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About Radiation in ^{nat}Gd for Neutron Capture Therapy

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Abstract: In the present work, based on publications dedicated to ^{nat}Gd natural gadolinium isotopes, characteristics of secondary particles are analysed in details for various neutron-induced reactions. Characteristics of the secondary particles produced in these reactions that make significant contribution to absorbed dose are estimated. It is also established that the main contribution to the absorbed dose is made by secondary particles produced in interactions of neutrons and ^{155}Gd and ^{157}Gd isotopes. From comparison of gamma-radiation spectra it is defined that the amount of γ-quanta with energies 0-400 keV (i.e. effective γ-quanta) produced in the (n,γ)-reaction by ^{155}Gd is higher than that by ^{157}Gd. Compared spectra of other particles (internal conversion electrons, Auger electrons, x-ray radiation) have shown that earlier used average values of their energy must be defined more precisely. When biological objects are irradiated for approximately 30 minutes by epithermal neutrons in the ^{nat}Gd NCT (Gadolinium-based neutron-capture therapy), one should take into account energies of secondary particles produced by ^{152}Gd, ^{154}Gd, ^{156}Gd, ^{158}Gd and ^{160}Gd isotopes as they have high linear energy transfer (LET). It is demonstrated that when combined, all these secondary particles can make significant contribution to the absorbed dose at neutron-irradiation of biological objects by the ^{nat}Gd NCT technique.

Key words: Nuclear reactions, natural gadolinium isotopes, secondary particles, conversion electrons, epithermal neutrons, neutron capture therapy, radiation, biological effect.

1. Introduction

Gadolinium-based neutron-capture therapy (^{nat}Gd NCT)—is one of the promising techniques in the neutron-capture therapy. In 1936, Locher was the first who demonstrated suitability of Gd for the NCT. For a long period time, ^{10}B was considered to be the main element due to its large thermal neutron capture cross-section, high energy and short secondary alpha-particles path in reactions with ^{10}B. Several years of studies have proved that some radioresistant tumours treatment requires preparations with capabilities to accumulate with high gradient in tumours rather than in healthy tissues, and elements having higher neutron-capture cross-sections than those of ^{10}B. Starting from 1960s, and especially after accepting Gd as a contrast agent in magnet-resonance imaging (MRI), attention was drawn to application of Gd in NCT. Therefore, Gd is relatively new nuclide in NCT. The major advantage of Gd is its high neutron-capture cross-section, which is 12.76 times higher than that of ^{10}B, and for ^{155}Gd and ^{157}Gd isotopes, composition of which in ^{nat}Gd is more than 30%, it is 15.84 and 66.4 times higher than that of ^{10}B. This in general allows reduction of irradiation time required to achieve needed dose and, consequently, to decrease risk of damage to healthy tissues. At present, ^{nat}Gd NCT is not applied in clinical experiments because of uncertainties in calculation of absorbed dose.

Importance of these studies is conditioned by the following reasons:

1. Analysis of publications showed that majority of authors (T. Matsumoto et al. [1], J. T. Masiakowski et al. [2] Martin et al. [3, 4] и Laster et al. [5]) use significantly simplified calculations to derive absorbed dose in ^{nat}Gd NCT. In particular, many authors [6-11] (R. F Barth et al. [6, 7], R. M Brugger et al. [8], B. Hofmann [11]), take into account only influence of (separately or in combination) Auger-electrons, internal conversion electrons, gamma-radiation and x-ray radiation from ^{nat}Gd produced in (n,γ) reaction.

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Consequently, some authors J. Carlsson et al. [9] and G. De Stasio et al. [10] have suggested that Gd must be delivered into cells to destroy tumour cells. But, by taking into account high cross-section of thermal neutrons and γ-radiation penetration depth, authors R. F. Barth et al. [6, 7] and R. M. Brugger et al. [8] have indicated possibilities to destroy tumour cells when Gd is outside of these tumour cells. By taking into account characteristics of secondary particles J. T. Goorley [12] has estimated possibilities for Gd application in the NCT by dividing into the following groups: ^{157}Gd NCT, ^{159}Gd RNT and Gd PAT, where RNT—radionuclide therapy, PAT—photon-activation therapy. He has also identified non-exclusiveness of these three individual therapy forms. Therefore, a combination of these two or three therapy forms has been proposed. To apply them, one should accurately evaluate prompt γ-quanta, internal conversion (IC) electrons, Auger-electrons and others. Other authors, namely S. A. Klykov [13], A-F. Miller et al. [14], J. Stepanek [15], C. K. C. Wang et al. [16], T. Goorley et al. [17], M. Rivard et al. [18], S. A. Klykov et al. [19], Y. Sakura et al. [20], I. Sheino et al. [21], in their calculations have taken into account only secondary particles produced in ^{155}Gd(n,γ)^{156}Gd and ^{157}Gd(n,γ)^{158}Gd reactions, since cross-sections of these reactions are very large, 60,800 and 255,000 barns, respectively. Therefore, they have drawn a conclusion that their contribution to the absorbed dose must be more than 90%. Contribution of these secondary particles produced in the ^{157}Gd(n,γ)^{158}Gd reaction to the absorbed dose is approximately 70%. These results are presented in the Table 1, and one can see that there are contradictions between some characteristics of these secondary particles.

