Accelerator based epithermal neutron source for NCT

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In paper presented investigations of patient treatment possibility by boron neutron capture therapy on special facility created in Institute for Physics and Power Engineering (IPPE) based on high current proton accelerator KG-2.5 with a $^{7}Li(p,n)^{7}Be$ reaction neutron source. Data on calculated absorbed dose distribution in patient tissue are presented.

1. Introduction

Nowadays neutron capture therapy looks very promising method of cancer treatment, especially for brain tumors by reason of selective damage cancer cells. Treatment effect of this method based on neutrons nuclear reaction with nuclides ^{10}B, ^{157}Gd. These nuclides have high cross-section of interaction with thermal neutrons. Unfortunately, thermal neutrons could enter only in near surface tissue and could not be used for deep localized tumors. This restriction limit such neutrons using only for surface tumors or for intraoperative therapy. For deep situated tumors looks more prospective to use epithermal neutrons with energy from 1 eV to 10 keV. These neutrons have much more penetrative ability and slow down in tissue till thermal energy. It makes possible neutron capture therapy for tumors located on depth up to 10 cm from surface. Important, that in epithermal neutron beam amount of fast neutrons must be as small as possible, because of dose from high-energy neutrons is main factor limited treatment process. Main critical factor is surface absorbed dose form reaction with fast neutrons. For treatment purposes necessary to have epithermal neutrons beam with size about 10x10 cm and neutron flux ~10^{9} s $^{-1}$ cm $^{-2}$.

Presently ^{7}Li(*p,n*)^{7}Be reaction looks are most appropriate neutron source for accelerator based facility for neutron capture therapy [1]. In set of papers reviewed approach based on neutron generation by protons with a high (about 2.5 MeV) energy [2-5]. Neutrons generated by such protons have high energy (up to ~0.8 MeV) and emitted in to all angles. So, it is necessary to create special moderator block (beam shaping assembly) to make satisfactory neutron beam for neutron capture therapy.

This paper investigated oncology patient treatment possibility by Neutron Capture Therapy (NCT) on created in IPPE facility based on high current accelerator KG-2.5 with using as a neutron source ^{7}Li(*p,n*)^{7}Be reaction. Detail calculations of a neutron yield, neutrons spatial-energy distribution and accompanying radiation for this reaction were done.

Based on these results were performed radiations transport calculations, were derived absorbed dose distribution in patient tissue for treatment planning.

2. Simulation of neutrons source

For detail representation of neutrons spatial distribution, the subinterval 1^{0} along the angle of neutrons flight escape to direction of protons beam was used [6]. The full calculated yield of neutrons under initial energy of protons 2.2 MeV, 2.3 MeV, 2.4 MeV, 2.8 MeV, for which the basic investigations were carried out, are $3.9\cdot10^{12}$, $6.3\cdot10^{12}$, $8.1\cdot10^{12}$ and $1.37\cdot10^{13}$ neutrons per second for the beam current 10 mA. These dates are in a good agreement with direct neutrons full yield measurements [3, 7].

Simultaneously with neutrons in lithium target gamma rays are born, which basic source are ^{7}Li(*p, p'γ*)^{7}Li reaction and radionuclide ^{7}Be. For the same protons energy full gamma rays yield were $2.3\cdot10^{12}$, $2.8\cdot10^{12}$, $3.2\cdot10^{12}$, $5.1\cdot10^{12}$ gamma quantum per second for beam current 10 mA. Its angular distribution is close to isotropic.

3. Simulation of radiation transport

Neutrons and gamma rays transport simulation was carried out by Monte Carlo method using program C95NCT and MCNP [8]. To investigate various materials properties as a moderator for creation of epithermal neutrons beam sphere moderator model was used. In its center was placed neutron source as a thin disk with diameter 4 cm to which the cylindrical cavity with the same diameter (fig.1) adjoins. Detectors were ring surfaces of sphere taken with subinterval 30º relative to directions of protons beam and having an opening angle ±15º. Calculations were carried out for sphere radius from 16 to 28 cm.

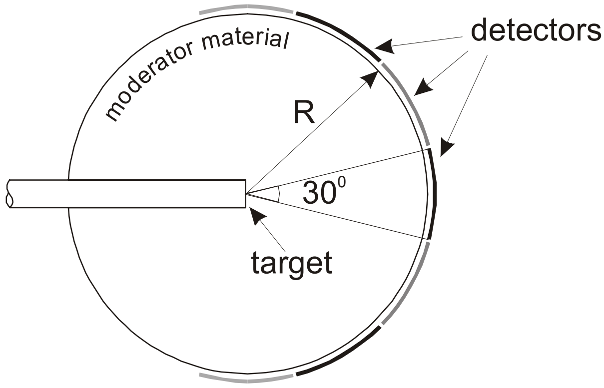

Fig. 1 Calculation model for evaluation in-air epithermal neutrons source characteristics.

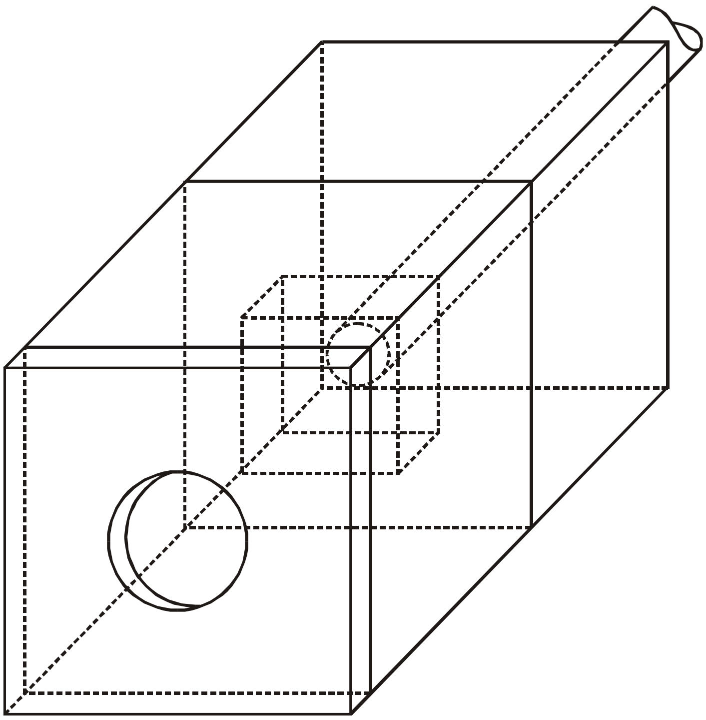

Fig 2. Beam shaping assembly calculation model for in-phantom absorbed dose distribution modeling.

