PROCEEDINGS OF SCIENCE

Manufacturing of boron thin films for the measurement of the $^{10}B(n,\alpha)^{7}Li$ reaction in BNCT

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The Boron Neutron Capture Therapy (BNCT) has been considered for the treatment of different types of aggressive cancers located in areas of difficult access or which already presented metastasis. The working principle of this therapy is the selective delivery of boron to the tumor cells, followed by the neutron irradiation that will induce the emission of α particles through the $^{10}B(n,\alpha)^{7}Li$ reaction used in BNCT. The high energy deposition rate of the product particles causes the death of the cells and this therapy becomes much effective if the healthy tissue is less exposed to this radiation. The objective of this work is to develop a method for measuring the rate of this reaction by using boron thin films that were manufactured with different concentrations of boric acid deposited over muscovite mica and then exposed to different irradiation time intervals at the reactor IEA-R1 located at IPEN, São Paulo. Here we show the first results on the density and uniformity of the boron thin films, where the detection of the particles is made using track detectors CR-39 and LR-115, their calibration and the first result for the $^{10}B(n,\alpha)^{7}Li$ reaction rate measurement.

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1. Introduction

An ideal therapy for cancer is one in which all tumor cells are selectively destroyed without damaging the normal tissue. Although, currently, the standard treatments (radiation therapy, chemotherapy, surgery) have cured many cancers, there are still gaps, such as the survival of tumor cells and subsequent recurrence and the patient's physical stress.

The Boron Neutron Capture Therapy (BNCT) is a therapy that have proven to be effective in the treatment of cancers located in areas inaccessible to surgery or those who already have presented metastases [1,2]. BNCT is based on the reaction of low energy neutron capture by ^{10}B (a stable isotope of boron); it is a binary radiotherapy, in other words, it brings together two components (low energy neutrons and atoms of boron) that when separated have only minor effects on cells [3]. The treatment consists in injecting boron into the tissue and then irradiating it with thermal neutrons (energy of about 0.025 eV); when the ^{10}B captures those neutrons, it goes to $^{11}B^*$ and decays into an alpha particle and ^{7}Li ion (with emission of a gamma). As the α and ^{7}Li emitted have high LET (linear energy tranfer; $LET_{\alpha} \sim 190$ keV/μm and $LET_{Li} \sim 160$ keV/μm [4]) and their ranges combined are of the order of the diameter of a typical cell (~ 12 μm) [5], BNCT causes damage mainly to the cell containing boron. Thus, if there is a higher concentration of boron in the tumoral cells than in the healthy ones, a higher dose will be delivered to the tumor during the neutron irradiation, making BNCT a local radiotherapy.

When irradiating tissues containing boron with thermal neutrons, although the main contribution to the dose will come from the $^{10}B(n,\alpha)^{7}Li$ reaction, neutron reactions with hydrogen and nitrogen must be considered: $^{1}H(n,\gamma)^{2}H$ and $^{14}N(n,p)^{14}C$ [6]. The cross section for thermal neutron capture by boron ($\sigma_{thermal\_10B}$ = 3840 barns) is much higher than the cross sections for the n + ^{1}H ($\sigma_{thermal\_1H}$ = 0.33 barns) and n + ^{14}N ($\sigma_{thermal\_14N}$ = 1.70 barns) reactions [7], but the concentration of these atoms in tissues are high and must be considered in the dose calculation.

There are some key aspects to make BNCT a successful cancer treatment: (1) development of boron compounds highly selective to the tumoral cells. In this way, the decay of boron into α and ^{7}Li occur mainly inside the cell that is intended to be damaged, causing minimum damage to healthy tissue; (2) development of neutron sources that can be placed inside hospitals (nowadays most of the research is done using nuclear reactors); (3) biodistribution of boron measurement and dosimetry must be precise, aiming a lower dose and shorter time treatment and (4) clinical protocols must be developed.

