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

Инженерная школа ядерных технологий
Направление подготовки 14.04.02 Ядерные физика и технологии
Научно-образовательный центр международного ядерного образования и карьерного сопровождения иностранных студентов ТПУ

МАГИСТЕРСКАЯ ДИССЕРТАЦИЯ

Тема работы
Изучение деградации и высвобождения лекарственных средств из микрокамерных структур, напечатанных на 3D-принтере из полимолочной кислоты

УДК 615.014.67-022.53.034:661.746.2

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School of Nuclear Science & Engineering
Field of training: 14.04.02 Nuclear Science and Technology
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Research and Training Centre for International Nuclear Education and Career, School of Nuclear Engineering

MASTER THESIS

Topic of research work
Degradation and drug release study of 3D printed polylactic acid microchamber structures

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Tomsk – 2023

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).

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Program Director
_____ Verkhoturova V.V.
«____» _____ 2023

ASSIGNMENT
for the Graduation Thesis completion

In the form:

Master Thesis

For a student:

Group	**Full name**
0AM1M	AWUAH COLLINS

Topic of research work:

Degradation and drug release study of 3D printed polylactic acid microchamber structures.	
Approved by the order of the Director of School of Nuclear Science & Engineering (date, number):	№ 30-89/c dated January 30, 2023

Deadline for completion of Master Thesis:	06.06.2023

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.)*	The work will be about a study on degradation and drug release of 3D printed polylactic acid microchamber structures. This will be a continuous experiment where measurements will be taken from the set-up daily and the results will be determined at the end of the research.

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).*	Review of technical literature on this subject, designing and building an experimental set-up for the study, investigations on the degradation of microchamber structure, measurements to determine the drug release profile as a result of degradation of the microchamber structures, analysing the data obtained.
List of graphic material *(with an exact indication of mandatory drawings)*	Technical drawings of study object, micrographs from various microscopic images, graphical representations of results.

Advisors to the sections of the Master Thesis
(with indication of sections)

Section	Advisor
Technical part (literature and practical)	Sven Rutkowski (PhD)
Financial part	Ekaterina V. Menshikova (PhD)
Social part	Yuriy V. Perederin (PhD)

Date of issuance of the assignment for Master Thesis completion according to the schedule	13.03.2023

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

Position	Full name	Academic degree, academic status	Signature	Date
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Assignment accepted for execution by a student:

Group	Full name	Signature	Date
0AM1M	Awuah Collins		

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

Level of education: Master degree program
Research and Training Centre for International Nuclear Education and Career, School of Nuclear Engineering
Period of completion: spring semester 2022/2023 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:	06.06.2023

Assessment date	**Title of section (module) / type of work (research)**	**Maximum score for the section (module)**
27.01.2023	Preparation of technical specifications and selection of research areas	10
24.02.2023	Development of a common research methodology	10
23.03.2023	Selection and study of materials on the topic	10
13.04.2023	Experimental research	20
27.04.2023	Processing received data	20
18.05.2023	Registration of the work performed	15
30.05.2023	Preparation for defending the dissertation	15

COMPILED BY:
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Nuclear medicine	Vera V. Verkhoturova	PhD		

ABSTRACT

This master's thesis consists of 134 pages, 28 figures, 36 tables, 100 references.

Keywords

Degradation, Drug Release, Polylactic Acid, 3d Printed, Microchamber, Biodegradable, Polymer

The subject of this research was on degradation and drug release study of 3D printed polylactic acid microchamber structures.

The goal of the study was to investigate the dynamics of degradation and the drug release profile of PLA microchambers under conditions which are similar to the human body.

In the course of this research, the literature on the subject was studied. Also, a 3D printed PLA microchamber was filled with a fluorescence cargo and covered with a thin layer made from of the PLA polymer. It was then placed in a solution that has physical and chemiscal conditions similar to that of the human blood constantly circulating at bodily temperature. Degradation analysis of the PLA covering layer, and the release profile of the cargo was determined.

From the results, there was gradual degradation of the covering layer which simulntaneously released the cargo during the degradation process.

Application area: cancer research laboratories, cancer centres, biomedical research laboratories.

Economic effcicency/significance of work: This technology could be used as an option for systemic radiation therapy and other froms of drug delivery where the radiopharmaceutical or the drug to be sued will be filled in the polymer and implanted in the patient.

CONTENTS

1. INTRODUCTION

1.1 Background of study

As science progresses, newer technologies are being developed in the micro size range. Nano and micro materials were developed for various needs in medicine and which have been investigated extensively over the last decades. Liposomal carriers, dendrimers, carbon micro or nano tubes, and inorganic metal-based micro formulations are among the most common and well-studied micro- and nano materials over the years. [1, 2, 3].

In recent times, there has also been the emergence of microchambers used as stande-alone implants or parts of the surface of implants in medicine. Microchambers are materials for the loading of microparticles with a size of 2.2 μm and solutions for continual release or release-on-demand of the cargo [4, 5]. These microchambers could be made of magnetic iron oxide, silica, [4, 5, 6, 7] as well as of biodegradable or non-biodegradable polymers [8,9].

Recently, there has been high incidence and prevalence of several complex medical conditions, which require innovative interventions. The success of these interventions can rely heavily on the integration of different medical disciplines. For this reason, it is necessary to integrate the technology of a polymeric microchamber system for drug release in both conventional and newer fields of medicine [10], including nuclear medicine.

Similar to how conventional medications may be employed as cargo in this fashion, it may be possible that radioactive compounds used in nuclear medicine can also be contained in polymeric microchambers and delivered gradually to the target site via the bloodstream.

For biomedical applications, biodegradable polymers including polylactic acid (PLA), poly(glycolic acid) (PGA), poly(lactic-co-glycolic acid) (PLGA) and

polycaprolactone (PCL), as well as their copolymers, are increasingly widely employed [11]. To fabricate microchambers for use as drug release systems, their synthetic forms can be 3D printed into customizable shapes and figures.

A polymer is considered biodegradable if it has the ability to decay naturally without harming the environment [12]. When biodegradable polymers such as PLA are printed in a 3D structure, and filled with a cargo in a form of any desired drug, and covered with a thin biodegradable polymeric layer, the polymer layer can degrade in a biological environment, such as living tissues, to release the drug.

Drug release can be described as an aspect of drug delivery; the process of administering medication or other pharmaceutical compounds to achieve a therapeutic effect [13]. The phenomenon of 'drug release' occurs when drugs migrate outward from their storage location to contact or to mix with the surrounding medium [14].

1.2 Problem Statement

Despite the significance of medication adherence, the World Health Organisation reports that 50% of people with chronic illnesses experience medication nonadherence on average [15]. Apart from this, non-adherence of chronic medications can account for up to 50% of treatment failures, around 125,000 deaths, and up to 25% of hospitalizations each year [16].

Due to a lack of understanding of the importance of taking medications, pharmacophobia or forgetfulness it is not unusual for people to miss an occasional dose or take it outside the regular time window, and this can aggravate the condition, or at least, have some negative health effects on the patients. This problem cuts across the various traditional drug delivery routes [17] such as oral, buccal, sublingual, pulmonary, ocular, nasal, transdermal, vaginal or anal [18].

Furthermore, it is proven that excipients added to drugs in drug synthesis can affect the chemical nature, the stability and bioavailability of drugs and,

consequently, their therapeutic efficacy and safety [19]. Therefore there is the need to develop a drug delivery system which may not require the addition of excipients for its administration.

From the above, undoubtedly, there is a pressing need to develop a drug delivery system and system of drug administration which overcomes these barriers.

1.3 Study Objectives

The goals of this study have been classified into two: the main objective, and the specific objectives. The main objective generally describes the overall aim of the research, whiles the specific objectives spells out the minor goals that are required to achieve the overall goal.

1.3.1 Main Objective:

The main objective of this study is to determine the extent of degradation of the covering of a filled 3D printed microchamber and the rate of release of the cargo in a flowing phosphate-buffered saline (PBS) solution under controlled conditions.

1.3.2 Specific Objectives:

The specified goals of this study are as follows:

i. Design, fabricate and seal a 3D printed PLA microchamber filled with a fluorescence cargo.

ii. Design a suitable continuous flow laboratory setup with the size of a human adult aorta in diameter that is suitable to be used in an incubator.

iii. Measure the fluorescence of the released cargo on daily basis for a period of 60 days

iv. Compare the morphological changes of the seal (cover) of the PLA microchamber within a period of 60 days.

v. Ascertain the dynamics of the roughness of the PLA microchamber cover because of degradation within a 60 day period.

vi. Determine the dynamics of wettability and surface energy of the PLA microchamber structure in a flowing PBS within a period of 60 days.

1.4 Significance of Study

This study attempts to project the feasibility of using drug-filled PLA microchamber implants as a system of drug delivery whereby there will be a constant release of a controlled amount of the drug in the living tissue due to the degradation process of the PLA microchamber structure.

Unlike other studies where the surrounding solution used in the experiment was stable, this study will determine the release trends of the cargo in a flowing liquid, which practically defines the novelty of this study.

The flowing liquid will be such a one that has ion concentrations similar to that of the human blood, such that the release kinetics can be likened to what may happen in the bloodstream in living tissues. This can give scientist a more precise view of how this can happen in living tissues.

Considering the limited research and publications in this area, this study will contribute to knowledge and as well be an important resource for scientist who may be interested in these aspects of biomedical applications to determine the release trends of PLA microchambers in a flowing liquid.

The essence of this study will not only be for biomedical applications alone, but also for other applications including environmental applications. For example: the concept may be used to reduce water contamination by placing the drug-filled and covered polymer in the contaminated water such that the released cargo will neutralize chemicals and such other contaminants which may be present in the water (Rutkowski, personal communication, 2022).

This study can be a significant alternative to conventional administration of drugs that is seen to be inconvenient, as well as for passive and active targeting in theranostics. For example, for patients diagnosed of chronic medical conditions

which require daily intake of drugs, this study can be a guide for further research in creating a drug delivery system in living tissues which will always administer drugs in desired quantities whiles implanted in the tissues [20].

2. LITERATURE REVIEW

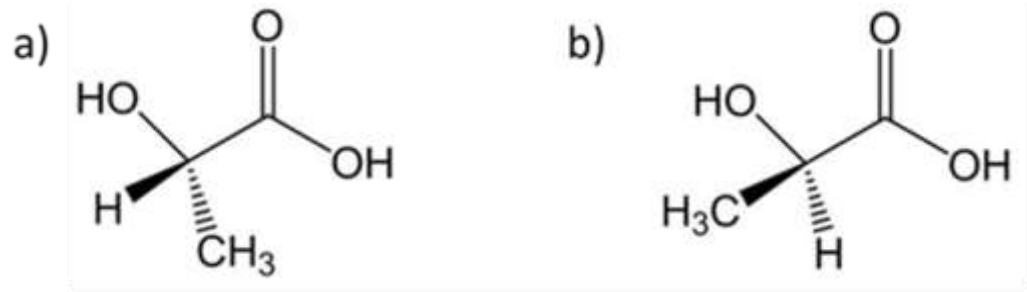
2.1 Polylactic Acid (PLA) as a biodegradable polymer for fabrication of drug release systems

A biodegradable polymer is highly suitable for drug release in living tissues if it is made from nontoxic and renewable feedstock. Polylactic acid (PLA) is seen to be one of the most promising biopolymers because of this attribute. It is also one of the most widely utilized biodegradable polymers because of its exceptional combination of qualities; including biocompatibility, biodegradability, mechanical strength, and processability. As such, it is much more preferable for the fabrication of polymeric microchamber implants for drug release [21].

2.2 Overview of Poly(lactic acid)

Poly(lactic acid) (PLA) is a member of the family of biodegradable and compostable aliphatic polyesters, which is frequently created from -hydroxy acids like polyglycolic acid or polymandelic acid [22].

PLA is a polymer with lactic acid as its monomer, which binds with another lactic acid monomer to form the PLA polymer. Lactic acid (2-hydroxy propionic acid) is the simplest hydroxypropionic acid with an asymmetric carbon atom and thus exists in two optically active configurations: The lactic acid L(+) and the D(-) lactic acid stereoisomers (Figure 1.x). L(+) isomer is produced by humans and other mammals, whereas both the D(-) and the L(+)-enantiomers are produced by bacterial systems [22].



(a) L(+) lactic acid and (b) D(-) lactic acid
Figure 2.1 – Stereoisomers of lactic acid

The bulk of lactic acid that is commercially generated across the world is a product of fermentation of carbohydrates by bacteria; employing homolactic organisms such different modified or optimised strains of the genus Lactobacilli, to make lactic acid [22].

PLA is one of the few polymers in which the stereochemical structure can be easily modified. This is usually done when a regulated blend of the L- or D-isomers is polymerized to produce high-molecular-weight (at over 100,000 daltons [22]) amorphous or crystalline polymers (Figure 1.2), and generally regarded as safe [23].