At first sight, from the Table 1 it seems that these characteristics are close, but when the absorbed dose is calculated with taking into account ^{155}Gd and ^{157}Gd neutron-capture cross-sections one can see pronounced deviations.

To our opinion, these calculation methods do not adequately take into account the nature and characteristics of epithermal neutron beam used for neutron-capture reaction generation. Analysis of characteristics of our beam and similar beams of other international nuclear research centres used for the NCT demonstrated that all these epithermal neutron beams contain fast neutrons and gamma-radiation components. In the case of ^{nat}Gd NCT it is incorrect to neglect contribution of these components to the absorbed dose. It is known that the ^{nat}Gd consists of seven stable isotopes: ^{152}Gd, ^{154}Gd, ^{155}Gd, ^{156}Gd, ^{157}Gd, ^{158}Gd and ^{160}Gd. Therefore, contribution of these isotopes to the absorbed dose should be evaluated for interaction of epithermal neutrons with the mentioned above ^{nat}Gd isotopes.

2. In the last decades, the progress made in the NCT was achieved by application of boron-containing preparations. For this reason, many boron-based concepts and calculation models are often directly transferred to ^{nat}Gd NCT studies. Such a direct transfer is not suitable for the ^{nat}Gd NCT, since in ^{nat}Gd NCT

Table 1

	E_{av}, keV	G_γ	E_{av}, keV	G_e	E_{av}, keV	G_{Ae}	$E_{x\text{-}ray}$, keV	G_x
Klykov [13]	2,860	2.86	68.6	0.66	3.9-4.8	4.1-9.7	10.7-38.4	0.33-0.84
Miller et al.[14]	7,871	3.29	91	0.732				
Stepanek [15]	2,219	1.56	45.39	0.647	3.94	4.8	10.5	5.77
Wang et al. [16]			65.91	0.725	4.8	6.7		
Goorley et al. [17]	2,437	1.83	45.9	0.69	4.19	4.93	10.73	0.84
Rivard et al. [18]	2,219	1.56	45.51	0.649	4.14	9.71	10.33	0.32
Klykov et al. [19]			45.51	65 ± 15				
Sakura et al. [20]			45.51	65 ± 15				
Sheino et al. [21]	2,206	1.55					24.1	0.63

Here G—yield of particles, i.e. yield of γ-quanta, internal conversion electrons, auger electrons and x-ray, respectively, for single neutron-capture reaction.

there are some secondary particles, like γ-quanta having penetration depth sufficient for knocking out orbital electrons from gadolinium atoms. These knocked out electrons can be used in photon-capture therapy of tumours. Such secondary particles can cause other reactions as well. From these reactions secondary particles with high linear energy transfer (LET) are produced. Therefore, we believe that the absorbed dose calculation model for ^{nat}Gd NCT is much more complex than that for ^{10}B NCT. Obviously, this calculation model must contain all possible neutron-capture reactions for gadolinium.

3. All models estimating biological effect of tumour tissue damage are based on a simplified approach, which includes two or three types of radiation. To our opinion, ^{nat}Gd NCT must include all range of all radiation types absorbed by biological objects. It is also important because combination of two-three radiation types can give a stronger damaging effect on tumour tissues (in clinical practice combination of gamma-radiation with other radiation types is used), and in this case one can have a spectrum contributed by several types of radiation that produces combined effect on biological tissue.

Based on these reasons, we have thoroughly analysed existing publications and performed our own additional calculations to study secondary particles emitted by gadolinium in interactions with reactor's epithermal neutrons. Obtained results make valuable corrections to dosimetric calculations for the ^{nat}Gd NCT.

2. Methods

In order to determine the number of particles produced in nuclear neutron-induced reactions in ^{nat}Gd we use well-known nuclear physics methods (A. I. Abramov et al. [22]). Under irradiation of a sample containing N nuclei with flux of neutrons Φ, number of interaction acts per a second is expressed as follows:

$$A = N\,\sigma\cdot\Phi \qquad (1)$$

where σ—reaction cross-section. On the other hand, this number of interaction acts allows one to determine the number of secondary particles produced in 1 second of irradiation time. Naturally, the same number of secondary particles will be produced every second. If nucleus produced as a result of a reaction is radioactive, then the number of nuclear transformations (i.e. specific activity of nuclides) after irradiation with flux of neutrons can be usually expressed as follows:

$$A = \lambda N = \sigma\,\Phi\,N_X[1\text{-}exp(-\lambda t_{irr})] = \sigma\,\Phi\,N_X\,[1\text{-}exp(-ln2\,t_{irr}/T_{1/2})] \qquad (2)$$

where λ—decay constant, N_X—number of nuclei of activated nuclide in target.

