TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

Министерство науки и высшего образования Российской Федерации
федеральное государственное автономное
образовательное учреждение высшего образования
«Национальный исследовательский Томский политехнический университет» (ТПУ)

Инженерная школа ядерных технологий
Направление подготовки 14.04.02 Ядерные физика и технологии
Отделение ядерно-топливного цикла

МАГИСТЕРСКАЯ ДИССЕРТАЦИЯ

Тема работы
Получение ^{177}Lu путем регенерации мишени Yb для ядерной медицины на исследовательском реакторе ИРТ-Т

УДК 621.384.664: 621.039.55: 615.615.84

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TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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«Национальный исследовательский Томский политехнический университет» (ТПУ)

School of Nuclear Science & Engineering
Field of training (specialty): 14.04.02 Nuclear Science and Technology
Specialization: Nuclear medicine
Nuclear Fuel Cycle Division

MASTER THESIS

Topic of research work
Production of ^{177}Lu by regenerating the Yb target for nuclear medicine at the IRT-T research Reactor

UDC621.384.664: 621.039.55: 615.615.84

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Tomsk – 2021

LEARNING OUTCOMES

Competence code	Competence name
Universal competences	
UC(U)-1	Ability to make critical analysis of problem-based situations using the systems analysis approach, and generate decisions and action plans.
UC(U)-2	Ability to run a project at all life-cycle stages.
UC(U)-3	Ability to organize and lead the teamwork and generate a team strategy to achieve the target goal.
UC(U)-4	Ability to use modern communication technologies to realize academic and professional interaction.
UC(U)-5	Ability to analyze and account for cultural diversity in the process of intercultural interaction.
UC(U)-6	Ability to set and pursue individual and professional activity priorities and ways to modify professional activity based on the self-esteem.
General professional competences	
GPC(U)-1	Ability to formulate goals and objectives of the research study, select assessment criteria, identify priorities for solving problems.
GPC(U)-2	Ability to apply modern research methods, evaluate and present the results of the performed research.
GPC(U)-3	Ability to present research outcomes in the form of articles, reports, scientific reports and presentations using computer layout systems and office software packages.
Professional competences	
PC(U)-1	Ability to maintain medical and technical documentation related to medico-physical aspects of radiation therapy, interventional radiology and radionuclide diagnostics and therapy.
PC(U)-2	Ability to ensure radiation safety of personnel, public, and the environment, to carry out monitoring of radiation exposure levels of patients, personnel, public, and the environment.
PC(U)-3	Ability to operate and maintain equipment and tools applied for the medical use of radiation.
PC(U)-4	Ability to manage the quality of physical and technical aspects within radiation therapy, diagnostics, interventional radiology and radionuclide diagnostics and therapy departments in accordance with the specific equipment requirements, regulatory requirements and staffing of a medical organization.
PC(U)-5	Ability to conduct and organize dosimetry planning, clinical dosimetry, quality assurance procedures for radiotherapy, interventional radiology, and radionuclide diagnostics and therapy.

PC(U)-6	Ability to apply knowledge of natural sciences, fundamental laws in the field of nuclear physics and technology, clinical and radiation standards, hygienic measures in nuclear medicine, which is sufficient to study issues associated with medical physics using modern equipment and information technology relying on the latest Russian and international experience.
PC(U)-7	Ability to develop reference books, tables and software containing data for clinical use in dosimetric planning of radiation therapy, radionuclide diagnostics and therapy.
PC(U)-8	Ability to take part in the design and physical and technical equipment development for radiation therapy, diagnostics, interventional radiology and radionuclide diagnostics and therapy, and radiation safety divisions.
PC(U)-9	Ability to conduct training sessions and develop instructional materials for the training courses within the cycle of professional training programs (bachelor degree programs).

TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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School of Nuclear Science & Engineering
Field of training (specialty): 14.04.02 Nuclear Science and Technology
Specialization: Nuclear medicine
Nuclear Fuel Cycle Division

APPROVED BY:
Program Director
_____ Verkhoturova V.V.
«____» _____ 2021

ASSIGNMENT
for the Graduation Thesis completion

In the form:

Master Thesis

For a student:

Group	**Full name**
0AM9M	Veronica Kgabisang Gouws

Topic of research work:

Production of ^{177}Lu by regenerating the Yb target for nuclear medicine at the IRT-T research Reactor	
Approved by the order of the Director of School of Nuclear Science & Engineering (date, number):	№ 104-43/c dated April 14, 2021

Deadline for completion of Master Thesis:	05.06.2021

TERMS OF REFERENCE:

Initial date for research work: (the name of the object of research or design; performance or load; mode of operation (continuous, periodic, cyclic, etc.); type of raw material or material of the product; requirements for the product, product or process; special requirements to the features of the operation of the object or product in terms of operational safety, environmental impact, energy costs; economic analysis, etc.)	To perform the experimental production of NCA ^{177}Lu with a recycling of the Yb target for nuclear medicine applications.
List of the issues to be investigated, designed and developed (analytical review of literary sources with the purpose to study global scientific and technological achievements in the target field, formulation of the research purpose, design, construction, determination of the procedure for research, design, and construction, discussion of the research work results, formulation of additional sections to be developed; conclusions).	• To review the theoretical background/literature • To calculate theoretical activity of ^{177}Lu from the given problem of Yb_2O_3, • To separate of Lu from Yb using the cementation methods. • To recycling of target (Yb_2O_3) through of separation of Yb and Hg using the distillation process. • To measure the activity using Gamma spectroscopy (HPGe GX1018 Canberra) detector. • To calculate the activity and specific activity of Yb and Lu from gamma-ray lines detected results.
List of graphic material (with an exact indication of mandatory drawings)	
Advisors to the sections of the Master Thesis (with indication of sections)	
Section	**Advisor**

Introduction	DR. Ivan Alekseevich Ushakov, School of Nuclear Science & Engineering, Tomsk Polytechnic University, Tomsk
Chapter One: Literature Review	DR. Ivan Alekseevich Ushakov, School of Nuclear Science & Engineering, Tomsk Polytechnic University, Tomsk
Chapter two: Materials and Method	DR. Ivan Alekseevich Ushakov, School of Nuclear Science & Engineering, Tomsk Polytechnic University, Tomsk
Chapter three: Results and Discussions	DR. Ivan Alekseevich Ushakov, School of Nuclear Science & Engineering, Tomsk Polytechnic University, Tomsk
Chapter four: Financial management resource efficiency and conservation	Associate Professor Spicyna Lubov Yurievna, Division for Social Sciences and Humanities TPU School of Core Engineering Education, Tomsk
Chapter five: Social Responsibilities	DR. Verigin Dan Aleksandrovich, School of nuclear science and engineering, Division for nuclear-fuel cycle, Tomsk Polytechnic University, Tomsk
Chapter six :Conclusions and future recommendations	DR. Ivan Alekseevich Ushakov, School of Nuclear Science & Engineering, Tomsk Polytechnic University, Tomsk

Date of issuance of the assignment for Master Thesis completion according to the schedule	05.06.2021

Assignment issued by a scientific supervisor / advisor (if any):

Position	**Full name**	**Academic degree, academic status**	**Signature**	**Date**

Associate professor	Naymushin Artem Georgievich	PhD		

Assignment accepted for execution by a student:

Group	Full name	Signature	Date
0AM9M	Veronica Kgabisang Gouws		

TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

Министерство науки и высшего образования Российской Федерации
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«Национальный исследовательский Томский политехнический университет» (ТПУ)

School of Nuclear Science & Engineering
Field of training (specialty): 14.04.02 Nuclear Science and Technology
Specialization: Nuclear medicine

Level of education: Master degree program
Nuclear Fuel Cycle Division
Period of completion: spring semester 2020/2021 academic year

Form of presenting the work:

Master Thesis

SCHEDULED ASSESSMENT CALENDAR
for the Master Thesis completion

Deadline for completion of Master's Graduation Thesis:	05.06.2021

Assessment date	**Title of section (module) / type of work (research)**	**Maximum score for the section (module)**
06.02.2021	Introduction and literature review	…
15.02.2021	Experimental method	…
30.04.2021	Results analysis and discussions	
07.04.2021	Report submission preparation	
13-04-2021	Financial management and Social Responsibility	
18.05.2021	Preparation for defense	
22.05.2021	Compilation of the dissertation (full report)	

COMPILED BY:
Scientific supervisor:

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Associate professor	Naymushin Artem Georgievich	PhD		

APPROVED BY:

Program Director	Full name	Academic degree, academic status	Signature	Date
Nuclear Power Installation Operation	Vera V. Verkhoturova	PhD		

Blank for diploma project section
«Financial management, resource efficiency and resource saving»

ASSIGNMENT FOR THR DIPLOMA PROJECT SECTION «FINANCIAL MANAGEMENT, RESOURCE EFFICIENCY AND RESOURCE SAVING»

Student:

Group	Name
0AM9M	Veronica Kgabsisang Gouws

School	School of Nuclear Science & Engineering	**Department**	Division for Nuclear-Fuel Cycle
Educational level	Master	**Specialization**	14.04.02 Nuclear medicine

Initial data for the section "Financial Management, Resource Efficiency and Resource Saving":	
1. The cost of scientific research resources: material, technical, energy, financial, informational and human	Budget of research not higher than 339102,99 rubles,
2. Norms and standards for spending resources	Supervisor' salary 89960,00 rubles per month; consultant' salary – 46540,00 rubles per month, Executor' salary- 11336,00 rubles per month
3. The system of taxation used, tax rates, volumes of payments, discounts and loans	Coefficient of incentive bonuses 10%, coefficient of incentives for the manager for conscientious work activity 27.1%; contributions for social funds are 30% totally
Problems to research, calculate and describe:	
1. Assessment of the commercial potential of engineering solutions	Comparison of the condensers' types
2. Planning of research and constructing process and making schedule for all periods of the project	Calendar plan/ Hierarchical of the project
3. Requirement for investments	Costs calculations
4. Budgeting an engineering project	Creation of the project budget

5. Calculation of resource, financial, social, budgetary efficiency of an engineering project and potential risks	List of resource requirements
Graphic materials	
1. «Portrait» of the consumer 2. Competitive power of the project 3. SWOT matrix 4. Assessment of the prospects of a new product 5. Plan of investments. The budget for scientific and technical research 6. Project Efficiency indicators 7. Project risks	

Assignment date	

Consultant:

Position	Name	Academic degree	Signature	Date
Associate professor	Luibov Y. Spicyna	PhD		

Student:

Group	Name	Signature	Date
0AM9M	Veronica Kgabisang Gouws		

Task for section
«Social responsibility»

To student:

group	Full name
0AM9M	Veronica Kgabisang Gouws

School	Nuclear Science and Technology	Department	Division for Nuclear fuel cycle
Degree	Master programme	Specialization	**Nuclear Medicine**

Title of graduation thesis:

Production of ^{177}Lu by regenerating the Yb target for nuclear medicine at the IRT-T research Reactor	
Initial data for section «Social Responsibility»:	
1. Information about object of investigation (matter, material, device, algorithm, procedure, workplace) and area of its application	NCA ^{177}Lu radioactive radioisotope used for treatment of cancer. Devices/equipment: Cementation, distillation equipment, HPGe (GX1018 Canberra). Workplace: Laboratory for Isotopic Analysis and Technologies Application area: Radiopharmaceutical facilities, hospitals.
List of items to be investigated and to be developed:	
1. Legal and organizational issues to provide safety: – Special (specific for operation of objects of investigation, designed workplace) legal rules of labor legislation; – Organizational activities for layout of workplace.	– Labour code of Russian Federation #197 from 30/12/2001 GOST 12.2.032-78 SSBT – Sanitary Rules 2.2.2/2.4.1340-03. Hygienic requirements for PC and work with it – Sanitary Rules 2.6.1.2523-09 Radiation safety standards
2. Work Safety: 2.1. Analysis of identified harmful and dangerous factors 2.2. Justification of measures to reduce probability of harmful and dangerous factors	– Enhanced electromagnetic radiation level – Insufficient illumination of workplace – Excessive noise

	– Deviation of microclimate indicators – Electric shock – Ionizing radiation
3. Ecological safety:	– Indicate impact of radionuclides production on hydrosphere, atmosphere and lithosphere
4. Safety in emergency situations:	– Fire safety;

Assignment date for section according to schedule	

The task was issued by consultant:

Position	Full name	Scientific degree, rank	Signature	date
Associate Professor	Verigin D.A.	PhD		

The task was accepted by the student:

Group	Full name	Signature	date
0AM9M	Veronica Kgabisang Gouws		

Abstract

The master's dissertation consists of 160 pages; 28 figures; 42 tables; and 81 references.

Keywords: NCA ^{177}Lu, cementation, ytterbium, recycling, radiopharmaceutical facilities

The goal of the study was to perform the experimental production of NCA ^{177}Lu with a recycling of the Yb target for nuclear medicine applications.

The purpose of the study was to separate the NCA ^{177}Lu from macroscopic amounts of the ytterbium target material by cementation process followed by recycling of Yb.

The activity of the third cementation process of radioactive Yb and Lu were 2.06±0.05 Bq and 96.97±4.16 Bq which corresponds to 1.4 mg and 7.6 μg, respectively. The amount of Yb left was 35.5 mg which can be recycled and used for new production. Application areas are radiopharmaceutical facilities, Hospitals.

Abbreviations

IARC- International Agency for Resear

ch on Cancer

TRT- Targeted radionuclide therapy

SA- Specific activity

CA-Carrier added

NCA-No-Carrier Added

RIT- Radioimmunotherapy

PRRT- peptide radionuclide therapy

BFCA- Bifunctional chelating agent

SPECT -Single-photon emission computed tomography

PET -Positron emission tomography

NAA-Neutron Activation Analysis

LET- Linear Energy Transfer

VEC-Verticals experimental

HEC-Horizontal experimental

INAA -Instrumental neutron activation analysis

RNAA -Radiochemistry neutron activation analysis

PGNAA- prompt gamma ray neutron activation analysis

DGNAA- delayed gamma ray neutron activation analysis

HPGe-High Purity Germanium detector

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Introduction

Cancer is the leading cause of death globally. The International Agency for Research on Cancer (IARC) recently estimated that 7.6 million deaths worldwide were due to cancer with 12.7 million new cases per year being reported worldwide. In the year 2018, the estimated total death was 9.6 million and globally, the number of cancer deaths are expected to increase from 18 million in 2018 to 29 million at the end of 2040 [1]. The cancer treatment was appreciated after the discovery of X-rays by Wilhelm Conrad Röntgen in 1895 [2]. The discovery of X-rays by Röentgen in 1895 led to the use of x-rays for diagnostics in hospitals throughout the world. The first medical x-rays at the University of Pennsylvania were taken in February of 1896 within 3 months after the discovery of the x-ray. The biologic effects of ionizing radiation were recognized. Experiments were performed by scientists and workers for experiencing a significant radiation effect. Physicians at St. Louis Hospital in Paris began treating patients with radiation after learning the effects of ionizing radiation. The use of ionizing radiation in the treatment of cancer began after they have found that radium can be used as an exposure to tumour [3].

Radiation therapy has been used in cancer treatment for many years ago [2]. Radiation uses the radiation techniques such as high-energy beams, X-rays, gamma rays, electron beams, or protons to cure cancer cells [4]. The main aim of radiation therapy is to maximize the radiation dose to abnormal cancer cells while minimizing exposure to normal cells. Radiation therapy has developed with speciality with Radiation Oncology being a discipline in which various health and science professionals from numerous disciplines work together, radiation therapy or radiotherapy remains an important modality used in cancer treatment [2]. Cancerous tumours can be treated using the following main methods such as chemotherapy, radiation therapy, and surgery. The radiation therapy is common to combine radiation therapy with surgery, chemotherapy, hormone therapy, or combination of the three techniques [3].

Nuclear medicine is a phenomenon which uses radioisotopes for diagnosis, treatment or theragnosis (combination of therapy and diagnosis) [5]. Every year, over 10,000 hospitals

in the world uses radionuclides for diagnostics and treating about 30-50 million of patients according to World Nuclear Association and the European Commission [6]. Radioisotopes are isotopes of a chemical element with excess of energy, which they release in the form of radiation. They can occur naturally or be produced artificially in research reactors and accelerators. Research reactors and accelerators are used to develop new radioisotopes for diagnostics and therapy in nuclear medicine, for non-destructive testing and radiotracer industrial applications and to use as the radiotracer studies in scientific research. Accelerators advantages over nuclear reactors for radioisotope production, such as safety and cheaper operating and decommissioning costs. They generate less than 10% of the waste, it uses electricity rather than fission reactions and accelerator-produced waste is less hazardous than waste produced by a research reactor and accelerators do not pose risks to nuclear weapon proliferation [7].

In the early 20th century, the use of radionuclides for treatment of disease has a long history and parallel isolation of radium by Marie and Pierre Curie. Radioisotopes are used for different application such as for medical product sterilization, cardiac diagnostic procedures, bone and tumour scans, and radioisotope therapy. Medical isotopes are produced by either reactors or cyclotrons. The neutron-rich radioisotopes, such as ^{99m}Tc, ^{60}Co, ^{192}Ir, ^{131}I, ^{166}Ho, ^{177}Lu, are produced in reactors either as fission products or though neutron capture analysis which are long-live radioisotopes. The neutron-deficient radioisotopes, such as ^{18}F, ^{201}Tl, ^{123}I, ^{67}Ga, are produced in cyclotrons by the reactions of (p,n) and (p,α) and are short half-lived radioisotopes [8]. Most of the therapeutic radionuclides are produced in nuclear reactors and are rich in neutrons and decay by β- emission. The demand for the production of therapeutic radioisotopes is still growing. High-purity thermal neutrons spectrum is required to produce the therapeutic radioisotopes [9]. Nuclear research reactors are commonly used to produce medical radiolanthanides using a high thermal neutron flux for high yield production and high specific activity. For non-carrier added production route, large quantities of the target material will remain leading to low specific activity, this makes the direct pathway route of irradiated

target material to be impossible. The production of radioisotopes in reactors is based on neutron capture in a target material, either by activation or generation of radioisotopes from fission of the target material by bombardment with thermal neutrons [10]. Russia traditionally plays an important role in supplying isotopes to the world market, its share is estimated to be 22% [11]. The following Figure 1.1 shows the countries nuclear reactor which are in commission of producing ^{177}Lu [1].

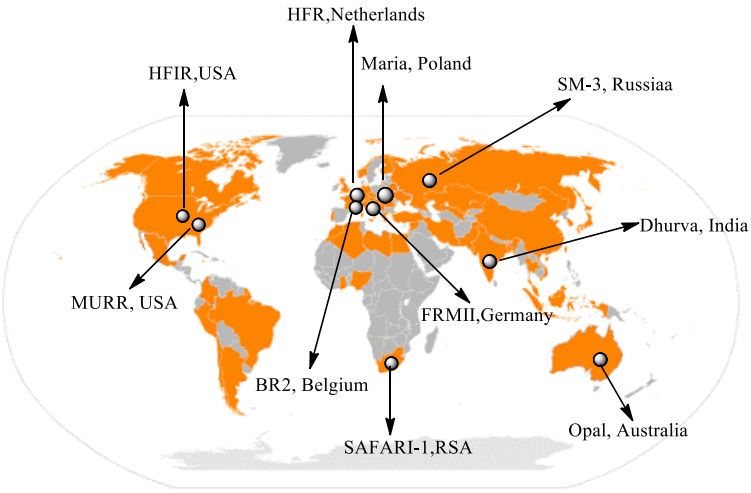


Figure 1.1-The map showing global production of ^{177}Lu nuclear reactors [1]

^{177}Lu-based radiopharmaceuticals have shown a growth in recent years among other radionuclides used for target therapy [12]. Several radiopharmaceuticals for treating of painful bone metastases have been developed and have shown good efficacy in relieving bone pain. Radiotherapy for bone pain is simple to administer and has been associated with improved mobility in many patients, reduced dependence on narcotic and non-narcotic analgesics, improved performance status and quality of life and, in some studies, improved survival. The use of ^{177}Lu radiopharmaceuticals is under clinical trials in many countries, and it is expected that the approved ^{177}Lu radiopharmaceuticals will be available in the near future. Its applicability has been studied in the treatment of colon cancer, metastic bone cancer, non-Hodgkin's lymphoma, lung, ovarian, and prostate cancer, and neuroendocrine and gastroenteropancreatic tumours [13]. The following Figure 1.2 shows that most of the radionuclides are attached to the targeting vector vie a chelator and linker [10].

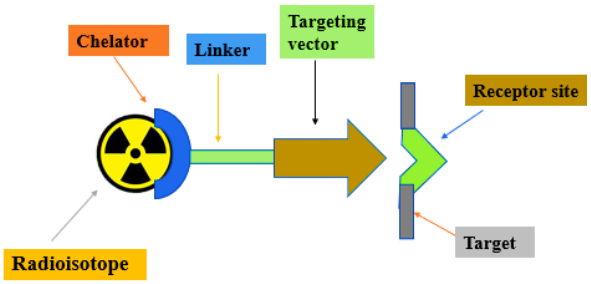


Figure 1.2- Schematic representing the radiopharmaceutical product [10]

Radioisotopes ^{177}Lu, is used in the form of labelled compounds for bone palliations, synovectomy, and the treatment of liver cancer [14]. ^{177}Lu is an important therapeutic radioisotope in nuclear medicine because of its high theranostic potential [10]. During the production of ^{177}Lu at the research reactor, a specific activity is determined by the route of production. The main aim of the production of ^{177}Lu for diagnostic and therapy methods is to reduce the mortality rate from cancer [15]. The direct production route of ^{177}Lu via the (n,γ) nuclear reaction which results in carrier added (CA) provide with limited achievable specific activity because of the presence of the target material. In order to obtain achievable specific activity, indirect route production of ^{177}Lu using a highly enriched ^{176}Yb target material which results in non-carrier added (NCA) may be used. The high specific activity of ^{177}Lu can be used for application of radioimmunotherapy (RIT) and peptide radionuclide therapy (PRRT) [16]. The main goal of this study was to perform the experimental production of NCA ^{177}Lu with a recycling of the Yb target for nuclear medicine applications. The particular objectives of this research is to determine the theoretical activity calculations of ^{177}Lu from a given problem using the target Yb_2O_3, to separate of Lu from Yb using the cementation methods, to check repeatability of the experiment, to separate Yb from mercury by distillation process, to recycle the target (Yb_2O_3) through of separation of Yb and Hg using the distillation process and purification of mercury, to measure the activity of Yb and Lu using the well-type HPGe gamma-ray detector and calculate the activity and specific activity of Yb and Lu from gamma-ray lines detected results.

Chapter 1- Literature review

1.1 Therapeutic Particle Emissions

Radionuclides emitting particles represent a high amounts of energy deposition in a small volume and are therefore suitable for most various cancers. The emission of therapeutic particles consists of Auger electrons, alpha particles, beta particles and conversion electrons. All these particles except for beta are classified as high-linear energy transfer (LET) electron emitters. Conversion electrons are monoenergetic and have a discrete range in tissues, and beta electrons have range of energies, thus have a maximum and average energy value [17].

Radionuclides that decay by β particle emission, α particle emission and auger electron emission are used in developing radiotherapeutic agent. Each type of particle emission has application treatment depending on the size of the tumor distribution, pharmacokinetics of the tracer. Beta emitters are frequently used for radiotherapy. The β^-particles are emitted from the nucleus with the range of energy from zero to maximum level. The range of beta in tissues of 1-10 mm which provide homogenous tumor dosage through their deposition in heterogenous in the target tissues. Some particular radio-lanthanides produced in research reactor have similar chemical characteristics, their production and the use in therapeutic radiopharmaceuticals can be based on similar principles [18].

Auger electrons are very effective in killing the cell to cellular DNA as a necessary requirement. Alpha emitting radionuclides are used for radiotherapy because of their high LET and its high cytotoxicity [19]. Alpha emitters are used for treatment of small and cluster cancerous cells and for medical application, alpha emitters are heavy particles with long-lived daughter products thus a small number of α particles can be used [18]. The altering of cellular homeostasis is another course of action, modifying signal transduction pathways, redox state, and disposition to apoptosis. The cellular changes enhance the killing of tumour cells while reducing the probability of normal cell death [20].The selection of a particle emitter depends on its nature, the extent and disease stage [17].

1.2 Decay scheme of ^{177}Lu

Lutetium ($^{177}_{71}Lu$) is a chemical element that belongs to the lanthanides group of the periodic table. The radioactive isotope with an atomic number of equals to 71 and the natural abundance which is 97.41% of the stable isotope of $^{175}_{71}Lu$ [21]. Lutetium-177 (half-life of 6.71 days) decays by β^- to the stable ground state of ^{177}Hf and decays to an excited state of ^{177}Hf that lies between 0.24967 MeV and 0.32132 MeV above the ground state, which de-excites to the ground state with the photon emission. The following Figure 2.1 shows the decay scheme for ^{177}Lu [22].

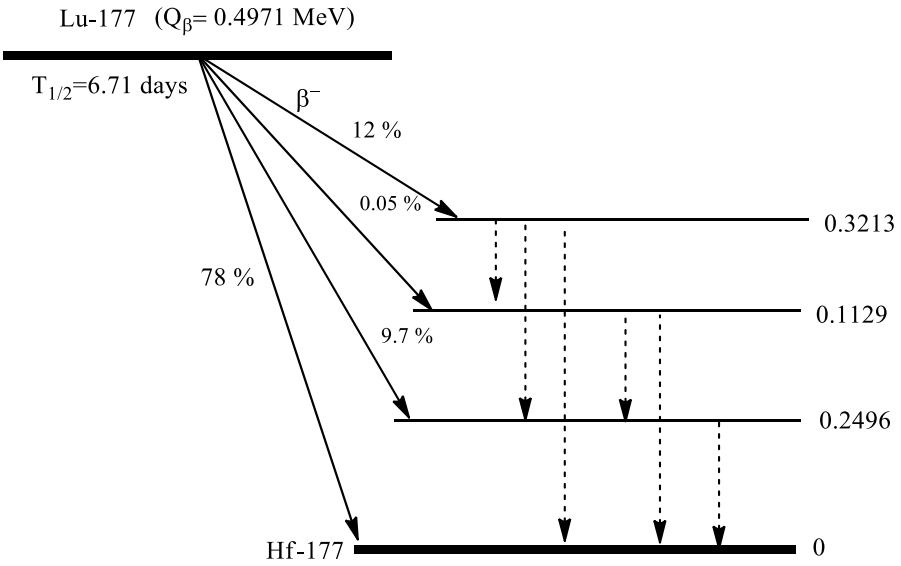


Figure 2.1- Simplified decay scheme of ^{177}Lu [22]

$^{177}_{71}Lu$ decays to $^{177}_{72}Hf$ by beta decay as illustrated in the reaction Equation (1) and (2) below [21].

$$n^0 \rightarrow p^+ + e^- + \nu_e^- \quad (1)$$

$$^{177}_{71}Lu \rightarrow ^{177}_{72}Hf + e^- + \nu_e^- \quad (2)$$

1.2.1 Spectrum of ^{177}Lu

$^{175}_{71}Lu$ is both β^- and γ emitting isotope. The energy of β^- particles which will give therapeutic effect are 498.3 keV at 79.4% of the total β^- emissions. The post-therapeutic imaging energy that will be used is 208.36 keV at 10.36% of the γ emissions [21]. The tissue penetration depth of 0.5 MeV of β^- is 2 mm which allows selective deposition of energy inside the tissue cells while sparing the surrounding of the healthy tissues. The gamma emission and beta energies of 208 keV and 133 keV allows the simultaneous imaging and diagnostic of the treatment of tumor and make it possible for ^{177}Lu to be used for theranostic. The advantage of the decay characteristics of ^{177}Lu makes it advantageous by other applied therapeutic β^- emitters such as ^{131}I and ^{90}Y.The tissue penetration depth of ^{90}Y is 11 m and that of ^{131}I is 2 mm but emits high energy photons in high abundance which results in extra radiation to non-target organs, and ^{90}Y damage the health surrounding tissues. The radioisotope ^{177}Lu in comparison with ^{131}I and ^{90}Y, has the gamma rays which are sufficient low energy which allows for imaging while not affecting the nearby tissues, so it is considered a better alternative to ^{131}I and ^{90}Y for radio-therapeutic applications [1].

