

Prototype of a real-time three-dimensional dosimetric imaging system for particle therapy

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Abstract

Particle radiotherapy possesses unique physical and biological advantages compared to photon radiotherapy. However, numerous sources of uncertainty still exist during the treatment process, such as setup errors, range fluctuations, incident particle errors, and other factors. The identification and control of these uncertainties are of great significance for achieving more precise treatment and reducing unnecessary or excessive doses received by patients. One of the key approaches to reducing treatment uncertainty is the implementation of three-dimensional (3D) dosimetry. Therefore, developing an independent technology capable of 3D dose reconstruction within the patient's body during treatment delivery is crucial for particle therapy centers.

This study aims to develop a real-time 3D dose imaging system for particle therapy to monitor the beam range and dose distribution within the patient during the treatment process. The study designed and evaluated a prototype of this imaging system, which consists of a beam monitoring system and a dose engine (DoRT). The beam monitoring system is used to measure pencil beam parameters in real-time during treatment, while DoRT is used to reconstruct the 3D dose distribution of the pencil beam within the target region.

We performed a functional evaluation of this prototype system using incident carbon ions at the Heavy Ion Medical Machine (HIMM) and compared its reconstructed dose distribution with Monte Carlo calculation results and film measurement results. For the investigated zigzag scanning delivery case, the prototype system achieved real-time dose reconstruction with a voxel size of 1 mm cubic, and the reconstruction time for a single pencil beam dose distribution was 46 ms. Benchmarking the reconstructed dose against Monte Carlo simulation results revealed an average Gamma pass rate (3 mm, 3%) of 95.36%.

Furthermore, the reconstructed lateral dose profiles showed good agreement with medical film measurements, with a median dose deviation of 1.56%. These experimental results confirm the feasibility of the system for 3D dose imaging. This study achieved real-time 3D dose reconstruction in particle therapy, with the ultimate goal of providing a new reference solution for real-time 3D dose imaging, thereby improving the accuracy of particle therapy.

Full Text

Preamble

Prototype of a real-time three-dimensional dosimetric imaging system for particle therapy* Fa-Ming Luo,^{1, 2} Chuan Huang,¹ Zheng-Guo Hu,^{1, 2}, † Yu-Cong Chen,¹ Xiu-Ling Zhang,¹ Juan Li,¹ Zhi-Guo Xu,^{1, 2}, ‡ Xin-Cai Kang,¹ Xin-Le Lang,^{1, 2} Zu-Long Zhao,¹ Jia-Li Fu,^{1, 2} Kai Zhou,¹ Xiao-Tao Liu,¹ Wei-Long Li,¹ Rui-Shi Mao,^{1, 2} and Guo-Qing Xiao^{1, 2} ¹Institute of Modern Physics, Chinese Academy of Sciences, Lanzhou 730000, China ²School of Nuclear Science and Technology, University of Chinese Academy of Sciences, Beijing 100049, China Particle radiotherapy offers unique physical and biological advantages over photon radiotherapy. However, it shows numerous uncertainties due to positioning errors, range straggling, incident particle errors, and other factors. Addressing and mitigating these uncertainties can lead to more precise treatment and reduce the unnecessary or excessive doses administered to patients. A critical approach to reducing uncertainties in treatment is the implementation of three-dimensional (3D) dosimetry. Thus, developing an independent technique for 3D dose reconstruction in patients during treatment delivery is crucial for particle therapy facilities. In this study, we aimed to develop a real-time 3D dosimetric imaging system for particle therapy to monitor the beam range and dose distribution in patients during particle therapy. A prototype of the imaging system was designed and evaluated using a beam-monitoring system and dose engine (DoRT). The beam-monitoring system was used to measure the parameters of a pencil beam in real-time during treatment, and DoRT was used to reconstruct the 3D dose distribution of the pencil beam in the target. We performed a functional evaluation of this prototype with carbon ions incident on a heavy-ion medical machine (HIMM) and compared the reconstructed dose distribution with those obtained from Monte Carlo calculations and film measurements. For the investigated zigzag-scanning delivery case, real-time dose reconstruction with 1 mm cubic voxels was achieved by this prototype, and the time required to reconstruct the dose distribution of an individual pencil beam was 46 ms. The reconstructed doses were benchmarked against Monte Carlo simulated results, where the average gamma index passing rate (3 mm, 3%) was 95.36%. In addition, the reconstructed lateral profile dose distributions were in good agreement with the medical film measurement results, and the median value of the dose deviation was 1.56%. These experimental results confirm the feasibility of the system for 3D dosimetric imaging. In this study, real-time 3D dose reconstruction for particle therapy is realized with the ultimate goal

of providing a new reference scheme for real-time 3D dosimetric imaging to improve the accuracy of particle therapy.

