TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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

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

МАГИСТЕРСКАЯ ДИССЕРТАЦИЯ

Тема работы
Оптимизация проведения сочетанного курса лучевой терапии рака шейки матки

УДК 616.849:618.14-006

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

MASTER THESIS

Topic of research work
Optimization of combined course radiotherapy for patients with cervical cancer

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Programme Director	**Full name**	**Academic degree, academic rank**	**Signature**	**Date**
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Tomsk – 2022

LEARNING OUTCOMES

Competence code	Competence name
Universal competences	
UC(U)-1	Ability to make critical analysis of problem-based situations using the systems analysis approach, and generate decisions and action plans.
UC(U)-2	Ability to run a project at all life-cycle stages.
UC(U)-3	Ability to organize and lead the teamwork and generate a team strategy to achieve the target goal.
UC(U)-4	Ability to use modern communication technologies to realize academic and professional interaction.
UC(U)-5	Ability to analyze and account for cultural diversity in the process of intercultural interaction.
UC(U)-6	Ability to set and pursue individual and professional activity priorities and ways to modify professional activity based on the self-esteem.
General professional competences	
GPC(U)-1	Ability to formulate goals and objectives of the research study, select assessment criteria, identify priorities for solving problems.
GPC(U)-2	Ability to apply modern research methods, evaluate and present the results of the performed research.
GPC(U)-3	Ability to present research outcomes in the form of articles, reports, scientific reports and presentations using computer layout systems and office software packages.
Professional competences	
PC(U)-1	Ability to maintain medical and technical documentation related to medico-physical aspects of radiation therapy, interventional radiology and radionuclide diagnostics and therapy.
PC(U)-2	Ability to ensure radiation safety of personnel, public, and the environment, to carry out monitoring of radiation exposure levels of patients, personnel, public, and the environment.
PC(U)-3	Ability to operate and maintain equipment and tools applied for the medical use of radiation.
PC(U)-4	Ability to manage the quality of physical and technical aspects within radiation therapy, diagnostics, interventional radiology and radionuclide diagnostics and therapy departments in accordance with the specific equipment requirements, regulatory requirements and staffing of a medical organization.
PC(U)-5	Ability to conduct and organize dosimetry planning, clinical dosimetry, quality assurance procedures for radiotherapy, interventional radiology, and radionuclide diagnostics and therapy.
PC(U)-6	Ability to apply knowledge of natural sciences, fundamental laws in the field of nuclear physics and technology, clinical and radiation standards, hygienic measures in nuclear medicine, which is sufficient to study issues associated with medical physics using modern equipment and information technology relying on the latest Russian and international experience.
PC(U)-7	Ability to develop reference books, tables and software containing data for clinical use in dosimetric planning of radiation therapy, radionuclide diagnostics and therapy.
PC(U)-8	Ability to take part in the design and physical and technical equipment development for radiation therapy, diagnostics, interventional radiology

	and radionuclide diagnostics and therapy, and radiation safety divisions.
PC(U)-9	Ability to conduct training sessions and develop instructional materials for the training courses within the cycle of professional training programs (bachelor degree programs).

TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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

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

Level of education: Master degree program
Nuclear Fuel Cycle Division
Period of completion: 2020/2021and 2021/2022 academic years

Form of presenting the work:

Master Thesis

SCHEDULED ASSESSMENT CALENDAR
for the Master Thesis completion

Deadline for completion of Master's Graduation Thesis:	06.06.2022

Assessment date	Title of section (module) / type of work (research)	Maximum score for the section (module)
27.01.2022	Preparation of technical specifications and selection of research areas	10
24.02.2022	Development of a common research methodology	10
23.03.2022	Selection and study of materials on the topic	10
13.04.2022	Experimental research	20
27.04.2022	Processing received data	20
18.05.2022	Registration of the work performed	15
30.05.2022	Preparation for defending the dissertation	15

COMPILED BY:
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APPROVED BY:

Program Director	Full name	Academic degree, academic status	Signature	Date
Nuclear medicine	Vera V. Verkhoturova	Ph.D		

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

Student:

