JOINT INSTITUTE FOR NUCLEAR RESEARCH

Final Report of INTEREST Program

Feasibility study of accelerator-based Boron Neutron Capture Synovectomy

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Participation period:

March 03 – April 12, Wave 12

Dubna, 2025

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Abstract

This report presents a first approach to a feasibility study on the application of accelerator-based Boron Neutron Capture Synovectomy (BNCS) as a therapeutic approach for rheumatoid arthritis (RA). BNCS integrates nuclear physics and biomedical engineering to achieve targeted ablation of inflamed synovial tissue using high-linear energy transfer particles generated through neutron capture by boron-10. The study focuses on the simulation and optimization of a neutron source based on the 7Li(p,n)7Be reaction using a 2 MeV proton beam, combined with two different Beam Shaping Assembly (BSA) configurations. Simulations were conducted using the Monte Carlo N-Particle Transport Code (MCNP6) to evaluate neutron flux and energy spectra at the BSA output. One configuration, using paraffin and graphite, produced a thermal neutron spectrum, while the other, using beryllium fluoride and magnesium fluoride, yielded an epithermal spectrum suitable for BNCS. Results demonstrate that the latter configuration effectively concentrates neutrons within the optimal energy range (10–20 keV), supporting its potential use in clinical settings for localized, minimally invasive RA treatment.

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

1. Introduction

1.1 Overview of Rheumatoid Arthritis

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease primarily characterized by persistent inflammation of the joints, which can lead to progressive joint destruction, functional disability, and decreased quality of life. The disease arises when the immune system mistakenly attacks synovial tissues, causing inflammation, pain, and swelling. Over time, this inflammatory response may extend beyond the joints to affect other organ systems.

Globally, RA affects approximately 18 million people, with a higher prevalence observed among women and older adults. The onset typically occurs between the ages of 30 and 60, and the disease exhibits a female-to-male ratio of approximately 3:1. If left untreated, RA can lead to severe complications, including cardiovascular disease, interstitial lung disease, and peripheral neuropathy. These systemic manifestations underscore the importance of timely and effective intervention strategies.

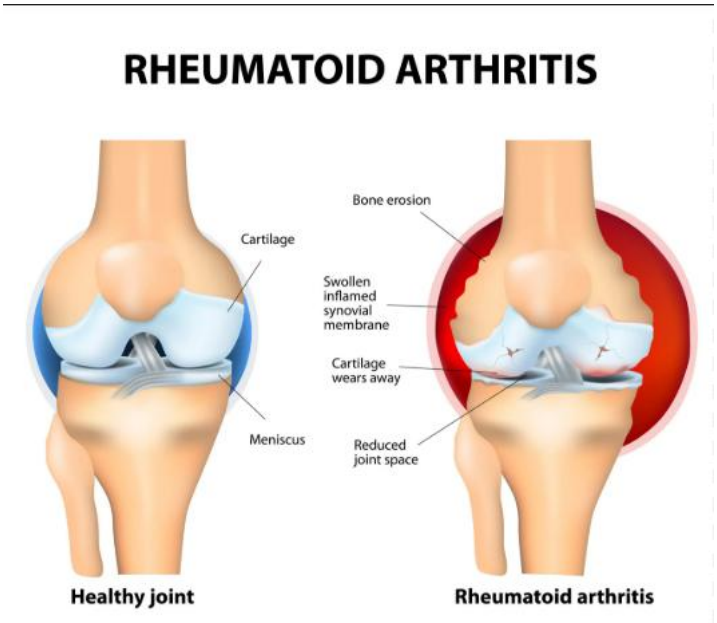

Figure 1. *Example of a comparison between a healthy joint and a joint with Rheumatoid arthritis*

Given the complex and systemic nature of RA, the development of advanced diagnostic tools and therapeutic monitoring techniques is of critical importance. In recent years, the integration of nuclear physics into biomedical research has enabled the application of high-resolution, non-invasive imaging modalities—such as positron emission tomography (PET) and single-photon emission computed tomography (SPECT)—to visualize and quantify inflammatory processes at the molecular level. These techniques, coupled with novel radiotracers targeting specific biomarkers of inflammation, offer promising avenues for early detection, patient stratification, and treatment assessment in RA.

