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Feasibility study of accelerator-based Boron Neutron Capture Synovectomy

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1) Abstract

This study investigates the feasibility of Boron Neutron Capture Synovectomy (BNCS) as a targeted treatment for rheumatoid arthritis using accelerator-based neutron sources. BNCS offers a non-invasive alternative to surgery by delivering high-linear energy transfer (LET) radiation directly to diseased synovial tissue through the $^{10}B(n,\alpha)^{7}Li$ reaction. A compact epithermal neutron beam was modeled using the $^{7}Li(p,n)^{7}Be$ reaction at 1.97 MeV, with an optimized moderator and reflector configuration. A detailed knee phantom was constructed, including tissue-equivalent layers such as skin, synovium, cartilage, and bone. Monte Carlo simulations were performed using MCNP6 to estimate neutron interaction and dose deposition in the synovium under various boron concentrations. The results demonstrated efficient dose delivery to the target region with minimal exposure to surrounding healthy tissues. These findings support the potential clinical applicability of BNCS, highlighting its effectiveness, safety, and adaptability for treating joint conditions in an outpatient setting.

2) Introduction

Rheumatoid arthritis is a systemic disease characterized by inflammation of the synovium, the membrane lining the inner joint capsule of articulating joints. The cause of this disease is still unclear. In normal joints, the synovium is very thin (the thickness of several cells). However, in joints with rheumatoid arthritis, after proliferation of the synovial cells, the synovium increases in thickness to several millimeters, and the amount of synovial fluid in the joint cavity increases as well. Rheumatoid arthritis is treated with[1] anti-inflammatory drugs, and, when these drugs fail, surgical removal of the synovial membrane is performed.

Radiation synovectomy is an alternative to surgery. In other countries, radiation treatment with beta radioisotopes has been widely adopted. During treatment, a beta-emitting radioisotope is injected into the synovial fluid, and the kinetic energy carried by the beta particles is deposited in the synovium, killing the cells. It is used extensively in Europe, Australia, and Canada. It is not widely used in the United States, however, because of concerns regarding healthy tissue irradiation caused by leakage of the beta emitter away
from the joint.

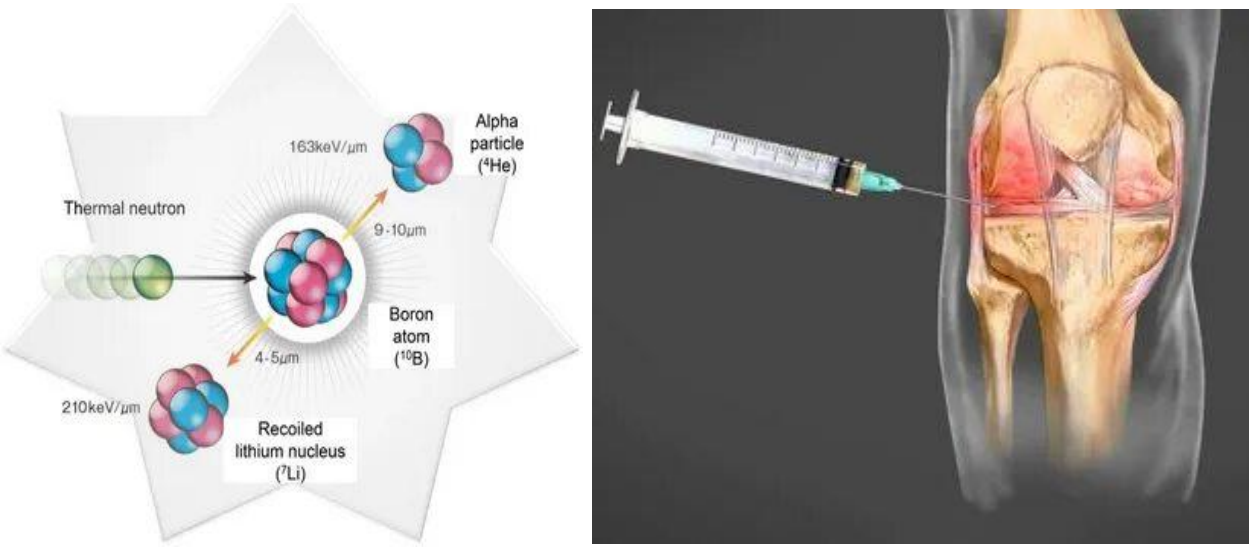

Figure 1: An illustration of Boron Neutron Capture Synovectomy.

Another alternative therapeutic approach is currently under investigation. This approach is **Boron Neutron Capture Synovectomy (BNCS)** which avoids the problems associated with the leakage of beta emitters from the joint, while still taking advantage of the merits of radiation synovectomy relative to surgery. BNCS is a two-part procedure illustrated schematically in Fig. 1 in which a nonradioactive compound[2] containing a nuclide with a high thermal neutron capture cross section (^{10}B) is first injected into the joint space; next, a beam of neutrons causes the nuclide to fission releasing two high-LET, high-RBE particles that travel distances less than the diameter of a cell.