1.2.2 No-Carrier-Added ^{177}Lu

Radionuclides have maximum theoretical specific activity values referred to as carrier-free when all the atoms contain one isotope of the element. Carrier free (CF) denotes a radionuclide having 100 % isotopic abundance. A radionuclide is characterized as no carrier added to which no carrier atoms have been added and for which precautions have been taken to minimize contamination with stable isotopes of the element in question. Carrier free is an idealistic situation for a preparation having a specific activity value that approaches the calculated maximum theoretical specific activity [22].

1.2.3 ^{177}Lu-Specific Activity

The specific activity, A_S, for a given radionuclide is defined as its activity divided by the total mass of all its radioactive and stable isotopes which is measured in Bq/mol or Bq/g. Specific activity is expressed in terms of disintegration rate per unit mass of the element [17].

The Equation (3) can be used for determining the specific activity of the radionuclide produced by (n,γ):

$$S = \frac{A}{m_o} \tag{3}$$

where A is the activity of the radionuclide measured and m_0 is the initial mass of the lutetium in the irradiated target [23].

Lutetium-177-labeled therapeutic radiopharmaceuticals comprising small molecules, large biomolecules and particles are currently being evaluated for myriad of clinical applications [24]. The targeted radionuclide therapy is based on selecting appropriate radiopharmaceuticals and targeting mechanisms for application on the number of target sites available for radiopharmaceutical. For instance, targeting to trabecular bone is considered a large capacity site and does not require highly specific activity of ^{177}Lu.

The advantage to produce radioisotope using the nuclear reactor, is the ability to reach high specific activity. High thermal neutron flux in the nuclear research reactor allows production of medical radioisotopes with high specific activity [25]. High specific activity is used for applications such as receptors sites for peptide and antibody therapy. Therapeutic applications such as peptide radionuclide therapy (PRRT), radioimmunotherapy (RIT), palliative treatment of bone metastases etc. uses high SA ^{177}Lu to express on the surface of the tumour [22]. Low specific activity can be used for applications in bone pain palliation and radiation synovectomy [25]. Specific activity of a radioisotope produced by particle-induced reactions is a direct function of the incident particle flux, an increase particle in the particle flux incident it results in an absolute increase in the specific activity of the product. Several isotopes have long physical half-lives and low production of cross-section which will require

long irradiation period. The increase of flux it does not only results in higher specific activity, but it will also result in conversion of the enriched target material. The increase of neutron flux for example, by a factor of two required half of the enriched target material to produce the same amount of radioactive product [10].

1.3 The importance of ^{177}Lu for treatment of cancer

The radioisotope ^{177}Lu, is emerging as an important radioisotope for treatment of the cancer such as breast, prostate, colon, and brain. The isotope with a half-life of 6.71 days, emits a low energy β^- with the maximum and average energies of 421 keV and 133 keV for the effective treatment of the small tumours. Also, it emits a low energy gamma radiation suitable for the simultaneous imaging. ^{177}Lu is a radioisotope having very good potential for use in in vivo therapy, because of its favourable decay characteristic. This radionuclide is important in nuclear medicine as it emit gamma photons used for imaging and beta radiations used for therapy [26].

^{177}Lu radionuclide has brought attention and, in the research, commercial and clinical communities for use in a variety of therapeutic procedures for over the last years. ^{177}Lu has also established a strong foothold at the forefront of targeted radionuclide therapy (TRT). ^{177}Lu in a short time span has virtually pervaded all areas of in vivo radionuclide therapy and may be become a key therapeutic radionuclide of choice for targeted radionuclide therapy. The use of ^{177}Lu in targeted molecular therapies has primarily developed for advances in molecular and cell biology, which include the use of peptides targeted to cell surface receptors, which are overexpressed on the surface of tumour cells [26].

The importance of ^{177}Lu as a targeted radionuclide is that the β^- emitted by ^{177}Lu mean penetration range in soft tissues is 670 μm. Lu-177 emits β^- particle which can penetrate 1 mm in soft tissues, allowing effective delivery of radiation to tumour cells while sparing the nearby healthy tissues. The isotope is effective in localizing cytotoxic radiation in areas where the tumors developed. The emission of energy from β^- and low energy photons results in low

dose and can be able to maintain high level activity of ^{177}Lu during the preparation of radiopharmaceutical. This property is important in medicine for the development of theranostic agents for combined diagnostic and therapeutic use that can deliver therapy to individual cells in affected tissues. ^{177}Lu is a radionuclide which can be used for radiolabelling of antibodies and it offers the period to be elongated for other procedure such as purification quality control. ^{177}Lu is an adequate radionuclide for therapy having both beta particle emissions with maximum energy of 497 (78.6%), 384 (9.1%) and 176 keV (12.2%) for therapeutic effect and gamma emissions 113 (6.4%) and 208 keV (11%) for imaging with a gamma camera. The major advantage of ^{177}Lu lies in the feasibility of its large-scale production with excellent radionuclide purity and adequate specific activity owing to the high thermal neutron capture cross-section of ^{176}Lu (2100 b) using moderate flux reactors [22].

The half-life of ^{177}Lu which is 6.71 days offers extended time periods, which may be required for the use of more procedures to radiolabel and purify ^{177}Lu-labeled radiopharmaceuticals, and for performing quality control and administration. The use of a longer-lived therapeutic radionuclide such as ^{177}Lu is suited for the radiolabelling of antibodies that have slow targeting kinetics. The relatively long 6.71 days physical half-life of ^{177}Lu not only minimizes decay loss, which may be encountered during the transportation and distribution to users, but also provides excellent logistical advantages for shipment to sites distant from the reactor production facility as well as radionuclide-processing facilities [22].

^{177}Lu reactor production and processing technologies along with the recent developments are of great importance. As radionuclide therapy is moving to the forefront of molecular-targeted radionuclide therapy of cancer and other diseases, the demand for ^{177}Lu is evolving. ^{177}Lu production, it is essential based on the technical and economic resources. ^{177}Lu has potential as a therapeutic radionuclide especially in developing countries with limited reactor facilities and for indigenous production capability of radiopharmaceuticals. The relatively longer half-life of ^{177}Lu provides logistic advantage for production, radiochemical processing, and transportation of finished radiopharmaceuticals [17].

1.4 ^{177}Lu Production Process

The production of ^{177}Lu in research reactors throughout the world indicates that all pertinent factors should be evaluated and assessed. The importance of production and processing strategy has been exploited to obtain ^{177}Lu in a chemical form having acceptable radionuclide and radiochemical purity [27]. ^{177}Lu is produced in a reactor by direct (n, γ) neutron radiation of the stable isotope ^{176}Lu.

However, in the process, only about 20% of ^{176}Lu atoms are converted to the wanted ^{177}Lu and it is very difficult to separate the radioisotopes from the non-radioisotopes since both compounds are chemically equivalent. Another method to produce ^{177}Lu is through indirect process using the stable isotope ^{176}Yb [26]. ^{177}Lu can be produced by direct and indirect in the reactor production routes can be used for application in nuclear medicine. The following Figure (2.2) shows the direct and indirect reactor routes for production of ^{177}Lu [27].

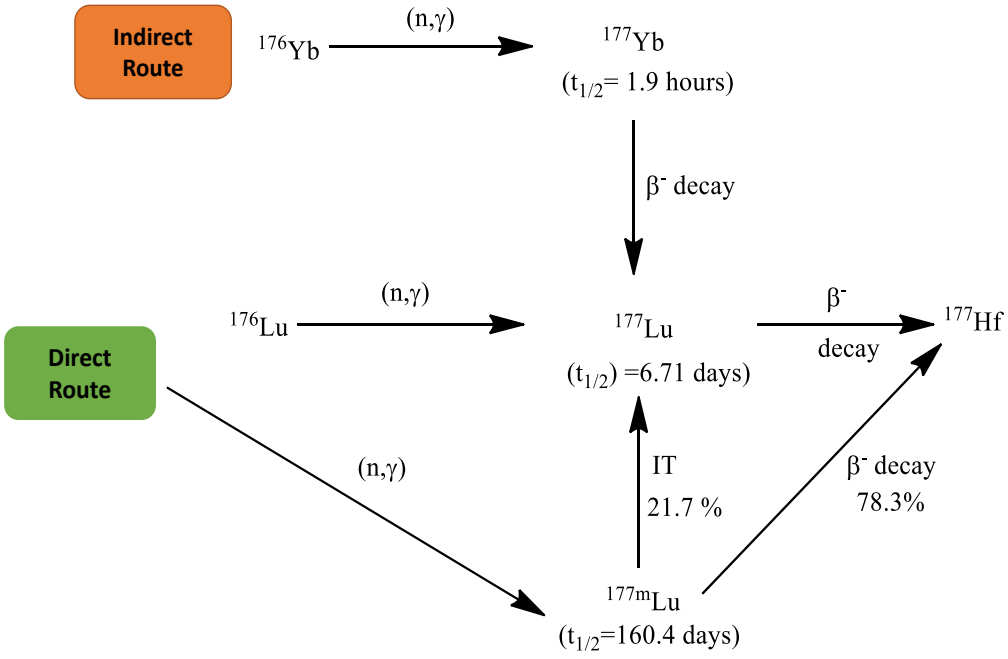


Figure 2.2- Different routes for reactor production of Lu atoms [27]

1.4.1 Direct Production Route [^{176}Lu(n,γ) ^{177}Lu]

The direct production route is based on neutron irradiation of ^{176}Lu targets by the ^{176}Lu(n,γ)^{177}Lu reaction. The direct production route offers the following advantages: The approach to target irradiation in a reactor and requires few design changes in reactor irradiation and processing facilities. It offers the potential to use the $^{176}Lu_2O_3$ target, which remains stable under irradiation conditions and is compatible with reactor irradiation. The irradiated target processing is easy, fast, and technically less demanding as simple target dissolution in dilute mineral acid on gentle warming suffices. The facility required for target processing is straightforward to install and maintain. The route has the flexibility to scale the increase or decrease levels of production in response to requirements by adjusting the target size. Processing generates negligible levels of radioactive waste, and this production method represents the most inexpensive option to obtain ^{177}Lu of requisite purity [28].

^{175}Lu and ^{176}Lu are the two naturally occurring isotopes of lutetium and only ^{175}Lu is stable radionuclide. ^{176}Lu decays by beta decay with a half-life of 4×10^{10} years. For the production of ^{177}Lu, the Lu_2O_3 is the preferred chemical form because of its chemical and thermal stability during irradiation and its solubility in dilute mineral acid. An enriched ^{176}Lu target is of a great interest in view for the need to obtain high specific activity ^{177}Lu amenable for radionuclide therapy. The targets used for production should have a high purity as isotopic impurities are likely to decrease the specific radioactivity of the produced ^{177}Lu owing to high target nuclide burn-up during high neutron-flux irradiation [29]. Direct route production of ^{177}Lu provides with varying specific activities which depend on the neutron flux and irradiation time used and indirect route provide with specific activity which is closed to the theoretical specific activity calculated which takes into the account radioactive decay law [15]. The direct (n, γ) production route offers the prospect of producing ^{177}Lu with specific activity adequate for preparing receptor-specific therapeutic radiopharmaceuticals. This is possible because ^{176}Lu has a very high thermal neutron capture cross section (σ=2090 b, I_0=1087 b) for formation of ^{177}Lu. The neutron capture cross section of ^{176}Lu does not follow

the 1/v law, and there is a strong resonance very close to the thermal region. This method can be prepared with high specific activity of ^{177}Lu with enriched irradiated ^{176}Lu target [27].

There are some concerns that have been raised on the use of this production route include despite the advantages of the direct route. The possibility of using enriched ^{176}Lu targets is necessary owing to the limited natural abundance (2.6 %) of ^{176}Lu in the unenriched target. The specific activity of ^{177}Lu obtained by this method is 740–1,110 GBq (20–30 Ci)/ mg versus the theoretical SA value of 4.07 TBq (110 Ci)/mg. This indicates that only 25 % of the atoms are ^{177}Lu, and 75 % consisting of the product mixture are non-radioactive which contaminate about $^{175/176}$Lu. The maximum specific activity can be achieved only with high-flux reactors is about 70 % of the theoretical value. These specific activity values are adequate for preparation of the ^{177}Lu-labeled agents used for bone pain palliation, synovectomy, treatment of liver cancer and some other applications activity [22].

1.4.2 Indirect Production Route [^{176}Yb(n,γ) ^{177}Yb β^{-} ^{177}Lu]

The indirect ^{176}Yb(n,γ)^{177}Yb→^{177}Lu production route necessitates a chemical separation of ^{177}Lu from the target ^{176}Yb target atoms. In order to obtain high specific activity, the indirect route of production can be considered using highly enriched ^{176}Yb target material. The ^{177}Lu produced by indirect method will be usable for all applications irrespective of the neutron flux in the reactor and irradiation conditions [15]. The indirect production route also has shortcomings, which may be expected to obstruct the path toward widescale utility. Low production yields due to the poor ^{176}Yb thermal neutron reaction cross section (2.5 barn) as compared to the 2090 barn for the direct production from ^{176}Lu. The effective separation of micro amounts of ^{177}Lu from macro amounts of the irradiated Yb target requires an elaborate radiochemical separation as well as purification procedure in order to generate the significant amounts of radioactive waste. This method of production is the most expensive option to obtain ^{177}Lu of requisite purity and it does not only require an enriched ^{176}Yb target but also its recovery and recycling [27]. The advantage of using the indirect route production of ^{177}Lu is the production of the radionuclide free from the long-lived ^{177m}Lu radionuclidic impurity

which is present when using direct route of production. The chemical separation of ^{177}Lu from the irradiated Yb_2O_3 target material is the major challenge of producing ^{177}Lu using this route. The specific activity of the product will be reduced by the presence of Yb [25]. The indirect production route offers the potential to provide ^{177}Lu of the highest possible radionuclide purity, the potential to provide ^{177}Lu of the highest possible radionuclide purity and the presence of long-lived radioactive impurities (e.g., ^{177m}Lu, $<10^{-5}$), below the detection limit, and is associated with minimum radiation protection and waste disposal issues. Specific activity is independent of neutron flux and it provide with the satisfactory radiolabelling performance. The ^{177}Lu obtained by this method has a longer shelf-life (up to 2 weeks). This method of production is the most expensive option to obtain ^{177}Lu of requisite purity and it does not only require an enriched ^{176}Yb target but also its recovery and recycling activity [24].

Another production route has been proposed which is via ^{177m}Lu/^{177}Lu as shown on Figure 2.2. The production route of ^{177m}Lu/^{177}Lu radionuclide generator is based on the production of ^{177}Lu from the decay of its long-lived isomer, ^{177m}Lu with a half-live of 160.4 days [27]. The generator has brough challenges in the separation of chemically and physically alike isomers, ^{177m}Lu and ^{177}Lu. Recently, [27] have provided the experimental evidence on ^{177m}Lu and ^{177}Lu separation thereby confirming the possibility of ^{177m}Lu/^{177m}Lu radionuclide generator based ^{177}Lu production [29]. Radionuclide generators have played an important role in the development and applications of radiopharmaceuticals [21].

^{177m}Lu/^{177}Lu radionuclide generator can be used for the production of ^{177}Lu radiopharmaceutical development by providing cost effective, carrier-free, on demand and onsite availability of ^{177}Lu. The main challenges are the large-scale production of ^{177m}Lu, the parent radionuclide needed for the ^{177m}Lu/^{177}Lu radionuclide generator. Is at the great importance if the nuclear research reactor infrastructure is available and capable of producing sufficient ^{177m}Lu activity to support the ^{177}Lu generator production. ^{177m}Lu is usually co-produced in small quantities during the direct route production of ^{177}Lu [1].

1.5 Targeted Radiotherapy (TRT)

The targeted radiotherapy is a field which have higher efficiency and less side effects to treatment of cancer than chemotherapy. The targeted radiotherapy (TRT) is the ability to deliver the radiation dose to cancerous cells even to unknown location of cancer cells developed which is the modality of treatment of cancer [22]. The targeted radionuclide therapy has radionuclides which are bounded to a target molecule to ensure there is interaction with the tumor cells. The radioisotopes are placed in the human body with cancerous cells by destroying the abnormal growth of cancerous cells by releasing the ionizing radiation during the radioactive decay. The biological effect of the targeted radionuclide therapy for tumor treatment is caused by the absorption of energy from the radiation emitted by the radionuclide. Targeted radiotherapy uses peptides or antibodies to cancer cells of which the specific receptors are over-expressed. This method ensures that there is a high degree of ionizing radiation that will focus only of cancerous cells without affecting the nearby healthy tissues [18]. This radionuclide therapy is effectively targeting the cancer cells inside the body of a human being as shown in the following Figure (2.3) below [1].

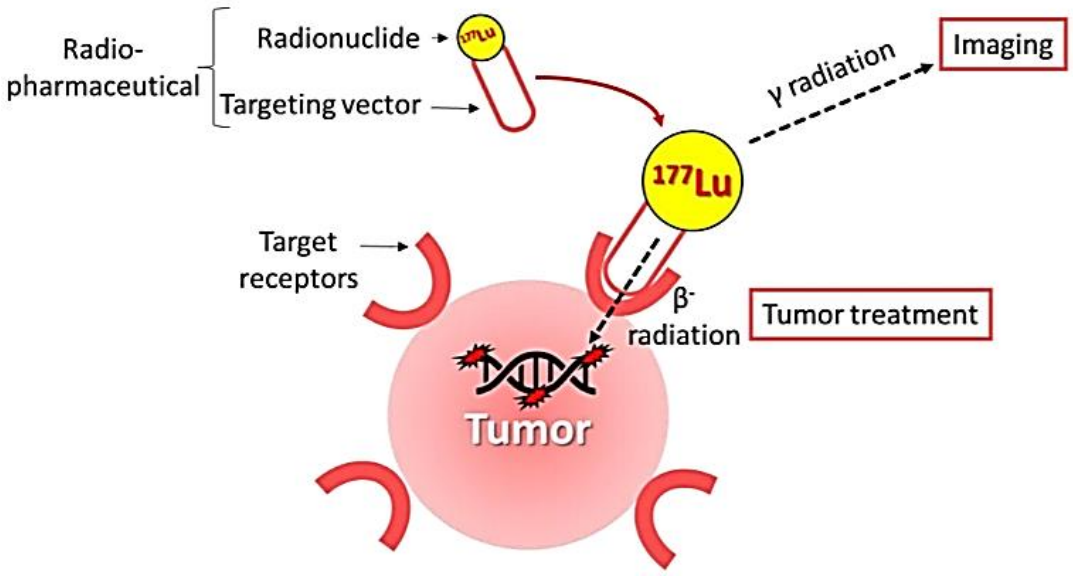


Figure 2.3- Schematic diagram showing the target radionuclide therapy using radiopharmaceutical comprising a targeting vector and lutetium-177 [1]

Targeted radionuclide therapy has been reported to be a success in the treatment of tumor with less side effects. There are combinations of several factors for the application of any radionuclide in targeted radionuclide therapy such as physical half-life, decay energy, decay product, tissue penetration depth, high specific activity of the radionuclide, and radionuclidic purity [1]. The use of ^{177}Lu in nuclear medicine procedures has been impressive, and widespread applications of ^{177}Lu therapeutic agents and been responsible for stimulating the growth of these therapeutic methods. The use of ^{177}Lu is evolving, as the targeted radionuclide therapy, and a broad spectrum of ^{177}Lu labelled therapeutic radiopharmaceuticals for treating a wide range of diseases.

In nuclear medicine the diffusion of ^{177}Lu has not only brought the developments in radionuclide therapy but has also prompted radiotherapeutic method toward the treatment of some diseases. The remarkable use of ^{177}Lu labelled radiopharmaceuticals in targeted radionuclide therapy have been the major factors among researchers and capturing the imagination of the clinical community though the advances in molecular and cellular biology [22]. The cost-effective availability of sufficient activity levels of ^{177}Lu that have the required as the key success of using ^{177}Lu in in vivo targeted therapy as ^{177}Lu-labeled radiopharmaceuticals. The interesting use of ^{177}Lu in targeted radionuclide therapy provide the review on the production and processing of this emerging radionuclide [22].

1.5.1 Basis of radiopharmaceuticals

Radiopharmaceuticals are radioactive compounds used for diagnosis and treatment of diseases which consists of radionuclide and pharmaceutical agent. About 95% of radiopharmaceuticals in nuclear medicine is used for therapeutic purposes. The pharmaceutical is chosen in designing the radiopharmaceutical in a localized organ. The suitable radionuclide is chosen to be administered into the patient on the chosen pharmaceutical [19].

The radiation emitted can be detected from the organ by external detector for assessment of structure and functioning of the organ. Several radiopharmaceuticals contain

^{177}Lu for clinical trials. DOTA is the most studied peptide used for peptide receptor radionuclide therapy such as [$DOTA^0, Tyr^3$] octreotide (DOTATOC) and [$DOTA^0, Tyr^3$] octreotate (DOTATATE) which is labelled with ^{177}Lu. DOTATATE is used to patient with somatostatin receptor-positive tumors e.g neuroendocrine tumors [24]. The ^{177}Lu-DOTATATE is FDA approved for treatment of gastroenteropancreatic, neuroendocrine tumors used for clinical applications worldwide. A paper was currently published for the treatment of prostate cancer using ^{177}Lu-PSMA based radiopharmaceutical. More than 50% of patients showed a respond of the treated cases. The ^{177}Lu based radiopharmaceutical can also be used for application in breast, colon, lung cancer treatment [1].

^{177}Lu for radiopharmaceuticals has been successfully developed and evaluated. The in vivo applications of key ^{177}Lu radiopharmaceuticals for a variety of therapeutic procedures include peptide receptor radionuclide therapy [29], bone pain palliation, radiation synovectomy [30] and radioimmunotherapy. There is an expanding list of ^{177}Lu-labeled radiopharmaceuticals that is currently being evaluated at the preclinical research or at product development stages, these may be used in vivo in humans for evaluation for radionuclide therapy [26].

Lutetium exists in the +3-oxidation state, which precludes reduction oxidation in any chemistry solution complications and commonly forms nine coordination complexes. This property provides the potential for radiolabelling of molecular carriers, which include small molecules, and peptides, proteins, and antibodies with the specific desired characteristics for therapy. Lu+3 chemical characteristics are suitable for peptide and protein radiolabelling by attachment of a bifunctional chelating agent (BFCA) through a metabolically resistant covalent bond [22]. The major diagnostic modalities used for imaging which include both planar and tomographic imaging technology are single-photon emission computed tomography (SPECT) and positron emission tomography (PET) [21].

1.6 Ytterbium target

Natural ytterbium consists of a mixture of seven stable isotopes, including ^{168}Yb, ^{170}Yb, ^{171}Yb, ^{172}Yb, ^{173}Yb, ^{174}Yb and ^{176}Yb, among which ^{174}Yb is the most abundant. The use of ytterbium metal as a target is considered for irradiation which oxidizes in air under oxygen [31]. The advantage of the use of Yb_2O_3 it possesses chemical and thermal stability during irradiation and the post irradiation target processing easy as simple target dissolution in dilute acid will suffice [32], and under irradiation in nuclear reaction has sufficient stability [24].

The concentrated acid is used to dissolve irradiated Yb metal. The isotopic abundance and their thermal neutron absorption cross section are summarized in the following Table 2.1:

Table 2.1- Isotopic abundance of the natural Yb and thermal neutron absorption cross- section [24]

Isotope	Abundance (%)	σ (b) for (n,γ)
^{168}Yb	0.13	2400
^{170}Yb	3.04	12
^{171}Yb	14.28	53
^{172}Yb	21.83	1.3
^{173}Yb	16.13	16
^{174}Yb	31.38	63
^{176}Yb	12.76	31

The possibility of obtaining a large-scale production of ^{177}Lu by indirect route method it depends on the possibility of the radiochemical separation of the target Yb and ^{177}Lu [33]. If the enriched ^{176}Yb is used instead of natural Yb as a target material for the production of ^{177}Lu, the specific activity expected to increase. Also using the enriched sample, ^{169}Yb can be removed as an unwanted radioisotope, which is produced by neutron bombardment of ^{168}Yb with very high σ(b), 2400 barn with these backgrounds.

1.7 Production equation

Radionuclides are classified as neutron-rich and neutron-deficiency. The neutron-rich radionuclides are those that are produced in the nuclear research reactor while the neutron-deficiency are produce by bombarding a target material with protons, deuterons, or helium particles and in most cases are non-carrier added radionuclides [17]. Radionuclides that undergo the neutron bombardment in the nuclear reactor, there is no Coulomb repulsion from positively charged nucleus, and these neutrons can easily penetrate the nucleus. Thermal neutrons have a low energy neutron with a large probability useful for production of radionuclides because these neutrons have distribution of energy of gas molecules in thermal equilibrium at room temperature [17].

The production of a given radionuclide is proportional to the number of the target nuclei N_t, number of incident particles and the cross-section σ. The radionuclide product undergoes radioactive decay, λN_p. Thus, the net rate of change in the number of radioactive product nuclei, N_p during the irradiation is given by the rate of formation less the rate of decay, or [17],

$$dN_p / dt = \varphi\sigma N_t - \lambda N_p \tag{4}$$

Since N_t is large to remain constant during irradiation, the solution to this differential equation is,

$$\lambda N_p = N_t\varphi\sigma(1-e^{-\lambda t}) \tag{5}$$

The activity of the product A_p, at the end of bombardment is λN_p, after the substitution the following radionuclide production Equation (6) is obtained,

$$A_p = N_t\varphi\sigma(1-e^{-\lambda t}) \tag{6}$$

where;

A -activity in disintegrations per seconds, dps;

N_t -number of target atoms=$W/M \times F \times$ Avogadro constant (6.023×10^{23} atoms per mole);

W - weight of the sample in grams;

M -atomic weight in grams/mole;

F -isotopic abundance;

φ - neutron flux in neutrons. $cm^{-2}.\sec^{-1}$;

σ - cross section in cm^2;

λ -decay constant of the product $=\ln 2/t_{1/2}$;

t - the irradiation time.

1.7.1 Theoretical specific activity of ^{177}Lu

It is important to discuss the importance of the specific activity (SA) of ^{177}Lu before its production and this is the key to success for the use in targeted radionuclide therapy [24]. The theoretical specific activity of carrier-free (CF) ^{177}Lu is calculated using the following Equation (7):

$$\frac{dN}{dT} = \lambda N = \frac{0.693\times N}{T_{1/2}} = \frac{0.693\times 6.023\times10^{23}}{6.65\times24\times60\times60\times177} \, Bq/g \qquad (7)$$

$$= \frac{0.693\times 6.023\times10^{23}}{6.65\times24\times60\times60\times177} \, Bq/mg = 4.10367 \, TBq/mg$$

$$110.91 \, Ci/mg$$

where; N - number of ^{177}Lu atoms, λ - decay constant of ^{177}Lu, $T_{1/2}$ - half-life of ^{177}Lu [24].