Furthermore, interdisciplinary approaches involving nuclear instrumentation, radiopharmaceutical development, and computational modeling have opened new possibilities for precision medicine in autoimmune diseases. The application of these methodologies in clinical and preclinical settings not only enhances our understanding of RA pathogenesis but also supports the design of targeted therapeutic strategies aimed at minimizing systemic damage and improving patient outcomes. As such, the convergence of nuclear science and rheumatology represents a pivotal advancement in the pursuit of innovative solutions for complex chronic diseases.

1.2 Treatment Modalities

Traditional treatment of RA includes a combination of pharmacological approaches—such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and disease-modifying antirheumatic drugs (DMARDs)—alongside non-pharmacological interventions like physical therapy and lifestyle modifications. While these methods can alleviate symptoms and slow disease progression, they often fail to achieve long-term remission or prevent irreversible joint damage in all patients.

In recent years, innovative treatment modalities have emerged, aiming to target RA at the molecular and cellular levels. Among these, novel radiotherapeutic techniques have shown potential in addressing both the local and systemic aspects of autoimmune joint diseases. One such promising approach is Boron Neutron Capture Synovectomy (BNCS), which integrates principles of nuclear medicine with targeted tissue ablation.

BNCS is based on the selective accumulation of boron-containing compounds within inflamed synovial tissue, followed by irradiation with low-energy neutrons. The nuclear reaction between boron-10 and thermal neutrons generates high-linear energy transfer (LET) particles—namely alpha particles and lithium nuclei—that induce localized cellular damage. Due to the short path length of these particles, the cytotoxic effect is confined to the boron-loaded cells, minimizing harm to surrounding healthy tissue. This selectivity presents BNCS as a potential alternative to conventional surgical synovectomy or systemic immunosuppression.

The integration of BNCS into clinical research frameworks underscores the growing relevance of nuclear techniques in personalized medicine. Advances in boron compound development, neutron beam optimization, and imaging-guided treatment planning have further refined the feasibility and safety profile of this approach. Moreover, the application of computational simulations and dosimetric modeling supports treatment precision and enhances understanding of radiobiological effects at the microscale.

In the context of chronic inflammatory diseases such as RA, BNCS represents a paradigm shift—moving from generalized systemic therapies toward highly localized, molecularly targeted interventions. Continued interdisciplinary research is essential to evaluate long-term efficacy, optimize delivery protocols, and translate preclinical success into standardized clinical practice.

1.3 Boron Neutron Capture Synovectomy (BNCS)

BNCS represents a novel therapeutic strategy designed to selectively destroy inflamed synovial tissue through a two-step process. This method is based on the principles of Boron Neutron Capture Therapy (BNCT), originally developed for cancer treatment. In BNCS, a boron-10 (^10B) enriched compound is first introduced and preferentially accumulates in the synovial membrane. This is followed by irradiation of the volume of interest with a beam of thermal neutrons.

The interaction between the epithermal neutrons and ^10B nuclei results in a nuclear reaction that produces high-energy alpha particles and lithium-7 nuclei. These particles have a very short path length (5–9 micrometers), enabling them to destroy targeted cells while sparing surrounding healthy tissues. This mechanism holds significant promise not only for rheumatoid arthritis but also for other pathologies involving localized tissue proliferation, such as synovial sarcoma or joint-associated metastases.

The present report focuses on designing a Beam Shaping Assembly (BSA) capable of producing epithermal neutrons within the energy range of 10–20 keV. This neutron energy spectrum is considered optimal for BNCS applications since it shifts to the necessary thermal energy on its path up to the volume to be treated. The ultimate aim is to evaluate the technical feasibility of implementing BNCS as a viable treatment for rheumatoid arthritis, thereby contributing to the development of precise, minimally invasive therapeutic options for autoimmune joint diseases.

Additionally, advanced computational simulations—such as those based on Monte Carlo transport codes—are employed to model neutron behavior and optimize BSA geometry. These simulations provide valuable insight into the spatial and energy characteristics of the neutron field.

By addressing the engineering and radiobiological challenges associated with BNCS implementation, this study contributes to the broader goal of advancing targeted radiotherapies for autoimmune diseases. The proposed system has the potential to provide a minimally invasive, highly localized alternative to conventional surgical or systemic treatments. As such, BNCS represents a promising direction in the integration of nuclear technologies with precision medicine in rheumatology and beyond.

2. Project Objectives

The objective of the work was for the student to become familiar with the use of MCNP code for the generation of a therapeutic neutron beam based on accelerators with the p+Li reaction to be used in the treatment of rheumatoid arthritis through BNCS.

