^{12}C nuclear reaction measurements for hadrontherapy.

B. Braunn, M. Labalme,G. Ban, J.Colin, D. Cussol, J.M. Fontbonne, F.R.. Lecolley, C. Pautard.
LPC Caen, France
F. Haas, D. Lebhertz, M. Rousseau, L. Stuttge
IPHC Strasbourg, France
M. Chevallier, D. Dauvergne, F. Le Foulher, C. Ray, E. Testa, M. Testa.
IPN Lyon, France
M.D. Salsac
CEA/IRFU/SPhN Saclay, France

Abstract

Hadrontherapy treatments require a very high precision on the dose deposition (±2.5% and ±1-2mm) in order to keep the benefits of the precise ions' ballistic. The largest uncertainty on the physical dose deposition is due to ion fragmentation. Up to now, the simulation codes are not able to reproduce the fragmentation process with the required precision. To constraint the nuclear models and complete fragmentation cross sections databases; our collaboration has performed an experiment on May 2008 at GANIL with a 95 MeV/u ^{12}C beam. We have measured the fluence, energy and angular distributions of charged fragments and neutrons coming from nuclear reactions of incident ^{12}C on thick water-like PMMA targets. Preliminary comparisons between GEANT4 (G4BinaryLightIonReaction) simulations and experimental data show huge discrepancies.

1 Introduction

Hadrontherapy consists in irradiating cancerous tumours with light ions (mainly p and ^{12}C), from 80 to 400 MeV/u. Compared to conventional radiotherapy, it presents two main advantages: a maximum of dose deposition at the Bragg peak and, for ions heavier than protons, an enhanced biological efficiency in the Bragg peak region.

Hadrontherapy treatments require a very high precision on the dose location in order to keep the benefits of the precise ions' ballistic. The energy amount deposited at the tumour and its location have to be determined with an accuracy of 1-2 mm and 2.5% respectively. The largest uncertainty on physical dose deposition relies on the ion fragmentation processes along their penetration path in the patient tissues (Ref. [1]). Fragments produced in these reactions contribute to the delocalization of a non-negligible proportion of the dose in the surrounding healthy tissues and a decrease of the dose at the tumour as shown in Fig. 1. Moreover, nuclear reactions along the path of the ions lead to an attenuation of the primary beam flux and an increase of lower Z fragments, with an increasing penetration depth, (in treatments less than 50% of incident carbon reach the tumour). These fragments contribute to the deposited dose in the Bragg-peak and must be taken into account for the biological dose evaluation.

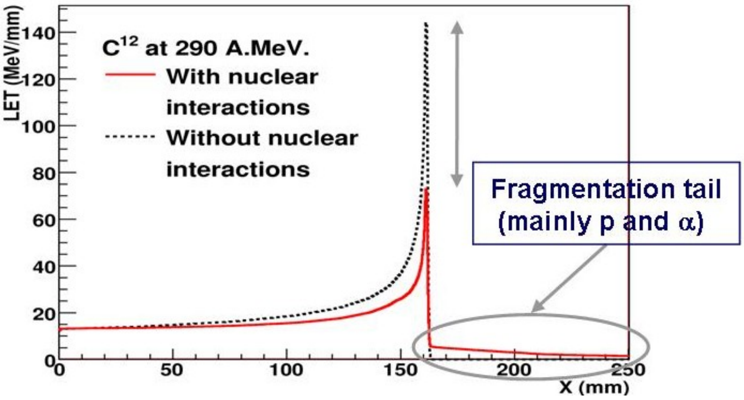

Fig. 1: GEANT4 simulations of the dose deposited in water with (full line) and without (doted line) activating nuclear reactions

Simulation codes are used to calculate the transport of ions in matter for hadrontherapy applications. They include deterministic codes: TRiP (developed at GSI Ref. [2][1]) or HIBRAC (Ref. [3]) and Monte Carlo codes: SHIELD-HIT, FLUKA, GEANT4, PHITS… (Refs. [4-6]). Experimental data, like the dose profile and Bragg peak depth (20 mm), are quite well reproduced by these codes. However, the accuracy is not sufficient to obtain a precision of about 2.5% on the deposited dose. The largest uncertainty on the dose calculations is due to the limited experimental data and to the subsequent uncertainties on fragmentation's cross sections that are critical inputs for these transport codes. Indeed, few experimental cross section data are available for light ions on light target in the energy range 30-250 MeV/u. The data used by transport codes are empirically extrapolated from experimental values at higher energies. Thus, to severely constrain the physics models used in the hadrontherapy (Z:E) range, fragmentation cross section measurements are absolutely needed.

