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APPLICATION OF GENERALIZED PERTURBATION THEORY TO SENSITIVITY ANALYSIS IN BORON NEUTRON CAPTURE THERAPY

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ABSTRACT

Boron neutron capture therapy – BNCT is a binary cancer treatment used in brain tumors. The tumor is loaded with a boron compound and subsequently irradiated by thermal neutrons. The therapy is based on the ^{10}B (n, α) ^{7}Li nuclear reaction, which emits two types of high-energy particles, α particle and the ^{7}Li nuclei. The total kinetic energy released in this nuclear reaction, when deposited in the tumor region, destroys the cancer cells. Since the success of the BNCT is linked to the different selectivity between the tumor and healthy tissue, it is necessary to carry out a sensitivity analysis to determinate the boron concentration. Computational simulations are very important in this context because they help in the treatment planning by calculating the lowest effective absorbed dose rate to reduce the damage to healthy tissue. The objective of this paper is to present a deterministic method based on generalized perturbation theory (GPT) to perform sensitivity analysis with respect to the ^{10}B concentration and to estimate the absorbed dose rate by patients undergoing this therapy. The advantage of the method is a significant reduction in computational time required to perform these calculations. To simulate the neutron flux in all brain regions, the method relies on a two-dimensional neutron transport equation whose spatial, angular and energy variables are discretized by the diamond difference method, the discrete ordinate method and multigroup formulation, respectively. The results obtained through GPT are consistent with those obtained using other methods, demonstrating the efficacy of the proposed method.

1. INTRODUCTION

Boron neutron capture therapy (BNCT) is a binary cancer therapy that is used especially for treatment of brain tumors. The tumor tissue is loaded with a ^{10}B-enriched compound, BPA-f (boronophenylalanine-fructose), and subsequently irradiated by neutrons with epithermal energies between 1 eV and 10 keV [10], which penetrate the tissue and are thermalized (0.0253 eV), producing little effect on healthy tissue [15].

The therapy is based on the $^{10}B\ (n, \alpha)\ ^{7}Li$ nuclear reaction, which emits two types of particles with high energy, alpha particles and the ^{7}Li nuclei. The total kinetic energy (2.79 MeV) released in this nuclear reaction, when deposited in the tumor region, destroys the cancer cells.

To plan BNCT treatment, in addition to considering the proper dose of the $^{10}B\ (n, \alpha)\ ^{7}Li$ nuclear reaction, it is necessary determinate the dose deposited by neutrons scattered in the healthy tissue surrounding the tumor. For this reason, it is important to have different selectivity between the tumor and healthy tissue. In this context, sensitivity analysis considering different boron concentration values is essential to reduce the damage to healthy tissue [7].

The objective of sensitivity analysis is to evaluate the effect of varying the parameters of a model or phenomenon on the final result of the simulation. In BNCT, the computational simulation is very important; because it helps planning the treatment by analyzing the absorbed dose rate and its possible effects on healthy tissues, so as not to expose patients to unnecessary doses.

The objective of this paper is to present a deterministic method based on generalized perturbation theory (GPT) to perform sensitivity analysis of the ^{10}B concentration. This sensitivity analysis is important to determine of the absorbed dose rate of patients undergoing BNCT. For this purpose, the method relies on the neutron transport equation to simulate the neutron flux in all brain regions. The spatial, angular and energy variables are discretized by the finite difference method (diamond difference-DD), the discrete ordinate method and multigroup formulation, respectively. Two-dimensional Cartesian geometry is applied. The generalized perturbation theory method's advantages, compared to methods traditionally used, is that the former calculates the optimized ^{10}B concentration and consequently the absorbed dose rate with a significant reduction in computational time. The results obtained with GPT are consistent with those obtained using the traditional methods [13], demonstrating the efficacy of the proposed method.

2. METHODOLOGY

2.1 Generalized Perturbation Theory (GPT)

The generalized perturbation theory (GPT) is a heuristic mathematical method used for sensitivity analysis of some physical phenomena. The initial applications of the theory were concentrated in the reactor physics field. The GPT formally uses the concept of an importance function and of conservation of particles, in relation to linear or linearized fields.

The importance function concept in GPT [3,4] corresponds to the contribution of a given particle, inserted at a given time t and a given point $\vec{r}$ of the phase space, to the response function.