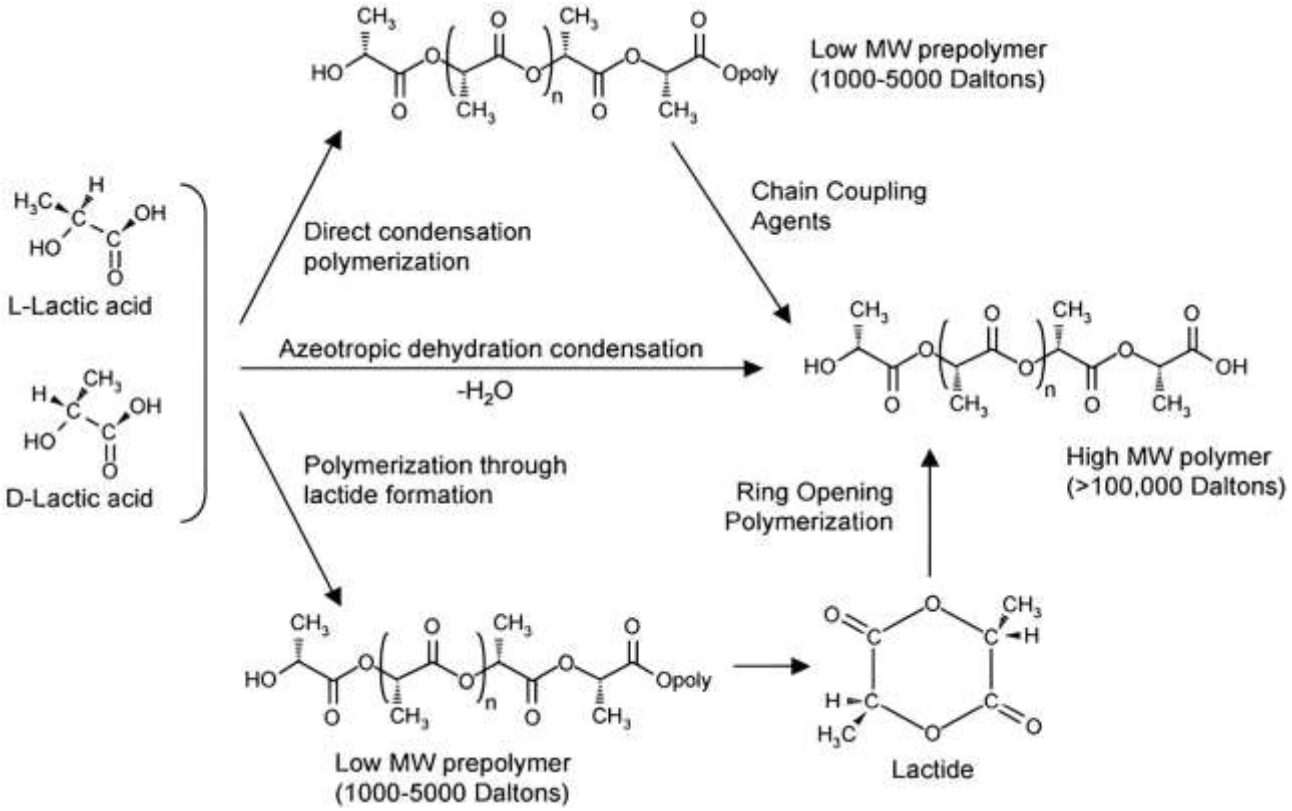


Figure 2.2 – Synthesis methods for high-molecular-weight PLA [23]

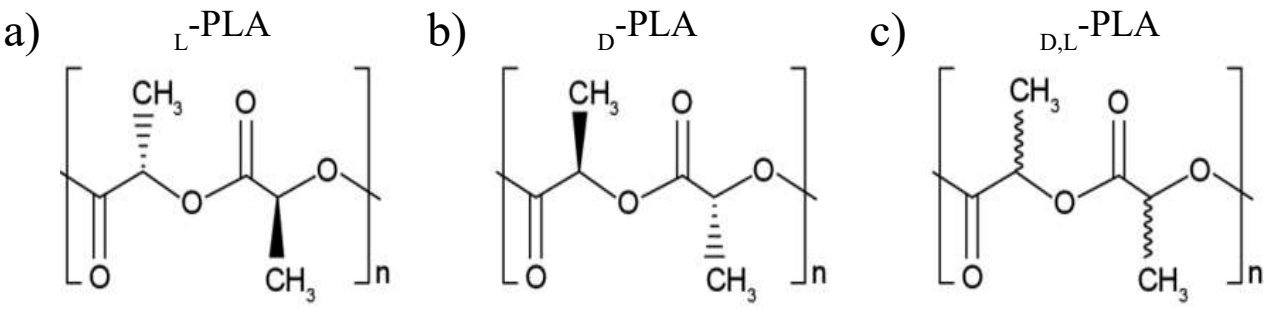
High-molecular-weight poly(lactic acid) is a thermoplastic polymer that is colorless, glossy, stiff, and has properties comparable to those of polystyrene. The majority of organic solvents, including tetrahydrofuran (THF), chlorinated solvents, benzene, acetonitrile, and dioxane, can dissolve amorphous PLA [25].

PLA that is crystallised is soluble in benzene and chlorinated solvents at high temperatures. Slow cooling, annealing it over the glass-transition temperature T_g, or strain crystallisation are all methods for crystallising poly(lactic acid) [25].

Without the need for enzymes to catalyse the ester bond hydrolysis, PLA may be broken down by straightforward hydrolysis. The object's size and shape, the isomer ratio, and the temperature of the hydrolysis all affect its rate of degradation. [25].

In order to create items for the market for biocompatible/bioabsorbable medical devices or for industrial packaging, thermoplastic, high-strength, high-modulus PLA may be created from resources that are renewable yearly. It is simply processed using standard plastics equipment to create moulded components, film, or fibres [25].

Three forms of PLA exist: poly-L-lactic acid (PLLA), poly-D-lactic acid (PDLA) and a racemate poly-DL-lactic acid (PDLLA) (Figure 1.x). Recently, the racemate PDLLA may have a high or low molecular weight. PDLLA of high molecular weight is found to have a high mechanical stability whiles PDLLA of low molecular weight has relatively lesser mechanical stability. For this reason, even though both of them can be useful biomaterials, their biomedical uses may slightly differ [26, 27, 28].



(a) Poly-L-lactic acid (PLLA), (b) Poly-D-lactic acid (PDLA), (c) Poly-DL-lactic acid (PDLLA) [29]

Figure 2.3 Structure of poly(lactic acid) isomers

2.3 Biocompatibility, biodegradation and biosafety of PLA in medical implants and theranostic systems

Although PLA polymer has been around for more than 150 years, it continues to be a valuable resource for biomedical research and the development of a fundamental knowledge of how artificial polymers may effectively function alongside biological systems [30].

The most widely utilised biodegradable polymer for therapeutic applications nowadays is polylactic acid (PLA). Examples of these uses include tissue engineering, temporary and long-term implanted devices, and drug delivery systems. These examples continually extend into new fields. This is mostly attributable to the polymer's advantageous biocompatibility and its safe degradation products [30]. In addition to other synthetic degradable polyesters [31], PLA has been widely utilised in surgery as dissolvable suture meshes for nearly three decades [32, 33]. Due to its commedable mechanical stability and outstanding biocompatibility, the stereoisomer D,L-PLA has recently been extensively investigated as a biomedical coating for orthopaedic material [2,3,4]. Additionally, low molecular weight D,L-PLA can be coupled with medications like growth stimulants, antibiotics, or thrombin inhibitors to create a locally acting drug-delivery system [30].

PLA starts to degrade once it comes into contact with biological medium, often by hydrolysis of the ester-bond backbone, into lactic acid (LA) or into carbon dioxide and water [30].

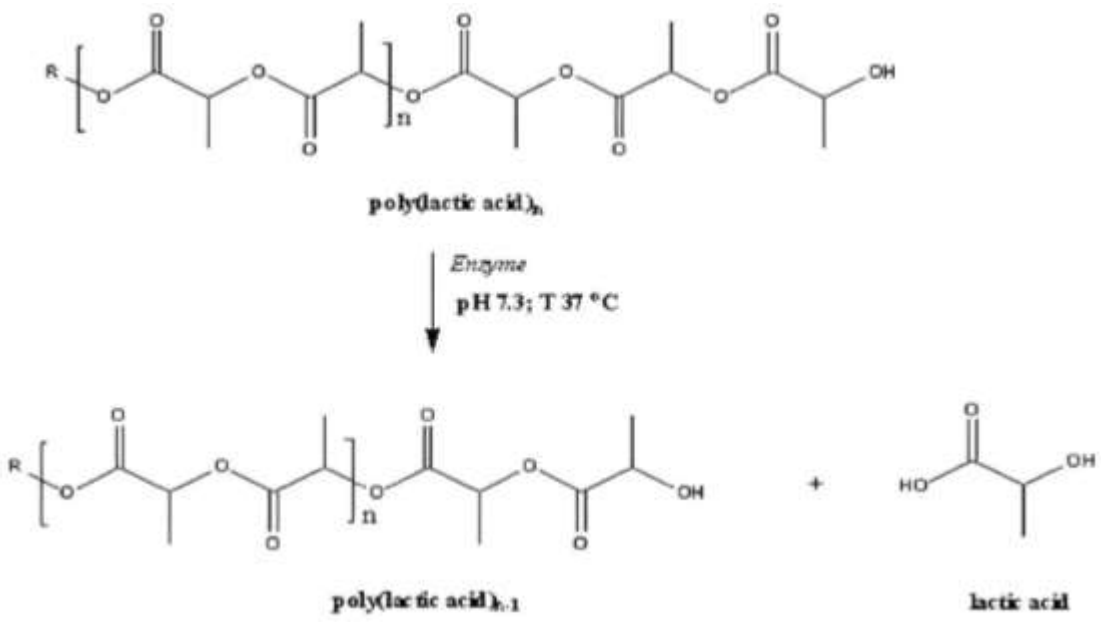


Figure 2.4 – Proposed schematic mechanism of PLA biodegradation [34]

For this reason, if it is filled with the desired drug, the drug gets exposed from the cover, and releases into the surrounding tissues and/or the blood stream during the degradation process. The degradants are, however, either intracellularly metabolised or eliminated by the breath and urine [30].

As a polymer, the functionality and efficiency of the PLA-made medical implants are affected by a number of variables. These variables can include degradation rate, polymer structure, composition (whether a monomer or a copolymer), physicochemical parameters (taking into account ionic charge, ionic strength, and pH), physical factors (taking into account shape and size), morphological aspect (whether amorphous, semi-crystalline (i.e. intravenous, subcutaneous, among others) [35, 36].

Whiles in the tissue, the pH, temperature, and chemistry of the cargo can also affect the degradation rate. Additionally, bacterial infection, or inflammation as a result of the presence of a foreign body also speed up the degradation of PLA through the secretion of enzymes that break down the polymeric matrix. Diffusion of water between the polymer chains whiles in the tissue, also allows biodegradation to take place on the surface of the polymer as well as inside the body of the polymer

[30]. As a result, the rate of degradation in the sites of inflammation will be higher than in healthy tissues [30].

The degradation rate is also influenced by chirality. D-PLA will degrade more quickly than L-PLA. This makes it possible to customise the implant for the desired organ and biomedical use. With an average half-life of 30 weeks, the half-life of PLA can be increased or decreased to meet therapeutic demands. By identifying the molecular composition and physical design of the microchamber, degradation kinetics may be adjusted. Utilizing the L- or the D- chirality of the LA will significantly increase or reduce the degradation rates, respectively [30].

2.4 3D Printing

3D printing, also known as additive manufacturing, is the process of making three dimensional solid objects from a digital file by the use of a 3D printer. Using additive methods, 3D printed objects are produced. In an additive process, an object is made by adding layers of material one after another until the product is made. It is possible to think of each of these levels as a finely sliced cross-section of the object [37].

Subtractive manufacturing, which involves hollowing out a piece of metal or plastic using a milling machine, for example, is the reverse of 3D printing. Complex forms may be created with 3D printing with less material compared with conventional production techniques [37].

2.4.1 3D Printing Techniques

Although the media frequently refers to all additive manufacturing technologies as "3D printing," there are several distinct procedures that differ in how layers are created. Depending on the material and machine technology employed, specific procedures will vary. As a result, in 2010, the American Society for Testing and Materials (ASTM) group "ASTM F42 - Additive Manufacturing" developed a set of standards that categorise a variety of additive manufacturing processes into seven groups. These techniques are: binder jetting, directed energy deposition,

material extrusion, material jetting, power bed fusion, sheet lamination, and vat photopolymerization. [38].

2.4.2 Binder Jetting

Binder jetting uses inkjet technology similar to that used in standard desktop inkjet printers. In this procedure, the liquid binder is applied to the powder dispersed in discrete areas by an inkjet printer head. It uses less energy since the ingredients are bound together without the use of heat. Additionally, because the powder is not heated, all leftover powder may be recycled completely. Materials frequently utilised in this approach include metals, polymers, and ceramics [37, 38, 39, 40]. The figure below illustrates Binder Jetting 3D printing.

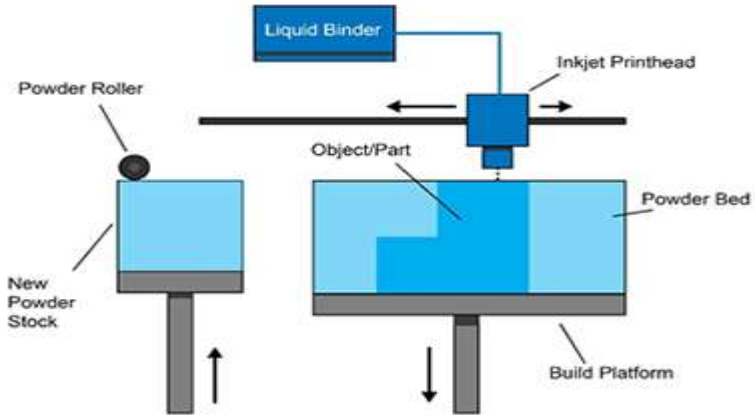


Figure 2.5 – Illustration of Binder Jaetting 3D printing technique [38]

The binder jetting technique operates according to the following: A roller is used to spread the powder material over the build platform. The binder adhesive is deposited on top of the powder by the print head. The build platform is lowered according to the layer thickness of the model. Over the previous layer, another layer of the powder is spread. The powder binds to the liquid to form the object. The entire object is eventually made by the repetition of the process [38].