To improve the knowledge of ^{12}C fragmentation, measurements have been achieved in Japan and in Europe. Measurements of light charged fragment production in water since 2003 have been started by Japanese treatment centres (Chiba & Hyogo). They have performed complete measurements of carbon ions fragmentation in water phantoms in the energy range 200-400 MeV/u (Refs. [7-9]). Similar measurements have also been performed by the GSI biophysics department: light charged ions and neutron production by fragmentation of a carbon beam in water in the energy range 150-400 MeV/u (Refs. [10-12]). All these measurements allow the determination of the integrated flux and energy distributions of the fragments according to the water depth. These data could be directly implemented in treatment planning systems (TPS) and/or compared to nuclear reaction codes.

An integral experiment, with a 95 MeV/u ^{12}C beam on PMMA targets has been performed by our collaboration on May 2008 at GANIL to complete the fragmentation data in the whole range of hadrontherapy energies.

2 Experimental Set-Up

The aims of our integral experiment are to determine the fluence and the energy distributions of light charged fragments and neutrons in ^{12}C collisions on PMMA tissue equivalent targets at 95 MeV/u and to estimate the uncertainties due to the extrapolations used by simulation codes.

It has been performed with the CHARISSA collaboration reaction chamber, ECLAN, at the GANIL G22 beam line. The setup is composed of five ΔE/E telescopes for charged particles detection and four DEMON detectors for neutrons measurements (cf. Fig. 2). The targets are set on a rotating wheel in the centre of the reaction chamber. The wheel support six PMMA—$C_5H_8O_2$; d=1.19 g/cm^3—targets of different thicknesses: 5, 10, 15, 20, 25 & 40 mm and an empty slot; the Bragg peak depth for 95 MeV/u ^{12}C is of 20 mm in PMMA.

