Validation of a track repeating algorithm for intensity modulated Carbon therapy with GEANT4

Qianxia Wang\textsuperscript{1,2}, Antony Adair\textsuperscript{1,2}, Yu Deng\textsuperscript{3}, Hongliang Chen\textsuperscript{3}, Michael Moyers\textsuperscript{3}, James Lin\textsuperscript{3}, and Pablo Yepes\textsuperscript{1,4}

\textsuperscript{1}Department of Physics and Astronomy, MS 315, Rice University, 6100 Main Street, Houston, TX 77005, USA and
\textsuperscript{2}Department of Radiation Physics, Unit 1420, The University of Texas MD Anderson Cancer, 1515 Holcombe Blvd., Houston, TX 77030, USA

(Dated: September 18, 2018)

The Fast Dose Calculator (FDC), a track repeating algorithm Monte Carlo method was initially developed for proton therapy. The validation for proton therapy has been demonstrated in a previous work. This method can be expanded to ion applications. Our purpose of this paper is to validate the FDC for carbon therapy. We compare the 3D dose distributions and dose-volume-histograms (DVH) for carbon calculated by FDC with a full Monte Carlo method, GEANT 4. 19 patients in total will be discussed, including 3 patients of prostate, 5 of brain, 3 of head and neck, 4 of lung and 4 of spine. We use gamma-index technique to analyse dose distributions and we do dosimetric analysis for DVH, a more direct and informative quantity for planning system assessment. The FDC calculations of both quantities agree with GEANT4. The gamma-index passing rates of all patients discussed in this paper are above 90% with the criterion 1%/1 mm, above 98% with the criterion 2%/2 mm and over 99.9% with the criterion 3%/3 mm. The Root Mean Square (RMS) of percent difference of dosimetric indices \(D_{02}, D_{05}, D_{50}, D_{95}\) and \(D_{98}\) are 0.75%, 0.70%, 0.79%, 0.83% and 0.76%. And all the difference are allowed for clinical use.

PACS numbers: 34.80.Lx, 52.20.Fs

I. INTRODUCTION

Particle therapy (Wilson 1946, Amaldi 2005) is considered to have a greater potential to spare healthy tissue than traditional photon-therapy. It can deliver dose to deep-seated or radioresistant tumors and cause less toxicity to the healthy tissue around the tumor (Castro et al 2004, Schulz-Ertner et al 2007, Ohno 2013, Poludniowski et al 2015 ). Thus in the last few years the number of particle therapy facilities has significantly increased (PTCOG website), in spite of their cost and technological challenges (Newhauser et al 2015). Compared with proton therapy, carbon therapy produces narrower lateral penumbra, which allows to minimize damage healthy tissue in the proximity the tumor. Moreover, carbon ions have higher relative biological effectiveness (RBE) than protons (Kraft 2000). This feature causes more DNA double strand breaks and lead to more non-repairable damage to tumor cells. Even though the cost of carbon therapy is 2-3 times more than proton therapy, these avantages has boosted its clinical use. Moreover, good clinical results with carbon therapy have been reported (Schulz-Ertner et al 2004, Tsujii et al 2004).

An essential component of any particle therapy treatment planning system is the dose calculation engine. Traditionally dose calculations was carried out with Pencil Beam Algorithms (PBS) (Petti 1992, Russell et al 1995, Hong et al 1996, Deasy 1998, Schneider et al 1998, Schaffner et al 1999, Szymanowski and Oelfke 2002, Taylor et al 2017), due to their calculation speed. However, it has been shown that Monte Carlo algorithms provide higher accuracy, especially in areas with large homogeneities (Taylor et al 2017). Traditional Monte Carlo code require calculations times orders of magnitude larger than PBS algorithms. However, in the last few years a variety of faster Monte Carlos have been developed (Yepes et al 2009a , b, Dallas MC, Mayo MC, whatever else we can found). Among them, the only fast Monte Carlo for ion therapy is (Mayo).