More detail information about epithermal neutrons beam characteristics was obtained following a calculations absorbed doze distribution in the phantom. In these calculations special moderator block configuration was used fig.2. It allows to simulate moderator block composed from different materials, and also to take into account real construction of the moderator block, including the accelerator target. In calculations same simplified model of the phantom was used (cube with rib 20 cm). The first two layers with thickness 0.5 and 0.8 cm simulate skin and skull accordingly, and rest of volume - substance of brain. The structure of tissue corresponds to the recommendations ICRU-46 [9]. The ring detectors with radius subinterval 1 cm are placed on the depth of phantom in its fore-part with subinterval 1 mm in the first two layers up to the depth 1.5 cm and with subinterval 0.5 cm on the greater depth in the phantom.

As a criterion for the choice of material and optimal size of moderator two parameters were selected: ϕ_{epi} - epithermal neutrons flux density (neutrons energy more 1 eV) on a moderator surface for proton beam current 10 mA, and $\dot{D}/\phi_{epi}$ - magnitude biologically weighed absorbed doze specific power created in the same point in tissue by neutrons and a gamma quantum, reduced to a single epithermal neutrons stream on a moderator surface. The kerma-factors values and relative biological effectiveness presented in [15], were used for calculation of biologically weighted dozes. The magnitude $\dot{D}/\phi_{epi}$ is equivalent relative biological effectiveness weighed kerma-factor for a tissue and it is desirable, that it did not exceed magnitude biologically weighed doze specific power arising under epithermal neutron transport in phantom which is ~ $2\text{-}3 \cdot 10^{-12}$ RBE Gy cm^2. These two parameters are usually neutron beam in air dosimetric qualities parameter. Calculations results in these coordinates visually illustrate the quality of moderator: the best result corresponds to the left top of the graph.

4. Moderator choice

Materials that can be used as moderator or filter for forming a epithermal neutrons beam calculation researches were carried out in a series of works [2-5]. Light elements materials with large fast neutrons scattering cross-section and small absorption cross-section and activation in the slow neutron range are the most preferable. Those materials are deuterium, oxides and fluorides of beryllium, magnesium, aluminum, graphite, composition of fluorine with carbon and other. Materials contained fluorine, which has large neutron inelastic scattering cross-section with excitation of low levels with energy 0.11 and 0.197 MeV and for energy higher than 150 keV are the most interest. When choosing moderator material and it optimum sizes for a accelerator based with ^{7}Li(*p,n*)^{7}Be reaction epithermal neutrons source, source size, energy distribution and spatial anisotropy has essential meaning. The last two factors influence also on a choice of optimum disposition of irradiated object with respect to direction of protons beam.

In carried out calculations we investigated the following chemical elements and isotopes: D, ^{7}Li, Be, C, N, O, F, Mg, Al, Ti, Ca in accessible chemical combination, such as D_2O, LiF, MgF_2 , CaF_2 , polytetrafluoroethylene $(CF_2)n$, C_6F_6, AlN, Fluental®. The last material represents a metallo-ceramiks with composition: 56% F, 43% Al, 1% LiF and was specially developed for the similar purposes [11] and is applied to forming of epithermal neutron beam in some reactors and accelerators [11, 12].

5. Results

5.1. In-air neutron beam characteristics

For various materials properties evaluation from point of view optimum epithermal neutron beam forming using ^{7}Li(*p, n*)^{7}Be reaction source calculations for moderator model as sphere (fig.1) with radiuses 16, 18, 20, 22, 24, 26 and 28 cm were carried out. Main calculations have performed for a neutrons source with starting protons energies 2.3 MeV and beam current 10 mA. Statistical error of calculations was less than 1%.

Calculations results for various materials are represented in fig. 3 - 4. From figures one can be seen that epithermal neutrons flux density on a moderator surface for most materials is similar on magnitude and as a first approximation corresponds to dependence $1/R^2$, that is a corollary of small neutrons absorption in moderator. Deuterium and beryllium possessing by large stopping ability, are elimination, therefore already for moderator thickness 16 cm the significant part of neutrons are slowing up to energies below than accepted epithermal area boundary 1 eV. As a result the epithermal neutrons flux density for deuterium and beryllium for moderator radius 16 cm appears 1.2-1.5 times smaller and corresponds to dependence $\sim 1/R^4$. The second feature of moderator from deuterium and beryllium, and also graphite, which have a smooth dependence of total cross-section from neutrons energy, is the considerable difference epithermal neutrons beam characteristics leaving moderator under angles 0º and 90º in relation to direction of proton beam (collinear and orthogonal geometry). Orthogonal geometry, as one can see from fig.3, for deuterium has some advantages, providing forming epithermal neutron beam with lower fast neutrons impurity and flux density 1.2 times greater. The similar result is observed for beryllium and carbon. For moderators including isotopes with resonance structure in total neutron cross-section (fluorine, magnesium, aluminum) difference between orthogonal and collinear geometries is insignificant. The results represented on fig. 4-7 are concerned to collinear geometry.

