VA Gribkov^{1,2*}, M Chernyshova³, AA Talab⁴, GG Giannini⁵ and F Longo⁵

¹A.A. Baikov Institute of Metallurgy and Material Science, Russian Academy of Sciences, Moscow, Russia

²The Abdus Salam International Centre for Theoretical Physics, Trieste, Italy

³Institute of Plasma Physics and Laser Microfusion, Warsaw, Poland

⁴Atomic Energy Authority, NRC, Plasma Physics and Nuclear Fusion Department, Egypt

⁵Department of Physics, University of Trieste, Trieste, Italy

*Corresponding Author: VA Gribkov, A.A. Baikov Institute of Metallurgy and Material Science, Russian Academy of Sciences, Moscow, Russia.

Received: June 05, 2019; Published: June 25, 2019

Abstract

The Dense Plasma Focus device "Bora" belonging to the Abdus Salam International Centre for Theoretical Physics, Trieste, Italy, has been used for experimental activity in the field of bio-medical applications, in particular for a specific modification of the boron-capture neutron therapy of cancer. The main goal was to provide investigations of the spectra changes by various moderators, in particular by plates made of tungsten. Thicknesses of the W plates were 43 and 83 mm. The blocks have been installed in the direction from the neutron source to the fast probe - a photomultiplier tube with a plastic scintillator. Measurements and calculations (carried out by means of the Geant4 toolkit) of time delays and shapes of the neutron pulses at different distances for two types of moderator materials have been provided with an aim to obtain by a time-of-flight technique its energy spectrum. The ultimate goal of the researches was to find a proper material and its thickness to fulfill demands that are necessary for the shock boron neutron capture therapy that is believed may overcome difficulties met by the classical technique.

Keywords: Neutron Pulse; Boron Neutron Capture Therapy; Cancer

Introduction

The Boron Neutron Capture Therapy [1] is a part of radiation therapy and it is one of the promising methods intended for treating of malignant tumors (in particular brain neoplasms) developing side by side with surgery, chemotherapy, hormone therapy, immunotherapy or a mixture of the four. It belongs to the type with the high linear energy transfer (LET) irradiation, which is the rate of energy loss along the path of an ionizing particle. It is based on the nuclear reaction on the non-radioactive boron-10, which makes up approximately 20% of natural elemental boron:

 ${}^{10}B + n \rightarrow [{}^{11}B^*] \rightarrow \alpha + {}^{7}Li + 2.31 \text{ MeV}$ (1)

To explore this reaction the boron-10 must be delivered into the cells of a malignant tumor but not to the surrounding normal tissues. To the moment a number of the delivery agents are under investigations [2]. Among them there are several ones that are quite promising, in particular those that are used nanoparticles in combination with antibodies (immunoglobulin). However, only two from these agents have currently been used in clinical trials. The first one is a polyhedral borane anion, sodium borocaptate or BSH ($Na_2B_{12}H_{11}SH$), and the second one is a dihydroxyboryl derivative of phenylalanine, referred to as boronophenylalanine or BPA.

Two main demands have to be fulfilled in the BNCT treatment: efficacy and selectivity. For the first point the dose must be 60-70 Gy. It is possible to have with present-day sources during the appreciable time period. For resolving of the second problem the difference in saturation by boron of malignant (concentration must be $20 - 50 \mu g/g$ in tumor) and disease-free cells should be about 20. Yet the existed agents are able to make it on the level of not more than 5 only. That is the main problem of classical BNCT.

Citation: VA Gribkov., et al. "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". EC Clinical and Medical Case Reports 2.4 (2019): 115-126.

Side by side with the action of neutrons according to the reaction (1) neutrons can produce the low LET gamma rays, resulting primarily from the capture of thermal neutrons by normal tissue hydrogen atoms [${}^{1}H(n,\gamma){}^{2}H$]. Hard X-rays and gammas may also appear during an irradiation of a tumor from the sources of neutrons (reactors and accelerators). These low LET radiations (photons) may produce in malignant cells free radicals that can also result in apoptosis of the cells yet not so effective.