If the half-life $T_{1/2}$ of radionuclide produced in the reaction is large, then the number of nuclear transformations is determined by expression (2). If the half-life $T_{1/2}$ of radionuclide produced in the reaction is not large, then efficient irradiation time must be $t_{irr} >> T_{1/2}$. In this case, the number of nuclear transformations can be determined by means of expression (1) (A. I. Abramov et. al. [22]). If the half-life of radionuclide produced in the reaction is $T_{1/2}$ = 1 s, then the number of nuclear transformations under irradiation of the sample for t_{irr} = 1 s can be determined from the following expression derived from the expression (2):

$$A_{act} = f\,\sigma\,m\,pN_A[1\text{-}exp(-ln2)]/A \qquad (3)$$

where f—flux of neutrons, m—quantity of irradiated element in grams, p—relative concentration of irradiated isotope in the chemical element (%), N_A—constant of Avogadro, A—atomic mass of the irradiated isotope.

It is known that natural gadolinium has seven isotopes: ^{152}Gd (0.205%), ^{154}Gd (2.23%), ^{155}Gd (15.10%), ^{156}Gd (20.60%), ^{157}Gd (15.70%), ^{158}Gd (24.50%), ^{160}Gd (21.60%). By using expressions (1)-(3) to determine the number of nuclear transformations per second for every neutron—induced reaction in ^{nat}Gd, we have calculated and evaluated characteristics of secondary particles for every particular isotope. We have used characteristics of WWR-SM INP AS RU epithermal neutron flux from publications of G. A. Kulabdullaev et al. [23], G. A. Abdullaeva et al. [24].

3. Analysis of Various Reactions with Neutron Interaction with ^{nat}Gd Isotopes

Neutron can cause in ^{152}Gd isotope the following reactions: ^{152}Gd(n,γ)^{153}Gd, ^{152}Gd(n,2n)^{151}Gd, ^{152}Gd(n,p)^{152}Eu, ^{152}Gd(n,t)^{150}Eu, ^{152}Gd(n,α)^{149}Sm. Among these reactions only ^{152}Gd(n,α)^{149}Sm has 0.2 nuclear transformations per second, others are negligibly small (reaction yield for them is within 1×10^{-9} and 5.8×10^{-6} transitions per second). The energy of ^{152}Gd(n,α)^{149}Sm reaction is 8.08 MeV. Formed ^{149}Sm nucleus has large (n,γ) reaction cross-section of approximately 46,000 barns. However, actually both ^{152}Gd and ^{149}Sm are α-decay nuclei with half-lives of 1.08×10^{14} years and 2.0×10^{15} years, respectively, and the α-decay energy is Q_α = 2,140 keV and Q_α = 1,869.9 keV (J. Tauren et al. [25] and R. B. Firestone et al. [26]), respectively.

Neutrons in ^{154}Gd isotope can cause the following reactions: ^{154}Gd(n,2n)^{153}Gd, ^{154}Gd(n,p)^{154}Eu, ^{154}Gd(n,t)^{152}Eu, ^{154}Gd(n,α)^{151}Sm. Among them only ^{154}Gd(n,t)^{152}Eu reaction has higher probability since it has 2 nuclear transformations per second. The energy of this reaction is unknown. Cross-section of (n,γ) reaction for produced ^{152}Eu nucleus is approximately 6,000 barns. Nucleus produced in the ^{154}Gd(n,t)^{152}Eu reaction can be in the excited state with spin 0 or 3. In the first excited state the life-time is 9.3116 h, and β^--decay (72%) and electron capture (28%) processes take place. In the second excited state the life-time is 13.537 years, and β^--decay (27.9%) and electron capture (72.1%) processes with Q_β = 1818.8 keV and Q_{EC} = 1874.3 keV, respectively, take place. The Table 2 shows characteristics of secondary particles produced in ^{154}Gd(n,t)^{152}Eu reaction.

Neutrons in ^{155}Gd isotope can cause the following reactions: ^{155}Gd(n,γ)^{156}Gd, ^{155}Gd(n,3n)^{153}Gd, ^{155}Gd(n,p)^{155}Eu, ^{155}Gd(n,d)^{154}Eu, ^{155}Gd(n,^{3}He)^{153}Sm, ^{155}Gd(n,α)^{152}Sm. Among these reactions, ^{155}Gd(n,γ)^{156}Gd and ^{155}Gd(n,α)^{152}Sm reactions have 1.783×10^7 and 14.8 nuclear transformations per second, and energies of 8.54 and 8.33 MeV, respectively. The rest of the reactions have negligibly small number of nuclear transformations per second from 1×10^{-6} to 1.17×10^{-4}. In ^{155}Gd(n,γ)^{156}Gd reaction, emitted higher probability γ-quanta with relative intensity ≥ 100 have the following energies (Table 3) shown in keV (J. Tauren et. al. [25] and R. B. Firestone et al. [26]).