The $^{10}B(n,\alpha)^7Li$ reaction delivers intense radiation damage to those cells that have previously been loaded with ^{10}B, or their nearest neighbors. Like radiation synovectomy, BNCS results in synovial ablation by the delivery of radiation energy to the diseased membrane. The procedure could be carried out on an outpatient basis and would require no rehabilitation. Unlike radiation synovectomy there is no radiation hazard associated with leakage of the injected compound out of the joint. The ^{10}B remains stable both before and after neutron bombardment. The radiation dose is only delivered while the tissue is undergoing neutron irradiation.

3) Study objectives

The primary objective of this research is to investigate the feasibility and effectiveness of Boron Neutron Capture Synovectomy (BNCS) using accelerator-based neutron sources. Specifically, the study aims to:

- Design and optimize an accelerator-driven epithermal neutron beam utilizing the 7Li(p,n) reaction to ensure adequate neutron flux suitable for BNCS applications.
- Calculate the absorbed dose in synovial tissue under varying boron concentrations using Monte Carlo simulations.
- Estimate key treatment parameters, including neutron flux, dose distribution, and boron uptake requirements, to support the implementation of BNCS.
- Evaluate the overall clinical feasibility and potential of BNCS as a novel treatment modality for joint disorders.

4) Background

a) Difference between BNCS and BNCT

First, the tumor ^{10}B uptake in BNCT is usually at the level of several to several tens of ppm (parts per million), whereas the synovial boron [1]concentration in BNCS is expected to be several thousands of ppm. Potentially, many more boron photons will be emitted from the synovium in BNCS, and the count rate of boron photons will be much higher than that at previous BNCT facilities. The advantages of a higher count rate include a better signal to noise ratio and a shorter detection time to achieve a statistically reliable count.

In BNCT, a very clean epithermal neutron beam is necessary. The boron concentration is low, and so is the boron dose rate. If the neutron beam is contaminated with fast neutrons, the healthy tissue dose from fast neutrons can be significant. However, in BNCS a neutron beam mixed with fast neutrons is acceptable. The boron concentration is high, and the irradiation time is expected to be short. Therefore, the healthy tissue dose from fast neutrons and incident photons is small.

The third difference comes from the depth and the shape of the target tissue. The depth of synovium is about 0.4 to 1.3 cm from the skin, in contrast with up to 7 to 10 cm for a deep-seated brain tumor. The size of joints (such as the knee or finger) may be quite variable, so the gamma ray telescope for BNCS must be adaptable to joints of a wide range of sizes.

b) Accelerator neutron beam

Accelerator-based neutron sources offer significant advantages for Boron Neutron Capture Synovectomy (BNCS), particularly due to their ability to be integrated into clinical environments. While only a few nuclear research reactors currently[3] conduct clinical BNCT trials, the widespread adoption of BNCS will require more accessible and compact neutron sources. Charged particle accelerators, especially those using protons, are promising candidates for this role. Although generating high beam currents (in the milliamp range) is technically challenging—due to the substantial heat deposited in the target and the need for efficient cooling—these systems enable shorter patient treatment times and greater flexibility in clinical deployment. Among potential reactions, the $^{7}Li(p,n)^{7}Be$ reaction stands out due to its favorable characteristics.

As shown in figure 2, It has a low energy threshold at 1.88 MeV and a broad cross-section plateau around 269 mb between 1.93 and 2.00 MeV, followed by a strong resonance peak at 2.25 MeV with a cross section nearing 590 mb. These features allow for the efficient production of relatively low-energy neutrons suitable for BNCS, particularly when high boron concentrations in superficial targets like the synovium permit the use of mixed or epithermal neutron spectra.