All products of the above reactions - the alpha particles, the lithium nuclei, free radicals and electrons - produce ionizations in the immediate vicinity of the reaction point, with a range of 5 - 10 μ m, which is approximately the characteristic size of the target cell. Additionally, selectivity of irradiation action may also be fulfilled by a special profiling of the neutron beam used for irradiation (so-called computational dosimetry and treatment planning [4]).

From the above-mentioned one may see that the main problem in BNCT of cancer is currently an execution of an increase of the selectivity factor in irradiation of malignant cells preserving living tissues unperturbed [3]. This task is mainly decided by investigation of new boron delivery agents. But we have proposed another approximation.

Pulsed BNCT

It was found [5] that three demands are important for the shock-like pulsed neutron treatment of a cancer by the boron-neutron capture therapy:

- 1. To obtain after the moderation a neutron spectrum of the type "epithermal" (energies should be in the range 0.5 eV -10 keV, but not more than 100 keV) when cross-section with the boron-saturated tissue is still high enough and at the same time a penetration depth to the human tissue (e.g. into brain) is relatively long (a few cm).
- 2. To preserve the neutron pulse duration after the above-mentioned moderation much less than the chemical reaction time with free radicals (about 1 μs) to gain a synergy effects with powerful shock-like action upon a tissue (see [6]).
- 3. Not to lose too much in the neutron stream intensity.

The main feature differs a so-called "pulsed radiation chemistry in its perfect sense" from continuous and long-pulse or short-pulse/ low-dose irradiation is the criterion that can be formulated in two principles kept simultaneously [6]:

- Micro-volumes of activity of primary (neutrons, X-ray photons) or secondary (nuclear reaction products, protons, α-particles, solvated electrons, free radicals) particles must be overlapped within the tissue (e.g. overlapping of spurs and blobs)
- 2) This overlapping must be fulfilled during the time interval short compared with duration of chemical/bio-chemical reactions (transformations) induced by the irradiation (e.g. duration of reaction with free radicals taking time of more than 1 microsecond).

One of the devices able to generate fusion neutrons (of 2.5- and 14-MeV energies) and X-rays (with 0.1...600.00-keV photons) during very short (1...50 nanoseconds) and powerful pulses is the device named "Dense Plasma Focus" (DPF) [7]. The interval of the bank energy feeding these devices is ranged from $E_b \sim 1$ J to ~ 1 MJ. It is an ecologically clean (of a "push-button" type and working at a somewhat low voltage - 10...25 kV), compact, relatively cheap device able at the same time to ensure dose power up to $10^8...10^9$ Gy/min in neutrons and $10^9...10^{10}$ Gy/min in X-rays [7,8].

Our analysis [5] has shown that a DPF has the following opportunities in its application for radiation therapy of cancer patients.

DPF devices of the medium size (5-10 kJ, ~ $1 \div 2 - m^2$ foot-print) can ensure the necessary dose of neutron irradiation in about 3 hours working with a moderator (epithermal neutrons) if it will be operated with a repetition rate of 100 cps with D₂ or with 1 cps with D-T mixture as a working gas. Devices of this scale with water-cooled electrodes and anode orifices have been tested successfully up to 16 cps and during a quarter of a million of shots without wearout replacements [9]. One of the innovative future possibilities to increase intensity of the neutron beam and simultaneously to localize its action in the wanted place (besides a collimation) is connected with using several Dense Plasma Foci all at once irradiating the tumor from different sides. It seems possible with medium-sized devices with $E_b \sim 5$ kJ and neutron yield $Y_n \sim 10^{11}$ of 14 MeV neutrons per pulse of about 10 ns width or a few times bigger (say of 30 kJ and 10^{12} n/pulse).

Citation: VA Gribkov., *et al.* "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". *EC Clinical and Medical Case Reports* 2.4 (2019): 115-126.