This work is related to the boron biodistribution measurement as its goal is to measure precisely the $^{10}B(n,\alpha)^{7}Li$ reaction rate, so that when tissues containing boron are irradiated the exactly damaged caused by α and ^{7}Li will be known. For this, boron thin films are manufactured and irradiated with thermal neutrons. It is important that the films of boron are thin, i.e. their thickness must be much less than the α and ^{7}Li ranges.

CR-39 (plastic polymer) and LR-115 (cellulose nitrate) will be used to detect the α and ^{7}Li tracks. The ion passage causes structural damaged that can be observed at the microscope after chemical etching [8]; it is possible then to count the tracks and determine the local concentration of ^{10}B (by measuring the track density).

2. Methodology

The method used for manufacturing the boron thin films is based on a method routinely used for the manufacturing of uranium and thorium thin films [9]. The technique consists in depositing a solution of boric acid (H_3BO_3) in water over muscovite mica, which is a very smooth surface. The film is then heated to transform the acid into oxide. Based on the neutron flux available for the irradiation of the boron thin films at the reactor IEA-R1 located at IPEN (~ 10^8 neutrons.cm^{-2}.s^{-1}) and the desired track density (that would be sufficiently great for statistical purposes but sufficiently small for not overlapping tracks), different concentrations of the boric acid solution have been prepared.

Three pieces of muscovite mica of 16 cm^2 (one piece for each concentration of boric acid solution) were the substrates for the films. To obtain a uniform spread of the solution over the mica surface, 20 μL ethyl alcohol, 400 μL ether and 20 μL Parlodion (nitrocellulose; 1.80 g Parlodion / 30 mL ether) were added to 400 μL H_3BO_3 solution.

Before heating the thin films, they were cut in four pieces of 4 cm^2, resulting in 12 boron thin films; six of them were heated at 400ºC and the other six at 750ºC (these temperatures were chosen based on the fact that it is desired that all boric acid is transformed into boron oxide [10]), all for four hours. After heating, each boron thin film was coupled with a detector (CR-39 with 9 cm^2 and LR-115 with about 2.5 cm^2), resulting in 12 different assemblies and then the boron thin films were irradiated with thermal neutrons (the lowest concentration films were irradiated for 60 minutes and the other films for 10 minutes).

For observing the tracks at an optical microscope (with an increase of 1000x), the detectors were chemically etched in a sodium hydroxide (NaOH) solution in water[1] at a thermal bath; the chemical etching damages the detector surface as a whole but the etching velocity is greater along the ion path, in such a way that channels are formed along the ion trajectory. Detailed information on the experimental procedures is shown in Table 1.

The α and ^{7}Li tracks can be counted and the superficial track density, which is proportional to the ^{10}B local concentration, is determined. For the $^{10}B(n,\alpha)^{7}Li$ reaction rate measurement, besides knowing the track density, it is necessary to calibrate the boron thin film and for this, a previously calibrated uranium thin film[2] is used; it is irradiated with the boron thin film that is going to be calibrated. In this work, only the boron thin film with the lowest acid boric solution concentration is calibrated, since the purpose is primarily to test the method.

[1] The desired amount of NaOH is dissolved in less than 100 mL of water and after stabilizing the solution at room temperature, it is completed with water to 200 mL.

[2] The uranium thin film was deposited over muscovite mica and the track detector used is also muscovite mica. It was irradiated for 60 minutes with thermal neutrons at a flux ~ 10^8 neutrons.cm^{-2}.s^{-1}. The chemical etching for revealing the fission tracks in the muscovite mica was done with 100 mL of hydrofluoric acid (48%) in a thermal bath at 15ºC for 90 minutes.

thin film of boron	solution concentration (g H_3BO_3 / L H_2O)	^{10}B superficial density (cm^{-2})	heating temperature (ºC)	detector	irradiation time interval (min)	chemical attack		
						(g NaOH / 200 ml final solution)	thermal bath (ºC)	bath time interval (min)
B1-1	0.03	~ 10^{13}	400	CR-39	60	50.02	70	30
B1-2				LR-115		19.98	60	20
B1-3			750	CR-39		50.07	70	30
B1-4				LR-115		20.01	60	20
B2-1	0.29	~ 10^{14}	400	CR-39	10	50.02	70	30
B2-2				LR-115		20.03	60	20
B2-3			750	CR-39		50.07	70	30
B2-4				LR-115		-	-	-
B3-1	2.99	~ 10^{15}	400	CR-39		50.02	70	30
B3-2				LR-115		-	-	-
B3-3			750	CR-39		50.07	70	30
B3-4				LR-115		-	-	-