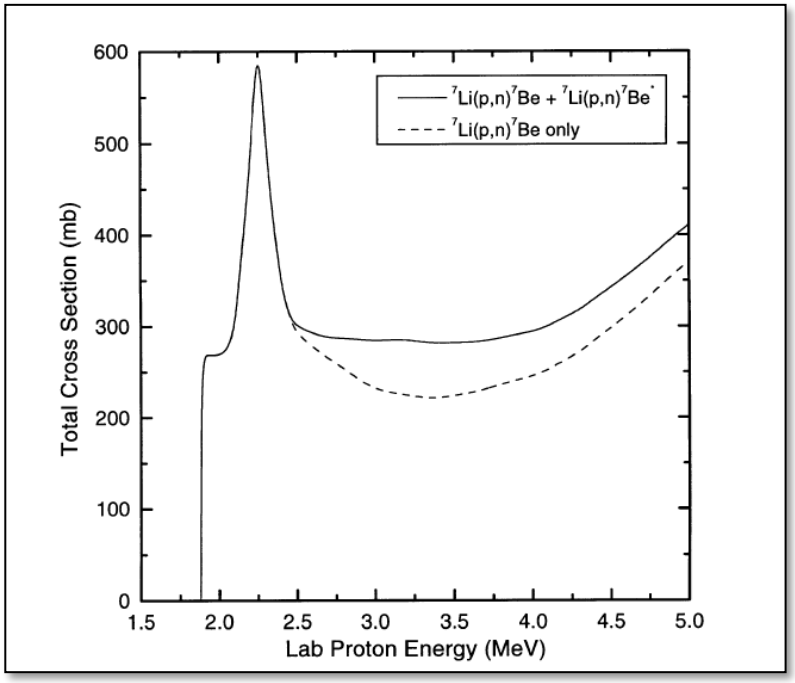

Figure 2: Total (p,n) Cross Section for 7Li. (H. Liskien and A. Paulsen 1975)

5) Methodology

a) Monte Carlo method

The Monte Carlo method is a statistical technique widely used in radiation transport simulations to model the complex interactions of particles with matter. By simulating the random paths of many individual particles, the method provides highly accurate [4] estimates of physical quantities such as particle flux, energy deposition, and dose distribution. In nuclear engineering and medical physics, Monte Carlo simulations are commonly used for systems with complex geometries, heterogeneous materials, and multiple interaction mechanisms. Codes like MCNP6 (Monte Carlo N-Particle) allow for detailed modeling of particle sources, transport, and interactions with various media, making them an ideal tool for evaluating treatment concepts such as Boron Neutron Capture Synovectomy (BNCS).

In this report, the MCNP6 code was utilized to model a proposed BNCS setup and assess its feasibility. The simulation involved defining a realistic accelerator based epithermal neutron beam and detailed synovial tissue geometry to analyze the interaction of neutrons with boron-loaded tissue. The F4 tally was used to compute the neutron flux as a function of energy, providing insight into the neutron spectrum within the target region. Additionally, the F6 tally was employed to estimate the dose distribution, based on energy deposition within the synovium. These tallies, combined with precise material definitions and source modeling, enabled a quantitative evaluation of the neutron field and its suitability for effective BNCS treatment.

b) Model setup

i) Accelerator based epithermal neutron beam

A schematic of the accelerator neutron beam configuration is shown in **Figure 3**. The nuclear reaction used for neutron production is $^{7}Li(p,n)^{7}Be$. Protons are accelerated to 1.97 MeV and directed to hit a lithium target with a thickness of 12.2 μm, located near the far end of the BNCS beam tube. The proton beam current was estimated to be 10mA. However, the lithium target is not included in the model figure due to its dimensions being on the order of tens of microns. The moderator thickness was optimized to achieve an epithermal neutron flux at the end of the BNCS beam and was chosen to be 6 cm in radius. The reflector was placed on both sides of the moderator and is represented by two cylinders, each with a radius of 10 cm. The beam tube was modeled as a vacuum, while the moderator and reflector were modeled as light water (H_2O) and aluminum oxide (Al_2O_3), respectively.