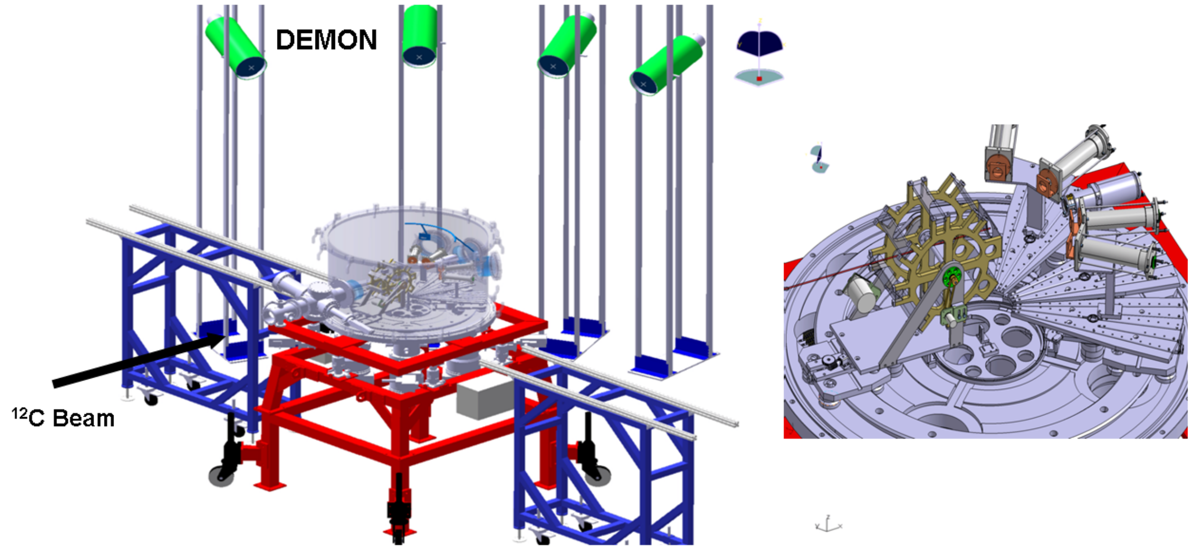

Fig. 2: Schematic views of the experimental set up. Right side: zoom on the inner part of the chamber.

2.1 Charged particles detectors

The experimental set-up included five three stages ΔE/E charged particle telescopes placed inside the reaction chamber, 20 cm behind the outside front of the targets. Each of them is mounted on the rotating arm of the ECLAN reaction chamber as shown on right side of Fig. 2. The covered angle from is from 0° to 70° with an acceptance of 4 mSr.

The five ΔE/E detectors are composed of two 300 mm^2 Si stages—80 µm & 500 µm thick—followed by one scintillator. Four of them are composed of a CsI scintillator—7.5 cm thick, 3 cm in diameter—and the forward angles telescope (covering angles from 0 to 10°) is composed of a BGO scintillator—7.5 cm thick, 2.5 cm in diameter— in order to measure protons up to 220 MeV.

2.2 Neutrons detectors

The setup included four neutron detectors based on DEMON detector modules. They allow measuring the all neutrons energy range (from 3 to 250 MeV) at four different angles: 18°, 28°, 46° and 70°. The four DEMON detectors are equipped with the charged particles veto detectors SYREP.

The detectors are composed of a cylinder—20 cm thick, 16 cm in diameter—filled with NE213 liquid scintillator. The neutron energy is determined by a time-of-flight technique and the discrimination from γ is achieved by a pulse shape analysis. They are placed outside of the reaction chamber, 260 cm behind the targets. This ToF distance and the GANIL cyclotron frequency lead to a neutron detection threshold of 6.7 MeV.

2.3 Beam monitor

The beam monitor is a critical tool for the accuracy of the cross section measurements. It is based on fluorescence X rays measurements emitted by a thin Ag foil—7 µm thick— placed in the beam before the reaction chamber. X rays are detected thanks to two detectors—Si(Li) & Ge—placed at 90°. These two detectors are calibrated at low beam intensity by means of a Scintillator+PM placed in the beam. Such a monitor is particularly well suited in the 10^4-10^9 ions/s intensity range and has given a precision of ~5% on the beam intensity during our experiment.

3 Data analysis and simulations

Data analysis is still under completion. Production rates and energy distributions, from proton to carbons, have been successfully measured at different angles (from 0 to 70°) for the six PMMA thicknesses (5 to 40 mm). Production rates and energy distributions of neutrons have also been measured at 4 angles.

Preliminary comparisons between GEANT4 (G4LightIonReaction activated for ion inelastic reactions; Ref [13]) simulations and experimental data are presented in this section.

3.1 Neutrons

The four DEMON detectors placed at 18, 28, 46 and 70° allow the discrimination between neutrons, gamma and charged particles. The time of flight analysis give the energy of the neutrons. Due to the ToF distance and the GANIL cyclotron frequency, the neutron detection threshold is of 6.7 MeV.

The neutrons energy spectra have been obtained behind the six PMMA thicknesses at the 4 angles. Figure 3 shows an example of energy distribution measured (prior to DEMON efficiency correction) for a 2 cm thick PMMA target at four angles. Enclosed is the DEMON efficiency for three different energy cuts: 2.5, 3 and 3.5 MeVee. The 3.5 MeVee cut corresponds to the neutron energy threshold of 6.7MeV. The production of neutrons is forward peaked and they reached energies up to 250 MeV at forward angles.

