeling of light fragment transports, particularly their lateral scattering.

Unlike pencil-beam algorithms, in which dose and particle spectra are calculated in water, MC methods explicitly simulate beam transport and fragmentation in heterogeneous patient anatomy. This provides accurate information on the particle spectrum in each voxel, allowing for accurate evaluation of the biological effect. Therefore, MC is a desirable tool for biological dose calculation and plan optimization. However, as a statistical method, MC simulations require a large amount of computations to reach sufficient precision. At present, full MC-based inverse treatment planning is still a computationally challenging problem for photon and proton therapy [18–24] and an even bigger challenge for carbon ion therapy's much more complicated biological dose calculation and optimization.

In 2010, Mairani et al. [25] implemented the local effect model [8] with FLUKA [26] to simulate carbon ion transport in patients and calculate biological dose distributions. Following this work, Glitzner et al. developed an MC-based treatment planning tool for ion therapy in 2013 [27]. Despite their success, FLUKA and other general-purpose MC codes for ion therapy, such as Geant4 [28], PHITS [29], MCNPX [30], and Shield-HIT [31], are running on traditional CPUs. The long computation time on these devices is a concern for practical applications. Recently, Kamp et al. [32] combined the Repair-Misrepair-Fixation Model (RMF) [13] with FLUKA-generated fragmentation spectra in water for biological treatment plan optimization. They achieved fast dose calculation and optimization, but used a pencil-beam algorithm.

In order to realize full MC-based IMCT treatment planning in a clinical routine, we recently developed a graphics processing unit (GPU)-oriented fast cross-platform MC engine called goCMC (GPU OpenCL Carbon MC) [33]. We demonstrated the accuracy of goCMC for physics simulations by comparing goCMC with Geant4-based MC simulations for various cases. Considerable acceleration was achieved: it takes 50 seconds to transport 10^7 carbon ions with an initial energy of 400 MeV/u and the resulting secondary particles in water using an NVidia GTX 1080 GPU. With this successful development, we started building a biological treatment plan optimization system on top of goCMC. This paper reports our progress toward this goal.

2. Methods and Materials

2.1 MC simulation

goCMC can simulate transport of carbon ion beams in voxelized geometry with energy up to 450 MeV/u. Both electromagnetic and nuclear interactions are simulated based on physics laws and/or tabulated physics data extracted from Geant4. goCMC tracks over 300 types of secondary ions and isotopes but ignores nuclear interactions of secondary particles. We adopted the Open Computing Language (OpenCL) programming framework to enable parallel computing on various devices, such as GPU and multi-core CPU. Detailed descriptions of the physics process, secondary particle transport, and dose scoring can be found in a recent publication that demonstrates the accuracy, efficiency, and portability of goCMC.

IMCT plan optimization requires spatial distributions of quantities related to biological effect estimation for each spot. To accelerate this process, we developed multi-GPU support so that calculations on different spots can be performed on different GPUs simultaneously. Inverse optimization and final dose calculation remained on a single GPU.

2.2 Biological dose calculation

Biological calculation in our system was designed within the framework of the widely used linear-quadratic (LQ) model [34]. The RMF model was implemented as the default choice. Other radiobiological models were supported through user-provided tables of radiosensitive parameters as functions of particle type and energy.

2.2.1 The RMF model—The RMF model [13] provides a mechanistic approach to explicitly link cell death to double strand break (DSB) induction and processing. Kamp et al. reported reasonable agreement between the RMF model and published experimental results for carbon ion beams with nuclear fragmentation accurately simulated [32]. In this model, radiosensitive parameters (α_q, β_q) for an ion are determined as a function of DSB induction Σ and the frequency-mean specific energy $\bar{z}_f$ [32,35]:

$$\alpha_q = \frac{\sum}{\sum_x} \left[\alpha_x + 2 \frac{\beta_x}{\sum_x} \left(\sum \bar{z}_f - \sum_x \bar{z}_{f,x} \right) \right], \quad \beta_q = \left(\frac{\sum}{\sum_x} \right)^2 \beta_x, \quad (1)$$

where (α_x, β_x), Σ_x , and $\bar{z}_{f,x}$ are corresponding parameters for reference X-rays. Typical values are $\Sigma_x = 8.27$ per Gy per giga-base-pair ($\text{Gy}^{-1} \text{ Gbp}^{-1}$) and $\bar{z}_{f,x} = 0.0019$ Gy for a ^{60}Co source. From track structure simulation results, Semenenko and Stewart [36] showed that Σ ($\text{Gy}^{-1} \text{ Gbp}^{-1}$) can be parameterized by

