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Monte Carlo Simulations for Beam Delivery Line Design in Radiation Therapy with Heavy Ion Beams

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1. Introduction

Hadrontherapy is an advanced technique in the field of radiation therapy. It guarantees a high efficiency in conforming a high level of dose to the tumor volume due to the Bragg peak characteristic. Monte Carlo simulations of the Beam Delivery Line (BDL) as well as the treated volume provide all the necessary information on the physical processes. The use of Monte Carlo numerical techniques allows tracking the single particle in different tissues and materials. It permits the evaluation of the dose delivered to the treated volume and the prediction the quality of the irradiation.

The information generated by those simulations can be used for the evaluation of the biological effect on cell survival. The radiobiological equivalent dose can be evaluated using combining Monte Carlo particle tracking with specific radiobiological models, like the Local Effect Model (LEM)(Elsasser and Scholz, 2007).

Monte Carlo simulations for the beam delivery line and for the treated volume provide all the necessary information on the physical processes and related dosimetry and provide a useful tools for the design of passive elements of a BDL. We have described the full BDL of the National Center of Oncologic Hadrontherapy (CNAO) in a Monte Carlo simulation. We estimate the impact of the passive elements of the BDL on the energy distribution on the treated volume.

The simulation is based on the package GEANT4 to estimate the actual distribution in the treated volume of particles and fragments and the corresponding energies. The treated volume is simulated defining different tissues. The evaluation of biological effects was studied using a code based on the LEM. The computational effort was performed using the distributed INFN Grid computing resources.

1.1 Dose delivery techniques

In the field of hadrontherapy two main kinds of beams are used: proton and carbon ion beams.

There are two main techniques for dose delivery used in the field of hadron therapy. The first technique is the passive scattering technique which is largely used for both proton therapy and carbon ion therapy. With this technique the beam is spread by placing scattering material into the path of the incoming particles.

A combination of collimators and compensators conforms the dose to the target volume. To spread out the Bragg peak, a set of range modulator wheels or ridge filters are added in the beam path in the BDL (Figure 1). The passive technique is commonly used with cyclotrons and requires an important effort in the definition of the modulating devices along the beam delivery line to reach a 3D-conformal dose distribution.

In the active scanning techniques, magnets deflect and steer the ion beams. With the guidance of the control system, the scanning magnet steer the single mono-energetic beam to paint voxel by voxel the target volume, in successive layers. The depth of penetration of the Bragg peak is adjusted by varying the initial kinetic energy of the beam (Figure 1). With syncrotons we are able to generate a range of energies which can reach steps of 0.5 mm precision in the particle range.
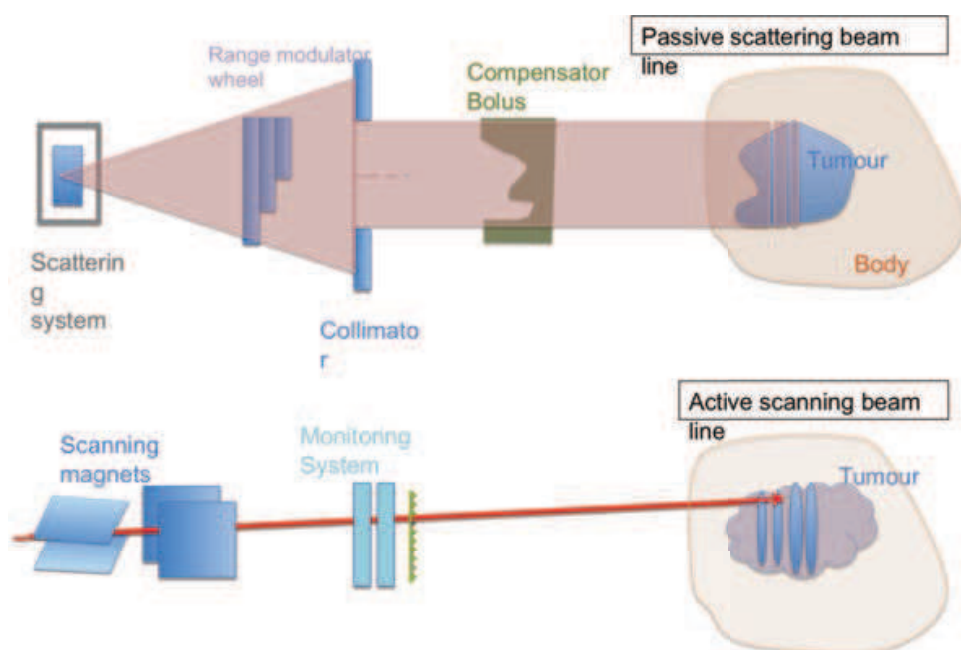

Fig. 1. Passive scattering and active scanning beam delivery systems.

Proton and carbon ion beams have a very sharp Bragg peak. For proton beams of energies smaller than 100 MeV, with a gaussian fit around the region of the maximum of the Bragg peak, we can measure a sigma smaller than 1 mm, while for carbon ion beams, the sigma measured in the same way is smaller than 1mm for energies up to 360 MeV.

In order to use proton and carbon ion beams in hadrontherapy and to achieve an acceptable homogeneity of the Spread Out Bragg Peak (SOBP), the peaks need to be broaden at least few millimeters by means of a properly designed *ripple filter*. The use of a ripple filter is mandatory in particular in conjunction with active scanning techniques for dose delivery, where it helps to reduce the numbers of energy switches necessary to obtain a smooth SOBP, leading also to shorter overall irradiation times.

In this work we studied the design and the simulation of ripple filters used on the BDL for the CNAO. We present a two steps study: the first one is dedicated to proton beams and the second one is for carbon ion beams. Radiobiological effects for ion beams are also evaluated,

since they modulate the shape of the radiobiological equivalent dose distribution around the Bragg peak accordingly to the specific ripple filter used.

2. Method and Materials: Beam Delivery Line for active scanning delivery technique

The final decision in the choice of the right design of the BDL elements depends on the impact of those passive elements on the energy distribution in the treated volume. A full BDL is simulated and modeled to estimate the actual distribution in the treated volume of particles and fragments and the corresponding energies and the total scattering of the original beam at the treatment volume.

The BDL is composed by a double online monitoring system (Box1 and Box2), a range shifter and the ripple filters. The monitoring system consists of an emsemble of pixel and strip chambers. We put the ripple filter as the last static device before the patient at 50 cm with respect the isocenter (see Figure 2).

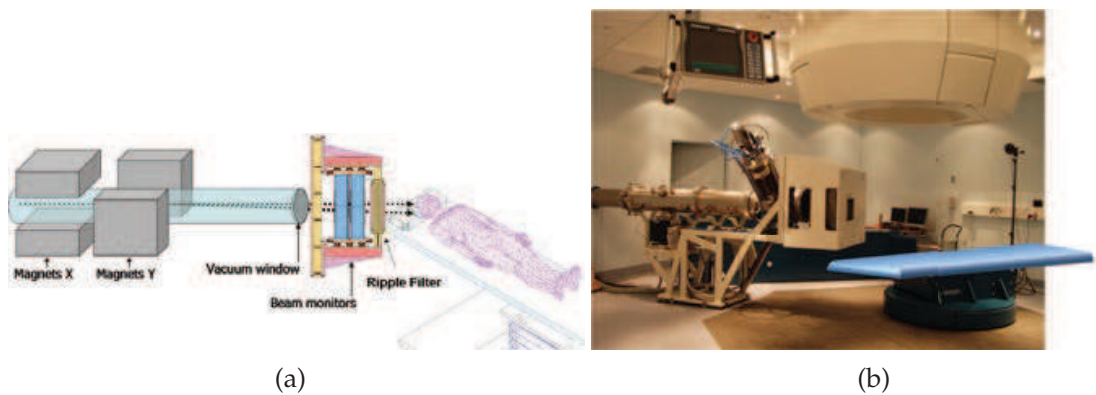(a)   (b)

Fig. 2. Beam delivery system including the scanning magnets , monitoring system and the ripple filter.