Keywords: Particle therapy; Real-time dosimetric imaging; 3D dose reconstruction; Quality assurance; Pencil beam

INTRODUCTION

Charged particles (protons and carbon ions) are widely used in clinical radiotherapy. The main physical advantages of particle therapy over conventional photon therapy are increased energy deposition toward the finite range of ions in the tissue and the Bragg peak, which allows precise dose delivery [1]. For particle therapy to be successful, the range of the beam and three-dimensional (3D) dose distribution within the patient must be accurately known. Conventional X-ray computed tomography (CT) is still used clinically to formulate particle-beam treatment plans for patients. However, X-ray attenuation is based on photoelectric effects and elastic and inelastic scattering, whereas particle interactions follow the Bethe-Bloch rule. The difference in physical interactions between photons and particles partially obviates the advantages of particle therapy [2, 3]. In addition, the patient setup, organ motion, and anatomical changes limit the accuracy of particle therapy [4]. Therefore, to accurately verify the location and quantity of the radiation dose, the irradiated region and 3D dose distribution in the patient must be monitored in real-time; this process enables the fast and reliable * This work was supported by the Scientific Instrument Developing Project of the Chinese Academy of Sciences (No.YJKYYQ20210013). † Corresponding author, luzg@impcas.ac.cn ‡ Corresponding author, xuzg@impcas.ac.cn verification of the consistency between planned and delivered doses. However, the accurate monitoring of the location of the Bragg peak and reconstruction of the 3D dose distribution during treatment are major challenges in precision particle therapy [5, 6]. This is a bottleneck in this field, with no perfect solution.

To date, several techniques have been explored for in-beam range verification and 3D dose measurements, including positron emission tomography (PET), prompt gamma (PG), and radiation-induced acoustics (RA). However, each has its own limitations and is not suitable for short-term clinical use.

Imaging methods based on PET and PG detection in single-photon emission computed tomography (SPECT) have recently been developed [7-10]. Both methods predict the detection of gamma quanta, which are produced by radioisotopes and excited nuclei resulting from the inelastic collisions of ions with tissues. In the case of proton beams, the production of the positron emitters ^{11}C , ^{14}N , and ^{15}O results in annihilation and production of two 0.511-MeV gamma quanta used to form PET images, whereas the emission of high energy gammas (2-15 MeV) accompanying the decay of the excited nuclear states of ^{12}C , ^{16}O , and ^{40}Ca forms the basis of SPECT [11-13]. Therefore, the images produced using these two methods represent the distribution of radionuclides rather than

the distribution of energy deposits. Furthermore, positron emitters induced by treatment beam irradiation are diffused or perfused in living tissues because of the biological washout effect during irradiation and imaging, which degrades the correlation between the activity and delivered dose distribution [14]. Because of factors such as the half-life of nuclides and image reconstruction algorithms, both methods currently require durations spanning few seconds to few minutes after irradiation to achieve image reconstruction with an accuracy of 1-2 mm [7, 15]; therefore, neither method can achieve real-time (tens of milliseconds) dose reconstruction during treatment.

In addition, RA has potential applications in both radiotherapy 3D dosimetry and treatment guidance and in low-dose radiological imaging. Unlike the gamma quanta emitted from radioisotopes and excited nuclei, acoustic waves are induced by the thermoacoustic effect in objects exposed to a pulsed beam of ionizing radiation. The RA signals arise from local temperature increases and subsequent volume expansion of the tissue, which responds directly to the energy imparted to the electrons [11]. Thus, the RA signals are derived from the collisional mass stopping power of the ions and provide a direct measure of the Bragg peak and location of the radiation dose. Previous studies demonstrate a relationship between the pressure signals (measured by transducers or hydrophones) from a pulsed proton beam and the dose delivered by the beam [16-21]. However, noise is a current limitation of this method, which requires novel and highly sensitive transducers with wide bandwidths for accurate signal detection at clinically relevant dose levels [22].

To develop a clinically viable diagnostic method for 3D dosimetric imaging, in this study, we designed a prototype of 3D dosimetric imaging system based on measured beam parameters and spatial distributions of secondary particles. We tested this prototype on a heavy-ion medical machine (HIMM) using a simple zigzag-scanning beam delivery case, and compared the reconstructed dose distributions with Monte Carlo simulations and the measured results of a medical film.

II. DESIGN OF THE PROTOTYPE SYSTEM A prototype real-time 3D dosimetric imaging system is designed in this study, consisting of a beam monitoring system and 3D dose reconstruction engine (DoRT). A schematic of the prototype is presented in Fig. 1 [FIGURE:1]. The beam-monitoring system is used to obtain the information of the current beam, and the 3D dose reconstruction engine is used to calculate the dose distribution generated by the current beam in the irradiated object. The beam-monitoring system consists of two integrated dose-position ionization chambers (IDPICs) and a scintillator module. Two IDPICs are placed upstream of the isocenter and perpendicular to the beam line, and the particle beam is extracted from the nozzle and passed through these two IDPICs to the patient (target). The incident angle, position, spot size, and delivered dose of the beam can be monitored via the synchronous operation of the two IDPICs. The scintillator module is placed on the

patient's side and used to measure the distribution of secondary particles emitted from the patient's body. The beam range can be predicted based on its distribution.