$$f(t) = u + \frac{(u - v)t}{t + w}. \quad (2)$$

Here, $u = 48.9$, $v = 164.5$, and $w = 759$ are constants, and $t \equiv Z_{\text{eff}}^2 / \beta^2$, in which β is the velocity relative to the speed of light, and $Z_{\text{eff}} = Z[1 - \exp(-125\beta Z^{-2/3})]$ is the effective charge of the incident ion. The frequency-mean specific energy $\bar{z}_f$ can be calculated as [13]

$$\bar{z}_f = 0.204 \times \frac{\text{LET}}{d^2} \quad (3)$$

where d is the target diameter with a typical value of $5 \mu\text{m}$, and LET is the ion's linear energy transfer. We implemented the above equations in goCMC such that, given (α_x, β_x) of a cell type, (α_q, β_q) can be calculated efficiently during ion transport.

2.2.2 Biological dose of mixed irradiation field—During carbon beam transport, a large number of secondary particles are produced from nuclear interactions, resulting in a mixed irradiation field consisting of multiple ion types in each voxel. To correctly accumulate the biological effect, we implemented on-the-fly scoring of dose-weighted radiosensitive parameters (a_D, b_D) as

$$a_D(x) = \frac{\sum_q \alpha_q D_q}{N_h}, \quad \sqrt{b_D(x)} = \frac{\sum_q \sqrt{\beta_q} D_q}{N_h}. \quad (4)$$

Here, q stands for a dose deposition event by a primary or secondary ion, and D_q is the deposited physical dose. (α_q, β_q) is calculated from Eq. (1). The summation is over all dose deposition events at voxel x . N_h is the number of simulation histories. After all particles are simulated, we can compute the biological effect (defined as the logarithm of cell survival) as

$$-\ln S = a_D N + \left(\sqrt{b_D} N \right)^2. \quad (5)$$

Here, N is the actual weight of the field defined as the number of primary carbon ions. The biological dose, i.e., the dose that needs to be delivered by the reference radiation (^{60}Co) to achieve the same biological effect, is thus calculated by

$$D_b = \sqrt{-\frac{\ln S}{\beta_x} + \left(\frac{\alpha_x}{2\beta_x} \right)^2} - \frac{\alpha_x}{2\beta_x}. \quad (6)$$

2.3 Treatment plan optimization

2.3.1 General considerations—For IMCT, the task of optimization is to generate a satisfactory biological dose distribution by adjusting the weight of each spot. To start a treatment planning process, a user first inputs several planning parameters, including the following. 1) Number and angles of fields: a typical IMCT plan contains two fields (three in very rare cases) with manually selected incident angles. 2) Spot spacing and depth (energy) increment: to ensure the homogeneity of dose distribution, it is usually desired to have a narrow spacing, e.g., ~2 mm for spots with ~6 mm full-width at half maximum (FWHM) [37]. 3) Weighting factors for optimization target volumes (OTVs) and organs at risk (OARs). 4) The ratio of the LQ parameters α_x/β_x for different structures.

Using the input plan configuration and patient data, the system automatically places spots to cover OTVs and spare OARs. Specifically, only spots with Bragg peaks inside or at the boundary of the OTVs are selected. For typical clinical cases, the number of voxels and spots is large. Because of the GPU's relatively small memory, only a subset of CT voxels is used for optimization. We follow the strategy suggested in a previous proton optimization study [38], whereby a CT image with a resolution of 512×512 on axial planes is down-sampled to 256×256 . The voxels selected for optimization include all the boundary voxels of each structure and all voxels inside the OTVs. For voxels inside an OAR, depending on the structure size V , we select all voxels if $V < 100 \text{ cm}^3$, one of every 2×2 voxels if $100 \text{ cm}^3 < V < 300 \text{ cm}^3$, one of every 3×3 voxels if $300 \text{ cm}^3 < V < 500 \text{ cm}^3$, and one of every 4×4 voxels if $V > 500 \text{ cm}^3$.

2.3.2 Objective function—Given the prescribed dose distribution $D_p(\mathbf{x})$ ($\mathbf{x}$ is the voxel array), the conventional optimization approach is formulated as minimizing an objective function $f(\mathbf{N}) \equiv |D_b(\mathbf{x}, \mathbf{N}) - D_p(\mathbf{x})|^2$ with respect to spot weights, denoted by a vector $\mathbf{N}$. Here, $|\cdot|$ denotes the L2 norm of a vector. In this approach, the complex dependence of $D_b(\mathbf{x}, \mathbf{N})$ on spot weight, namely Eq. (4)–(6), makes the optimization problem hard to solve. In our study, we chose to directly optimize the biological effect, $-\ln S$ [39]. Specifically, $D_p(\mathbf{x})$ was converted to prescribed biological effect by the LQ model, i.e.,