2.4.3 Directed Energy Deposition (DED)

DED uses focused heat input to fuse the material that is deposited in layers using a multi-axis nozzle to construct objects. Laser, electron beam, and arc are a few examples of the heat inputs utilized for DED [41]. The material feedstock can

be a wire or a powder. DED is primarily utilized for the repair of metal objects [42]. The figure below illustrates the DED 3D printing technique.

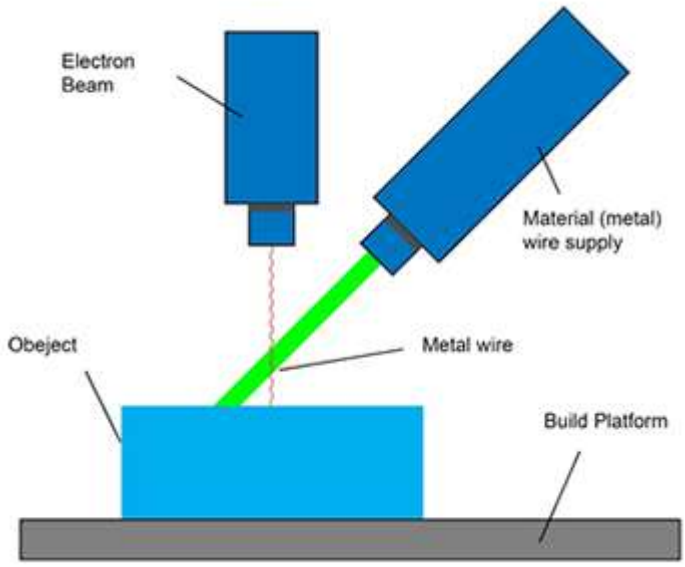


Figure 2.6 – Illustration of DED 3D prining technique [38]

The process involved in this technique is such that A4 or 5 axis arm with nozzle moves around a fixed object whiles the nozzle deposits material unto existing surfaces of the object. The material, either in wire or powder form, is melted upon deposition using electron beams, a laser or plasma arc. Subsequently, there is layer by layer addition of further material. This solidifies to create or repair new features on the existing object [38].

2.4.4 Material Extrusion

Material extrusion involves the fused deposition modelling (FDM) technique. Thermoplastic filaments are heated in this process before being extruded via a nozzle tip. Then, layer by layer, the extruded molten material is added in accordance with the digital model of that part of the object. To cut costs and speed up manufacturing, FDM is frequently used for developing concept models in the early phases of product development. For FDM, filament materials are easily available, which makes it advantageous. Additionally, a variety of FDM filaments with various strengths and

temperature characteristics can be obtained [38]. Material extrusion 3D printing technique is illustrtated in the figure below:

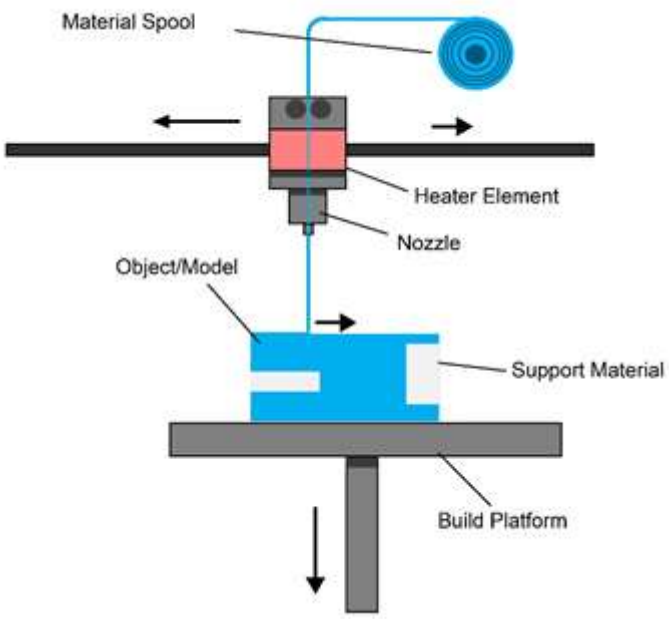


Figure 2.7 – Illustration of Material Extrusion 3D priniting technique [38]

In this technique, the first layer is built as nozzle deposits material to build the first layer according to the required cross sectional area of first object slice. Subsequent layers are added on top of previous layers, and as the material is in a melted state, layers are fused together upon deposition [38].

2.4.5 Material Jetting

In terms of how it works, material jetting is identical to a conventional inkjet printer. Photopolymer droplets are carefully placed on the build surface during this procedure. After the initially deposited material has solidified, the build platform height is adjusted to repeat the deposition. This procedure involves the use of a variety of materials, including composites, polymers, and ceramics [42]. Material Jetting 3D printing technique is illustrated in figure 2.4 below:

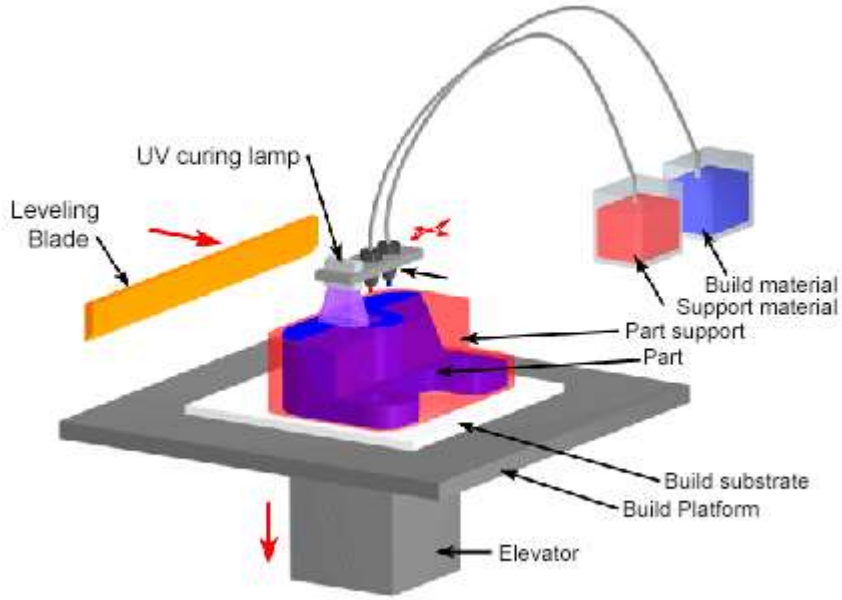


Figure 2.8 – Material Jetting 3D printing technique illustration [38]

The procedure in this technique is such that the print head is positioned above build platform to allow for the use of either thermal or piezoelectric method deposition of Droplets from the print head onto the required surface. Droplets of then material solidify and make up the first layer. Further layers are then built up as before on top of the previous. Layers are allowed to cool and harden or are cured by UV light. Post processing includes removal of support material [38].

2.4.6 Power Bed Fusion (PBF)

In PBF, deposited material layers are melted or sintered to produce a single object using high power energy sources. Based on the kind of power source, there are different distinct PBF methods: selective laser melting (SLM) and selective laser sintering (SLS) [38]. PBF may be performed using a variety of material classes, including as metals, artificial polymers, and ceramics [38]. PBF 3D printing technique is as illustrated in figure 2.5 below:

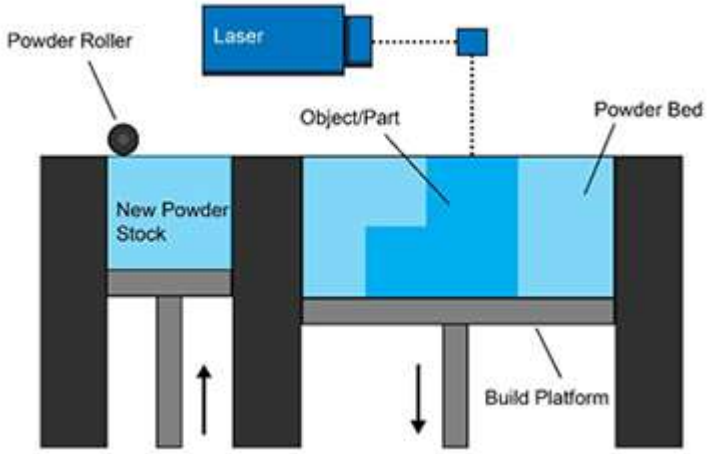


Figure 2.9 – Illustration of Power Bed Fusion 3D printing technique [38]

A layer of material, typically 0.1mm thick, is spread over the build platform. The first layer or first cross section of the model is fused by another layer. A roller spreads the new layer of powder across the previous layer. There is further fusion and addition of layers or cross sections. The entire model is created by repetition of the process [38].

2.4.7 Sheet Lamination

In contrast to other 3D printing techniques, sheet lamination uses sheets as the material feedstock rather than powder or wire. This process involves layer-by-layer stacking of precisely cut layers of metal or polymer that are then joined by diffusion to create the finished product [46]. Sheet Lamination technique of 3D printing is illustrated in figure 2.6 below:

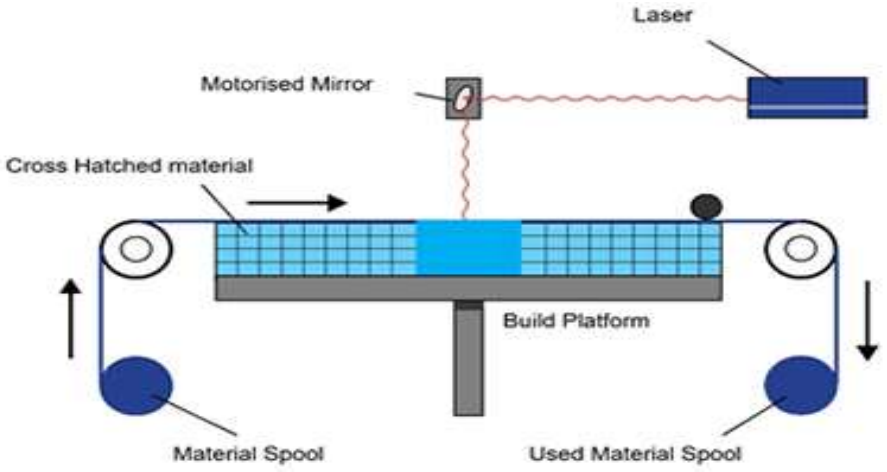


Figure 2.10 – Illustration of Sheet Lamination 3D printing technique [38]

On the cutting bed, the material is positioned in place, and then bonded in place over the previous layer using an adhesive. By the use of a knife or a laser, the required shape is the cut from the layer, and the subsequent layer is added [38].

2.4.8 Vat Photopolymerisation (VP)

VP is a 3D printing technique that creates 3D objects by curing photoreactive materials with a light source or regulated UV radiation. In this technique, thickness of the layer lowers the build platform from the top of the resin vat downwards, then a UV light cures the resin layer by layer. After this, there is a continuous movement of the platform downwards, and additional layers are built on top of the previous. In some machines a blade which moves between layers is used in order to provide a smooth resin base to build the next layer on. After completion, the vat is drained off the resin and the object removed. The figure below illustrates this technique:

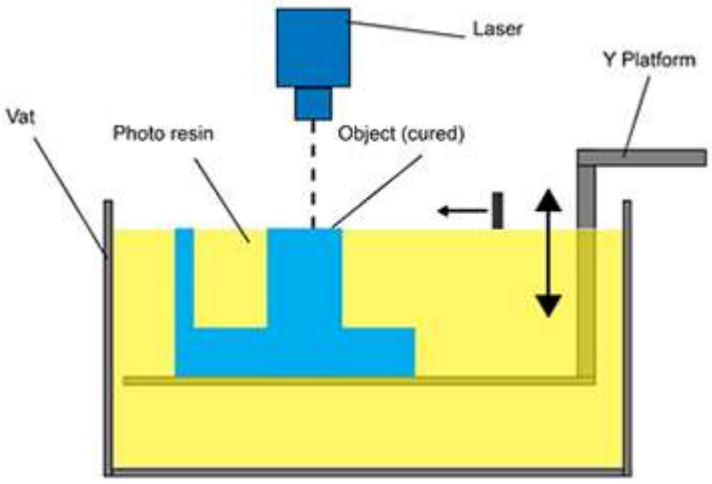


Figure 2.11 – Illustration of VAT photopolymerization 3D printing [38]

Examples of VP include stereolithography (SLA) and digital light processing (DLP). SLA employs ultraviolet light as its light source, whereas DLP uses an arc lamp [22]. The most accurate method, stereolithography, is utilised to produce high-quality prototypes with detailed and complicated geometrical designs. Additionally, it can create items with a good surface polish and a high dimensional tolerance. But the high resin usage drives up the price of stereolithography technology [38].

2.5 3D Printed PLA Microchambers

The manufacture of high-resolution polylactic acid (PLA) structures desirable for various biomedical applications, is made possible, in particular, by nozzle-based technologies such as 3D printing. 3D printed microchamber structures have appealing uses in biomedical applications and regenerative medicine. For example, such microchambers can be used as biodegradable templates for tissue regeneration, drug release structures, and also as 3D in-vitro platforms for studying cell response to various microchamber conditions [43].