The large DPF of the energy of several hundred kJ (occupying $\sim 20 - 30 \text{ m}^3$ volume) operating with the D-T mixture at 1 cps will be able to make this job in a few minutes. In the work [8] we found that there is almost no difference in consequences of neutron irradiation of dissimilar bio-test objects by a DPF or a neutron generator of classic type or a fission reactor operating below the above-mentioned dose power ($\leq 10^9 \text{ Gy/min}$).

It is already an important result opening an opportunity to use in neutron therapy this 20-kV compact and cheap device instead of less ecologically friendly, expensive and cumbersome fission reactors, isotopes and MeV-accelerators. However one can expect here some synergetic effects with DPF if it will be used either with just fast/epithermal neutrons of the nanosecond (ns) pulse duration producing high concentration of their secondary products (α -particles and Li nuclei and/or free radicals) in cells or at the combined application of fast/epithermal neutrons and hard X-Rays for a suppression of malignant cells at the dose power exceeding 10⁹ Gy/min.

Possible reasons for these expected effects are:

- A simultaneous break of both spirals of DNA (double-strand rapture) and diffusion of rubbles during the ns period of time produced by a high-intensity neutron flux and/or a high concentration of secondary products of nuclear reactions on boron and of free radicals;
- A threshold-like behavior of radiation damage of malignant cells within a neutron field having a high concentration.

The last opportunity, which might increase a selectivity and efficacy of the neutron therapy, must be explained here in more details.

Indeed at present time chemicals used for an increase of boron capture by malignant tissues of the intracranial tumors for the subsequent BNCT provide an increase of boron concentration in cancerous cells as it was mentioned above by about \leq 5 times higher compared with the living cells (e.g. blood) due to different penetrability of their blood-brain barriers and because of some other reasons [10] instead of necessary 20.

However if we shall ensure the above-mentioned overlapping of micro-volumes of activity of secondary particles at the irradiation in the case of the action of present-day chemicals in the malignant cells only - but not in the living tissues (due to the above-mentioned 5-times boron concentration difference) - in that case we might have the expected synergetic effect. It could be managed in the analogy with our previous experiments where such effect was observed in the case of the low LET X-ray photon irradiation of enzymes and photoresists [5,6,11].

Both the above opportunities open ways for a low-dose (and probably a single-pulse) therapy of cancer. However, to start experimental works we need to clarify several important questions that can be modeled by numerical calculations.

Numerical simulations

In this work we focus on the development of a detailed simulation of interaction of short-pulse radiation from a DPF with a moderator to estimate output spectrum and pulse duration for this dynamic case.

Geant4 [12-15] is a Monte Carlo toolkit for the simulation of the passage of particles through matter. It is one of the first main high energy physics (HEP) software tools to use the methods of Object Oriented Programming (in C++). It is developed and maintained by the international Geant4 Collaboration. Its application areas include high energy and nuclear physics, medical physics, dosimetry, accelerator developments and space physics experiments.

Two different DPF configurations were simulated. They differ mainly for the external dimensions. While the first one generates a spectrum of "quasi"-monochromatic neutrons of 2.45-MeV energy, the second one is usually used to generate also almost mono-energetic neutrons of the energy peaked at 14 MeV. Full width at half maximum (FWHM) of the spectral distribution of neutrons is about 3 - 5% of the maximal energy of them for both cases. Use the Geant4 toolkit allowed simulating both configurations without changing the rest of the Monte-Carlo Software.

Citation: VA Gribkov., et al. "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". EC Clinical and Medical Case Reports 2.4 (2019): 115-126.

The evaluation of the FluentalTM moderator size was done by means of the above simulation. A pulse of quasi monochromatic neutrons (with an energy spread - FWHM of 3 - 5%) was generated at the center of the DPF device, where the plasma column was situated. The size of the moderator is critical to generate epithermal isotropic neutrons (suitable for BNCT applications) as well as for changing the time profile of the neutron spectra. The latter parameter is the most crucial one, since to use the expected synergetic effect of the neutron pulse and probably in a combination with the X-ray pulse both generated by the DPF, and then not too much affected by the moderator, we need the neutron pulse duration to remain well shorter than 1 μ s.