Table 1: Detailed manufacturing caracteristics for each one of the boron thin films: it was used three different concentrations of boric acid solution in water (0.03 g H_3BO_3/L H_2O, 0.29 g H_3BO_3/L H_2O and 2.99 g H_3BO_3/L H_2O) for the deposition over muscovite mica and two different heating temperatures (400ºC and 750ºC); the thin films were coupled with track detectors (CR-39 and LR-115) resulting in 12 different assemblies that were irradiated with thermal neutrons (flux ~ 10^8 neutrons.cm^{-2}.s^{-1}). To reveal the tracks left by the α and ^{7}Li in the detectors, chemical attacks with sodium hydroxide were made (at controlled temperatures and time intervals, depending on the detector).

3. Results and discussion

3.1 Deposition method

Examples of the tracks, seen on the detectors CR-39 and LR-115, are displayed in Figure 1, showing that the method for manufacturing boron thin films using boric acid deposits ^{10}B atoms over the muscovite mica surface.

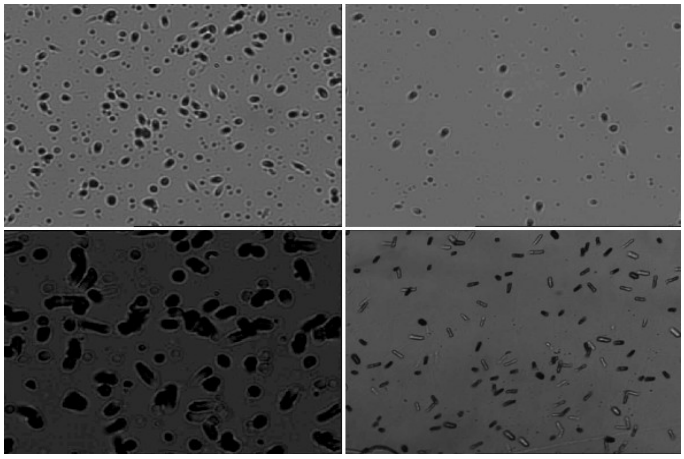

Figure 1: *Top left:* region of detector CR-39 coupled with the boron thin film (increased by 1000x); *top right:* region of the detector CR-39 that was not coupled with the boron thin film (increased by 1000x); *bottom left:* region of detector LR-115 coupled with the boron thin film (increased by 1000x); *bottom right:* region of muscovite mica coupled with the uranium thin film used for calibrating the boron thin film (increased by 200x).

Since the CR-39 pieces were larger than the boron thin films, we could check the regions of the detector which were not coupled with the thin film and there appeared some backgroud tracks (about 10% of the tracks found at the region coupled with the thin film)[3]. This background is currently being investigated and the most probable cause is that they are generated by recoil atoms from the carbon reaction with the fast neutrons, still an important part of neutron spectrum. It is also worth noting that the detectors were chemically etched for times much shorter (30 minutes) than the standard etching (400 minutes), not revealing completely the tracks; This procedure was necessary to avoid overlapping tracks.

3.2 Spatial homogeneity of boron thin films

To evaluate the spatial homogeneity of the boron thin films, we applied the χ^2 test on two types of histograms: one-dimensional histograms fitted with a Poisson distribution and two-dimensional histograms fitted with a plan. The one-dimensional histograms represents our events distribution and since the decay of $^{11}B^*$ is a rare event it obeys the Poissonian statistics; the two-dimensional histograms represents the spatial distribution of tracks and as it is desired that the boron thin films are spatially homogeneous, those histograms were fitted with a plan whose only free parameter is its height.