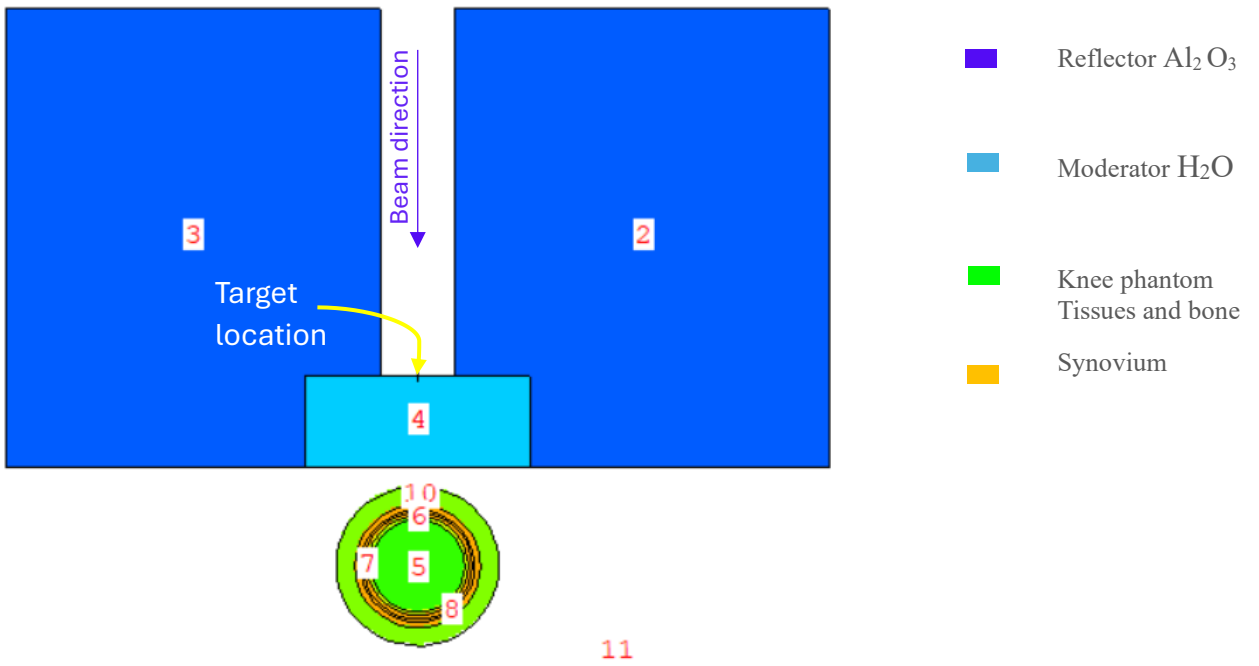

Figure 3: Geometry of MCNP model used for BNCS feasibility study

ii) Knee phantom

The synovium membrane and its surrounding structures in a knee phantom was modeled as shown in figure 4. The data used to model knee phantom were taken from references Yanch et al. (1999), Yanch et al.(1997) and Vega-Carrillo and Manzanaresacuna (2003). For dose calculations, a knee phantom that has an outer diameter of 6.85cm has been used. The phantom is divided into six tissue-equivalent sections, namely skin, sub- synovium, synovium, fluid space, cartilage and bone. The knee phantom has the following sections with corresponding thickness: skin and soft tissue (0–1.3cm), synovium(1.3–1.45cm), synofluid (1.45– 1.65cm), articular cartilage (1.65–1.85cm)and bone(1.85–6.85c m). The elemental composition of each tissue is shown in **Table 1**.

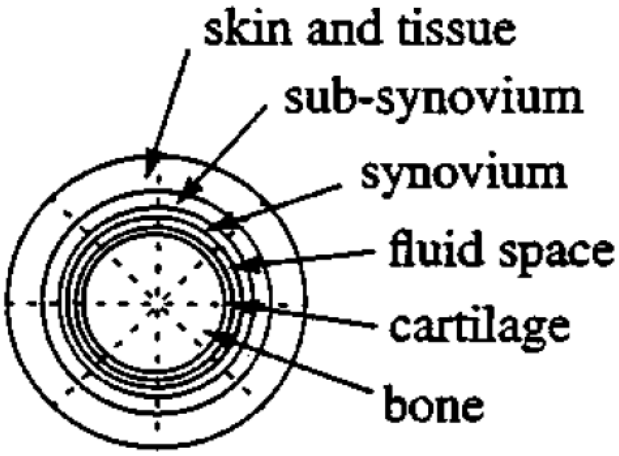

Figure 4: Knee phantom schematic

Table 1

Elemental composition of knee phantom constituents (wt%)(Vega-Carrillo and Manzanares Acuna,2003).

Element	Articular cartilage	Bone	Joint fluid	Tissue
Hydrogen	9.60	3.40	11.10	10.00
Carbon	9.90	15.50	-	14.90
Nitrogen	2.20	4.20	-	3.50
Oxygen	74.40	43.50	88.9	71.60
Magnesium	0.50	-	-	-
Phosphorous	-	0.20	-	-
Sulfur	2.20	10.30	-	-
Calcium	0.09	-	-	-
Chlorine	0.03	22.50	-	-
Density (g/cm3)	1.10	1.92	1.00	1.00

c) Neutron absorption and boron dose in the synovium

Monte Carlo simulations were conducted to estimate the number of $^{10}B(n,\alpha)$ reactions occurring in the synovium at varying boron concentrations. Simultaneously, the absorbed dose in the synovial tissue was determined using two different tally options in the MCNP6 code. The first method employed the F6 tally, which directly calculates the energy deposited per unit mass of the material. Both F6:n and F6:n,p tally options were utilized. In the F6:n tally, only the kinetic energy deposited by neutrons through heavy charged particles—resulting from reactions such as (n,α), (n,n), and (n,n′)—is recorded. However, it does not account for the photon energy deposited in the tissue from (n,γ) and (n,n′γ) reactions.

In contrast, the F6:n,p tally includes both the energy deposited by heavy charged particles and the contribution from secondary photons generated by neutron interactions, providing a more comprehensive estimate of the total energy deposition in the synovium.

The energies of secondary particles, like ^{4}He and ^{7}Li produced through the $^{10}B(n,\alpha)^{7}Li$ reaction, if they are not to be tracked (i.e., not included on the MODE card) will be deposited at the point of the interaction. Nuclear recoil energy will be deposited at the point of interaction unless heavy ion transport is specified (i.e., MODE #), but this can be a good approximation because the range of these ions is a few microns.