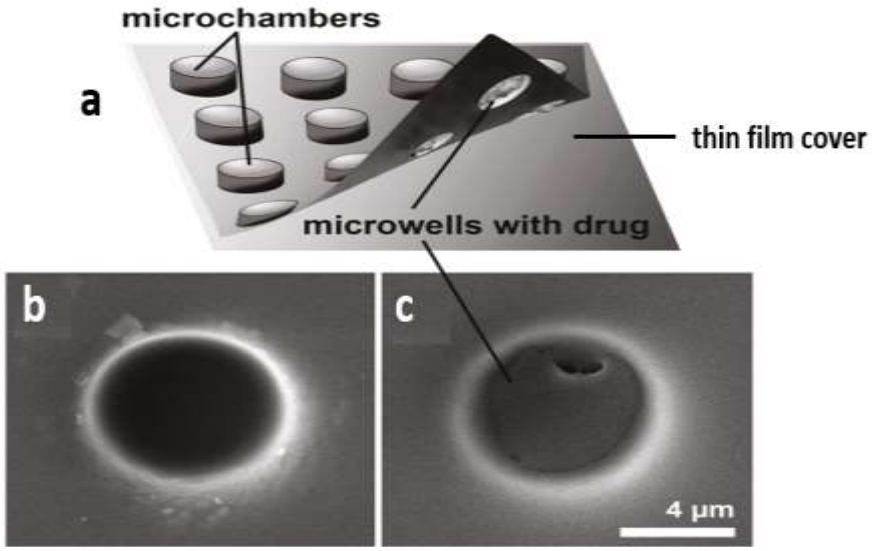
The material utilised to construct the 3D structure, its geometry and internal architecture, as well as the final surface qualities, all affect the operation of the microchamber, and are essential factors that determines the effectiveness of 3D printed microchambers. In addition to highlighting the significance of these factors in microchamber fabrication, this remark also highlights how adaptable these PLA microchambers are as a potential tool in regenerative medicine and other areas of medicine [43].

2.6 Microchambers and Drug Delivery

The application of microchambers in drug delivery is one of the most important issues of microchambers in pharmaceuticals.

There are two ways of synthesizing microchambers for drug delivery. The microchamber can be a in a form of a sphere (nanosphere or microsphere), which is a matrix in which the drug is uniformly scattered. It can also be in a form of a capsule (nanocapsule or microcapsule); which is a cavity in which the drug is embedded and surrounded by a polymeric membrane [44]. Polymeric microchambers that have substantial components made of PLA can be much more efficient in drug delivery [44].

In fabricating polymeric microchambers for drug release, the polymer's chemical properties must not interfere with the activity of the cargo. Also, the polymer's physical properties must be uniform and reproducible [46].



(a) Schematic overview, (b) SEM micrograph of the well structure from a microchamber (c) SEM micrograph of a single microwell filled with a drug

Figure 2.12 – Microchamber structure: [47].

2.7 PLA microchamber drug delievery in nuclear medicine and theranostics

In nuclear medicine and theranostics, PLA microchambers may be used as a drug release system to target cancer tissues while preventing radiation from spreading to surrounding healthy tissue.

Scientists have discovered that particular organs absorb particular chemicals. For instance, the thyroid absorbs iodine and the brain absorbs glucose. It is possible to monitor blood flow to the brain, liver, lung, heart, and kidneys and also to treat various forms of cancers in these organs using diagnostic and therapeutic radiopharmaceuticals respectively [48].

PLA microchambers used for this purpose and/or their cargo (radiopharmaceutical used) may have to be present in the body within a calculated

period for the release of the required amount of the radiopharmaceutical such that extended patient exposure to radiation may be avoided [49].

2.7.1 Radiopharmaceuticals for therapy

Therapeutic agents containing radioactive species work by concentrating radioactive substances in an organ or place for long enough to deliver a therapeutic dosage of radiation. Radioactive alpha and beta species can be employed to provide the therapeutic effect because they allow for extremely high ionization per length of trip [50, 51].

Radionuclide therapy offers the benefit of delivering a highly concentrated absorbed dose to the targeted tissues while sparing the healthy tissues in the surrounding area [51].

The best radiopharmaceutical (radioactive species) for therapy is determined by two considerations. Physical factors such as type of emission, energy radiation, daughter product, method of production, radiopharmaceutical purity, and effective halflife (a relationship between physical and biological half-lives) influence medical internal radiation dosimetry (MIRD) and linear energy transfer (LET); it should be very high for therapeutic radiopharmaceuticals. The second category comprises biological aspects such tissue targeting, tumor retention, stability, and toxicity [52].

Radiation therapy uses particles of radiation to kill or weaken cancer cells [53]. Similar to how it is used for diagnostic purposes, the radionuclide that produces the radiation are usually absorbed in a particular organ. Beta radiation frequently results in the death of cancer cells [53]. For instance, ^{177}Lutetium (^{177}Lu) is produced from ^{176}Ytterbium (^{176}Yb), and this forms ^{177}Yb after beta irradiation, and then quickly transforms back into ^{177}Lu, which is used as a theranostic radiopharmaceutical for advanced metastatic prostate cancer [53]. Also Non-Hodgkin lymphoma and liver cancer, for example, can be treated with ^{153}Samarium (^{153}Sm), ^{131}Iodine (^{131}I), ^{90}Yttrium (^{90}Y), and 32 Phosphorus (^{32}P) according to the same phenomenon of being localized in a particular organ when administered into

the patient. In certain circumstances, ^{103}Pd, ^{223}Ra and ^{131}Cs, are used as well [53], and the treatment is governed by the same phenomenon. The table below shows some major radionuclides used in cancer therapy and their main properties.

Table 2.1 – Main radionuclides used in therapy and their main properties [52]

Radionuclides	Half-Life	Radiation
177 Lu	6.73 days	B: 0.490 MeV
1535m	1.93 days	y and X-ray: 0.113 MeV (3%), 0.210 MeV (11%)
1311	8.02 days	B: 0.810 MeV (20%), 0.710 MeV (30%), 0.640 MeV (50%) and y photons of 103 keV (28%)
32 p	14.26 days	B: 0.607 MeV (89.6%), 0.334 MeV (7.23%) and y photons of 0.364 MeV (81.5%), 0.284 MeV (6.12%) 0.637 MeV (7.14%)
89 5r	50.53 days	B: 1.71 MeV (100%)
907	64.10 h	B: 1.501 MeV (99.99%)
117mSn	13.60 days	B: 2.280 MeV (99.98%)
169 Er	9.40 days	IT: y photons 0.158 MeV (86.4%) and 0.156 MeV (2.11%)
186 Re	3.72 days	B: 0.351 MeV (55%) and 0.342 MeV (45%)
188 Re	17.00 h	B: 1.071 MeV (70.99%), 0.934 MeV (21.54%) and y photon of 0.137 MeV (9.47%)
223 Ra	11.44 days	EC: X-ray of 50.32 KeV (3%)

Secondary c-radiation decay can be observed in several b-emitting radiopharmaceuticals. These radiopharmaceuticals, in this circumstance, allow not only therapy but also diagnosis and the completion of the whole terminology of theranostics [55]. Furthermore, radiopharmaceuticals that emit energetic a- or b-particles are most commonly used to treat dense and large tumors; otherwise, Auger electrons emitting radiopharmaceuticals are preferred for treating small clusters of cancer cells or small tumors due to their high-level cytotoxicity and short-range biological effectiveness [55, 56].

2.7.2 Radionuclides for Imaging

Imaging, using radionuclides is a one-of-a-kind approach that allows for molecular and sub-molecular imaging of an individual [57, 58]

It is always necessary to identify the target organ in order to select the right radiopharmaceutical to be used for the imaging [59, 60, 61]. The most used radionuclides for diagnosing (and treating) various human bodily organs are shown in the figure below:

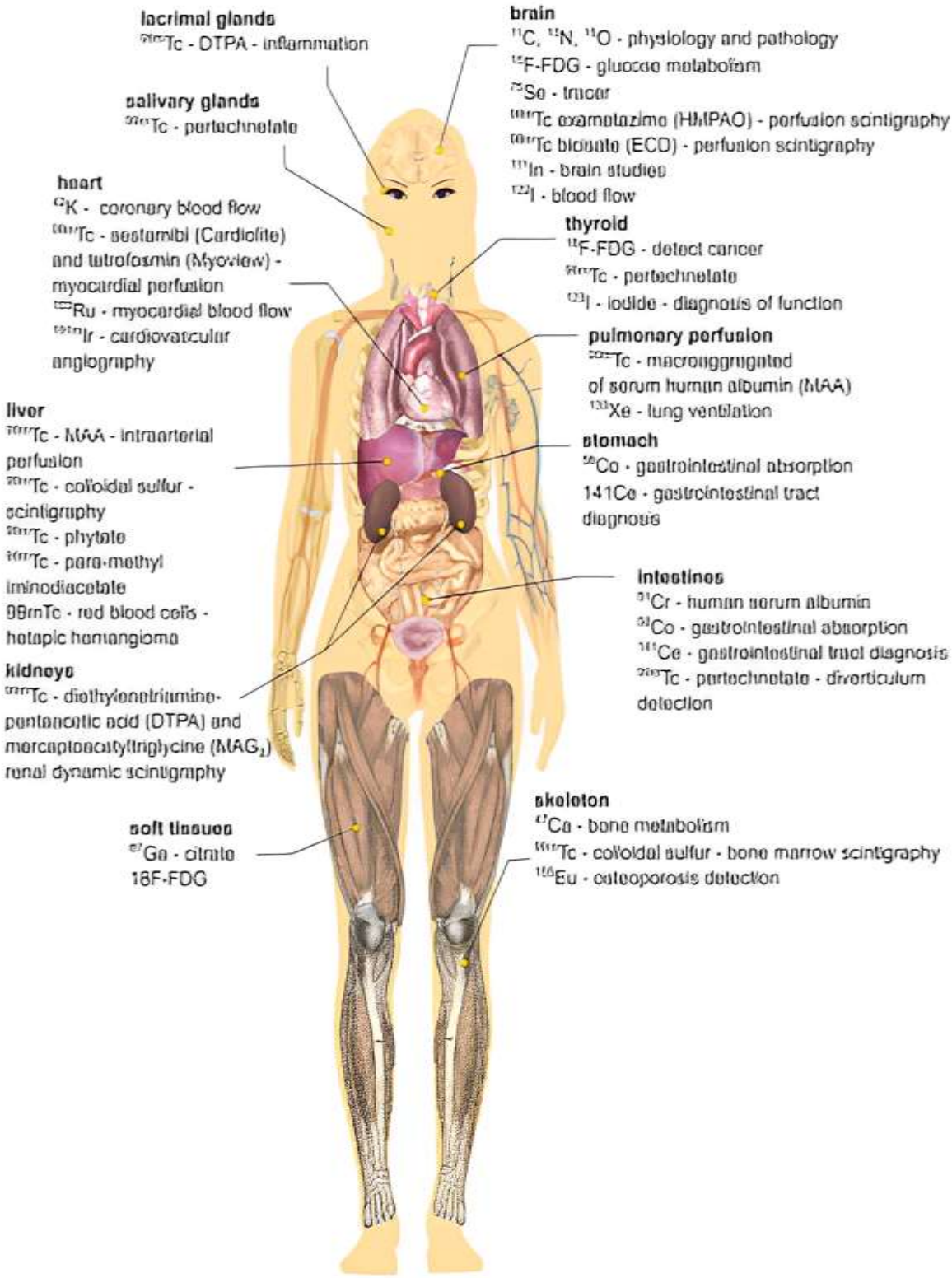


Figure 2.13. Different radiopharmaceuticals and target organs for cancer diagnostics and therapy [59, 60, 61]

In this way, selecting the appropriate radionuclide is a critical step in developing efficient radionuclides by taking into account a targeted and normative approach that takes into account physical half-life, decay mode, and emission parameters. The table below shows a summary of these properties and the respective diagnostic radiopharmaceuticals.

Table 2.2 – Main radionuclides used in imaging and their properties [52]

Radionuclide	**Production**	**Emission type**	**Half-life**	**Emax(c) (keV)**
^{131}I	^{130}I(n,c)^{131}Te(b)^{131}I	c (81.2%), b	8.0 days	284, 364, 637
^{67}Ga	^{68}Zn(n,p)^{67}Ga	C	78.3 h	93, 184, 300, 393
^{111}In	^{111}Cd(p,n)^{111}In	Auger, c	67.2 h	171, 245
^{123}I	^{121}Sn(a,2n)^{123}I	Auger, c	13.2 h	159
99mTc	99Mo/99mTc - generator	C	6.0 h	140
^{18}F	^{18}O(p, n)^{18}F	Positron	1.83 h	Eb Þ 635
^{64}Cu	^{64}NI(p, n)^{64}Cu	Positron	12.7 h	Eb Þ 656
^{76}Br	^{76}Se(p, n)^{76}Br	Positron	16.0 h	Eb Þ 3941
^{124}I	^{124}Te(p, n)^{124}I	Positron	100.2 h	Eb Þ 2134, 1533

2.8 Mechanism of targeting cancer cells with radiopharmaceuticals

When an extracellular molecule come into contact with cells, cells have certain proteins inside their mitochondria, or in their cytoplasm or on the cell membranes, known as receptors. The receptors receive signals specifically from the molecule, and then allows the molecule to bind or permeate into the cell [62].