With the χ^2 and the number of degrees of freedom of each fitting function, it is possible to calculate the P-value of the distribution, expressing the statistical significance of the data (for this analysis it is desired that P-value > 0.05) [11].

In Table 2 and Figure 2, there are some results for the uniformity of events from a Poisson distribution fit to one-dimensional histograms; the main interest here is to analyze the four thin films that can be calibrated, i.e. that were irradiated with the uranium thin film (B1-1, B1-2, B1-3 and B1-4).

thin film of boron	*P-value (from Poisson fit)*
B1-1	0.27
B1-2	0.19
B1-3	0.04
B1-4	0.51
B2-1	0
B3-1	0.01

Table 2: P-values obtained from fitting a Poisson distribution to one-dimensional histograms of track counts distribution for each boron thin film.

[3] These track densities were subtracted from the track densities in the region where the detector was coupled with the boron thin film.

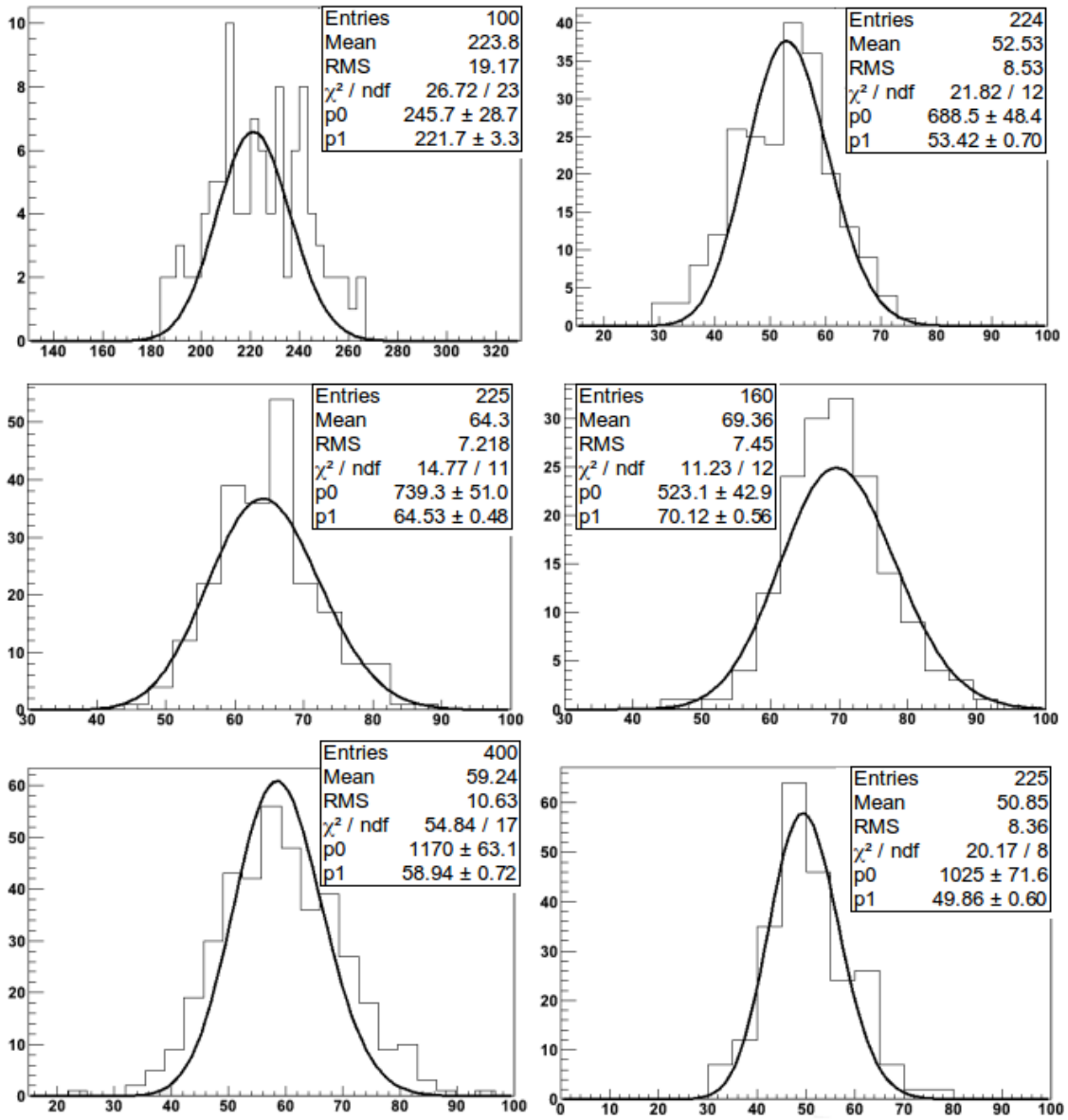

Figure 2: *Top left:* track count distribution for the boron thin film B1-1 fitted with the Poisson distribution, giving P-value ~ 0.27; *top right:* track count distribution for the boron thin film B1-3, with P-value ~ 0.04; *middle left:* track count distribution for the boron thin film B1-2, with P-value ~ 0.19; *middle right:* track count distribution for the boron thin film B1-4, with P-value ~ 0.51; *bottom left:* track count distribution for the boron thin film B2-1, with P-value ~ 0; *bottom right:* track count distribution for the boron thin film B3-1, with P-value ~ 0.01.

Results for the spatial homogeneity of the boron thin films, obtained from the plan fit of two-dimensional histograms. Note that most thin films does not appear to be homogeneous (P-values < 0.05), but since those thin films are large (~ 4 cm^2), it is possible to cut them into four pieces of about 1 cm^2; therefore, dividing them into four pieces (analysis shown in Table 3), better results are achieved.