3. Methodology

This study employed the Monte Carlo N-Particle Transport Code (MCNP6) to model and simulate the production and moderation of neutrons for applications in **Boron Neutron Capture Synovectomy (BNCS)**. The methodology focuses on the simulation of a compact, accelerator-based neutron source coupled with a Beam Shaping Assembly (BSA) designed to moderate fast neutrons into the epithermal energy range (10–20 keV), which is optimal for therapeutic irradiation of inflamed synovial tissues.

3.1 Simulation Framework and Overview

The simulation was performed using MCNP6, which allowed for the detailed modeling of neutron transport, interactions, and energy moderation through heterogeneous materials. The complete geometry included:

- The doble-differential spectrum of the neutron beam resulting from the reaction 7Li(p,n)7Be for Ep = 2MeV.
- Two Beam Shaping Assembly (BSA) each one composed of multiple moderating and shielding layers with different materials.
- Tallies and detectors placed in the forward direction at the end of both BSAs to characterize the neutron field so can be used for further comparison

The model aimed to reproduce realistic physics for the proton-lithium interaction and neutron moderation, as well as the spatial and angular distribution of emitted neutrons.

3.2 Accelerator-Based Neutron Source

Neutron production was modeled via the nuclear reaction:

7Li(p,n)7Be

with 2 MeV protons impinging on a layer of lithium-7. The neutron emission spectrum was configured using energy-angle-dependent data consistent with the physical characteristics of the reaction. Importantly, the **angular distribution of the emitted neutrons was constrained to the forward hemisphere**, specifically from **0° to 89°** in the direction of proton beam propagation. This directional bias reflects realistic kinematics of the (p,n) reaction at 2 MeV and was implemented using the SDEF card in MCNP6, with the DIR parameter used to limit the emission to this angular interval.

This directional setup ensured that the majority of the neutrons entered the BSA in a forward-focused cone, increasing moderation efficiency and minimizing neutron loss due to backscattering or leakage.

3.3 Beam Shaping Assembly (BSA) Design

Two BSA geometries were proposed using different materials. In the first case, hydrogenated materials such as paraffin were used, which produced a thermal neutron beam (***Figure 3***). In the second case, a mixture of beryllium fluoride and magnesium fluoride was used, which produced an epithermal neutron beam (***Figure 2***).