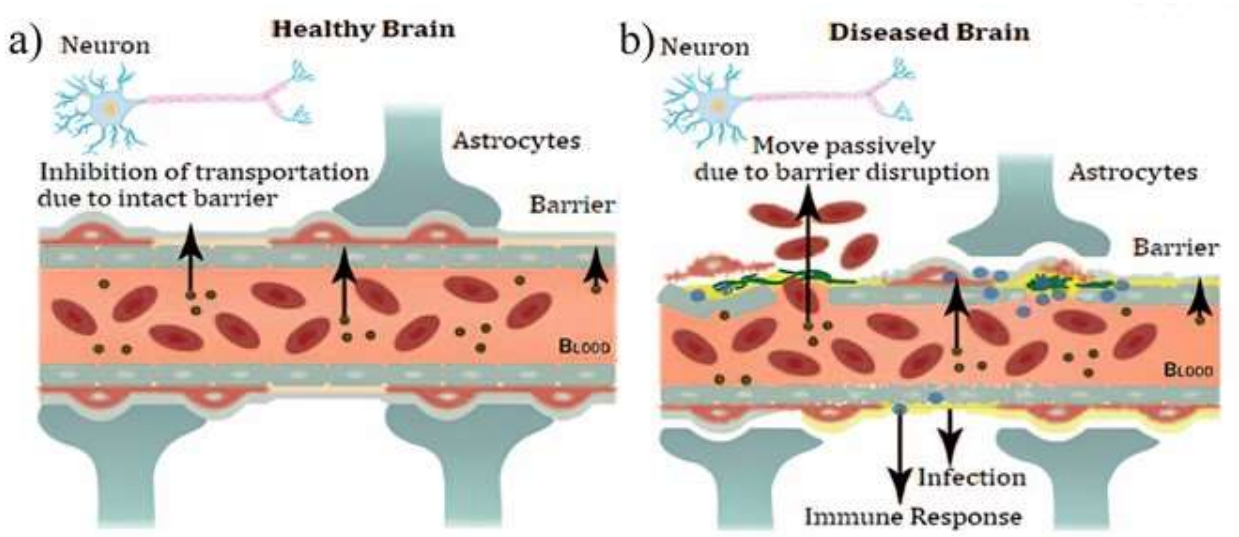
Unlike normal cells, specific cancer cells have a unique set of cell surface receptors that serve as potential targets for tumour theranostics. Specific radiopharmaceuticals can, thus, be synthesized to target these receptors for the purpose of diagnostics or treatment of the cancer [63].

For the purpose of easy transportation via the bloodstream and targeting of the specific cancer cell, radiopharmaceuticals are usually binded with radiolabeled

ligands to target only specific cancer cells with respect to the special set of receptors in the cancerous cells [64]. Once the ligand binds with the cancer cell, there is neurotransmission between the receptor of the cell and the brain, which allows for the binding or permeation of the cell [65] by the particular radiopharmaceutical.

Usually, for radiolabelled complexes, whiles the ligand is designed to be hydrophilic, the radiopharmaceutical itself is lipophilic, therefore since blood is hydrophilic and cells (cancer cells) are hydrophobic by nature, the hydrophilic ligand easily transports the hydrophobic/lipophilic radiopharmaceutical via the bloodstream unto the cell [66], and at this point, the radiopharmaceutical permeates the membrane of the cancer cell, or binds with the cancer cell to produce a diagnostic or therapeutic effect [67]. This mechanism does not destroy adjacent normal cells since normal cells do not express such receptors that will cause the radiopharmaceutical to bind with the cell [67].

A typical radiopharmaceutical for brain imaging is 99mTc-DTPA. It is designed to target folate receptors which are overexpressed in cancer cells of the brain [68]. When administered, it cannot permeate across the cell membranes of normal brain cells easily because these cells do not express the receptors needed to receive signals from the 99mTc-DTPA radiopharmaceutical (See Figure 1(A)). However, when the cells become cancerous, they overexpress receptors that disrupts the cell membrane of the cancerous cells to allow for the passive movement of 99mTc-DTPA radiopharmaceutical into the cell, which subsequently accumulate in the infected area of brain (See Figure 1(B)) to allow for imaging [69]. The figure below shows this illustration:



(a) Illustration of intact barrier in the brain cells that disallows 99mTc-DTPA to permeate normal brain cells, (b) disruption of the cell mebrane physiology to allow for the passive movement of 99mTc-DTPA in abnormal (cancerous) brain cells as a result of overexpression of folate receptors

Figure 2.14 – Mechnanism by which radiopharmaceuticals target cancerous cells and spares normal cells [69]

99mTc-DTPA has a biologic half-life of 1–2 hours [69]. With 70 minutes being the halftime for clearance of plasma, in 24 hours the urinary system eliminates 90% of the tracer from the body [69].

TASK FOR SECTION
«FINANCIAL MANAGEMENT, RESOURCE EFFICIENCY AND RESOURCE SAVING»

To the student:

Group	Full name
0AM1M	Awuah Collins

School	School of Nuclear Technology Engineering	**Division**	Nuclear Fuel Cycle
Degree	Master Degree	**Educational Program**	14.04.02 Nuclear Physics and Technology

Input data to the section «Financial management, resource efficiency and resource saving»:	
1. *Resource cost of scientific and technical research (STR): material and technical, energetic, financial and human*	– Salary costs – 259 thousand rubles – STR budget – 1.112.819,65 rubles
2. *Expenditure rates and expenditure standards for resources*	– Electricity costs – 5,8 rub per 1 kW
3. *Current tax system, tax rates, charges rates, discounting rates and interest rates*	– Labor tax – 27,1 %; – Overhead costs – 30%;
The list of subjects to study, design and develop:	
1. *Assessment of commercial and innovative potential of STR*	– comparative analysis with other researches in this field;
2. *Development of charter for scientific-research project*	– SWOT-analysis;
3. *Scheduling of STR management process: structure and timeline, budget, risk management*	– calculation of working hours for project; – creation of the time schedule of the project; – calculation of scientific and technical research budget;
4. *Resource efficiency*	– integral indicator of resource efficiency for the developed project.
A list of graphic material *(with list of mandatory blueprints):*	
1. *Competitiveness analysis* 2. *SWOT- analysis* 3. *Gantt chart and budget of scientific research* 4. *Assessment of resource, financial and economic efficiency of STR* 5. *Potential risks*	

Date of issue of the task for the section according to the schedule	

Task issued by adviser:

Position	Full name	Scientific degree, rank	Signature	Date
Associate professor	E.V. Menshikova	PhD		

The task was accepted by the student:

Group	Full name	Signature	Date
0AM1M	Awuah Collins		

5.0 FINANCIAL MANAGEMENT

In modern times, the expectations with regards to scientific and engineering research are ascertained not on just the level of it discovery, but rather considered on a commercial scale in the development of the sector involved. Moreover, being able to draw a commercial plan for a discovery or invention helps to search for sources of funding for the research and the commercializing the results. The aspect of commercialization seems to be more important since the commercial attractiveness of the scientific research should not be based on just exceeding technical parameters over the already existing ones, but also on how efficient the developer will be appreciated for his or her work as demanded by the market. Taking into considerations the price, customer satisfaction, project budget and many more helps to measure the worth of the research and can promote future ongoing research in the field as well. Hence, the aim of the section "Financial Management, Resource Efficiency and Resource savings" is to measure the prospects and success of a research project in order to design a mechanism for managing and acquiring special supports during the implementation stage of the project to enhance productivity. (Paramasivian, n.d).

This study aims at inventing a technology made of 3D printed PLA microchamber structures which may be used as used as biomedical implants for drug release in living tissues. In nuclear medicine, for instance, radiopharmaceuticals, this technology can be used as a new technology for systemic radiation therapy: Whiles the polymer keeps on degrading, radiopharmacetical filled in the microchamber structure gets released into the surrounding medium and targets cancer cells.

Apart from biomedical applications, in environmental and water management, these drug release systems can be used for waste water purification and water decontamination as the polymer degrades and releases chemicals that were already filled in the structure to neutralize contaminants in contaminated water.

5.1 Potential consumers of the research results

The target consumers of this project work can be the government facilities, private operators, educational and scientific research centers whose scope of work is in relation with biomedical implants or water technology. Nevertheless, this study can be useful in further scientific research in many other scientific disciplines; including the aspects of nuclear technologies.

5.1.1 Target market

The target market includes consumers interested in applying this technology in their industries; including hospitals, medical and biomedical facilities, research institutions and environmental protection facilities.

Particularly in nuclear medicine, the target market for the application of this technology may include cancer hospitals/clinics (radiotherapy and oncology departments) and research institutions interested in oncology and systemic radiation therapy.

The results of this research would be useful for further research; such as in vivo, and clinical trials to ascertain the feasibility of the technology in living tissues. Again, this study can be employed by environmental protection experts in neutralizing contaminants in contaminated water.

5.2 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.

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 the research and competitors is evaluated for each indicator on a five-point scale, where 1 is the weakest position and 5 is the strongest. The weights of indicators determined in the amount should be 1. Analysis of competitive technical solutions is determined by the formula:

$$C = \sum P_i \cdot W_i,$$

where C – the competitiveness of research or a competitor;

W_i– criterion weight;

P_i – point of i-th criteria.

For the competitive analysis of technical solution in relation to this study can many depending on how this technology will be used. However, for the purpose of this thesis, this analysis will be limited to its possible applications in nuclear medicine.

In nuclear medicine, the competitors to this novel drug release technology of 3D printed PLA microchamber structures can be the traditional means of systemic radiation therapy.

Traditional means of systemic radiation therapy involves the injection or swallowing of a radioactive substance, such as, radioactive iodine or a radioactively labelled monoclonal antibody, after which the drug travels through the blood to target and kill tumor cells in the affected organ [81]. In this this method of cancer treatment, excipients that may be added to the drug can reduce the potency of the drug [19]. Also, the patient will be required to take frequently take several shots of injections or swallowing of the drug until the cancer is totally treated, which can take up to several months. Whiles the inconvenience that comes with this method can cause the patient to stop the medication in general, other patients may potentially skip the medication, which may affect the desirable results from this method.

If the technology of 3D printed PLA microchamber structures are used in systemic radiation therapy, excipients may not be necessary in the drug design, keeping the potency of the drug intact. Again, this will be a one-off surgical process that will bring an end to the inconvenience of taking drugs and its associated issues, such as forgetfulness or prescription abandonment; both of which may affect the treatment process.

Table 5.1 – Evaluation map for comparison of competitive technical solutions

Evaluation criteria	**Criterion Weight** *Wi*	**Points**			**Competitiveness**		
		P_{pol}	P_{drg}	P_{pla}	C_{pol}	C_{drg}	C_{pla}
1	2	3	4	5	6	7	*8*
Technical criteria for evaluating resource efficiency							
1. Noise immunity	0.06	44	22	55	00.24	00.12	00.30
2. Minimum dose load on critical organs	0.20	44	33	44	00.80	00.60	00.80
3. Ease of operation	0.04	33	22	44	00.12	00.08	00.16
4. Possibility to set the required size	0.25	33	33	55	00.75	00.75	10.25
5. Tissue equivalence	0.20	44	44	55	00.80	00.80	10.00
Economic criteria for performance evaluation							
1. Development cost	0.10	44	55	55	00.40	00.50	00.50
2. Estimated service life	0.10	55	33	44	00.50	00.30	00.40
3. Research funding	0.05	44	44	44	00.20	00.20	00.20
Total	**1**	**--**	**--**	**--**	**30.81**	**30.35**	**40.61**

Legend

P_{pol}: Points for other polymers

P_{drg}: Points for model drug used

P_{pla}: Points for polylactic acid

This analysis suggests that the study is effective because it provides acceptable quality results. Further investment in this development can be considered reasonable. Hence, the technology of 3D printed microchamber structures can be used as an alternative for systemic radiation therapy.

5.3 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. The second stage consists of identifying the compatibility of the strengths and weaknesses of the project with the external environmental conditions. This compatibility or incompatibility should help to identify what strategic changes are needed.

The description of each step for executing the SWOT analysis should be accurate and following the meaning of each topic, as;

Strengths: Factors that characterize the competitive side of the research project. It shows a specific advantage or a special resource in terms of competition, that means is the resources or opportunities for achieving the main objective.

Weaknesses: Limitation of a research project that hinders the achievement of its objectives, or basically the insufficient capabilities or resources compared to competitors.

Opportunities: Occurrence of environmental situations that may interfere in the project, which may improve the competitive position of the project. Threat: Situation not expected and not desired, may be destructive or threatening for the project competitiveness. All analysis is presented in the table below:

Table 5.2 – SWOT analysis

	Strengths: S1. Environmental friendliness of manufacturing technology; S2. Application of modern additive technologies for the manufacture of polylactic acid microchambers S3. Innovative method to improve drug delivery	**Weaknesses:** W1. Longer time frame of research. W2. Research demanded timely measurements W3. Research involved extensive knowledge in various aspects of science
Opportunities: O1. Availability of laboratories and equipment for the study O2. Supportive supervisor and other colleagues O3. Opportunity to apply previous scientific knowledge and laboratory skills in the study	***Strategy which based on strengths and opportunities:*** 1. Interdisciplinary knowledge in designing and carrying out the study. 2. Teamwork and collaborative skills in carrying out lab tasks 3. Knowledge and skills in laboratory works	***Strategy which based on weaknesses and opportunities:*** 1. Daily monitoring of experimental set-up 2. Timely measurements of desired parameters 3. Extensive research on various aspects of the study
Threats: T1. Inadequate literature about the study T2. Study was novel and its success was not predictable. T3. Research involved the use of chemicals which may be toxic	***Strategy which based on strengths and threats:*** 1. Student utilized research skills in searching for related literature 2. Student was creative and innovative in achieving research goals 3. Student was cautious, and also applied safety precautions in handling chemicals in the laboratory	***Strategy which based on weaknesses and threats:*** 1. Deeper search and consultation of several resource materials and persons 2. Time management and diligence in carrying out tasks 3. Student read and applied information of the handling and storage of various chemicals used in the research

Based on the results of the analysis of this matrix, it can be concluded that the difficulties and challenges that this research may face are offset by the existing strengths of the research.

5.4 Project Initiation

In the initiation processes, the initial purpose and content of the project are determined. The initial financial resources are fixed. The internal and external stakeholders of the project are determined, which will interact and influence the overall result of the research project are determined.

5.5 Project Goals and Results

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. Information about the stakeholders of the project is presented in the table below.