$$-\ln S_p = \alpha_x D_p + \beta_x D_p^2. \text{ The objective function is}$$

$$f(\mathbf{N}) \equiv \sum_i w_i |\ln S(\mathbf{x}, \mathbf{N}) - \ln S_p(\mathbf{x})|_{\mathbf{x} \in \text{OTV}_i}^2 + \sum_i w_i |(\ln S(\mathbf{x}, \mathbf{N}) - \ln S_p(\mathbf{x})) \Theta(-\ln S(\mathbf{x}, \mathbf{N}) + \ln S_p(\mathbf{x}))|_{\mathbf{x} \in \text{OAR}_i}^2, \quad (7)$$

in which w_i are structure weighting factors and Θ is the Heaviside function. The first L2 norm is the fidelity term of biological effect in all OTVs. The second is the penalty term, if biological effect in any sub-region within OARs exceeds its upper limit. $-\ln S(\mathbf{x}, \mathbf{N})$ is the combined biological effect distribution from all spots in the treatment plan and is given by

$$-\ln S(\mathbf{x}, \mathbf{N}) = \langle \mathbf{a}_D(\mathbf{x}), \mathbf{N} \rangle + \left\langle \sqrt{\mathbf{b}_D(\mathbf{x})}, \mathbf{N} \right\rangle^2. \quad (8)$$

Here, for each voxel x_j , $a_{Di}(x_j)$ and $\sqrt{b_{Di}(x_j)}$ are dose-weighted linear and quadratic parameters contributed by the i^{th} spot and determined by spot simulation using Eq. (4). The angle bracket $\langle \dots \rangle$ means vector inner product.

2.3.3 Inverse optimization—The objective function in Eq. (7) can be rewritten in matrix form as

$$f(\mathbf{N}) = \left| \sqrt{\mathbf{W}} \cdot \left(\mathbf{A}\mathbf{N} + \mathbf{B}\mathbf{N} \cdot \mathbf{B}\mathbf{N} - \left(\boldsymbol{\alpha}_x \cdot \mathbf{D}_p + \boldsymbol{\beta}_x \cdot \mathbf{D}_p^2 \right) \right) \cdot \boldsymbol{\Theta} \right|^2, \quad (9)$$

where

$$\mathbf{A} = \begin{pmatrix} a_{D1}(x_1) & a_{D2}(x_1) & a_{D3}(x_1) & \cdots & a_{DQ}(x_1) \\ a_{D1}(x_2) & a_{D2}(x_2) & a_{D3}(x_2) & \cdots & a_{DQ}(x_2) \\ a_{D1}(x_3) & a_{D2}(x_3) & a_{D3}(x_3) & \cdots & a_{DQ}(x_3) \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ a_{D1}(x_P) & a_{D2}(x_P) & a_{D3}(x_P) & \cdots & a_{DQ}(x_P) \end{pmatrix}, \quad (10)$$

$$\mathbf{B} = \begin{pmatrix} \sqrt{b_{D1}(x_1)} & \sqrt{b_{D2}(x_1)} & \sqrt{b_{D3}(x_1)} & \cdots & \sqrt{b_{DQ}(x_1)} \\ \sqrt{b_{D1}(x_2)} & \sqrt{b_{D2}(x_2)} & \sqrt{b_{D3}(x_2)} & \cdots & \sqrt{b_{DQ}(x_2)} \\ \sqrt{b_{D1}(x_3)} & \sqrt{b_{D2}(x_3)} & \sqrt{b_{D3}(x_3)} & \cdots & \sqrt{b_{DQ}(x_3)} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \sqrt{b_{D1}(x_P)} & \sqrt{b_{D2}(x_P)} & \sqrt{b_{D3}(x_P)} & \cdots & \sqrt{b_{DQ}(x_P)} \end{pmatrix}, \quad (11)$$

P is the length of the scoring grid, and Q is the number of spots. $\sqrt{W}$, Θ and (α_X, β_X) are vector forms of the weighting factors, Heaviside function, and radiosensitive parameters. The dot $\cdot$ in Eq. (9) means elementwise product.