The Monte Carlo simulation is implemented with GEANT4 (GEANT4, release september 2010) and it is linked to Root interface (Root, cern Package) which provides an online follow-up of the events generated during the simulation along the beam path. The goal of the implemented simulations is the study the effect of the monitoring system and of the ripple filter on the therapeutic beams. We simulated both proton and carbon ion beams and we check for both beams the 3-dimensional deposited dose distribution.

2.1 Monte Carlo with GEANT4

The physics of the therapeutic carbon ion beams transport was simulated with the GEANT4 Monte Carlo simulation toolkit version 9.3 with patch 01.

GEANT4 is a flexible object oriented code, designed originally for high-energy physics applications but now it is extended to low energies used in heavy ion therapy. For this study, the GEANT4 physics for the electromagnetic processes is activated using the setting of 'Option3' recommended by the electromagnetic working groups of Geant4 collaboration. This setting is designed for applications requiring higher accuracy of electrons, hadrons and ion tracking without magnetic field. To set up the hadronic interaction we used the following hadronic models: 'G4HadronQElasticPhysics' for hadronic elastic model, 'G4HadronInelasticQBBC' for hadronic inelastic models for proton and neutrons and 'G4IonBinaryCascadePhysics' for hadronic inelastic models for ions.
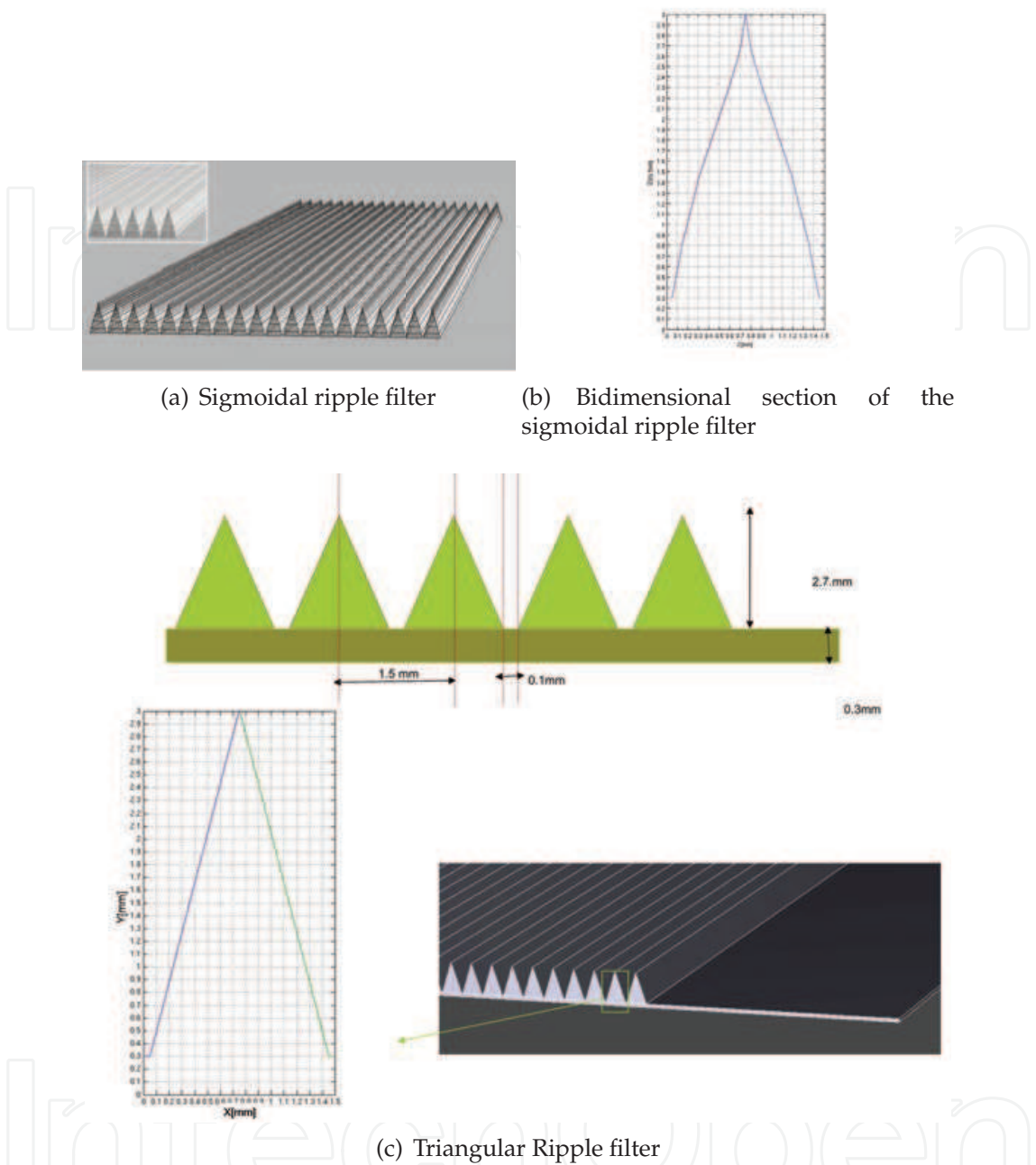
(a) Sigmoidal ripple filter   (b) Bidimensional section of the sigmoidal ripple filter

(c) Triangular Ripple filter

Fig. 3. Sections of ripple filters as described by (Weber and Kraft, 1999) of 3 mm (Type B) and the new triangiular one (type A)and as designed and described in the Monte carlo simulation with Geant4 (see also (Bourhaleb et al, 2008)).

2.2 Design of a ripple filter

We simulated the beam delivery line supporting both proton and carbon ion beams using different energies of the beams. We compared the effect of different kind of ripple filters and their advantages.

The effects of different kind of ripple filters are studied in different possible configurations. We designed two different shapes of ripple filters of almost the same dimension. The first one (type A) has a simplified section (triangular section) and a thin base of plexiglass (PMMA) of

20 mm × 200 mm × 0.3 cm and a total thickness respectively of 2 mm and 3 mm (see Figure 3). The second shape (type B) has a sigmoidal section as described by (Weber and Kraft, 1999), as we can see in Figures 3. The sigmoidal shape of the type (B) filter satisfy the requisite to produce filtered Bragg peaks with a gaussian shape that permits a better uniformity when they are added up in a SOBP.

In our study we used PMMA plates of $1.19 \mathrm{g}/cm^3$ density. The momentum spread for both protons and carbon ions was fixed at $\Delta p/p = 0.05\%$.

The shape of the Bragg peak resulting from the passage of the ion beam through the beam delivery line is strongly depending on the scattering and the straggling processes that affect the final spatial distribution of the beam energy loss. In fact, as we will see in details in the following section, proton beams, that have higher straggling effects than carbon ions, are deflected and broadened easily and are less sensitive to the shape of the ripple filter. Conversely, carbon ion beams needs more accuracy in the design and the mechanical production of the adequate ripple filter.