The following traditional equation (8) is used to project the irradiation yields [24]:

$$\frac{dN^{177}Lu}{dt} = \left(\frac{dN^{177}Lu}{dt}\right)growth - \left(\frac{dN^{177}Lu}{dt}\right)decay \quad (8)$$

OR

$$\frac{dN^{177}Lu}{dt} = N^{176}Lu\sigma^{177}Lu\varphi - N^{177}Lu\lambda^{177}Lu \quad (9)$$

where;

$N^{176}Lu$ -number of target atoms ^{176}Lu;

$^{176}Lu\sigma$ -neutron capture cross section of ^{176}Lu (cm^2);

$N^{177}Lu$ -number of radioactive atoms ^{177}Lu formed;

$\lambda^{177}Lu$ -decay constant of ^{177}Lu (s^{-1});

φ -neutron flux $(cm^{-2}.s^{-1})$.

$$\frac{N^{176}Lu\varphi\sigma^{176}Lu}{\lambda^{177}Lu}\left(1-e^{-\lambda^{177}Lut}\right)$$

$$\frac{dN^{177}Lu}{dt} = \left(\frac{dN^{177}Lu}{dt}\right)growth - \left(\frac{dN^{177}Lu}{dt}\right)decay - \left(\frac{dN^{177}Lu}{dt}\right) \text{ product burn up}$$

$$N^{176}Lu\sigma^{176}Lu\varphi - N^{177}Lu\lambda^{177}Lu - N^{177}Lu\varphi\sigma^{177}Lu$$

$$N^{177}Lu = N_0{}^{176}Lue^{-\varphi^{176}Lut}$$

$N_0{}^{176}Lu$ =initial number of target atoms ^{176}Lu

$$N^{177}Lu = \frac{N_0{}^{176}Lu\varphi\sigma^{176}Lu}{\lambda^{177}Lu - \varphi\sigma^{176}Lu}\left(e^{-\varphi^{176}Lut} - e^{-\varphi^{177}Lut}\right) \quad (10)$$

The Equation (10) is used provides the neutron capture cross section in the thermal neutron area and is inversely proportional to the neutron velocity (the $1/Vn$ law) [21].

1.7.2 Irradiation Yield for indirect route production

$$^{176}\mathrm{Yb}\,(\mathrm{n},\gamma)\,{}^{177}\mathrm{Yb} \xrightarrow{\beta^-} {}^{177}\mathrm{Lu} \quad (11)$$

In this case, the net production rate of nuclide ^{177}Lu is given by Equation (12):

$$\frac{dN_{Lu}}{dt} = N_{Yb}(1 - e^{-\lambda_{Yb}t})\phi\sigma_{Yb} \quad (12)$$

If the number of target atoms, N_{Yb} , remains constant (no considerable target burn-up) and $N_{Yb} = N_{Lu} = 0$ at $t = 0$ (start of irradiation), integration of Equation (13) gives rise to:

$$N_{Lu} = N_{Yb}\phi\sigma_{Yb}\left[\left(\frac{1 - e^{-\lambda_{Lu}t}}{\lambda_{Lu}} + \frac{e^{-\lambda_{Yb}t} - e^{-\lambda_{Lu}}}{\lambda_{Yb} - \lambda_{Lu}}\right)e^{-\lambda_{Yb}t_d} + \frac{\left(1 - e^{-\lambda_{Yb}t}\right)\left(e^{-\lambda_{Yb}t} - e^{-\lambda_{Lu}t_d}\right)}{\lambda_{Lu} - \lambda_{Yb}}\right] \quad (13)$$

where;

N_{Yb} - the initial number of ^{176}Yb atoms;

σ_{Yb} - is the cross section of the ^{176}Yb (n,γ) ^{177}Yb reaction;

ϕ - the neutron flux of the irradiation source;

t - the irradiation time;

t_d - the decay time after irradiation,

λ_{Yb} and λ_{Lu} - decay constants of ^{177}Yb and ^{177}Lu, respectively [19].

1.8 Research reactor for radioisotopes production

In nuclear reactors, radioisotopes are produced mostly by (n,γ) reactions, they are neutron rich and decay by β^- particle emission [34]. This route (n,γ) is widely used with thermal neutrons. The production of radioisotopes in reactors is based on neutron capture in a target material, either by activation or generation of radioisotopes from fission of the target material by bombardment with thermal neutrons. There are different types of neutrons which are classified according to their energy which are thermal, epithermal, and fast neutrons [34].

Thermal neutrons are those neutrons which are in thermal equilibrium with energy of 0.025 eV at the temperature of 20°C. The energy distribution can be represented by Maxwellian. Epithermal neutrons are neutrons which are moderated which have not reached thermal equilibrium. Their energy ranges are 1eV to ~ 100 keV. The 1/En (where En is the energy of neutrons) law can approximately represent the distribution of epithermal neutrons. Fast neutrons are neutrons with high energy (above 0.1MeV). They have small significance in thermal reactors and for radioisotope production [34].

The uses of research reactors include the analysis and testing of materials, and production of radioisotopes. The applications are mainly in the nuclear industry, fusion research, environmental science, advanced materials development, drug design and nuclear medicine. It could also be used for academic and applied research in the areas of nuclear and neutron related sciences and engineering. The extent of the utilization of the reactor is basically determined by the reactor power, which determines the neutron flux available, as well as on its operational cycle. Small power levels and short operational cycles (only few hours of operation each day) are particularly inconvenient, both for high quality research and also for the production of useful radioisotopes [35]. The use of neutron activation for producing the radioisotopes, widely used in industry and medicine, by bombarding particular elements with neutrons analysis atoms are made radioactive by exposure to neutrons in a reactor. The characteristic radiation each element emits can then be detected [36].

1.8.1 IRT-T research reactor

The TPU Research Nuclear Reactor is the one and only in Tomsk and Russia determines its role in national and international research projects. The growth of interest in research activities in the area of neutron activation analysis (NAA). NAA allows measuring ultra-small concentrations of an element in substance and carrying out mass and express analyses. The University core scientific equipment includes the nuclear research reactor IRT-T (W = 6 MW). There are 14 vertical experimental channels (VEC) placed outside the reactor core and 10 beam ports (HEC): 8 radial beam ports with diameter of 100 mm and 2 tangent of 150 mm diameter [35]. Beryllium is used as the moderator. The beryllium reflector has the thickness of 69 mm around the core perimeter. In the central channel, the maximum neutron flux with the beryllium moderator is 1.7×10^{14} for thermal and $2\times10^{13} n/\left(cm^2 s\right)$ for fast neutrons. The energy of the neutron flux ranges within 10-1000 eV and with Monte Carlo simulation estimation of $1.6\times10^{13} n/\left(cm^2 s\right)$ [35].

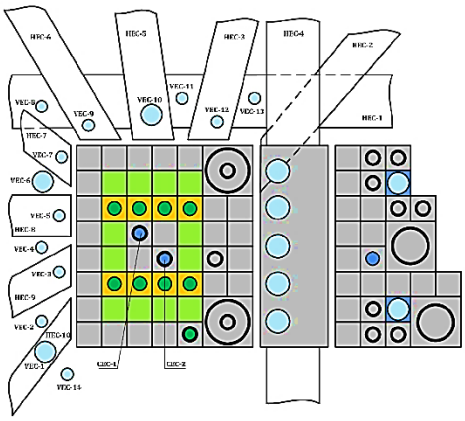


Figure 2.4- Diagram showing the IRT-T reactor core [37]

1.8.2 Neutron Activation Analysis

Neutron activation analysis was first introduced by George Von Hevesy and Hilde Levi in 1936. It is a technique to measure amounts of chemical elements in a sample, based on the conversion of stable nuclei to other, mostly radioactive nuclei, by neutron irradiation

of the material [38]. The technique is based on the nuclear reaction between neutrons and target nuclei [39]. Neutron activation analysis (NAA) is also a technique used for qualitative and quantitative elemental analysis of multiple major, minor, and trace elements in samples and is the useful method for the determination of elements from various sources in the ppb-ppm range without or with chemical separation [40].

Samples are bombarded with neutrons in order to transform stable isotopes of most element constituting samples into radioactive isotopes by neutron capture. The target is bombarded by neutrons such that neutron capture occurs, and atom will either remain stable or become unstable. If the nuclei are in an excited state and undergo β-decay emitting γ- rays, this can be detected using an HPGe detector [41]. The activated nuclides decay according to a characteristic half-life emitting beta particles only, but other nuclides emit gamma-photon with specific energies. The sensitivities and accuracies of neutron activation analysis are dependent on the concentration of a particular element and radionuclide parameters such as parent isotope abundance, neutron cross-section, half-life, and gamma ray abundance [38].

1.8.2.1 Types of Neutron Activation Analysis

Instrumental neutron activation analysis (INAA) is based on short-lived radionuclide production by nuclear reactions, such as reactor neutrons (i.e., thermal neutrons). INAA has advantages such as better sensitivity, low detection limit, simple and no reagent blank correction [42]. In INAA, the sample does not undergo chemical separation and can be used when other radioactive isotopes do not interfere with measurement of the element of interest.

Radiochemistry neutron activation analysis (RNAA) involves sample decomposition and separation of elements. Through separation method, the interfering elements are separated from elements of interest [39]. INAA can be classified into two: prompt gamma ray neutron activation analysis (PGNAA) where measurements are performed immediately after irradiation and delayed gamma ray neutron activation analysis (DGNAA) where measurements follow after radioactive decay.

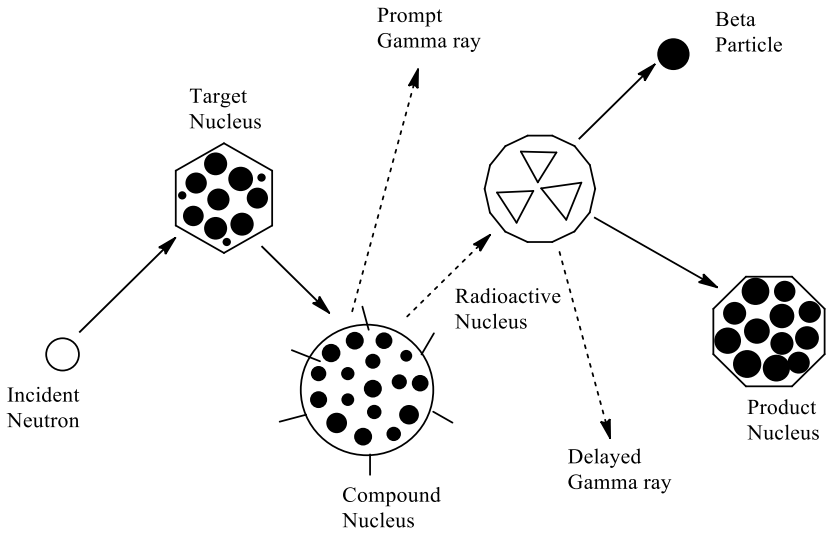


Figure 2.5- Method of NAA [40]

1.8.2.2 Neutron sources

The probability of a neutron interacting with a nucleus for a particular reaction is dependent on the kind of nucleus involved and the energy of the neutron. Isotropic neutron sources are most frequently used as neutron sources. They consist of an alpha emitting radioactive nucleus mixed with beryllium. The neutron sources are provided by neutron chain reactors utilizing the fission reaction and neutron irradiation is commonly used as an activation technique in a nuclear reactor. These neutron sources are applied in accelerators where a convenient target material is bombarded by accelerated charged particles and are produced in a nuclear reaction [41]. Neutrons are generated at a certain type of reaction has the advantage of the isotropic neutron sources which can be made portable and generate a stable neutron flux, but the neutron flux is rather low in comparison to a nuclear reactor [38]. The nuclear activation process can be expressed using the following Equation (14):

$$ {}^{m}_{z}X + {}^{1}_{0}n \rightarrow {}^{m+1}_{z}Y \xrightarrow{\beta^-} {}^{m+1}_{z+1}K + \gamma \qquad (14) $$

where; X - atomic number z and mass number m of stable isotope, Y radioisotope which emit beta particle accompanied by gamma-rays, n - neutrons, γ - gamma-ray released.

1.8.2.3 Cross section for Nuclear Reactions

The probability of a neutron interacting with a nucleus for a particular reaction is dependent on the kind of nucleus involved and the energy of the neutron. The absorption of a thermal neutron in most materials is much more probable than the absorption of a fast neutron and probability of interaction will vary depending upon the type of reaction involved. [41]. The probability of a particular reaction occurring between a neutron and a nucleus is called the microscopic cross section (σ) of the nucleus for the particular reaction (Reaction Rates). The microscopic cross section is regarded as the effective area the nucleus present to the neutron for the reaction. The following Equation (15) shows the number of atoms at time t after irradiation is expressed as [41]:

$$N_y(t) = N_y(t_0)e^{-\lambda y(t-t_0)} \tag{15}$$

For a nuclear reaction of the type (n,γ), the induced activity (A_t) in the disintegration per second at the end of irradiation of time (t) is given by Equation (16):

$$A_t = N\sigma\phi(1-e^{-\lambda t}) = N\sigma\phi\left(1-e^{\frac{0.693}{t_{1/2}}}\right) \tag{16}$$

where σ is thermal neutron capture cross section in $\sec^{-1}$. The unit of cross section is the barn (1 barn= 10^{-24} cm^2), ϕ is thermal neutron flux in neutrons $cm^{-2}\sec^{-1}$, λ is decay constant of the product nuclide ($\lambda = 0.693/t_{1/2}$, $t_{1/2}$ is half-life of the product nuclide, N is number of atoms of in the target [41].

1.9 Separation techniques of ^{177}Lu from neutron irradiated ^{176}Yb

Radiochemical separation is a method which is considered for separation for success of NCA ^{177}Lu production. In periodic table, Yb and Lu are adjacent trivalent lanthanides and have similar chemical and physical properties. The separation of irradiation of ^{177}Lu from

^{176}Yb is the challenges for preparation of NCA which will require separation of microscopic levels of ^{177}Lu from the macroscopic levels of the ^{176}Yb target. [33].

There is some consideration that must be followed to achieve the success which are, the specific activity of ^{177}Lu must be higher and there should be a high decontamination factors from ytterbium provided by the separation process. The process should provide high yield of ^{177}Lu (>85%). The Lutetium should have a suitable chemical form (ionic form) for radiolabelling. The criteria for separation of Lu from Yb are the ^{177}Lu/Yb separation efficiency and the time spent for this separation. The methods of separation of ^{177}Lu from Yb are based on ion-exchange chromatography, solvent extraction, electrochemical separation, extraction chromatography. The separation is based on the difference in the properties of these elements such as the capability of Yb for reduction and amalgam formation [33].

1.9.1 Cementation process for Yb and Lu

Cementation is the method of electrochemical displacement of metals from compounds by other from their compounds. The process is based on the contact of alkali metal amalgams and acetate, citrate, or other compounds of rare earth metal. The cementation method is based on the selective reduction of ytterbium and its extraction on mercury by amalgamation [43]. The reduction is described with the following Equation (17):

$$Yb^{3+} + Na \rightleftharpoons Yb^{2+} + Na^{+} \quad (17)$$

In this process, the irradiated Yb_2O_3 is dissolved in hydrochloric acid, sodium acetate is added to form sodium amalgam followed by extraction of Yb by sodium amalgam from Cl^{-}/CH3COO^{-} electrolytes taking advantage of higher solubility of metallic Yb than Lu in mercury. The procedure of this method has some limitation such that the recovery yield of ^{177}Lu and product quality is appealing, the time-consuming requirement at some point complicated the process by involving multiple cementation cycles together with the elaborate purification steps emerged as the major impediment that would be expected to restrict its wide-scale applicability [33].

The chloride ion addition in the form of their sodium or potassium salts increases the rate of cementation by sodium amalgam. Boldyrev et al. [43] suggested alternation of electrolysis on mercury cathode separation for the cementation reduction of Yb to eliminate the apparent technology imperfection. The electrochemical procedure for the Yb/Lu separation is electrolysis on a mercury cathode, based on the capability of Yb for reduction to the elemental state of the following reaction shown in Equation (18) followed by the formation of ytterbium amalgam [33].

$$Yb^{3+} \rightarrow Yb^{2+} \rightarrow Yb^{0} \quad (18)$$

Ytterbium amalgam in acid solution is unstable and decomposes immediately after its formation. The intense hydrolysis of trivalent elements is formed because of an increase in pH of the solution. The formation of amalgams is prevented due to the hydroxides formed. The electrolysis should be performed in neutral solutions of organic salts preventing the precipitation of hydroxides. The electrolysis on a mercury cathode is often accompanied by the mercury dispersion [33].

This method is the separation of lanthanides with sodium amalgam. The method was reported by Lebedev et al. is based on the selection reduction of ytterbium and its extraction on mercury by amalgamation [24]. This method was optimised for the separation of NCA ^{177}Lu from 200 mg ytterbium target by Lebedev et al [44]. It is based on the selective reductive separation of ytterbium with sodium amalgam and followed by cation-exchange purification. The reduction is described as follows Equation (19):

$$Yb^{3+} + Na \rightleftharpoons Yb^{2+} + Na^{+} \quad (19)$$

The electro-amalgamation process is based on the mercury-pool cathode developed by Chakravarty et al. [45], which is based on the two-cycle in lithium citrate medium. This process provides ^{177}Lu with > 99.99% Radionuclidic purity with an overall separation yield of ~ 99% within 3-4 hours [24].

The recovery of the target is important because of the high cost of enriched ^{176}Yb. The recovery of the target from mercury amalgam needs chemical processing [46]. Dash et al. [24] demonstrated the flow chart of electro-amalgamation process which is used for routine production and chemical separation of ^{177}Lu by indirect route production. The flow chart is show in Figure 2.6 below.

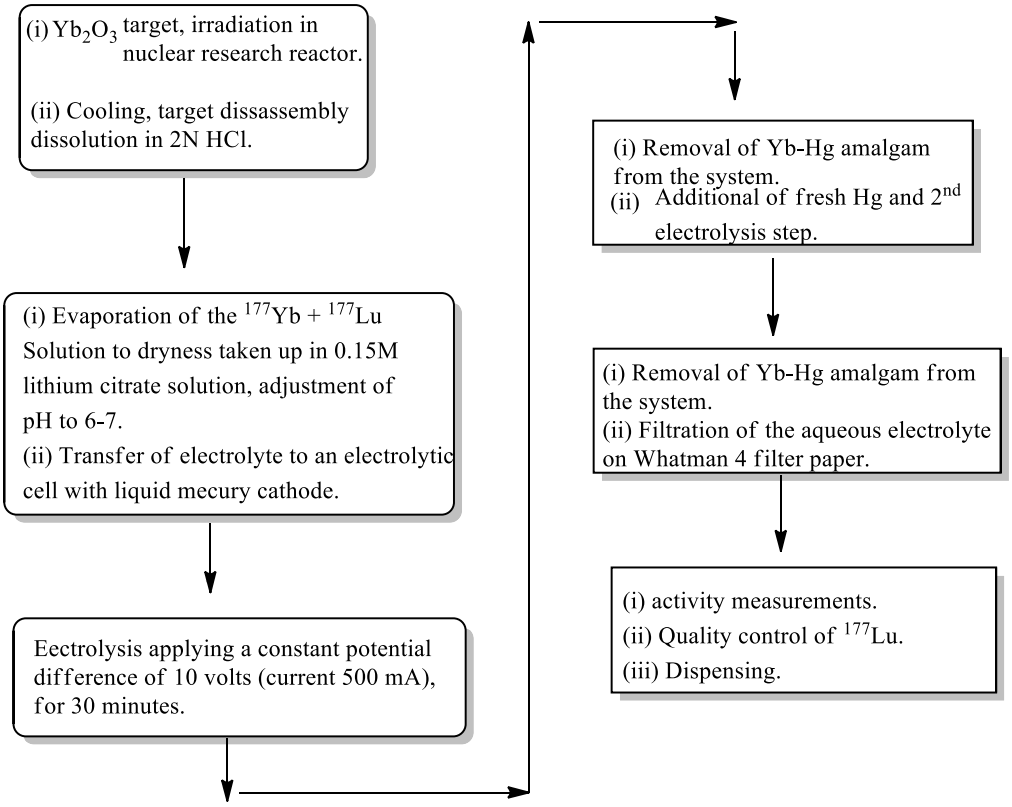


Figure 2.6-Production flow chart [24]

1.9.2 Electrochemical Method

Electrochemical separation was applied for production of NCA ^{177}Lu. Electrochemical separation strategy uses electrolytic medium to selectively deposit the radionuclide of interest between the standard reduction potentials of two radionuclides under controlled applied potential. This electrochemical method consists of selective reduction of Yb^{3+} to Yb^{2+} and its preferential transfer onto a mercury cathode exploiting the ability of Yb^{2+} to form amalgams with Hg [22]. There are some strategic methods that must be followed for the separation method such as the examination of the redox potentials of the Yb and Lu which indicates the

possibility of Yb forming the bivalent state and bivalent state of Lu is unknown. Yb^{2+} is known to form an amalgam, Lu^{3+} cannot [24].

Therefore, Lu is difficult to deposit on the Hg cathode from aqueous electrolytes. The possibility of electrolytic reduction of Yb^{3+} to Yb^{2+} in acidic solution owing to its high hydrogen over-voltage. Such an attribute ensures no reoxidation of Yb^{2+} and offers easy handling and deposition of Yb onto Hg [24]. The electrochemical separation method is essentially based on the formation of the Yb amalgam by electrolysis into a mercury cathode or extraction into an amalgam aimed at its removal from the Yb-Lu mixtures [22].

1.9.3 Purification of Yb from impurities

Ytterbium (Yb) is a rare-earth element and in the earth's crust, is a mixed composite oxide mineral resource. Ytterbium metal has a high vapor pressure and is hard to refine and contains large amounts of volatile elements and the like as impurities [47]. It is possible to obtain high purity rare earth metals in which the oxygen content is 300 ppm or less and having few impurities. The refining method is proposed for obtaining high purity rare elements by adding Mg or Zn to Ta-containing rare earth metals as impurities, melting this in a crucible.

High purity ytterbium can be obtained by heating ytterbium oxide in a vacuum together with reducing metals and reducing the product with reducing metals and simultaneously distilling the same. The purification of ytterbium involves the method of high temperature saturated dissolution, low temperature recrystallization, high temperature reduction and vaporization-based removal of impurities [48].

1.10 Radionuclidic purity

The method of examination for gamma emitters for Radionuclidic purity is gamma spectrometry [89]. Radionuclidic purity is the ratio which is expressed as a percentage of the radioactivity of ^{177}Lu to the total radioactivity content of the sample. Gamma spectroscopy is used to determine the Radionuclidic purity of ^{177}Lu. For quantitative and qualitative analysis of ^{177}Lu impurities, the detector must be calibrated for both energy and efficiency calibrations. The calibration sources that should be used is ^{152}Eu containing radionuclides with different gamma photon energies [22].

1.10.1 High Purity Germanium (HPGe) detector

Gamma rays are emitted during radioactive decay or nuclear reactions [49]. The detection of gamma gives information about the nuclear energy levels in which their energy and intensity determines the position levels, the emission of gamma measure the lifetimes of levels in which it gives the deformation parameters, their polarization, their angular distributions, and the correction provide spin information, magnetic moment, and static quadrupole moments [50].

Gamma spectroscopy is a technique used to identify and measure radionuclides in different samples. The environmental samples can differ by chemical composition and structure for efficiency calibration for measurement of samples [51]. High resolution gamma spectroscopy is a method which is used to determine the radionuclides in any sample in which the radioactivity measurements are determined. This is achieved by means of HPGe detectors. HPGe is a semiconductor crystal detector which consists of a cylinder-shaped n type germanium crystal. The high purity germanium detector is used for analysis of concentration of radionuclide in environmental samples and for environmental radioactivity. The calibration of the detector is important for the environmental radioactivity measurements, to improve efficiency and reduce the amount of radioactive waste produced. The calibration of the detector is performed by counting a sample and the standard source [52].

Germanium(Ge) detectors have a large energy resolution which detect activity concentration measurements of different radioisotopes of different gamma emission [50]. High Purity Germanium (HPGe) detector has been used in many environmental studies to quantify the parent radionuclide in the samples on gamma peaks of its daughter radionuclide [51]. The detector used gamma ray interacting with matter to produce signals from particles entering the system. The energy of the gamma-ray is transferred to electrons creating electron pairs during the interaction [53]. Compared to well-type and planar, coaxial detector has low efficiency at low gamma energy [54]. Broad energy germanium detector (BEGe) is one of the HPGe detector which has high sensitivity at high gamma energy [51].

There is intrinsic uncertainty in radioactivity analysis. Uncertainty can be due to many components such as matrix, weighing, the content of water, radioactivity and homogeneity, instrumentations which include the special acquisition, background and efficiency calibration, and properties of nuclear which include radioactive decay, emission probability and the half-life [55]. Long time of counting, large sample size and sample-detector distances that are small are recommended for better statistics when using the detector in gamma spectrometry. However, a sample with a large volume results in self-absorption and large counting time causing short-lived radionuclides to decay during the measurements [56].

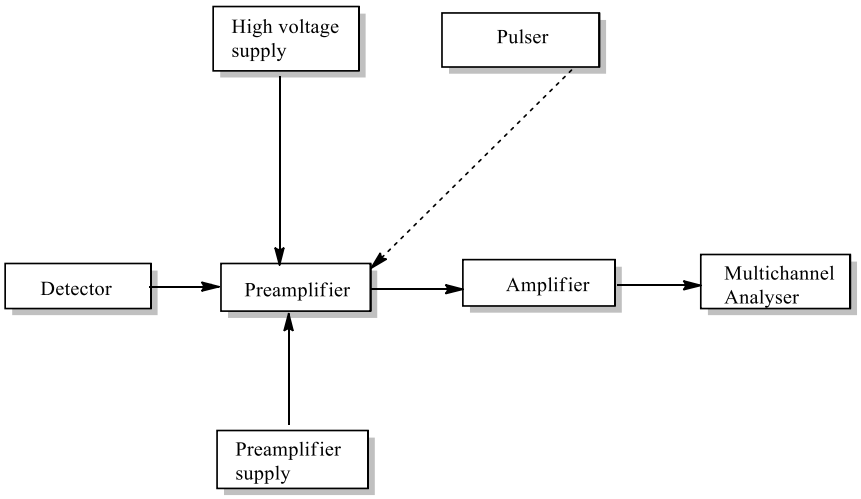


Figure 2.7- An electronic system schematic for gamma-ray spectrometry [53]

Figure 2.7 shows a schematic diagram of for the electronic system of HPGe semi-conductor detector. The detector is based on interaction of gamma ray with matter to produce a signal for every particle entering the system. The energy of the gamma-ray is transferred to electrons by creating electron on the active volume of material of the detector during the interactions. The number of charge carriers produced per interaction is proportional to the amount of gamma-ray energy deposited in the detector. External high voltage called detector bias is connected to the detector. The voltage withdraws the electron-hole pairs created within the depletions region of the detector for all the charge carriers are connected by the amplified to a proportional size of the gamma-ray energy absorbed [57].

BEGe can cover energy range from 3 keV to 3 MeV [58], it can be used in the application of nuclear physics [59], medical science [60] and the environmental studies. Monte Carlo (MC) is a simulation method used to calibrate the detector [61]. Bronson tested source less efficient calibration software using MC simulation for 13 detectors and concluded the method is more convenient quicker [58]. The Monte Carlo simulation was used to correction factors such as coincidence summing and self-absorption effects for some measurements [62].The Monte Carlo method has been applied to simulate the detection process to obtain spectrum peaks and to determine the efficiency curve for each geometry.

HPGe-detectors are calibrated for the energy response, peak resolution and counting efficiency using a multi-channel analyser and the spectrophotometry software These properties depend on the energy of the incident radiation from $^{241}Am/^{152}Eu$ source with different gamma-ray energies. The detector characterization is performed using Genie 2000 software [63]. The measured energy of a gamma-ray corresponds to the type of element and its isotope, while the number of counts corresponds to the abundance of the radioactive source present in the measured sample [52].