The IDPIC consists of a dose monitoring unit and a beam-profile monitoring unit. The dose-monitoring unit is a large-area parallel-plate ionization chamber (IC) composed of a negative high-voltage electrode and a dose signal electrode.

The beam-profile monitoring unit is a multistrip ionization chamber (MSIC) that can measure the size and position of the beam spot [23–25]. The MSIC comprises a positive high-voltage electrode and two multistrip signal electrodes. The signal electrodes are made of 76 μm FR4 (Tera-Function epoxy with filler and fiberglass), covered with 17.5 μm copper. These electrodes are engraved by a standard printed circuit board technique to obtain 256 strips (0.8 mm wide, with a pitch of 1 mm) and have a scoring area of 256 mm \times 256 mm. The high-voltage electrode is made of a 13- μm -thick Kapton® foil with aluminum layers on both sides. This design optimizes the space utilization while improving the accuracy and efficiency of beam monitoring. The entire detector has a front-to-back window spacing of 37 mm, with a water equivalent thickness of 0.38 mm under the irradiation of a 230-MeV proton beam. Consequently, the energy loss and angle deviation after the beam passes through the detector can be ignored, and the changes in the beam can be monitored in real-time after calibration. The scintillator module measures the location of the Bragg peak of the beam in the target by monitoring the distribution of secondary particles generated under the beam irradiation on the target.

It consists of 80 probes arranged in a 5 \times 16 array, each of which consists of a CeBr3 crystal, with a size of ϕ 20 mm \times 5 mm, coupled to a silicon photomultiplier.

The hardware architecture of the monitoring system is illustrated in Fig. 2 [FIGURE:2]. The IDPIC detector consists of a single-channel IC and 512-channel MSIC. The current signal generated by the IC is converted into digital pulses using a charge-to-frequency converter. The frequency of these digital pulses corresponds to the input current from the IC, and these digital pulses are then conveyed to the data acquisition and processing (DAQ) system through the data input and output interface. The 512-channel signal interface of the MSIC with the DAQ system through an analog front end is equipped with two application-specific integrated circuit (ASIC) chips. Each ASIC chip is composed of a 256-channel analog-to-digital converter. The DAQ system consists of a System-on-Chip Field-Programmable Gate Arrays (SoC FPGA) core processor and its peripheral support modules. The SoC FPGA processes and transmits these signals as well as exchanges data with other devices via Ethernet interfaces and small form-factor pluggable modules. The CeBr3 probes of the scintillator module convert the detected signals into weak voltage signals, which are further converted into transistor-transistor logic signals by the front-end readout board and then transmitted to a multichannel counter. Two IDPICs and the scintillator module perform synchronous measurements, which

are processed by the front-end electronics and SoC FPGA before being transmitted to the data summary module. This module packages the data and sends a packet to the host every 46 ms via the Ethernet interface.

Fig. 1. (Color online) Schematic of the prototype of real-time 3D dosimetric imaging system.

Fig. 2. (Color online) The hardware architecture of the beam monitoring system.

III. PRINCIPLE AND METHOD OF DOSE IMAGING A. Beam monitoring To measure the incident angle and position of the beam, two IDPICs were used for synchronous measurements, as shown in Fig. 3 [FIGURE:3]. The distance between IDPIC1 and IDPIC2 is LAB and the distance between IDPIC2 and the front end of the target is LBC. According to the definition of the 3D basis, we specify that the centers of the rightmost, anterior, and inferior (cid:17) voxel in a cube of size $m \times n \times p$ have coordinates $O(0, 0, 0)$. Consequently, the coordinates of the central voxel in the up- (cid:16) m per plane are $O(0, 0, 0)$. When the beam is irradiated to the target, the incident position C (x_C, y_C, z_C) on the front end of the target can be calculated according to the beam spot position A $(x_A, y_A, -LAB - LBC)$ measured by IDPIC1 and the beam spot position B $(x_B, y_B, -LBC)$ measured by IDPIC2.

The calculation formulas are given by Eq. (1). $LAB + LBC$ $LAB + LBC$ $z_C = 0$ $(x_B - x_A) + x_A$ $(y_B - y_A) + y_A$ The beam irradiation angles are defined as θ and ϕ . As shown in the Fig. 3, we define θ as the azimuthal angle in the x-y plane from the x-axis with $0 < \theta < 2\pi$ and ϕ as the polar angle from the positive z-axis with $0 < \phi < \pi$. Therefore, the incident angle of the beam can be calculated using Eq. (2), and Eq. (3). (cid:113) $\phi = \tan^{-1} \sqrt{(x_B - x_A)^2 + (y_B - y_A)^2} / z_C$ $\theta = \tan^{-1} (y_B - y_A) / (x_B - x_A)$ In addition, the dose delivered by the beam is monitored using the dose monitoring unit of IDPIC2. The irradiation dose is typically represented by monitor unit (MU), which is a measure of the machine output from a clinical accelerator for radiation therapy [26].