2.3 Pre-simulation analytical studies

The full Monte Carlo simulation of the passive elements and the water phantom requires a fairly amount of CPU time, and the iteration over different shapes and dimensions of the ripple filter is a lengthy procedure. To shorten this time and get an approximated solution we studied an algorithm to solve analytically the problem based on a *linear filter approach*. By convolving the shape of the non-filtered Bragg curves with a longitudinal *filter transfer function* one can estimate the energy deposition depth dose curves as modified by the ripple filter

$$D = f * D_0, \tag{1}$$

where f is the transfer function associated to the specific ripple filter, D is the dose distribution in the volume of interest, which includes the effect of the ripple filter, and D_0 is the dose distribution without the ripple filter.

The transfer function was derived from the profiles of the ripple filters while the non-filtered Bragg curves D_0 were obtained from a Monte Carlo simulation of the full beam line and water phantom but without filter.

With this technique, which has been briefly introduced, one can quickly estimate the effects of the different filter shapes for any given set of proton beam energies. Applying the method to the two types of filters, type A and type B, (an example is reported in Figure 4), we can observe that the profiles of the filtered peaks are very similar and that the differences are less than 3% at the maximum dose.

In the next sections we discuss the impact of the ripple filters on the longitudinal and trasversal energy deposition curves obtained with a full simulation for both proton and carbon ion beams.

2.4 Effect of ripple filters on the Bragg peak
2.4.1 Proton beams

In this study we considered two type (A) filters with a maximal thickness of 2 mm and 3 mm respectively (see Figure 5(a)). For different configurations we compared the longitudinal Bragg peak width (sigma) and the dose uniformity at the SOBP.

The kinetic energies used in proton-therapy with active scanning covers the range between 70 and 250 MeV (see Figure 5(b)). As expected the present study shows that the effects of the ripple filter is more critical for low kinetic energies. At 70 MeV the sigma of the maximum of dose deposition curve along the beam direction is almost doubled by the insertion of the
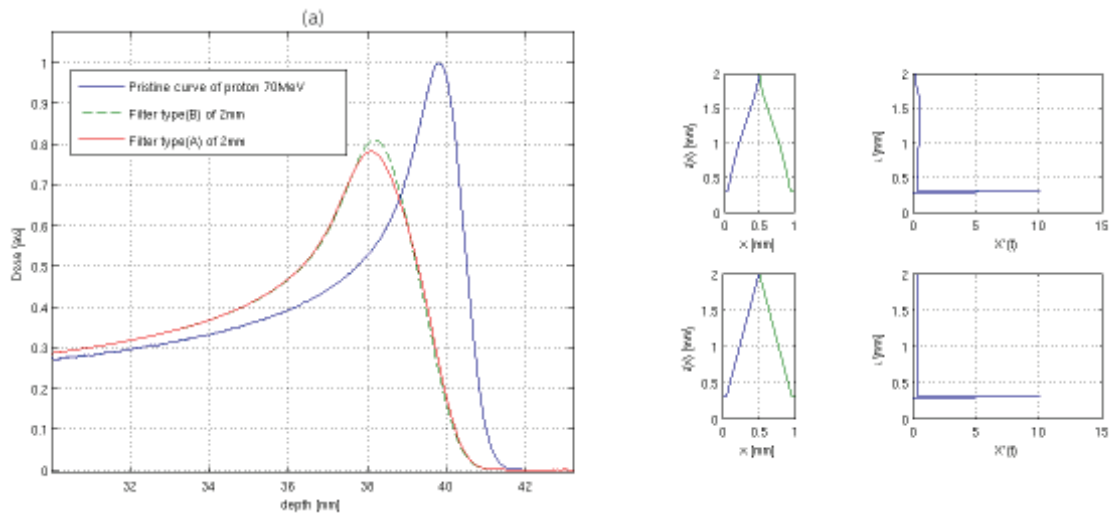
Fig. 4. Comparison of the Bragg curves using the sigmoidal shaped ripple filer and the triangular one with proton beam at 70 MeV.
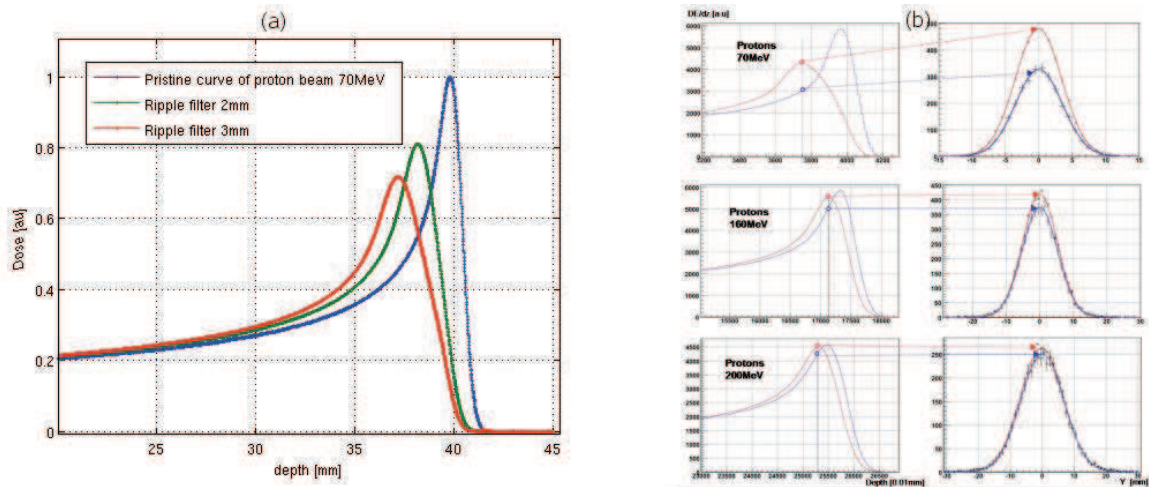

Fig. 5. Comparison of the Bragg curves using triangular ripple filters of 2mm and 3mm thickness with proton beam at different energies.

ripple filter, whilst the difference between 2 and 3 mm thick filter is of the order of 10%. For beam energies greater than 100 MeV the insertion of the ripple filter gives a marginal increase of the sigma (< 10%), which has already a value of several millimeters. The Bragg peak sigma values are reported for three different energies in Table 1. In the same table there are reported the widths for the 2 and 3 mm thick type (A) filters respectively. Even at low energies, the impact on the width of the peaks due to the two ripple filters is negligible (< 10%). However at 70 MeV the shape of Bragg peak falloff (see Figure 5,a) is quite affected by the filter, even if the width does not change by more than 10 %.

In Figure 5,b the longitudinal and transverse energy deposition curves are shown at three beam energies (70, 160, and 200 MeV) for a 2 mm thick type(A) filter and without filter. The energy deposition curves in the transverse plane with respect to the beam direction refer to the longitudinal position of the Bragg peak for the filtered case.

	70 MeV	160 MeV	200 MeV
No ripple filter	0.8	3	4.3
Ripple filter of 3 mm	1.9	3.3	4.4
Ripple filter of 2 mm	1.6	3.0	4.3

Table 1. Sigma values in [mm] from gaussian fits performed on a $\pm 1\sigma$ range around the Bragg peak

2.4.2 Carbon ion beams

It is well known that for carbon ion beams the Bragg peak is narrower than for the proton beams. Similar consideration applies also to the transverse plane. In this case it can be necessary to enlarge the Bragg peak width by using a configuration of two ripple filters used simultaneously (see comparison of peak shapes at Figure 11).