It is known, that this reaction induces the internal electron conversion process in the excited ^{156}Gd isotope. The highest probability has γ-radiation of the excited ^{156}Gd isotope with E_γ—energies and N_{ICC}—internal conversion coefficients (ICC) (Table 3). There are also: 110 γ-radiation processes with energies from 190.215 to 1,040.47 keV with ICC (0.01-0.096), 200 γ-radiation processes in the energies range from 356.446 to 1,334.401 keV with ICC (0.001-0.0096)

Table 2

E_{β^-}, keV	I_{β^-}	E_{β^+}, keV	I_{β^+}	E_γ, keV	I_γ
175.39	1.819	224.41	0.923	367.79	0.861
384.78	2.43	294.87	2.085	411.12	2.234
549.75	1.59	344.51	24.92	503.47	0.149
695.62	13.78	640.45	17.41	586.265	0.459
1,063.4	0.9	788.42	21.73	678.623	0.471
		956.55	26	778.90	12.942
		1,063.85	1.30	970.35	0.588
1,474.52	8.1	1,507.82	0.90	1,089.737	1.727
		1,752.52	0.74	1,299.14	1.623
				1,314.67	0.931

Here E—energy, I—intensity (in relative units) of secondary particles in relevant reactions.

Table 3

E_γ (I_γ), keV (relative units)			E_γ (N_{ICC})	E_x (I_γ)	E_{Ae} (I_{Ae})
89.0(1)	947.0(3)	1,965.1(20)	79.9(5.91)	5.4(0.27)	6.7(43-K, 85-L_3)
131.1(2)	949.1(10)	1,981.5(4)	89.0(3.93)	6.0(0.70)	7.4(20-K, 70-L_2)
161.6(5)	960.5	2,017.7(3)	112.0(1.5)	6.0(0.09)	7.8(1.4-K, 43-L_1)
170.2(7)	961.0(6)	2,026.7(3)	116.0(1.3)	6.1(6.3)	33.5(0.58-K)
192.8(1)	969.9(8)	2,032.4(3)	131.1(0.9)	6.7(0.07)	33.9(0.76-K)
199.2(1)	984.4(10)	2,092.3(5)	147.7(0.65)	6.7(3.9)	34.4(0.07-K)
228.3(4)	993.3(1)	2,097.8(4)	148.9(0.61)	6.8(0.12)	34.6(0.70-K)
296.5(3)	1,008.8	2,110.7(4)	155.2(0.58)	6.9(0.06)	35.1(1.4-K)
321.8(4)	1,014.5(1)	2,127.5(3)	155.7(0.58)	7.1(1.32)	35.7(0.68-K)
333.4	1,026.5(2)	2,152.1(13)	160.2(0.51)	7.2(0.01)	40.0(0.22-K)
339.5(6)	1,040.5(8)	2,167.6(7)	168.4(0.40)	7.8(0.67)	40.2(0.16-K)
350.5(5)	1,053.3(5)	2,170.8(7)	170.2(0.45)	7.9(0.01)	40.3(0.15-K)
356.4(5)	1,059.1(4)	2,180.9(12)	171.9(0.37)	8.1(0.02)	40.4(0.12-K)
380.4(5)	1,065.2(2)	2,205.2(8)	190.0(0.30)	8.1(0.03)	40.6(0.03-K)
399.8(7)	1,067.2(2)	2,211.8(12)	0.2	41.9(0.01)	40.6(0.01)
407.2(5)	1,073.5(12)	2,227.9(5)	204.2(0.21)	42.3(26.8)	40.7(0.01-K)
411.1	1,074.5(2)	2,234.0(5)	212.8(0.23)	43.0(48.3)	40.8(0.25-K)
436.5	1,079.2(8)	2,255.5(5)	219.8(0.19)	48.5(4.79)	41.1(0.01-K)
443.2(24)	1,107.0(2)	2,293.3(5)	224.7(0.21)	49.0(9.27)	41.1(0.11-K)
450.9(2)	1,114.0(3)	2,357.2(5)	225.9(0.15)	49.0(0.15)	41.1(0.04-K)
469.6(2)	1,119.9(11)	2,361.2(3)	238.5(0.15)	50.0(3.10)	41.3(0.24-K)
472.7(5)	1,121.1(8)	2,367.6(7)	253.0(0.15)	50.1(1.20)	41.4(0.25-K)
479.4	1,153.5(14)	2,403	269.1(0.13)		41.5(0.05-K)
481.0	1,159.0(8)	2,450	276.0(0.1)		41.6(0.03)
488.5	1,162.4(9)	2,656	276.7 (0.21)		41.6(0.03)
508.4(3)	1,168.0(4)	2,785			41.8(0.04)
515.3	1,174.2(11)	2,974			41.8(0.04)
526.9(7)	1,180.3(15)	3,010			41.8(0.01)
530.1	1,180.9(1)	3,050			41.8(0.01)
534.3(7)	1,187.2(2)	3,070			41.8(0.01)
542.5	1,193.8(4)	3,096			41.9(0.03)
551.3(6)	1,218.7(13)	3,122			42.0(0.01)
557.2	1,220.5(11)	3,218			42.0(0.05)
563.6	1,230.7(3)	3,225			42.2(0.01)
576.0	1,242.5(10)				42.3(0.01)
583.5(10)	1,252.6(10)				42.3 (0.01)
599.4	1,254.8(5)				42.6(0.02)
609.4	1,258.1(14)				42.7(0.05)
599.5	1,264.6(5)				42.7(0.05)
609.6(25)	1,266.4(12)				42.9(0.01)
614.5(9)	1,284.6				42.8 (0.01)
626.3(5)	1,291.7(2)				43.0(0.01)
652.4	1,322.4(3)				43.0(0.01)
658.9	1,324.8(1)				43.0(0.01)
700.1	1,334.5(23)				46.5(0.02)
704.4(9)	1,357.5(10)				46.7(0.02)