To compare the potential damaged cells of synovium vs. health tissue energy deposition tally (MeV/g/source particle) from all particles averaged over cell can be calculated for the knee phantom structures.

6) Results

We started the simulation by a simple geometry of the proton beam, target, moderator and reflector. To check the neutron energy vs flux produced in the target. A run was performed using tally F4 at the lithium target with number of particles 10^8 . The calculated neutron flux expressed in units [neutrons/proton/seg/cm^2] is acceptable for BNCS because accelerators with proton currents of about 10mA are currently being designed. This represents an output of $6.241509x10^{16}$ protons per second.

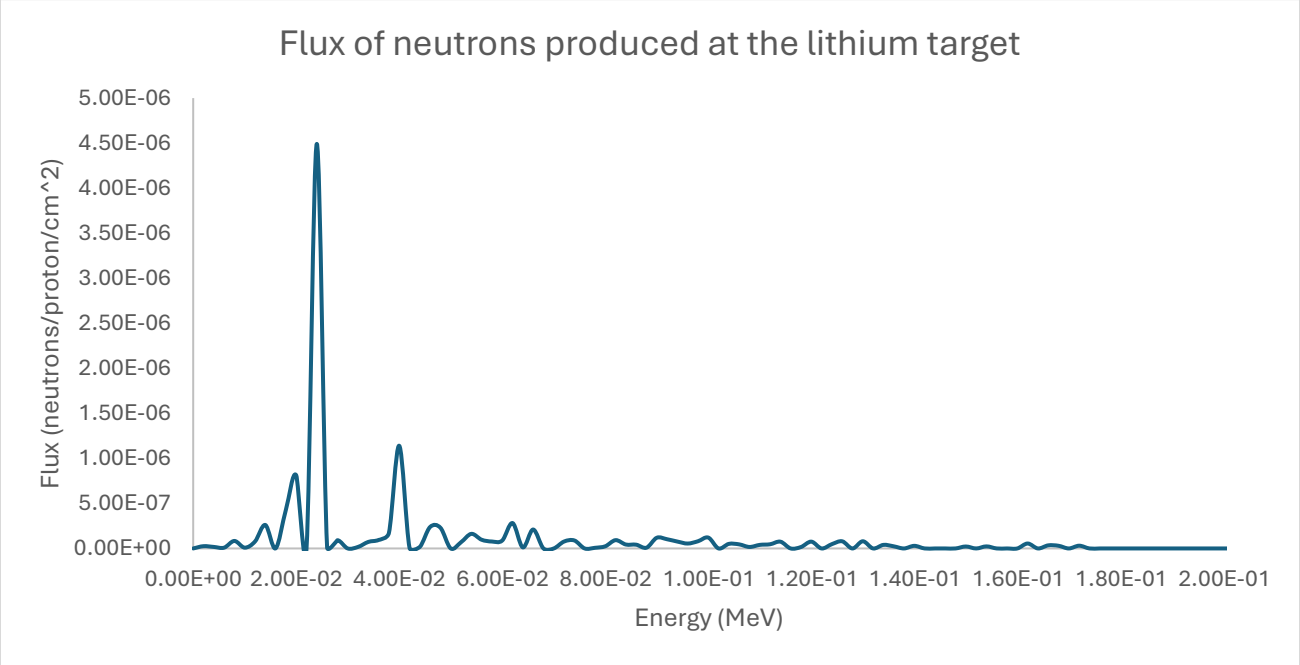

Figure 5: Neutron flux at lithium target

The neutron flux peak in **Figure 4** is at 20 keV, but still there is some other neutrons greater and smaller than 20 keV. That's why the neutrons need to be moderated to the epithermal region.
The next step was to estimate the neutron flux vs energy at the moderator.