Furthermore, while for protons the effect of a deviation of the ripple filter shape from the ideal one tends to be washed out by the relatively large straggling, the carbon ion Bragg curve is far more sensitive to the shape of the ripple filter.
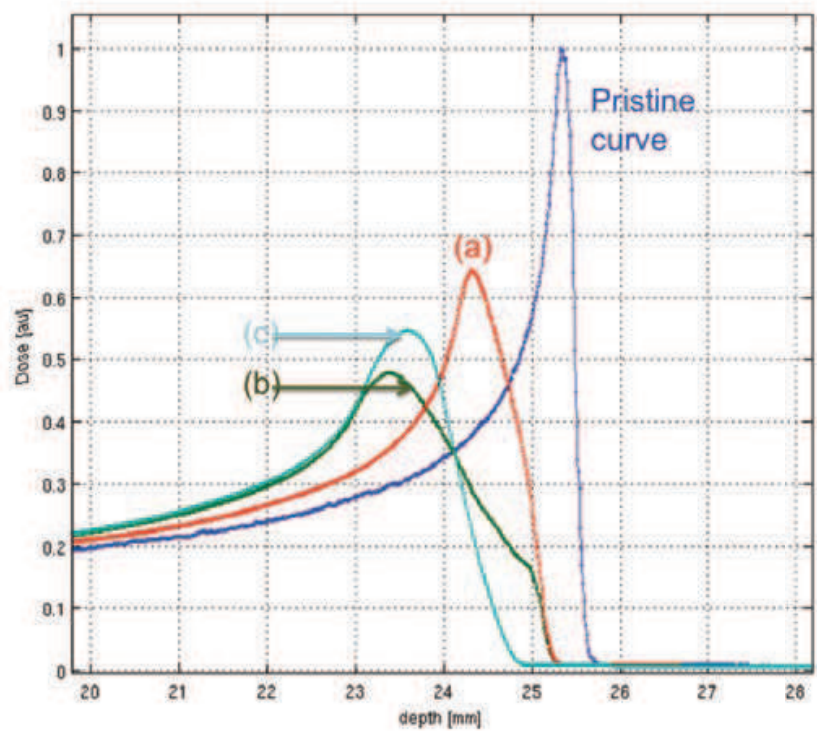

Fig. 6. a) Single triangular ripple filter (2 mm). b) Single triangular ripple filter (3 mm). c) Final design of the *double ripple filters* (2 mm + 2 mm) for carbon ion beams.

The carbon beams energies clinically used and simulated in this study range from 100 MeV/u up to 400 MeV/u. We simulated a *double filter*, with the first filter placed just after the exit window and the second ripple filter at 30 cm from the first, placed at the end of the monitoring system, right before the water tank. The two filters simulated are both of type (A) with 2 mm maximum thickness. For comparison we investigated the single ripple filter setup (2 and 3 mm) with a beam with kinetic energy of 100 MeV/u.

In Table 2) we see the effects of the simple and double filtering on the beam and the accuracy (normalized χ^2) of the gaussian fit performed on a $\pm 1\sigma$ range around the Bragg peak.

	100 MeV/u	270 MeV/u	360 MeV/u
σ (No ripple filter)	0.2	0.7	1.1
σ (One ripple filter of 2 mm)	1.1	1.4	1.6
χ^2 (One ripple filter of 2 mm)	185	35	19
σ (Two ripple filters of 2 mm)	1.6	1.9	2.1
χ^2 (Two ripple filters of 2 mm)	26	2.6	1.0

Table 2. Sigma value in [mm] from gaussian fits performed on a $\pm 1\sigma$ range around the Carbon ion Bragg peak and the corresponding value of the normalized χ^2 of the fit.

From the normalized χ^2 of the fit the similarity of the longitudinal dose deposition shape to a gaussian curve improves as the beam energy increase, but a good fit is obtained only with a double filter. Thus, for a carbon ion beam we conclude that the configuration with double filtering results in a shape which is closer to a gaussian curve with respect to the single filter. With a separate simulation, we probed the single type (B) filter and we found results very similar to the double filtering with type (A). This observation substantiates the original hint that the filter shape, for carbon ions, has a enormous impact on the resulting Bragg curve.

The results of the simulations were also compared with the experimental data taken at *Laboratory Nazionali del Sud* (LSN) in Catania, Italy, where carbon ion beam accelerated with a cyclotron at 62 MeV/u are used with different ripple filter configurations. The simulations are in complete agreement with the experimental data, as it ca be seen in Figure 7.
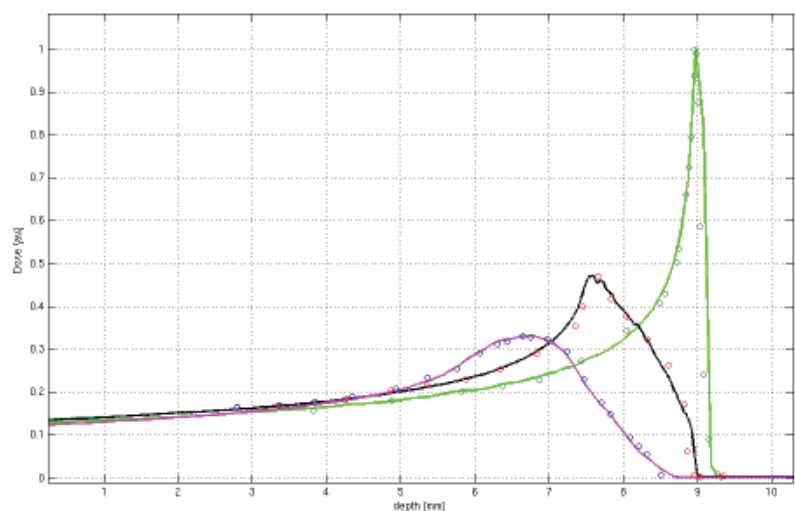

Fig. 7. Experimental measurements of carbon ion beam of 62MeV/u at Laboratori Nazionali del Sud (LNS) at the carbon ion beam line with and without ripple filters and compared to simulated curves.

2.5 Radiobiological effect

An investigation on the impact of the BDL elements for such configurations on particles yields and LET distribution in the treated volume is also performed. This knowledge is important, in particular in the case of carbon ion beams, to estimate the impact on the relative biological effectiveness (RBE) and the biological equivalent dose distribution (i.e. the dose weighted with the knowledge of the RBE) of the passive elements of the beam delivery line. In the case of carbon ions, the RBE usually presents variationin the irradiation fieldm, $1 < RBE < 5$, and

consequently the shape of the biological equivalent dose at Bragg peak is different from the corresponding physical dose. Hence, the evaluation of the transfer functions characterizing each of the element should involve a rigorous estimation of the biological effects.

With the Monte Carlo simulation we get the actual distribution in the treated volume of particles and fragments and the corresponding energies. The evaluation of biological effects was studied using a self developed code based on the LEM. The LEM provides a method to evaluate cell survivals starting from the knowledge of the track dose profiles and from the photon dose response curve. The model is based on the calculation of local biological effects, it thus preserves the details of track structure without averaging of the ionization density over cellular dimensions.

In this study we show a possible procedure to disentangle of the effects of the actual set-up of the beam line, from the information stored in the radiobiological look-up tables used in a treatment planning system (TPS). In principle, new simulations are mandatory for any change in the set-up, for example, the introduction of new ripple filters in the beam line. However, this needs a long computational effort, in particular for the evaluation of the biological effects. This method permits to avoid the re-calculation of the whole radiobiological database and the relative look-up tables when we have a change in the beam line set-up. In this way the TPS can be easily adapted to different beam line setup.