Table 3 continued

E_γ (I_γ), keV (relative units)	E_γ (N_{ICC})	E_x (I_γ)	E_{Ae} (I_{Ae})
709.9(9)	1,605.2(19)		47.0(0.02)
717.1(2)	1,646.2(18)		47.0(0.04)
727.1(8)	1,682.2(15)		47.1(0.02)
727.6(18)	1,722.1(7)		47.4(0.01)
743.7(13)	1,728.6(7)		47.5(0.01)
747.4(10)	1,732.4(6)		48.0 (0.01)
752.7	1,738.9(3)		48.1 (0.01)
762.3(8)	1,826.0(3)		48.1(0.01)
803.9	1,827.7(4)		48.2(0.01)
898.2(12)	1,845.5(24)		48.3(0.01)
905.1(1)	1,857.4(23)		48.3(0.01)
927.0(10)	1,872.9(3)		48.4(0.01)
943.9(1)	1,958.9(4)		48.4(0.01)

Here N_{ICC}—internal conversion coefficient.

and 15 radiation processes from 1,080.60 to 1,449.897 keV with ICC (0.00059-0.00099). In electron orbits rearrangement processes taking place in atom, the following observed x-ray radiation with energies (intensities) shown in keV and Auger electrons with high values of energies (intensities) shown in keV are presented in the Table 3 [25]. In the case of ^{155}Gd(n,α)^{152}Sm reaction, stable ^{152}Sm nucleus can also occur to be in the excited state with excitation of lower levels with energies of 121.7817(3), 366.4795(9) and 684.701(15) keV. Life-times of these levels are 1.400(11) ns, 57.7(8) ps and 6.2(4) ps, respectively. De-excitation takes place through γ-transitions to the ground state of ^{152}Sm nucleus.

Neutrons in ^{156}Gd isotope can cause the following reactions: ^{156}Gd(n,p)^{156}Eu, ^{156}Gd(n,d)^{155}Eu, ^{156}Gd(n,t)^{154}Eu, ^{156}Gd(n,α)^{153}Sm, ^{156}Gd(n,2n)^{155}Gd. Among them only ^{156}Gd(n,2n)^{155}Gd reaction has 19.6 transformations per second, whereas the rest have negligibly small number of nuclear transformations per second from 5.2×10^{-8} to 1.6×10^{-4}.

In the ^{156}Gd(n,2n)^{155}Gd reaction, stable ^{155}Gd nucleus can also occur to be in the excited state with excitation of lower levels with energies from 88.970 to 288.187 keV. Life-times of these levels are 3.02(4) ns, 172(4) ps in ^{154}Sm and 2.21(2) ns, 111.9(17) ps in ^{156}Gd. De-excitation takes place through γ-transitions to the ground state.