We implemented a gradient descent method to minimize $f(N)$. Specifically, the algorithm iterates as $N^{k+1} = N^k - \mu_k \nabla f(N^k)$, in which

$$\begin{aligned} \nabla f(N) = & A^T \left(\sqrt{W} \cdot \left(AN + BN \cdot BN - (\alpha_X \cdot D_p + \beta_X \cdot D_p^2) \right) \cdot \theta \right) \\ & + B^T \left[BN \cdot \left(\sqrt{W} \cdot \left(AN + BN \cdot BN - (\alpha_X \cdot D_p + \beta_X \cdot D_p^2) \right) \cdot \theta \right) \right]. \end{aligned} \quad (12)$$

The step size μ_k is determined based on the Armijo rule [40]. $N \geq 0$ is enforced by projecting its negative components to 0 in each iteration. The initial value N^0 is a user input with default value of 0. The stopping criterion is

$$\frac{|N^{k+1} - N^k|^2}{|N^k|^2} < \text{tol}, \quad (13)$$

in which tol is a user-provided parameter with a default value of 10^{-4} .

2.4 Integration with the Eclipse TPS

We developed the inverse optimization algorithm on top of goCMC as a standalone module. To facilitate its clinical translation, we embedded the whole system into the Varian Eclipse TPS [41]. A user-friendly operation environment and graphic user interfaces (GUI) were enabled through Varian Eclipse Scripting Application Programming Interface.

The system consists of a client-end served by the Eclipse planning environment and a GPU server-end performing the actual calculations (Figure 1). At the client-end, a user can set up treatment planning parameters. The patient and plan data are preprocessed and transferred to the server-end along with the planning request. After that, goCMC and the optimization module are launched to perform spot simulation and inverse planning. Finally, the biological dose distribution calculated with the optimized weights is sent back to the client-end for visualization and analysis. The user can adjust planning parameters through the GUI, if needed. If any of the plan configurations, such as beam angle, spot size, or resolution are changed, or new structures are added, all spots will be re-simulated. Otherwise, the optimization process is launched again without re-computing spots.

2.5 Evaluations

We evaluated the system in both 1-dimensional (1D) and 3D scenarios. First, we calculated biological dose distributions for three mono-energetic beams in water. Then, we produced a 1D biological spread-out Bragg peak (bSOBP) in water by a field with 25 spots. For 3D cases, we generated IMCT plans for three patients: a prostate cancer patient with two

laterally opposed fields; a pancreatic cancer patient with two fields irradiating from the left side; and a brain cancer patient with two non-coplanar fields. The prescription dose, CT dimension, and voxel size were 78 Gy(RBE), $256 \times 256 \times 170$, $1.95 \times 1.95 \times 2.5$ mm³ for the prostate case, 55 Gy(RBE), $256 \times 256 \times 84$, $1.95 \times 1.95 \times 2.5$ mm³ for the pancreas case, and 50 Gy(RBE), $256 \times 256 \times 198$, $1.79 \times 1.79 \times 1.5$ mm³ for the brain case. In all cases, spot resolution was 3.0 mm $\times$ 3.0 mm laterally and 0.3 g/cm² longitudinally. We used a relatively simple beam model, such that spot lateral FWHM at the beam entrance was ~6 mm and energy spread was 0.5% of the spot central energy. Although the user can set different α_X/β_X values for different structures, we used a constant $\alpha_X/\beta_X = 3.125$ Gy for all structures in these studies for simplicity.

3. Results

3.1.1 1D bSOBP

Figure 2(a) shows the depth dose curves of three mono-energetic carbon ion beams (100 MeV/u, 250 MeV/u and 400 MeV/u) in water calculated by goCMC. 3×10^7 histories were simulated for each beam, and the mean relative uncertainty was less than 1% in regions with dose greater than 10% of the maximum dose. Simulation time was 7.4 s, 60.9 s, and 152.2 s on an NVidia GTX 1080 GPU. Figure 2(b) shows a 1D bSOBP and the corresponding physical dose in water. The prescription dose was 1 Gy(RBE) from 100 mm to 160 mm. A field with 25 spots was simulated and optimized to generate the bSOBP.

3.1.2 Patient cases

Figure 3 presents the 3D IMCT treatment plans for the three patient cases. Plan details and performance measurements are summarized in Table 1. In all cases, OTVs were well covered ($V_{100\%} \sim 95\%$). An enhanced biological effect in OTVs can be clearly observed by comparing the biological dose and physical dose and the corresponding dose-volume histograms. With four NVidia GTX 1080 GPUs, total plan generation time was 0.6 hours for the prostate case, 0.2 hours for the pancreas case, and 0.3 hours for the brain case. Figure 4 is a screenshot of a final biological dose distribution displayed in Eclipse.

To better understand the impact of nuclear fragmentation on the total dose distribution, physical doses from various ion types are presented in Figure 5 for the prostate patient case. Secondary ions contribute around 30% of the total physical dose. Lighter fragments ($Z \leq 6$) account for over 99% of this secondary dose.