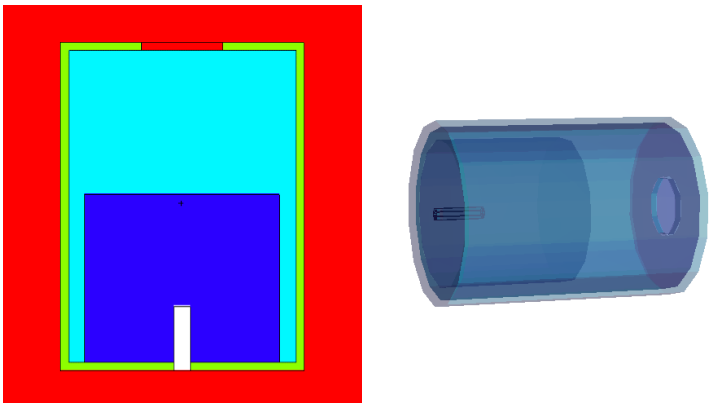

Figure 2. *Beam Shaping Assembly (BSA) for epithermal neutrons*

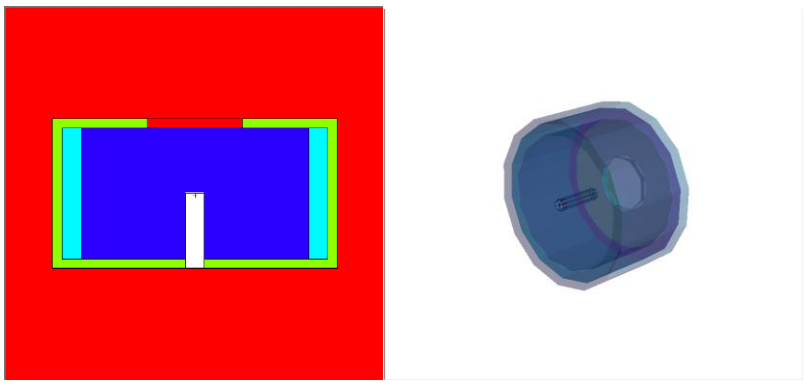

Figure 3. *Beam Shaping Assembly (BSA) for thermal neutrons*

4. Results

4.1 Analysis of the source spectrum

The presented graph in ***Figure 4*** illustrates the integral spectrum of the neutron source used in the simulation. The X-axis represents the energy of the generated neutrons, ranging from 0 to 230 keV. This range is critical for understanding how neutrons behave in the context of therapy. On the Y-axis, the number of detected neutron counts is observed, reaching a maximum between 8E−2 and 1E-1. This data is fundamental as it indicates the intensity of the signal within the most relevant energy range.

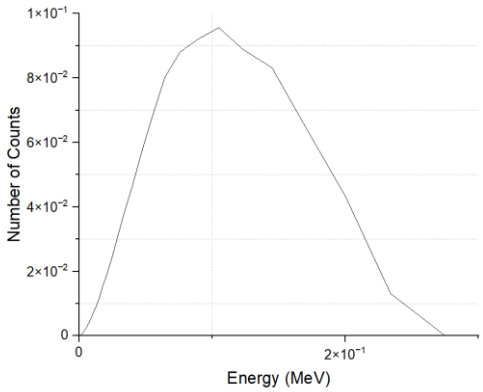

Figure 4. *Integral spectrum of the neutron source*

The shape of the curve is nearly symmetrical, peaking in the central region and gradually declining towards the extremes. This characteristic suggests that the majority of the generated neutrons possess energies in a medium range, which is ideal for therapeutic applications. The symmetry of the curve also indicates a balanced distribution, which can be advantageous in medical treatments.

The peak in the graph indicates a significant concentration of neutrons within a specific energy range. This is particularly beneficial for the application in Boron Neutron Capture Synovectomy (BNCS), as it seeks a spectrum that maximizes treatment efficacy by focusing on energies that optimize neutron interaction with inflamed tissue

The graph presented in ***Figure 5.*** show the spectral distribution of neutrons emitted by the source used, considering two specific directions: 0° and 90°. The graph is plotted on a logarithmic scale (base 10) for both the energy (MeV) and probability axes. The first curve, corresponding to the 0° direction, shows a distribution where the probability of neutron emission increases with energy, reaching a clear maximum around 0.03 MeV (30 keV), and then decreases. This behavior indicates a significant concentration of neutrons within the epithermal range, which is favorable

for applications such as Boron Neutron Capture Synovectomy (BNCS), where neutrons in that energy interval are required.

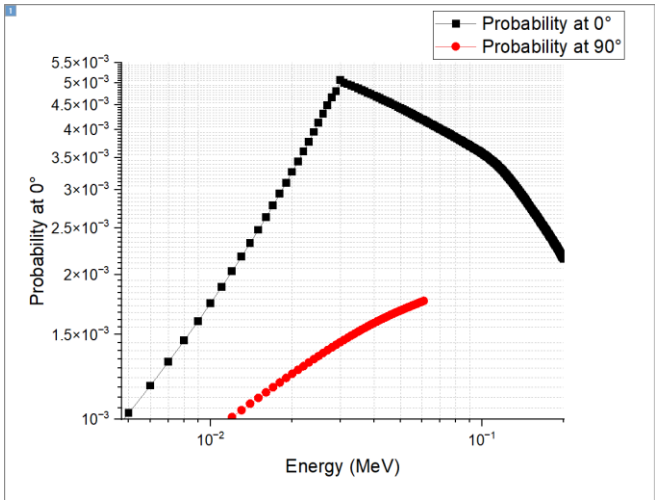

Figure 5. *Spectral distribution of neutrons emitted by the source at 0° and 90°*

In contrast, the curve corresponding to the 90° direction shows a different distribution. In this case, the probability also increases with energy, but there is no well-defined peak within the analyzed range. Instead of being concentrated at a specific energy, the curve suggests a broader distribution, with a greater proportion of neutrons at relatively higher energies. Unlike the frontal direction, where a clear energy selection is observed, the lateral direction exhibits a more extended spectrum.

When comparing both curves, it is evident that the 0° direction provides a higher probability of neutron emission within the epithermal range, while at 89° the emission is more dispersed toward higher energies. This behavior is consistent with the kinematics of the (p,n) reaction, in which neutrons are preferentially emitted along the beam direction, resulting in a spectrum more aligned with the energy requirements of the proposed clinical application.