Neutrons in ^{157}Gd isotope can cause the following reactions: ^{157}Gd(n,γ)^{158}Gd, ^{157}Gd(n,p)^{157}Eu, ^{157}Gd(n,d)^{156}Eu, ^{157}Gd(n,t)^{155}Eu, ^{157}Gd(n,^{3}He)^{155}Sm, ^{157}Gd(n,α)^{154}Sm, ^{157}Gd(n,nα)^{153}Sm, ^{157}Gd(n,2n)^{156}Gd. Among them: ^{157}Gd(n,γ)^{158}Gd, ^{157}Gd(n,α)^{154}Sm and ^{157}Gd(n,2n)^{156}Gd reactions have 7.67×10^7, 21.8 and 15.2 nuclear transformations per second, and the rest have negligibly small number of nuclear transformations per second, from 3.6×10^{-7} to 1.41×10^{-2}. Energies of the reactions with higher probability are 7.94, 7.28 and 7.87 MeV, respectively. In ^{157}Gd(n,γ)^{158}Gd reaction, emitted γ-quanta with higher probability with relative intensities higher than 100 have the following energies in keV (Table 4) (J. Tauren et al. [25] and R. B. Firestone et al. [26]).

It is known that this reaction induces the internal electron conversion process in the excited ^{158}Gd isotope. The highest probability has γ-radiation of excited ^{158}Gd isotope with E_γ—energies and N_{ICC}—internal conversion coefficients (ICC) (Table 4). There are also 50 γ-radiation processes with energies from 695.742 to 1,300.85 keV with ICC (0.00117-0.00887). In the ^{158}Gd atom, electron orbits are identical to those of ^{156}Gd, and moreover, the internal conversion process mainly takes place in atom shells located close to nucleus, therefore, produced x-ray radiation and Auger

Table 4

	E_γ (I_γ), keV(relative units)		E_γ (N_{ICC})		
79.5(14)	998.4(5)	1,782.0(5)	79.5(6.02)	417.9(0.01)	944.1
181.9(4)	1,000.8(7)	1,835.9(6)	114.5(0.20)	421.2(0.04)	962.1
213.0(4)	1,005.8(9)	1,857.0(4)	117.3(1.4)	423.7(0.02)	977.1
255.7(5)	1,007.2(7)	1,878.3(7)	135.3(0.86)	435.5(0.01)	998.4
277.5(7)	1,010.2(5)	1,943.4(5)	154.9(0.09)	438.8(0.03)	1,000.8
332.7(8)	1,028.3(8)	1,955.9(6)	159.0(0.05)	446.1(0.02)	1,007.2
365.4(5)	1,034.5(6)	2,040.6(6)	181.9(0.31)	475.2(0.01)	1,010.2
435.5(11)	1,062.3(9)	2,180.3(3)	188.8(0.05)	475.8(0.01)	1,028.3
446.1(5)	1,097.0(5)	2,260.7(3)	200.1(0.18)	479.6(0.01)	1,034.5
516.2(5)	1,107.6(7)	2,367.7(3)	213.0(0.18)	491.7(0.01)	1,097.0
539.6(17)	1,116.5(5)	2,451.2(6)	217.7(0.04)	493.8(0.01)	1,107.6
606.4(20)	1,119.2(6)	2,566	218.2(0.04)	498.7(0.01)	1,116.5
637.2(5)	1,184.0(8)	2,640(2)	235.4(0.03)	502.8(0.01)	1,119.2
688.8(25)	1,186.0(8)	2,743	236.2(0.03)	516.2(0.01)	1,186.0
743.1(30)	1,215.7(4)	2,804	251.9(0.09)	518.8(0.02)	1,219.9
750.1(3)	1,219.9(8)	2,842	253.9(0.02)	528.0(0.01)	1,237.5
780.0(5)	1,237.5(9)	2,844(2)	255.7(0.02)	528.2(0.01)	1,323.4
782.3(4)	1,312.1(12)	2,986	277.5(0.08)	531.9(0.02)	1,327.1
820.1(4)	1,323.4(5)	3,039	280.6(0.07)	539.6(0.02)	1,348.0(13)
824.1(4)	1,327.1(8)	3,081	282.7(0.02)	540.3(0.01)	1,372.9
832.9(5)	1,372.0(2)	3,108	283.9(0.02)	561.7(0.01)	1,377.8
870.9(5)	1,372.9(14)	3,161	291.9(0.02)	592.9(0.02)	1,437.9
887.7(5),	1,377.8(12)	3,179	295.7(0.02)	606.4(0.01)	
897.4(20)	1,392	3,192(1)	315.0(0.01)	646.1(0.01)	
902.0(6)	1,433.7(3)	3,201(1)	329.8(0.08)	688.8(0.01)	
915.0(5)	1,437.9(12)	3,288	330.3	743.0(0.01)	
917.5(5)	1,639.9(5)	3,299	332.7	750.1(0.01)	
922.5(5)	1,663.7(20)	3,428	336.2(0.01)	782.3(0.01)	
944.1(5)	1,691.6(7)	3,470	365.1(0.01)	824.1	
962.1(4)	1,693.4(3)	3,577	365.4	915.0	
977.1(13)	1,738.0(3)	3,740	388.8(0.01)	922.5	