2.5.1 Linear-quadratic filter approach for the biological effects

The idea is to approximate the beam line setup in a way similar to the linear filter approach described in a previous section. In general, in the linear filter approximation we assume that the output of the beam line is sufficiently similar to the *pencil-beam*, i.e. a very narrow monoenergetic beam evaluated without any element in the beam line, and that the form can be reproduced from the latter via a linear operation. The proper transfer function of the beam line can be obtained experimentally with the deconvolution of the measured dose distribution in a water phantom, D, and the distribution, D_0, of the simulated monoenergetic pencil beams in the same phantom, inverting the convolution operation $D = f * D_0$.

In the case of the equivalent biological dose, we assume a Linear Quadratic (LQ) formalism for the description of the cell survival as a function of the physical dose. In order to obtain the actual biological parameters α and β from the pencil-beam ones, α_0 and β_0, is possible to consider the convolution integral as a superposition of several infinitesimal pencil-beams and use the same kind of approach used for the evaluation of the biological effects for mixed-fields irradiations. In this approach the effective LQ parameters are evaluated as:

$$\bar{\alpha} = \frac{\sum \alpha_i}{\sum D_i} \tag{2}$$

$$\bar{\beta} = \frac{(\sum \sqrt{\beta_i} D_i)^2}{(\sum D_i)^2}, \tag{3}$$

that, applied to the linear filter formalism brings to a linear-quadratic convolution:

$$D = f * D_0 \tag{4}$$

$$\alpha = f * [\alpha_0 D_0]/D, \tag{5}$$
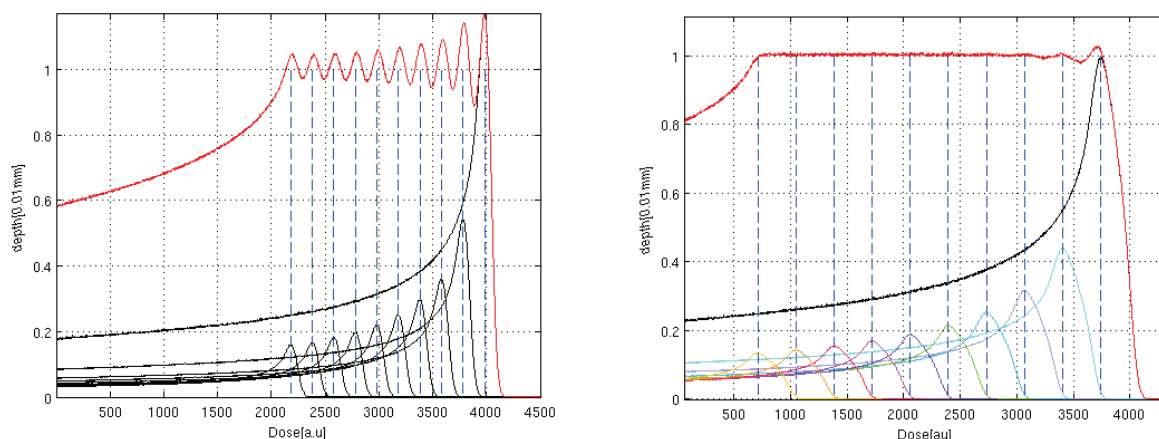
$$\beta = (f * [\sqrt{\beta^0} D^0]/D)^2, \tag{6}$$

Fig. 8. Spread out of the Bragg peak for proton beam of 70 MeV respectively without ripple filter and with ripple filter type(A) of 3 mm.

Where α_0 and β_0 are LQ parameters evaluated for the pencil-beam set-up while α and β correspond to the beam line set-up. Note that all the linear parameters are not constant but vary within the volume of interest as well as D and D_0.

2.5.2 Monte Carlo physical and biological simulations
In order to verify the linear-quadratic filter method, a set of carbon ions pencil-beams, as well as beams evaluated through a full beam delivery line are simulated. The used beam line is the beam line of the CNAO. The treated volume is simulated defining different material associated to the tissues in the head and neck region. The evaluation of biological effects was obtained using Monte Carlo simulations based on LEM (applied to Chinese Hamster Ovary (CHO) cells).
The LEM code use the particle tracks generated with GEANT4 Montecarlo simulation as an imput to evaluate the local effects in the cell nucleus. The microscopic resolution used in the simulations (of the order of the μm) for the creation of the radio biological data is very time consuming. Thus, the computational effort was performed using the distributed INFN Grid computing resources.

3. Results

3.1 SOBP calculation and dose uniformity
To evaluate the SOBP dose uniformity we overlap several curves as obtained with the simulation of a specific energy to mimic the dose delivery technique. Each curve has been displaced by a given amount with respect to the adjacent one and the dose delivered has been adjusted to obtain a flat average dose deposition. A sketch of the procedure using 10 different positions fixing the step between Bragg peaks as a function of the kinetic energy is depicted in Figure 8.
With this technique we compared the dose uniformity on the SOBP with and without ripple filters. The study was done with the ripple filter type (A) of 3 mm. For 70 MeV protons with the ripple filter and using a step of 3.36 mm the peak-to-peak dose uniformity is found to be $\pm 1\%$ error (see Figure 8). Without ripple filter the deviation increases to $\pm 15\%$ even if the step has been drastically reduced to 2 mm. Similar results for carbon ions of 100 MeV/u are reported also in Figure 9. In this figure we compare the SOBP profile for three different cases: a) no ripple filter and 0.5 mm steps; b) 2 mm type (A) filter and 1 mm steps; c) double
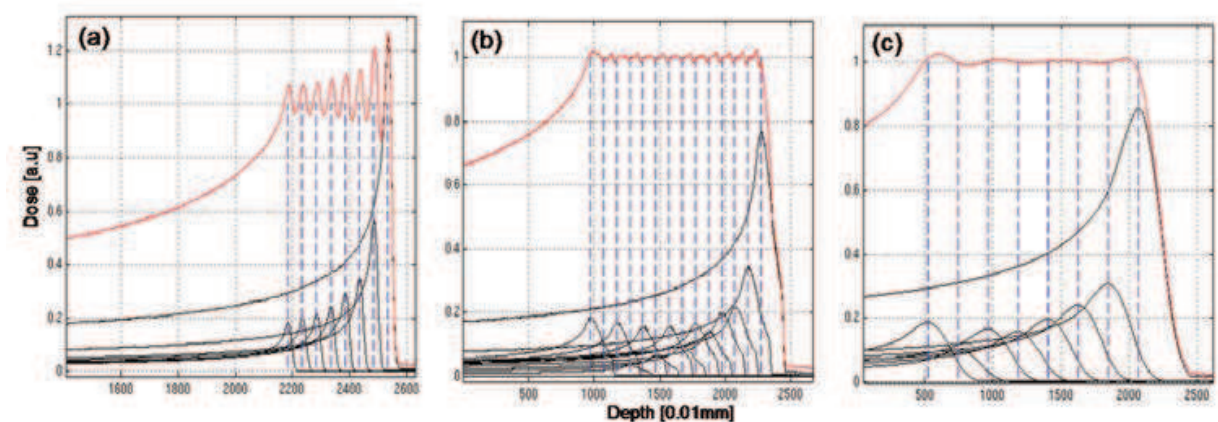
Fig. 9. Spread out Bragg peak of carbon ion beam of 100 MeV/u with: (a) pristine Bragg curve using 8 spots at 0.5 mm step, (b) Bragg curve after passing through one ripple filter type (A) of 2 mm, using 14 single spots at 1 mm step, and (c) Bragg curve after passing through two ripple filters type(A) distant 30 cm, using 8 single spots with step of 2.2 mm.