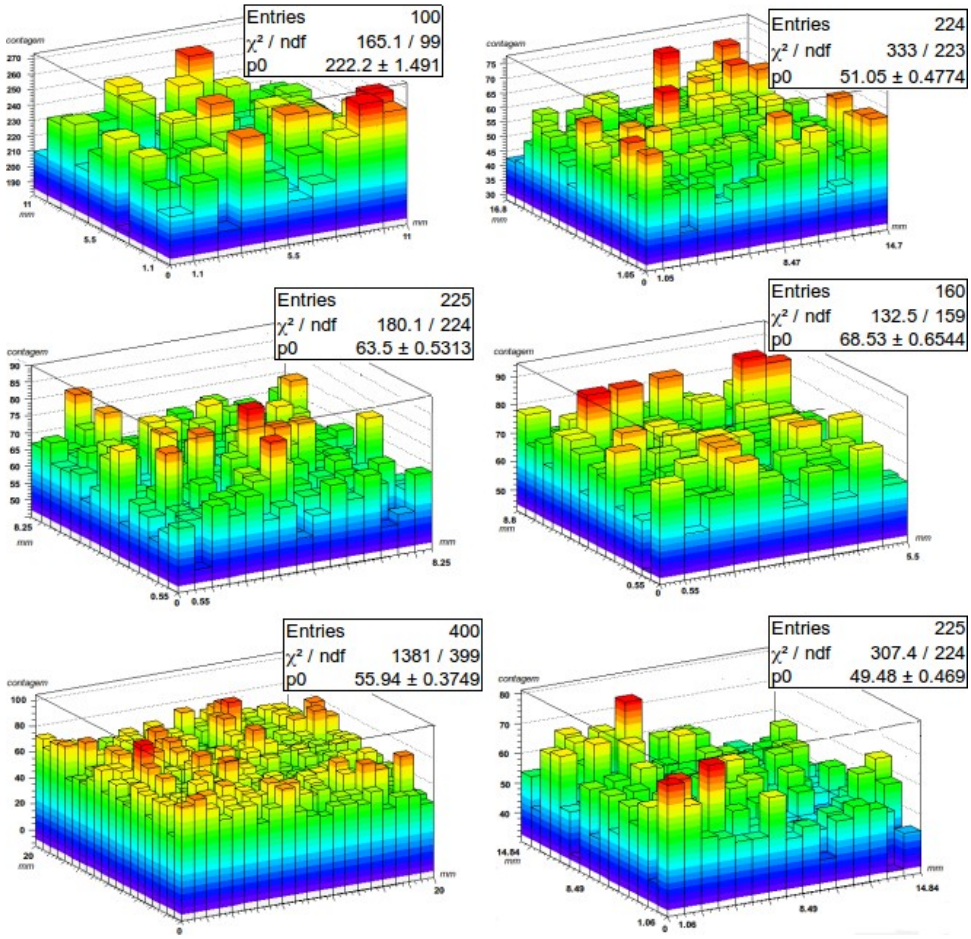

Figure 3: *Top left:* track count spatial distribution for the boron thin film B1-1 fitted with a plan, giving P-value ~ 0; *top right:* track count spatial distribution for the boron thin film B1-3, with P-value ~ 0; *middle left:* track count spatial distribution for the boron thin film B1-2, with P-value ~ 0.99; *middle right:* track count spatial distribution for the boron thin film B1-4, with P-value ~ 0.91; *bottom left:* track count spatial distribution for the boron thin film B2-1, with P-value ~ 0; *bottom right:* track count distribution for the boron thin film B3-1, with P-value ~ 0.

thin film of boron	*P-value (from plan fit)*	*P-value of each of its four smaller regions (from plan fit)*			
B1-1	0	0.11	0.01	0.82	0.04
B1-2	0	0.85	0.97	0.88	0.70
B1-3	0.99	0.04	0.82	0.47	0.90
B1-4	0.91	0.82	0.89	0.39	0.96
B2-1	0	0	0.01	0	0
B3-1	0	0.44	0.77	0.01	0.14

Table 3: P-values obtained from fitting a plan to two-dimensional histograms of track counts for each boron thin film and P-values obtained for each of its four smaller regions.

3.3 Calibration of boron thin films: $^{10}B(n,\alpha)^{7}Li$ reaction rate measurement

Calibrating boron thin films is to associate its track density, ρ_B, with the neutron fluence and ultimately with the $^{10}B(n,\alpha)^{7}Li$ reaction rate. For this, we calculate ρ_B (from the tracks