Chapter 2-Methodology

2.1 Chemicals and instruments

The apparatus and equipment used in the experimental work are double distiller, analytical balance, muffle: for conversion to oxide, measuring beakers, pipettes, power supplies, chemical vessels, vacuum pump, liquid nitrogen, pH meter, heating stove, gamma spectrometer, cementation diagram, and vacuum mercury distillation plant. The solution used for all processes in this work were measured using a weighing balance and were prepared in the fume hood to eliminate the exposure to strong and hazardous chemicals. In the experiment processes for all the preparations, the deionized water was used. The required acids solutions were prepared by dilution of commercial concentrated HCl and HNO_3. The glass columns and dispensers were washed with deionized water before preparations of solutions. After all experiment procedures, all radioactive waste solutions were collected and disposed in authorized storage area. All the solids, liquids were measured to check the level of radioactivity. The preparations of reagents used, and their chemical structures are show in the following Figure 3.1:

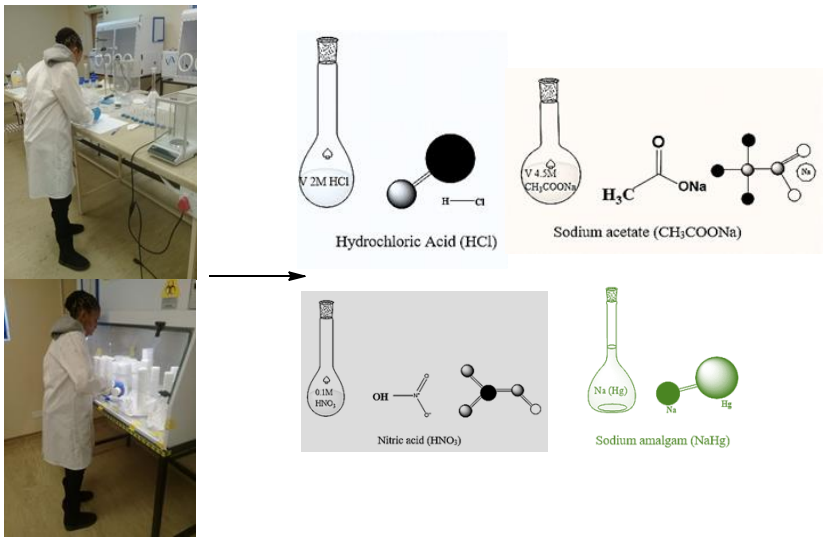


Figure 3.1- Chemical structures and formulas of different reagents prepared

2.2 Energy and Efficiency Calibration

The gamma-ray spectroscopy system is characterized by energy calibration, efficiency calibration and energy resolution. These properties should be measured using the source with different gamma-ray energies. The HPGe gamma spectroscopy detector was calibrated using ^{152}Eu standard source because it covers multiple gamma peaks of the entire region of interest and prior to the recording of gamma ray spectra. The detector was characterized using the ^{152}Eu source of range 121.78 keV to 1408.0 keV. The gamma photons from the ^{152}Eu source were detected by introducing the source to the detector using sample changer. The detector was calibrated concerning efficiency calibration was performed.

The calibration procedure of the detector is important to improve efficiency and reducing the amount of radioactive waste produce. Calibration is performed before measuring the sample to eliminate any shift spectra and maintain the quality of the measurements. The efficiency calibration is done determining the full energy peak efficiency, as a function of energy using two low activity point sources with complex decay schemes. ^{152}Eu was chosen because it consists of multiple energy peaks that cover a large energy region. After the calibration, the spectrum of ^{152}Eu was obtained. The spectrum of ^{152}Eu calibration of the HPGe detector is presented in Figure 3.2.

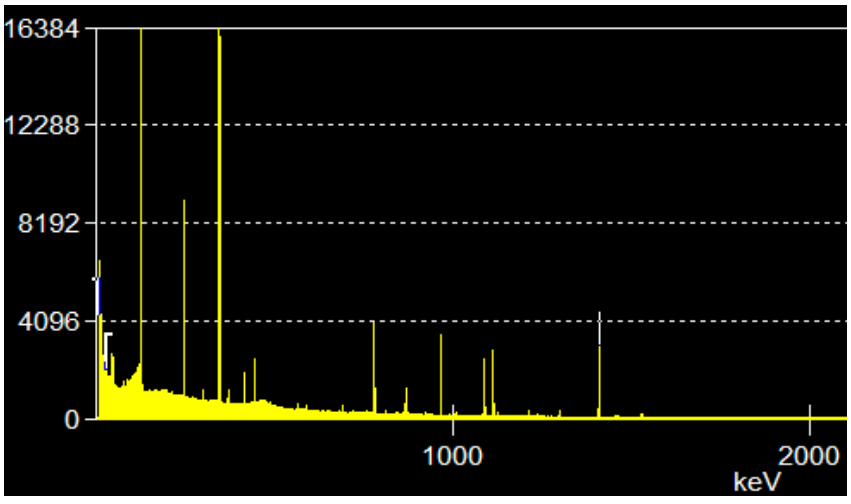


Figure- 3.2 spectrum of ^{152}Eu

The centroid channels were plotted against the energy peak lines for efficiency calibration, and the energy peak lines were plotted against the generated efficiency values [64]. Figure 3.3 below shows the efficiency as function of gamma-ray energy for the HPGe detector.

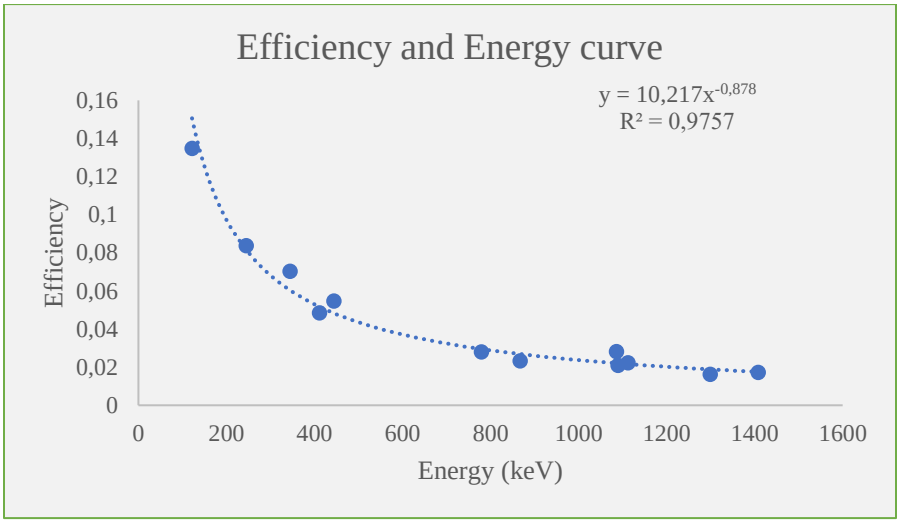


Figure 3.3- Efficiency as function of gamma-ray energy for the HPGe detector

2.3 Theoretical ^{177}Lu activity calculations

The theoretical activity of ^{177}Lu from 10 mg of Yb_2O_3 was determined using the irradiation time of 60, 1440, and 7200 minutes and with thermal neutron flux of 4×10^{13} n.cm^{-2}.s^{-1} using the Equation (6).

2.4 Activation of solution using radioactive tracers (^{177}Lu, ^{169}Yb)

The solution was activated using a radiative tracer of ^{177}Lu and ^{169}Yb. Radioactive tracers were made from irradiation of natural isotope of Lu and Yb at the nuclear research reactor. The mixed isotope of Lu which are found during the irradiation are ^{175}Lu and ^{176}Lu and the mixed isotope of Yb exposed to irradiation at the research reactor are ^{168}Yb, ^{170}Yb, ^{179}Yb, ^{173}Yb, ^{174}Yb, and ^{176}Yb. The main target of isotopes during irradiation are ^{176}Lu and ^{168}Yb which decay to produces ^{177}Lu and ^{169}Yb as radioactive tracers of the study.

The radioactive tracer of ^{169}Yb was used which can be made possible to conduct multiple technological experiments during the development of the method for the separation of ytterbium and lutetium. The use of radioactive tracers to is to determine the concentration distribution of the solution or to measure the activity of the sample.

In the literature review, the mass ratio of Yb/Lu is in the range of 800-1200. The ratio between Yb/Lu was chosen to be 1000 for simplicity in the literature review. The 10 µg mass of Lu_2O_3 from the prepared radioactive tracers is equivalent to the 1000 ratio between Yb/Lu. The volume of HCl added was 5.85 ml with concentration of 2 M and the volume of sodium acetate added was 4.15 ml with concentration of 4.2 M into the solution. In the prepared solution, there is non-radioactive 10 mg mass of Yb, 0.01 mg radioactive Yb and radioactive 0.01 mg (10/1000) of Lu.

The following Figure 3.4 shows the activation of solution using a radiative tracer of ^{177}Lu and ^{169}Yb. After the the target material of Yb_2O_3 exposed to radioactive labels, the reaction ^{177}Yb ($t_{1/2}$=1.9 hours) from ^{176}Yb (n,γ) and transformed to ^{177}Lu via beta-particle and emitting gamma-photon.

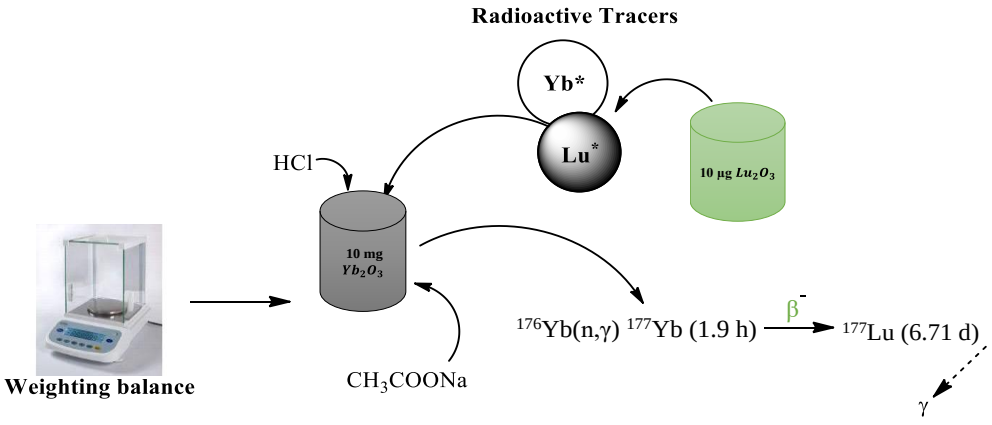


Figure 3.4 -Activation of solution using radioactive tracers (^{177}Lu, ^{169}Yb)

10 mg of Yb_2O_3 was theoretically used in the study. This target material of 10 mg of Yb_2O_3, can be irradiated in the pool-type research reactor of the IRT-T with thermal neutron flux of 4×10^{13} n.cm^{-2}.s^{-1}. The irradiation can be carried out in a beryllium neutron trap (NT)

of the IRT-T reactor as shown in the Figure 3.5. The radioactive tracers have the same chemical properties as irradiation at the research reactor.

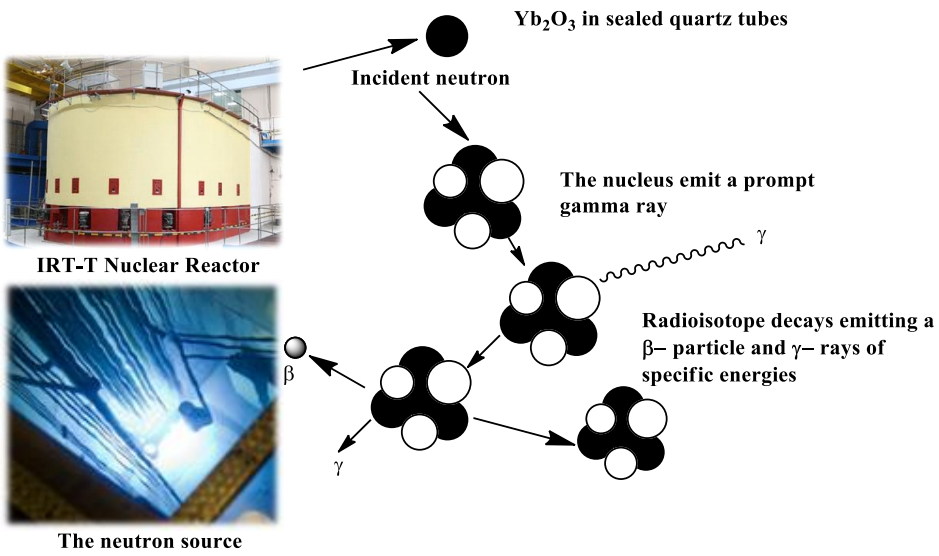


Figure 3.5- Pool type nuclear research reactor IRT-T

2.5 Cementation process of Yb and Lu

The cementation method was used for the separation of ytterbium and lutetium. The process of cementation was conducted from five cementations experiments each with three cycles of cementation.

2.5.1 Yb translated into chloride

The mass of non-radioactive of Yb_2O_3 target were weight as 10.2, 10.4, 10.3, 10.2, and 10.3 mg using an analytical weighting balance. The non-radioactive mass of Yb_2O_3 represent the weight mass of first to fifth cementation experiment. The non-radioactive 10 mg Yb was translated it into chloride by dissolving it in hydrochloric acid and evaporate it into the heating stove as follows:

$$Yb_2O_3 + HCl = YbCl_3 + H_2O \quad (20)$$

Balance equation: $Yb_2O_3 + 6HCl \rightarrow 2YbCl_3 + 3H_2O$ (21)

2.5.2 Five cementation experiments

The gamma spectrometry was acquired using a high purity germanium detector coupled to a multichannel analyser (GX1018 Canberra). The solution containing HCl and CH_3NOONa was measured for 7200 seconds using HPGe detector. The activity of Lu and Yb were measured in disintegration and the results were recorded. This was the initial cementation cycle measured before cementation process, to determine how many counts of Lu and Yb in the solution.

5 ml of sodium amalgam (NaHg) was prepared per cementation experiment. The sodium amalgam was washed with water and ethanol. The amalgam starts to decompose, and a high amount of Na is needed. The amount of sodium amalgam was determined. In the vessel, the solution containing hydrochloric acid and sodium acetate with radioactive Yb and Lu, and non-radioactive Yb were added into the sodium amalgam which contains molecules Na and Hg. The pH was continuously measured using pH meter as the solution was dissolving in the sodium amalgam. To keep the pH in the constant level, CH_3COONa were added into the solution. After the chemical reaction between Yb and sodium amalgam, some amount of Yb and Lu was dissolving in Hg. After two minutes, the whole solution together with sodium amalgam was measured with HPGe detector. This was the first cementation cycle of the first cementation experiment. The activity of Lu and Yb were measured in disintegration and the results were recorded. After the first cycle of cementation measurement, the sodium amalgam was removed.

After the first cementation cycle, the 5 ml of fresh sodium amalgam was prepared for the second cementation cycle. The fresh sodium amalgam was used in order to remove trace amount of Yb that may be present in the ^{177}Lu. The dissolved solution from the first prepared amalgam was added to the fresh sodium amalgam. The solution was waited for two minutes to dissolve, and pH was continuously measured. The aqueous solution containing NCA ^{177}Lu was separated and collected in the beaker. After two minutes, the whole solution together with sodium amalgam was measured with HPGe detector. The activity of Lu and Yb were

measured in disintegration and the results were recorded. This was the second cementation cycle of the first cementation experiment. The sodium amalgam was removed.

Another fresh 5ml sodium amalgam was prepared for the third cementation cycle. The dissolved solution in sodium amalgam from second cementation cycle was added to a fresh sodium amalgam. The solution was waited for two minutes to dissolve, and pH was continuously measured using pH meter. After two minutes, the whole solution together with sodium amalgam was measured with HPGe detector. The activity of Lu and Yb were measured in disintegration and the results were recorded. And this was the thirst cementation cycle of the first cementation experiment. The sodium amalgam was removed. The second, third, fourth and fifth cementation experiment were conducted using the procedure of the first cementation experiment. The following Figure 3.6 show the process of cementation method.

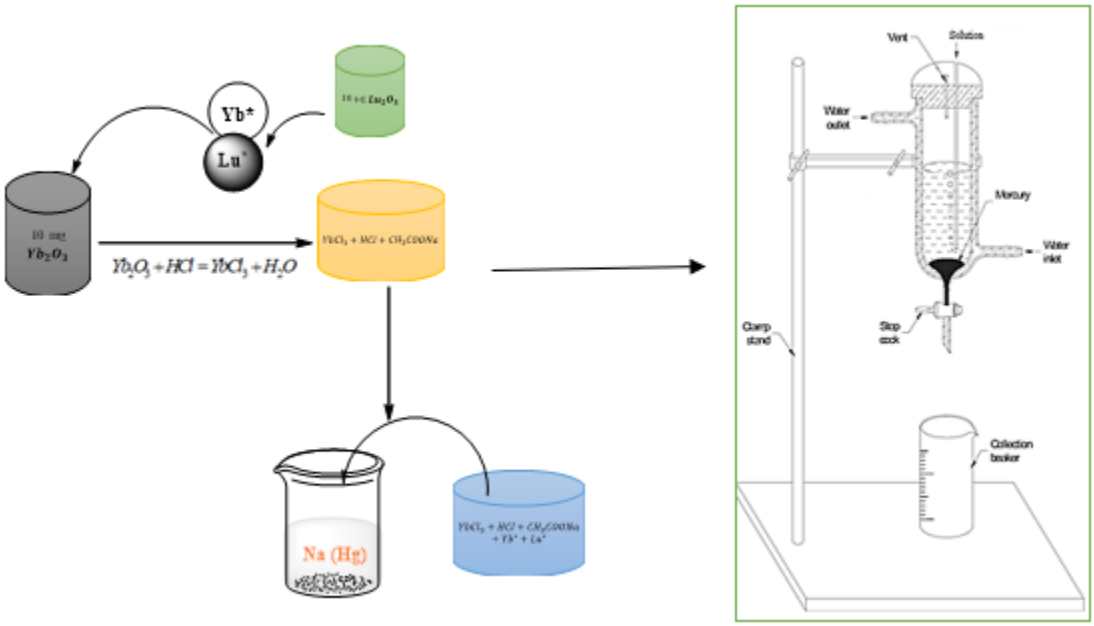


Figure 3.6-Diagram showing the solution procedure and cementation process

2.6 Gamma spectroscopy measurements

The measurement of activity concentrations of solution was carried out by γ-spectrometry. The γ-spectra were acquired using a high purity germanium detector coupled

to multichannel analyzer (GX1018 Canberra). The HPGe detector has a 1.5 keV resolution at 1333 keV and range from 1.8 to 2 MeV was used for analysis of ^{177}Lu in the presence of Yb.

The solution was analysed by gamma ray spectroscopy using a HPGe detector after an appropriate dilution of the sample. These gamma-ray peaks were detected in the composition of the solution of Yb and Lu. The activity of Lu and Yb were measured in disintegration and the results were recorded. The following Figure 3.7 is the gamma spectrometry system used for measuring the activity of ^{177}Lu and Yb.

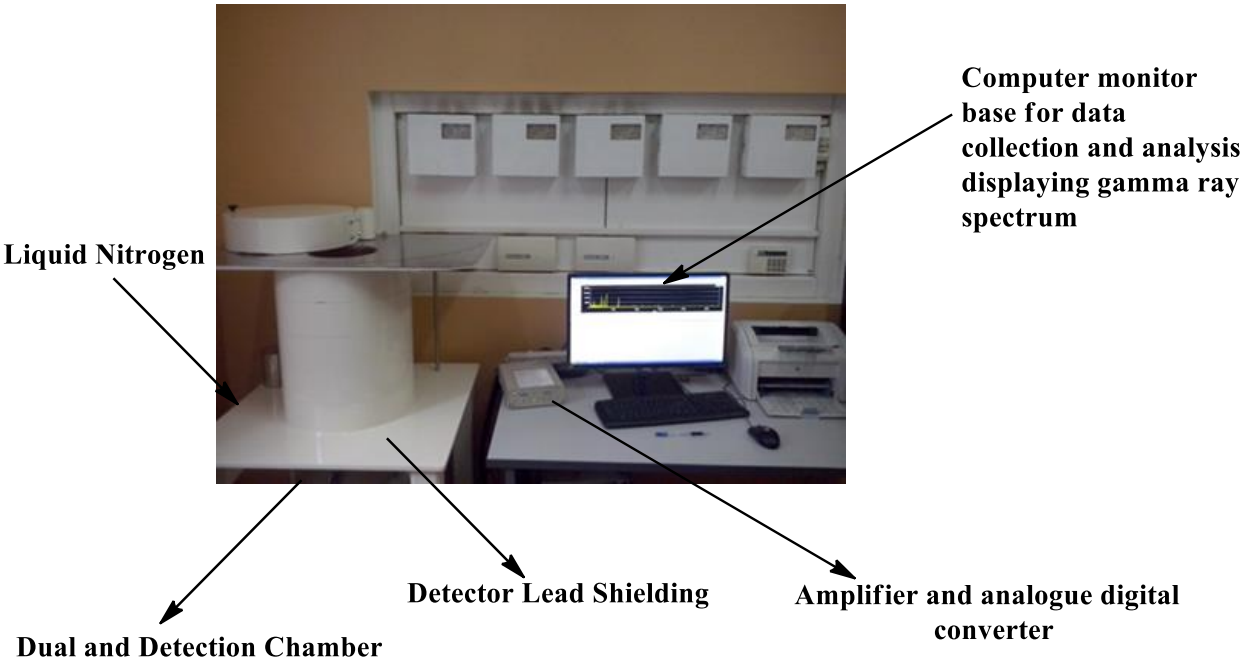


Figure 3.7- Block diagram of a basic gammas spectrometry system (GX1018 Canberra)

2.7 Distillation process experiment without radioactivity

Distillation is the process commonly used for separating liquid mixtures in which a large amount of energy is used. It can be used separate mixtures in the chemical and pharmaceuticals industries [66]. The separation of the liquid mixtures depends on the differences in boiling points of the individual components and the components distribution between the phase of solid and liquid in the mixture. This process depends on the vapor

pressure characteristics of the liquid mixture, and this vapour pressure is formed by heat application as a separating agent [67]. Distillation process is used to separate Yb from mercury and purification of mercury, recycling Yb in new production.

The distillation experiment without radioactivity was carried out at pressure of 850 mbar (vacuum) with the volume mercury of 20 ml. After 20 minutes, mercury was boiled and evaporated at the temperature of 250-252° C. For 1 hour and 20 minutes, mercury left a minor amount of less than 0.5 ml. The installation was sacrificed with pre-washing 0.1 M of nitric acid (HNO_3). Mercury pairs were controlled in the air with paper filled in a solution of Kl and Na. All mercury (with radioactive Yb) was distilled. Mercury was cleaned on filter paper (perforated) and falling into a receiver with 0.1 M nitric acid (HNO_3). After 13 minutes, mercury began to boil at a pressure of 870 mbar and temperature of 246° C. The solution was filtered through filter paper in order to remove residual impurity of mercury/amalgam. The rate of evaporation was decreased. White powder with black enclosure ($YbCl_2$) were obtained and during the cooldown, side surface red (HgO) and black (Hg_2O) powder was obtained. White powder was obtained at the bottom of the flask.

A 5 ml 4M of hydrochloric acid was poured onto the bottom of the distillation flask. All the powder was dissolved. Aliquots were selected at 1 ml. And the activity of Yb and Lu from the solution of the aliquots was measured using HPGe detector and the results were recorded in disintegration. The following Figure 3.8 shows the Vacuum Mercury Distillation Plant.

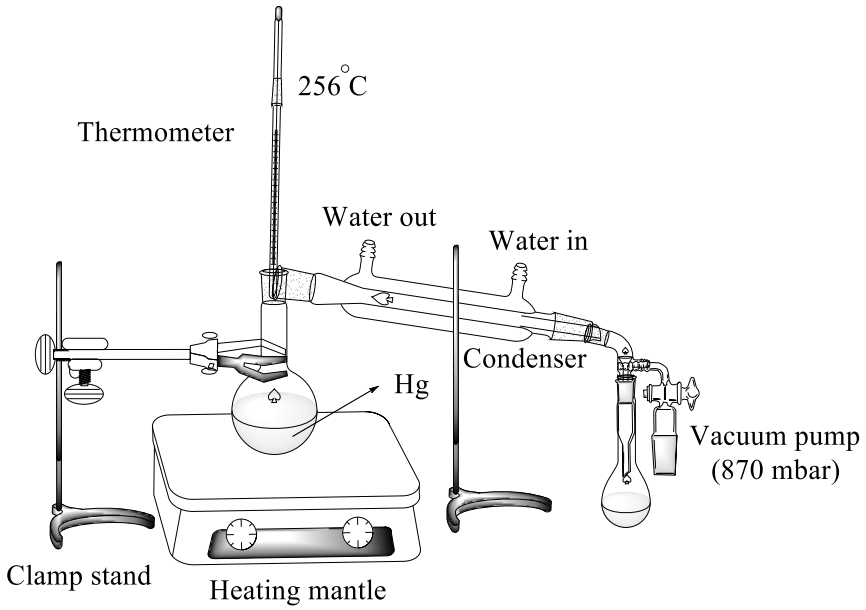


Figure 3.8- Vacuum Mercury Distillation Plant

2.8 Activity and specific activity calculations

Activity, A, is the term used to measure the decay rate of a radionuclide. Activity has units of disintegrations per second or dps. The decay constant, λ represents the probability that a radioactive atom will decay and is dependent on the half-life of the nuclide [65]. The γ-peak is used to calculate the activity of the isotopes. The activity of each cycle of cementation of Yb and Lu from five cementation experiments was calculated according to the Equation (22).

$$A = \frac{I[counts]}{t.\varepsilon.Intensity/100} \tag{22}$$

where;

A -is the activity concentration of a certain radioactive nuclide in the decay series;

I -is the number of counts (Area);

ε -is the absolute efficiency of the detector;

$Intensity$ -is the intensity of a specific energy photo peak;

t is time for collecting the spectrum of the sample [23].

The specific activity of a radionuclides produces by (n,γ) route of production is determined using Equation (3).

2.9 Radionuclidic purity

Gamma spectroscopy is used to examine the Radionuclidic purity. The radionuclide impurities are directly related to the production process of a radionuclides. The technical limitations and safety requirements limits have been set for Radionuclidic impurities in preparations of radiopharmaceuticals which is expressed as a percentage of the total radioactivity [89]. Radionuclidic impurity of Yb and Lu was calculated form the final product using the Equation (23) and was expressed as a percentage of the total radioactivity.

$$P_{RN}(\%) = \frac{N}{N_i} \times 100 \tag{23}$$

where;

N - number of atoms of the radionuclide of interest;

N_i - number of atoms summing for all the radionuclide present in the sample.

Chapter 3-Results and Discussion

3.1 Introduction

^{177}Lu is the isotope of interest which can be used for in-vivo target therapy radiopharmaceuticals. The production NCA of ^{177}Lu is suitable for the development of target-therapeutic agents. In the last few years, NCA ^{177}Lu was produced in several papers and were reported [45]. The production of ^{177}Lu by indirect method is ideal because only one isotope, ^{177}Lu, is produced in the process. However, the advantage of the preparation of this method allows the preparation of the product which correspond to the theoretical specific maximum activity of 110.91 $Ci.mg^{-1}$ only during the measurement of impurities using different techniques required [33].

^{177}Lu separated by this method could be successfully used for preparation of high specific activity ^{177}Lu-DOTA-TATE, an agent presently being used for treating in-operable neuroendocrine tumors over-expressing somatostatin receptors. And ^{177}Lu obtained by this technique is suitable for the preparation of targeted therapy agents, with adequate purity as well as specific activity for radiopharmaceutical preparation [45].

The aim of the study was to produce large amount of ^{177}Lu by the indirect route ^{176}Yb(n,γ) ^{177}Yb of production . It can be assumed that the ^{177}Yb quantitatively decays to ^{177}Lu due to the short half-life at high neutron flux and there are no significant losses through when it undergoes neutron activation to be expected. It is required to enrich the target material Yb to obtain a high irradiation yield and high specific activity of ^{177}Lu.