Table 5.3 - Stakeholders of the project

Stakeholders of the project	**Stakeholders of the project expectations**
Biomedical Engineering Industries	Efficient and fit for purpose Marketable technology Versatile technology
Hospitals	Keep patients from prescription abandonment Maintains drug efficacy Easier treatment method
Research Institutions	Versatile technology Technology has prospects for further research Technology can be a tool for other discoveries
Tomsk Polytechnic University (TPU)	The acquired results could be a ground breaking finding for research in TPU.

Information about the hierarchy of project goals and criteria for achieving goals is given in table 5.4.

Table 5.4 - Project goals and results

Project goals	Assessed the dynamics of degradation and release of cargo which was already filled in 3D printed PLA microchamber structures in a circulating medium with basic physical conditions similar to that of a human body
Expected results of the project	Based on the conducted research, the thin film PLA cover of 3D printed microchamber structures gradually released the cargo into the circulating medium upon gradual degradation and opening of the microwells of the structure.
Acceptance criteria of the project result	Well hypothesized and well conducted research with reproducible results
Requirements to the project results	The project is completed on time.
	The results will be used for further studies such as in vivo studies and clinical trials, and then may be approved and commercialized as a technology in the treatment of medical conditions

5.6 Organizational Structure of the Project

The organizational structure of the project involves all participants or people who participated in the research work, the number of hours they spent and the roles they played in the research. In this research work, there were two participants. The organizational structure of the project is presented in the table below.

Table 5.5 - Project Working Group

№	Name	Role in the Project	Functions	Hours spent (working days × 6 hours)
1	Rutkowski Sven	Scientific Supervisor	Coordination of work activities, guidance and assistance in project implementation. Verification of results obtained.	168
2	Awuah Collins	Student	Work on project implementation.	2436
Total:				**4404**

Assumptions and constraints

Limitations and assumptions are summarized in table below.

Table 5.6 - Limitations and assumptions

Factor	Limitations/assumptions
1. Project budget	3195136,15
1.1 Source of budgeting	Research grants and TPU
2. Project timeline:	25 June, 2022 – 31 March, 2023
2.1 Date of approval of the project management plan	11 May, 2022
2.2 Project completion date	17 May, 2023
3. Other	-

As a result of the initialization of the project, the goals and expected results were formulated, the stakeholders of the project and the financial framework were

identified, which is very important for the successful completion of the project and its implementation.

5.7 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.

5.7.1 Hierarchical structure of project activities

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.

5.7.2 Deadlines for the project stages

Project Schedule

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

Table 5.7 – Project duration and timeline for various processes.

Job title	**Duration, working days**		**Start date**	**Date of completion**	**Participants**
	Student	**Supervisor**			
Drawing up the technical assignment	-	1	16/12/2021	16/12/2021	Scientific supervisor
Literature review and supervisor's corrections	14	2	24/12/2021	07/01/2022	Student, Scientific Supervisor
Experimental design	5	1	17/02/2022	22/02/2022	Scientific supervisor, student
Gathering of apparatus, equipment and materials, labs and personnel	30	2	23/03/2022	22/04/2022	Scientific supervisor, student

Building of experimental set-up and supervisor's advice	20	1	25/06/2022	14/07/2022	Student, Scientific supervisor
Laboratory experiments and supervisor's advice	240	5	15/07/2022	31/03/2023	Student, Scientific supervisor
Processing of experimental data and supervisor's corrections	30	4	30/04/2022	06/05/2022	Student, Scientific supervisor
Analysis of lab results and supervisor's advice	30	1	09/05/2022	11/05/2022	Student, Scientific supervisor
Writing of thesis and supervisor's corrections	30	7	14/05/2022	23/05/2022	Student, Scientific supervisor
Defense Preparation and supervisor's corrections	7	2	24/05/2022	31/05/2022	Student, Scientific supervisor
Total	**406**	**28**			

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 - Gantt chart showing the timeline of the project

№	Activities	Participants	T_c, Days	Duration of the project											
				December 2021 to March 2022			April 2022 to July 2022			September 2022 to December 2022			January 2023 to May 2023		
				1	2	3	1	2	3	1	2	3	1	2	3
1	Drawing up the technical assignment	Scientific supervisor	7												
2	Literature review and supervisor's corrections	Student	14												
3	Experimental design	Scientific supervisor, student	5												

4	Gathering of apparatus, equipment and materials, labs and personnel	Scientific supervisor	30	
5	Building of experimental set-up and supervisor's advice	Student, Scientific supervisor	20	
6	Laboratory experiments and supervisor's advice	Student Scientific Supervisor,	240	
7	Processing of experimental data and supervisor's corrections	Student, Scientific supervisor	30	
8	Analysis of lab results	Student	30	
9	Writing of thesis and supervisor's corrections	Student, Scientific supervisor,	30	
10	Defense Preparation and supervisor's Guidance	Student, Scientific supervisor,	7	

 - Scientific supervisor

 - Student

Thus, the duration of the task performed by the student and the supervisor. In general, the duration of work in calendar days for a student is 83 days, and for a supervisor is 26 days. The total number of working days is 91.

5.8 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 planned costs are grouped according to the items presented in the table below:

Table 5.9 – Grouping costs by articles

Name	**Cost, rubles**
1. Material costs	419475.00
2. Equipment depreciation costs	24119.13
3. Basic salary	498037.4
4. Additional salary	49803.74
5. Labor tax	148464.95
6. Overhead	164352.35
7. Other direct costs	48406.80
Total	**1352659.37**

This article includes the costs of purchasing all types of materials, components, and semi-finished products necessary to perform work on this topic. The amount of material assets required is determined according to the consumption rates.

The project budget fully reflects all types of planned expenditures necessary for the implementation of the project. To find the final cost value, all calculated costs for individual items related to the manager and the student are summed. These costs include office supplies, printing costs, various equipment required for paperwork, and all costs that are associated with the purchase of special equipment (for example, instruments, instrumentation, stands, devices and mechanisms) necessary for the project.

Calculation of material costs

The calculation of material costs is carried out according to the formula:

$$C_m = (1 + k_T) \cdot \sum_{i=1}^{m} P_i \cdot N_{consi}$$

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).

Table 5.10 – Material costs

Name	Unit per measurement	Quantity (units, amount)	Price (rubles)
PLA spool	Unit	1	2500
PLA granules (Biomedical)	Packet	1 kg	390000
Rhodamine B	Unit	25 g	1000
Chloroform	Bottle	500 mL	6000
Total cost of materials			399500
Total transportation and purchasing costs (5%)			19975
Total			**419475**

Costs of special equipment

This work includes all the costs associated with the acquirement of special equipment necessary to carry out work on a particular topic. The cost of depreciation of equipment is calculated by the equation (5.2):

$$A = \frac{C_{in} \cdot H_a}{100} = \frac{C_{in}}{T_{serv}}, \quad (5.2)$$

A – annual amount of depreciation;

C_{in} – initial cost of the equipment;

$H_a = \frac{100}{T_{serv}}$ – rate of depreciation;

T_{serv} – life expectancy.

Table 5.11 – Depreciation of special equipment (+software)

№	Equipment identification	Total cost of equipment, rub	Life expectancy, year	Days of operation	Depreciation for the duration of the project, rub
1.	Ultimaker 3D-printer	600000	10	15	2465.75
2	Motic optical microscope with computer	327000	10	20	1791.78
3	Thermostat	132000	10	270	9764.38
4	Fluorat Fluorescence spectrometer with computer	390000	10	70	7583.33
5	Atomic force microscope with computer	520000	10	15	2166.67
6	Contact angle device with computer	250000	10	5	347.22
Total:		**2219000**	**Total:**		**24119.13**

Basic salary

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 equation:

$$S_b = S_d \cdot T_w, \quad (5.3)$$

where S_b – basic salary per participant;

T_w – the duration of the work performed by the scientific and technical worker, working days;

S_d – the average daily salary of a participant, rub.

The average daily salary is calculated by the formula:

$$S_d = \frac{S_m \cdot M}{F_v}, \quad (5.4)$$

where S_m – monthly salary of a participant, rub;

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

at holiday in 48 days, M = 10,4 months, 6 day per week;

F_v – valid annual fund of working time of scientific and technical personnel (251 days).

Table 5.12 – 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 - isolation period - sick absence	48
The valid annual fund of working time	251

Monthly salary is calculated by equation:

$$S_{month} = S_{base} \cdot (k_{premium} + k_{bonus}) \cdot k_{reg}, \quad (4.5)$$

where S_{base} – base salary, rubles;

$k_{premium}$ – premium rate;

k_{bonus} – bonus rate;

k_{reg} – regional rate.

The results of base salary calculation are presented in the table below:

Table 5.13 – Calculation of the base salaries

Performers	S_{base}, **rubles**	$k_{premium}$	k_{bonus}	k_{reg}	S_{month}, **rub.**	S_d, **rub.**	T_w, **work days**	S_{base}, **rub.**
(Supervisor) Sven Rutkowski, Associate professor	39300	-	-	1,3	51090.00	2116.90	28	59273.20
(Master's student) Awuah Collins	20064				26083.20	1080.70	406	438764.20
Total:								**498037.4**

Additional salary

This point includes the number 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:

$$S_{add} = k_{extra} \cdot S_{base}, \quad (5.6)$$

where S_{add} – additional salary, rubles;

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

S_{base} – base salary, rubles.

Table 5.14 – Additional salary

	Supervisor	**Master's student**
Salary, rubles	59273.20	438764.20
Additional salary, rubles	5927.32	43876.42
Sub Total	***65200.52***	***482640.62***
Total:	**547841.14**	

Labor tax

Tax to extra-budgetary funds is 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 equation:

$$P_{social} = k_b \cdot (S_{base} + S_{add}), \quad (5.7)$$

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 5.15 – Labor tax

	Supervisor	**Master's student**
Coefficient of deductions	0.271	
Salary (basic and additional), rubles	65200.52	482640.62
Labor tax, rubles	17669.34	130795.61
Total labor tax	**148464.95**	

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 base and additional salary of employees.

Overhead is calculated according to the equation:

$$C_{ov} = k_{ov} \cdot (S_{base} + S_{add}), \quad (4.8)$$

where k_{ov} – overhead rate.

Table 5.16 – Overhead costs

	Supervisor	**Master's student**
Overhead rate	0.3	
Salary, rubles	65200.52	482640.62
Overhead, rubles	19560.16	144792.19
Total:	**164352.35**	

5.8.1 Other Direct Costs

Energy costs for equipment are calculated by the formula:

$$C = P_{el} \cdot P \cdot F_{eq},$$

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

P − power of equipment, kW;

F_{eq} − equipment usage time, hours.

Table 5.17 – Other direct costs

Equipment	Power rates, kWh	Power of equipment, kW	Equipment usage time, hr	Energy cost, rubles
Motic optical microscope with computer	5.8	0.5	492	1426,80
Peristaltic pump	5.8	0.5	6480	18792,00
Thermostat	5.8	0.5	6480	18792,00
Fluorat Fluorescence spectrometer with computer	11.6	1.0	270	3132,00
Atomic force microscope with computer	11.6	1.0	180	2088,00
Contact angle device with computer	11.6	1.0	180	2088,00
3D printer with computer	11.6	1.0	180	2088,00
Total				**48406.80**

5.9 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.

5.10 Evaluation of the Absolute Effectiveness of the Project

Determination of efficiency is based on the calculation of the integral indicator of the effectiveness of scientific research. Its finding is associated with the definition of two weighted average values: financial efficiency and resource efficiency.

The integral indicator of the financial efficiency of a scientific study is obtained in the course of estimating the budget for the costs of three (or more) variants of the execution of a scientific study. For this, the largest integral indicator of the implementation of the technical problem is taken as the calculation base (as the denominator), with which the financial values for all the options are correlated.

The integral financial measure of development is defined as:

$$I_f^p = \frac{F_{p_i}}{F_{max}}$$

Where I_f^p – integral financial indicator of current project;

F_{p_i} – price of i-th variant of execution;

F_{max} – the maximum cost of execution of the research project (including analogues).

In this project, $F_{p_i} = 1112819{,}65$. It is assumed that, $F_{max} = 1200000{,}00$.

Hence, the integral financial indicator is:

$$I_f^p = \frac{1112819{,}65}{1200000{,}00} = 0{,}93$$

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). The integral financial indicator is equal to 0,93. This means that, the corresponding numerical reduction in the cost of development times is 0,93.

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

$$I_m^a = \sum_{i=1}^{n} a_i b_i^a \qquad I_m^p = \sum_{i=1}^{n} a_i b_i^p$$

where I_m – integral indicator of resource efficiency for the i-th version of the development;

a_i– the weighting factor of the i-th version of the development;

b_i^a, b_i^p– score rating of the i-th version of the development, is established by an expert on the selected rating scale;

n – number of comparison parameters.