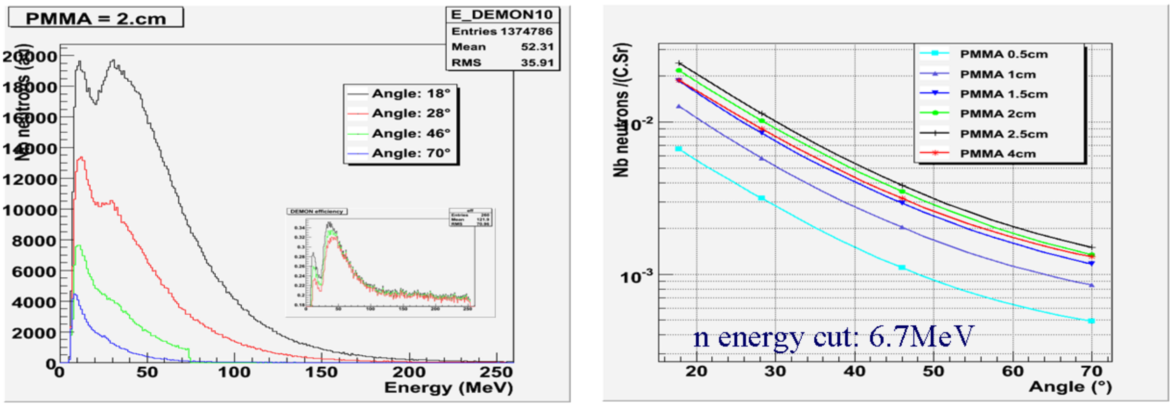

Fig. 3: Preliminary results. Left side, neutron energy spectra measured by the four DEMON behind the 2 cm thick PMMA target. Right side, production rates (per incident ^{12}C and Steradian) for the six PMMA thicknesses with a neutron energy threshold of 6.7 MeV

The neutrons distributions measured at 18, 28, 46 and 70° are shown on the right side of Fig. 3 for the six different targets thicknesses. These results have been obtained with a stactistical precision better than 5% at all angles. They emphazized, the increased of the neutron production with the PMMA thickness, up to 25 mm (^{12}C Bragg peak: 20 mm) following by an attenuation and an angular dispersion of the neutrons for the thickest—40 mm—PMMA target.

These results are still preliminary, the systematic errors have to be evaluated and the results compared to simulations.

3.2 Charged particles

The calibrations of the 5 telescopes is achieved, discrimination in Z has been obtained for the forward telescope with the BGO scintillator and discrimination in A for the four other.

The energy dependence with Z has been obtained for the six PMMA thicknesses and ~10 angles. Figure 4 shows two examples of Z=1 and Z=2 energy spectra measured at 7° for incident ^{12}C on a 20 mm thick PMMA target. Protons have been obtained with energies >200 MeV at forward angles. The experimental results are compared to GEANT4 simulations (G4LightIonReaction activated for ion inelastic reactions).

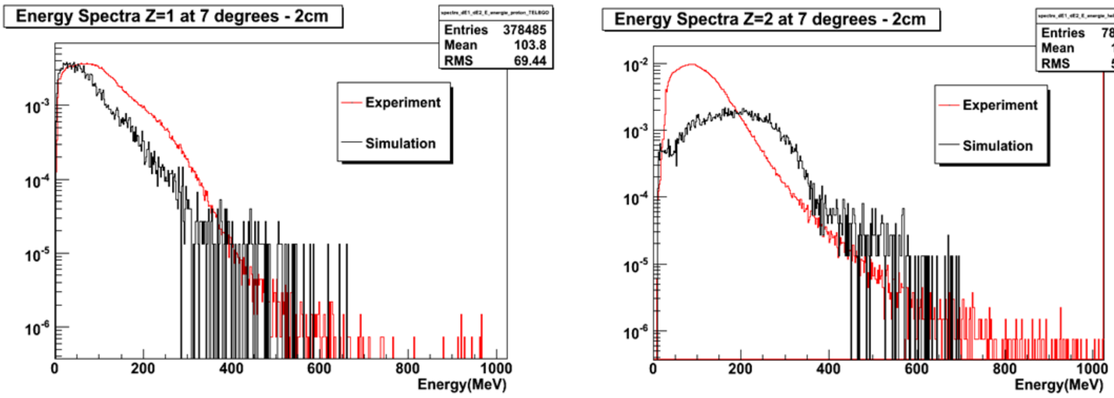

Fig. 4: Energy spectra measured by the 7° telescope behind the 20 mm thick PMMA target.
Left side: Z=1; Right side: Z=2.