Second feature defined epithermal neutron beam quality is value of the equivalent kerma-factor $\dot{D}/\phi_{epi}$ averaged on a neutron spectrum. It value is determined, mainly, by protons recoil, is directly connected with fast neutrons number in spectrum and is 20-30 times for researched materials. The kerma-factor $\dot{D}_\gamma/\phi_{epi}$, connected with gamma rays from accompanying reactions in the target and gamma rays born in moderator, for investigated materials does not exceed 10 % from $\dot{D}/\phi_{epi}$. From figures 3-4 one can see, that the best characteristics have epithermal neutrons beams formed by moderators from MgF_2, BeF_2 and polytetrafluoroethylene. The most perspective materials are magnesium fluoride (density 3.14 g/cm^3) and polytetrafluoroethylene (density 2.1 g/cm^3). Both these are produced by an industry and have high purity. Beryllium fluoride moderator not looks prospective because of high beryllium and it compounds toxicity. As could be seen from the fig. 3, 4 using the ^{7}Li (*p,n*) ^{7}Be reactions for proton energy 2.3 MeV as a neutron source, Fluental® is less suitable moderator in a comparison with MgF_2 and polytetrafluoroethylene.

So, the most perspective moderators for source of epithermal neutron based on ^{7}Li(*p,n*)^{7}Be reaction are MgF_2 and polytetrafluoroethylene. These moderator materials are formed epithermal neutrons spectrum, which give the most accordance with BNCT demands. The comparison of neutron spectrum from sphere with radius 20 cm from MgF_2, polytetrafluoroethylene, Fluental® and carbon moderators are given on Fig. 5, 6. Clear that MgF_2 and polytetrafluoroethylene give the smallest part of fast neutron and have the sharp peak in distribution region 1-20 keV.

Besides elastic and inelastic scattering radiative capture are occurred when neutron transport in moderator of MgF_2 and polytetrafluoroethylene. As a result of capture the radioactive nuclides ^{20}F with $T_{1/2}$ = 11.4 sec. and ^{27}Mg with $T_{1/2}$ = 10 min are generated. Their decay accompanying with emission 0.8-1.6 MeV gamma ray. ^{20}F and ^{27}Mg production rate calculation in MgF_2 and polytetrafluoroethylene moderators with radius 20 cm showed that total activities in full moderator volume for protons starting energy 2.3 Mev and current 10 mA are $3.8\cdot10^{10}$ Bq и $6.7\cdot10^{8}$ Bq accordingly and corresponding kerma factor $\dot{D}_{\gamma\,act}/\phi_{epi}$ is not exceed 1 % from $\dot{D}/\phi_{epi}$ value.

Epithermal neutron source optimization arisen problem proton beam energy choice. With proton energy increasing total neutron yield from thick target is increased too. At the same time primary neutron energy is increased, so moderator size must be increased too. When protons energy increasing thermal power in target is increased too and additional technical difficulties will be appear. To estimate these effects calculations for different proton energy were made. Calculation results for MgF_2 moderator are given on Fig. 7. These results are shown that suitable energy value is in interval 2.3 – 2.8 Mev.

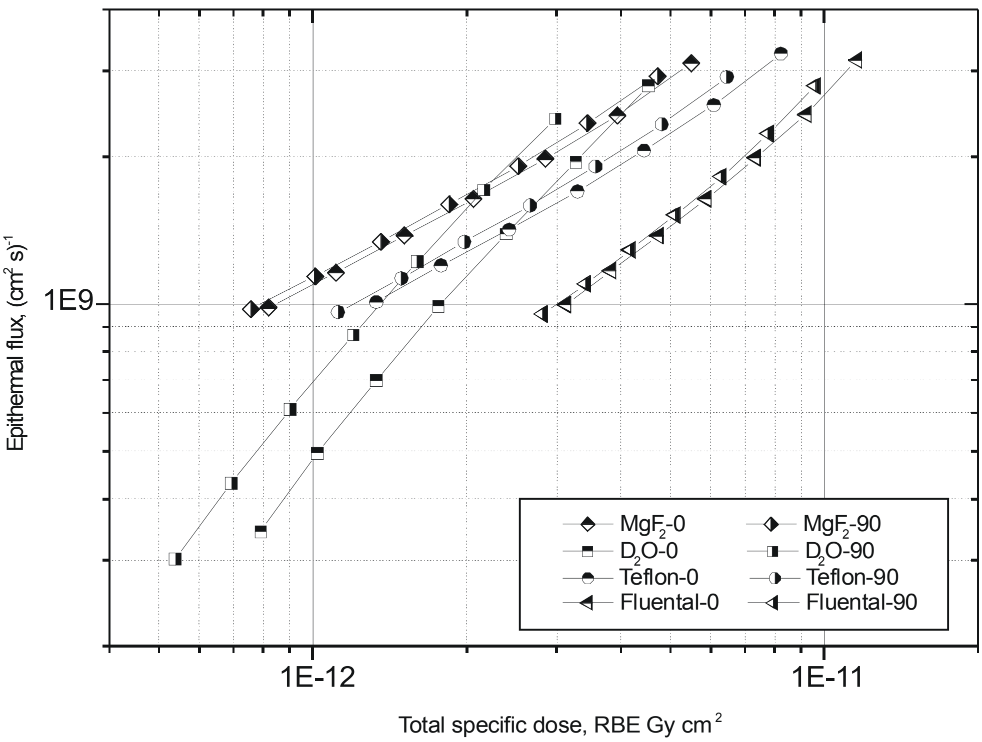

Fig 3. Epithermal neutron flux & total specific dose for various materials and moderator sizes for collinear and orthogonal geometry. Moderator radius from left to right 28, 26, 24, 22, 20, 18, 16 cm. For thick lithium-7 target, proton energy 2.3 MeV, proton current 10 mA.