2 mm type (A) filter and 2.2 mm steps. One can clearly appreciate the improvement of the uniformity going from a) to c) even if the steps are increased from 0.5 mm to 2.2 mm.

The situation is less critic when the beam energy is above 100 MeV. In fact at 160 MeV, using the ripple filter we have a dose uniformity within ±2% and ±3.5% without filter for a scanning step of 6 mm both. For beam energy of 200 MeV the dose uniformity is not depending any more on the use of the ripple filter: we evaluated a peak-to-peak dose uniformity of ±2% with or without filter for scanning steps ranging from 3 mm to 7.6 mm.

To enhance the impact of the filtering on the widening of the Bragg peak we simulated a setup with an aligned double filter. We compared the effect of different longitudinal positions and different way of coupling two type (A) ripple filters of 2 mm to optimize the conditions of the double filtering.

As shown before, the impact of the filter on proton beams is marginal above 100 MeV, thus we checked the effect of the double filter only at 70 MeV. In Figure 10 we compare the Bragg peaks obtained with the configuration without filters to other configurations: type (A) 2 mm thick single filter, and two same type double filter configurations. In one case the filters are 2 cm apart close to the patient and in another case one filter of the pair is placed right after the exit window and the second in front of the patient (30 cm apart).

With a double filter the shape of the resulting Bragg peak is more regular and is a better approximation of a gaussian than the single filtered peak. We deduce that one way to enlarge the Bragg peak preserving the gaussian shape of the peak with a ripple filter of type (A) is to use a double filtering where the first filter should be at the exit windows of the beam and the second one as far as possible from the first. This configuration corresponds to the convolution of two linear transfer functions giving as a result a non-linear transfer function.

The final design of the double ripple filter used in the CNAO beam line is reported in Figure 11. The simulated SOBP is reported in Figure 12.

3.2 Total Scattering effect

During the commissioning phase the full characterization of the beam line and the calculation of the total lateral scattering effect of the passive elemnts, for both proton beam and carbon ion beams, is mandatory. We performed also this kind of study for the commissioning of the CNAO beam line. The results are reported in Figure 13.
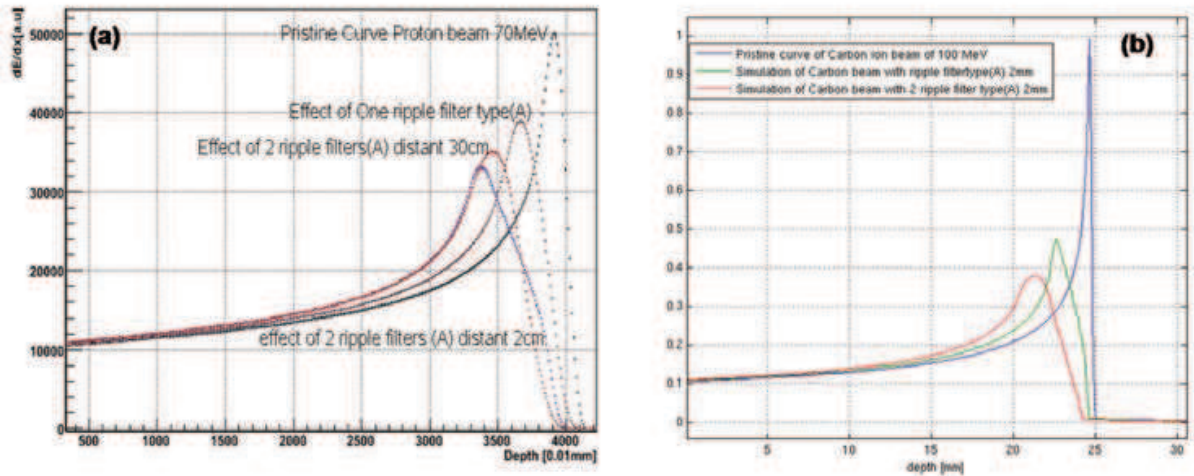
htbp

Fig. 10. a) Geant4 simulations of energy losses as functions of depth for different setting of ripple filters in the proton beam path before the water tank; b) Comparisons between depth-dose curve simulated with respectively one and two ripple filters for carbon ion beam of 100 MeV/u.
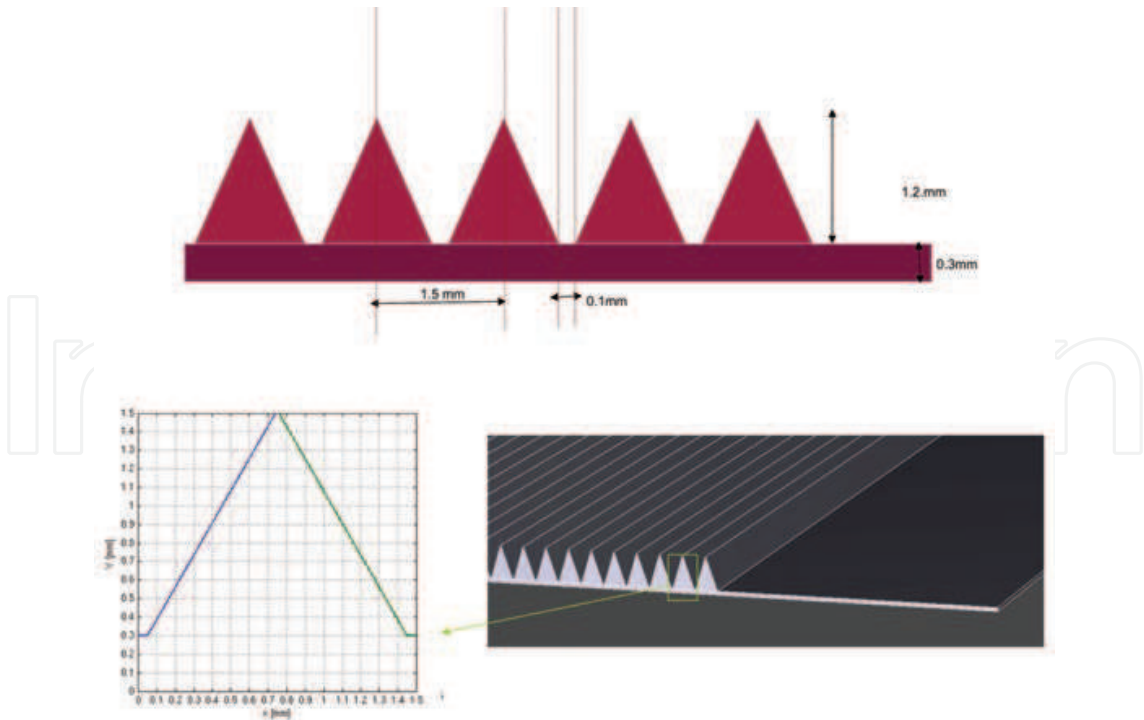