Figure 4 clearly shows that GEANT4 (G4LightIonReaction) do not reproduce energy distributions. This is also the case for heavier particles and all the angles. That emphasised the inability of GEANT4 simulation to reproduce the energy distribution of charged fragment emitted during a hadrontherapy treatment.

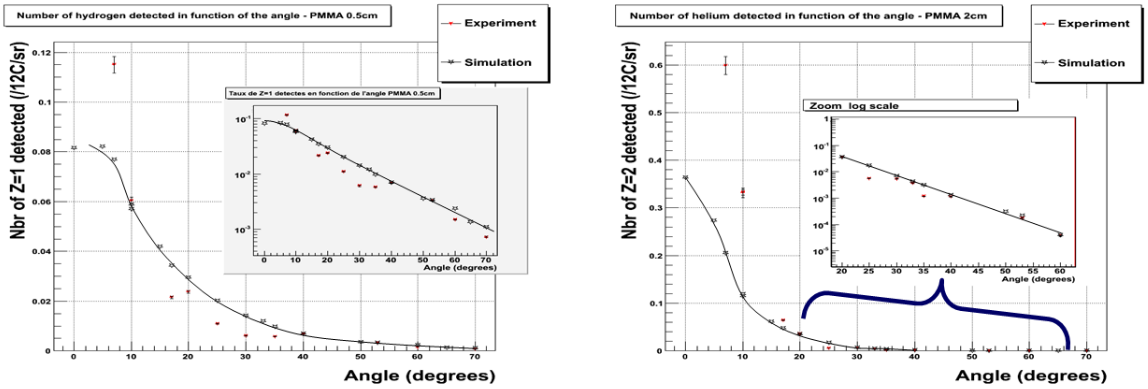

Fig. 5: Angular distributions of Z=1 (left side) and Z=2 (right side) production behind respectively targets of 5 mm and 20 mm thicknesses (only statistical errors are represented in this figure).

As shown in Fig. 5, GEANT4 do not reproduce the angular distribution of the particle productions. For the two angular distributions presented in Fig. 5, GEANT4 clearly underestimate the production of Z=1 and Z=2 at forward angles for all the PMMA thicknesses.

Figure 6 shows the production of charged fragments from Z=1 to Z=6 at 10° behind two PMMA thicknesses. These production rates have been obtained with statistical errors better than 5%. The preliminary estimation of the systematic errors are of the order of 10% for Z≥2 and 25% for Z=1.