counts in the detectors) and also the superficial track density of the reference uranium thin film[4], ρ_U. As stated previously, only those boron thin films, which were irradiated along with the uranium thin films can be calibrated.

$$\rho_U = N_U \varepsilon_U \sum_i C_{iU} \int_0^\infty \frac{d\sigma^{iU}(E)}{dE} \phi(E) dE \quad (1)$$

$$\rho_B = N_B \varepsilon_B \int_0^\infty \frac{d\sigma^{B}(E)}{dE} \phi(E) dE \quad (2)$$

Here, as a first approximation, it is considered that only thermal neutrons will induce the reactions with boron and uranium, so the only relevant isotopes are ^{235}U (for eq. 1, C_{235U} = 0.72% and $\sigma_{U\_thermal}$ = 580.6 barns [12]) and ^{10}B (for eq. 2, $\sigma_{B\_thermal}$ = 3840 barns [12]); besides, since those films were irradiated together, the incident neutron fluency is a constant parameter for the irradiation. It is also assumed that the track count efficiency for the mica is $\varepsilon_U \sim 1$ [9]; it is not the interest now to determine the track count efficiency for the boron thin films (ε_B).

$$\frac{\rho_B}{\rho_U} = \frac{K \sigma^B_{térmico}}{N_U C_{235_U} \sigma^U_{térmico}} \quad (3)$$

After some manipulation, it is possible to obtain the constant of calibration for each boron thin film, K (which depends on each film and on the observer since it contains ε_B; $K = N_B \varepsilon_B$). The calibration factors for the smaller regions of each boron thin film that are spatially homogeneous are shown in Table 4.