electrons have identical spectrum, as in the case of ^{156}Gd (Table 3). In the ^{157}Gd(n,α)^{154}Sm reaction, the energy of reaction is shared between α-particle and recoil-nucleus. ^{154}Sm is stable isotope, but as result of the reaction it can occur in the excited state with excitation of lower levels of nucleus with energies of 81.976 and 266.79 keV. In the ^{157}Gd(n,2n)^{156}Gd reaction lower levels with energies of 88.970 and 288.187 keV are excited in the ^{156}Gd nucleus. Life-times of these levels are 3.02(4) ns, 172(4) ps for ^{154}Sm and 2.21(2) ns, 111.9(17) ps for ^{156}Gd. De-excitation takes place through γ-transitions to the ground state of ^{156}Gd nucleus.

Neutrons in ^{158}Gd isotope can cause the following reactions: ^{158}Gd(n,γ)^{159}Gd, ^{158}Gd(n,p)^{158}Eu, ^{158}Gd(n,d)^{157}Eu, ^{158}Gd(n,t)^{156}Eu, ^{158}Gd(n,^{3}He)^{156}Sm, ^{158}Gd(n,α)^{155}Sm, ^{158}Gd(n,2n)^{157}Gd. Among them, the ^{158}Gd(n,γ)^{159}Gd and ^{158}Gd(n,2n)^{157}Gd reactions have 0.053 and 23.8 nuclear transformations per second, respectively, whereas those numbers are negligibly small for the rest of reactions (from 2.33×10^{-5} to 1.48×10^{-2}). In the ^{158}Gd(n,γ)^{159}Gd reaction, ^{159}Gd nucleus is β^--radioactive with life-time of 18.475 h. The β^--particles are emitted with energies of 970.6(62.5%), 912.61(25.4%), 833.1(0.017%), 622.32(0.31%) and 607.6(11.7%) keV, respectively, and γ-quanta with

energies of 57.99, 137.5, 348.28 and 363.54 keV, respectively (see J. Tauren et al. [25] and R. B. Firestone et al. [26]). For ^{158}Gd(n,2n)^{157}Gd reaction, final ^{157}Gd nucleus is stable. Although, it can occur to be in the excited state with excitation of lower levels of ^{157}Gd with energies [corresponding life-times] of 54.533(6) keV [130(8) ps], 63.917(5) keV [0.46(4) ns], 131.455(9) keV [95(5) ps], 180.229(11) keV [no data available], 227.31(5) keV [16.7(15) ps].

Neutrons in ^{160}Gd isotope can cause the following reactions: ^{160}Gd(n,γ)^{161}Gd, ^{160}Gd(n,2n)^{159}Gd, ^{160}Gd(n,p)^{160}Eu, ^{160}Gd(n,d)^{159}Eu, ^{160}Gd(n,t)^{158}Eu, ^{160}Gd(n,α)^{157}Sm, ^{160}Gd(n,nα)^{156}Sm. Among them, ^{160}Gd(n,γ)^{161}Gd and ^{160}Gd(n,p)^{160}Eu reactions have highest probability with 12.9 and 0.812 nuclear transformations per second, respectively, whereas those numbers are negligibly small (from 8.42×10^{-4} to 2.489×10^{-2}) for the rest of reactions. In the case of ^{160}Gd(n,γ)^{161}Gd reaction, produced nucleus is β^--radioactive with the life-time of 3.66 min, Q_β—energy of β^--particles is Q_β = 1,955.6 keV. ^{161}Gd nucleus decays into ^{161}Tb, which is also β^--radioactive with the life-time of 6.88 days. In the case of ^{160}Gd(n,p)^{160}Eu reaction, ^{160}Eu nucleus is also β^--radioactive with the life-time of 38 sec, and energy Q_β = 4,580 keV. This ^{160}Eu nucleus decays into stable ^{160}Gd nucleus (J. Tauren et al. [25] and R. B. Firestone et al. [26]).