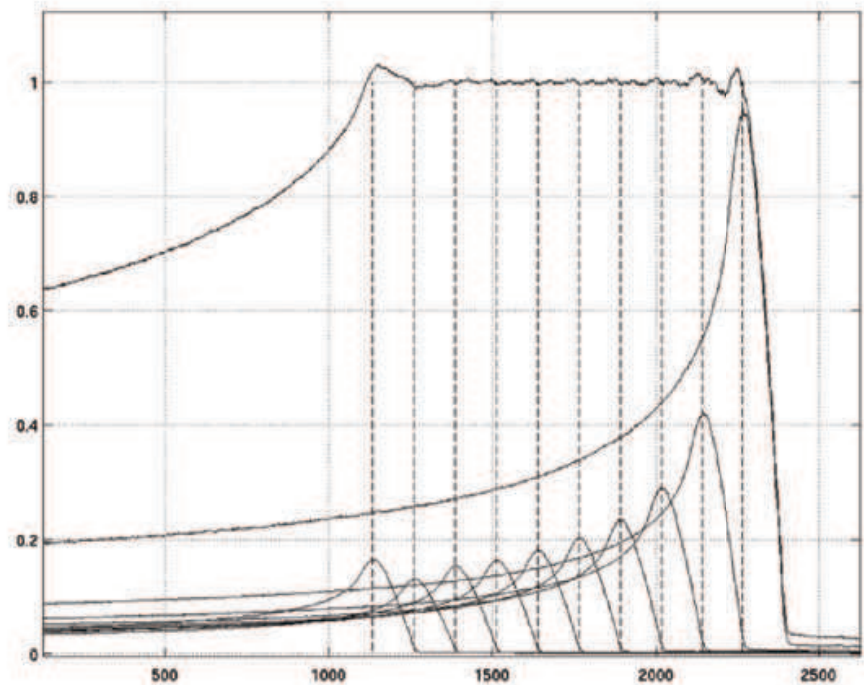Fig. 11. Final design of the couple of ripple filters for carbon ion beams.

Fig. 12. SOBP corresponding to the final design of the couple of ripple filters for carbon ion beams.

3.3 Radiobiological aspects

3.3.1 Shape of biological equivalent dose using a ripple filter

In order to verify the linear-quadratic filter method, we first studied the case of a simple beam line set-up where only one ripple-filter is inserted. The characterization of the ripple filter is obtained from the knowledge of the transfer function f that can be experimentally and also analytically determined. The result of this comparison is reported in Figure 14, where the α and β curves as a function of depth in the volume, evaluated via full Montecarlo simulations (GEANT4 + LEM), are compared with those produced with the linear-quadratic filter approach. The figure shows a very good agreement of the two methods.

We completed our analysis simulating also the complete full CNAO BDL. We verified the method through the comparison of the radiobiological MC simulations and results using the linear filter approach. The resulting evaluated profiles of the physical and biologiacl equivalent dose are reported in Figure 15.

3.3.2 Ripple filters for radiobiological measurement

Radiobiological equivalent dose is strongly depending on the accuracy of the electromagnetic and hadronic processes modeled in the simulation Monte Carlo package. For the Study of the effect of ripple filter on the shape of the Bragg peak also is important the accuracy of the radiobiological model and its parameters is more important and it has a direct impact on the final shape of dose distribution around the Bragg peak.

The radiobiological cell survival measurements at the Bragg peak have the problem of uncertainties in the positioning of cell samples in the peak region. This due to the very sharp shape of the maximum of energy deposition for carbon ion beams (the guausian fit at the peak is less than 0.1mm sigma). We designed for this specific purpose a special ripple filter
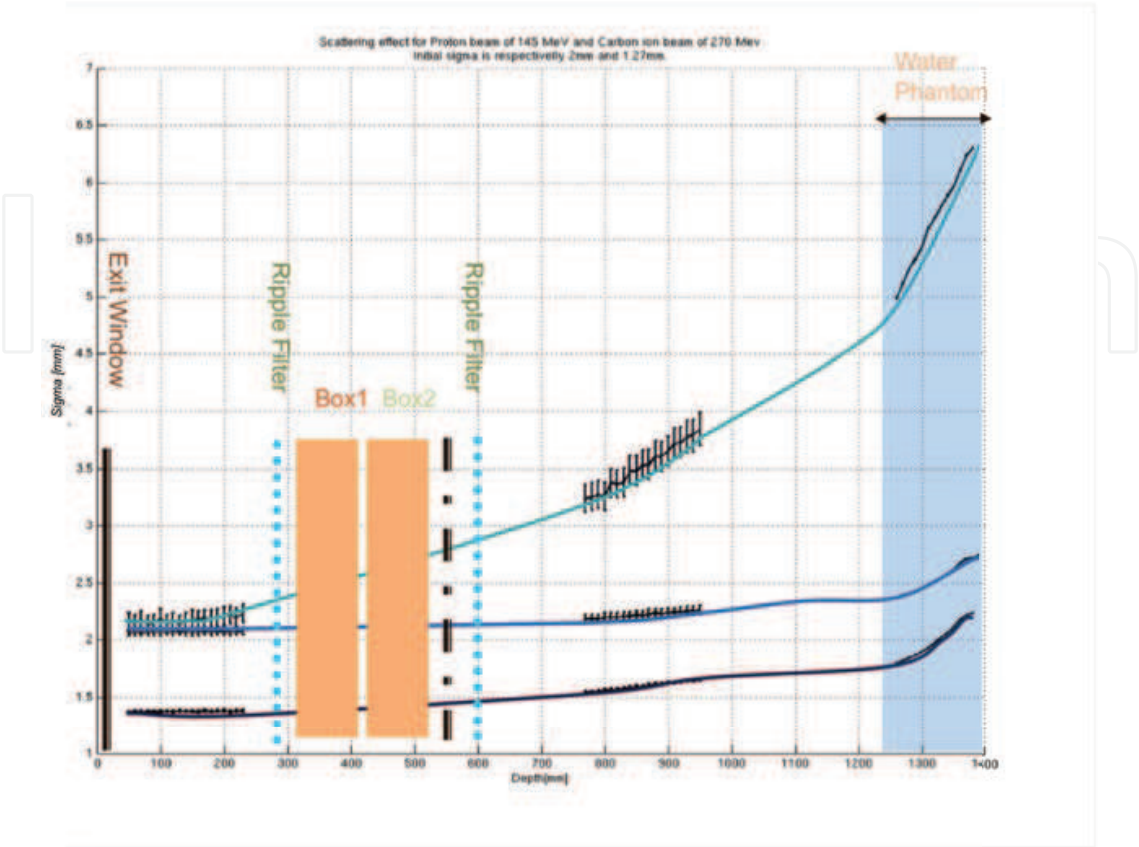
Fig. 13. Scattering effect along the beam delivery for carbon ion beam of 270 MeV/u and proton beam of 145 MeV.
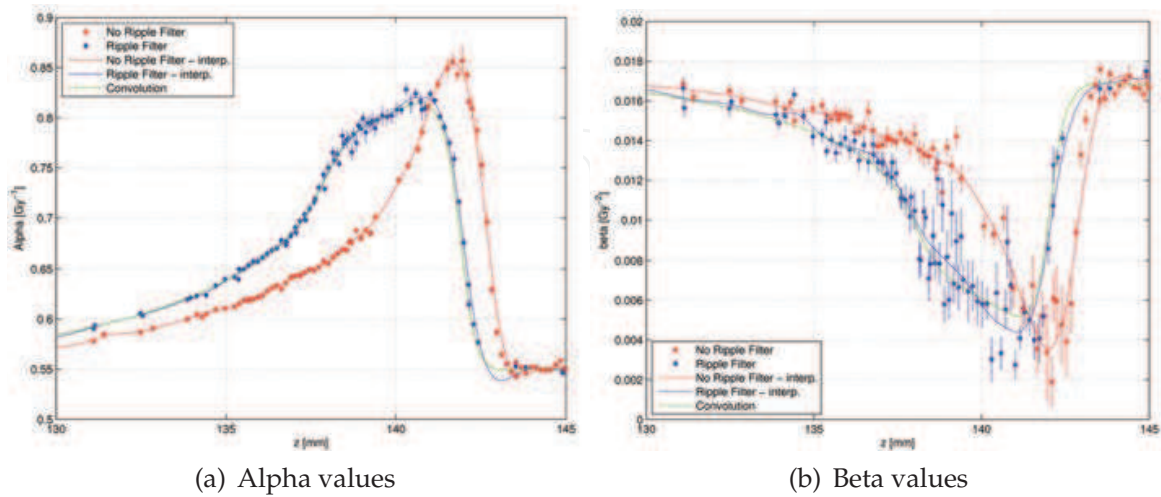