The calculation of the integral indicator of resource efficiency is presented in the form of table as shown below:

Table 5.18 – Evaluation of the performance of the project

Criteria	**Weight criterion**	**Points**	
		I_m^p	I_m^a
1. Risk of malfunctioning of drug release implant	0,18	5	3
2. Dose homogeneity	0,13	4	4
3. Dose on organs at risk	0,2	5	5
4. Effectiveness of drug release	0,14	4	4
5. Risk of treatment failure	0,1	5	4
Economic criteria for performance evaluation			
1. Competitive methods	0,08	4	4
2. Expected lifecycle	0,07	5	5
3. Development cost	0,1	4	4
Total	**1**	**4,55**	**4,09**

$$I^p{}_m = \sum_{i=1}^{n} a_i b_i^a$$

$$I^p{}_m = (0{,}18 \times 5) + (0{,}13 \times 4) + (0{,}2 \times 5) + (0{,}14 \times 4) + (0{,}1 \times 5) + (0{,}08 \times 4) + (0{,}07 \times 5) + (0{,}1 \times 4)$$

$$I^p{}_m = 4{,}55$$

$$I^a{}_m = \sum_{i=1}^{n} a_i b_i^a$$

$$I^a{}_m = (0{,}18 \times 3) + (0{,}13 \times 4) + (0{,}2 \times 5) + (0{,}14 \times 4) + (0{,}1 \times 4) + (0{,}08 \times 4) + (0{,}07 \times 5) + (0{,}1 \times 4)$$

$$I^a{}_m = 4{,}09$$

The integral efficiency indicator of the scientific research project (I^p_{fin}) and of the analog (I^a_{fin}) is determined according to the formula of the integral basis of the financial integral resource efficiency:

$$I^a_{fin} = \frac{I^a_m}{I^a_f};\ I^p_{fin} = \frac{I^p_m}{I^p_f};$$

$$I^a_{fin} = \frac{4{,}09}{1} = 4{,}09;\ I^p_{fin} = \frac{4{,}55}{0{,}93} = 4{,}89$$

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

$$E_{av} = \frac{I^p_{fin}}{I^a_{fin}}$$

Where E_{av} - is the comparative project efficiency; I^p_{fin} - integral indicator of project; I^a_{fin} - integral indicator of the analog.

$$E_{av} = \frac{4{,}89}{4{,}09} = 1{,}20$$

Thus, the effectiveness of the development is presented in table 5.19.

Table 5.19 – Efficiency of development

Indicators	**Points**	**Analog**
	Project	**Conventional drug delivery**
Integral financial indicator	0,93	1
Integral resource efficiency indicator	4,55	4,09
Integral efficiency indicator	4,89	4,09

Comparison of the values of integral performance indicators allows scientific supervisors and students to understand and choose a more effective solution to the technical problem based on the financial and resource efficiency. Based on the calculation of the integral indicator with the definition of two weighted average values: financial indicator and resource efficiency of scientific research, we can conclude that the comparative assessment of the current project is relatively higher than analog; which involves conventional or traditional means of radiotherapy.

5.11 Chapter Conclusion

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

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.

TASK FOR SECTION "SOCIAL RESPONSIBILITY"

To the student:

Group	Full name
0AM1M	Awuah Collins

School	SNTE	Research and Education Center	DNFC
Level of education	Masters	Direction/ specialty	14.04.02 Nuclear Physics and Technology / Nuclear Medicine

Subject FQW:

Initial data for the section "Social responsibility":	
1. Characteristics of the research object (substance, material, device, algorithm, technique, working area) and its scope	- a model for the registration of γ-quanta by a system of NaI (Tl) detectors formed in the study of reactions of synthesis of light nuclei; experimental nuclear physics
List of questions to be researched, designed and developed:	
1. Legal and organizational security issues: - special (typical for the operation of the research object, the projected working area) legal norms of labor legislation; -organizational measures for the layout of the working area.	- Federal law of 09 Jan. 1996 No. 3-F3 "On radiation safety of the population" - SanPiN 2.2.2 / 2.4.2732-10 "Hygienic requirements for personal computers and work organization - SanPiN 1.2.3685-21 - other
2. Industrial safety: **2.1. Analysis of the identified harmful and dangerous factors** **2.2. Rationale for mitigation measures**	Harmful and dangerous factors: - deviation of microclimate indicators; - increased noise level; - insufficient illumination of the working area; - increased level of electromagnetic radiation; - psychophysiological factors; - increased level of ionizing radiation; - danger of electric shock.
3. Safety in emergencies:	- selection and description of a typical emergency - fire; - justification of measures to prevent emergencies; - the order of actions in the event of an emergency.

Date of issue of the task for the section on a line chart	13.03.2023

The assignment was given by the consultant:

Position	Full name	Academic degree, title	Signature	Date
Associate Professor	PerederindYuriy Vladimirovich	Ph.D		

The student accepted the assignment:

Group	Full name	Signature	Date
	Awuah Collins		

6. SOCIAL RESPONSIBILITY

This research was conducted at the Weinberg Research Center of the Tomsk Polytechnic University – Room 019 in the Academic Building 19 of the Tomsk Polytechnic University, Usova 4 Street, Tomsk, Russia.

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 processing the acquisition data with sophisticated software and computer-based programs. Hence, the workplace involved an enclosed room stocked with high speed computers and other gadgets to aid in the processing of data and necessary simulations.

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 [82]. 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.

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.

6.1 Legal and Organizational Items in Providing Safety

The Constitution of the Russian Federation is the basis of the legislative provision of safety. The legal basis for ensuring safety of life consists of relevant laws, regulations, as well as subordinate legislation. Laws and other legal acts adopted in the Russian Federation must not contradict the Constitution of the Russian Federation.

The legal basis for environmental safety in the country and ensuring necessary working conditions is Federal Law № 52 «On the sanitary and epidemiological welfare of the population» (1999) [83]. The most important legislative act aimed at ensuring environmental safety is the Law of the Russian Federation «On Environmental Safety» 4 (2002) [83].

The legal basis for organizing work in emergency situations and mitigating their consequences is provided by the laws of the Russian Federation; such as laws on Fire Safety [84].

The main legislative act on occupational safety and health is the Labor Code of the Russian Federation, which establishes the basic legal guarantees in the field of occupational safety and health. Occupational safety is a system of legislative, socio-economic, organizational, technological, hygienic and therapeutic and prophylactic measures and tools that ensure the safety, preservation of health and human performance in the work process [85].

Guarantees and compensations for harmful working conditions are ways of social protection of production workers that have a negative impact on their health. The state establishes various guarantees and compensations for workers, depending on the hazard category of the production:

- reduced working hours (working hours are limited to 30 hours per week in the presence of hazardous working conditions);
- additional annual leave (additional 7 days of annual leave, which is paid by the employer);

- extra pay for hazardous working conditions (an increase in wages of at least 4% of the employee's salary);
- early retirement;
- special and therapeutic meals (employees receive free therapeutic and prophylactic meals, which are aimed at maintaining health and prevention of occupational diseases);
- compulsory periodic medical examinations at the expense of employer [82].

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.

Basic ergonomic requirements for the correct location and arrangement of researcher's workplace: the workplace when working with a PC should be at least 4,2 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 nothing 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 [85].

6.2 Occupational Safety

In this section, harmful and hazardous factors that may occur during research in the laboratory, during the development or operation of the designed solution are analyzed. The analysis will be based on hazardous factors that may occur during the research at the B.P. Weinberg Research Center of the Tomsk Polytechnic University – Room 019 in the Academic Building 19 of the Tomsk Polytechnic University, Usova 4 Street, where this research was conducted.

To identify potential factors, it is necessary to use GOST 12.0.003- 2015 “Dangerous and harmful production factors. Classification".

Working conditions in the workplace are characterized by the presence of hazardous and harmful factors, which are classified into groups of elements: physical, chemical, biological, psycho-physiological [83].

A dangerous factor is a factor whose exposure to certain conditions results in injury or other sudden, acute health deterioration.

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

The object of the study is based on Degradation and drug release of 3D printed microchamber structures. This research was conducted at the B.P. Weinberg Research Center in the Academic Building 19 of the Tomsk Polytechnic University on the Usova 4 Street, Room 019. The 3D-printed microchamber structures will be filled with a radioactive cargo, and the release of the cargo will be expected as the object degrades in a polar medium. Consequently, the object of study may create a detriment of elevated levels of ionizing radiation when it gets released into the surrounding medium.

The dangerous and harmful factors are presented in the table 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 1.2.3685-21. "Hygienic standards and requirements for ensuring the safety and (or) harmlessness of environmental factors for humans" [86].
2. Excessive noise	-	+	+	Sanitary rules 1.2.3685-21. "Hygienic standards and requirements for ensuring the safety and (or) harmlessness of environmental factors for humans" [86].
3. Increased level of electromagnetic radiation	+	+	+	Sanitary rules 1.2.3685-21. "Hygienic standards and requirements for ensuring the safety and (or) harmlessness of environmental factors for humans" [86].
4. Insufficient illumination of the working area	-	+	+	Sanitary rules 1.2.3685-21. "Hygienic standards and requirements for ensuring the safety and (or) harmlessness of environmental factors for humans" [86].
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 currents" [89].
6. Increased levels of ionizing radiation	+	+	+	Sanitary rules 2.6.1.2523-09. Radiation Safety Standards (NRB-99/2009) [90].

A student working with a computer and also in the laboratory is exposed to physical factors such as temperature and humidity, noise, static electricity, electromagnetic fields of low purity, illumination; presence of radiation and chemicals. Psychophysiological dangerous and harmful factors are divided into:

physical overload (static, dynamic) and mental stress (mental overstain, monotony of work, emotional overload) [83].

6.3 Analysis of Hazardous and Harmful Production Factors

The main parameters that characterize working conditions are the microclimate, noise, electromagnetic field, and illumination.

This subsection describes the influence of the detected harmful and dangerous factors on the organism and determination of compliance with compliance with the regulatory value.

6.4 Deviation of Microclimate Indicators

The air of the working area (microclimate) is determined by the following parameters: temperature, surface temperature, relative humidity, air speed, heat exposure intensity. The optimal values of the microclimate characteristics are established in accordance with [86] and given in table below.

Table 6.2 – Optimal parameters of the microclimate [86]

Period of the year	**Temperature, °C**	**Surface temperature, °C**	**Relative humidity, %**	**Air speed, m/s**	
				Actual value	**Permissible value**
Cold period	19 – 24	18 – 25	55 – 62	0.1	0.1
Warm period	20 – 28	19 – 29	55 – 62	0.1	0.1 – 0.3

By examining the parameters of the microclimate at the workplace, which are maintained at an optimal level by water central heating system and natural ventilation, and comparing them with the allowable standards, we can conclude that the limits of allowable values [91] are not violated.

Calculating the air flow rate, G;

$$G = V \cdot K_{air},$$

Where; G is the air flow rate;

V is the volume of room 48 m^3.

Area = 15 m^2 and height 3.2 m;

K_{air} is the air exchange rate 2 h^{-1}.

$$G = 48 \cdot 3.2 = 153.6\, m^3/h\,.$$

There are 4 seats in the laboratory room, each of which will have a flow rate of 38.4 m^3/h and the flow rate, G must not be less than 20 m^3/h per seat with an air exchange rate not less than 2.

6.5 Excessive Noise

Noise 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 in the laboratory, the noise level in the workplace should not exceed 70 dB [86]. Noise levels did not exceed 70 dB in the laboratory where this research work was conducted.

6.6 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 [86], the intensity of the electromagnetic field at a distance of 50 cm around the screen along the electrical component should be no more than indicated in the table 4.3 below.

Table 6.3 – Permissible levels of intensity and density of the electromagnetic field [86]

Name of parameters	**Frequency range**	**Value acceptable level**
Electromagnetic field strength	5 Hz – 2 kHz	25 V/m
	2 kHz – 400 kHz	2.5 V/m
Magnetic flux density	5 Hz – 2 kHz	250 nT
	2 kHz – 400 kHz	25 nT

The intensity and density of electromagnetic levels at the laboratory (B.P. Weinberg Research Center of TPU, Usova 4, Building 19, Room 019) were within the permissible range.

6.7 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 [87, 88].

According to the standard, the illumination on the table surface in the area of the working documents should be 300 lux. Lighting should not create glare on the surface of monitor. Illumination of the monitor surface should not be more than 300 lux. For general artificial lighting, light sources with a color rendering index of ≥ 85% should be used. In rooms of various functional purposes with workstations equipped with a PC, the pulsation coefficient should not exceed 5% [92].

The brightness of the lamps of common light in the area with radiation angels from 50 to 90 °C should be no more than 200 cd/m, the protective angle of the lamps should be at least 40 °C. The safety factor for lamps of common light should be assumed to be 1.4 [92].

The work was conducted in laboratory room number 019 of the B.P. Weinberg Research Center in Building 19 of the Tomsk Polytechnic University. The area of the room is 15 m^2 (length, A – 5 m, width, B – 3 m and height, H – 3.2 m). Work surface height h_{ws} – 0.8 m. It is required to create illumination E – 300 lux. Wall reflection coefficient ρw – 50 %. Ceiling reflectance ρc – 70 %. Safety factor K_z – 1.5, non-uniformity factor Z – 1.1. The value of integral optimum criteria, λ of lamps position for fluorescent lamps with protective grille is in the range 1.1 – 1.3 for standard type LPO-71-4× 18-552. The value, λ = 1.3 is chosen for this [92].

Calculation of the general fluorescent lighting system. Distance of luminaires from ceiling (overhang) h_{ov} – 0.5 m [92]. Estimated height h, the height of the luminaire above the work surface is:

$$h = H - h_{ov} - h_{ws} = 3.2 - 0.5 - 0.5 = 1.9\ m\ .$$

The distance between the luminaires L is defined as:

$$L = \lambda \cdot h = 1.3 \cdot 1.9 = 2.47\ m\ .$$

Number of rows of downlights in the room = 2, number of downlights in one row = 3. The total amount of downlights will be 6.

The figure below shows the arrangement of downlights positions in the working room (all distance in m).