The importance function equation is obtained directly, whereas that the contribution response of a particle, introduced into a system of the phase space at a given initial time t, is conserved until a final time t_F (importance conservation principle). In this paper, we consider the stationary problem based on [3], so that the response function T, which represents the neutron absorption rate by the ^{10}B, is defined for two-dimensional geometry as:

$$T = \int_{A_R}\int_{4\pi}\int_0^{\infty} S^+(x,y,E,\hat{\Omega})\,\varphi(x,y,E,\hat{\Omega})\,dE\,d\hat{\Omega}\,dA \tag{1}$$

where A_R is a determined region of the brain, $\varphi(x,y,E,\hat{\Omega})$ is the neutron angular flux at the point (x,y) in A_R, which is the solution of the linear transport equation, defined as,

$$L\,\varphi(\vec{r},E,\hat{\Omega}) = S_{ext}(\vec{r},E,\hat{\Omega}) \tag{2}$$

where $S_{ext}(\vec{r},E,\hat{\Omega})$ is the external source and L the linear neutron transport operator, such that,

$$L = \hat{\Omega}\cdot\vec{\nabla}(\bullet) + \Sigma_t(\vec{r},E)(\bullet) - \int_{4\pi}\int_0^{\infty}\Sigma_S(\vec{r},E'\to E,\hat{\Omega}'\to\hat{\Omega})(\bullet)dE'\,d\hat{\Omega}' \tag{3}$$

The parameters $\Sigma_t(\vec{r},E)$ and $\Sigma_S(\vec{r},E'\to E,\hat{\Omega}'\to\hat{\Omega})$ are the total macroscopic cross section and the differential scattering macroscopic cross section of neutrons at point (x,y) with energy E and traveling in direction $\hat{\Omega}$ that will be scattered in an energy interval dE' about E' at a solid angle $d\Omega'$ about $\hat{\Omega}'$ [11].

The source term $S^+(x,y,E,\hat{\Omega})$, in the region A_R, is represented by:

$$S^+(x,y,E,\hat{\Omega}) = \begin{cases}\Sigma_a(x,y,E) & \text{para } (x,y)\in A_R\\ 0 & \text{para } (x,y)\notin A_R\end{cases} \tag{4}$$

The value $\sum_a(x,y,E)$ is the absorption macroscopic cross section of ^{10}B at a point (x,y) of A_R, such that,

$$\Sigma_a(x,y,E) \equiv N_B\sigma_a^B(x,y,E)\,. \tag{5}$$

The values of N_B and $\sigma_a^B(x,y,E)$ are, respectively, the atomic number density and the absorption microscopic cross section of ^{10}B at point (x,y) of A_R.

If a neutron with energy E, traveling in direction $\hat{\Omega}$, at time t, is introduced into a system in position $\vec{r}$, an increase in angular neutron flux results in an increase δT of the absorption rate T considered. This variation can be produced directly for this neutron or, in multiplicative systems, by its descendents (importance conservation principle). Therefore, the increase δT is defined as the neutron importance. This importance can be denoted by $\psi^*(\vec{r},E,\hat{\Omega})$, which is a function that depends on the space, angle and energy, and is a solution of the equation:

$$L^*\psi^*(\vec{r},E,\hat{\Omega}) = S^+(\vec{r},E,\hat{\Omega})\,, \tag{6}$$

where L^* is the adjoint neutron transport operator, defined by:

$$L^* = -\,\hat{\Omega}\cdot\vec{\nabla}(\bullet) + \Sigma_t(\vec{r},E)(\bullet) - \int_{4\pi}\int_0^{\infty}\Sigma_S(\vec{r},E\rightarrow E',\hat{\Omega}\rightarrow\hat{\Omega}')(\bullet)dE'\,d\hat{\Omega}'\,. \quad (7)$$

By considering the linear system and the importance concept it is possible to obtain the relationship known as the "source reciprocity relationship" [4]:

$$T = \int_V\int_{4\pi}\int_0^{\infty} S^+(\vec{r},E,\hat{\Omega})\varphi(\vec{r},E,\hat{\Omega})\,dE\,d\hat{\Omega}\,dV = \int_V\int_{4\pi}\int_0^{\infty}\psi^*(\vec{r},E,\hat{\Omega})S(\vec{r},E,\hat{\Omega})\,dE\,d\hat{\Omega}\,dV\ , \quad (8)$$

where

$$S(\vec{r},E,\hat{\Omega}) = S_{ext}(\vec{r},E,\hat{\Omega}) + S_S(\vec{r},E,\hat{\Omega})\,, \quad (9)$$