In our previous work [27, 28], we proposed a noninvasive method to measure the beam range in depth, which calculates the depth by measuring the distribution of secondary particles emerging from the irradiated object. This is because the spatial distribution of the secondary signals correlates with both the dose distribution and beam range [29]. Based on this the beam in the tissue. Unlike conventional CT data (photon attenuation images), the patient data used in this study are ion CT data (RSP images) obtained using ion radiography [31].

In addition, to facilitate the import of patient data, we equipped DoRT with a Digital Imaging and Communications in Medicine (DICOM) import module, which allowed for the conversion of DICOM data (CT set) into a custom patient data format. Consequently, patient data must be converted only once. The engine's DICOM import functionality requires the PyDicom library of Python

because we rely on built-in functions to import DICOM data. DICOM imports can be started via a graphical user interface (GUI). During the DICOM import, the grid resolution for the resulting CT cube can be adapted using trilinear interpolation. By default, the grid resolution is $1 \text{ mm} \times 1 \text{ mm} \times 1 \text{ mm}$. The resolution automatically defined the dose-grid resolution used later for dose calculation. Currently, the engine cannot calculate the dose on a grid with a resolution different from that of an interpolated CT cube.

3. Dose calculation

To realize real-time 3D dose distribution imaging, a fast and efficient dose calculation method was employed to realize this work.

In this method, dose distribution data are obtained by transforming and modifying the basic dose distribution data matrix. Usually, a full treatment is equivalent to superimposing a few thousand pencil beams on a given volume. We calculated the dose distribution for each pencil beam individually and superimposed the dose distributions for all pencil beams to obtain the full dose distribution.

The beam parameters were measured in real-time using a beam-monitoring system. We assume that the current beam can be described as (R, x, y, θ, ϕ) , where R is the depth range of the target, (x, y) are the coordinates of the beam spots on the isocentric plane, and (θ, ϕ) is the incident angle of the beam. The dose calculation method of DoRT consisted of three steps. 1) The first step is to calculate the 3D dose distribution of the current beam in a homogeneous medium (water), M at (w) . If the parameters of the current beam are the same as those of the beam in the database, the 3D dose distribution data of the beam can be used as the dose matrix of the current beam deposited in water. Thus, the consumption of computer resources is reduced and the reconstruction speed is increased.

If the parameters of the current beam are different from those of the beams in the database, then the dose matrices M at $(R1)$ and M at $(R2)$ are extracted from the database, where $R1, R2$ and R satisfy the condition $R1 = R \cos(\phi) - R2$.

The elements M at $(R1)$ and M at $(R2)$ were circularly shifted $\Delta R1 = R - R1$ and $\Delta R2 = R - R2$ along the Z direction, respectively, to obtain the dose matrices M at $(R2)$.

Thus, the dose distribution of the current beam irradiated into water perpendicular to the x - y plane can be calculated as $(R1)$ and M at Fig. 3. (Color online) Schematic for calculating the incidence angle and position of the beam. study, a similar method is used for real-time depth-range measurements. We use a scintillator module composed of CeBr_3 crystal probes to measure the distribution of secondary ions and predict the beam range in depth using a support vector regression framework. In addition, this method achieves sufficient sta-

tistical accuracy without necessitating the identification of secondary particle species, provided that the energy deposition of secondary particles within the scintillator module surpasses a specified threshold.

B. Reconstruction of 3D dose distribution

1. Base data

The basic data required by the DoRT dose imaging engine is the 3D dose distribution of different pencil beams in water, which includes the integrated depth dose profile and the lateral beam profile at different depths. In a previous study, we designed an integrated system (PBDOSE) to measure the 3D dose distributions of pencil beams, which consisted of a reference MSIC, mobile MSIC, motion control system, and water tank [30]. The lateral profile dose distribution at various depths is measured using the mobile MSIC and normalized by the measurements of the reference MSIC to reduce the effect of beam instability. Based on this result, a 3D dose distribution is created by stacking these profiles in the depth direction.

The 3D dose distribution of pencil beams with different energies (120–400 MeV/u carbon ion beams) in water is measured using PBDOSE, and a basic database is constructed using these measured data. To facilitate the use of data measured by PBDOSE, all data are converted into dose matrices with a grid resolution of $1\text{ mm} \times 1\text{ mm} \times 1\text{ mm}$ and labeled with the depth range R_i . In addition, these data are stored as a single file in Matlab's native format and loaded dynamically into DoRT depending on the current beam state.

2. Patient data

Patient data comprise anatomical information about the patient's body, which is used to calculate the dose distribution of $M_{at}(R) = R_2 - R_1$ ($R_1 + R_2 - R_1$ is constructed based on this relationship). Consequently, according to the RSP map obtained from the ion CT, the fitting coefficient of each medium in the target can be retrieved from the RSP-a lookup table.

