Geant4 simulation for a study of a possible use of carbon ion pencil beams for the treatment of ocular melanomas with the active scanning system at CNAO

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Abstract. The aim of this work was to study a possible use of carbon ion pencil beams (delivered with active scanning modality) for the treatment of ocular melanomas at the Centro Nazionale di Adroterapia Oncologica (CNAO). The promising aspect of carbon ions radiotherapy for the treatment of this disease lies in its superior relative radio-biological effectiveness (RBE). The Monte Carlo (MC) Geant4 10.00 toolkit was used to simulate the complete CNAO extraction beamline, with the active and passive components along it. A human eye modeled detector, including a realistic target tumor volume, was used as target. Cross check with previous studies at CNAO using protons allowed comparisons on possible benefits on using such a technique with respect to proton beams. Experimental data on proton and carbon ion beams transverse distributions were used to validate the simulation.

1. Introduction
The ocular melanoma is nowadays the most common early intraocular tumor in adulthood, a malignant tumor which tends to grow both inside the bulb, invading and disrupting the intraocular tissues and outside it, infiltrating the sclera and orbital tissues. Several possible modalities are available to treat the disease such as conventional radiotherapy, brachytherapy and hadrontherapy with protons. Since the depth profile of protons’ stopping power has a significant increase in dose at the end of the range in matter, protons or heavy ions treatments can improve the visual prognosis; the energy is delivered to the target tissue with very little exposure of surrounding healthy tissues.

The depth of Bragg peak is a function of the initial ion beam energy: by varying it during irradiation in a controlled way, a superimposition of many narrow Bragg peaks can be obtained (the Spread Out Bragg Peak - SOBP) This series of Bragg peaks, integrated over time, provide a uniform depth dose deposition.

In clinical practice of eye proton-therapy, the currently worldwide accepted technique for dose
delivery is represented by the passive scattering modality; however, the active scanning modality applied to ocular treatment can be a valid alternative. The CNAO Center (Centro Nazionale di Adroterapia Oncologica) is a synchrotron based medical center opened in Pavia in early 2010, were it is possible to treat deep-seated tumors both with protons and carbon ion beams. Its dose delivery system is represented by the full active scanning modality using a commercial general-purpose image-based treatment planning system (TPS). During the initial phase of the CNAO activity a beam line dedicated to the ocular treatment was not available, but currently one of the treatments room is going to be adapted and made suitable for this purpose [1]. Previous studies [2] were performed to investigate the possibility to use the active scanning technique to irradiate ocular melanomas at CNAO using protons. In this work we exploit a possible use of carbon ion beams instead of proton beams for eye’s treatments, aware of their higher RBR and narrow focusing. By switching the Monte Carlo simulation from Geant4 9.6 to Geant4 10.00, the full CNAO transport beam line previously developed [3] was adapted to carbon ions and validated against CNAO experimental data.

2. Methods

2.1. MC simulation and beam line geometry

The CNAO synchrotron is able to produce carbon ion beams with a FWHM ranging from a minimum of $4.5 \pm 0.45$ mm to a maximum of $8 \pm 0.8$ mm at the standard target center (isocenter), inversely depending on the beam energy. For protons, the FWHM ranges from $7.0 \pm 0.7$ mm to $22.3 \pm 2.23$ mm. The CNAO beam’s energy ranges from 120 MeV/u to 400 MeV/u, for carbon ions and from 63 MeV to 250 MeV for protons, with an uncertainty of 0.05%. Figure 1(a) shows the final part of the CNAO transport beam line, with all its elements, simulated by using the Geant4 10.00 toolkit.

The CNAO beam line consists of:

- Vacuum extraction beam pipe (~ 6 m) sealed by a 0.6 mm thick carbon shutter;
- Fixed structure called nozzle [4] inside of which two beam-monitoring chambers (Box1 and Box2, represented in Fig. 1) are embedded to measure in real-time the beam fluence and position. Passive elements such as ripple filters [5] and range shifters can be housed inside the nozzle external case (Fig. 1(b)).
- Standard target center (isocenter) located at a distance of 64 cm from the downstream edge of the nozzle, were the patient is positioned.

