NUCLEAR REACTIONS IN HUMAN-LIKE TISSUES DURING PROTON THERAPY*

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During particle therapy, the beam of protons or heavier ions can induce secondary particles, like neutrons, or produce radioisotopes, which decay with emission of β and γ radiation. These provide information about the beam or the tissues and are at the origin of an additional dose to surrounding tissues. This work is mainly focused on secondary neutrons that can interact with a tissue by indirect ionization or induce different nuclear reactions, *e.g.* $^{12}\mathrm{C}(n, n2\alpha)^{4}\mathrm{He}$, which may result in high biological effectiveness. The neutron flux induced by a proton beam was estimated using a GATE/Geant4 simulation for the calculation of neutron energy spectrum, and the Neutron Activation Analysis (NAA) method. Additionally, the cross sections for the $^{12}\mathrm{C}(p, np)^{11}\mathrm{C}$ reaction were measured.

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1. Introduction

The increasing number of patients that are treated with hadron therapy motivates experiments dedicated to studying the secondary or minor effects of this treatment and detailed knowledge of the radioisotopes produced in tissues during irradiation becomes more relevant. The most important secondary particles are the neutrons. Figure 1 shows the energy distribution of neutrons produced in a 1 cm thick average human tissue during proton irradiation. This spectrum was calculated using GATE/Geant4 with a physics list based on the Liège Intranuclear Cascade model (INCLXX). In the same figure, the quality factor of the neutron beam is presented that indicates how unsafe are the neutrons with a given energy.

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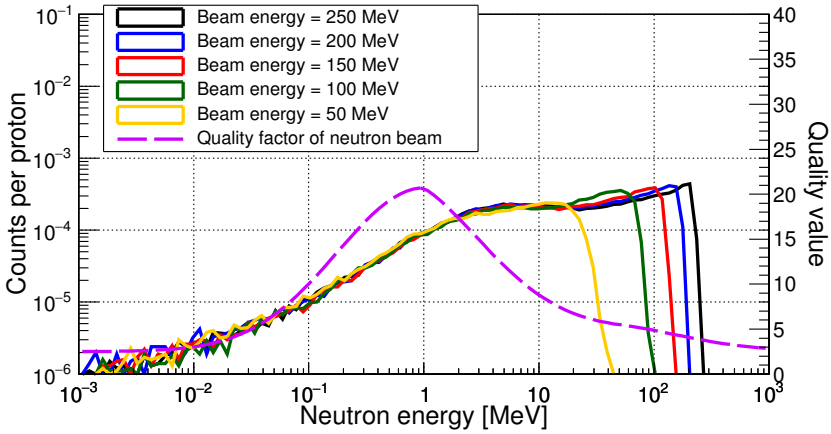

Fig. 1. (Colour on-line) Neutron energy spectrum for different energies of the proton beam interacting with a 1 cm thick averaged human tissue. Calculations were done using the GATE/Geant4 toolkit [1, 2] with the INCLXX physics list. The dashed/purple line presents the quality factor of the neutron beam.

In 2018, Cirrone *et al.* [3] have observed that a little amount of ^{10}B and ^{11}B added to the tissue unexpectedly increases the effectiveness of irradiation. The explanation of this phenomenon is related to the induced radioactivity in the irradiated tissues during hadron therapy and its influence on the treatment effects. Up to now, it is assumed that the dose and various effects originating from the secondary radiation (induced by the primary beam nuclear interaction) are negligible and can be completely omitted in the planning of particle therapy treatment. This simplification seems to be too strong and the effects of secondary radiation have to be quantitatively studied.

The main goals of the present project are:

1. Identification of isotopes produced during irradiation using γ-ray spectroscopy and lifetime measurements;

2a. Determination of the amount of produced radioisotopes;

2b. Reconstruction of the spectrum of neutrons originating from the tissues;

3. Appraisal of the additional dose from radioactive interactions;

4. Estimation of the biological effects of the additional dose.

2. Materials and methods

To achieve the above-mentioned goals, various techniques are needed. For the measurement of induced radioactivity in tissues and estimation of the cross sections for radionuclide production, a stack of human-like tissue targets (sixteen 2 mm thick samples placed one on another) was prepared, irradiated by a proton beam with a dose in the range from 30 Gy to 500 Gy and measured using a set-up presented in Fig. 2. During the experiment, a pair of $LaBr_3$:Ce [4] and a pair of NaI detectors with lead shields were used. The data acquisition system for the $LaBr_3$:Ce detectors was based on Caen DT5790, which is a complete digital acquisition system including an HV power supply. In the case of the NaI detectors, a standard acquisition system based on an amplifier (Silena7611) and an MCA (Tukan8K) was used.