4. Discussion

In a similar study [32], Kamp et al. used FLUKA to simulate carbon ion transport and nuclear fragmentations in water. They recorded spectra of ions as input for the RMF model to produce a table of dose-averaged radiosensitive parameters and physical dose distributions for 32 carbon ion beams with different energies. The table was then used in a dose-to-water pencil-beam algorithm for plan optimization. Compared with that study, the system presented here simulates carbon ion transport directly in the patient anatomy to account for heterogeneous material distributions. Hence, this approach potentially yields a more accurate simulation of physics processes. In particular, for nuclear fragmentation, simulation in water

only captures carbon-hydrogen and carbon-oxygen collisions. In contrast, goCMC includes carbon-carbon and carbon-calcium collisions. In bony structures and surrounding area, such interactions may have non-negligible contributions.

Biological dose calculation and plan optimization in this work was based on the RMF model, the accuracy and limitations of which have been discussed elsewhere [13,32,35]. Because of the uncertainty of biological models, this system should be validated comprehensively before it can be applied to patients. Future work in this direction should include comparing biological dose calculations and inverse planning with other treatment planning systems, such as TRiP [14–16], and with experimental measurements [42,43].

An important issue that impacts both speed and plan quality is the number of histories in spot simulation. It is desired to use a small number of particles per spot to speed up the computation. But the uncertainty in spot simulation will impact subsequent plan optimization and resulting plan quality. In this work, we used 10^5 histories per spot based on a previous MC study for intensity modulated proton therapy (IMPT) treatment planning [38]. Both plan quality and relative dose uncertainty were found to be satisfactory for a prostate IMPT plan with 10^5 histories per spot. However, in IMCT, the impact of number of histories per spot on inverse optimization and the final plan quality is still unclear. We will investigate this issue in different settings with different tumor sites, field configurations, spot resolutions, etc.

5. Conclusions

Based on a previously developed GPU-based MC engine, goCMC, we have successfully built a fast treatment plan optimization system for IMCT. Tests in different cases have demonstrated the function and efficiency of our system. To our knowledge, this is the first time that full MC-based IMCT inverse planning has been achieved in a clinically acceptable timeframe.

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Summary

A Monte Carlo (MC)-based biological treatment plan optimization system was developed for intensity modulated carbon ion therapy. A graphics processing units (GPU)-oriented cross-platform MC engine goCMC was employed. The repair-misrepair-fixation model was implemented for biological effect calculation. By using multi-GPU acceleration, full MC-based inverse optimization of biological dose was achieved for real patient cases within a clinically viable time frame.

Figure 1.

The overall system structure. The left column shows user-system interactions on a local client computer; the right column includes MC simulation and inverse optimization running on a remote GPU server.

Figure 2.

(a) Depth distributions of biological dose D_b and physical dose D_p of three mono-energetic carbon ion beams in water. (b) 1D bSOBP and the corresponding physical dose in water.

Figure 3.

Patient treatment plans generated by the system. First and second rows are biological dose and physical dose in the prostate, pancreatic, and brain (from left to right) cancer patients overlaid on CT images. Color bar indicates dose levels relative to the prescription dose. Arrows indicate beam directions. The bottom row is the corresponding Dose-volume histograms (DVHs). Solid lines and dashed lines denote biological dose and physical dose, respectively.

Figure 4.
Final biological dose distribution displayed in the Eclipse TPS.

Figure 5.

Top: An axial slice of the prostate patient CT and biological dose distribution. Bottom: Biological dose, physical dose, and doses of various ion types along the dashed line in the top subfigure. For each secondary ion type, contributions of all isotopes are added together. All doses are normalized by prescription dose.

Table 1

Summary of the patient treatment plan optimization and performance measurements with different hardware configurations. All times are in seconds. Number of histories is 10^5 per spot in MC spot simulation, and 10^7 per plan in final dose calculation.

		Prostate	Pancreas	Brain
	Number of spots	8282	3795	6714
	Number of voxels for optimization	25001	15510	26335
NVidia GTX Titan Black	MC Spot simulation time	5977	1793	2698
	Inverse optimization time	106	6	31
	Final dose calculation time	265	251	236
	Peak memory usage	43%	12%	39%
AMD Radeon R9 290x + NVidia GTX Titan Black	MC spot simulation time	3318	942	1496
	Inverse optimization time	102	6	31
	Final dose calculation time	257	240	233
	Peak memory usage	65%	18%	59%
4 × NVidia GTX 1080	MC spot simulation time	1866	565	834
	Inverse optimization time	96	5	29
	Final dose calculation time	251	232	219
	Peak memory usage	32%	9%	29%