4.2 Analysis of the neutron energy spectrum at the BSA outlet

The the graphic shown in ***Figure 6*** display the neutron energy spectra obtained for different material configurations used in the design of the moderation system. These plots help analyze how each material combination affects the energy distribution of the neutrons.

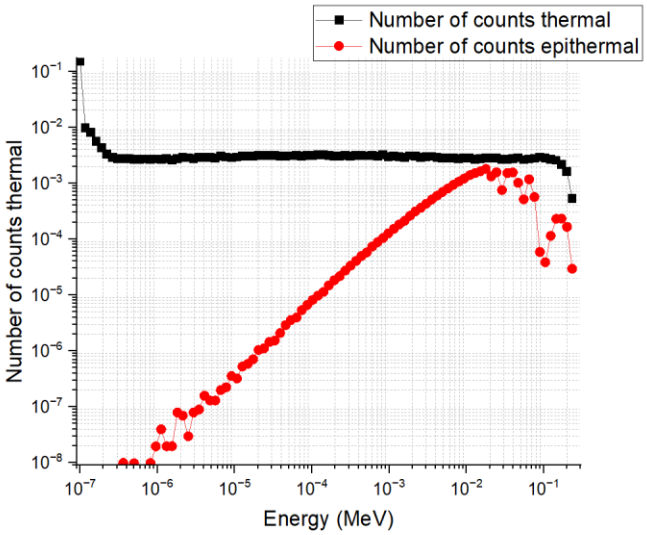

Figure 6. *Neutron energy spectra obtained for a BSA for thermal neutron spectrum and a BSA for epithermal neutron spectrum*

The first curve, corresponding to the system composed of paraffin and graphite as moderator and reflector materials respectively, shows a high number of counts at very low energies, around 1E-7 MeV. This is followed by a sharp drop in the number of detected events, and then a nearly flat plateau ranging from approximately 1E-6 to 1E-1 MeV. Finally, near the right end of the graph, around 1E-1 MeV, another decrease in counts is observed. This distribution indicates that the system effectively moderates neutrons, reducing their energy and maintaining them in a low and stable range. The flat central part of the spectrum suggests a fairly uniform presence of thermal or slow neutrons, which is characteristic of moderating materials such as paraffin.

The second curve, representing the system composed of beryllium fluoride and magnesium fluoride, shows a different trend. At very low energies, below 1E-5 MeV, the number of counts is low. However, as energy increases, the number of detected events rises progressively until reaching a well-defined peak around 10 to 20 keV, which falls within the epithermal neutron range. After the peak, the curve drops sharply. This behavior suggests that the materials used do not significantly slow down neutrons, resulting in a spectrum dominated by neutrons in the epithermal range.

When comparing both curves, it can be concluded that the paraffin and graphite system acts as an efficient moderator, generating a spectrum rich in thermal neutrons, which may be suitable for specific clinical applications such as treatment of skin melanoma. In contrast, the system based on beryllium fluoride and magnesium fluoride produces a higher concentration of epithermal neutrons, which is ideal for treatments such as Boron Neutron Capture Synovectomy (BNCS), particularly in the management of diseases like rheumatoid arthritis. In this context, the presence of a clear peak within the epithermal range makes the second system more appropriate for clinical applications where such neutron energies are required.

5. Conclusions

The study successfully modeled and simulated an accelerator-based neutron source suitable for Boron Neutron Capture Synovectomy using the MCNP6 code. Two BSA designs were tested: one using paraffin and graphite, effective for producing thermal neutrons; the other employing beryllium fluoride and magnesium fluoride, which generated a neutron spectrum rich in epithermal energies. The epithermal neutron spectrum, peaking between 10–20 keV, is ideal for BNCS applications due to its ability to precisely target boron-loaded inflamed synovial tissue. Simulation results confirmed that the directional emission of neutrons, particularly at 0°, aligns well with the energy needs for BNCS, maximizing therapeutic effectiveness while minimizing collateral tissue damage. These findings support the technical feasibility of implementing BNCS as a non-invasive and highly localized treatment modality for rheumatoid arthritis and potentially other localized joint disorders. Further research is needed to refine neutron beam shaping, optimize boron delivery agents, and validate clinical protocols for safe and effective implementation.

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