(a) Alpha values

(b) Beta values

Fig. 14. Effect of the ripple filter on the parameters α and β characterizing the biological equivalent dose for a carbon ion beam of 270 MeV/u.
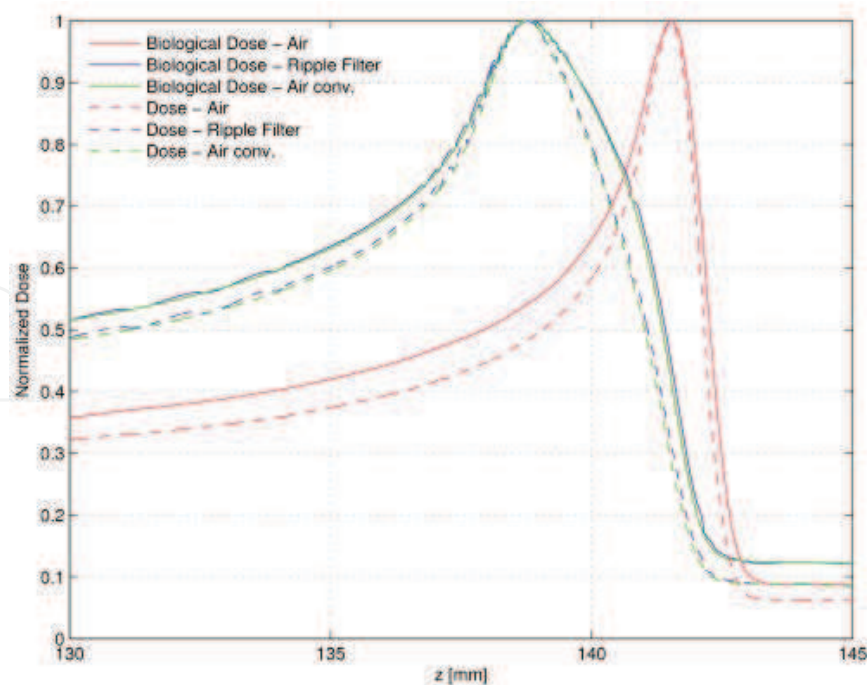
Fig. 15. . The shape of the physical dose at Bragg peak is different from the corresponding biological dose. Though the transfer functions characterizing each of the element should involve a rigorous evaluation of the biological effects.

in order to producea small broadening of the peak region to allow a more reliable positioning of cells samples. The modelization and estimation of the effects of the used ripple filter on the radiobiological response is mandatory in order to have a meaningful analysis of the radiobiological experimental data.

We used a Monte Carlo simulation with GEANT4 already benchmarked for a carbon ion beam of 62 MeV (see Figure 7). The beam line is principally composed of the following elements:the exit window, teh monitoring system, a first ripple filter and s second ripple filter. Actually instead of a detailed monitoring system (MS) we used an 'equivalent MS' in terms of water equivalent thickness. The two ripple filters are designed in such away that the Bragg peak have a guassian shape of about 0.4 mm. We built two ripple filter of 0.75 mm thickness each, and with a triangular shape (see Figure 16).

4. Conclusion

Monte Carlo simulations are a powerful tool helping in the optimization of resources during the design phase of the BDL, particularly in the field of advanced radiation therapy technique, where the accuracy of the dosimetric analyses is a crucial step for an accurate delivery of the treatment to the patient. Furthermore it is a powerful means to estimate the radiobiological effect of heavy ion beams when crossing different elements of the BDL.

The aim of this work is creating a flexible tool for full characterization of the beam delivery line including the biological impact. This characterization can be used in the TPS for modeling the possible effects of the passive elements in the beam line and to design new elements of the beam line. A step in this characterization consists in defining the transfer function and the linear filters related to the beam line elements.

Usually the passive elements on the beam line are optimized only for physical dose profiles. However, it is necessary to consider the biological effect and their impact on the dose
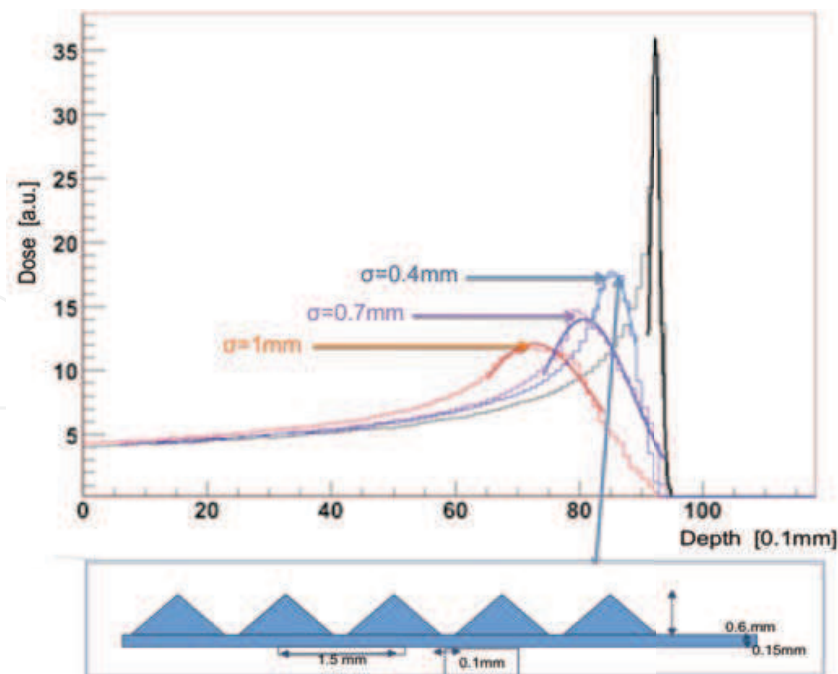
Fig. 16. Design of ripple filters for radiobioilogical measurments with carbon ion beams.

distribution, especially in the Bragg peak region for a correct estimation of the peak spread. A full characterization of the beam delivery line considering the biological impact provides a flexible tool in the treatment planning system for modeling the possible effects.

We estimate the impact on the relative biological effectiveness (RBE) and the biological dose distribution of the passive elements of the beam delivery line. The shape of the physical dose at Bragg peak is different from the corresponding biological dose. Though the transfer functions characterizing each of the element should involve a rigorous evaluation of the biological effects and to evaluate the correct shape of the effective dose.

In particular a biological linear-quadratic transfer function can be a flexible tool in a TPS, for a complete modeling of the biological effect, and in the design and the analysis of radiobiological measurements of cell survival around the Bragg peak region.

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This volume is an eclectic mix of applications of Monte Carlo methods in many fields of research should not be surprising, because of the ubiquitous use of these methods in many fields of human endeavor. In an attempt to focus attention on a manageable set of applications, the main thrust of this book is to emphasize applications of Monte Carlo simulation methods in biology and medicine.

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