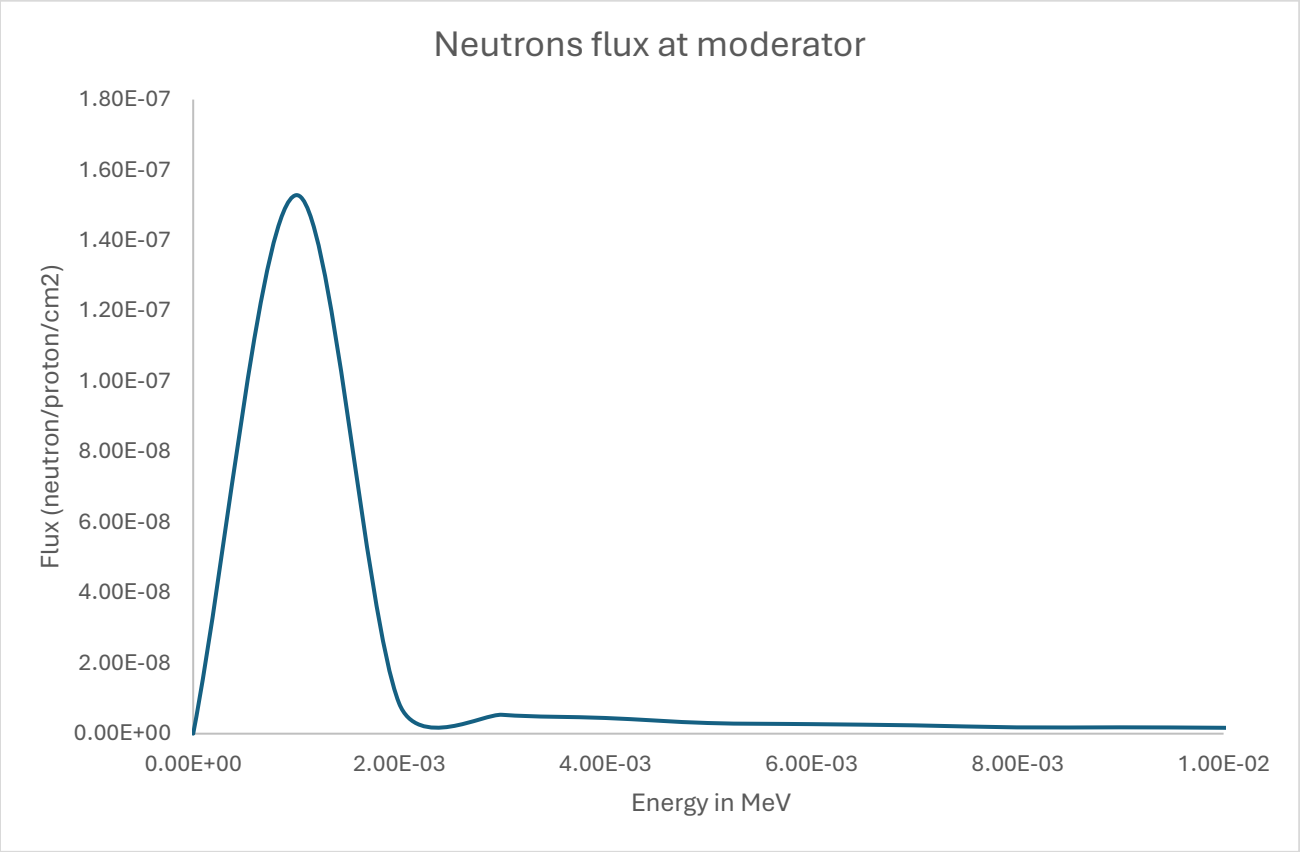

Figure 6: Neutrons flux obtained at moderator

The obtained neutrons shown in **Figure 5** have energy in the range of 1 keV and below. This energy is near to the epithermal neutron energy which is suitable for the boron neutron capture reaction.

Before modeling the whole knee phantom, we began by a tissue sphere of radius 4 cm located at the same position of the knee phantom.