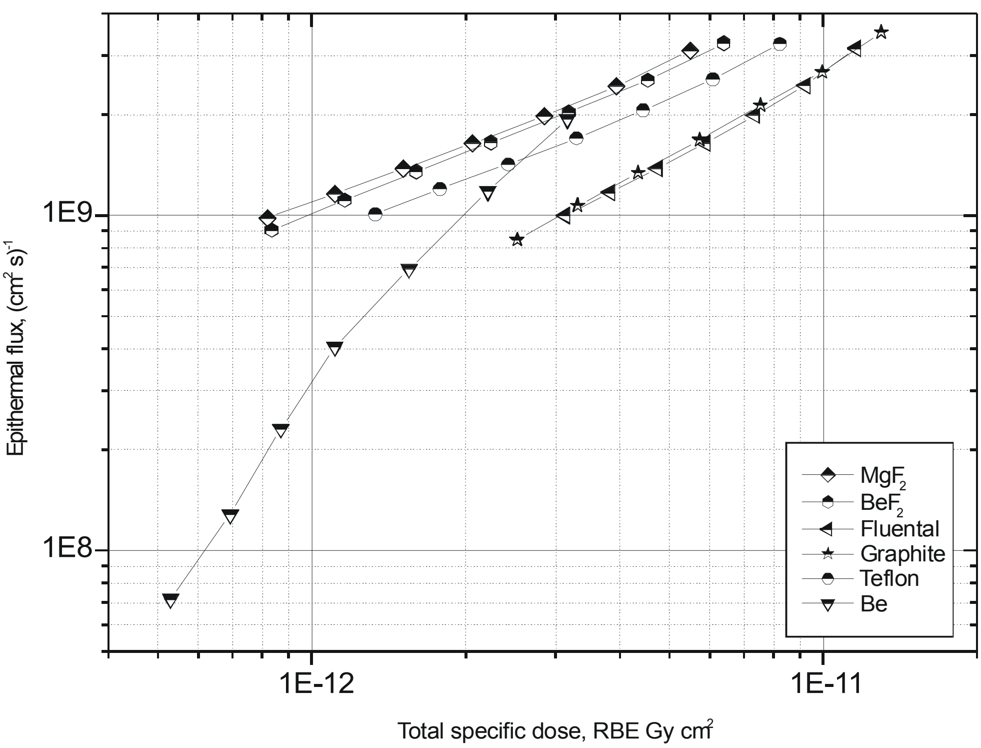

Fig 4. Epithermal neutron flux & total specific dose for various materials and moderator sizes for collinear geometry. Moderator radius from left to right 28, 26, 24, 22, 20, 18, 16 cm. For thick lithium-7 target, proton energy 2.3 MeV, proton current 10 mA.

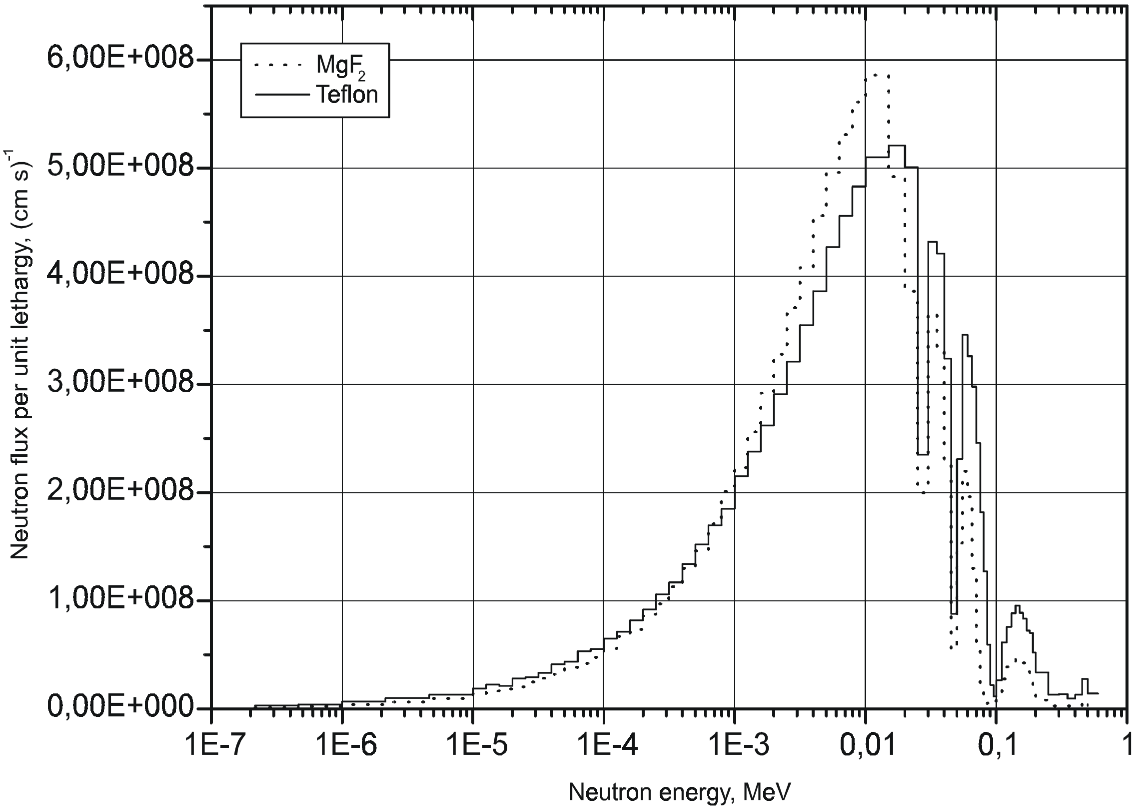

Fig. 5. Neutron spectra from MgF2 and Teflon moderators with radius 20 cm on a proton beam direction. Proton energy 2.3 MeV, current 10 mA.