Then, a dose matrix $M_{at}(R)$ can be calculated by rotating the matrix $M_{at}(R)$ around the y-axis by an angle ϕ and then rotating the angle θ around the z-axis. Similarly, the dose distribution matrix of the current beam in water $M_{at}(w)$ can be obtained by circularly shifting the elements of the matrix (R) in the x- and y-directions, respectively. The number of elements of the circular shift can be calculated as: $(cid:26)\Delta x = [l \tan(\phi) \cos(\theta) + x]$ $\Delta y = [l \tan(\phi) \cos(\theta) + y]$ Here, Δx and Δy are the numbers of elements of a circular shift in the x- and y-directions, respectively, and l is half the number of elements of the dose matrix $M_{at}(R)$ in the z-direction. 2) The second step is to calculate the dose distribution of the current beam in an inhomogeneous medium (human tissue) based on the dose distribution in a homogeneous medium $M_{at}(w)$. As human tissue is an inhomogeneous medium, the dose distribution of the beam in human

tissue is different from that in water; therefore, correcting the dose distribution data in the water phantom is necessary. In this study, DoRT corrected this dose distribution based on a method involving the water equivalent thickness (WET).

The relationship between the depth range and energy of the particle beam in different media can be fitted using Eq. (6), where E is the energy of the beam, R is the depth range in the medium, and a and b are fitting coefficients.

$R = aEb$ According to this formula, two beams with the same energy E_0 are incident into water and the medium, respectively; then, the ranges in water (R_w) and the medium (R_m) can be expressed as:

$R_w = aE_0b_w$ $R_m = aE_0b_m$ Previous studies found that the fitting coefficients b for different media are very similar [32]. Therefore, according to Eq. (7) and Eq. (8), the ratio of the depth range of a beam with the same energy in different media is equal to the ratio of the fitting coefficient a , as shown in Eq. (9). Each type of medium with a different RSP has a specific fitting coefficient, a . Monte Carlo simulations were performed to calculate the depth range of different energy beams in various media with different RSP and to fit the energy and depth ranges according to Eq. (6), we can establish a relationship between the RSP and the fitting coefficient [33]. An RSP- a lookup table Fig. 4 [FIGURE:4]. (Color online) Schematic of the calculation of WET for an inhomogeneous medium.

Figure 4(a) shows the depth-dose curve of a beam with energy E_0 in water, where R_w is the beam depth range.

Figure 4(b) shows the depth-dose curve of the same beam in an inhomogeneous medium. $d_1, d_2, d_3, \dots, d_n$ are the thicknesses of media $m_1, m_2, m_3, \dots, m_n$, respectively.

$R_{m1}, R_{m2}, R_{m3}, \dots, R_{mn}$ are the depth ranges of the beams incident on the media. The WET of this inhomogeneous medium can be expressed as $WET = \rho_1 d_1 + \rho_2 d_2 + \dots + \rho_n d_n$ (10) According to the definition of WET, a beam loses the same amount of energy when passing through two different media with the same WET. Therefore, as illustrated in Fig. 4, when voxel v_i in an inhomogeneous medium and voxel i in water have the same WET along the direction of the beam, the beam will have the same energy and speed upon reaching both voxels. In addition, according to the Bethe-Bloch formula, the rate of energy loss of charged particles is proportional to the atomic number and density of matter when the same charged particles are incident on matter at the same speed. Therefore, the relative dose of voxel v_i in a heterogeneous medium can be calculated based on the dose value and relative density of voxel v_i in water. By calculating all voxels in the direction of radiation exposure, the relative dose distribution data M at(in) in an inhomogeneous medium can be obtained. However, this is only the dose distribution generated by the particle beam of one MU, and the dose data generated by the current pencil beam can be expressed as:

Figure 5

Figure 1: Figure 5

$M_{at}(t) = M_{at}(in) \times NMU$ where NMU is the total number of MU detected by the beam-monitoring system.

To improve the efficiency of DoRT, the primary fluence considered for the calculation of $M_{at}(t)$ is restricted to the projection of the target onto the beam's eye view for every beam orientation. Therefore, the irradiated object geometry is transferred beamwise into the beam's eye-view coordinate system for dose calculations. 3) By performing the previous two steps, the dose distribution of each pencil beam in the irradiated object is obtained.

The third step is to calculate the cumulative dose distribution of all the pencil beams in the treatment plan and fuse the dose distribution data with CT images to achieve data visualization. The calculated dose distribution data are reverse-rotated and interpolated to assign a dose to the original CT grid.

In addition, DoRT is equipped with a data export module capable of exporting CT and dose-volume data to `.mat`, `.vtk` and `*.mha` file formats.

4. GUI and workflow

As shown in Fig. 5

, we developed a GUI for DoRT using the PyQt5 library, which enables developers to create powerful applications using Python. This GUI allows visualization and exploration of CT and a superimposed transparent dose distribution. Furthermore, the workflow of the dose calculation engine can be controlled from the GUI.