Figure 1 shows the results of the application of a 5-cm Fluental[™] moderator on the small chamber of the Bora device (see below), while figure 2 shows the effect of a 15-cm Fluental[™] moderator on the same device.



Figure 1: Energy spectrum of neutrons obtained by simulating a monochromatic neutron pulse of 10 ns of 2.45 MeV in the small chamber of the "Bora" device with the 5-cm FluentalTM moderator.



Figure 2: Energy spectrum of neutrons obtained by simulating a monochromatic pulse of 10 ns of 2.45-MeV neutrons in the small chamber of the "Bora" device with 15 cm Fluental[™] moderator.

Citation: VA Gribkov., et al. "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". EC Clinical and Medical Case Reports 2.4 (2019): 115-126.

Both the outgoing neutron spectrum and its time profile are shown. It is clearly seen that with the 15-cm layer the amount of epithermal neutrons is greatly increased.

Our simulations have also shown that similar moderation could be done when using a tungsten moderator. In figure 3 similar results are presented for the large chamber of the "Bora" device. This time a 15-cm tungsten moderator was used with the 14.5 MeV quasimonochromatic neutron pulse of the same pulse shape as above (10 ns). A comparison of 5 and 15 cm thicknesses in log-log scale is also presented for better impression on thickness influence on appearance of epithermal neutrons. Comparisons with experimental data are then foreseen to validate the present results.



Figure 3: Neutron energy spectrum obtained by simulating a monochromatic neutron pulse of 10 ns of 14.5-MeV energy in the large chamber of the "Bora" device with 15 cm tungsten moderator: the comparison of two energy spectra are presented in log-log scale for 5 cm (the upper curve) and 15 cm (the lower one) of tungsten moderator thicknesses.

The most important results of this set of calculations can be summarized as follows:

- Thickness 15 cm of both moderators used (Fluental[™] and tungsten) convert almost monochromatic initial spectra of neutrons generated by DPF with pure deuterium and deuterium-tritium mixture as working gases into spectra with well-developed epithermal "tails" (yet having an appreciable number of fast neutrons)
- 2) Use of both types of moderators makes neutron pulse duration longer; however in both cases their full widths at half maximum (FWHM) remain shorter than the duration of chemical reactions with free radicals (that is $\sim 10^{-6}$ seconds or more).

As it was mentioned above the resulting spectra have in our cases a sizable component of fast neutrons. However, there is a number of works published in literature that is devoted to this point. Some of the authors count a combination of fast and epithermal neutrons as a good tool to improve treatment of brain tumors.

Experimental Results

We have provided experimental investigations of changes in time behaviour and spectrum of neutron streams that pass from the Bora device through a tungsten moderator (See figure 4).

Citation: VA Gribkov., *et al.* "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". *EC Clinical and Medical Case Reports* 2.4 (2019): 115-126.



Figure 4: Configuration of the experiment on measurement of modifications in neutron pulse duration and spectrum after passing the neutron radiation through the tungsten moderator.

We installed near the small DPF chamber filled with pure deuterium one or two tungsten plates having thicknesses of 40 and 44 mm correspondingly. We placed our PMT+S probe at different distances from the assembly of DPF+W moderator. The idea is to measure an increase in neutron pulse duration produced by the moderators when the PMT+S probe is placed in close vicinity to the assembly "DPF + moderator". At the same time a long distance between the source + moderator and the PMT+S probe (large time-of-flight - TOF - base) will give us information on the spectrum modification. The experimental results are presented in subsequent figures.

The measured by means of PMT+S time of flight can easily be recalculated into the energy of this neutron group producing the neutron pulse maximum by a formula (2) taking from [16,17]:

$$E_{MeV} = (72.24 \, l_m / t_{ns})^2 \tag{2}$$

where neutron energy E_{MeV} is in [MeV], distance l_m is in [m] and time t_{ns} is in [ns].