With

$$S_S(\vec{r},E,\hat{\Omega}) = \int_{4\pi}\int_0^{\infty}\Sigma_S(\vec{r},E'\rightarrow E,\ \hat{\Omega}'\rightarrow\hat{\Omega})\,\varphi(\vec{r},E,\hat{\Omega})\ dE'\,d\hat{\Omega}'\,. \quad (10)$$

The main interest when performing sensitivity analysis of physical phenomenon is to evaluate the variation δT of T due to perturbation δp_i of the parameter set $p_i(i=1,2,...,I)$ that are relevant to the phenomenon. The variation δT can be defined as:

$$\delta T = \int_{t_0}^{t_F}\{\sum_i\frac{\partial T}{\partial p_i}\delta p_i + \frac{1}{2!}\sum_{i,j}\frac{\partial^2 T}{\partial p_i\partial p_j}\delta p_i\delta p_j + \frac{1}{3!}\sum_{i,j,k}\frac{\partial^3 T}{\partial p_i\partial p_j\partial p_k}\delta p_i\delta p_j\delta p_k + \ldots,\} \quad (11)$$

The first-order sensitivity coefficient considered in this paper can be defined by:

$$\beta_i \equiv \frac{p_i}{T}\int_{t_0}^{t_F}\frac{\partial T}{\partial p_i}\,dt\,. \quad (12)$$

Each reaction of the neutrons and boron deposits energy due to the α particle and ^7Li atoms. Thus, the sensitivity analysis of the neutron absorption rate by ^{10}B serves to support treatment planning for patients undergoing BNCT, because it provides an estimate of the number of ^{10}B (n,α) ^7Li reactions per unit of time. This information is important to calculate the absorbed dose rate due to the neutrons, which according to [12] is calculated by the equation:

$$D(x,y) = c\,\phi_g(x,y)\,\sigma_{a,g}NA(x,y)E_T\,, \quad (13)$$

where D(x,y) is the absorbed dose rate at point (x,y) in the medium in Gy/h, $\phi_g(x,y)$ is the thermal scalar neutron flux at point (x,y) in n/cm^2.s, NA(x,y) is the number of the specified nuclei/gr at point (x,y), $\sigma_{a,g}$ is the absorption microscopic cross section for thermal neutrons in cm^2, E_T is the energy released in the reaction in MeV and g is the energy group, which is considered to be thermal. The constant c = 5.76 x 10^{-7} is the conversion coefficient, converting MeV/gr into Gy/h.

2.2 Sensitivity Analysis in BNCT using GPT

The sensitivity analysis concerning the neutron absorption rate by ^{10}B in the brain (healthy and tumor tissue) is performed using the generalized perturbation theory (GPT), considering the boron concentration as the principal parameter [5].

The equation that represents the variation of T, equation (1), according to the boron concentration, is calculated as follows:

$$\frac{\partial T}{\partial N_B} = \int_{A_R}\int_0^\infty\int_{4\pi}\left\{\frac{\partial S^+(x,y,E,\hat{\Omega})}{\partial N_B}\varphi(x,y,E,\hat{\Omega}) + S^+(x,y,E,\hat{\Omega})\frac{\partial \varphi(x,y,E,\hat{\Omega})}{\partial N_B}\right\} d\hat{\Omega}\, dE\, dA \tag{14}$$

From equation (2), the following equation is defined,

$$L\left(\frac{\partial\varphi(x,y,E,\hat{\Omega})}{\partial N_B}\right) + \frac{\partial L}{\partial N_B}\varphi(x,y,E,\hat{\Omega}) = 0 \,. \tag{15}$$

Then,

$$L\left(\frac{\partial\varphi(x,y,E,\hat{\Omega})}{\partial N_B}\right) = -\frac{\partial L}{\partial N_B}\varphi(x,y,E,\hat{\Omega}) \equiv \widehat{S}(x,y,E,\hat{\Omega}) \tag{16}$$

with

$$\widehat{S}(x,y,E,\hat{\Omega}) = \begin{cases} \int_0^\infty\int_{4\pi}\sigma_S^B(E'\to E)\,\varphi(x,y,E',\hat{\Omega}')\,d\hat{\Omega}'dE' - \\ \sigma_t^B(E)\varphi(x,y,E,\hat{\Omega}) & \text{para}\,(x,y)\in A_R \\ 0 & \text{para}\,(x,y)\notin A_R \end{cases} \tag{17}$$