Figure 1. (a) 3D view of the simulated beam line in the Geant4 implementation and (b) a schematic view of the CNAO beam line. The red arrow represents the beam direction.
The simulation reference frame was chosen with beam propagation direction parallel with $X$ axis. The simulated beam line elements were placed inside a $14 \times 14 \times 14 \text{ mm}^3$ air mother volume.

### 2.2. Geant4 readout geometry

To validate the simulation a detector with the same composition of Gafchromic$^{TM}$ EBT3 radiochromic film (International Specialty Products, Wayne NJ, USA) was developed to simulate beam spot and scanned field lateral profiles. The results obtained with the MC simulation were compared with experimental measurements performed with real EBT3 films. A detailed description of the human eye with its internal components was then used to build an *eye-detector*, a detector that faithfully reproduces a real human eye.

#### 2.2.1. EBT3 film and water box detector

Radiochromic films are an important tool to verify dose distributions in highly conformal radiation therapy. In particular, Gafchromic EBT3 are widely used in various radiotherapy treatment modalities due to a good resolution as 2D dosimeter [6]. In order to perform the simulation validation, radiochromic EBT3 films were implemented in Geant4 for a cross check with CNAO experimental measurements performed with Gafchromic films.

According to the manufacturer’s data sheet [7] EBT3 films are made by laminating an active layer ($\sim 28 \mu\text{m}$ thick) between two identical transparent polyester substrates ($\sim 100 \mu\text{m}$ thick). The molecular formula of the layers was used to simulate the Geant4 materials with the correct number of elements in the correct stoichiometric proportion, by the *AddElement* method of the *G4Material* class (Tab. 1).

| Element    | H   | C   | O   | Li  | N   | Na  | Cl  | Br  |
|------------|-----|-----|-----|-----|-----|-----|-----|-----|
| Polyester layer | 36.40% | 45.50% | 18.10% | -   | -   | -   | -   | -   |
| Active layer  | 58.30% | 29.60% | 29.60% | 0.80% | 0.10% | 0.10% | 0.20% | 0.10% |

**Table 1.** Chemical composition of EBT3 films [7]

At CNAO, the Bragg peak position in water for different energies is measured for both proton and carbon ion beams through the PTW Peakfinder water column (PTW, Freiburg, Germany). To cross check the Geant4 simulation with CNAO experimental data a cubic water box ($500 \times 500 \times 500 \text{ mm}^3$) was also implemented in Geant4 as sensitive detector, to evaluate the beam energy deposited.

#### 2.2.2. The eye detector

The first step in building the eye-detector was to assign to all the eye components a simpler geometry to be implemented in Geant4. Figure 2 shows the simplified eye design used to reproduce the eye components in a simplified geometric shape that could be implemented in Geant4.

The eye dimension were parametrized as a function of the outer sclera radius, to be easily scaled according to the patients’ eyes.

The eye components, including a tumor, were accurately simulated and custom materials were defined to well reproduce all their chemicals [2]. They defined an *eye-world* volume inside the world volume; in this way it was possible to rotate or translate the eye maintaining their components in the same mutual positions. Each eye’s element was made *sensitive* to evaluate the energy deposition by single particles in different tissues.
Figure 2. (a) Simplified design of an human eye with the inner structures and (b) the side view of the eye-detector implemented in Geant4. During the irradiation the eye was rotated of an angle of 40° in the vertical direction to spare healthy tissues [8].

3. Results

3.1. Simulation validation

Before the eye-detector irradiation a validation of the Geant4 simulation with CNAO experimental data was carried out with both carbon ions and protons. Important beam parameters such as the transverse FWHM and scanned radiation field’s uniformity were tested within the simulation and compared with experimental measurements at CNAO Center. Experimental data used in this section are courtesy of Dott.Ciocca of the CNAO Medical Physics Unit.