In figure 5 one may see a typical oscilloscope traces (OT) obtained from magnetic probes installed near each of the 4 capacitors of the Bora device.



Figure 5: OTs from MPs taking current derivative curves from each of 4 capacitors of the device.

Citation: VA Gribkov., et al. "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". EC Clinical and Medical Case Reports 2.4 (2019): 115-126.

A typical neutron pulse observed in a certain distance from the DPF chamber after its passage through the tungsten plate moderator is presented in the figure 6.



Figure 6: The oscilloscope trace (OT) of a neutron pulse obtained after its penetration through a moderator plate made of tungsten of a thickness equal to 43 mm; the PMT+S probe is situated in this case in a distance of 464 cm from the chamber of the Bora device.

Cables' lengths from magnetic probes (MP) and PMT were selected in a manner to compensate the delay in time of operation of the PMT.

The DPF chamber has been positioned vertically. So, the neutrons were observed in the perpendicular direction to the Z axis of the chamber and they have their peak energy near 2.5 MeV.

Without tungsten moderator and at a distance of PMT+S fast probe from the DPF chamber 20 cm the arrival of the vertical front of the hard X-ray (HXR) pulse delayed to its appearance inside the chamber of Bora device by 0.67 ns (what is << of temporal resolution of the PMT+S) whereas for 2.5-MeV neutron pulse this delay is equal to:

$\Delta t_n = 72.24 \cdot 0.2 / \sqrt{2.5} = 9.14 \text{ ns} \approx 10 \text{ ns}$

Experiment has shown that the beginning of the neutron pulse is delayed in relation to the HXR pulse front by 30 ns whereas its maximum at the mean neutron pulse duration of 40 ns additionally delayed by 20 ns (in a sum by 50 ns). At the same time the HXR pulse front is coincide with the beginning of the current abruption phenomenon [18] (with a precision of the time resolution of both detectors - PMT+S and MP - \approx 3 - 5 ns).

For epithermal neutrons with energy 10 keV (or 100 keV) = 0.01 MeV (or 0.1 MeV):

$t_{ns} = 72.24 \times 8.89 / \sqrt{0.01} (0.1) = 6422 \text{ ns} (2032 \text{ ns}) = 6.4 (2.0) \ \mu\text{s}$

Our measurements of signals with and without blocks of W moderators and at different distances from DPF Bora chamber to the PMT+S probe have given the results as follows.

Without W; l = 0.2 m (See figure 7)

Date: 23.07.2014, Set 3, shot No 6, Neutron yield $Y_n = 130$ counts.

Two pulses are clearly seen at the figure 7*c* - the hard X-ray (HXR) pulse and the neutron one. Front of the HXR pulse (practically vertical) coincides with the moment of the current abruption phenomenon (with the first peak of the current derivative peculiarity -

Citation: VA Gribkov., *et al.* "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". *EC Clinical and Medical Case Reports* 2.4 (2019): 115-126.

lower OT). Duration of the HXR pulse at its pedestal is $\Delta t_{_{HXR}} = 10$ ns. Delay of the neutron pulse beginning to the moment of the abruption is 40 ns (in reality inside the chamber of PF-6 - (40 ns - 10 ns = 30 ns)). Its duration at the full width of half maximum is 40 ns (so its spatial size is a bit less than 1 m) whereas Δt_n (pedestal) = 60 ns.



Figure 7: OT of current derivative (3 signals from 3 magnetic probes - MP - a), one OT of current derivative (the lower sweep) versus PMT+S signal (the upper OT) showing synchronization, and the OT of HXR (the first one) and of neutron (the second one) pulses.

With W plate of 44 mm thickness; *l* = 0.2 m (See figure 8)

23.07.2014, Set 4, No 7. $Y_n = 147$

HXR pulse is absent (due to absorption in the W block). Delay of the beginning of the neutron pulse to abruption (first current derivative peak): 90 ns (in reality inside the chamber of the Bora device: 90 ns - 10 ns = 80 ns) and for its maximum - 110 ns (100 ns). Its duration at the full width of half maximum is 55 ns whereas Δt_a (pedestal) = 130 ns.