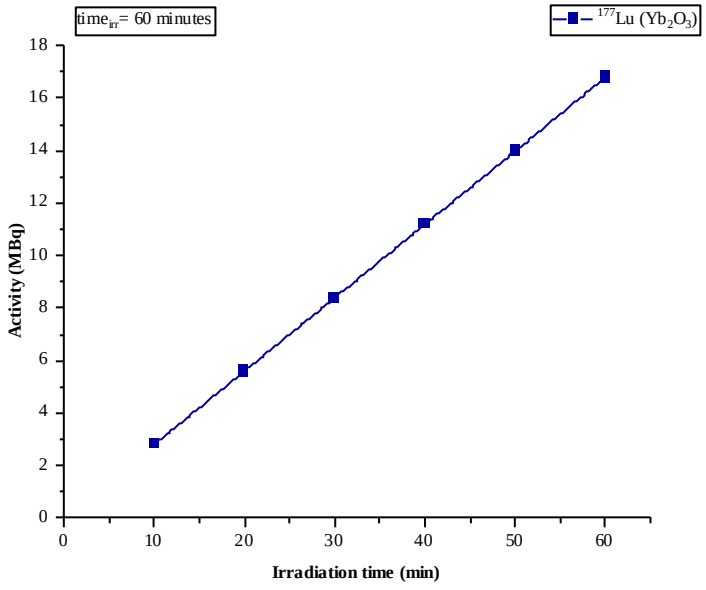
For this study, all reagents were prepared, the amount of ^{177}Lu was produced by cementation process by separation of Yb from Lu. The distillation process was also used for separation of Yb from mercury, purification of mercury, recycling of target (Yb_2O_3) through the separation of Yb and Hg. The activity was measured using HPGe detector and all the results were recorded.

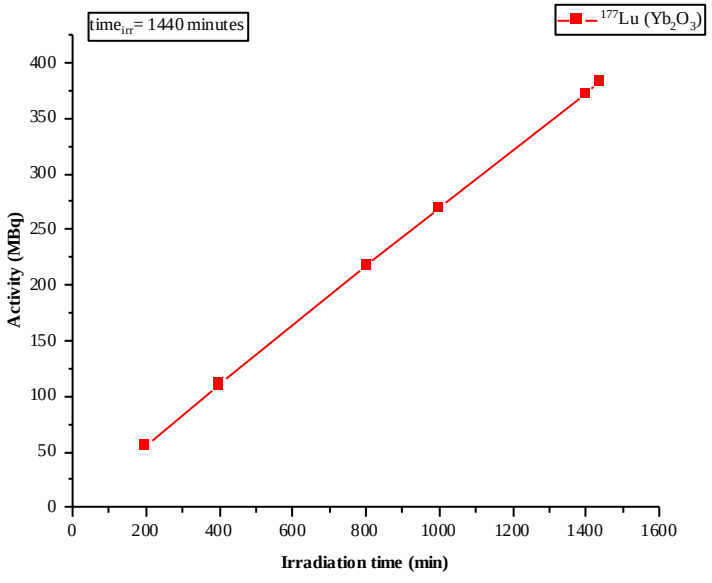
3.2 Theoretical activity of ^{177}Lu calculations

The theoretical activity of 10 mg of Yb_2O_3 during the irradiation time of 60, 1440, and 7200 minutes were theoretically calculated. The theoretical number of atoms and activity of ^{177}Lu from Yb_2O_3 was calculated using Equations (7) and (6). Specific activity was calculated using the Equation (3). Table 4.1 Summarize the theoretical activity and specific activity of ^{177}Lu and are further illustrated in Figure 4.1.

Table 4.1- Theoretical Activity and specific activity of ^{177}Lu from Yb_2O_3

Mass (mg)	Number of moles atoms/mol	λ (day^{-1})	T (min)	Activity (MBq)	Specific Activity (MBq/mg)	Specific Activity (Ci/mg)
10	3.4215×10^{19}	0.1033	60 1440 7200	16.8 383.6 1573.6	1.68 38.36 157.36	4.54×10^{-5} 1.04×10^{-3} 4.25×10^{-3}





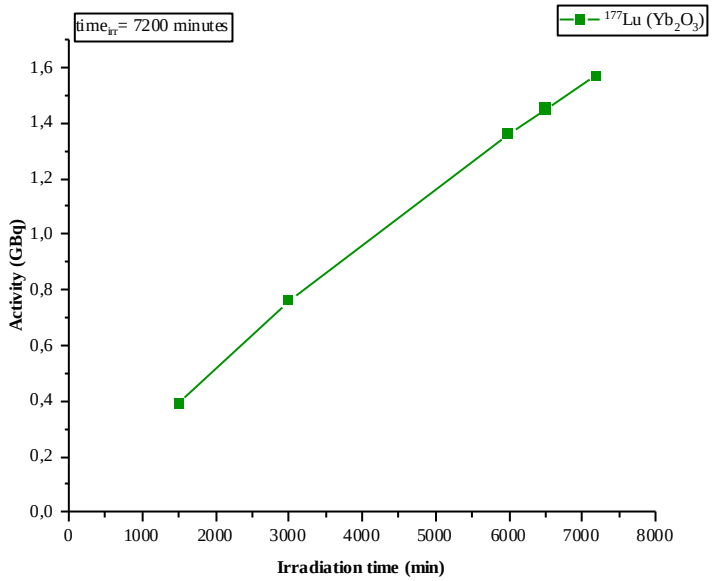


Figure 4.1-Activity of the Lu-177 from Yb_2O_3 during the irradiation time 60, 1440 and 7200 minutes

The theoretical activity during the irradiation time of 60, 1440, and 7200 minutes and was found to be 16.8, 383.6 and 1573.6 MBq with specific activity of 1.68, 38.36 and 157.36 (MBq/mg), respectively.

In Figure 4.1, the activity of ^{177}Lu increases with irradiation time and attain a maximum activity. The maximum activity corresponds to the when target started to irradiate in different time of irradiations. This shows during the production of ^{177}Lu, it will reach a maximum point after a certain duration of irradiation. It is evident that the yield of ^{177}Lu is achievable when the irradiation is carried out for the duration of 1, 3 and 5 days at the above specified thermal neutron flux. In some cases, there will be the decrease of the activity, and this could be a due to decay or rapid burning. According to theoretical predictions, the activity of ^{177}Lu formed in the irradiated lutetium target is increasing linearly during the first several hours of the irradiation. Later the burn-up of the target material becomes evident and the irradiation yield reaches a maximum value [68].

The actual specific activity of ^{177}Lu is different from the value obtained by dividing the production yield of ^{177}Lu by mass of the target irradiated, since the actual mass of the

lutetium present in the system post irradiation is different from the initial mass of the irradiated target which is reported by Zhernosekov et al. [68]. The maximum values of the ^{177}Lu specific activity are proportional to the thermal neutron flux.

The specific activity of ^{177}Lu from Yb_2O_3 provides for the possibility of variation of the time over the range without loss in the ^{177}Lu yield, as well as the specific activity which is close to the theoretical value. The specific activity of ^{177}Lu by indirect route of production depends on the amount of the lutetium in the target material. Even upon the irradiation with high thermal neutron flux ($\phi = 4 \times 10^{13}$ n.cm^{-2}.s^{-1}), the presence of stable lutetium isotope in the target material would lead to the decrease of specific activity of ^{177}Lu [69]. The higher the thermal neutron flux of the reactor, shorter will be the time of irradiation for attaining maximum activity [69]. This applies when ^{177}Lu is produced using enriched ^{176}Lu. Therefore, to obtain a maximum specific activity using enriched ^{176}Lu as a target material, the time of irradiation must depend on the neutron thermal flux for the irradiation [70].

The specific activity is very important for quantity determination in nuclear medicine. The specific activity is related to the initial mass of the present element in the target when it is produced by the (n, γ) reaction. The radionuclides with high specific activity are required for application in nuclear medicine. A maximum specific activity is when the radionuclide is the only isotope of the element present in the system. If the burn-up of the target is neglected, the calculated specific activity agrees with the real value. If the cross section of the reaction is high, of which the target element is used during the irradiation process, the specific activity should be related to the actual mass of the actual mass of the respective element [68].

Lu-177 with specific activity that is higher than 15-20 Ci/mg is required for peptide receptor radionuclides [68]. Lu-176 has a high thermal neutron capture cross section among other lanthanides in which its activation product ^{177}Lu decays into a stable, which does not compete with ^{177}Lu during the labeling of radiopharmaceuticals [68]. During the indirect route production, NCA ^{177}Lu is produced, the theoretical specific activity, however, can be obtained

when ^{176}Yb is irradiated and completely separated from the ^{177}Lu. The specific activity achieved can be lower because of the target ytterbium containing some stable lutetium impurity, the target is not monoisotopic which can contain few percent of ^{174}Yb which causes the production stable ^{175}Lu in the system via the reaction of ^{174}Yb (n,γ) ^{175}Yb$\rightarrow$ ^{175}Lu. This reason contributes to the total mass of lutetium mass in the system is significant due to the high ^{174}Yb content in the target, the high thermal neutron captures cross section of ^{174}Yb, and shorter half-life of ^{175}Yb as compared to that of ^{177}Lu. The other reason is that some amounts of ytterbium always remain in the system after the separation of Lu from Yb. During labeling of radiopharmaceuticals, ytterbium competes with lutetium, the specific activity must be related to the total mass of the lutetium and ytterbium in the system [68].

3.3 Cementation process results

The production of ^{177}Lu by indirect method depends on the possibilities of the radiochemistry separation of the starting of Yb and produced ^{177}Lu. There are other different types of separation techniques to separate Yb from Lu (Electrolysis, Separation using the Resin, high performance liquid chromatography (HPLC).

For separation of Yb and ^{177}Lu, the efficiency required for separation is determined by relative concentration of Yb in the fraction of Lu [33]. The separation of ^{177}Lu from ytterbium target is the key steps to determine the specific activity and Radionuclidic purity quality of the produced preparation of ^{177}Lu. The mass ratio of Lu/Yb in the target is one of the properties to determine the success application of the selected separation method. The lower the mass ratio of Lu/Yb, the more feasible the separation [68].

During cementation process, non-radioactive Yb_2O_3 was translated into chloride by dissolving it into hydrochloric acid and evaporate it into the heating stove. The introduction of the addition of the chloride in the form of sodium into the solution increases the rate of cementation by sodium amalgam. The cementation of the aqueous solution makes to process fast on sodium amalgam while increasing the pH of the solution depending on the duration of

amalgam, and the stirring method [43]. It is known that the cementation of aqueous solutions of ytterbium proceeds fast on sodium amalgam with the increase in pH of the working solution depending on the duration of contact with the amalgam [44].

Yb and Lu have the same chemical properties which is one of the disadvantages to separate the two isotopes. The cementation process was performed from five cementation experiment (each with three cementation cycle). Cementation process was conducted using different masses of Yb , namely 10.2, 10,4, 10.3, 0.2, 10.3 mg and 10 μg amount of Lu.

Five different masses were used to verify the consistency and reproductivity of the procedure. For irradiation process of natural Yb_2O_3 target, the process leads to the coproduction of multicurie level of ^{175}Yb as impurity. Though the ^{169}Yb and ^{175}Yb impurities could be efficiently removed by the separation process, this will give unnecessary radiation dose to the working personnel. The separation must be caried out in a lead shielded facility to provide radiation protection. The level of impurities in the irradiated target and in the final product can be minimized to a great extent using enriched Yb_2O_3 target [45].

3.4 Activity measurements results

The initial cycle of the cementation was measured before the cementation process. The activity of the initial cycle of each cementation experiment was measured using a calibrated MCA coupled HPGe detector in disintegration. The activity was measure for 7200 seconds. The energy and efficiency calibration of the detector was performed using ^{152}Eu source covering the energy range from 121.78 keV (25.58 %) to 1408 (21%). The activity of the ^{177}Lu was quantified by measuring the 208 keV (11%) gamma-ray peak and the amount of Yb present in it was determined by the 196 keV (35.9 %) gamma-ray peak emitted from the ^{169}Yb isotope, respectively. The other gamma-ray energy peaks detected in the spectrum are ^{169}Yb (130.5 keV), ^{175}Yb (137.7 keV), ^{175}Yb (144.9 keV), ^{169}Yb (177.2 keV), ^{177}Lu (208 keV) and ^{177}Lu (249.6 keV), respectively. Owing to its short half-life, ^{177}Yb ($T_{1/2}$=1.9 h),

would have been decayed and could not be detected in the sample. The gamma-ray spectra of the Lu and Yb is shown in the following Figure 4.2.

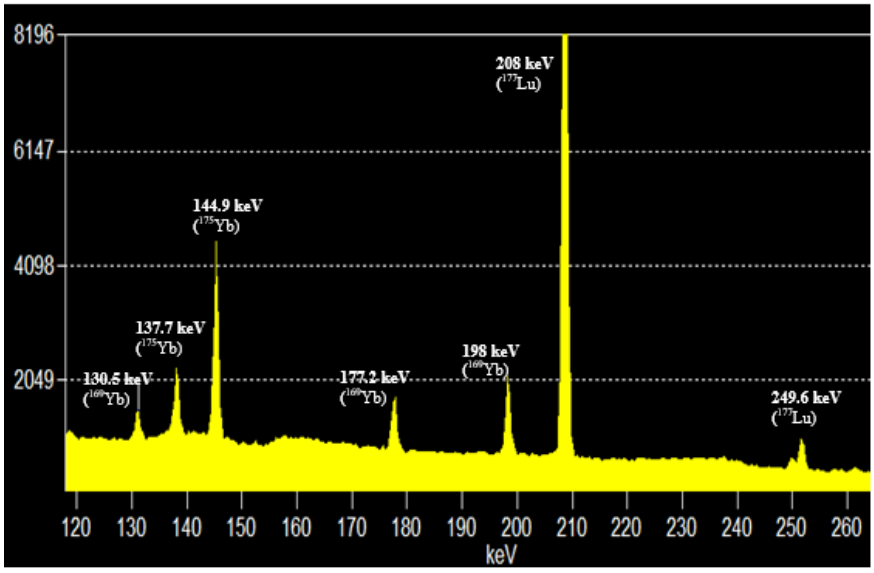


Figure 4.2- Gamma-ray spectra of Lu and Yb mixture

The following Tables 4.2 to 4.6 shows the results of cementation of radioactive Yb and Lu of five cementation experiment. HPGe detector (GX1018 Canberra) was used to measure the disintegration of each cementation experiment. After the initial cementation cycle of each cementation experiment, the disintegration of the first, second and third cementation was measured using HPGe detector (GX1018 Canberra).

Table 4.2- Cementation process of radioactive Yb and Lu disintegration results

	Cementation number	Radioactive Yb (disintegration)	Mass (mg) of Yb_2O_3	Radioactive Lu (disintegration)
First cementation experiment	0	3670	10.2	10903
	1	3233		9918
	2	1803		9003
	3	510		8162

Table 4.3- Cementation process of radioactive Yb and Lu disintegration results

	Cementation number	Radioactive Yb (disintegration)	Mass (mg) of Yb_2O_3	Radioactive Lu (disintegration)
Second cementation experiment	0	3593	10.4	10976
	1	3160		9950
	2	1755		9041
	3	465		8210

Table 4.4- Cementation process of radioactive Yb and Lu disintegration results

	Cementation number	Radioactive Yb (disintegration)	Mass (mg) of Yb_2O_3	Radioactive Lu (disintegration)
Third cementation experiment	0	3702	10.3	10884
	1	3258		9894
	2	1800		8992
	3	503		8114

Table 4.5- Cementation process of radioactive Yb and Lu disintegration results

	Cementation number	Radioactive Yb (disintegration)	Mass (mg) of Yb_2O_3	Radioactive Lu (disintegration)
Forth cementation experiment	0	3807	10.2	11300
	1	3352		10220
	2	1852		9280
	3	523		8844

Table 4.6- Cementation process of radioactive Yb and Lu disintegration results

	Cementation number	Radioactive Yb (disintegration)	Mass (mg) of Yb_2O_3	Radioactive Lu (disintegration)
Fifth cementation experiment	0	3504	10.3	10358
	1	3080		9416
	2	1715		8560
	3	483		7750

From the above results, it was observed that the disintegration from the initial to the third cementation cycles of radioactive Yb and Lu decreases for each cementation experiments. The decrease of the disintegration corresponds to the different mass of radioactive Yb and Lu as the solution dissolves in sodium amalgam.

The effects of macroscopic amounts of Yb on the cementation separation method of NCA ^{177}Lu were investigated by conducting experiments using Lu/Yb mixture containing inactive Lu and Yb equivalent to 10 mg of Yb and 10 μg of Lu. The separation was carried out and the activity of the content of the recovered ^{177}Lu was measured to determine the cementation separation yield.

Table 4.7 Summarizes the results of the mass ratio of non-radioactive of Yb_2O_3 and Lu_2O_3 from cementation experiment one to five of non-radioactive mass Yb_2O_3, 10.2, 10.4, 10.3, 10.2 and 10.3 mg and 10 μg of Lu_2O_3 and the results are further illustrated in Figure 4.3.

Table 4.7- The mass differences of non-radioactive of Yb_2O_3 and Lu_2O_3 of cementation experiments

Cementation Experiment	Non-Radioactive Mass of Yb_2O_3	Mass loss of Yb (mg) from initial to third cementation cycles	Non-Radioactive Mass of Lu_2O_3	Mass loss of Lu (µg) from initial to third cementation cycles
1	10.2	1.41		7.49
2	10.3	1.43		7.47
3	10.4	1.39	10	7.45
4	10.3	1.40		7.42
5	10.2	1.41		7.48

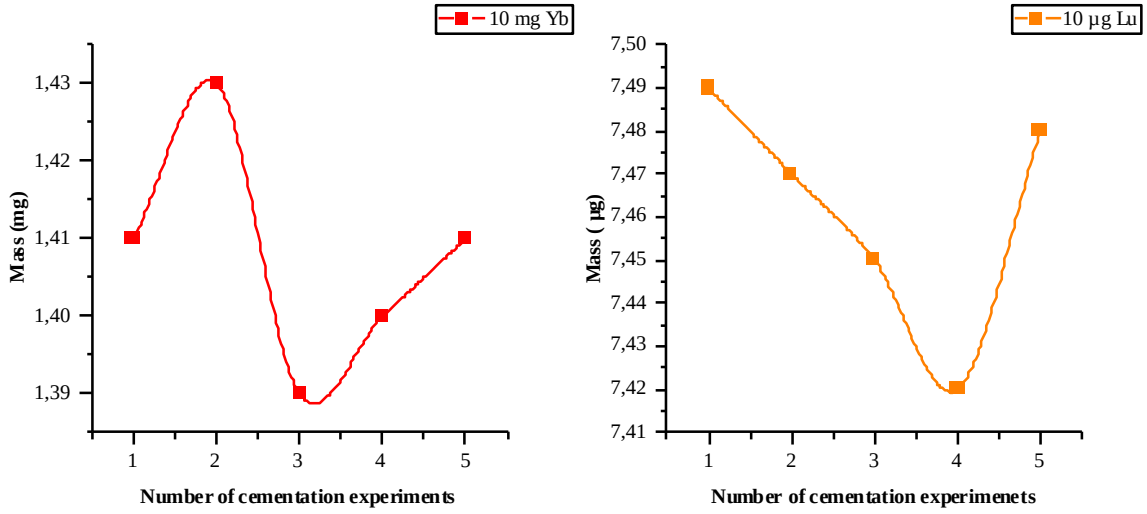


Figure 4.3 -Comparison of the mass differences between Lu and Yb on the separation of the Lu/Yb

In Figure 4.3, this result shows the effect of the mass difference from first to fifth of each cementation experiment using the original mass of 10 mg of Yb_2O_3 and 10 µg of Lu_2O_3. In each cementation cycle, there are some variations of the loss of mass. As seen in Figure 4.3, the third cementation experiment is better than the first and second cementation experiments from 10 mg of Yb of the initial mass, and on the 10 µg of Lu, the forth cementation experiment is better that the first, second, third and fifth cementation experiment.

For these results, it is normal situation in separation methods to have reduction of mass. Yb is resisting in dissolving sodium acetate. The different of the initial masses (10.2, 10.3, 10.4, 10,3 and 10.2 mg of Yb and 10 μg of Lu) shows that there were some errors during the dissolving of sodium acetate or preparation of sodium amalgam. This shows that each step of the experiment, different results were obtained. In the graph of 10 μg Lu, the first experiment has a big error, this shows in the graph that forth cementation experiment had a good accuracy.

When conducting the same experiments, the accuracy was obtained as you can see in the graphs displayed in Figure 4.3. The errors between the first and third cementation is 1.5 % difference, which is normal and good accuracy as compared to analytical methods having errors around 20 %. Therefore, this result shows it is good error and the results are accurate.

In some circumstances, this can also be explained in terms of the effect of mass ration (Yb:Lu) of Yb/ Lu during the separation. For 10 mg of Yb_2O_3, the mass start to increase with number of cementation experiment, reaches a maximum point and start to decrease. It can be observed that on the fourth and fifth cementation experiment, the mass of Yb start to increase. The slightly increase of mass of Yb shows that some amount of Yb might be left in the solution. This variation of masses can be used to explain the error attained during the experiment.

For 10 μg Lu, the mass started to decrease from first and fourth cementation experiment and start to increase from fourth to fifth cementation experiment. It is shows that the amount of Lu in the solution was reducing during the separation of Yb/Lu. It is shown that the Yb and Lu can be separated completely with no overlapping and broadening on the two peaks.

From this observation, these results indicate that the Lu can effectively separate from Yb target. The Yb/Lu mass ratio in the target is one of the properties to determine the success of the selected separation method. From above results, there is 7.14 times (10mg/1.4 mg) Yb

decrease, and 1.32 times (10 µg/7.6 µg) times decrease of Lu. The decrease can be implemented by increasing the number of cementation experiment. Therefore, the lower the Yb/Lu mass ratio, the more feasible the separation of Yb and Lu [67].

Table 4.8- The amount left for each cementation cycle of Yb and Lu after first cementation experiment

Cementation experiment	Cementation cycle number	Radioactive Yb (disintegration)	Amount of Yb (mg) left	Radioactive Lu (disintegration)	Amount of Lu (µg) left
1	0	3670	10	10903	10
	1	3233	2.96	9918	9.09
	2	1803	1.65	9003	8.26
	3	510	0.48	8162	7.49

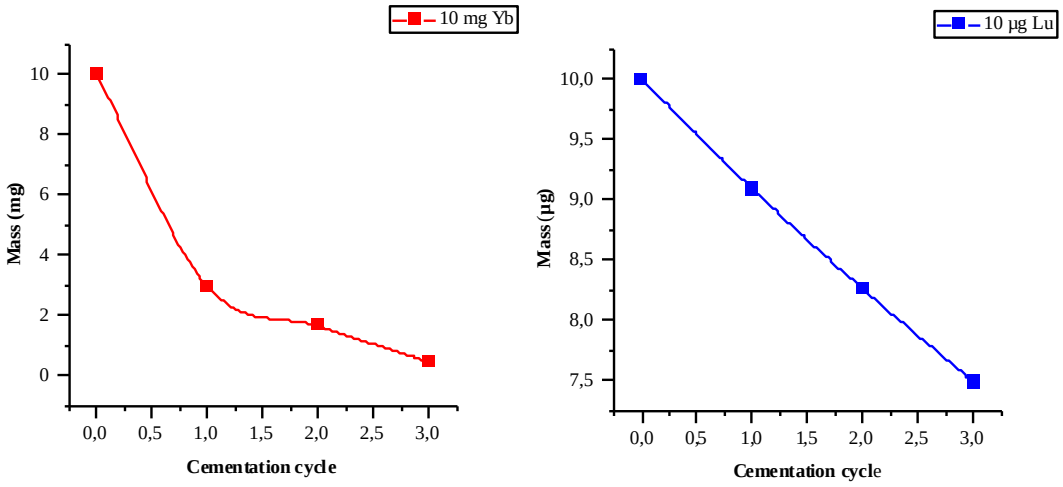


Figure 4.4 -Comparison of the amount left between Lu and Yb after first cementation experiment

Table 4.9- The amount of each cementation cycle with Yb and Lu after second cementation experiment

Cementation experiment	Cementation cycle number	Radioactive Yb (disintegration)	Amount of Yb (mg) left	Radioactive Lu (disintegration)	Amount of Lu (µg) left
2	0	3593	10	10976	10
	1	3160	2.88	9950	9.07
	2	7155	1.59	9041	8.24
	3	495	0.45	8210	7.45

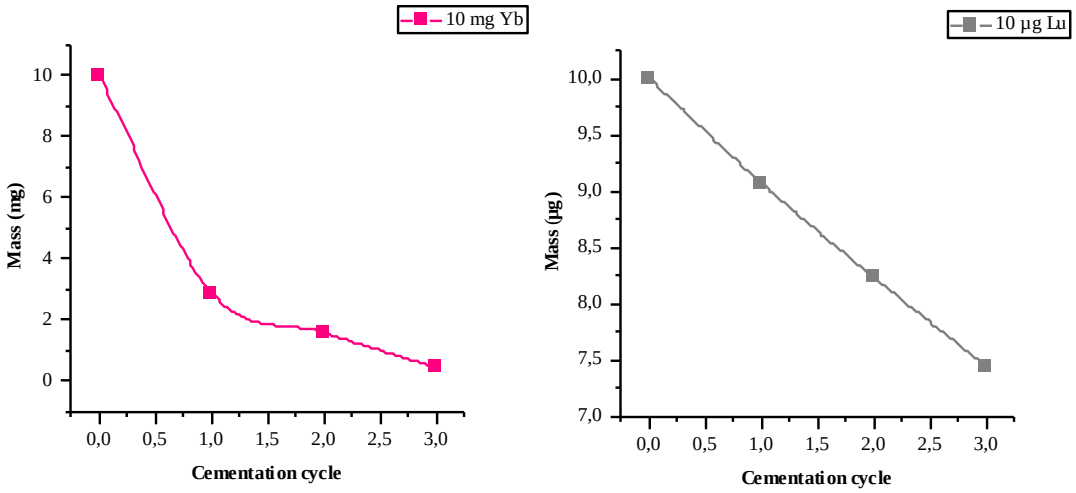


Figure 4.5 -Comparison of the amount left between Lu and Yb after second cementation experiment

Table 4.10- The amount left for each cementation cycle with Yb and Lu after third cementation experiment

Cementation experiment	Cementation cycle number	Radioactive Yb (disintegration)	Amount of Yb (mg) left	Radioactive Lu (disintegration)	Amount of Lu (µg) left
3	0	3702	10	11884	10
	1	3258	2.99	9894	9.09
	2	1800	1.65	8992	8.26
	3	503	0.46	8114	7.45

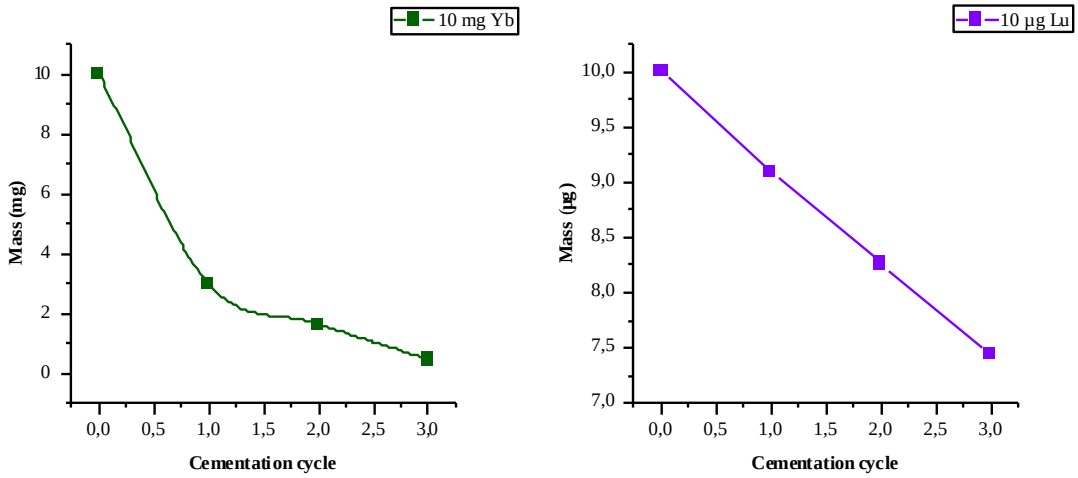


Figure 4.6 -Comparison of the amount left between Lu and Yb after third cementation experiment

Table 4.11- The amount left for each cementation cycle with Yb and Lu after fourth cementation experiment