The beam FWHM was measured along the simulated beam line, in air at isocenter, for 7 different beam nominal energies for protons (62.730 MeV, 81.560 MeV, 97.54 MeV, 119.05 MeV, 148.80 MeV, 174.87 MeV, 198.11 MeV) and 9 for carbon ions (from 115.32 MeV/u to 380.45 MeV/u). Figure 3 shows the comparison between simulated data (black dots) and CNAO measured data (red dots) whose experimental uncertainties were evaluated to be about 10% [1]. Simulated data for protons were produced with $2.5 \times 10^5$ events generated in 5 statistical independent runs. For carbon ions, due to the long computational times, the events number was reduced to $4 \times 10^3$. EBT3 films were use both for simulation and experimental measurements.

Figure 3. Comparison between simulated (black dots) and experimental (red dots) beam FWHM, for protons (a) and carbon ions (b), for different energies. The simulated detector for these measurements was the EBT3 film.

Experimental data and simulation for proton beams well overlap, within experimental uncertainties, with a good agreement. For carbon ions, the mean FWHM value of simulated and experimental data matches ($\sim 6$ mm), however the trend of the two series of points are different, in particular for the energies at the extremes of the CNAO delivery range. This is due to the choice of Geant4 physics list, and further studies are currently in progress. The percentage depth-dose deposited was simulated in the cubic water phantom for 4 different nominal beam energies, both for protons and for carbon ions. Fig. 4 shows simulation plots and CNAO
experimental measurements. Data were produced by simulating $5 \times 10^3$ carbon ions and $10^5$ protons.

The discrepancy between the Bragg peak range of CNAO data and simulation is within 0.1 mm, which is the maximum deviation tolerance. A good overlap between simulated and experimental data is achieved for proton and carbon ion beams.

Figure 4. Percentage depth-dose deposited in a water phantom by proton (a) and carbon ion beams (b) with 4 different nominal energies. Curves are normalized at the dose deposited by the beam with lower energy (81.56 MeV for protons and 115 MeV/u for carbon ions). For carbon ions 2 ripple filters (each 2 mm thick) were added.

3.2. Radiation scanned fields

The CNAO active scanning technique was achieved in Geant4 through a dedicated event generation; the code was validated by generating an uniform irradiation in the plane transversal to the beam axis. A $40 \times 40$ mm$^2$ squared radiation field was simulated for 100.51 MeV protons and 115.23 MeV/u carbon ions (Fig. 5). Data were produced by simulating $9 \times 10^5$ events for protons and $18 \times 10^4$ for carbon ions.

In order to minimize the beam broadening and lateral penumbra a new isocenter was defined at 11 cm from the end of the nozzle and the range shifter was positioned at a very close distance (6.5 cm) upstream the new isocenter. To cut the undesired lateral penumbras of the field, that must be eliminated for a good eye treatment, a 10 mm thick brass collimator with a 20 mm diameter circular aperture, was positioned at 5 cm upstream the isocenter.

The simulated material for the brass collimator was an alloy of 61.5% of copper, 35.2% of zinc and 3.3% of lead (percentages in mass). The mean values with the correspondent standard deviations and the lengths of the lateral penumbras (respectively for protons and carbon ions) are listed in Tab. 2 and 3 for both vertical and horizontal profiles, with and without the brass collimator. The values refer to the dose deposited in the simulate EBT3 film. The addition of the brass collimator best focuses the dose deposition on the central area and halves the lateral penumbra in both the transversal profiles.

| No collimator | Field size 50% | Y profile | X profile | Collimator | Field size 50% | Y profile | X profile |
|---------------|----------------|-----------|-----------|------------|----------------|-----------|-----------|
| Homogeneity 70% | 5.70 % | 5.20 % | 7.00 mm | 7.00 mm | Fall-off 80 %-20% | 2.50 mm | 2.50 mm |

Table 2. Field size, lateral penumbra and homogeneity obtained with 2D proton beam scan.
3.3. Spread Out Bragg Peak