Figure 8: OT of current derivative (4 signals from 4 magnetic probes - MP - a), one OT of current derivative (the lower sweep) versus PMT+S signal (the upper OT) showing synchronization, and the OT of HXR (the first one) and of neutron (the second one) pulses.

With W plate of 84 mm thickness; l = 0.2 m (See figure 9)

23.07.2014; Set 7, No 7; Y_n = 364

HXR pulse is absent (absorption in the double W block). Delay of the beginning of the neutron pulse to abruption (the first current derivative peak): 120 ns (in reality inside the chamber of the PF-6: - 120 ns - 10 ns = 110 ns) and for its maximum - 140 ns. Its duration at the full width of half maximum is 47 ns (so its spatial size is about 1 m) whereas Δt_a (pedestal) = 110 ns.

Citation: VA Gribkov., *et al.* "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". *EC Clinical and Medical Case Reports* 2.4 (2019): 115-126.

23.07.2014; Set 8 No 9; Y_n = 284: Delay of the beginning of the neutron pulse to abruption (the first current derivative peak): 110 ns (of its maximum - 140 ns). Its duration at the full width of half maximum is 32.5 ns whereas Δt_n (pedestal) = 120 ns.



Figure 9: OT of current derivative (4 signals from 4 magnetic probes - MP - a), one OT of current derivative (the lower sweep) versus PMT+S signal (the upper OT) showing synchronization, and the OT of HXR (the first -double - one) and of neutron (the second one) pulses.

Thus, in the close vicinity of the PF-6 chamber (20 cm) the duration of the neutron pulse is increased by a factor of about 2 times mainly due to its pedestal (a long tail of the pulse). But the value of the neutron pulse duration after the two-fold W moderator of 84 mm thickness is much lower than the typical time interval for the chemical and bio-chemical reactions with boron.

Then we have moved PMT+S to the distances 194 cm and 464 cm from the PF-6 chamber and repeated measurements of the same type. In these distances the OTs of neutron pulses represent a mixture of temporal and spectral features.

After these steps we have placed the fast probe PMT+S at the location of 889 cm apart from the PF-6 chamber. So, in this case the TOF distance is about an order of magnitude higher than the spatial size of the neutron pulse. It means that we can expect in this case a transformation of the temporal behavior of the neutron pulse into its spectral distribution because of conversion of neutrons' speeds into distances (and, eventually, into the temporal distribution).

First we put the PMT+S probe at a distance of 1.94 m from the DPF+moderator assembly. Here we obtained the oscilloscope trace of the neutron pulse shown in figure 10.



Figure 10: Oscilloscope trace of the neutron pulse obtained at the distance 1.94 m after the double-plate moderator.

Citation: VA Gribkov., *et al.* "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". *EC Clinical and Medical Case Reports* 2.4 (2019): 115-126.

From this figure one may see that in this relatively close vicinity to the moderator our neutron pulse change its duration in a very small degree: the FWHM in its peak appeared to be equal to 24.5 ns. Yet the pulse obtained a relatively long tail (about 200 ns) as a result of the neutron spectrum moderation. But still we can establish that its duration is preserved on the level that is much shorter compared with the duration of chemical and bio-chemical reactions with free radicals (that are > 1 μ s).

Then we moved our PMT+S fast probe from the source to the longer distances. In figure 11*a* the oscilloscope trace (50 ns per division) is presented for the case when a TOF base l_{TOF} is equal to 4.64m and the x-ray and neutron pulses are registered without moderator. Taking into consideration that usually a neutron pulse peak inside the DPF chamber of Bora device appears at $\Delta t \approx 10$ -20 ns later in comparison with the peak of hard X-ray pulse, calculations with using a formula (2) show that the energy of neutrons in its peak is about 2.5 MeV. It is expected for the neutrons irradiated in a side-on direction to Z-axis of the DPF chamber. At this regime and in this very "shot" (a discharge) of the DPF Bora operation the neutron pulse duration was about 13 ns (FWHM).