4. Calculations and Discussions

As one can see from the above analysis, as a result of irradiation of ^{nat}Gd with epithermal neutron flux a large number of secondary particles with different LET are produced. It is also of interest to determine their number and energies during the ^{nat}Gd NCT. The studies of Magnevist preparation pharmacokinetics by G. Abdullaeva et al. [27] demonstrate that the optimal irradiation time for the ^{nat}Gd NCT is approximately 30 min after intra-tumoural introduction of the preparation. Such an irradiation of ^{nat}Gd (1 g) with epithermal neutron flux for 30 min causes ^{152}Gd(n,α)^{149}Sm reaction as a result of which 360 α-particles are produced with energy of Q_α = 1,869.9 keV. In the ^{154}Gd(n,t)^{152}Eu reaction, 3,600 tritons with energies Q_t~2-3 MeV; β^--particles with energies from 175.39 to 1,474.52 keV; β^+-particles with energies from 224.41 to 1,752.52 keV; γ-quanta with energies from 367.79 to 1,314.67 keV are produced. In the ^{155}Gd(n,γ)^{156}Gd reaction with 3.2×10^{10} nuclear transformations per second, γ-quanta with energies from 79.878 to 3,225 keV, electrons with energies from 79.878 to 1,040.47 keV, x-ray radiation with energies from 5.3620.266 to 50.099 keV and Auger electrons with energies from 6.701 to 48.424 keV are mainly produced. In this reaction, 26,640 α-particles can be produced with the values of energy ranging between Q_α = 1-3 MeV. The ^{156}Gd isotope produces 29,880 neutrons with energies of 2-3 MeV. In the ^{157}Gd(n,γ)^{158}Gd reaction, the ^{157}Gd isotope with 1.38×10^{11} nuclear transformations per second mainly produces γ-quanta with energies from 79.5104 to 3,841 keV, electrons with energies from 79.5104 to 1,437.89 keV, x-ray radiation with energies from 5.3620 to 50.099 keV and Auger electrons with energies from 6.701 to 48.424 keV, respectively. In this reaction, 39,240 α-particles and 27,360 neutrons with the values of energy ranging between Q_α = 2-3 MeV and 1-3 MeV, respectively, can be produced. In the ^{158}Gd(n,γ)^{159}Gd and ^{158}Gd(n,2n)^{157}Gd reactions, 42,840 neutrons with energies 3-4 MeV, 100 β^--particles with energies from 607.6 to 970.6 keV and γ-quanta with energies from 54.533 to 227.31 keV are produced. In the ^{160}Gd(n,γ)^{161}Gd and ^{160}Gd(n,p)^{160}Eu reactions with 12.9 and 0.812 nuclear transformations per second, 23,320 β^-- particles with energy of Q_β-1,955.6 keV and 1,561 β^--particles with energy Q_β-4,580 keV and γ-quanta with the values of energies 56.3, 77.4, 102.3, 165.2, 283.6, 338.1, 360.9 and 480.1 keV are emitted. Analyzed spectra of these particles demonstrated that the particles produced in these reactions have small paths, namely t-, α-, β-particles, internal conversion electrons, Auger electrons and x-ray radiation with different LET. The major part of

their energy is lost within several centimetres of biological tissue. Apart from these, the particles with larger penetration depth, like neutrons and γ-quanta are produced. In turn, these particles can cause other nuclear reactions and can knock out orbital electrons, like in the case of photon-capture therapy.

The results of our analysis are in a good agreement with conclusions drawn by other authors regarding the fact that the main contribution to the absorbed dose is made by those secondary particles produced by with ^{155}Gd and ^{157}Gd isotopes in the (n,γ) reactions. But their contribution to the absorbed dose must be less than 90%. This contribution to the absorbed dose made by the ^{155}Gd and ^{157}Gd isotopes through the (n,γ) reaction must be almost of the same value. This fact is supported by comparing γ-spectra of neutron-capture by ^{155}Gd and ^{157}Gd (Table 3 and 4). Here, one can see that in ^{155}Gd the most effective (absorbed in 4-5 cm of biological tissue) γ-quanta with energies ranging between 0 and 400 keV are reproduced more than in ^{157}Gd at (n,γ)-reaction. Such γ-quanta mainly lose major fraction of their energy in 4-5 cm thick biological tissue. Those γ-quanta with higher energies participate in orbital electron knock out processes taking place in surrounding tissues. Compared spectra of other particles (internal conversion electrons, Auger electrons, x-ray radiation) demonstrates that mean values of their energies used earlier in the absorbed dose calculations [13-21] need to be determined much more precisely (Table 1). To obtain more accurate data on characteristics of these particles, complex precise measurements are required by using detectors of such particles. There is also an indirect method in the framework of which biological tissue cells damage by such particles can be modelled, irradiated and studied by means of histological analysis of the irradiated samples allowing one to evaluate characteristics of such particles. There is an additional conclusion that can be added to those mentioned above, that ^{nat}Gd NCT must take into account contribution of secondary particles produced by ^{152}Gd, ^{154}Gd, ^{156}Gd, ^{158}Gd and ^{160}Gd isotopes to the absorbed dose. As a total, all these secondary particles with certain characteristics can make sufficient contribution to the absorbed dose in the Gd NCT. The applied epithermal neutron flux has low intensity of accompanying gamma-quanta in the direct flux, that is why, their contribution to the absorbed dose is neglected. For a maximally precise calculation of the absorbed dose in the Gd NCT, the processes must be modelled and calculated with taking into account contribution of these secondary particles, which is the topic of our further studies.

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