Based on the source reciprocity relationship of GPT,

$$\int_{A_R}\int_0^\infty\int_{4\pi} S^+(x,y,E,\hat{\Omega})\frac{\partial\varphi(x,y,E,\hat{\Omega})}{\partial N_B}\, d\hat{\Omega}\, dE\, dA = \int_{A_R}\int_0^\infty\int_{4\pi}\psi^*(x,y,E,\hat{\Omega})\,\widehat{S}(x,y,E,\hat{\Omega})\, d\hat{\Omega}\, dE\, dA \tag{18}$$

where $\psi^*(x,y,E.,\hat{\Omega})$ is the importance function defined in equation (6).

The first-order sensitivity coefficient β_B, based on equation (12), is calculated as follows:

$$\beta_B \equiv \frac{N_B}{T}\int_{A_T}\int_0^{\infty}\int_{4\pi}\left\{\sigma_a^B(E)\varphi(x,y,E,\hat{\Omega}) + \psi^*(x,y,E,\hat{\Omega})\hat{S}(x,y,E,\hat{\Omega})\right\}d\hat{\Omega}\, dE\, dA\ , \qquad (19)$$

so that

$$\delta T = \beta_B \frac{\delta N_B}{N_B} T\ . \qquad (20)$$

Since the GPT method uses the importance function concept and conservation principles and also the source reciprocity relationship, to perform the sensitivity analysis, equations (2) and (6), which define the values $\varphi(x,y,E,\hat{\Omega})$ and $\psi^*(x,y,E.,\hat{\Omega})$, are solved only once. These values are then used to determine the values of T and β_B, considering a reference boron concentration value. For any other boron concentration value, δT is always calculated by equation (20), which is very simple.
Calculation of δT by the direct method uses the following equation:

$$\delta T = T_F - T_i\ , \qquad (21)$$

where T_i is the neutron absorption rate for an initial boron concentration (reference value) and T_F is the neutron absorption rate for another boron concentration value considered. Thus, to perform sensitivity analysis by the direct method it is necessary solve equation (2) every time the boron concentration value is changed, making the computational simulation very time consuming.
The use of GPT to perform sensitivity analysis in BNCT is very advantageous, because it reduces the computational time to calculate the response variations of interest when the parameters are altered.

3. RESULTS

In this paper, the sensitivity analysis calculations are based on generalized perturbation theory and consider the boron concentration as the parameter of interest.
The geometric shape of the spatial distribution of thermal neutron irradiation of brain tumors allows up to 6 cm without surgical procedures [6,8]. For this reason, here we simulate a case with a tumor of dimension (6x6) cm^2, considering the brain as being a square with dimension (18x18) cm^2, energies (1 eV to 10 keV); mesh (4x4). The diamond difference method is used to solve the equation (2) which considers the S_4 discrete ordinate formulation, P_3 method (anisotropic scattering) and vacuum boundary conditions. For numerical solution of the fixed source problem is used the “source iteration” method [11], with 10^{-4} as convergence criterion. The boron concentration reference values are 10 ppm in the healthy tissue and 30 ppm in the tumor. To perform the sensitivity analysis, we considered 40 ppm, 100 ppm and 125 ppm in the tumor.
Figure 1 shows the geometrical configuration. Besides the tumor (R5 region), regions R2, R4, R6 and R8 are also considered, which are healthy tissue adjacent to the tumor.

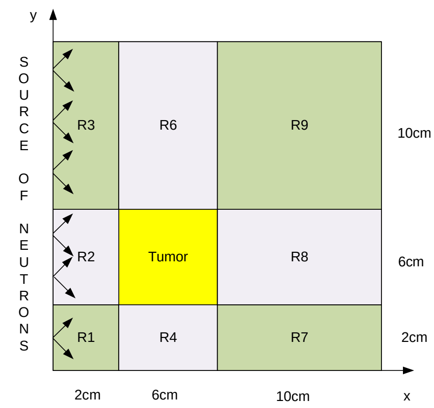

Figure 1. Configuration of brain considering a tumor measuring (6x6) cm^2

The computational code used to solve the neutron transport equation by the diamond difference (DD) numerical method [11] was developed by [1]. The nuclear data of the elements of human tissue and tumor were obtained from the ENDF/B-VI.8 database [14,2]. The atomic densities (1g/cm3) of these elements are shown in Table 1 and Table 2 [12].