Among the fast Monte Carlos, the Fast Dose Calculator (FDC), a track-repeating Monte Carlo algorithm for protons was developed by Yepes et al. (Yepes et al 2009a , b), which can increase the calculation speed with respect to traditional MC by few orders of magnitude. FDC was validated versus full Monte Carlo, GEANT4, for proton therapy in (Yepes et al 2016) In this work, we report in the extension of FDC to ion therapy and its validation.
II. METHODS

III. FDC EXTENSION TO IONS

A stand-alone code, referred to as GEANT4, based on GEANT4 version 10.1.0 (Agostinelli et al 2003, Allison et al 2006), with the physics list FTF_BERT was used for two purposes. Firstly it was utilized to generate the database of trajectories of carbon ions, C\textsuperscript{12}, in water that was used as an input for FDC. Secondly it was employed to generate the reference dose distributions for treatment plans for validation.

The database of C\textsuperscript{12} trajectories in water was generated by simulating 10K carbon ions with an energy of 5200 MeV impinging on a water phantom with the dimension of 510x510x2500 mm\textsuperscript{3}. For each impinging carbon, all the particles (ions, protons, neutrons, electrons, and gammas) produced from it were stored. In addition, all the steps of the original particle and of all its daughters were recorded in the database, along with the energy loss, the length, and direction for each step.

In addition to the trajectory database, parameters to scale the step length for different particles and materials were calculated and stored in a parameter repository. Similarly to the proton case, we considered a list of 49 biological and other materials commonly encountered in radiation therapy (lucite, brass, etc). For each material and a charged particle (ions, protons, and electrons), a table of the Relative Stopping Power (RSP) was stored as a function of particle kinetic energy in 1 MeV steps. RSP is defined as the stopping power of the material relative to water. The stopping power was obtained from the method ComputerTotalDEDX from G4EmCalculator for each particle, material and particle energy.

As for protons (Yepes et al 2016), the particle scaling parameters for scattering angles were obtained by taking the ratio of the scattering angle in the material relative to water. However, this was implemented as function of particle energy in 1 MeV steps, while in previous versions of the algorithm ratios were averaged over particle energies. Scattering angles of particles through a uniform slab of materials of thickness 0.02 g/cm\textsuperscript{2} were calculated with the Moliere approximation, as implemented by Lynch and Dahl (1991).

The basic track-repeating principle in FDC remains as in the proton case (Yepes 2009 a, 2009 b). However, the algorithm was updated to handle ions by utilizing the extended parameter repository with the length and angle scaling parameters for ions produced in carbon collisions, as explained in the previous section.

IV. PATIENT COHORT

We selected 19 patients from different clinical sites treated at the University of Texas MD Anderson Cancer Center (MDACC) with Intensity Modulated Proton Therapy (IMPT). The five clinical sites include prostate, brain, head & neck, lung and spine. For each type, 2 to 5 patients were selected for the study in this paper. The retrospective planning or dose calculations studies are conducted within purview of a generic protocol approved by an MD Anderson Internal Review Board.

Since we did not have clinical ion plans available to us, we started with clinically used proton plans, and converted them into carbon treatment plans. Such conversion was achieved by replacing for each energy layer the proton phase-space files describing the proton beam with carbon phase-space files, where protons of a given range were replaced with carbons ions with the same range. Obviously, the dose distributions for the proton and carbon plans are not exactly the same, because of the different properties of protons and carbon ions. For example, carbon Bragg peaks are sharper than those for protons, and they have a forward tail due to carbon fragmentation. In spite, of such differences, the resulting plans are meaningful for our comparison between FDC and GEANT4.

The target volume, prescribed dose, total voxel numbers, voxel size and maximum and minimum energies used in making plan are presented in Table I.

V. FDC-GEANT4 COMPARISONS

Like in previous studies (Yepes et al 2016), we validate FDC by comparing its dose distributions to those obtained with GEANT4, a full-fledged Monte Carlo validated against measurements and widely utilized in the hadron therapy research. Each selected treatment plan is processed with FDC and GEANT4. Both methods are provided with the Radiation Therapy plan, the CT images and the structure in DICOM format from the clinical treatment planning system.