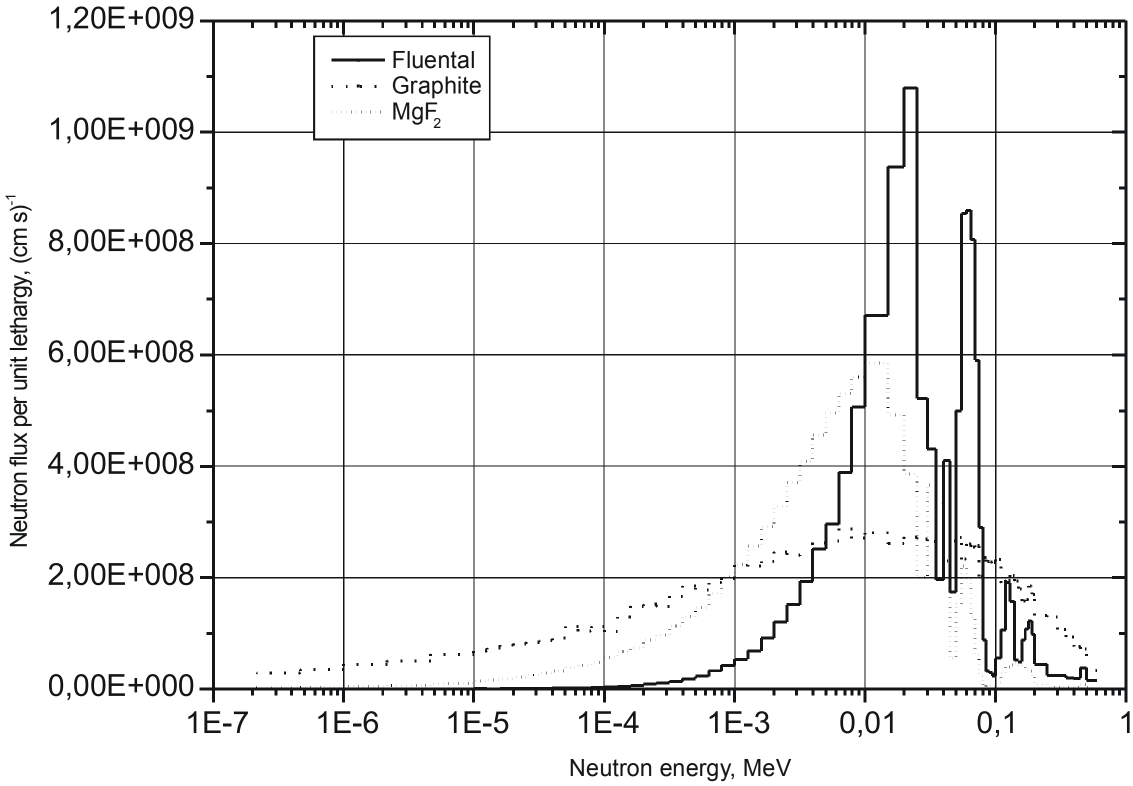

Fig. 6. Neutron spectra from Fluental, Graphite and MgF2 moderators with radius 20 cm on a proton beam direction. Proton energy 2.3 MeV, current 10 mA.

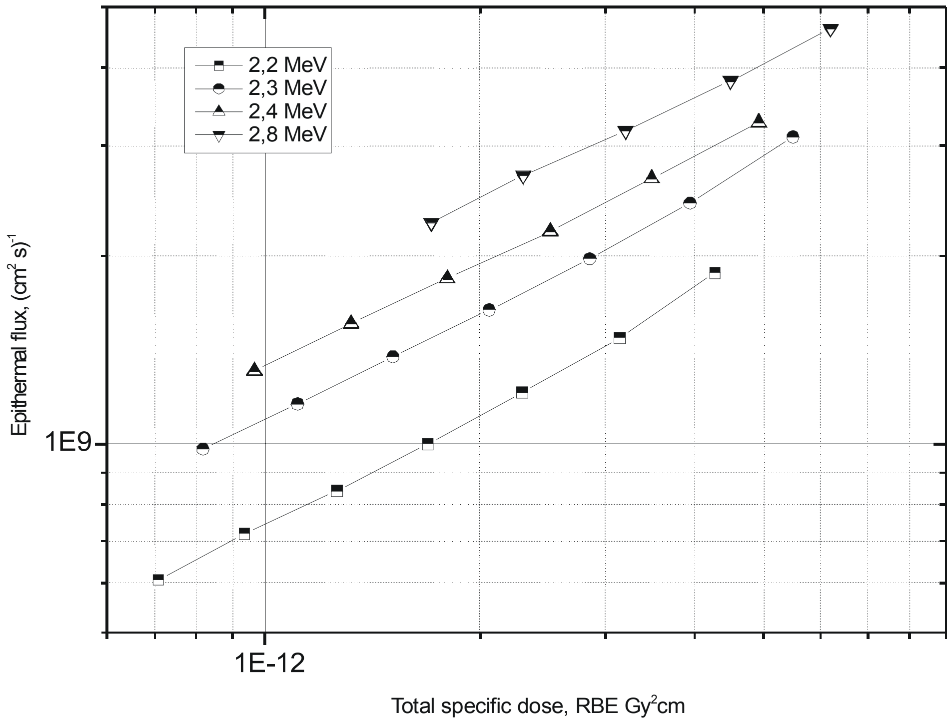

Fig 7. Epithermal neutron flux & total specific dose for MgF2 moderator, various moderator sizes, collinear geometry. Moderator radius from left to right 28, 26, 24, 22, 20, 18, 16 cm. Thick lithium-7 target, proton energy 2.2, 2.3, 2.4, 2.8 MeV, proton current 10 mA.

5.2. In-phantom dose distributions

Main epithermal neutron beam characteristic from BNCT point of view is in-phantom biological weighted doses. For providing these studies moderator block configuration given on Fig.2 and phantom described in section 3 were used. The main calculations were done for moderator blocks with size 40 x 40 cm for initial proton energy 2.3 Mev. Biologically weighted dose distributions on the phantoms depth for three moderators materials are given on fig. 8-10. In dose calculations were assumed that ^{10}B concentration in health tissue is 18 ppm, in tumor tissue is 65 ppm, $^{10}B(n,\alpha)^{7}Li$ reaction CBE products - 1.3 and 3.8 [13, 14]. Kerma-factors and RBE for neutron are taken from [10].