Figure 11: Oscilloscope trace of hard x-ray and neutron pulses in different conditions for the distance from the source to the PMT+S probe equal to 4.64m.

The same calculations for Figure 11*b* (200 ns per division) when we preserved our PMT+S probe in the same distance from the source but the trace was registered with the above-mentioned moderator (84 mm of tungsten) gave us for TOF a figure $t_{TOF} \approx 800$ ns. Calculations using formula (2) have shown that neutron energy in the pulse peak is equal to $E_n = 180$ keV. It means that we have obtained a noticeable moderation of neutrons energy. The total pulse duration (at the level 0.1 of its amplitude) increased up to 435 ns (\approx 200 ns FWHM). Besides, at this situation the "tail" of the neutron pulse was extended till the 1.4 µs. It means that the energy of the appreciable amount of neutrons at the end of this tail are decreased till the value $E_n < 50$ keV (it is already a range of the "epithermal" neutrons). However here we have to mention that taking into consideration our original neutrons pulse duration these figures are still not gave us a pure spectrum of neutrons. Rather they combine temporal and spectral characteristics of the neutron radiation.

Then we moved our PMT+S probe to the TOF base equal to 8.89 m. We obtained here the oscilloscope traces shown in figure 12.



Figure 12: Oscilloscope traces obtained for the distance from the source to the PMT+S probe equal to 8.89 m: a) - without tungsten blocks, b) with 2 tungsten plates of 84-mm total thickness.

Citation: VA Gribkov., et al. "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". EC Clinical and Medical Case Reports 2.4 (2019): 115-126.

At this distance in a majority of shots the hard X-ray pulse was very weak or even absent due to strong absorption and scattering in tungsten. So, we have made synchronization for the Figure 12*b* by means of the signal of a current derivative as above.

Again in figure 12*a* we have here a neutron signal obtained without moderator. One may see that the pulse duration was increased till the value about 16 ns (FWHM).

The analogous oscilloscope trace obtained with the two plates of tungsten at this distance is shown in figure 12b.

From the trace number 2 (red) it is possible to determine the TOF of neutrons along this base and to calculate corresponding values of energy. It appears to be equal:

- 750 ns and 730 keV for the beginning of the pulse
- 937 ns and 470 keV for the beginning of its peak
- 1387 ns and 210 keV for the end of its peak, and
- 1681 ns and 140 keV for the tail of the pulse.

It means that the visible part of the neutron pulse here has duration of about 1 μ s. In the trace No. 4 a part of the pulse (100 ns) is represented with better time resolution. One may see that the pulse has an oscillatory character. It should be mentioned here that relatively poor sensitivity of our probe does not give us an opportunity to see a presence of epithermal neutrons (10 - 50 keV) at this last TOF base.

Conclusions

- It is shown that the Shock-like Boron Neutron Capture Therapy (SBNCT) been a promising approach in brain cancers treatment strongly depends on feasibility of three indispensable conditions under application of powerful nanosecond neutron flashes from Dense Plasma Focus devices: moderation of energy of fast fusion neutrons till epithermal values; preservation of neutron pulse durations after the above-mentioned moderation with values much less than the chemical/biochemical reaction time with free radicals (about 1 μs) to gain a synergy effects with powerful shock-like action upon a tissue; keeping the neutron stream intensity in a maximal degree.
- 2) Results of the Geant4 application for modelling of the moderation effects at usage of tungsten and Fluental[™] moderators has demonstrated the possibility of using these materials of moderate thicknesses for the task with good results in all three abovementioned directions for the powerful nanosecond pulses of 2.5- and 14-MeV neutrons generated in a Dense Plasma Focus (DPF) device.
- 3) The Dense Plasma Focus device of medium energy storage (up to 6 kJ in a battery) Bora (ICTP, Trieste, Italy) is fitted for examination of the problems under discussion.
- 4) Experiments on investigation of changes produced by tungsten moderator in the neutron pulse delay time, its duration and in spectra of neutron pulses passed through the W blocks of 44 and 84 mm thickness has shown a possibility to ensure the demanded conditions.
- 5) Numerical and experimental results with tungsten moderators appeared to be in a reasonable qualitative agreement.