After the dose-imaging engine communicates with the beam-monitoring system, the first step of the workflow is to load the base data consisting of the dose distribution data of different pencil beams (see Sec. III B 1), and patient data comprising a CT dataset (see Sec. III B 2). The loading data can be obtained using an import interface. Next, the depth range, number of MU, incident position, and angle of the current beam were calculated based on the data uploaded by the beam-monitoring system. Subsequently, DoRT conducts dose calculations based on beam parameters and patient data (see Sec. III B 3). The resulting dose distributions are saved in files and displayed in the GUI, which also supports the depth-dose curve computation.

IV. EVALUATION OF THE PROTOTYPE beam is accelerated from 7 MeV/u to an extraction energy ranging from 120 to 400 MeV/u [35]. The beam is extracted from the synchrotron via slow resonant extraction with a flux of up to 1×10^9 particles per second (pps) [36-38]. The beam extraction directions of the four treatment terminals were horizontal,

horizontal & vertical, and vertical, and 45° . A fixed horizontal beam transport line was used to evaluate the performance of the imaging system.

When using the beam-scanning method for particle-beam therapy, the target volume is divided into many iso-energy slices and irradiated slice-by-slice. To evaluate the functionality of this prototype, we used pencil beams of different energies for scanning along a simple zigzag path. Table 1 lists the parameters (energy, spot position coordinates, and delivered dose) of the pencil beam irradiated at each point along the scanning path.

Table 1. Parameters of the scanning pencil beam. Pencil Energy (MeV/u) Coordinates x (mm) y (mm) To facilitate the verification of the dose distribution, a polymethyl methacrylate box filled with water is employed as the irradiation object. Three Gafchromic™ EBT3 films (Lot No.10312201) are placed in a box perpendicular to the beamline and used to measure the lateral profile dose distribution at different depths (80, 90, and 100 mm). The ion CT data for this target are obtained using a composite ionization chamber detector, which is a preliminary prototype of the carbon-ion radiography system developed by our group [39]. The experimental layout of the prototype real-time dose imaging system is shown in Fig. 6 [FIGURE:6].

A. Experimental setup B. Data processing and analysis In this study, we performed a functional evaluation of a prototype using carbon-ion beams. All carbon ion irradiation experiments were conducted on the HIMM, which was co-developed by the Institute of Modern Physics, Chinese Academy of Sciences (IMP-CAS), and its subsidiary company Lanzhou Ion Therapy Co., Ltd. [34]. The HIMM consists of an electron cyclotron resonance (ECR) ion source, cyclotron injector, compact synchrotron, and four treatment terminals. The beam generated by the ECR ion source is pre-accelerated by the cyclotron to an energy of 7 MeV/u and then injected into the synchrotron via charge exchange, where the To evaluate the accuracy of the 3D dosimetric imaging, a general-purpose Monte Carlo toolkit Geant4 was used, where the parameters of the incident particles and detector geometry extracted from the experimental setup were implemented in the simulation code. Based on the simulation results, we evaluated the imaging accuracy of the 3D dose and depth-dose distributions. A gamma analysis [40] with a distance to agreement of 3 mm and dose difference criterion of 3% is employed to evaluate the 3D dose distribution. In addition, only dose points exceeding 10% of the maximal dose value are considered for the gamma analysis.

Fig. 5. (Color online) GUI of DoRT, which is grouped into several functional blocks. In addition, a triple-channel analysis method was used for processing the film data [42].

Computation speed is critical in workflows. To investigate the dose calculation performance in DoRT, multiple treatment planning scenarios with different numbers of pencil beams were defined based on a specific irradiated object. The

parameters of these beams were transmitted to DoRT by another computer using the TCP/IP protocol. Using CPU settings (Intel® Core™ i9-13980HX), each was executed five times and the average runtime was calculated. In addition, the runtimes of the individual pencil beam dose distribution calculations in different scenarios were calculated.

Fig. 6. (Color online) Experimental layout of the real-time dosimetric imaging prototype.

C. Results

1. Comparison of dose distribution

In addition, we measured the lateral profile dose distributions using radiochromic films. A point-to-point comparison of the calculated and measured results was performed to evaluate the accuracy of the lateral profile dose distribution imaging. The film specimen was scanned on a flatbed Epson Expression 12000XL scanner in transmission mode at 24 h post-irradiation. We positioned the film specimen at the center of the scanner to reduce the lateral scan artifacts [41]. To maintain the flat specimen on the scanner, a glass compression plate was positioned on top of the specimen. The specimen was scanned at a resolution of 75 dpi and 48-bit color depth. All color-correction features were deactivated, and the specimens were scanned as positive films in the transparency mode, as recommended by the Gafchromic Film QA Protocol. To evaluate the performance of the prototype for 3D dosimetric imaging, a comparison between the simulated 3D dose distribution and the reconstructed result from DoRT is shown in Fig. 7 [FIGURE:7]. Plot (a) shows the 3D dose distribution simulated by Geant4 according to the experimental settings, and plot (b) shows the results reconstructed from the dosimetric imaging prototype. The simulation results provide more details of the dose distribution, particularly in the fragmented tail (post-peak) region. This is because the primary fluence considered for the calculation in DoRT is restricted to the projection of the target onto the beam's eye view for every beam orientation. Simultaneously, the fragmentation tail region of each pencil beam dose distribution in the basic data was truncated to reduce the resource consumption of DoRT. Gamma analysis (3mm, 3%) was applied to the results, and the prototype appeared to be generally suitable for 3D dose imaging with a mean pass rate of 95.36%.