The quality of epithermal neutron beam is usually characterized by next principal parameters:

1. Advantage depth (AD) – depth on which the biologically weighted dose in tumor equal with maximum dose in healthy tissue.
2. Advantage depth dose rate (ADDR), which characterizes time for achievement dose on the depth AD.
3. Therapeutic ratio (TR) dose in tumor to maximum dose in healthy tissue.
4. Advantage rate (AR) - full dose in tumor tissue to full dose in healthy tissue, integrated from surface to depth AD.
5. Current to flux, J_{epi}/ϕ_{epi}, characterizing the expansion of epithermal neutron beam.

Calculated therapeutic ratio for moderators from MgF_2, polytetrafluoroethylene, Fluental® and dosimetrical measurements therapeutic ratio for FCB MIT epithermal beam [13, 14] are given on fig. 11.

Comparison is shown that moderator of MgF_2 has the best characteristics parameters close to ones obtained on the reactor beam FCB MIT. Polytetrafluoroethylene, as a moderator, worse than MgF_2 on its characteristics but significant better than Fluental®. Because this material is more cheaper than MgF_2, calculations were made for combined moderator, which central part is presented as a 20 x 20 cm^2 cross-section parallelepiped consisted of MgF_2, remaining part consisted of polytetrafluoroethylene. Moderator thickness was varied in limit from 16 to 24 cm. Obtained results are given on fig. 12 and shown that the optimal moderator length of MgF_2 equals approximately 20-22 cm. Principal combined moderator characteristics from MgF_2 and polytetrafluoroethylene with size 40 x 40 cm and optimal length are given in table. For comparison characteristics of FCB MIT beam [13, 14] are given in Table 1 too. Fig. 13 is given the principal parameters comparison for combined moderator from MgF_2 and polytetrafluoroethylene with calculation results for moderator, which will be used on Birmingham University facility. This moderator consist of Fluental® and carbon [12]. It is shown that proposed combined moderator has preference by all parameters as compare proposed to use in Birmingham.

Basic characteristics comparison of accelerator based facility with beam shaping assembly made from MgF_2 and polytetrafluoroethylene and FCB MIT [13, 14] facility.

Table

	AD, cm	TR_{max}	ADDR, RBE cGy/min	AR	J_{epi}/ϕ_{epi}
Accelerator facility with BSA	9.1	6.2	100 (current 10 mA)	5.6	0.64
FCB MIT	9.3	6.4	125	6	0.84

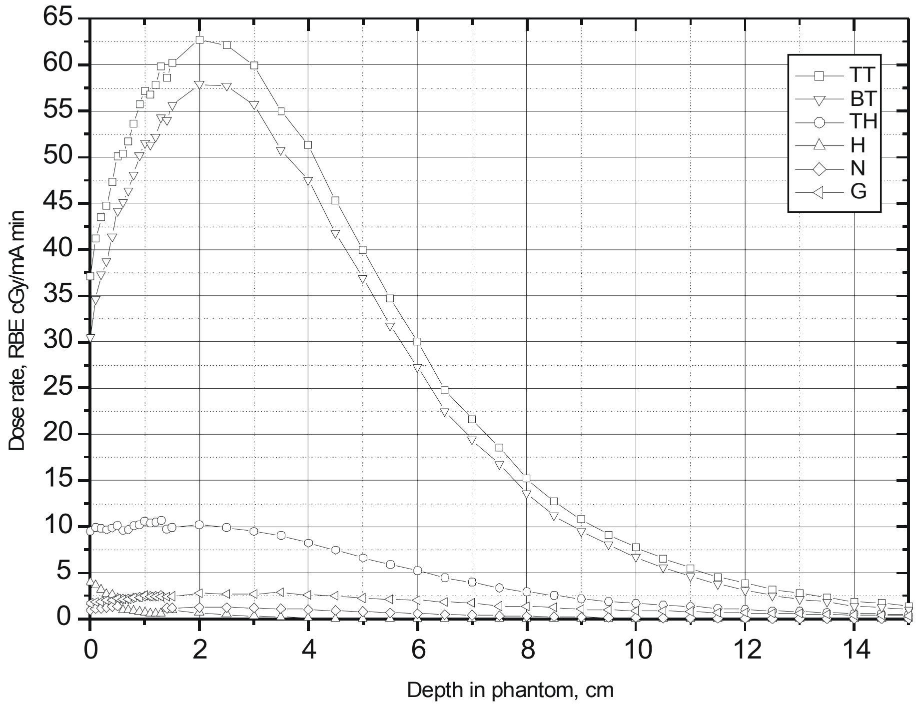

Fig. 8. Absorbed doses rates as function of depth in phantom. MgF_2 moderator, size 40x40x40 см, proton energy 2.3 MeV, beam current 1 mA. TT – tumor total dose, BT – boron dose in tumor, HT – total dose in healthy tissue, H – proton recoil dose, N – dose from nuclear reaction with nitrogen, G – gamma ray dose.