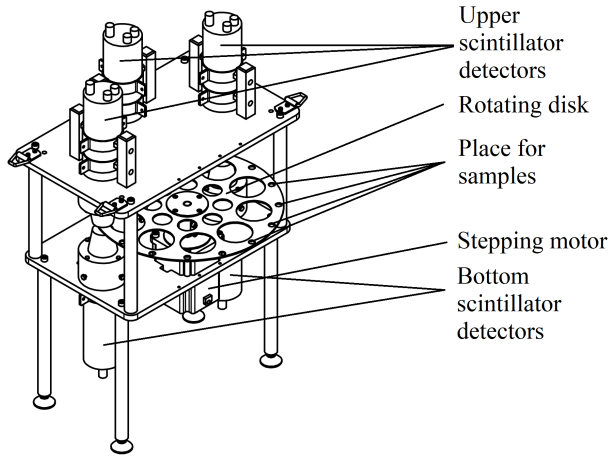

Fig. 2. Measurement set-up with rotating disk for up to 16 samples and up to 6 detectors. The activity of up to three samples can be measured simultaneuously using 3 pairs of detectors (two detectors per sample are needed to measure the activity using coincidence and anti-coincidence techniques).

The other aim of the present project is to measure the yield of neutrons emitted during particle therapy using the Neutron Activation Analysis (NAA). The targets for such measurements were designed in a geometry as follows: a cylindrical tissue (soft and removable part) was surrounded by a metal pipe (stiff part). The idea was to irradiate the tissue by protons, but not the stiff part of the target, which is neutron-sensitive. The preparation of the target samples for this experiment was challenging because of two reasons: (1) the neutrons are not exclusively produced in the human-like tissues and (2) the target is activated by the proton beam in a similar way

as by the neutrons. To mitigate the first effect, two sets of targets were prepared, with and without the tissue. The latter was irradiated to estimate the neutron flux emitted from the beamline, including the collimator. For radiological reasons, the proton beam was stopped in a paraffin block located behind the neutron target. The diameter of the proton beam was around 25 mm and to eliminate the second effect, a collimator was used to reduce the beam spot to a size slightly smaller than the diameter of tissue in the target. The scheme of the target geometry is presented in Fig. 3. During the experiment, a pig liver was chosen as the soft part (*tissue* in the figure) while steel, Cu and Al were used as the stiff one (*absorber* in the figure).

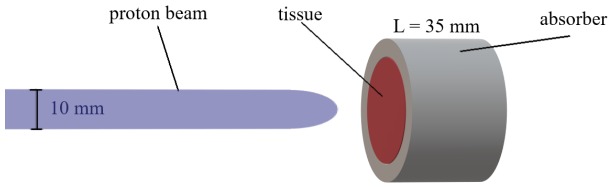

Fig. 3. Irradiation geometry for neutron spectrum measurements.

The irradiations were performed at the Institute of Nuclear Physics of the Polish Academy of Science. A 60 MeV proton beam delivered by the AIC-144 accelerator was used. The targets were placed in the eye radiotherapy treatment room using a brass collimator, which reduced the beam diameter to 10 mm.

3. Measurements

To estimate the neutron flux using the NAA method, literature data on the products of neutron interactions (*e.g.* energies of emitted γ rays, half-lives) were used (see Table I).

TABLE I

Nuclear reactions used for the neutron spectrum estimation with information about their product decay and the neutron energy threshold.

Reaction	Half-life [h]	Decay type	E_γ [keV]	I_γ [%]	E^{thresh} [MeV]
^{65}Cu(n,p)^{65}Ni	2.52	β^-	1481.8	23.5	3.95
^{56}Fe(n,p)^{56}Mn	2.578	β^-	846.8	98.9	5.40
^{27}Al(n,α)^{24}Na	15.0	β^-	1368.6	100	6.75
^{63}Cu(n,3n)^{61}Cu	3.408	β^+	656.0	10.1	22.5
^{54}Fe(n,3n)^{52}Fe	8.275	β^+	168.7	99.2	27.45

After the irradiation, the stiff parts of the targets (without the tissue material) were placed on a HPGe detector. In the spectrum of γ rays emitted from steel (figure 4), beside the lines coming from the decay of ^{52}Fe and ^{56}Mn, a very strong annihilation peak is observed, which originates both from the decay of ^{52}Fe and those of the radioisotopes that were produced by strongly scattered protons.

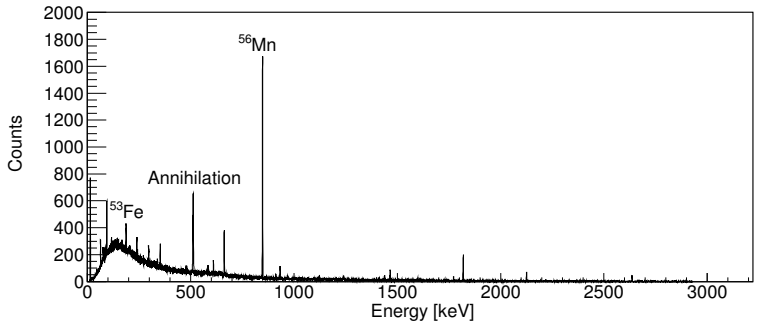

Fig. 4. Gamma-ray spectrum of the steel sample irradiated together with a tissue.