Fig. 7. (Color online) 3D dose distribution simulated from Geant4 (a) and reconstructed by DoRT (b). The dose values of all the voxels are normalized to 0-100, and the color represents the relative dose value.

To determine the statistical and systematic uncertainty in the beam range and dose, a relative dose line plot along the Z-axis of the target was compared between the Monte Carlo simulated data and DoRT reconstructed images, as shown in Fig. 8 [FIGURE:8]. The reconstruction via DoRT matched the simulation well, with an average relative deviation of all points on the curve of

1.25%. The comparison results show that the points with large dose deviations were mainly located in the Bragg peak region.

Because the film we used was not calibrated for absolute dosimetry, we compared the relative dose distribution of the film measurements with the reconstructed results. The lateral profile dose validation results are presented in Fig. 9 [FIGURE:9]. For comparison, the dose values in both results were normalized to 0–100. Evidently, the reconstructed dose distributions were in good agreement with the film-measured results at the three representative depths of 80, 90, and 100 mm. A point-to-point comparison of the results showed that the median value of the dose difference was 1.56% and the maximum relative dose deviation was 19.59%.

Fig. 8. (Color online) Comparison of simulated (solid black line) and reconstructed (red dots) depth–dose curves.

2. Runtimes

In addition to high reconstruction accuracy, fast computation is critically important for clinical applications. Regarding full-dose reconstruction during clinical treatment, Fig. 10 FIGURE:10 shows the total runtimes for 3D dosimetric imaging using the CPU hardware. This prototype can calculate the full dose distributions in 15.5 seconds on average and less than 24 s even for the plan with more than 2100 pencil beams, which includes the required time for all steps from loading base data and patient data from files (about 2 s on average), necessary CT rotations and interpolations (about 1.5 s), dose calculation by DoRT (about 19 s), and interpolating the final dose distribution back to the original CT grid (about 1.5 s). Figure 10(b) shows the mean runtimes for calculating the dose distribution of an individual beam for different treatment plans. Based on the test results, we found that the dose reconstruction runtime of this prototype for an individual pencil beam was less than 11 ms, which meets the requirements for real-time 3D dosimetric imaging in conventional particle therapy.

V. DISCUSSION In this study, we designed a prototype real-time 3D dosimetric imaging system and performed a functional evaluation of the system using an HIMM. Based on our previous work [27, 28], the prototype calculates the beam depth range (beam energy) by monitoring the distribution of secondary particles' distribution, and monitors the incidence angle and position of the pencil beam using IDPIC. To achieve real-time 3D dose distribution imaging, a fast 3D dose distribution calculation algorithm was employed in the dose calculation engine DoRT of the prototype.

Usually, in-beam PET and PG imaging techniques are used for the detection of gamma quanta, which are produced by radioisotopes and excited nuclei resulting from the inelastic Fig. 9. (Color online) Comparison of dose distribution in the lateral profile measured by EBT3 films and reconstructed by the prototype.

Dosimetric images (beam eye' s view) at three different depths (80, 90, and 100 mm from the entrance) are shown. From left to right: the displayed 2D slices are perpendicular to the beam along the beam depth. collisions of ions with tissues. Owing to factors such as the half-life of nuclides and low detection efficiency, both meth- ods require seconds to minutes after irradiation to achieve image reconstruction [12, 13]. To achieve real-time (tens of milliseconds) dose reconstruction during treatment, the sig- nal detected by the scintillator in this system was the num- ber of secondary particles whose energy exceeded a speci- fied threshold. Therefore, The system is not required to dif- ferentiate between particle types during measurements. The primary advantage of this approach is that the scintillator achieves optimal counting statistics within a reduced acquisi- tion time. Additionally, because the secondary particles must pass through a certain thickness of the medium and air before reaching the scintillator, the size of the target influences the counting statistics of the detectable secondaries. This issue arises for PET and PG imaging.