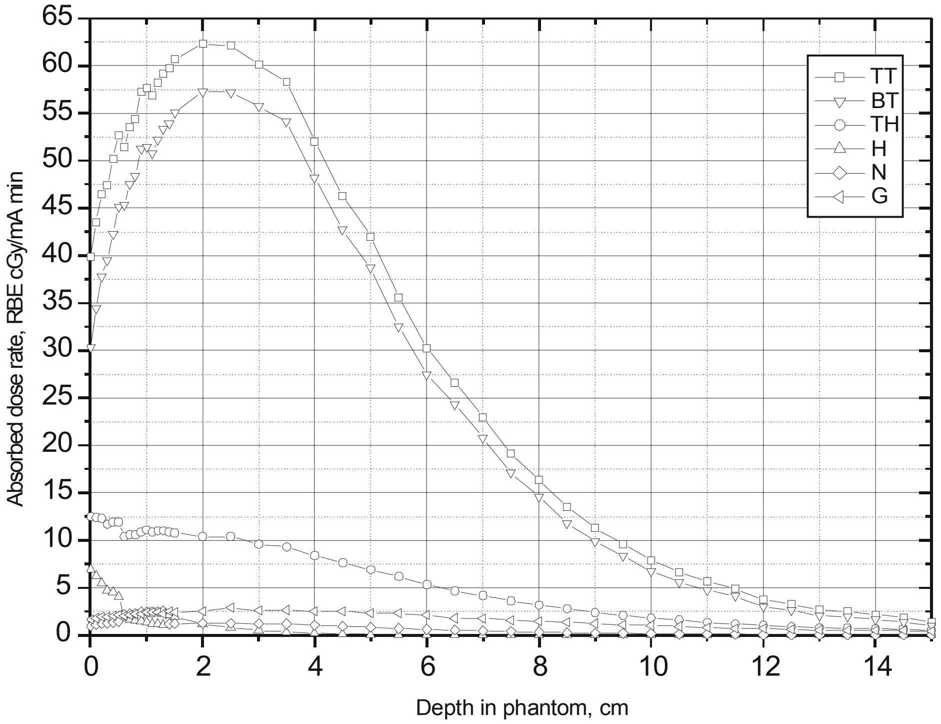

Fig. 9. Absorbed doses rates as function of depth in phantom. Polytetrafluoroethylene moderator, size 40x40x40 см, proton energy 2.3 MeV, beam current 1 mA. TT – tumor total dose, BT – boron dose in tumor, HT – total dose in healthy tissue, H – proton recoil dose, N – dose from nuclear reaction with nitrogen, G – gamma ray dose.

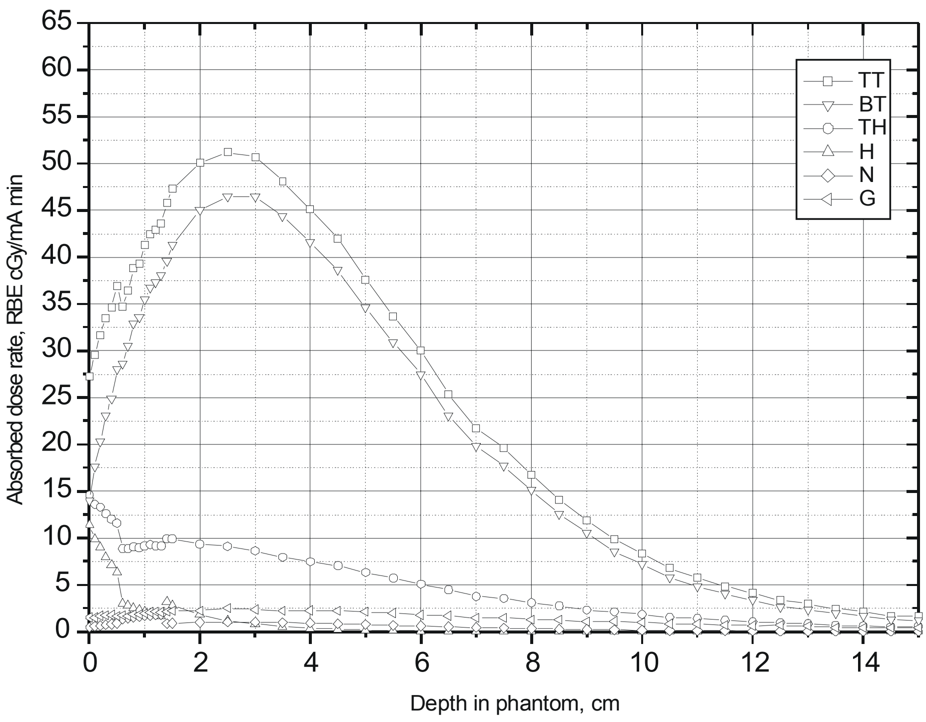

Fig. 10. Absorbed doses rates as function of depth in phantom. Fluental moderator, size 40x40x40 см, proton energy 2.3 MeV, beam current 1 mA. TT – tumor total dose, BT – boron dose in tumor, HT – total dose in healthy tissue, H – proton recoil dose, N – dose from nuclear reaction with nitrogen, G – gamma ray dose.

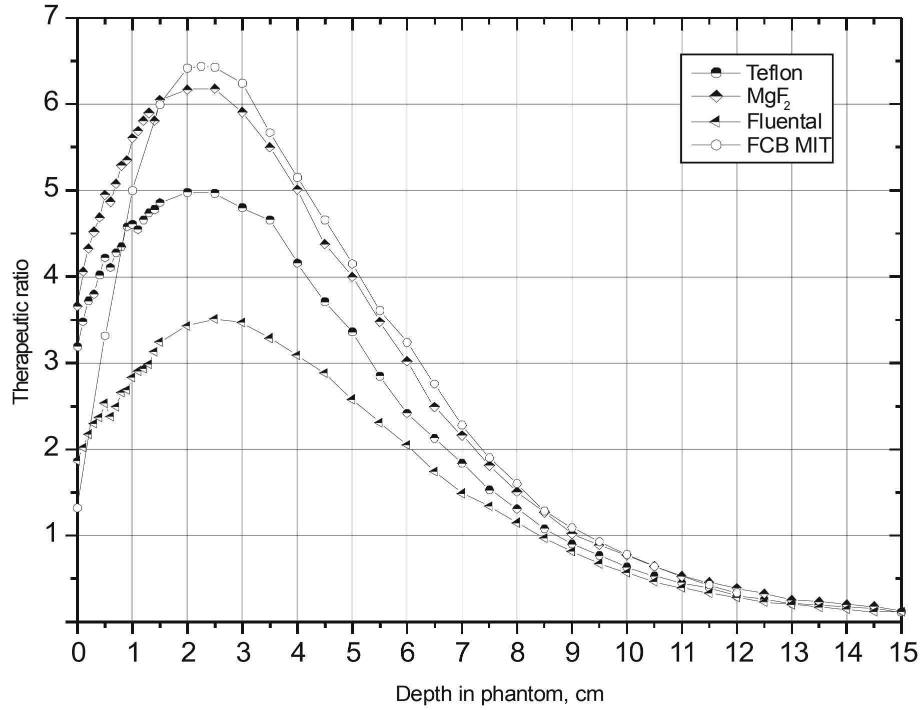

Fig. 11. Therapeutic ratio for different moderator materials as function of depth in phantom, moderator size 40x40x40 cm (proton energy 2.3 MeV) and reactor based beam [13].