4. Results

Figure 5 presents the decay in time of two γ-ray lines: 656 keV and 846.8 keV, emitted from ^{61}Cu and ^{56}Mn, respectively. The measured ^{56}Mn activity (right graph in figure 5) is higher for a tissue-filled target than for an empty cylinder, while for ^{61}Cu an opposite trend was observed. Additionally, one can see that the number of counts for the ^{61}Cu decay is lower than that for ^{56}Mn. The most probable reasons of such situation are (1) thermalization of neutrons in the non-irradiated part of the tissue and (2) emission of neutrons along the beam direction.

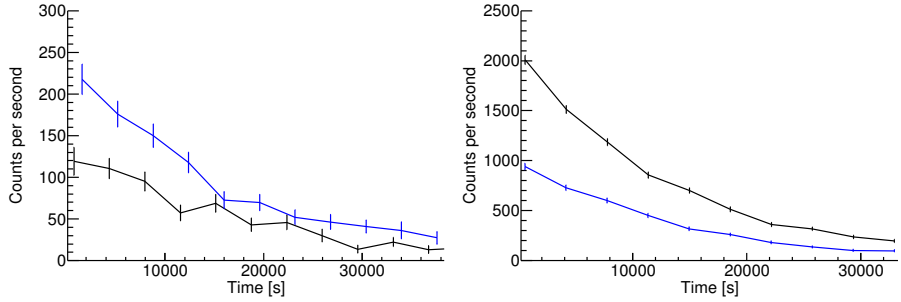

Fig. 5. (Colour on-line) Decay in time of two γ-ray lines, coming from the decay of ^{61}Cu (left) and ^{56}Mn (right). In grey/blue and black, the data for targets irradiated without and with a tissue, respectively.

The metal part of the targets is reached only by thermal neutrons. In the case of steel, which is an alloy that contains 10% of Mn, the most abundant isotope of manganese, ^{55}Mn, can easily capture thermal neutrons. Furthermore, because of a cylindrical shape of the neutron-sensitive part of the target, most neutrons escape without interaction with this part.

In order to estimate the cross sections for the production of radionuclides in tissues, an additional test was performed. The target was composed of a stack of natural carbon pellets, which were irradiated with a dose of 30 Gy. The measurement lasted for 3 hours, but significant signals could be observed during the first 100 minutes. Each sample was measured for 2 minutes. Very preliminary results are presented below (figure 6).

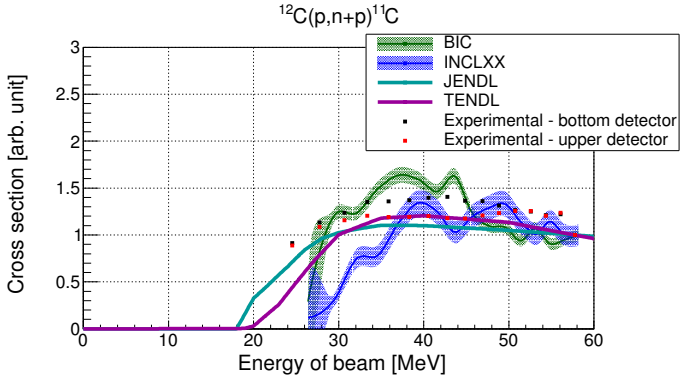

Fig. 6. Comparison of relative cross sections for experiment (points), simulation (bands) and theory (solid lines).

The experimental results are in quite good agreement with the theoretical calculations as well as with the simulation. The simulation was performed using the Geant4/GATE package with the BIC or INCLXX physics lists. The analysis of the experimental data for tissues is in progress.

5. Conclusions

The designed set-up has been verified to provide accurate data for cross-section measurements. The obtained cross sections for the $^{12}\mathrm{C}(p,np)^{11}\mathrm{C}$ reaction agree quite well with the theoretical predictions. The NAA method is very useful for the neutron spectrum analysis. For future studies, the target geometry should be modified, as in the present work the neutron flux was probably absorbed in the tissue, which suggests that the target should be thinner. The results of the present project, combined with those of our earlier work [5] will provide an estimate of the contribution of secondary radiation to the biological effectiveness.

6. Forthcoming research

New measurements will be performed to collect better statistics for tissues and other materials. For the neutron spectrum analysis, the geometry of the target will be modified. During irradiation for NAA, the neutron flux will be measured simultaneously using liquid scintillator detectors based on the BC-501A scintillator. There are also plans to perform irradiations with more energetic protons (> 60 MeV) and heavier beams (*e.g.* α or ^{12}C).

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