We performed a functional evaluation of the prototype us- ing carbon ions. For dose deliveries, the gamma index pass- ing rate (3 mm, 3%) against the Geant4 simulated result was 95.36%. The depth-dose curve acquired from this system was comparable to the simulated result, with an average rel- In addition, the reconstructed lateral ative error of 1.25%. profile dose distributions agreed well with the film measure- ment results, and the median value of the dose deviation was 1.56%. Although the dosimetric validation is conducted solely with the relative dose in water, DoRT also offers the capability to reconstruct doses in highly heterogeneous pa- tient geometries, achieving a processing time of less than 11 ms per spot. Using a GPU for dosimetric image rendering, the dose-imaging frame rate of this system can theoretically reach 90 frames per second (FPS). However, a decrease in the data acquisition period of the scintillator module leads to a statis- rameters. As a visionary challenge, this system can be employed to trigger an interruption of delivery in case of sig- nificant discrepan- cies between planned and delivered doses, which would limit the burden on the personnel and allow an accurate report of the delivery during the treatment with no further actions required. In addition, the dose reconstructed using this method represented the physical dose distribution.

By applying a selected relative biological effectiveness (RBE) model to the cal- culated physical dose and incorporating rel- evant biological parameters, the physical dose distributions can be converted into biological dose distributions. There- fore, the method proposed in this study has the potential to achieve RBE weighted dose distribution imaging, which is not possible using other methods.

In this study, we propose the use of ion CT images instead of X-ray CT images for dose calculation, which can over- come the uncertainties associated with the derivation of an RSP map from a map of the linear attenuation coefficient of X-rays. However, ion CT technology currently faces chal- lenges such as subop- timal image resolution and quality, com- plex particle path reconstruction and energy loss correction algorithms, and limited spatial and temporal resolutions

of detector systems. The integration of ion CT into routine clinical practice has been impeded by technical challenges, alongside the necessity for further clinical validation and standardization. Although clinically viable ion radiography systems have not yet been developed, we believe that the results of this study are valuable for achieving precise particle therapy.

With the development and clinical application of ion CT technology in future, the 3D dosimetric imaging method proposed in this study will have broader application prospects. Consequently, in this study, we focus on examining the feasibility of using this method to realize online 3D dosimetric imaging and aim to provide a new reference scheme for improving the accuracy of particle therapy.

VI. CONCLUSION In this paper, we propose a dosimetric imaging system that includes specific hardware and software capable of performing 3D real-time dose reconstruction. We tested this system on the HIMM, compared the reconstructed dose distributions with Monte Carlo simulations, and measured the results for radiochromic films, respectively. This feasibility study demonstrated that the prototype 3D dosimetric imaging system can monitor the beam range and dose distribution in an irradiated object during particle therapy, which is necessary to achieve precise particle therapy. However, the primary function of the system is to detect any discrepancy between administered and planned doses promptly through a fully automated process. This information is intended to be communicated to the treating physicians and can be potentially utilized for both online and offline adaptation. Therefore, the following steps include experiments in more complex scenarios, such as anthropomorphic phantoms, which are necessary before the ultimate goal is to test the system in real patients.

In addition, more accurate dose calculation algorithms will Fig. 10. (Color online) Full (a) and individual beam (b) dose reconstruction runtime of the prototype. Time required to recalculate planned dose distributions with DoRT using an Intel® Core™ CPU. The data points are marked with black squares, and the red line serves only as a visual guide. Shaded areas denote the 95% confidence interval. tical fluctuation in the secondary particle measurement and increases the deviation in the depth range measurement. As a result, the acquisition time of the beam parameters in the prototype was set to 46 ms, such that the total time required for the entire acquisition and reconstruction procedure was less than 57 ms. Because the acquisition time was longer than the reconstruction time, dose reconstruction for the previous cycle could be performed concurrently with data acquisition for the current cycle, thus achieving an image update of 21 FPS.

With millisecond-order acquisition and reconstruction times, this system provides high frame rates, which are at least a factor of six higher than those provided by RA imaging [43].

The dose reconstruction algorithm employed in DoRT is under further development and testing, and a more exhaustive validation will be reported in future publications.

In addition, this algorithm will be tested with more complex phantoms that account for tissue heterogeneities, which may affect the accuracy of the reconstructed doses. In this case, the introduction of Dij matrix and ray tracing in the dose engine can mitigate the inaccuracies related to the analytical dose engine [44, 45]. In addition, the inclusion of deep learning dose prediction models will be investigated.

The presented prototype was tested with carbon ions; however, it can be applied to protons, and switching between particles does not affect the processing time. Moreover, switching between different accelerators requires only the corresponding base data to calculate the dose and integration with the beam-monitoring system to receive the real-time beam parameters developed in the future to reduce the deviations in dose reconstruction. [1] Rinaldi, S. Brons, J. Gordon et al., Experimental characterization of a prototype detector system for carbon ion radiography and tomography. *Phys. Med. Biol.* 58, 413 (2013). DOI: 10.1088/0031-9155/58/3/413 [2] K. Parodi, Heavy ion radiography and tomography. *Phys. Med.* 30, 539-543 (2014). DOI: 10.1016/j.ejmp.2014.02.004 [3] R. Schulte, V. Bashkirov, T.F. Li et al., Conceptual design of a proton computed tomography system for applications in proton radiation therapy. *IEEE Trans. Nucl. Sci.* 51, 866-872 (2004).

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