Table 1. Atomic density of the human tissue elements

Elements	W%	Atomic Density x 10^{24}
H	10.7	0.064
O	71.4	0.0269
C	12.1	0.00602
N	4.5	0.00118

Table 2. Atomic density of the boron

^{10}B Concentration	Atomic Density x 10^{24}
10ppm	5.57E-07
30ppm	1.67E-06
40ppm	2.22E-06
100ppm	5.57E-06
125ppm	6.96E-06

The neutron absorption rate for the reference values (10 ppm-30 ppm, tissue and tumor) were calculated and the results of this simulation are presented in Table 3.

Table 3. The T and D_B values for the R_2, R_4, R_6, R_8 regions and tumor

Regions	Neutron Absorption Rate T	Absorbed Dose Rate D_B (Gy/h)
Tumor	1.93E-03	9.75E-13
R_2	7.63E-03	1.26E-11
R_4	3.72E-04	2.09E-13
R_6	2.95E-04	12.2E-14
R_8	2.41E-08	6.21E-15

The results obtained show that the value of the absorbed dose rate is higher in the R2 region (which represents healthy tissue, 10 ppm ^{10}B) than in the tumor region. The consequence of this fact is more neutrons absorbed in healthy tissue, which results in severe damage and destruction of healthy cells.

Sensitivity analysis is performed to increase the selectivity (tumor/tissue). In the first calculation, we determined the sensitivity coefficient β_B, which was 1.0034. After that, we calculated the variations δT considering the following boron concentration increases in the tumor region: 30ppm-40ppm, 30ppm-100ppm and 30ppm-125ppm, as shown in Table 4.

Table 4. Result of sensitivity analysis in tumor region obtained by GPT

Variation of 30ppm to:	Variation of δT	Neutron Absorption Rate T
40 ppm	1.00E-03	2.90E-03
100 ppm	4.50E-03	6.40E-03
125 ppm	6.10E-03	8.00E-03

The results presented in Table 4 show that to achieve higher tumor selectivity, the ^{10}B concentration must be greater than 125ppm in this region, because to any value less than this the neutrons absorption rate T will be higher in healthy tissue. However, the selectivity with difference 1:12.5 (10ppm in tissue and 125ppm in tumor) is not yet achieved with the boron compounds used. However, some studies in humans, as shown by [9], use a combination of different compound, such as borocaptate sodium (BSH) and BPA-fructose, to increase the ^{10}B concentration in the tumor. This would be a viable solution in cases like the one presented.

Another important consideration is related to the incident neutron energy. In the simulations performed by [13], for neutrons originating from a source with energies between (1eV and 3keV), the absorbed dose rate in the tumor region, with 4 cm in diameter (spherical geometry), was high only in the first two centimeters of the tumor.

To verify the behavior observed by [13], we ran a simulation considering the first two centimeters of the tumor, the ^{10}B concentrations in the tissue (10ppm) and tumor (30ppm) and energies between 1eV and 10keV.

Table 5. T values for different tumor dimensions

Tumor Dimension	Neutron Absorption Rate T
2cm x 6cm	1.25E-02
6cm x 6cm	1.93E-03

According to the result, shows in Table 5, similar behavior occurs. Therefore, in this case, the energy range between 1 eV and 10 keV is not sufficient for successful therapy. As most neutrons are absorbed in the first two centimeters of the tumor some cancer cells cannot be destroyed. The greater the distance between the neutron source and tumor, the greater must be the incident neutron energy so that the neutron absorption by ^{10}B is sufficient to destroy all the cancer cells.

In their simulations [13], concluded that with energies between 10 keV and 100 keV, the boron dose is more evenly distributed in the tumor, which provides greater selectivity between the tumor and surrounding tissue. Simulating this energy range in the example proposed in this paper, we obtained the results presented in Table 6.