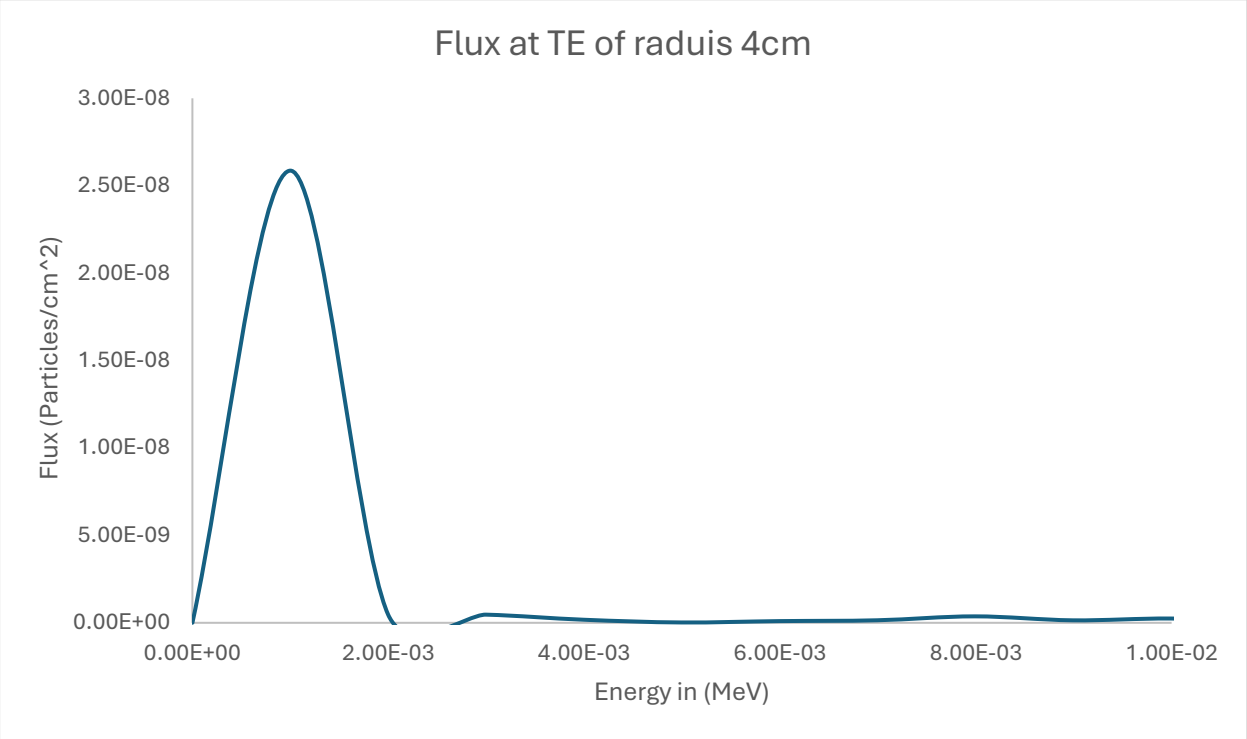

Figure 7: Flux of neutrons at tissue equivalent sphere

Figure 6 illustrates that neutrons undergo further moderation within the tissue-equivalent (TE) sphere. A noticeable reduction in the flux peak is observed, indicating that some neutrons were either absorbed by the tissue or scattered out of the system.

To assess secondary radiation, an additional tally was introduced to measure gamma production within the tissue. The resulting gamma flux was found to be **2.56113E-09**, which is relatively low. This is attributed to the use of a thin lithium target and a proton beam energy not positioned very close to the neutron production threshold, both of which limit gamma generation.

Subsequently, the full knee phantom geometry was incorporated into the model to evaluate the neutron flux reaching the synovium in the absence of boron loading. As shown in **Figure 7**, the presence of multiple moderating layers before the synovium leads to a further reduction in neutron flux compared to the values observed with the TE sphere alone.

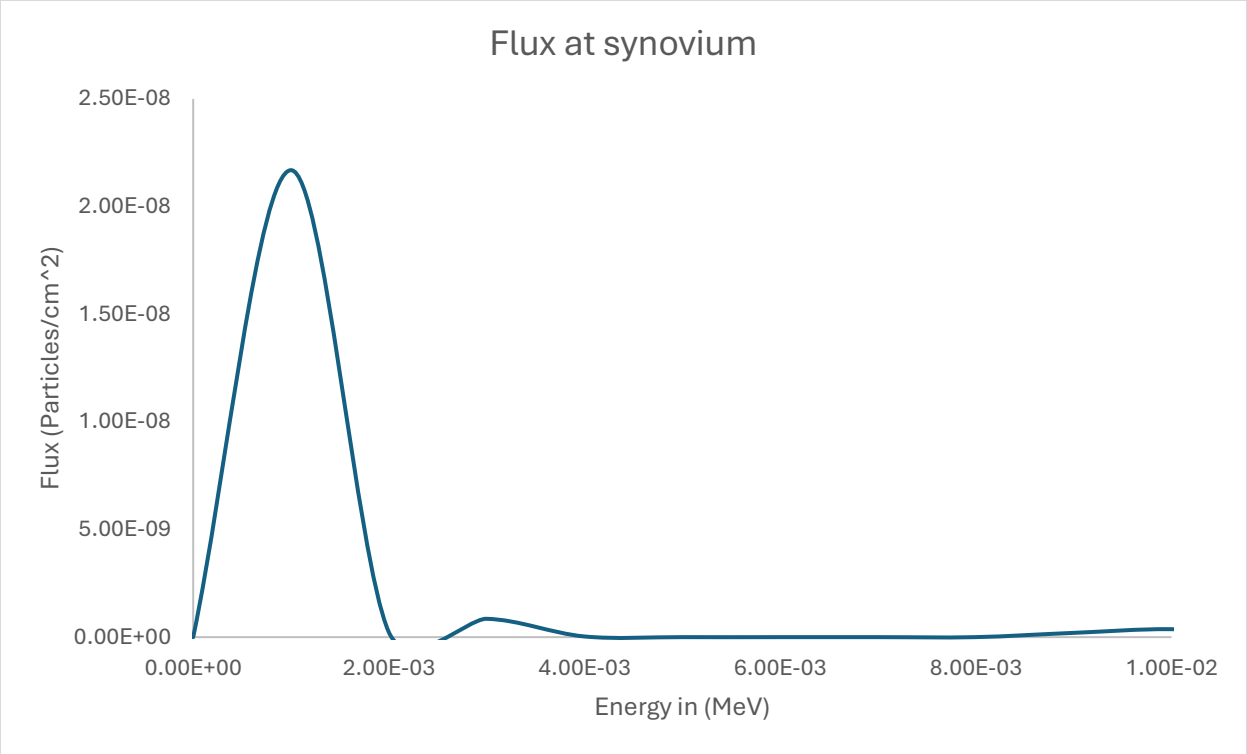

Figure 8: Neutron flux counted at the synovium

The energy deposition for various synovial boron concentration and 1 ppm only for the other tissue is shown in **table 2**.