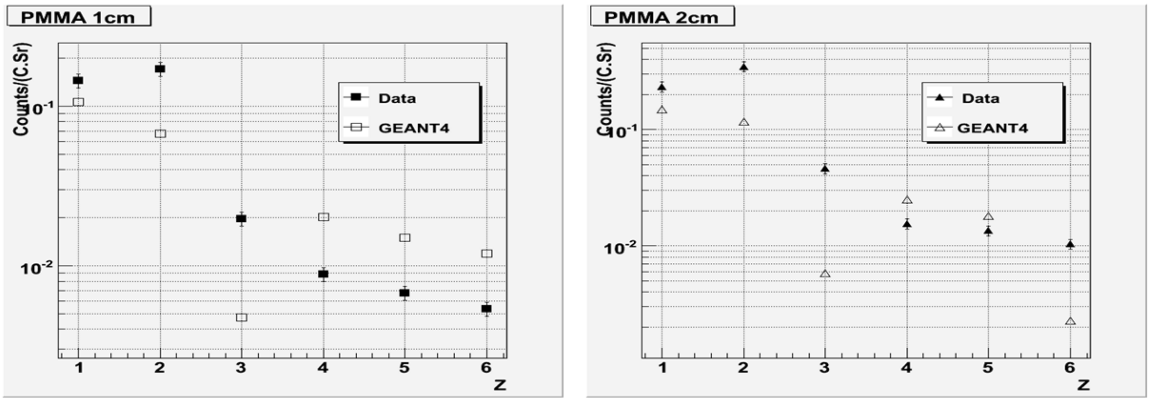

Fig. 6: Preliminary comparison between experimental data—full symbol—and GEANT4 simulations data—open symbol— of charged fragments productions (from Z=1 to 6) behind two PMMA thicknesses: 10 and 20 mm

Preliminary comparisons between Geant4 simulations (G4LightIonReaction for ion inelastic reactions) and experimental data show huge discrepancies especially for the production of Z=3 that is not reproduces at all. A clear underestimation of Z=2 is also emphasized that could be explain by the underestimation of the α-cluster structure of the ^{12}C by the G4LightIonReaction model of GEANT4.

The experimental results and the simulations are still preliminary but energy spectra and particle productions are not reproduced by GEANT4 simulations (discrepancies of a factor 2 and even more for Z=3) whatever the angle is.

4 Conclusion and outlooks

A first integral experiment has been achieved at GANIL in 2008 with a 95MeV/u ^{12}C incident beam on thick PMMA targets. Preliminary results have been obtained for six different PMMA thicknesses from 5 to 40 mm—Bragg peak depth: 20 mm—. The energy spectra and production rates have been measured for neutrons at four angles (18, 28, 36 & 70°) and for charged particles (protons to carbons) at 10 angles (0 to 70°).

Preliminary comparisons performed with GEANT4 (G4LightIonReaction) simulations emphasized discrepancies with experimental data. Extensive comparisons with Geant4 simulations have to be achieved in order to evaluate the accuracy of its different hadronic models (INCL4+ABLA, QMD, GEMINI, SMM, Fermi Break-Up) by activating or de-activating specific physical processes (e.g.: G4BinaryLightIonReaction, G4BinaryCascade, G4QMD…).

The experimental results will also be compared to other Monte Carlo codes like Fluka and HIPSE and to transport codes with different nuclear reaction models activated and/or used to develop a new model for “hadrontherapy like” nuclear reactions

These results will allow completing the fragmentation production data at ~100MeV/u and could be integrated in treatment planning systems (TPS). They have shown the inability of simulations to reproduce the dose deposition with the 2.5% required accuracy. It emphasizes the necessity to improve the nuclear reaction models by measuring double cross section data on thin target for C-C, C-O, C-H and C-Ca reactions in the hadrontherapy energy range (80-400MeV/u) with a ~10% accuracy. Our collaboration will propose new experiments on thin targets at GANIL: C-C, C-H, C-O, C-Ca… at 95 MeV/u (2010-2013).

References

[1] D. Schardt et al., *Adv. Space Res.* **17** (1996): 87-94.

[2] Jäkel et al., *Physica Medica* **XIV/1** (1998): 53–62.

[3] Tsao et al., *Phys. Rev. C***47** (1993): 1257

[4] Gudowska et al., *Phys. Med. Biol.* **49** (2005): 1933-1958

[5] Pshenichnov et al., *Phys. Med. Biol.* **50** (2005): 5493-5507

[6] La Tessa et al. 2007

[7] Matsufuji at al., *Phys. Med. Biol.* **48** (2003): 3393-3403.

[8] Matsufuji et al., *Phys. Med. Biol.* **50** (2005): 3393-3403.

[9] Toshito et al., *Phys.Rev. C* **75** (2007): 054606

[10] Shall et al., *NIM. B* **117** (1996): 221.

[11] Gunzert-Marx, *Rad. Prot. Dosim.* **110** (2004): 595-600.

[12] Gunzert-Marx et al., *New J. Phys.* **10** (2008): 075003.

[13] http://geant4.web.cern.ch/geant4/UserDocumentation/UsersGuides/PhysicsReferenceManual/fo /PhysicsReferenceManual.pdf.