Table 6. Neutron absorption rate in the tumor and R_2 regions for 10 keV to 100 keV

Regions	Neutron Absorption Rate T	Absorbed Dose Rate (Gy/h)
Tumor	1.89E-02	2.51E-09
R_2	8.42E-03	11.20E-11

Again the behavior is the same for the neutron absorption rate as in the simulations of [13], which show that the generalized perturbation theory method is effective to perform sensitivity analysis in BNCT.

4. CONCLUSION

Since the radiation field in BNCT consists separately of the dose of multiple components (different physical properties and biological effects), the value of the dose due to the radiation component varies not only with the boron concentration in the tumor region, but also with the selectivity between tumor and tissue, the energy spectrum of incident neutrons and the tumor location in of the region of interest. For this reason, the sensitivity analysis of these parameters is important to plan proper treatment.

The results of the studies performed in the adjacent region to the tumor are important to minimize the effects on healthy tissue because they allow estimating parameter values relevant to therapy to increase the differential of dose deposition between tumor and tissue. These results also show the compatibility of the results obtained by the method proposed in this work with other previous studies employing other methods.

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REFERENCES

1. ABREU, M. M. P., *Solução Numérica do Problema de Transporte de Nêutrons Independente do Tempo na Formulação de Ordenadas Discretas*, Programa de Engenharia Nuclear, COPPE/UFRJ, Rio de Janeiro, RJ, Brazil (1994).
2. FERREIRA, C. R.; SANTOS, A; *"Análise de Criticalidade Utilizando-se os Sistemas NJOY, AMPX-II e KENO-IV"*, Anais do VII ENFIR, Encontro Nacional

de Física de Reatores e Termohidráulica, Vol. 1, p. 215-225, Recife-PE, Brazil, (1989).

3. GANDINI, A., J. Nucl. Energy, 21, p. 755, (1967).
4. GANDINI, A., *Generalized Perturbation Theory (GPT) Methods*. A Heuristic Approach. Advanced in Nuclear Science, 19: 205-380, J. Lewins and M. Becker Eds. Plenum Press (1987).
5. GARCIA, V. S., *Estudos de Sensibilidade em BNCT Usando a Teoria de Perturbação Generalizada*, Programa de Engenharia Nuclear, COPPE/UFRJ, Rio de Janeiro, Brazil, (2009).
6. HARLING, O.K., ROBERT, K.A., MOULING, D.J., ROGUS, R.D., *Head phantoms for neutron capture Therapy*. Med Phys, 22: 579-583 (1997).
7. INTERNATIONAL ATONIC ENERGY AGENCY (IAEA), *Current Status of Neutron Capture Therapy*, In: IAEA – Tecdoc – 1223, IAEA, Wien (2001).
8. KATZ, D., *Treatment planning for boron neutron capture therapy at the New England Medical Center*. (Thesis) MIT, Massachusetts (1996).
9. KAWABATA, S., MIYATAKE, S., KAJIMOTO, *The early successful treatment of glioblastoma patients with modified boron neutron capture therapy*, Journal of Neuro-Oncology 65: 159 – 165 (2003).
10. LEE, C.L., ZHOU, X.-L., HARMON, J.F., et al., *Thermal Neutron Flux Mapping in a Head Phantom*, Nuclear Instruments and Methods in Physics Research A 422: 106 – 110, (1999).
11. LEWIS, E. E., MILLER JR., W. F., *Computational Methods of Neutron Transport*, American Nuclear Society, Inc, La Grange Park, Illinois, USA (1993).
12. MARASHI, M. K., *Analysis of Absorbed Dose Distribution in Head Phantom in Boron Neutron Capture Therapy, Nuclear Instruments and Methods in Physics Research*, A 440: 446 – 452, (2000).
13. NIEVAART, V.A., *"Spectral Tailoring for Boron Neutron Capture Therapy"*, Ph.D dissertation, Delft University of Technology, Amsterdam, Netherlands (2007).
14. NUCLEAR ENERGY AGENCY (NEA), 1989. Available at: http://www.nea.fr/dbforms/data/eva/evatapes/endfb_6_rel, retrieve in (2009).
15. VAN RIJ, C. M., WILHEN, A. G., VAN LOREN, A. C., SAUERWEIN, W. A. G., *Boron Neutron Capture Therapy for Glioblastoma Multiforme*. Pharm World Sci, 27: 92 – 95 (2005).