Table 2

Boron concentration (ppm)	F6:n,p (MeV/gram/neutrons)	F6:n (MeV/gram/neutrons)
1	9.09937E-12	9.19443E-12
1,000	3.14451E-09	3.11460E-09
2,000	6.44031E-09	6.34670E-09
3,000	9.31327E-09	9.21816E-09
5,000	1.13212E-08	1.13681E-08
10,000	2.23359E-08	2.22343E-08

The results presented in the **Table 2** clearly demonstrate the effect of neutron self-shielding as boron concentration increases. As the concentration of ^{10}B in the synovium rises, the dose contribution per ppm of boron steadily decreases. This indicates that additional boron does not result in a proportionate increase in dose, as neutrons are increasingly absorbed near the surface of the tissue before reaching deeper regions. Consequently, not all boron atoms contribute equally to the reaction, reducing overall dose efficiency. Notably, the suppression of thermal neutron flux is already evident at concentrations as low as 1,000 ppm, highlighting that the self-shielding effect plays a significant role across the entire practical range of boron concentrations considered for BNCS. Additionally, the boron dose is clearly dominant in BNCS, and the photon dose and the neutron dose through other nuclear reactions adds negligible dose to the total dose when the boron concentration is over 5,000 ppm.

Table 3

Other Tissues with 1 ppm boron concentration	F6:n,p (MeV/gram/neutrons)	F6:n (MeV/gram/neutrons)
bone	8.36809E-11	1.21858E-11
art.cart	1.20373E-10	2.07486E-11
Joint fluid	7.46101E-11	9.79329E-12
sub-synovium	7.73821E-11	7.30591E-12
tissue	4.64815E-10	3.96403E-10

In most tissues—such as bone, articular cartilage, joint fluid, and sub-synovium—photon contributions as shown in **Table 3** account for over 80% of the total energy deposition, indicating that photon interactions play a dominant role in overall dose delivery. In contrast, soft tissue shows a much smaller difference between F6:n and F6:n,p values, suggesting that neutron-induced charged particle interactions are the primary contributors to dose in this region. The high photon contribution in denser tissues like bone can be attributed to their composition, which enhances photon absorption. These results emphasize the importance of using F6:n,p for accurate dose assessment, as relying on neutron-only tallies would significantly underestimate the actual dose, particularly in photon-sensitive or high-density tissues.

7) conclusion

The neutron spectrum obtained from the reaction ^{7}Li+p is suitable for the implementation of the Boron Neutron Capture Synovectomy. Therefore, despite the practical difficulties in the manufacture of Lithium targets for high proton currents, several research groups consider and promote the development of accelerator-based neutron sources using this reaction. Compared to the other reactions that generate neutrons, it is undoubtedly that using a relatively simple BSA an ideal epithermal neutron spectrum for BNCS can be obtained.
Our expectations this binary therapeutic modality is based on the possibility of injecting the borated compound directly to the infected synovium. And thus, obtain concentrations of ^{10}B in the diseased cell hundreds of times higher than those obtained in the case of BNCT.

8) Acknowledgement

I would like to express my sincere gratitude to the Joint Institute for Nuclear Research (JINR) for granting me the invaluable opportunity to participate in this wave. This experience has significantly enhanced my software and research skills, while also enriching my personal and scientific knowledge.
I am especially thankful to my supportive supervisor, Dr. Ivan Padron Diaz, for his continuous guidance, patience, and encouragement throughout the project. His mentorship was instrumental in making this a fruitful and rewarding journey of learning and discovery.

9) Reference

[1] Jiang, H. (2003). *Development of a gamma ray telescope for online synovial dosimetry in boron neutron capture synovectomy* (Doctoral dissertation, Massachusetts Institute of Technology).
[2] Yanch, J. C., et al. (1999). Boron neutron capture synovectomy. *Medical Physics, 26*(3), 364–375.
[3] Lee, C. L. (1998). *The design of an intense accelerator-based epithermal neutron beam prototype for BNCT using near-threshold reactions* (Doctoral dissertation, Massachusetts Institute of Technology).
[4] MCNP® Code Version 6.3.0 Release Notes LA-UR-22-33103 Rev. 1 January 10, 2023. Los Alamos National Laboratory. USA.