Group	Name
0AM0M	Esther Kwashie

School	School of nuclear technology engineering	School division	Division of Nuclear Fuel Cycle
Level of qualification	Master degree	Field of study	14.04.02 Nuclear Physics and Technology

Initial data for chapter «Financial management, resource efficiency and resource saving»:	
The cost of scientific research resources: material, technical, energy, financial, informational and human	*Project budget 1 112 819,65 rubles:* *The cost of purchasing equipment – 653 thousand rubles, the cost of a salary for a supervisor – 136 thousand rubles, the cost of a salary for a design engineer – 123 thousand rubles. etc.*
The system of taxation used, tax rates, volumes of payments, discounts and loans	*According to clause 3 of subclause 16 of Art. 149 of the Tax Code of the Russian Federation, this project is not subject to taxation. Based on Chapter 34 of the Tax Code of the Russian Federation, since 2016, the rate of 30.2% of the wage fund has been used to calculate contributions to extra-budgetary funds.*
Problems to research, calculate and describe:	
Project initiation	Project goals and results, project structure, assumptions and limitations, planning, budgeting, etc.
Economic model development	Calculation of initial investment, calculation of funds obtained from fuel savings, calculation of cash flows over 20 years
Determining the effectiveness of projects	Net Present Value Calculation and Sensitivity Analysis
Final decision making	Selecting and evaluating criteria, weighing the criteria and calculating the most appropriate solution
Graphic materials:	
«Portrait» of the consumer *Competitive power of the project* *SWOT matrix* *Assessment of the prospects of a new product* *Plan of investments. The budget for scientific and technical research*	

Assignment date	

Consultant:

Position	Name	Academic degree	Signature	Date
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Student:

Group	Name	Signature	Date
0AM0M	Esther Kwashie		

TASK FOR SECTION
«SOCIAL RESPONSIBILITY»

For a student:

Group	Name
0AM0M	Esther Kwashie

School	School of nuclear technology engineering	School division	Division of Nuclear Fuel Cycle
Level of qualification	Master degree	Field of study	14.04.02 Nuclear Physics and Technology

Topic of research work:

Optimization of combined course radiotherapy for patients with cervical cancer	
Initial data for section «Social Responsibility»:	
1. Information about object of investigation (matter, material, device, algorithm, procedure, workplace) and area of its application	*The object of investigation is multimodality imaging application in Brain tumor Radiation therapy planning.* *The applications and limitations of different imaging modalities under study will be analysed and recommendations given, which may be useful for oncology institutions and hospitals.*
List of items to be investigated and to be developed:	
1. Legal and organizational issues to provide safety: – Special (specific for operation of objects of investigation, designed workplace) legal rules of labor legislation; – Organizational activities for layout of workplace.	– Labour code of Russian Federation #197 from 30/12/2001 GOST 12.2.032-78 SSBT – Sanitary Rules 2.2.2/2.4.1340-03. Hygienic requirements for PC and work with it
2. Work Safety: 2.1. Analysis of identified harmful and dangerous factors 2.2. Justification of measures to reduce probability of harmful and dangerous factors	– Enhanced electromagnetic radiation level – Insufficient illumination of workplace – Excessive noise – Deviation of microclimate indicators – Electric shock
3. Ecological safety:	– Indicate impact of MRI, CT and SPECT machines on hydrosphere, atmosphere and lithosphere
4. Safety in emergency situations:	– Fire safety;

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

The task was issued by adviser:

Position	Full name	Academic degree, academic rank	Signature	Date
Associate Professor	Yuriy V. Perederin	Ph.D		

The task was accepted by the student:

Group	Full name	Signature	Date
0AM0M	Esther Kwashie		

Contents

1. The Incidence of Gynecological Cancer

"Cancer incidence" can be defined as an indication of the average risk of cancer in a community. It shows the burden of newly diagnosed patients in a given region, expressed in absolute case numbers per year [3]. The influence of avoidance strategies based on reducing population exposure to pathogenic risk factors (e.g., tobacco use or human papillomavirus (HPV) infections, etc.) or the early detection and treatment of precancerous lesions (e.g., cervical cancer screening) is measured based on [3] decreased incidence. Mortality rates are affected by incidence rates and history of the disease, the effectiveness of treatments and the delivery of health services [3]. It is unsuitable to use mortality rate as an indirect estimate of cancer incidence when doing a comparison among distinct populations, presuming equal survival/fatality rates in the populations being compared, which is seldom true [3].