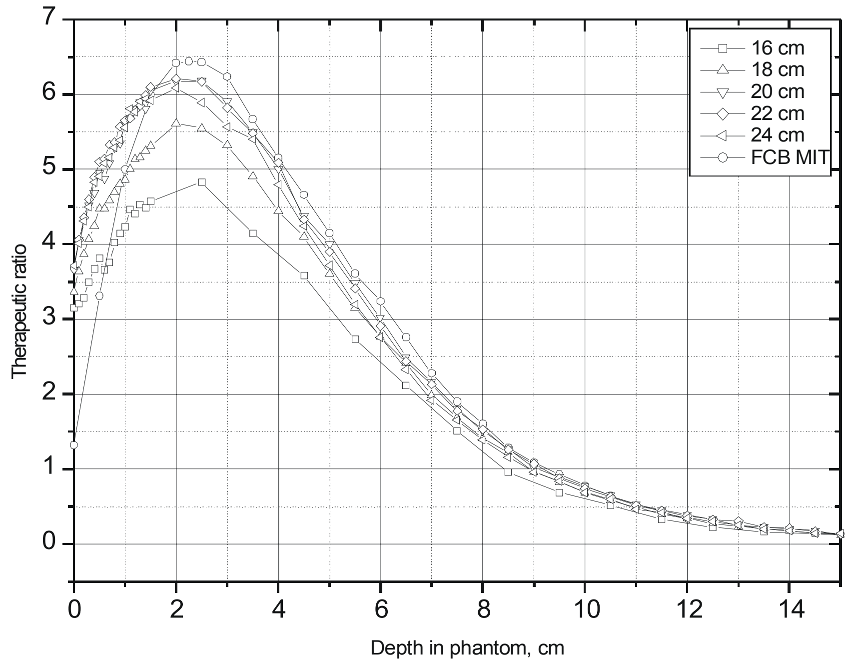

Fig. 12. Therapeutic ratio for MgF2 – polytetrafluoroethylene moderator (size 40x40x40 cm) with various MgF2 block length. Proton energy 2.3 MeV. FCB MIT – reactor based beam [13].

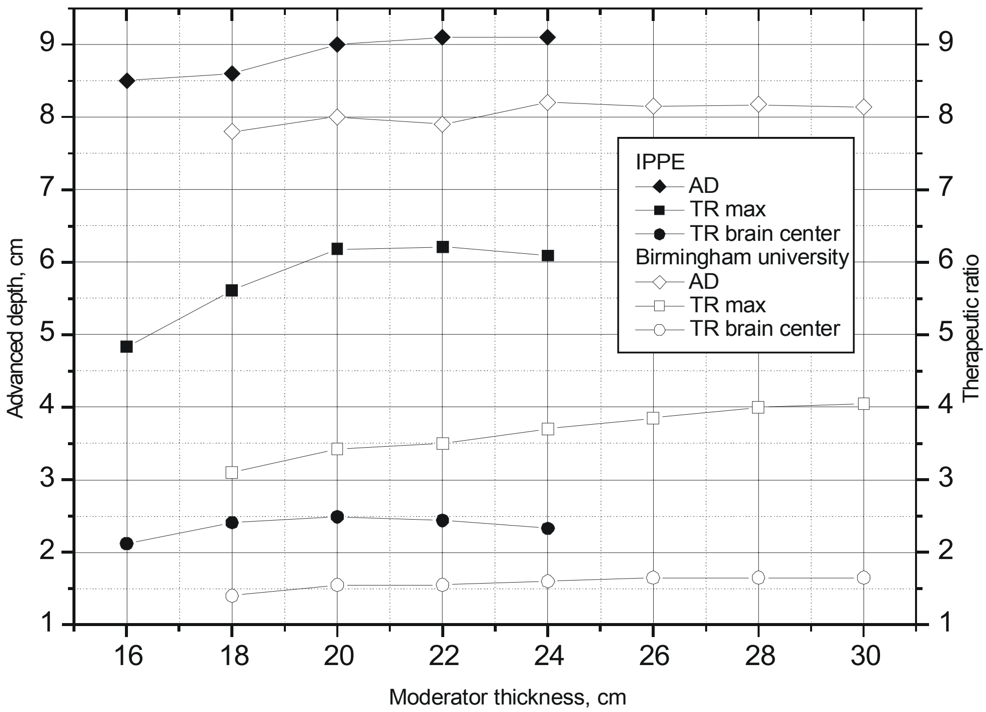

Fig. 13. Moderators characteristics comparison for MgF2 – polytetrafluoroethylene moderator (proton energy 2.3 MeV) and moderator suggested by Birmingham University team [12] (proton energy 2.4 MeV).

Conclusion

Calculation studies on best moderator materials for accelerator based epithermal beam creation for BNCT were made. It is shown that MgF_2 have the best characteristics. Optimal configuration of combined moderator consisted of MgF_2 and polytetrafluoroethylene was proposed. As a result of dose distribution calculations was shown that when using this moderator with 2.3 MeV protons and beam current 10 мA advantage depth is 9cm, therapeutic ratio on the depth ~3 cm is 6, advantege depth dose rate on the depth 9 cm is ~1 RBE Gy per minute, that corresponds to maximum time of therapy 12 minutes.

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