After the studies of the beam shaping, a PMMA (Polymethyl Methacrylate) range shifter was introduced in the transport beam line, in order to degrade the too high beam energy supplied by the CNAO synchrotron. Since monochromatic proton beams are usually too narrow to cover the whole tumor volume, to have a clinically correct dose distribution it is necessary to add Bragg peaks shifted in depth and weighted in order to create a spread out Bragg peak (SOBP) [9]. By varying the number of peaks, the extent of this uniform region can be varied. An algorithm was implemented to calculate the set of correct weights necessary to obtain a SOBP and a simulated SOBP was produced inside a water cube detector ($25 \times 25 \times 25$ mm$^3$) positioned at the new isocenter both for protons (Fig. 6a) and carbon ions (Fig. 6b). The distal fall-off and homogeneity values together with the range shifter thickness are shown in Tab. 4 for protons and carbon ions. In the flat region the homogeneity is within the CNAO maximum tolerance value (5%), endorsing the simulation accuracy.
3.4. Eye irradiation

The eye-detector was irradiated through a two dimensional transverse beam scan at different depths by adding a range shifter (RS) 41 mm thick for protons and 20 mm thick for carbon ions. The RS and the brass collimator (with an ellipsoidal aperture of $20 \times 22 \text{ mm}^2$) were placed respectively 65 mm and 50 mm upstream the isocenter.

The eye-detector was rotated of an angle of $40^\circ$ in the vertical direction, in order to misalign the tumor from healthy tissues in front of it. With this setup, the treatment uniformity on the tumor in the eye-detector was tested for both proton and carbon ion beams. Fig. 7a and Fig. 8a show the top and lateral 2D dose distributions views of the irradiated eye-detector respectively for protons ($3.5 \times 10^6$ simulated events) and carbon ions ($5 \times 10^5$ events).

For a more quantitative description of the deposited dose in the eye-detector and for the evaluation of the ratio between the dose deposited in the tumor and the other eye components, proton and carbon DVHs (Dose Volume Histograms) were compared. Looking at the protons’ DVH in Fig. 7b, the 100% of the tumor volume results to have received an energy release of 20 MeV, while the same dose was received by only the 70% of the vitreous humor volume. The energy deposited in the other eye components across their volume ranges from 50% to 10% or less. In particular in the optic nerve and the cornea, the most radiation sensitive sub components, 20 MeV have been deposited within 30% of their volume or less. For carbon ions (Fig. 8b) the percentage of tissue absorbing 7 MeV or more was 100% of the tumor volume but only the 50% of the vitreous humor volume. Only the 30% or less of optic nerve and cornea volumes received 7 MeV.

Figure 6. Spread Out Bragg Peak (blue curve) for protons (a) and carbon ions (b) obtained by superimposing Bragg Peaks curves for 10 consecutive energies (colored curves).

Figure 7. (a) Top and lateral 2D view of the energy deposited by proton beams in the eye detector. The tumor is represented by the yellow line in the right side of the eye. (b) Comparative Dose Volume Histograms for proton beams.
Figure 8. (a) Top and lateral 2D view of the energy deposited by carbon ion beams in the eye detector. The tumor is represented by the yellow line in the right side of the eye. (b) Comparative Dose Volume Histograms for carbon ion beams.

4. Conclusions
The CNAO beam line and eye detector geometry was implemented, the beam setup was optimized for ocular treatments and the simulation was validated against CNAO experimental data. The uniform 3D dose distribution in the tumor volume was studied both for protons and carbon ions; carbon ions showed less lateral penumbra (1.5 mm) due to a more collimated beam. Due to the long computational time for carbon ions, the number of events simulated was less than that of protons; however we are going to adapt the code to the multi-threaded option included in Geant4 10.00 to increase the number of generated events by reducing simulation time. Anyway, the good preliminary results so far obtained by this work, point out and confirm the possibility of using carbon ions delivered with active scanning beams to treat the ocular melanomas.

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