Developed countries constitute New Zealand, Australia, North America, Europe and Japan. The remaining regions constitute "developing countries". New cases of cervical, vaginal, ovarian, uterine, vulvar and choriocarcinoma together accounted for 942,000 cases, or 18.6% of all female cancers worldwide. Out of the 2.9 million female cancer deaths worldwide, 15.3% accounted for gynecological cancers (excluding malignancies of the vagina, vulva and placenta); of the total cases prevalent over 5 years, gynecological cancer accounts for 20.9% of cases [3]. Table 1.1 shows the incidence rates, deaths and 5-year prevalence of cervical, ovarian and uterine cancers for developed and developing countries and 18 regions across the globe.

From the Table 1.1 data, the less developed countries recorded the highest cases of cervical cancer. This could be as a result of the lack of effective screening methods in these developing countries. According to the data, ovarian cancer cases were recorded as the second highest number of cases. The third was uterine cancer and then vulvar and vaginal cancers represented as the rarest types of gynecological cancers.

Table 1.1 - Cancers of the cervix, uterine body and ovary [3]

	Cervix			Uterus			Ovary			All		
	Cases	Deaths	5-year prev.	Cases	Deaths	5-year prev	Cases	Deaths	5-year prev.	Cases	Deaths	5-year prev.
World	492800	273200	1409200	198600	50200	775400	204200	124700	538400	895600	448100	2723000
Developed countries	83400	39500	309900	136300	29100	557400	96700	62200	262300	316400	130800	1129600
Developing countries	409400	233700	1099300	62300	21100	218000	107500	62500	276100	579200	317300	1593400
Eastern Africa	33900	27100	57200	2400	800	8600	4700	3300	10400	41000	31200	76200
Middle Africa	8200	6600	13900	700	200	3000	1100	800	2600	10000	7600	19500
Northern Africa	8100	6500	14000	1500	600	5200	1800	1300	4200	11400	8400	23400
Southern Africa	7600	4400	13100	600	200	2100	1000	600	2200	9200	5200	17400
Western Africa	20900	16700	35700	1400	500	5100	3600	2500	7900	25900	19700	48700
Caribbean	6300	3100	18400	1600	800	5400	800	400	2000	8700	4300	25800
Central America	17100	8100	49300	2400	1000	8600	4000	1900	10100	23500	11000	68000
South America	48300	21400	139200	10600	3200	34900	12700	6100	31500	71600	30700	205600
Northern America	14600	5700	58200	51500	6300	223200	25100	16000	74400	91200	28000	355800
Eastern Asia	61100	31300	191900	20200	4700	80000	30600	15000	88000	111900	51000	359900
South-Eastern Asia	42500	22500	132500	9100	3200	32400	16800	9200	43300	68400	34900	209200
South central Asia	157700	86700	446100	13100	5400	45600	32500	22800	83500	203300	114900	575200
Western Asia	4400	2100	13700	4100	1900	13800	4000	2400	10200	12500	6400	37700
Eastern Europe	30800	17100	107700	29600	10100	111500	23600	15200	56700	84000	42400	275900
Northern Europe	5600	2800	21100	10500	2200	39500	10500	7100	24700	26600	12100	85300
Southern Europe	10600	4100	40900	15800	3600	61600	11600	6400	32000	38000	14100	134500
Western Europe	12700	5600	49200	21000	4500	86700	17600	12100	48400	51300	22200	184300
Oceania	2000	800	6500	2000	400	7500	1700	1000	4500	5700	2200	18500

The information is primarily obtained from the World Health Organization's International Agency for Cancer Statistics (IARC) systematic global norm statistics (WHO). The information is gathered by regularly gathering information on all diagnosed new cancer cases in a defined resident population in each geographical

region on a continuous basis. The limitation on this data however is that many countries lack cancer registries and as such many populations are not covered in the data collection. It is clear that the estimates of cancer burden vary in accuracy for different countries, based on the scope and validity of the available data for each country. Table 1.2 shows the incidence and number of cases of vaginal, vulvar and choriocarcinoma in 2002.