Cementation experiment 4	Cementation cycle number	Radioactive Yb (disintegration)	Amount of Yb (mg) left	Radioactive Lu (disintegration)	Amount of Lu (µg) left
	0	3807	10	11300	10
	1	3352	2.97	10220	9.04
	2	1852	1.64	9280	8.21
	3	523	0.46	8840	7.82

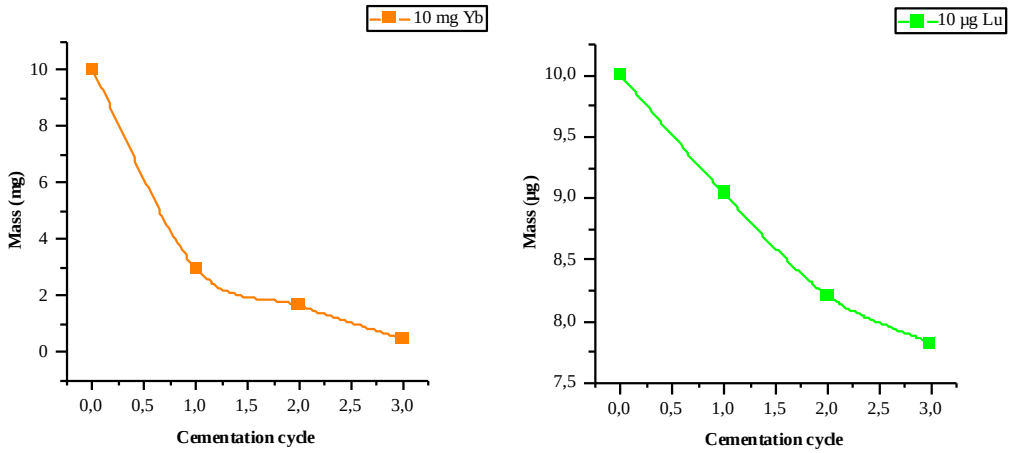


Figure 4.7-Comparison of the amount left between Lu and Yb after fourth cementation experiment

Table 4.12- The amount left of each cementation cycle with Yb and Lu after fifth cementation experiment

Cementation experiment	Cementation cycle number	Radioactive Yb (disintegration)	Amount of Yb (mg) left	Radioactive Lu (disintegration)	Amount of Lu (µg) left
5	0	3504	10	10358	10
	1	3080	2.97	9416	9.09
	2	1715	1.66	8560	8.26
	3	483	0.47	7750	7.48

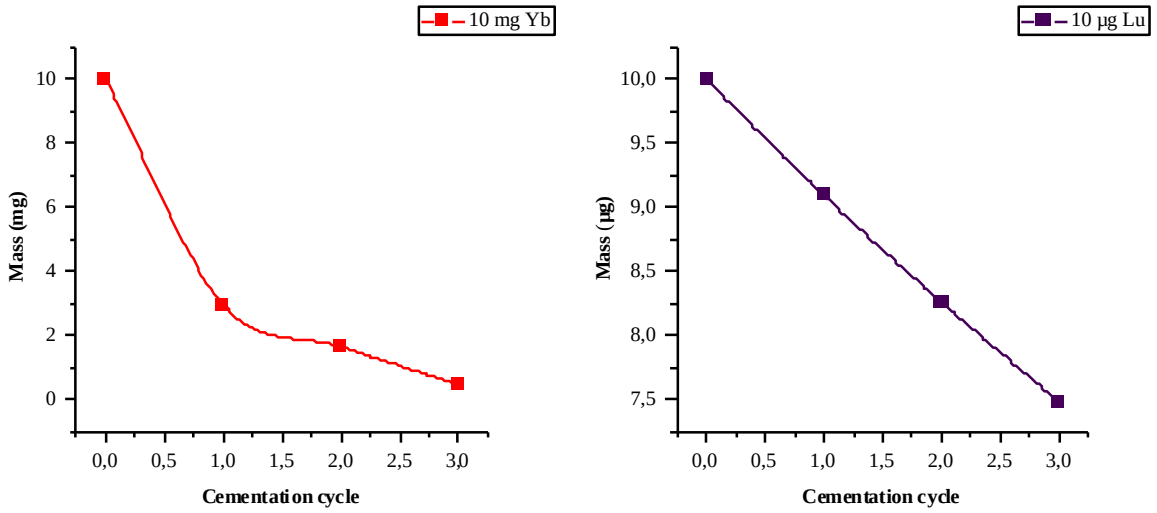


Figure 4.8-Comparison of the amount left between Lu and Yb after fourth cementation experiment

Tables 4.8 to 4.12 shows the results of the amount of each cementation cycle with Yb and Lu from first to fifth cementation experiment. The results are further illustrated from Figures 4.4 to 4.8. The results show the effective separation of the macro quantities of ytterbium from the ^{177}Lu/Yb mixture without the loss of ^{177}Lu. In each cementation cycle, there is loss of mass. It is normal situation in separation methods to have reduction of mass.

The results show the effect of mass of Yb and Lu dissolving in the solution. As shown on the Figures 4.4 to 4.8, Yb dissolve better than Lu. ^{177}Lu has no amalgam which forms, it was reported that some amount of ^{177}Lu can be removed from electrolyte with ytterbium [71].

Lu has no amalgam forming property where as Yb forms an amalgam readily and this property could be satisfactory exploited to achieve their separation. The results illustrated indicate that NCA ^{177}Lu can effectively separate in the presence of 10 μg. Yb is resisting in dissolving in the sodium acetate. There are some forces which make Yb to resist in dissolving sodium acetate. After each cementation cycle, there are some chemical, physical forces acting which inhibit the Yb dissolving in mercury.

Yb has a less impurities with large masses of non-radioactive Yb than Lu. This implies that one counts of Yb correspond to the larger masses of non-radioactive Yb. Lu has small non-radioactive mass, therefore, so to find the change in 10 μg of Lu, more counts must be determined to be observable.

As see in Figures 4.4 to 4.8, the graphs of Lu are straight line and the graphs of Yb are curvy or exponential. The straight line explains the fact that Lu has small mass and the inter-dependence of Lu and NaHg is too small.

The process of dissolution is when one atom changes to another or is the consistence movement of molecules in the solution. When Yb and Lu dissolve in sodium amalgam, Yb takes away some amount of Lu. This means when Yb atoms moves to NaHg in a situation, it will transfer its atoms to Hg, therefore, it takes away some amount of atoms of Lu. Another reason is that the mass of Lu reduces faster than the mass of Yb because of the small mass of Lu, thus showing a straight line.

After a total of five of these cementation experiments, an amount of the ytterbium was removed from the aqueous solution. The NCA ^{177}Lu is isolated from the solution. The feasibility of cementation method, both in terms of yield and purity of the ^{177}Lu, can be used for preparation of radiopharmaceuticals.

As stated in the literature, the separation of neighbouring lanthanides is challenging. The effective separation of micro amounts of ^{177}Lu product from macro amounts of Yb target material needs a special attention since high separation are required [72]. The

efficient method of the separation of the ytterbium and lutetium is based on the ability of the ytterbium to be reduced to the bivalent state on a mercury cathode in basic solutions in the presence a chelator [69]. A chelator can be introduced to modify the behavior of the two atoms with respect to the stationary phase [18].

The separation of Lu and Yb with sodium amalgam by formation of ytterbium amalgam was demonstrated by Marsh [73]. Lebedev described the attempt to application of the isolation process of ^{177}Lu from irradiated Yb procedure [33]. The method reported by Lebedev et al [44] was involving eight cementation cycles. Chakraborty et al [74] reported the production of ^{175}Yb by irradiation of natural Yb_2O_3 target material and ^{175}Yb labelled polyamino phosphate, as a potential agent for bone palliation [75].

The method was based on the selective ytterbium and its extraction on mercury by amalgamation. the target material Yb_2O_3 was irradiated and dissolved in hydrochloric acid, sodium acetate was also added to form sodium amalgam. The method was followed by extraction of Yb by sodium amalgam from Cl^-/CH_3COO^- electrolytes. The remaining of ytterbium and was then precipitated together with lutetium as hydroxides. The solution of ^{177}Lu obtained after precipitation was 1 mg Yb (III) from 50 mg of the irradiated target of Yb_2O_3 [24].

After the cementation cycle, the separation of ^{177}Lu contained about 10 μg Yb (III) from 200 mg of neutron irradiated Yb_2O_3. In this cementation process, it was possible to precipitate macroscopic quantities of Yb up to 200 mg on Na (Hg) amalgam electrode. However, the use of mercury it was in a critical point for preparation of radiopharmaceutical grade radionuclides [44]. The cementation proceed should be repeated for 4 to 5 times in each cycle in order to separate 99% of ytterbium. The addition of the fresh amalgam requires a series of transitions operation, which leads to significant loss [33].

Boldyrev came with an alternative suggestion of the cementation reduction of Yb with its separation by electrolysis on a mercury. The cementation process with sodium amalgam,

the electrolysis, is accompanied by the acidification solution and the process is repeated for the preparation of the second cementation cycle. This method of separation offers the higher purity benefit while reducing the overall times of processing. The method is simple, not susceptible to radiolytic damage and it generate minimum amount of radioactive waste and provides sufficient purity of ^{177}Lu for nuclear medicine applications [33].

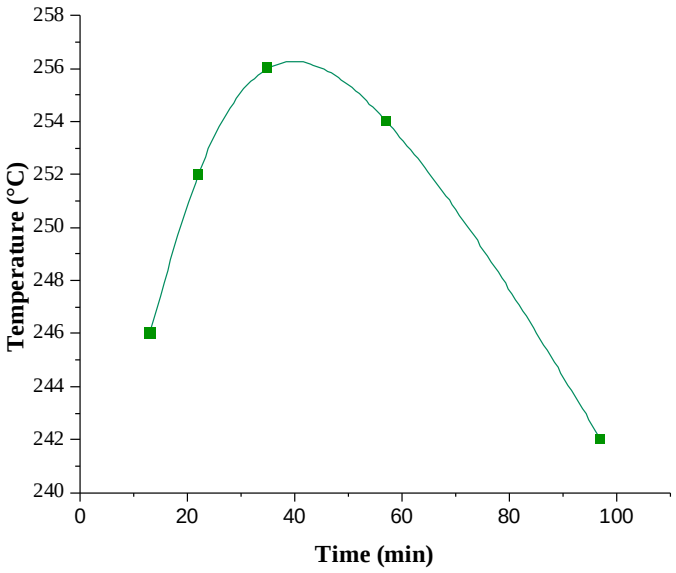
The cementation separation method offers a benefit of higher purity product while reducing overall processing time. The method is inexpensive, not susceptible to radiolytic damage, generates minimum radioactive waste and provides sufficient purity for nuclear medicine applications. The experiment setup is robust, compact, easy to operate and amenable for making automated systems. This technique for producing NCA ^{177}Lu could act as positive factor in the growth of ^{177}Lu-based radiopharmaceutical [45].

3.5 Distillation process results

After cementation process, all mercury were collected and distilled. The following Table 4.13 shows the results of pressure and temperature with time during boiling point of mercury for distillation process which are further illustrated in Figures 4.9 and 4.10. The distillation experiment was performed without radioactivity at pressure of 850 mbar (vacuum) with the volume mercury of 20 ml.

Table 4.13-Pressure and temperature with time during boiling point of mercury

Time (min)	Pressure (mbar)	Temperature (°C)
13	870	246
22	880	252
35	890	256
57	900	254
97	900	242



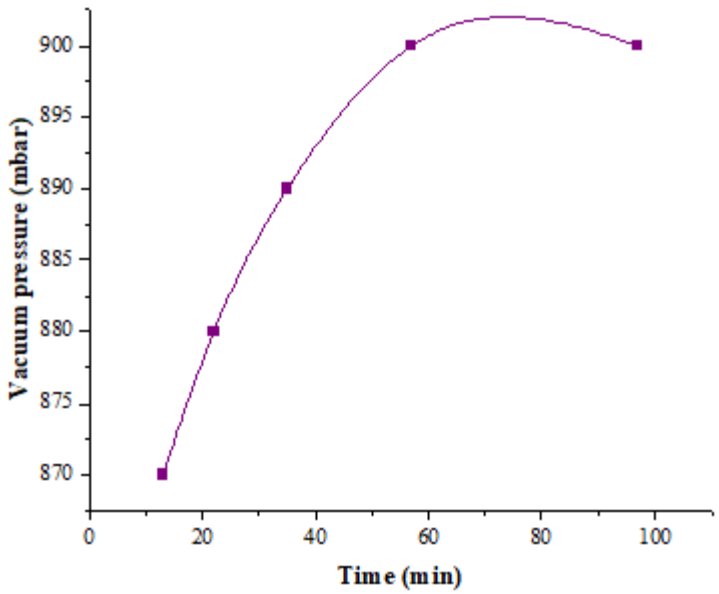


Figure 4.9-Dependance of temperature on time Figure 4.10-Dependance of pressure on time

In Figure 4.9, the temperature increases with time, it reaches a maximum point and start to gradually decrease. This happened when there is decrease of evaporation during boiling of mercury. At the low time, the temperature is very small. The temperature at time 25 minutes is 256 °C which is greater than the temperature at time 20 minutes which is 252 °C, respectively. There is fluctuation of temperature during the heating. In the vessel, the top area is large, thus there is an increase of temperature during the evaporation of mercury. During the evaporation, the level area of the vessels starts to decrease. The decrease of temperature after 50 minutes, is due to the decreasing level of mercury from the top of the vessel or because there was no mercury that is left in the vessel.

The measurement of the experiment of the single vapor pressure of mercury, the boiling point was measured in 1801 by Dalton [76], who obtained 662 K and in 1803, Crichton [77], said that the normal boiling point is above a temperature. in this experiment, the vacuum pressure is relative pressure rather than an absolute pressure (0 mbar). In the initial, the vacuum pressure is more than the atmospheric air pressure. In the beginning of evaporation, the vacuum pressure decreases. In Figure 4.10, the vacuum pressure starts to increase at time 13 minutes, in which at point of 900 mbar reaches a maximum value and start to decrease at time 80 minutes. The pressure is not directly measured, rather is calculated from converting

the concentration of the mercury into a gas steam to a spatial pressure which is of the vapour pressure of the sample. Temperature and pressure depend on the level of mercury and evaporation. At the end of evaporation of mercury, the vacuum pressure increases, because of the pump, and in the vessels no evaporation is taking place.

After the decrease of the rate of evaporation and cooling down of the solution in the vessel, white powder with black enclosure ($YbCl_2$) were obtained and during the cooldown at the bottom of the flask, side surface red (HgO) and black (Hg_2O) powder was obtained. The black powder (Hg_2O) is not stable, it will transfer to red powder (HgO), this happens when the temperature of the vessel decreases. On the right vessel of the distillation plant, liquid mercury is left.

5 ml 4M of hydrochloric acid was poured on the bottom of the distillation flask using a pipette. 1 ml of aliquots was selected, and the solution was measure in HPGe detector for 7200 seconds. The hydrochloric acid was added to avoid the dissolving red and black powered. Table 4.14 Illustrate the results of the amounts of Yb (mg) and Lu (µg) dissolving in mercury (Hg) and Table 4.15 shows the disintegration results of Yb and Lu from 1 ml of measurement and 5 ml theoretical, the amount of Yb and Lu left after it has dissolved in mercury.

Table 4.14 -Results of the amounts of Yb (mg) and Lu (μg) dissolving in mercury (Hg)

Cementation cycle	Sum of disintegration counts of Yb	Sum of disintegration counts of Yb differences	Amount (mg) of Yb which dissolved in mercury	Sum of disintegration counts of Lu	Sum of disintegration counts of Lu differences	Amount of Lu (μg) which dissolved in mercury
0	18276	15762	44.33	54421	13345	12.26
3	2514			41076		

Table 4.15 -Results of the amounts of Yb (mg) and Lu (μg) left after dissolving in mercury (Hg)

Yb counts	Lu counts	Sum of masses (mg) of Yb	Sum of masses (μg) of Lu	Measurements	Amounts of Yb (mg) recycling	Amounts of Lu (μg) recycling
2523	2130	51.4	50	1 ml measure	35.5	9.8
12615	10650			5 ml theoretical		

The distillation process is used to separate Yb from mercury and purification or extractions of mercury. The amount of Yb and Lu dissolving in mercury are 44.33 mg and 12.26 μg as shown in Table 4.14. The amount of Yb and Lu left after it has dissolved in mercury are 35.5 mg and 9.8 μg. The counts number of 12615 for Yb correspond to the amount 35.5 mg of Yb which can be recycled for a new production.

3.6 Activity and specific calculations

The following Table 4.16 shows the results detected from gamma spectrometry of the initial cementation cycle before cementation process.

Table 4.16- Gamma-ray line of ^{169}Yb and ^{177}Lu results

Energy (keV)	Isotope	Efficiency	Intensity	Counts	Time (sec)
198	Yb-169	0.096947267	0.349	2523	7200
208	Lu-177	0.100563489	0.117	2130	7200

The experiments on Yb amalgamation were performed at the room temperature while maintaining the pH at the constant level. The activity of each cycle of cementation of radioactive Yb and Lu was calculated using information from γ-line of 208 keV (^{177}Lu) with intensity of 11.7 % and 198 keV (^{169}Yb) with intensity of 34.9 %. From the results of Table 4.16 of gamma-ray line for ^{169}Yb and ^{177}Lu, Equations (22) and (3) was used to calculate activity and specific activity of Yb and Lu of each cementation cycle. The results are shown in Table 4.17 and are further illustrated in Figure 4.11.

Table 4.17-Activity of the cementation cycles (disintegration) of Yb and Lu

Cementation no of cycles	Activity of Yb (Bq)	Specific activity of Yb (Bq/mg)	Activity of Lu (Bq)	Specific activity of Lu (Bq/μg)
0	15±0.42	1.5±0.04	128.47±3.57	12.85±0.36
1	13.20±0.37	3.22±0.03	116.62±3.07	11.66±0.31
2	7.32±0.19	0.73±0.02	105.94±2.75	10.59±0.27
3	2.06±0.05	0.21±0.01	96.97±4.16	9.69±0.42

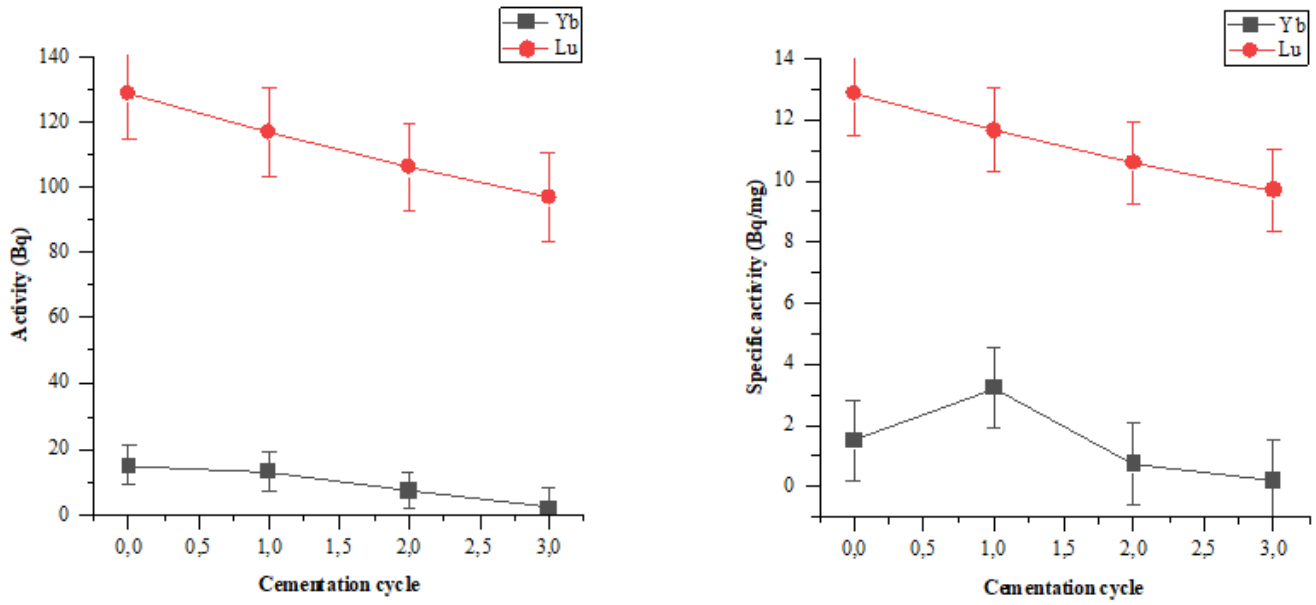


Figure 4.11 Comparison between activity and specific activity of Yb and Lu calculated with cementation cycles

The time used for measurement of disintegration of ^{169}Yb and ^{177}Lu calculation was 7200 seconds. As shown in the Figure 4.11, the activity and specific activity of Lu (red line) and Yb (black line) decreases. The activity of radioactive Yb and Lu after the of third cementation cycle were 2.06±0.05 Bq and 96.97±4.16 Bq which corresponds to 1.4 mg and 7.6 µg, respectively. It evident that the activity and specific activity of Lu (red line) is higher than the activity of Yb (black line). And there is a rapid decrease of the activity and specific activity of Yb.

3.7 Radionuclidic purity

Radionuclidic impurity of Yb and Lu was calculated form the final product using the Equation (23) and was expressed as a percentage of the total radioactivity. The following Table 4.18 shows the results of the Radionuclidic impurity of Yb and Lu.

Table 4.18-Radionuclidic purity of Yb and ^{177}Lu

Isotope	Half-life	λ (sec^{-1})	Activity (Bq)	Number of atoms (atoms/mol)	Sum of the Number of atoms (atoms/mol)	Percentage %
Lu-177	6.71 d	1.19 x 10^{-6}	96.97	8.15 x 10^{7}	8.97 x 10^{7}	90.86
Yb-169	32.02 d	2.50 x 10^{-7}	2.06	8.24 x 10^{6}		9.18

The Radionuclidic purity of ^{169}Yb and ^{177}Lu was found to be 9.18 % and 90.86 %, respectively. The effective separation of ^{177}Lu from ytterbium target is one of the key steps to determine the quality (specific activity and Radionuclidic purity) of the produced ^{177}Lu preparation. In order to obtain high specific activity of ^{177}Lu is to separate ^{177}Lu from the target material Yb as soon as after the end of bombardment and also to prevent the lower specific activity. This is because the isotope ^{175}Lu formed by decay of ^{175}Yb can lower the specific activity [45]. According to Knapp et al., [78] to produce ^{177}Lu through direct route of $^{176}\text{Yb}\,(n,\gamma)\rightarrow{}^{177}\text{Lu}$ provide lower production yield in comparison with direct neutron capture route. This technique is an option which can be used for assessing NCA ^{177}Lu using medium neutron flux nuclear research reactors and it can also make it possible for growth of ^{177}Lu-based radiopharmaceuticals [45].

The importance of ^{177}Lu for labelled target specific radiopharmaceuticals is growing rapidly and the adequate specific activity and Radionuclidic purity is likely to increase with time globally [23]. When calculating the activity of Lu and Yb in the (n,γ) reaction, one should consider, the cross section for thermal neutron captures so as the target is not considered to be constant during the irradiation. The value of neutron flux for indirect production does not have effect on the quality of ^{177}Lu obtained but the higher flux makes the makes the production more effective and it is easy to separate Lu/Yb.

Some amount of ytterbium always remains in the system after separation of Yb/Lu. Ytterbium competes with lutetium during labelling of radiopharmaceuticals, so the specific activity has to be related to the total mass of lutetium and ytterbium in the system [67]. The critical impurities are those which have the high abundance of the isotopes with high thermal neutron capture cross section and the half-life in the range of several days. Longer half-life of radionuclides is important because they increase the volume of radioactive waste which need to be stored or disposed in an appropriate way [67]. It is important after the ^{177}Lu isolation, the target material ^{176}Yb may be recycled and used for the repeated irradiation. This will however increase the efficiency of the utilization of the expensive target material [79].

South Africa is one of the countries that in commission of producing radioisotope ^{177}Lu. Maage and Knoesen [80] produced a non-carrier added ^{177}Lu by indirectly irradiating enriched ytterbium-176 (^{176}Yb) at SAFARi-1 nuclear research reactor of the South African Nuclear Energy Corporation (NECSA).

For indirect route of production, 1 g of 99.56% enriched ^{176}Yb and Yb_2O_3 irradiated with a neutron thermal flux of 5.94×10^{14} n.cm^{-2}.s^{-1} for 6-14 days followed by decay interval up to 14 days. The specific activity of indirect were 105.3 and 100.2 Ci/mg. After 14 days, the decay values decrease to 93.4 and 80.4 Ci/mg for indirect. The specific activity of NCA ^{177}Lu is 3.6 times higher than CA ^{177}Lu. Therefore, the indirect route provides with high specific activity of NCA ^{177}Lu preferred for peptide receptor radiation therapy (PRRT). This result shows that NTP at Necsa , has the ability to produce ^{177}Lu which can be distributed in nearby radiopharmaceuticals facilitites and hospitals of South Africa and other neighbouring African countries for treatment of cancer and other diseases.

The low activity obtained for this study can be used for biological synthesis of molecule, ^{177}Lu-DTPA and other more applications. As compared to the results in Table 4.16, this scientific study, the specific activity of ^{177}Lu was low as compared to 105.3 and 100.2 Ci/mg of Maage and Knoesen [80]. The results show a huge difference, and this might be due to the fact that the high amount of Yb was left in the final product, therefore the results

are comparable since the Yb separated from ^{177}Lu using cementation separation technique. Therefore, to improve the results, the concentration of sodium acetate should be increased which has impact on the final activity of the product, to increase the cementation experiment to ten instead of five to reduce the amount of Yb in the final product. The NCA ^{177}Lu is possible to deliver to the end medical users from the production facility and radionuclide-processing facility, because ^{177}Lu has the relatively long 6.71 days physical half-life of and will not only minimizes decay loss but may also be encountered during the transportation.

Tomsk polytechnic university creates the trial batch of chemical element lutetium which is used for the treatment of cancer. The scientists of TPU were the first to produce radioisotope ^{177}Lu at the IRT-T reactor. The isotope is still used in the leading clinic in Germany and Israel. The IRT-T research reactor can produce ^{177}Lu by direct and indirect route This shows that TPU is of importance in the Tomsk Regions and the entire country of Russia, since it can produce this ^{177}Lu radioisotope which can be distributed to hospital for nuclear medicine application in treatment of cancer [81].

The developed technique of cementation separation technique for separation of NCA ^{177}Lu from Yb through activation of solution using radioactive labels of the could be used for the routine production of NCA ^{177}Lu, especially in the developing countries with limited nuclear research reactors, to explore ^{177}Lu as a therapeutic radionuclide.

Chapter 4-Financial management, resource efficiency and resource saving

Financial management is the activity of management concerned with the planning, procuring and controlling of the firm's financial resources. “Financial management may be defined as that area or set of administrative function in an organization which relate with arrangement of cash and credit so that organization may have the means to carry out its objective as satisfactorily as possible." - by Howard & Opton.

The purpose of this section discusses the issues of competitiveness, resource efficiency and resource saving, as well as financial costs regarding the object of study of Masters' thesis. Competitiveness analysis is carried out for this purpose. SWOT analysis helps to identify strengths, weaknesses, opportunities, and threats associated with the project, and give an idea of working with them in each particular case. For the development of the project requires funds that go to the salaries of project participants and the necessary equipment, a complete list is given in the relevant section. The calculation of the resource efficiency indicator helps to make a final assessment of the technical decision on individual criteria and in general.

In addition, it would help determine the accomplishment of the research work so as to develop a mechanism for managing and supporting specific project solutions at the implementation stage of the project lifecycle to increase productivity. The financial management solves the following objectives:

- Planning and preparation of research work.
- Budget calculation for research work.
- Development of evaluation of commercial potential.