In Table II we also give the statistical uncertainty of each voxel for Geant4 and FDC, which are shown on the 3rd and 4th column, respectively. The statistical uncertainty is related to the target volume and number of histories used.
### TABLE I: Calculation details for all patients, which include target volume, prescribed dose, total number of voxel and minimum and maximum energies

| Type  | Index | Target Volume (cm$^3$) | Prescr. Dose (Gy) | Voxel # | Voxel size (mm$^3$) | Min Energy (MeV/n) | Max Energy (MeV/n) |
|-------|-------|------------------------|-------------------|---------|---------------------|-------------------|-------------------|
| Prostate | 1 | 21 | 65 | 17,796,597 | 1.95×1.95×1.0 | 264 | 361.26 |
| | 2 | 31 | 22.0 | 21,294,338 | 1.95×1.95×1.0 | 267.7 | 381.9 |
| | 3 | 18 | 38 | 11,408,683 | 1.95×1.95×1.25 | 303 | 375.5 |
| Brain | 1 | 39 | 54 | 12,424,230 | 1.56×1.56×1.25 | 137 | 270.5 |
| | 2 | 63 | 54 | 11,195,197 | 1.56×1.56×1.25 | 135 | 294.5 |
| | 3 | 11 | 55.4 | 11,067,150 | 1.95×1.95×1.25 | 173 | 250.5 |
| | 4 | 24 | 50.0 | 9,564,310 | 1.95×1.95×1.25 | 169 | 278.5 |
| | 5 | 63 | 30.6 | 9,026,964 | 1.95×1.95×1.25 | 135 | 247 |
| H & N | 1 | 24 | 70.0 | 6,482,515 | 1.95×1.95×2.5 | 270.5 | 346.5 |
| | 2 | 7 | 66.0 | 18,624,294 | 1.95×1.95×1.0 | 182.5 | 357.5 |
| | 3 | 14 | 66.0 | 22,667,190 | 1.95×1.95×1.25 | 219.5 | 286.5 |
| Lung | 1 | 36 | 70.0 | 6,401,252 | 1.95×1.95×2.5 | 158 | 298.5 |
| | 2 | 33 | 66.0 | 10,125,024 | 1.95×1.95×2.5 | 181 | 250.5 |
| | 3 | 117 | 63 | 5,101,360 | 2.07×2.07×2.5 | 204 | 377 |
| | 4 | 125 | 66 | 4,270,560 | 2.34×2.34×2.5 | 274.5 | 387.5 |
| spine | 1 | 138 | 9.0 | 23,230,350 | 1.95×1.95×2.0 | 237 | 316.5 |
| | 2 | 48 | 45.5 | 6,794,229 | 1.95×1.95×2.5 | 209.5 | 332.5 |
| | 3 | 333 | 70 | 10,505,404 | 1.95×1.95×2.5 | 135 | 298 |
| | 4 | 36 | 50 | 11,393,369 | 1.95×1.95×2.5 | 215.5 | 312.5 |

**TABLE II: Summary of gamma-index passing rates and difference between the GEANT4 and FDC dosimetric indices for the target volume for all patients.** Three different criteria are used for gamma-index calculation: 1%/1mm (P1), 2%/2mm (P2), and 3%/3mm (P3). D02, D05, D20, D50, and D95 are the maximum dose covering 2%, 5%, 50%, 95% and 98% of the target. Values in the last line are root mean square of all patients.

in the calculation. Higher number of histories will bring down the statistical uncertainty. And larger target volume needs more number of histories to get lower statistical uncertainty.