thin film of boron		*ρ (10^6 tracks.cm^{-2})*	*K (10^{15} atoms ^{10}B.cm^{-2})*
CR-39	*400°C*	2.21 ± 0.01	0.92 ± 0.03
		2.22 ± 0.01	0.93 ± 0.04
	750°C	2.83 ± 0.02	1.18 ± 0.04
		2.87 ± 0.02	1.20 ± 0.04
		2.78 ± 0.02	1.16 ± 0.04
LR-115	*400°C*	2.57 ± 0.02	1.08 ± 0.04
		2.58 ± 0.02	1.08 ± 0.04
		2.54 ± 0.02	1.06 ± 0.04
		2.57 ± 0.02	1.08 ± 0.04
	750°C	2.83 ± 0.02	1.18 ± 0.04
		2.66 ± 0.02	1.11 ± 0.04
		2.81 ± 0.02	1.18 ± 0.04
		2.80 ± 0.02	1.17 ± 0.04

Table 4: Constants of calibration for each boron thin film.

It is also possible to calculate the incident thermal neutrons fluency that induced the $^{10}B(n,\alpha)^{7}Li$ reaction, which results in $\phi_{thermal} = (6.22 \pm 0.22).10^{11}$ neutrons.cm^{-2}. Since the nominal neutron flux during the irradiation was of about 10^8 neutrons.cm^{-2}.s^{-1} and the thin films were irradiated for 60 minutes, the value found for the neutron fluency is in the expected magnitude.

[4] The number of uranium nuclei per cm^2 in the uranium thin film used is $N_U = (5.96 \pm 0.14).10^{16}$ cm^{-2} and its superficial tracks density is $\rho_U = (1.55 \pm 0.04).10^5$ tracks.cm^{-2}.

Finally, the $^{10}B(n,\alpha)^{7}Li$ reaction rate, $R = \sigma_{B\_thermal}\ \phi_{thermal}$, is calculated and the value found for it is $R = (2.39 \pm 0.08).10^{-9}$ neutrons/decay.

4. Conclusions

The employed method to deposit the boron thin films showed to be very effective, since after irradiating those thin films the tracks left by α particles and ^{7}Li ions in the detectors could be counted and their superficial track densities were determined, making possible the calibration of the boron thin films and calculate the $^{10}B(n,\alpha)^{7}Li$ reaction rate.

The boron thin films were heated at two different temperatures, 400ºC and 750ºC, for four hours so that the boric acid was converted to oxide and the hydrogen present at the acid would not interfere in the $^{10}B(n,\alpha)^{7}Li$ reaction rate measurement. From the track densities, showed at Table 4, there is no significant difference between those two temperatures. Besides that, given the low cross sections of the n + H reactions[5] even if the boron thin films were composed exclusively of boric acid, just ~ 4% of the tracks would not be from the $^{10}B(n,\alpha)^{7}Li$ reaction.

When comparing the CR-39 and LR-115 detectors, as expected, there is no significant difference between them (tracks densities at Table 4); for the energies and ranges[6] of the α and ^{7}Li produced by the neutron capture reaction, both detectors have similar efficiency detection [14].

For the calibration of the boron thin films we assumed as a first approximation that only thermal neutrons would interact with the atoms of boron and uranium; this can be improved by irradiating the boron thin films boron with thorium thin films (as well as the uranium thin film) which will separate the contribution of higher energy neutrons [15].

The high densities of tracks make it more difficult to chemically etch the detectors for longer periods of time (there would be overlapping of tracks, situation in which track count is far more difficult); for better results it is important to manufacture thinner films of boron. This is one of the next challenges to be overcome. The other is to study the observed background and identify its cause.

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[5] $\sigma\ (\ ^{1}H(n,n)^{1}H\ ) = 55$ barns and $\sigma\ (^{1}H(n,\gamma)^{2}H\ ) = 0.33$ barns.

[6] At 96% of $^{10}B(n,\alpha)^{7}Li$ reactions: $E_{\alpha} \sim 1.47$ MeV and $E_{Li} \sim 0.84$ MeV → from SRIM simulations: Δx_{α}(CR-39) ~ 6.3 μm, Δx_{α}(LR-115) ~ 6.2 μm and Δx_{Li}(CR-39) ~ 3.2 μm, Δx_{Li}(LR-115) ~ 3.3 μm [13].

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