4.1 Pre-research analysis

To analyze consumers of research results, it is necessary to segment the market. This research focuses on production of ^{177}Lu by indirect route method using non-radioactive Yb_2O_3. Radioactive tracers ^{169}Yb and ^{177}Lu were used for activation of solution. Yb and Lu

must undergo separation process after activation. Cementation method was used to separate Yb from Lu. A trace amount of Yb and Hg was found in the solution, distillation process is used to separate Yb from mercury and purification of mercury, recycling Yb in new production.

Target market - the market that includes consumers interested in the results of the research who would buy the good/service connected with the student's investigation. For this research, the ^{177}Lu produced in the study can be distributed to radiopharmaceuticals companies and hospital would use the results for treatment of cancer.

Segmentation is the division of buyers into homogeneous groups, each of which may require a specific product (service). It is possible to apply geographic, demographic, behavioral and other criteria for segmenting the consumer market, it is possible to use their combinations using such characteristics as age, gender, nationality, education, favorite occupations, lifestyle, social affiliation, profession, income level. Depending on the category of consumers (commercial organizations, individuals), appropriate segmentation criteria must be used. For example, for commercial organizations, segmentation criteria can be: location; industry; manufactured products; size, etc. For individuals, segmentation criteria can be: age; gender; nationality; education; income level; social belonging; profession, etc.

4.1.1 Competitiveness analysis of technical solutions

In order to find sources of financing for the project, it is necessary, first, to determine the commercial value of the work. Analysis of competitive technical solutions in terms of resource efficiency and resource saving allows to evaluate the comparative effectiveness of scientific development. This analysis is advisable to carry out using an evaluation card (see Table 5.1).

The outcome of the research is very sensitive on producing radioisotope of interest for nuclear medicine applications. The production route is indirect route where Yb target is enriched before irradiation. The cementation method was used for the separation of

ytterbium and lutetium followed by distillation process used to separate Yb from mercury and purification of mercury, recycling Yb in new production. The measurement of activity concentrations of Lu in the presence of Yb was carried out by γ-spectrometry. The γ-spectra were acquired using a high purity germanium detector coupled to multichannel analyzer (GX1018 Canberra).

However, this project tends to focus more on the nuclear medicine and all related medicine industries produces isotopes for treatment of cancer. In these medical industries, large number of radioisotopes are tested and the development of radiopharmaceuticals using radioisotope ^{177}Lu are under clinical trials. Therefore, this research was embarked to reduce the time of examination and to reduce the cost involved to enrich Yb target since is expensive and to reduce large amount of nuclear waste materials. This ultimately leads to a reduction in the economic costs of purchasing and enrichment of Yb target material.

There are different types of separation methods used to separate NCA ^{177}Lu from Yb which can also be considered:

- Cementation process – P_f .
- Electrochemical method – P_{i1} .
- High pressure liquid chromatography – P_{i2} .

Cementation process was used and appeared to be an attractive method and feasible proposition. The cementation separation method offers a benefit of higher purity product while reducing overall processing time. The method is inexpensive, not susceptible to radiolytic damage, generates minimum radioactive waste and provides sufficient purity for nuclear medicine applications.

First of all, it is necessary to analyze possible technical solutions and choose the best one based on the considered technical and economic criteria.

Evaluation map analysis presented in Table 5.1. The position of your research and competitors is evaluated for each indicator by you on a five-point scale, where 1 is the weakest position

and 5 is the strongest. The weights of indicators determined by you in the amount should be 1. Analysis of competitive technical solutions is determined by the formula:

$$C = \sum P_i \cdot W_i, \quad (24)$$

where;

C - the competitiveness of research or a competitor;

W_i– criterion weight;

P_i – point of i-th criteria.

Table-5.1- Evaluation card for comparison of competitive technical solutions

Evaluation criteria ***example***	**Criterion weight**	**Points**			**Competitiveness** Taking into account		
		P_f	P_{i1}	P_{i2}	C_f	C_{i1}	C_{i2}
1	2	3	4	5	6	7	8
Technical criteria for evaluating resource efficiency							
1. Growth in User' productivity	0.15	4	3	3	0,5	0,5	0,06
2. Convenience in operation (meets the requirements of consumers)	0.02	4	3	4	0,6	0,4	0,3
3. Immunity	0.05	3	3	3	0,5	0,03	0,05
4. Energy efficiency	0.2	3	4	4	0,2	0,15	0,5
5. Reliability	0.05	3	4	3	0,2	0,2	0,4
6. Safety	0.05	4	4	3	0,5	0,2	0,5
7. Noise level	0.02	2	3	3	0,6	0,15	0,4
8. Demand for memory resources	0.05	3	3	4	0,3	0,04	0,3
9. Functional capacity	0.15	4	3	3	0,5	0,3	0,06

10. Ease of operation	0.02	5	4	3	0,4	0,5	0,5
11. Intelligent interface quality	0.02	3	4	3	0,3	0,2	0,2
12. Ability to connect to a computer network	0.05	4	3	3	0,05	0,06	0,02
Economic criteria for performance evaluation							
1. Development cost	0.1	5	4	3	0,6	0,4	0,05
2. Market penetration rate	0.02	3	3	3	0,04	0,06	0,06
3. Expected lifecycle	0.05	3	3	3	0,4	0,3	0,04
4. Price	0.05	3	3	4	0,05	0,6	0,2
5. After-sales service	0.02	4	3	3	0,06	0,2	0,6
6. Estimated life-time	0.02	4	3	3	0,04	0,5	0,4
Total	**1**	**64**	**60**	**58**	**5,85**	**4,79**	**4,64**

The results of the competitiveness analysis show that cementation process have the highest value of competitiveness. This shows that the cementation process is the best for feasible separation of Yb from Lu. The study is effective because it provides acceptable quality results. Further investment in this development can be considered reasonable.

4.1.2 SWOT analysis

Complex analysis solution with the greatest competitiveness is carried out with the method of the SWOT analysis: Strengths, Weaknesses, Opportunities and Threats. The analysis has several stages. The first stage consists of describing the strengths and weaknesses of the project, identifying opportunities and threats to the project that have emerged or may appear in its external environment.

Strengths. Strengths are the factors that characterize the competitive side of a research project. Strengths indicate that a project has a distinctive advantage or special resources that are special in terms of competition. In other words, strengths are the resources or capabilities

available to the project management that can be effectively used to achieve the goals set. At the same time, it is important to consider the strengths both from the point of view of the project management and from the point of view of those who are still involved in it.

Weaknesses. A weakness is a flaw, omission, or limitation of a research project that hinders the achievement of its goals. This is something that does not work well within the project or where it has insufficient capabilities or resources compared to competitors.

Opportunities include any preferred situation in the present or future that occurs in the project environment, such as a trend, change, or perceived need that supports the demand for a result that allows the project management to improve their competitive position.

Table 5.2-SWOT matrix

	Strengths of the research project: S1. Energy and Efficiency calibration of HPGe detector. S2. Able to work in high activity in the laboratory results using gamma spectroscopy and results analysis. S3. Production costs is low. S4. Does not require higher electrical energy to operate.	Weaknesses of the research project: W1. All reagents, chemicals and data of results were prepared and collected by qualified stuff. W2. Data collections of the results took a lot of time.

	S5. Reduction in time for the collection of data.	
Opportunities: O1. The data collection of activity can be used to calculate the specific activity of the ^{177}Lu final product using gamma spectroscopy (GX1018 Canberra). O2. Calibration of the detector using mixed standard sources. O3. Data will be applicable in TPU for record to be used in future analysis. O4. To use other technique for precise and accurate of the results. O5. The optimization of other separation method.	1. To obtain other methods to calibrate the HPGe detector. 2. To use an alternative technique for measuring activity of the yield product. 3. To produce high activity of ^{177}Lu using a different route of production. 4. To create a new direction of production of ^{177}Lu to be used for diagnostics and imaging.	1. Ability to understand the whole experimental procedure for preparations of chemical reagents and other processes. 2. To obtain data in record time and according to the research planning.
Threats: T1. Lack of hands on in the working laboratory. T2 Lack of demand for the use of another	**Strategy which based on strengths and threats**: 1. Improve the opportunity of student hand on	**Strategy which based on weaknesses and threats:** 1. The collection of the results took

technique, such as beta spectroscopy. T2. 1. Strong competition of alternate package from other sources.	practical experiments. 2. The ability to use beta spectroscopy to be able to identity other beta radionuclides needed for the study.	time due to lack of involvement. 2. Writing conference abstract and attending conference will increase the awareness of the scientific research.

The challenges of this research based on conclusions can easily be solved and overcome for future.

4.2 Project Initiation

The initiation process group consists of processes that are performed to define a new project or a new phase of an existing one. As part of the initiation processes, the initial goals and content are determined, and the initial financial resources are recorded. The internal and external stakeholders of the project that will interact and influence the overall outcome of the research project are identified. This information is fixed in the project Charter. The project charter documents the business needs, the current understanding of the needs of the project customer, as well as the new product, service, etc. is the result that is planned to be created.

4.2.1 The goals and results of the project

This section provides information about the project stakeholders, the hierarchy of project goals, and the criteria for achieving the goals. Project stakeholders are persons or organizations that are actively involved in the project or whose interests may be affected both positively and negatively during the execution or as a result of the completion of the project.

They can be contractors, sponsors, the public, etc. Provide information on the project's stakeholders.

Table 5.3-Stakeholders of the project

Project stakeholders	**Stakeholder expectations**
Research Institute (TPU reactor-IRT-T) and other nuclear research Institutions producing radioisotopes, and radiopharmaceutical	The approval of the scientific research was done under TPU. To produce radioisotopes with high specific activity using direct and indirect route for nuclear medicine applications. To using the produced yield of ^{177}Lu for preparations of radiopharmaceuticals.
Hospital and radiopharmaceutical companies	The radioisotope ^{177}Lu to be transferred to radiopharmaceutical companies and hospital institute for special treatment.
People with cancer disease and experimental methods	To use radiopharmaceuticals ^{177}Lu to be administered for treatment of cancer by minimizing the neighboring tissues and to be used for synthesis of biological molecules.
South African government companies that produces radioisotopes	To embarkment of knowledge and experience gained to put in the resources of South Africa, since it has technologies to produce the isotope of interest.

Table 5.4- Purpose and results of the project

Purpose of project:	To perform the experimental production of NCA ^{177}Lu with a recycling of the Yb target for nuclear medicine applications. To separation of NCA ^{177}Lu from macroscopic amounts of the ytterbium target material by cementation process based on sodium amalgam and recycling of target (Yb_2O_3) through of separation of Yb and Hg using the distillation process.
Expected results of the project:	Low activity of ^{177}Lu and high amount of Yb in the final product was observed which can be used for biological systhesis of molecules and ^{177}Lu DTPA.
Criteria for acceptance of the project result:	The results must be improved by to carry out optimization for better separation of Yb and Lu. To recycle the Yb amount obtained for new production of ^{177}Lu.
Requirements for the project result:	The results must be in agreement with other published authors.
	Further studies should be conducted using the results obtained.
	To use alternative separation method to reduce high amount of Yb in the production yield.

	Industrial application: the results would help in other nuclear medicine application which requires a low activity of ^{177}Lu.

4.2.2 The organizational structure of the project

At this stage of the work, the following issues need to be resolved: who will be included in the working group of this project, determine the role of each participant in this project, and also specify the functions performed by each of the participants and their labor costs in the project. In this research work, there were four participants.

- Scientific supervisor
- Consultant

Table 5.5- Working group of the project

№	Participant	Role in the project	Functions	Labor time, hours × (6 hours)
1	Naymushin Artem Georgievich, Deputy Director-Head of the Research Nuclear Reactor Educational and Scientific Center	Scientific Supervisor	Responsible for authorization and implementation of the resources used, and coordinated the activity of the scientific research.	18 x 6= 96
2	Veronica Kgabisang Gouws, TPU masters student	Executor	Introduction and Review of literary writing, experimental	33 x 6= 198

			method format, results discussions, conclusions, Writing the master's thesis.	
3	Ivan Alekseevich Ushakov, an Engineer of Laboratory for Isotopic Analysis and Technologies	Consultant	Proposed a scientific research topic, aim and objective of the study. Review results, discussions and conclusions of the study. Corrections on the format of the dissertation, grammar, results analysis.	79 x 6= 474
Total				768

4.2.3 Project limitations

Project limitations are all factors that can be as a restriction on the degree of freedom of the project team members.

Table 5.6-Project limitations

Factors	Limitations / Assumptions
3.1. Project's budget	339102,99 RUB
3.1.1. Source of financing	TPU, Laboratory for Isotopic Analysis and Technologies,
3.2. Project timeline:	01-02-2021 to 28-05-2021

3.2.1. Date of approval of plan of project	14-03-2021
3.2.2. Completion date	28-05-2021
3.3. Other restrictions	-

4.3 Planning of scientific and technical project management

The planning process group consists of the processes that are carried out to determine the overall content of the work, clarify the goals, and develop the sequence of actions required to achieve these goals. The scientific project management plan should include the following elements.

4.3.1 Project Schedule

As part of planning a science project, you need to build a project timeline and a Gantt Chart.

Table 5.7- Project Schedule

Job title	Duration, working days	Start date	Date of completion	Participants
Development of tasks and technical specifications	5	01-02-2021	06-02-2021	Scientific supervisor
Determination of research direction	11	06-02-2021	11-02-2021	Scientific supervisor and Consultant
Place of the on-job training and experimental performance	2	11-02-2021	15-02-2021	Scientific supervisor and Consultant

Introduction and Theoretical literature review	23	15-02-2021	14-02-2021	Executor
Preparations of chemical reagents	3	14-02-2021	19-02-2021	Consultant
Conduction of experimental method collection of data from HPGe detector	2	19-02-2021	30-02-2021	Consultant
Results discussions and conclusions	3	30-02-2021	13-03-2021	Executor
Compiling the final document of dissertation	15	13-03-2021	29-03-2021	Executor
Adding and compiling new results to the document and results discussions	5	29-03-2021	07-04-2021	Executor
Implementation of the corrections of the whole document	5	07-04-2021	13-04-2021	Executor

Preparation of research diary	6	13-04-2021	30-04-2021	Executor
Research summary and format	7	30-04-2021	18-05-2021	Executor
PowerPoint presentations check-up and preparations of defence	15	18-05-2021	28-05-2021	Consultant and Executor

As part of planning a science project, you need to build a project timeline and a Gantt Chart. Hierarchical Work Structure (HWS) - detailing the enlarged work structure. In the process of creating an HWS, the content of the entire project is structured and defined. It may be presented in schemes.

As part of planning a science project, you need to build a project timeline and a Gantt Chart. A Gantt chart, or harmonogram, is a type of bar chart that illustrates a project schedule. This chart lists the tasks to be performed on the vertical axis, and time intervals on the horizontal axis. The width of the horizontal bars in the graph shows the duration of each activity.

Table 5.8- A Gantt charts

№	Activities	Participants	T_c, days	Duration of the project											
				February			March			April			May		
				1	2	3	1	2	3	1	2	3	1	2	3
1	Development of tasks and technical specifications	Scientific supervisor	5												
2	Determination of research direction	Scientific supervisor and Consultant	11												
3	Place of the on-job training and experimental performance	Scientific supervisor and Consultant	2												
4	Introduction and Theoretical literature review	Executor	23												

5	Preparations of chemical reagents	Consultant	3												
6	Conduction of experimental method, collection of data from HPGe detector	Consultant	2												
7	Results discussions and conclusions	Executor	3												
8	Compiling the final document of dissertation	Executor	15												
9	Adding and compiling new results to the document and results discussions	Executor	5												

10	Implementation of the corrections of the whole document	Executor	5												
11	Preparation of research diary	Executor	6												
12	Research summary and format	Executor	7												
13	PowerPoint presentations check-up and preparations of defence	Consultant and Executor	15												

Scientific supervisor Consultant Executor

4.4 Scientific and technical research budget

When planning the budget of scientific research, it should be ensured that all types of planned expenditures necessary for its implementation are fully and reliably reflected. In the process of forming the budget.

The calculation of material costs may be also carried out according to the formula:

$$C_m = (1 + k_{\text{T}}) \cdot \sum_{i=1}^{m} P_i \cdot N_{consi}, \quad (25)$$

where;

m – the number of types of material resources consumed in the performance of scientific research;

N_{consi} – the amount of material resources of the i-th species planned to be used when performing scientific research (units, kg, m, m^2, etc.);

P_i – the acquisition price of a unit of the i-th type of material resources consumed (rub./units, rub./kg, rub./m, rub./m^2, etc.);

k_T – coefficient taking into account transportation costs.

Prices for material resources can be set according to data posted on relevant websites on the Internet by manufacturers (or supplier organizations).

Energy costs are calculated by the formula:

$$\text{C} = P_{el} \cdot \text{P} \cdot F_{eq}, \quad (26)$$

where;

P_{el} − power rates (5.8 rubles per 1 kWh);

P − power of equipment, kW;

F_{eq} − equipment usage time, hours.

4.4.1 Special equipment for scientific experiments

This article includes all the costs associated with the purchase of special equipment (instruments, control and measuring equipment, stands, devices and mechanisms) necessary for carrying out work on a specific topic. The cost of special equipment is determined according to the current price lists, and in some cases at the agreed price.

Table 5.9-Cost calculation for the article «Special equipment for scientific experiments

№	Name of equipment	Quantity, units	Price per unit, money, rub	Total cost for position, money
1	New laptop	1	42 000,00	42 000,00
2	Pens	2	250,00	500,00
	Books	2	157,00	314,00
3	Transportation	2	320,00	640,00
	Total			43454,00

When purchasing special equipment, it is necessary to include in the costs its delivery and installation in the amount of 15 % of its price. The cost of equipment used in the implementation of a specific scientific project and available in this scientific and technical organization is accounted in the form of depreciation charges.

4.5 Calculation of the depreciation

Depreciation is not charged if an equipment cost is less than 40 thousand rubles, its cost is taken into account in full.

If you use available equipment, then you need to calculate depreciation:

$$A = \frac{C_{\text{перв}} * \text{Н}_\text{а}}{100} \quad (27)$$

where;

A - annual amount of depreciation;

$C_{перв}$ - initial cost of the equipment;

$\text{Н}_\text{а} = \frac{100}{\text{Т}_{\text{сл}}}$ - rate of depreciation;

$T_{сл}$ - life expectancy.

For this research, a HPGe detector (GX1018 Canberra), cementation and distillations equipment which cost 450 000,00 rubles, 233 520,00 rubles, 277 300 ,00 rub les were used. The gamma detector and the laptop both had a life expectancy of 5 years whiles that of the climatic chamber was 10 years. The depreciation for the gamma detector, climatic chamber and laptop can be calculated as follows:

HPGe detector (GX1018 Canberra):

$$D = \frac{Cost}{Time} \tag{28}$$

$D = \frac{450\,000}{5\times365} = 246{,}58\frac{rubles}{day}$

Since the equipment was used for 6 days

$$A = 246{,}58 \times 6 = 1479{,}48\, rubles$$

Cementation equipment:

$$D = \frac{Cost}{Time}$$

$$\mathrm{D} = \frac{233\,520}{10 \times 365} = 63{,}98\frac{rubles}{day}$$

Since the equipment was used for 2 days

$$A = 63{,}98 \times 2 = 127{,}96\, rubles$$

Distillation equipment:

$$D = \frac{Cost}{Time}$$

$$\mathrm{D} = \frac{277\,300}{10 \times 365} = 75.97\frac{rubles}{day}$$

Since the equipment was used for 2 days

$$A = 75{,}97 \times 2 = 151.94\, rubles$$

Table 5.10- Depreciation of special equipment (+software)

№	Equipment identification	Quantity of equipment	Total cost of equipment, rub.	Life expectancy, year	Depreciation for the duration of the project, rub.
1.	HPGe detector (GX1018 Canberra)	1	450 000,00	10	1479,48
2.	Cementation equipment	1	233 520,00	10	127,96
3	Distillation equipment	1	277 300,00	10	151,94
Total					1756,38

4.6 Basic salary

This article includes the basic salary of scientific and engineering workers, workers of model workshops and experimental production facilities directly involved in the performance of work on this topic. The amount of salary expenses is determined based on the labor intensity of the work performed and the current system of remuneration. The basic salary includes a bonus paid monthly from the salary fund (the amount is determined by the Regulations on Remuneration of Labor).

This point includes the basic salary of participants directly involved in the implementation of work on this research. The value of salary costs is determined based on the labor intensity of the work performed and the current salary system. The basic salary (S_b) is calculated according to the following formula:

$$S_{\text{b}} = S_a \cdot T_{\text{w}} \,, \tag{29}$$

where;

Sb – basic salary per participant;

T_{w} – the duration of the work performed by the scientific and technical worker, working days;

Sa - the average daily salary of an participant, rub.

The average daily salary is calculated by the formula:

$$S_d = \frac{S_m \cdot M}{F_{\text{v}}} \,, \tag{30}$$

where;

S_m – monthly salary of an participant, rub.;

M – the number of months of work without leave during the year:

at holiday in 48 days, M = 11.2 months, 6 day per week;

F_{v} – valid annual fund of working time of scientific and technical personnel (251 days).

Table 5.11-The valid annual fund of working time

Working time indicators	
Calendar number of days	365
The number of non-working days - weekend - holidays	 52 14
Loss of working time - vacation - sick absence	 48
The valid annual fund of working time	251

Monthly salary is calculated by formula:

$$S_{month} = S_{base} \cdot (k_{premium} + k_{bonus}) \cdot k_{reg}, \quad (31)$$

where;

S_{base} – base salary, rubles;

$k_{premium}$ – premium rate;

k_{bonus} – bonus rate;

k_{reg} – regional rate (for Tomsk region is equal 1.3).

Table 5.12- Calculation of the basic salary

Performers	S_{base}, rubles	$k_{premium}$	k_{bonus}	k_{reg}	S_{month}, rub.	W_d, rub.	T_p, work days	W_{base}, rub.
Scientific supervisor	69200,00	-	-	1,3	89960,00	3087,81	18	55580,58
Consultant	35800,00				46540,00	1597,45	33	52715,85
Executor	8720,00				11336,00	642,53	79	50759,87
Total								159056,30

4.6.1 Additional salary

This point includes the amount of payments stipulated by the legislation on labor, for example, payment of regular and additional holidays; payment of time associated with state and public duties; payment for work experience, etc.

Additional salaries are calculated on the basis of 10-15% of the base salary of workers:

$$W_{add} = k_{\text{extra}} \cdot W_{base}, \quad (32)$$

where;

W_{add} – additional salary, rubles;

k_{extra} – additional salary coefficient (10%);

W_{base} – base salary, rubles.

Table 5.13-Salary of scientific research project performers

Salary	Scientific supervisor	Consultant	Executor
Basic salary	55580,58	52715,85	50759,87
Additional salary	5558,06	5271,59	5075,99
Total payments at article C_{sal}	15905,64		

4.6.2 Social security pays (Labor tax)

Social security pays (so-called labor tax) to extra-budgetary funds are compulsory according to the norms established by the legislation of the Russian Federation to the state social insurance (SIF), pension fund (PF) and medical insurance (FCMIF) from the costs of workers.

Payment to extra-budgetary funds is determined of the formula:

$$P_{social} = k_b \cdot (W_{base} + W_{add}) \quad (33)$$

where; k_b – coefficient of deductions for labor tax.

In accordance with the Federal law of July 24, 2009 No. 212-FL, the amount of insurance contributions is set at 30%. Institutions conducting educational and scientific activities have rate - 27.1%.

Table 5.14-Labor tax

	Scientific supervisor	Consultant	Executor
Coefficient of deductions	27.1%		
Salary, rubles	61138,64	57987,44	55835,86
Labor tax, rubles	16568,57	15714,60	15131,52
Total	47414,69		

4.7 Scientific and industrial business trips

This article includes the travel expenses of scientific and production personnel associated with the direct implementation of a scientific research project, the amount of which is assumed to be 10% of the main and additional salaries of all personnel engaged in the implementation of this topic.

4.7.1 Pays for work performed by other firms

This item includes the cost of counterparty work, i.e. work performed by third-party organizations and enterprises on the order of this scientific and technical organization, the results of which are used in a scientific research project. In addition, this item of expenditure includes the payment of consultations, the use of the Internet, etc. The amount of these costs is determined according to the contractual terms.

4.7.2 Overhead costs

Overhead costs include other management and maintenance costs that can be allocated directly to the project. In addition, this includes expenses for the maintenance, operation and repair of equipment, production tools and equipment, buildings, structures, etc.

Overhead costs account from 30% to 90% of the amount of basic and additional salary of employees.

Overhead is calculated according to the formula:

$$C_{ov} = k_{ov} \cdot (W_{base} + W_{add}) \quad (34)$$

where; kov – overhead rate.

Table 5.15-Overheads

	Scientific supervisor	Consultant	Executor
Overhead rate	40%		
Salary, rubles	61138,64	57987,44	55835,86
Overhead, rubles	24455,46	23194,98	22334,34
Total	69984,78		

4.8 Other direct costs

Energy costs for equipment are calculated by the formula:

$$C = P_{el} \cdot P \cdot F_{eq}, \quad (35)$$

where;

P_{el} − power rates (5.8 rubles per 1 kWh);

P − power of equipment, kW;

F_{eq} − equipment usage time, hours.

Table 5.16- Other direct costs

	Power rates, kWh	**Power of equipment, kW**	**Equipment usage time, hr**	**Energy cost, rubles**
HPGe detector (GX1018 Canberra)	5.8	0.5	480	1392
Cementation equipment	5.8	0.5	24	69,60
Distillation equipment	5.8	0.5	24	69,60
Total				1531,2

4.9 Determination of resource (resource-saving), financial, budgetary, social and economic efficiency of research

The effectiveness of a scientific resource-saving project includes social efficiency, economic and budgetary efficiency. Public efficiency indicators take into account the socio-economic consequences of the implementation of an investment project for society as a whole, including the direct results and costs of the project, as well as costs and benefits in related sectors of the economy, environmental, social and other non-economic effects.

The indicators of the economic efficiency of the project take into account the financial implications of its implementation for the enterprise implementing the project. In this case, the performance indicators of the project as a whole characterize from an economic point of view, technical, technological and organizational design solutions.

Budgetary efficiency is characterized by the participation of the state in the project in terms of expenditures and revenues of budgets of all levels.

In addition to the above types of efficiency, the resource effect can be distinguished (characterized by indicators reflecting the influence of innovation on the volume of production and consumption of one or another type of resource), scientific and technical (evaluated by indicators of novelty and usefulness), etc.

4.9.1 Formation of budget costs

The calculated cost of research is the basis for budgeting project costs. Determining the budget for the scientific research is given in the table 5.17.

Table 5.17- Items expenses grouping

Name	Cost, rubles
1. Material costs	43454,00
2. Equipment costs	1756,38
3. Basic salary	159056,30
4. Additional salary	15905,64
5. Labor tax	47414,69
6. Overhead	69984,78
7. Other direct costs	1531,2
Total planned costs	**339102,99**

4.10 Evaluation of the comparative efficiency of the scientific research project

Determination of efficiency is based on the calculation of the integral indicator of the efficiency of scientific research. Its finding is associated with the determination of two weighted averages: financial efficiency and resource efficiency.

An integral indicator of the financial efficiency of a scientific research is obtained in assessing the budget of costs of three (or more) variants of the implementation of a scientific research. For this, the largest integral indicator of the implementation of a technical problem

is taken as the basis of the calculation (as the denominator), with which the financial values for all execution options are correlated.

Integral financial indicator is determined in the formula:

$$I_f^p = \frac{F_{pi}}{F_{max}}, \quad (36)$$

where;

I_f^p – integral financial indicator of current project;

F_{pi} – price for *i*-th variant of execution;

F_{max} – maximum cost of execution of a research project (including analogs).

The resulting value of the integral financial indicator of development reflects the corresponding numerical increase in the budget of development costs in times (a value greater than one), or the corresponding numerical reduction in the cost of development in times (a value less than one, but higher than zero).