Acknowledgement

This research was provided partially in the frame of the R.F. state task no. № 075-00746-19-00 and was supported by the International Atomic Energy Agency (grants IAEA CRP nos. 17167, 19248, 19253, 22745 and 23664).

Bibliography

- 1. Moss RL. "Critical review with an optimistic outlook on boron neutron capture therapy (BNCT)". *Applied Radiation and Isotopes* 88 (2014): 2-11.
- 2. Barth RF, et al. "Boron delivery agents for neutron capture therapy of cancer". Cancer Communications 38.1 (2018): 35.

Citation: VA Gribkov., *et al.* "Moderators Influence on the Short Powerful Neutron Pulse in View of their Applications in the Shock Boron Neutron Capture Therapy of Cancer". *EC Clinical and Medical Case Reports* 2.4 (2019): 115-126.

- 3. Yu TL. "Prof. Rolf F. Barth: the future of boron neutron capture therapy will depend on the clinical trials of accelerator-based boron neutron capture therapy". *Therapeutic Radiology and Oncology* 2 (2018): 58.
- 4. Nigg DW. "Computational dosimetry and treatment planning considerations for neutron capture therapy". *Journal of Neuro-Oncology* 62.1-2 (2003): 75-86.
- 5. Giannini G., *et al.* "Opportunities afforded by the intense nanosecond neutron pulses from a plasma focus source for neutron capture therapy and the preliminary simulation results". *Physica Scripta* 86 (2012): 055801.
- 6. Gribkov VA and Orlova MA. "On various possibilities in pulsed radiation biochemistry and chemistry". *Radiation and Environmental Biophysics* 43.4 (2004): 303-309.
- 7. Bernard A., et al. "Scientific status of plasma focus research". Journal of the Moscow Physical Society 8.2 (1998): 93-170.
- 8. Gribkov VA., *et al.* "The development of methods and apparatus for cancerous growth diagnostics and therapy on the base of neutron and X-ray radiation pulse generator". Issues of Atomic Science & Technology, Nuclear Instrument-Building, Editor-in-chief: Yu.N. Barmakov, All-Russia Research Institute of Automatics, Issue #1 (27), Moscow (2010): 178.
- 9. Lee S., *et al*. "High Rep Rate High Performance Plasma Focus as a Powerful Radiation Source". *IEEE Transactions on Plasma Science* 26.4 (1998): 1119-1126.
- 10. Chen W., *et al.* "Selective boron drug delivery to brain tumors for boron neutron capture therapy". *Advanced Drug Delivery Reviews* 26.2-3 (1997): 231-247.
- 11. Gribkov VA., *et al.* "Opportunities Afforded by New Generation of Pulsed Radiation Sources in Flash Radiation Physics and Chemistry". *Research Journal of Chemistry and Environment* 9.4 (2005): 11-19.
- 12. Agostinelli S., et al. "Geant4 a simulation toolkit". Nuclear Instruments and Methods in Physics Research A 506.5 (2003): 250-303.
- 13. Allison J., et al. "Geant4 developments and applications". IEEE Transactions on Nuclear Science 53.1 (2006): 270-278.
- 14. http://geant4.cern.ch/
- 15. http://geant4.cern.ch/support/proc_mod_catalog/physics_lists/referencePL.shtml
- 16. Curtiss LE. "Introduction to Neutron Physics". Princeton, NJ: Van Nostrand (1959).
- 17. Vlasov NA. "Neutrons (Neitrony)". M: Nauka (in Russian) (1971).

Volume 2 Issue 4 July 2019 ©All rights reserved by VA Gribkov*., et al.*