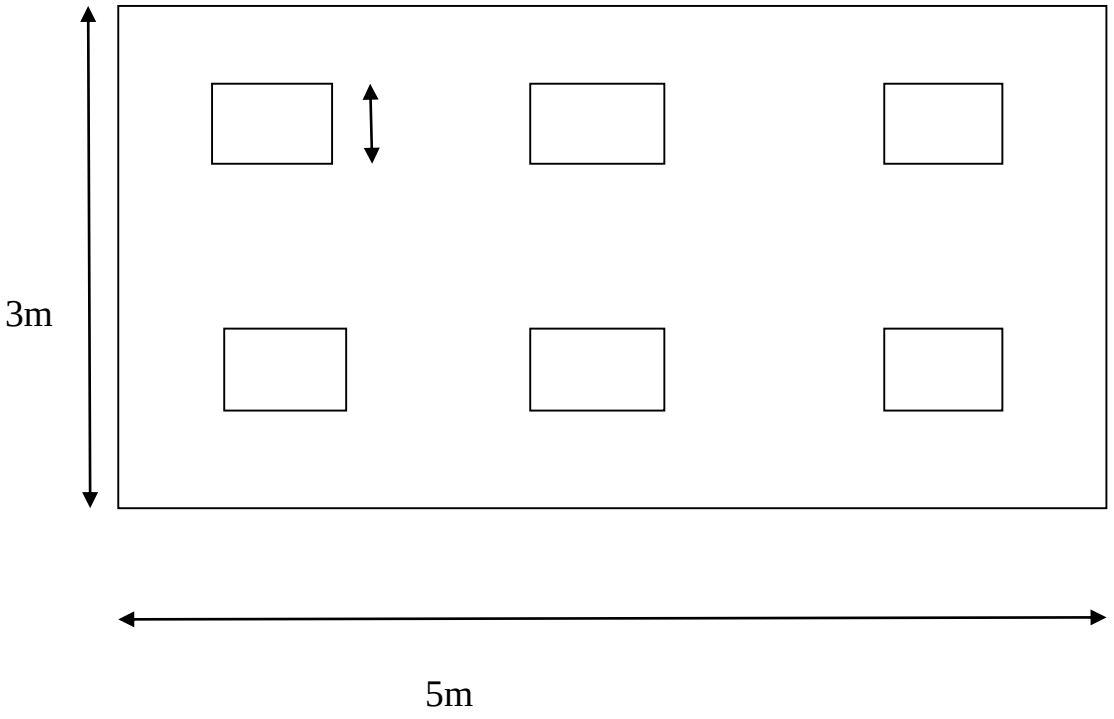


Figure 6.1 – Downlights positions in the working room

Room index is calculated as;

$$i = \frac{S}{h \cdot (A + B)} = \frac{5 \cdot 3}{1.9 \cdot (5 + 3)} = 0.99 .$$

According to the reference values, the coefficient of use of the luminous flux is determined η – 0.51. The luminous flux utilization coefficient shows what part of the luminous flux of the lamps falls on the working surface. It depends on the index of the room i, the type of luminaire, the height of the luminaires above the working surface h and the reflection coefficients of the walls ρ_w and the ceiling ρ_c.

The luminous flux of the lamp is determined by the formula:

$$F = \frac{E_n \cdot K_z \cdot Z \cdot S}{\eta \cdot N},$$

where E_n - normalized minimum illumination according to [86]; S – the illuminated area, m^2; K_z – safety factor considering luminaire pollution; Z – is the ratio of average illumination to minimum (usually taken equal to 1.1-1.2, let Z = 1.1); N – number of lamps in the room; η – luminous flux utilization factor, 0.6 [7].

$$F = \frac{300 \cdot 1.5 \cdot 1.1 \cdot 15}{0.51 \cdot 6} = 2427\ lm .$$

In accordance with the luminous flux, a standard LB lamp 80-4 with a flow of 2500 lm, the lighting system of the laboratory room corresponds to the standard. [91].

6.8 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 75 % for a long time), high temperature (more than 35 °C), the presence of 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 [86]. 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;
– Short-circuited in high-voltage units: power supply and display unit [86].

The upper limits for values of contact current and voltage are shown in Table 6.4 below.

Table 6.4 – Upper limits for values of contact current and voltage [86]

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

In accordance with [89], the lighting system of the laboratory room corresponds to the standard. The equipment used were first class equipment which have voltage not exceeding 1000 V, which were also acceptable for this research [89].

6.9 Increased Levels of Ionizing Radiation

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 effect. Deterministic effects (harmful tissue reactions) due to exposure with high doses and 12 stochastic effects due to DNA destruction and mutations (for example, induction of cancer) [90]. To provide radiation safety with using sources of ionizing radiation one must use next principles:

– Keep individual radiation doses from all radiation sources no higher than permissible exposure;
– Forbid all activity with using radiation sources if profit is low than risk of possible hazard;
– Keep individual radiation doses from all radiation sources as low as possible. According to [90], there are three groups of people related to work with radiation:

– Personnel A – personnel who work directly with radiation sources;
– Personnel B – personnel who do not directly work with radiation sources, but are exposed to them;
– Population [90].

Table 6.5 shows dose limits for all three groups of people.

Table 6.5 – Basic dose limits [93]

Quantity		**Dose limits**	
Effective dose		**Personnel A**	**Population**
		20 mSv per year in average during 5 years, but not more than 50 mSv per year.	1 mSv per year in average during 5 years, but not more than 5 mSv per year.
Equivalent dose per year	Eye's lens	150 mSv	15 mSv
	Skin	500 mSv	50 mSv
	Hands and feet	500 mSv	50 mSv
*Dose limits for personnel B are quarter part of dose limits of staff A.			

According to [90], the levels of ionizing radiations in the laboratory were acceptable.

6.10 Justification of Measures to Reduce the Levels of Exposure to Hazardous and Harmful Factors on the Researcher (worker)

Safe working conditions are such working conditions in which the impact of harmful or hazardous production factors on the working person is excluded, or their levels of exposure do not exceed the established standards. In order to prevent the adverse effects of the microclimate, protective measures should be used (for example, local air conditioning systems; air showering; compensation for the adverse effects of one microclimate parameter by changing another; overalls and other personal protective equipment; rooms for rest and heating; regulation of work time: breaks in work, reduction of the working day, increase in the duration of vacation, reduction of work experience, etc.). One of the effective collective means of protection against thermal radiation of workers is the creation of a certain thermal resistance in the path of the heat flow in the form of screens of various designs - transparent, translucent and opaque [83]. 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 [94].

The parameters of microclimate in the work space regulated by the central heating system, have the following values: humidity 58 %, air spread 0.1 m/s, warm period temperature 20-25 °C, in cold period 19-23 °C. Natural ventilation is provided in the work space. 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.

In this paper, 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, seals are installed around the perimeter of the doors and windows [95].

There are the following ways to protect against electromagnetic radiation:

- 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.

Fatigue of the organs of vision can be associated with both insufficient illumination and excessive illumination [83].

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 [96].

Desktops should be placed in such a way that the monitors are oriented sideways to the light openings, so that natural light falls mainly on the left.

Also, as a mean of protection to minimize the impact of the factor, local lighting should be installed due to insufficient lighting, window opening should be equipped with adjustable devices such as blinds, curtains, external visors [96].

To ensure the safety of work in electrical installation, next steps should be performed:

- Disconnecting the installation (part of the installation) from the power source;
- Checking the absence of voltage;
- Mechanical locking of the drives of switching devices, removal of fuses, disconnection of the ends of supply lines and other measures that exclude the possibility of erroneous supply of voltage to the place of work;
- Grounding of disconnected live parts (application of portable earthing switches, switching on ground knives);
- Fencing of the workplace or live parts that remain under voltage, which can be touched or approached to an unacceptable distance during operation [97].

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 decision about interference in the case of radiation accidents, contamination of the environment and buildings with radionuclides [90].

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 level of personnel and population [90].

The main controlled parameters are:

- Annual effective and equivalent doses;
- Intake and body content of radionuclides;
- Volume of 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 [90].

Radiation protection office establish control levels of all controlled parameters in according to not exceeding control levels radiation protection officers start investigation of exceed causes and take actions to eliminate this exceeding.

During 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 after matches;
- Number of persons irradiated with doses higher than controlled limits of doses;
- Analysis of actions for providing radiation safety, meeting requirements rules, standards of irradiation safety;
- Analysis of irradiation doses obtained by groups of population from all ionizing radiation sources [90].

6.11 Fire and Explosive Safety

According to the explosion and fire hazard, the premises are divided into categories «А, Б, В1-В4, Г, Д», and buildings into categories «А, Б, В1-В4, Г, Д». Categories of premises and buildings are determined based on the type of combustible substances and materials in the premises, their quantity and fire hazard properties, as well as on the basis of space-planning decisions of the premises and the characteristics of the technological processes carried out in them [98].

The potential causes of fire are:

- non-compliance with fire safety regulations;
- short circuits in the power supply;
- work with open electrical equipment;
- malfunction of current-carrying parts of installations;
- presence of combustibles such as documents, doors, tables, cable insulation, etc.in close proximity to an electrical installation.

Explosion and fire hazard categories of premises are shown in Table 6.6 below.

Table 6.6 – Categories of premises for explosion and fire hazard [98]

Room category	**Characteristics of substances and materials (circulating) located in the room.**
А increased explosion and fire hazard	Combustible gases, flammable liquids with a flash point of not more than 28 °C in such an amount that they can form explosive vapor-gas-air mixtures, the ignition of which develops an estimated excess explosion pressure in the room exceeding 5kPa and/or substances and materials that can explode and burn when interacting with water, atmospheric oxygen or with each other in such an amount that the calculated overpressure of the explosion in the room exceeds 5kPa.
Б explosion hazard	Combustible dusts of fibers, flammable liquids with a flash point of more than 28 °C, flammable liquids in such an amount that they can form explosive dust-air or vapor-air mixtures, the ignition of which develops an estimated excess explosion pressure in the room exceeding 5kPa.
В1 – В4 Fire hazard	Combustibles and slow-burning liquids, solids combustibles and slow-burning substances and materials (including dust and fibers), substances and materials that can only burn when interacting with water, atmospheric oxygen or with each other provided that the premises in which they are located (contact), do not belong to category А or Б.
Г moderate fire hazard	Non-combustible substances and materials in a hot, incandescent or molten state, the processing of which is accompanied by the release of radiant heat, sparks and flames and/or combustible gases, liquids and solids that are burned or disposed as fuel.
Д reduced fire hazard	Non-flammable substances and materials in a cold state.

Classification of the premises to category B1, B2, B3 or B4 is carried out depending on the number and method of placing the fire load in the specified room and its space-planning characteristics, as well as on the fire hazardous properties of substances and materials that make up the fire load according the document [99].

The room where the research was conducted is in category B4 [98]. The research was conducted in a manner where all such fire hazards were avoided.

6.12 Substantiation of Measures for the Prevention of Emergencies and the Development of Procedures in Case of Emergencies

Measures that can be used in prevention of fire are grouped into: organizational, technical, operational and regime.

Organizational measures seek to correct operation of equipment, provide 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 mostly deal with 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 [100].

The regime measures establish rules for the organization of the work and compliance with fire-fighting measures. In order to prevent fire from short circuits, overloads, etc., the following fire safety rules recommended to 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 fireworks);
- 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; for example: fire emergency, it is necessary to inform the management (duty officer), call the Emergency Service or the Ministry

of Emergency Situations telephone 112, take measures to eliminate the accident in accordance with the instructions; as for the case of fire emergencies [84].

The most likely emergencies that may occur at the workplace are fire or electrocution with their proposed prevention and emergency plan. Possible emergency situations, their preventions and emergency plan are presented in Table 6.7 below.

Table 6.7 – Possible Emergency situations, their preventions and emergency plan

No.	Emergency situation	Prevention	Emergency plan
1	Fire outbreak	– prevention of spontaneous combustion of substances, restriction of fireworks); – Compliance with fire regulations; – proper operation of equipment; – proper placement of flammables	– Call the emergency service – telephone 112; – inform management; – take measures to mitigate potential consequence in accordance with instruction; – providing luminaires for evacuation
2	Person being electrocuted	– Avoid working with naked cable; – not operating electronic device in conditions of high humidity and high temperature; – compliance with electric regulations	– Inform management or supervisor; – call the emergency service – telephone 112; – insulating the person from the electric source using a wooden or plastic rod
3	Chemical spillage	– wearing personal protective equipment; – safe handling and storage of chemicals	– Inform management and supervisor; – call the emergency service – telephone 112; – take measures to mitigate the consequence of the accident

6.11 Chapter Conclusion

In the social responsibility section the hazardous and harmful factors considered were:

- deviation of microclimate indicators [83];
- excessive noise [83];

- increased level of electromagnetic radiation [83];
- insufficient illumination of the working area [83];
- abnormally high voltage value in the circuit, the closure which may occur through the human body [89];
- increased levels of ionizing radiation [90].

The category of the laboratory premises for explosion and fire hazard were classified under category B4 [98].

First class equipment which have voltage not exceeding 1000 V were used for this research, and this is acceptable for electrical safety [89].

All relevant safety measures and precautions to lower the likelihood of accidents and traumas during investigation were brought to light. The most likely emergencies that could have occur at the workplace are fire and electrocution. These were dealt with having strategized for their prevention and emergency plan.

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.

CONCLUSION

The wettability and surface energy measurements of the structure was successfully measured by optical tensiometry. The contact angles of the PLA covering layer were altered at different points in time, which showed the surface of the covering layer was undergoing morphological changes at the molecular level to possibily effect a degradation process.

In general, the research was successful, and all objectives of the study were achieved.

Inference

From the results, it can be inferred that PLA polymers can be used for drug release purposes, and possibly as drug release implants in humans because of its biodegradable tendencies.

Recommendation

It is recommended that further research including in vitro and in vivo studies, should be done concerning the use of PLA microchamber structures as drug release systems, especially by the use of radiopharmaceuticals.

The study was considerably economical, socially acceptable and undercarried under the safety regulations according to the laws of the Russian Federation. The scope of application of this study could be cancer research laboratories and also as a novel form of systemic radiation therapy at cancer centres.

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