The statistical uncertainty $\sigma$ can be calculated in the following steps:

$$D = \frac{1}{N} \sum_{i=1}^{N} D_i$$
\[ \sigma = \sqrt{\frac{1}{N} \sum_{i=1}^{N} (D_i - \bar{D})} \]

where \( i \) is the index of the each voxel, \( D_i \) is the dose deposit for each particle in every step in a particular voxel, and \( \bar{D} \) is the mean dose deposit. Note that for those voxels with dose below 10% of the maximum dose are ignored. It requires extra storage space. So it is only kept for voxel energy, then transformed into statistical uncertainty in Dose. The number of histories is 30 M for each beam when performing FDC calculation. Because the computing time for GEANT4 is usually about 7000 to 18000 times more than FDC, we did not use the same number histories as FDC. The number of histories selected for GEANT4 is to make sure the statistical uncertainty blow 0.4. For all patients discussed in this paper, the number of histories is between 10M to 65M for each beam. As can be noted, by comparing the 6th column with the 5th one, most of the statistical errors for FDC are lower than that for GEANT4 because the number of histories used in FDC is higher than that in GEANT4.

VI. RESULTS AND DISCUSSION

A. Dose distribution

The gamma-index analysis is done for all patients with three different criteria, 1 mm/1%, 2 mm/2% and 3 mm/3%. The passing rates with different criteria for all patients were listed in the 5th, 6th and 7th column of Table II. For all the patients, their passing rates are over 90.2% for 1 mm/1%, 98.9% for 2 mm/2% and 99.9% for 3 mm/3%. The RMSs are listed in the last line of Table II, which are 97.91, 99.83 and 100 for different criteria. The high passing rates demonstrate that the FDC dose distributions agree well with that calculated by GEANT4. These passing rates are visualized in Figure 1 [image reference], from bottom to top of which are 1 mm/1% (P11 black dots), 2 mm/2% (P22, red squares) and 3 mm/3% (P33, green triangles). Figure 1 showed that the cohort of brain, H\&N and spine patients have higher gamma-index passing rates than other three types.

We select a head \& neck patient (Index 1) as an example to show the FDC-dose, GEANT4-dose and their difference distributions for a specific section in Figure 2 [image reference]. The first plot in this figure is the dose distribution projected in the transverse plane with z=100 mm calculated by FDC. The one in the middle is the dose projection in the same plane from GENAT4. The last panel is the dose difference between two methods (FDC - GEANT4). As shown in the first two plots, the dose distributions simulated by the two methods are similar to each other. Their difference displayed in the last panel shows that the maximum dose difference is of the order of 1 Gy, which confirms that the two methods agree with each other.

The dose distributions in x (lateral), y(anterior-posterior) and z (superior-inferior) projections for all the patients were also compared for a fast evaluation of the agreement. As an example, Figure 3 [image reference] displays the x, y and z projections for the same patient discussed above. The curves of three projections calculated by the two methods coincide.

B. Dose-Volume-Histogram

\( D_{02}, D_{05}, D_{50}, D_{95} \) and \( D_{98} \) for target volum for all patients are calculated by GEANT4 and FDC. For each index of DVH, the relative difference between the GEANT4 and FDC values was calculated and listed in columns 8-12 of
FIG. 1: Gamma-index passing rates for all patients of five different sites studied in this paper. From bottom to top, the criteria used for Gamma-index calculation are 1 mm/1% (P11, black dots), 2 mm/2% (P22, red squares) and 3mm/3% (P33, green triangles).

Table II. The RMS of each index for all patients was calculated and listed in the last line of Table II. The difference in percentage is below 1.5% for D02, 1.45% for D05, 1.69% for D50, 1.58% for D95 and 1.64 for D98. The RMSs of differences in D02, D05, D50, D95, D98 calculated by two codes are 0.75%, 0.70%, 0.79%, 0.83% and 0.76% respectively, which confirm that the DVH calculated by two codes agree well with each other. All these values of difference between GEANT4-DVH and FDC-DVH for target are displayed in Figure 4. The agreement for brain and spine patients is better than the other three types patients, which is consistent with the comparison of dose distribution.