Where;

F_{pi} – the cost of the research work for using cementation cycle = 339102,99;

And F_{max} – the maximum cost of execution of research project using an electrochemical method = 420 000,00.

$$I^p{}_f = \frac{F_{pi}}{F_{max}}$$

$$I^p{}_f = \frac{339102,99}{420\ 000,00}$$

$I^p{}_f$ =0.81

$$I^a{}_f = \frac{F_a}{F_{max}}$$

$$I^a{}_f = \frac{420\,000{,}00}{420\,000{,}00}$$

$I^a{}_f = 1$

The integral indicator of the resource efficiency of the variants of the object of research can be defined as follows:

$$I_m^a = \sum_{i=1}^{n} a_i b_i^a \quad , \quad I_m^p = \sum_{i=1}^{n} a_i b_i^p \quad , \qquad (37)$$

where;

I_m^a is an integral indicator of resource efficiency of options;

a_i- the weight coefficient of the i-th parameter;

b_i^a, b_i^p - the score of the i-th parameter for the analog and development, set by an expert method on the selected rating scale;

n - the number of comparison parameters.

It is recommended to calculate the integral resource efficiency indicator in the form of a table, an example of which is given below.

Table 5.18-Comparative evaluation of the characteristics of the project execution options

Criteria	Parameter weighting factor	Scientific research project	Analog 1 (electrochemical method)
Growth in User' productivity	0.1	3	5
Convenience in operation (meets the requirements of consumers)	0.15	4	4
Immunity	0.15	2	4
Energy efficiency	0.20	4	2
Reliability	0.25	4	3
Material consumption	0.15	3	5
Total	1	20	23

$I^a{}_m$ = 3*0,1+4*0,15+2*0.15+4*0,20+4*0,25+3*0,15=3,45

Analog's 1 = 5*0,1+4*0,15+4*0,15+2*0,20+3*0,25+5*0,15=3,60

An integral efficiency indicator of the scientific research project ($I_{fin}{}^p$) and of the analog ($I_{fin}{}^a$) are determined according to the formula of the integral basis of the financial integral resource efficiency:

$$I_{fin}{}^p = \frac{I_m^p}{I_f{}^p}, \qquad I_{fin}{}^a = \frac{I_m^a}{I_f{}^a} \qquad \ldots \tag{38}$$

$$I^p{}_{f1} = \frac{I^p{}_m}{I^p{}_f} = \frac{3,45}{0,81} = 4,26$$

$$I^a{}_f = \frac{I^a{}_m}{I^a{}_f} = \frac{3,60}{1} = 3,60$$

Comparison of the integral indicator of the efficiency of the current project and analogs will determine the comparative efficiency the project. Comparative project efficiency:

$$E_{av} = \frac{I_{fin}^{p}}{I_{fin}^{a}} \quad (39)$$

where;

E_{av} is the comparative project efficiency;

I_{fin}^{p} - integral indicator of project;

I_{fin}^{a} - integral indicator of the analog.

$$E_{av} = \frac{4,26}{3,60} = 1.18$$

Table 5.19-Comparative project efficiency

№	Indicator	Project	Analog 1 (electrochemical method)
1	Integral financial indicator	0,81	1
2	Integral resource efficiency indicator	3,45	3,60
3	Integral efficiency indicator	1,18	1
4	Comparative evaluation of the project execution variants	1,18	1

Comparison of the values of integral indicators of efficiency allows master's students to choose a more effective solution to the technical problem in the master's thesis basing on financial and resource efficiency.

Conclusions of Financial Management

Observations from the calculated results above, it can be concluded that the best place to conduct this research work is project which is the university, in order to attain resource and financial efficiency.

Thus, in this section was developed stages for design and create competitive development that meet the requirements in the field of resource efficiency and resource saving.

These stages include:

- development of a common economic project idea, formation of a project concept;
- organization of work on a research project;
- identification of possible research alternatives;
- research planning;
- assessing the commercial potential and prospects of scientific research from the standpoint of resource efficiency and resource saving;
- determination of resource (resource saving), financial, budget, social and economic efficiency of the project.

In the course of performing the economic part of the qualification master work, calculations were made of the planned cost of research and the time spent. The total cost of work is 339102,99 RUB, the main component of which is the cost of wages to perform scientific and technical research.

Chapter 5-Social responsibility

5.1 Introduction

The social responsibility concerning the workplace is very paramount to the safety and well-being of the workers and the people around. The human life is so important that nothing can replace it when damaged or death. This is the reason why there should be radical improvement in safety techniques in the working environment to reduce accident rates.

The working environment involved in this research is mainly based on producing ^{177}Lu from natural enriched Yb_2O_3 target (indirect route) for nuclear medicine applications. Hence, the workplace involved the laboratory rooms which includes preparation of chemicals and gamma spectroscopy equipment for collection of data and results analysis.

The objective of the study is to determine the theoretical specific activity of ^{177}Lu. The theoretical activity and specific activity calculations of ^{177}Lu from the given problem of Yb_2O_3. Cementation process using non-radioactive amount of Yb_2O_3 and distillation process. To measure the activity using the well-type HPGe gamma-ray detector (GX1018 Canberra). To calculate the activity of Yb and Lu from gamma-ray lines detected results.

Cementation process is performed to separate Yb from Lu followed by the extraction of Hg using distillation process. The radioisotope ^{177}Lu produced by indirect route may produces a low specific activity due to low thermal cross section of Yb, therefore, suitable separation method is required for producing high yield of ^{177}Lu.

5.2 Legal and organizational items in providing safety

Nowadays one of the main ways to radical improvement of all prophylactic work referred to reduce Total Incidents Rate and occupational morbidity is the widespread implementation of an integrated Occupational Safety and Health management system. That means combining isolated activities into a single system of targeted actions at all levels and stages of the production process.

Occupational Safety in the workplace is a system of legislative, socio-economic, technological, organizational, therapeutic and prophylactic actions and tools that is taken to ensure the safety, protection of the human health and the optimum performance of the human during working hours [1]. However, there should be laid down rules for labor protection and safety tactics that should be enacted in the working environment in order to prevent accidents and to guarantee safe and reliable working atmosphere on the part of the workers as obligatory. These should cover all workers from the highest hierarchy to the lowest rank in exception to none.

According to the Labor Code of the Russian Federation, every employee has the right:

- to have a workplace that meets Occupational safety requirements;

- to have a compulsory social insurance against accidents at manufacturing and occupational diseases;

- to receive reliable information from the employer, relevant government bodies and public organizations on conditions and Occupational safety at the workplace, about the existing risk of damage to health, as well as measures to protect against harmful and (or) hazardous factors;

- to refuse carrying out work in case of danger to his life and health due to violation of Occupational safety requirements;

- be provided with personal and collective protective equipment in compliance with Occupational safety requirements at the expense of the employer;

- for training in safe work methods and techniques at the expense of the employer;

- for personal participation or participation through their representatives in consideration of issues related to ensuring safe working conditions in his workplace, and in the investigation of the accident with him at work or occupational disease;

- for extraordinary medical examination in accordance with medical recommendations with preservation of his place of work (position) and secondary earnings during the passage of the specified medical examination;

- for warranties and compensation established in accordance with this Code, collective agreement, agreement, local regulatory an act, an employment contract, if he is engaged in work with harmful and (or) hazardous working conditions.

The labor code of the Russian Federation states that normal working hours may not exceed 40 hours per week. The employer must keep track of the time worked by each employee.

Rules for labor protection and safety measures are introduced in order to prevent accidents, ensure safe working conditions for workers and are mandatory for workers, managers, engineers and technicians.

In the industries, there are dangerous factors whose impact under certain circumstances might led to trauma, sudden shock and severe worsening of the health of the worker. Therefore, a harmful factor or an industrial health hazard is a factor whose effect on a worker under certain conditions may result to a decrease in the working capacity which has a direct negative influence on productivity of the workplace.

5.3 Basic ergonomic requirements for the correct location and arrangement of researcher's workplace

The workplace when working with a PC should be at least 6 square meters. The legroom should correspond to the following parameters: the legroom height is at least 600

mm, the seat distance to the lower edge of the working surface is at least 150 mm, and the seat height is 420 mm. It is worth noting that the height of the table should depend on the growth of the operator.

The following requirements are also provided for the organization of the workplace of the PC user: The design of the working chair should ensure the maintenance of a rational working posture while working on the PC and allow the posture to be changed in order to reduce the static tension of the neck and shoulder muscles and back to prevent the development of fatigue.

The type of working chair should be selected taking into account the growth of the user, the nature and duration of work with the PC. The working chair should be lifting and swivel, adjustable in height and angle of inclination of the seat and back, as well as the distance of the back from the front edge of the seat, while the adjustment of each parameter should be independent, easy to carry out and have a secure fit.

5.4 Occupational safety

A dangerous factor or industrial hazard is a factor whose impact under certain conditions leads to trauma or other sudden, severe deterioration of health of the worker [1].

A harmful factor or industrial health hazard is a factor, the effect of which on a worker under certain conditions leads to a disease or a decrease in working capacity.

5.4.1 Analysis of harmful and dangerous factors that can create object of investigation

The object of NCA ^{177}Lu is radioactive material which is used for treatment of cancer for patients, therefore cannot causes any harmful and dangerous factors.

5.4.2 Analysis of harmful and dangerous factors that can arise at workplace during investigation

The workplace is characterized by circumstances involving hazardous and harmful factors. These factors are grouped into distinct categories namely; biological, physical, chemical, and psychophysiological. The main elements of the production process that form dangerous and harmful factors are presented in Table 6.1 below.

Table 6.1 - Possible hazardous and harmful factors

Factors (GOST 12.0.003-2015)	Work stages			Legal documents
	Development	Manufacture	Exploitation	
1. Deviation of microclimate indicators	+	+	+	Sanitary rules 2.2.2 / 2.4.1340–03. Sanitary and epidemiological rules and regulations "Hygienic requirements for personal electronic computers and work organization."
2. Excessive noise		+	+	
3.Increased level of electromagnetic radiation	+	+	+	
4.Insufficient illumination of the working area		+	+	

				Sanitary rules 2.2.1 / 2.1.1.1278–03. Hygienic requirements for natural, artificial and combined lighting of residential and public buildings. Sanitary rules 2.2.4 / 2.1.8.562–96. Noise at workplaces, in premises of residential, public buildings and in the construction area. Sanitary rules 2.2.4.548–96.

				Hygienic requirements for the microclimate of industrial premises.
5. Abnormally high voltage value in the circuit, the closure which may occur through the human body	+	+	+	Sanitary rules GOST 12.1.038-82 SSBT. Electrical safety. Maximum permissible levels of touch voltages and currents.
6. Increased levels of ionizing radiation	+	+	+	Sanitary Rules 2.6.1. 2523 -0 9. Radiation Safety Standards (NRB-99/2009).

There are several factors that have great influence on the person working on the computers and these factors are classified based on physical and psychophysiological effects are as follows.

The following factors effect on person working on a computer:

- physical:
    - temperature and humidity;
    - noise;
    - static electricity;
    - electromagnetic field of low purity;
    - illumination;
    - presence of radiation;
- psychophysiological:
    - psychophysiological dangerous and harmful factors are divided into:
        - physical overload (static, dynamic)
        - mental stress (mental overstrain, monotony of work, emotional overload).

The following Table 2 explain further these factors:

5.4.2.1 Deviation of microclimate indicators

The air of the working area (microclimate) is determined by the following parameters: temperature, relative humidity, air speed. The optimum and permissible values of the microclimate characteristics are established in accordance with [2] and are given in Table 6.2.

Table 6.2 – Physical and psychophysiological factors and its effects in a computer based working environment.

Physical factors	Temperature and humidity: Sometimes, humans in general feels so tired and disturbed due to the hotness, coldness and the moisture content in an enclosed environment. Hence, these conditions may sometimes reduce the productivity and affects the physical well-being of the worker.
	Noise: Continual background noise from the computer systems sometimes has a physical damage on the hearing organ of the worker. This damage may continue to affect the person each day, weeks, months and years.
	Static electricity: this an inequity of electrical charges on the surface or within a material which exist around a field until its able dissipate through an electric current or an electrical discharge. One main physical effect of static electricity to the worker is having an airborne particulate influence on him. For instance, if a worker is positively charged, it has the possibility of attracting negatively charged particles from the air around him, hence setting up static electric field which is unhygienic and causes other problems. Many scientific findings have established that electric fields around a person intensely increase the plate-out rate of airborne particulates. Hence, from speculations, it's been point out that incase such particulates has an allergic effect,

	the plate-out might cause an incidence of skin irritation or disease, though has not proved.
	Electromagnetic field of low purity
	Illumination: Lightening from the monitor screen of the computer has a direct effect on the eye of the worker involved. Spending many hours working with the computer has a blurry effect on the eye and as a sign of digital strain on the eye. The most damaging of all is too much exposure of the eyes to blue light.
Psychophysiological	Physical overload (static, dynamic)
	Mental stress: Sitting at one place for a long time with the computer by straining the eye, involving the brain with much work may result in mental overstrain, monotony of work, emotional overload and many more that have psychophysiological effects on the worker.

Table 6.3 - Optimal and permissible parameters of the microclimate

Period of the year	Temperature, C	Relative humidity,%	Speed of air movement, m/s
Cold and changing of seasons	23-25	40-60	0.1
Warm	23-25	40	0.1

5.4.2.2 Excessive noise

Noise and vibration worsen working conditions, have a harmful effect on the human body, namely, the organs of hearing and the whole body through the central nervous system. It results in weakened attention, deteriorated memory, decreased response, and increased number of errors in work. Noise can be generated by operating equipment, air conditioning units, daylight illuminating devices, as well as spread from the outside. When working on a PC, the noise level in the workplace should not exceed 50 dB.

5.4.2.3 Increased level of electromagnetic radiation

The screen and system blocks produce electromagnetic radiation. Its main part comes from the system unit and the video cable. According to [2], the intensity of the electromagnetic field at a distance of 50 cm around the screen along the electrical component should be no more than:

- in the frequency range 5 Hz - 2 kHz - 25 V / m;
- in the frequency range 2 kHz - 400 kHz - 2.5 V / m.

The magnetic flux density should be no more than:

- in the frequency range 5 Hz - 2 kHz - 250 nT;
- in the frequency range 2 kHz - 400 kHz - 25 nT.

5.4.2.4 Abnormally high voltage value in the circuit

Depending on the conditions in the room, the risk of electric shock to a person increases or decreases. Do not operate the electronic device in conditions of high humidity (relative air humidity exceeds 75% for a long time), high temperature (more than 35 ° C), the presence of conductive dust, conductive floors and the possibility of simultaneous contact with metal components connected to the ground and the metal casing of electrical equipment. The operator works with electrical devices: a computer (display, system unit, etc.) and peripheral devices. There is a risk of electric shock in the following cases:

- with direct contact with current-carrying parts during computer repair;

- when touched by non-live parts that are under voltage (in case of violation of insulation of current-carrying parts of the computer);

- when touched with the floor, walls that are under voltage;

- short-circuited in high-voltage units: power supply and display unit.

Table 6.4 - Upper limits for values of contact current and voltage

	Voltage, V	Current, mA
Alternate, 50 Hz	2	0.3
Alternate, 400 Hz	3	0.4
Direct	8	1.0

5.4.2.5 Insufficient illumination of the working area

Light sources can be both natural and artificial. The natural source of the light in the room is the sun, artificial light are lamps. With long work in low illumination conditions and in violation of other parameters of the illumination, visual perception decreases, myopia, eye disease develops, and headaches appear.

According to the standard, the illumination on the table surface in the area of the working document should be 300-500 lux. Lighting should not create glare on the surface of the monitor. Illumination of the monitor surface should not be more than 300 lux.

The brightness of the lamps of common light in the area with radiation angles from 50 to 90° should be no more than 200 cd/m, the protective angle of the lamps should be at least 40°. The safety factor for lamps of common light should be assumed to be 1.4. The ripple coefficient should not exceed 5%.

5.4.2.6 Increased levels of ionizing radiation (Gamma spectroscopy)

Ionizing radiation is radiation that could ionize molecules and atoms. This effect is widely used in energetics and industry. However, there is health hazard. In living tissue, this radiation could damage cells that result in two types of effects. Deterministic effects (harmful tissue reactions) due to exposure with high doses and stochastic effects due to DNA destruction and mutations (for example, induction of cancer).

To provide radiation safety with using sources of ionizing radiation one must use next principles:

a) keep individual radiation doses from all radiation sources not higher than permissible exposure;
b) forbid all activity with using radiation sources if profit is low than risk of possible hazard;
c) keep individual radiation doses from all radiation sources as low as possible.

There are two groups of people related to work with radiation: personnel, who works with ionizing radiation, and population.

Quantity	Dose limits	
	personnel	population
Effective dose	20 mSv per year in average during 5 years,	1 mSv per year in average during 5 years,

	but not higher than 50 mSv per year	but not higher than 5 mSv per year
Equivalent dose per year in eye's lens	150 mSv	15 mSv
skin	500 mSv	50 mSv
Hands and feet	500 mSv	50 mSv

Effective dose for personnel must not exceed 1000 mSv for 50 years of working activity, and for population must not exceed 70 mSv for 70 years of life.

In addition, for women from personnel of age below 45 years there is limit of 1 mSv per month of equivalent dose on lower abdomen. During gestation and breast feeding women must not work with radiation sources.

For students older than 16, who uses radiation sources in study process or who is in rooms with increased level of ionizing radiation, dose limits are quarter part of dose limits of personnel.

5.4.3 Justification of measures to reduce the levels of exposure to hazardous and harmful factors on the researcher

5.4.3.1 Deviation of microclimate indicators

The measures for improving the air environment in the production room include: the correct organization of ventilation and air conditioning, heating of room. Ventilation can be realized naturally and mechanically. In the room, the following volumes of outside air must be delivered:

- at least 30 m^3 per hour per person for the volume of the room up to 20 m^3 per person;

- natural ventilation is allowed for the volume of the room more than 40 m^3 per person and if there is no emission of harmful substances.

The heating system must provide sufficient, constant and uniform heating of the air. Water heating should be used in rooms with increased requirements for clean air.

The parameters of the microclimate in the laboratory regulated by the central heating system, have the following values: humidity 40%, air speed 0.1 m / s, summer temperature 20-25 ° C, in winter 13-15 ° C. Natural ventilation is provided in the laboratory. Air enters and leaves through the cracks, windows, doors. The main disadvantage of such ventilation is that the fresh air enters the room without preliminary cleaning and heating.

5.4.3.2 Excessive noise

In research audiences, there are various kinds of noises that are generated by both internal and external noise sources. The internal sources of noise are working equipment, personal computer, printer, ventilation system, as well as computer equipment of other engineers in the audience. If the maximum permissible conditions are exceeded, it is sufficient to use sound-absorbing materials in the room (sound-absorbing wall and ceiling cladding, window curtains). To reduce the noise penetrating outside the premises, install seals around the perimeter of the doors and windows.

5.4.3.3 Increased level of electromagnetic radiation

There are the following ways to protect against EMF:

- increase the distance from the source (the screen should be at least 50 cm from the user);

- the use of pre-screen filters, special screens and other personal protective equipment.

When working with a computer, the ionizing radiation source is a display. Under the influence of ionizing radiation in the body, there may be a violation of normal blood

coagulability, an increase in the fragility of blood vessels, a decrease in immunity, etc. The dose of irradiation at a distance of 20 cm to the display is 50 μrem / hr. According to the norms [2], the design of the computer should provide the power of the exposure dose of x-rays at any point at a distance of 0.05 m from the screen no more than 100 μR / h.

Fatigue of the organs of vision can be associated with both insufficient illumination and excessive illumination, as well as with the wrong direction of light.

5.4.3.4 Increased levels of ionizing radiation

In case of radiation accident, responsible personnel must take all measures to restore control of radiation sources and reduce to minimum radiation doses, number of irradiated persons, radioactive pollution of the environment, economic and social losses caused with radioactive pollution.

Radiation control is a main part of radiation safety and radiation protection. It is aimed at not exceeding the established basic dose limits and permissible levels of radiation, obtaining the necessary information to optimize protection and making decisions about interference in the case of radiation accidents, contamination of the environment and buildings with radionuclides.

The radiation control is control of:

- Radiation characteristics of radiation sources, pollution in air, liquid and solid wastes.
- Radiation factors developed with technological processes in working places and environment.
- Radiation factors of contaminated environment.
- Irradiation dose levels of personnel and population.

The main controlled parameters are:

- Annual effective and equivalent doses
- intake and body content of radionuclides

- volume or specific activity of radionuclides in air, water, food products, building materials and etc.
- radioactive contamination of skin, clothes, footwear, working places and etc.
- dose and power of external irradiation.
- particles and photons flux density.

Radiation protection office establish control levels of all controlled parameters in according to not exceed dose limits and keep dose levels as low as possible. In case of exceeding control levels radiation protection officers start investigation of exceed causes and take actions to eliminate this exceeding.

uring planning and implementation of radiation safety precautions, taking any actions about radiation safety and analysis of effectiveness of mentioned action and precautions one must value radiation safety with next factors:

- characteristics of radioactive contamination of the environment;
- probability of radiation accidents and scale of accidents;
- degree of readiness to effective elimination of radiation accidents and its aftermathches;
- number of persons irradiated with doses higher than controlled limits of doses;
- analysis of actions for providing radiation safety, meeting requirements, rules, standards of radiation safety;
- analysis of irradiation doses obtained by groups of population from all ionizing radiation sources.

5.4.3.5 Abnormally high voltage value in the circuit

Measures to ensure the electrical safety of electrical installations:

- disconnection of voltage from live parts, on which or near to which work will be carried out, and taking measures to ensure the impossibility of applying voltage to the workplace;

- posting of posters indicating the place of work;

- electrical grounding of the housings of all installations through a neutral wire;

- coating of metal surfaces of tools with reliable insulation;

- inaccessibility of current-carrying parts of equipment (the conclusion in the case of electroporating elements, the conclusion in the body of current-carrying parts) [3].

5.5 Ecological safety

5.5.1 Analysis of the impact of the research object on the environment

Sources of ionizing radiation used in medicine could be divided into two groups: radioactive substances and radiation generators. The difference is that radiation generators like accelerators and x-ray tubes emit ionizing radiation only when they are turned on.

In ordinary work with necessary safety precautions, there are insignificant impact of using sources of ionizing radiation on environment. The immediate effect of ionizing radiation is ionization of air in room, but after a specified time the ionization disappears.

The danger of using radioactive materials could occur only in accidents with stealing and loosing these materials due to high toxicity.

5.5.2 Analysis of the environmental impact of the research process

Process of investigation itself in the thesis do not have essential effect on environment. One of hazardous waste is fluorescent lamps. Mercury in fluorescent lamps is a hazardous substance and its improper disposal greatly poisons the environment.

Outdated devices goes to an enterprise that has the right to process wastes. It is possible to isolate precious metals with a purity in the range of 99.95–99.99% from computer components. A closed production cycle consists of the following stages: primary sorting of equipment; the allocation of precious, ferrous and non-ferrous metals and other materials; melting; refining and processing of metals. Thus, there is an effective disposal of computer devices.

5.5.3 Justification of environmental protection measures

Pollution reduction is possible due to the improvement of devices that produces electricity, the use of more economical and efficient technologies, the use of new methods for generating electricity and the introduction of modern methods and methods for cleaning and neutralizing industrial waste. In addition, this problem should be solved by efficient and economical use of electricity by consumers themselves. This is the use of more economical devices, as well as efficient regimes of these devices. This also includes compliance with production discipline in the framework of the proper use of electricity.

Simple conclusion is that it is necessary to strive to reduce energy consumption, to develop and implement systems with low energy consumption. In modern computers, modes with reduced power consumption during long-term idle are widely used.

5.6 Safety in emergency

5.6.1 Analysis of probable emergencies that may occur at the workplace during research

The fire is the most probable emergency in our life. Possible causes of fire:

- malfunction of current-carrying parts of installations;
- work with open electrical equipment;
- short circuits in the power supply;

- non-compliance with fire safety regulations;
- presence of combustible components: documents, doors, tables, cable insulation, etc.

Activities on fire prevention are divided into: organizational, technical, operational and regime.

5.6.2 Substantiation of measures for the prevention of emergencies and the development of procedures in case of emergencies

Organizational measures provide for correct operation of equipment, proper maintenance of buildings and territories, fire instruction for workers and employees, training of production personnel for fire safety rules, issuing instructions, posters, and the existence of an evacuation plan.

The technical measures include compliance with fire regulations, norms for the design of buildings, the installation of electrical wires and equipment, heating, ventilation, lighting, the correct placement of equipment.

The regime measures include the establishment of rules for the organization of work, and compliance with fire-fighting measures. To prevent fire from short circuits, overloads, etc., the following fire safety rules must be observed:

- elimination of the formation of a flammable environment (sealing equipment, control of the air, working and emergency ventilation);
- use in the construction and decoration of buildings of non-combustible or difficultly combustible materials;
- the correct operation of the equipment (proper inclusion of equipment in the electrical supply network, monitoring of heating equipment);
- correct maintenance of buildings and territories (exclusion of the source of ignition - prevention of spontaneous combustion of substances, restriction of fire works);

- training of production personnel in fire safety rules;
- the publication of instructions, posters, the existence of an evacuation plan;
- compliance with fire regulations, norms in the design of buildings, in the organization of electrical wires and equipment, heating, ventilation, lighting;
- the correct placement of equipment;
- well-time preventive inspection, repair and testing of equipment.

In the case of an emergency, it is necessary to:

- inform the management (duty officer);
- call the Emergency Service or the Ministry of Emergency Situations - tel. 112;
- take measures to eliminate the accident in accordance with the instructions.

Conclusions of Social Responsibilities

In this section about social responsibility the hazardous and harmful factors were revealed. All necessary safety measures and precaution to minimize probability of accidents and traumas during investigation are given.

Possible negative effect on environment were given in compact form describing main ecological problem of using nuclear energy.

It could be stated that with respect to all regulations and standards, investigation itself and object of investigation do not pose special risks to personnel, other equipment and environment.

References of Social Responsibilities

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3. GOST 12.1.038-82 Occupational safety standards system. Electrical safety.
4. Fire and explosion safety of industrial facilities. GOST R12.1.004-85 Occupational safety standards system. Fire safety

Chapter 6-Conclusions and Future Recommendation

The goal of the study was to perform the experimental production of NCA ^{177}Lu with a recycling of the Yb target for nuclear medicine applications. The radioisotope ^{177}Lu was separated from Yb target material for NCA experiment for nuclear medicine applications. The theoretical activity and specific activity of ^{177}Lu from Yb_2O_3 were determined. The theoretical activity of ^{177}Lu from 10 mg of Yb_2O_3 for 5 days is approximately 1 GBq. The cementation process was performed with five cementation experiments (each with three cementation cycles) using the ratio Lu/Yb 1000 followed by the recycling Yb.

HPGe detector (GX1018 Canberra) was calibrated with ^{152}Eu source for analysis of ^{177}Lu in the presence of Yb. Gamma-ray peak of 208 keV for ^{177}Lu and 198 keV for ^{169}Yb were detected in the system. The activity of the third cementation process of radioactive Yb and Lu were found to be 2.06±0.05 Bq and 96.97±4.16 Bq which corresponds to 1.4 mg and 7.6 μg, respectively.The repeatability of the experiment was < 3.0 %, respectively. The ratio Yb/Lu of the third cementation process is about 184.2, separation factor is 5.4. After the cementation process, Yb target was extracted by distillation process, and the amount of Yb (mg) which that can be recycling is 35.5 mg from 51.4 mg (>69%) for new production. After the cementation process, high amount of mass of Yb was observed. In conclusion, it is necessary to carry out optimization for better separation of Yb and Lu. The goal of this research was accomplished towards the production of radioisotopes ^{177}Lu.

For future recommendations, the optimization must be carried out by changing the concentration $NaCH_3COONa$, increase number of cementation cycles for better separation. To conduct the experiment with high activity. To determine the radionuclide and radiochemical purity. To measure the amount of impurities in production and to determine the synthases of ^{177}Lu-DOTA-TATE. The outcome will ultimately provide evidence-based information, to the policy makers, about the contribution of the produced ^{177}Lu to be used for diagnostic, imaging or as a peptide receptor radionuclide therapy for treatment of cancer.

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