Figure 5 displays DVHs of the same head & neck patient mentioned above for four selected structures: GTV (black), Hypothalamus (red), Brain_Stem (green) and Frontal_Lobe (light blue). The open squares and solid line are for FDC and GEANT4 calculations, respectively. The comparisons show that the DVHs calculated by the two methods agree well with each other. Especially, the DVHs for Brain_Stem and Frontal_Lobe from the two methods are virtually indistinguishable.
FIG. 2: Gamma-index passing rates for all patients of five different sites studied in this paper. From bottom to top, the criteria used for gamma-index calculation are 1 mm/1% (P\textsubscript{11}, black dots), 2 mm/2% (P\textsubscript{22}, red squares) and 3mm/3% (P\textsubscript{33}, green triangles).

FIG. 3: Dose distribution projection in the direction superior to inferior (x), left to right (y) and anterior to posterior (z) for the same patient calculated by FDC (black line) and GEANT4 (red line).

VII. CONCLUSIONS

In this paper, we used GEANT 4, a widely used full-fledged Monte Carlo code as the standard to verify the accuracy of the Fast Dose Calculator (FDC) code in carbon patients calculation. We compared dose distributions and dose-volume-histograms (DVH) calculated by FDC and GEANT4. The gamma-index passing rates with the criterion 2%/2 mm are above 98.5% for all patients, and the passing rates are above 99.9 for all patients if 3%/3 mm is used. For DVH, the Root Mean Square (RMS) for the difference of five selected slices (D\textsubscript{2}, D\textsubscript{5}, D\textsubscript{50}, D\textsubscript{95}, D\textsubscript{98}) calculated by FDC and GEANT4 are below 0.75%, 0.70%, 0.79%, 0.83% and 0.76% respectively. Therefore, the FDC accuracy amply satisfies the requirement for clinical use.
FIG. 4: Difference of five different indices of target volum DVH: $D_{02}$, $D_{05}$, $D_{50}$, $D_{95}$, and $D_{98}$. Negative difference means FDC-DVH is small than GEANT4-DVH.

VIII. ACKNOWLEDGEMENT

Agostinelli S et al 2003 GEANT4a simulation toolkit Nucl. Instrum. Methods A 506 250-303.
Allison J et al 2006 Geant4 developments and applications IEEE Trans. Nucl. Sci. 53 270-8.
Amaldi U and Kraft G 2005 Radiotherapy with beams of carbon ions Rep. Prog. Phys. 68 1861-82.
Castro J R, Petti P L, Blakely E A and Daftari I K 2004 Particle radiation therapy Textbook of Radiation Oncology S A Leibel and T L Phillips (Philadelphia, PA/Amsterdam: Saunders/Elsevier) pp 1547-68.
Deasy J O 1998 A proton dose calculation algorithm for conformal therapy simulations based on Moliere theory of lateral dections Med. Phys. 25 476-83.
Hong L, Goitein M, Bucciolini M, Comiskey R, Gottschalk B, Rosenthal S, Serago C and Urie M 1996 A pencil beam algorithm for proton dose calculations Phys. Med. Biol. 41 1305-30
Kraft G 2000 Tumor Therapy with Heavy Charged Particles Prog. Part. Nucl. Phys. 45 S473-544.
Newhauser W D, Zhang R 2015 The physics of proton therapy Phys. Med. Biol. 60 R155-209
Ohno T Particle radiotherapy with carbon ion beams. EPMA J 2013 4-9.
Petti P L 1992 Differential-pencil-beam dose calculations for charged particles Med. Phys. 19 137-49
Poludniowski G, Allinson N M and Evans P M 2015 Proton radiography and tomography with application to proton therapy Br. J. Radiol. 88 20150134.
Particle Therapy Cooperative Group (PTCOG) webpage (https://www.ptcog.ch/).
Russell K R, Grusell E and Montelius A 1995 Dose calculations in proton beams: range straggling corrections and energy
FIG. 5: Dose-volume histograms of a head & neck patient (Index 1) calculated with FDC and GEANT4.