Table 1.2 - Cancer of the vulva, vagina and choriocarcinoma [3].

	Estimated number of cases and ASR (World) per 100000 (all ages) in 18 world regions (2002)						
	Vulva (C51)		Vagina (C52)		Choriocarcinoma (C58)		All
Area	Cases	Rate	Cases	Rate	Cases	Rate	Cases
Eastern Africa	0.5	0.8	0.3	0.34	0.5	0.46	1.3
Middle Africa	0.2	0.56	0.1	0.31	0.1	0.18	0.3
Northern Africa	0.2	0.35	0.2	0.3	0.0	0.04	0.5
Southern Africa	0.2	0.78	0.1	0.25	0.1	0.40	0.3
Western Africa	0.4	0.57	0.4	0.5	0.3	0.33	1.1
Caribbean	0.2	1.09	0.1	0.75	0.0	0.03	0.4
Central America	0.4	0.87	0.3	0.53	0.1	0.13	0.8
South America	2.4	1.46	1.1	0.68	0.5	0.26	4.0
Northern America	4.0	1.63	1.2	0.47	0.1	0.08	5.4
Eastern Asia	2.3	0.26	1.7	0.2	1.3	0.15	5.2
South-Eastern Asia	1.2	0.55	0.6	0.26	1.2	0.43	3.0
Southern Asia	2.6	0.46	4.1	0.7	1.0	0.13	7.7
Western Asia	0.4	0.61	0.2	0.24	0.2	0.16	0.8
Eastern Europe	4.8	1.61	1.3	0.47	0.2	0.10	6.2
Northern Europe	1.5	1.58	0.4	0.43	0.0	0.04	1.9
Southern Europe	2.4	1.45	0.5	0.36	0.0	0.05	2.9
Western Europe	2.7	1.33	0.8	0.45	0.0	0.05	3.5
Oceania	0.3	1.51	0.1	0.45	0.0	0.07	0.4
World	26.9	-	13.2	-	5.8	-	45.9

The data is produced consistently gathering data on all diagnosed new cancer cases in a community in a given geographical region. Estimates were obtained from

neighboring countries for many developing countries for which information was unavailable (such as Cambodia, Democratic Republic of the Congo).

Gynecological cancer incidence was estimated, in precedent order, from:

- the national incidence data [3];
- the national mortality data [3], with incidence estimation using sets of regression models that are peculiar to location, gender and age, generated from local cancer registry data (incidence plus mortality);
- the local incidence in a country from the regional cancer registries;
- data from hospital registries or pathology [3] records, on frequency.

The country-specific rates for countries with no data available were calculated from neighboring countries for which estimates were made.

1.1 Cervical cancer

Cervical cancer is the second common cancer in females around the world. It has a mortality rate of 52 %. 86 % of the cases of cervical cancers are diagnosed [5] in developing countries. The existence of screening and vaccination programs has an impact on rates of occurrence and fatality worldwide. In developed countries, these preventive measures have contributed to a decrease of 75 % in the number of cervical cancer cases in the last 50 years [6].

The true female pelvis contains and protects the urinary bladder, urogenital diaphragm, rectum, ovaries, femoral heads and internal reproductive organs. The fibro-muscular urinary bladder typically lies mid-line, and is covered superior by parietal peritoneum. It can contain 50-1000 ml of urine [7]. The cervix is located at the bottom of the uterus. It serves as a passageway between the vagina and the uterus because it connects the two structures. Due to its different anatomy and histology, it is considered to be a separate anatomical structure from the uterus [8].

The cervix serves two primary purposes, which are as follows:

It makes it easier for sperm to travel through the vaginal canal and into the uterine cavity. The expansion of both the external and interior os are necessary to accomplish this goal [8].

Ensures that the upper part of the female reproductive tract remains sterile. All structures that are superior to the cervix, including the cervix itself, are sterile. This prevents bacterial invasion of the uterine cavity and the upper genital canal. It is maintained by regular endometrial shedding, a thick cervical mucus and a thin external os [8]. Figure 1.1 shows the female pelvis with its organs, including the location of the cervix.

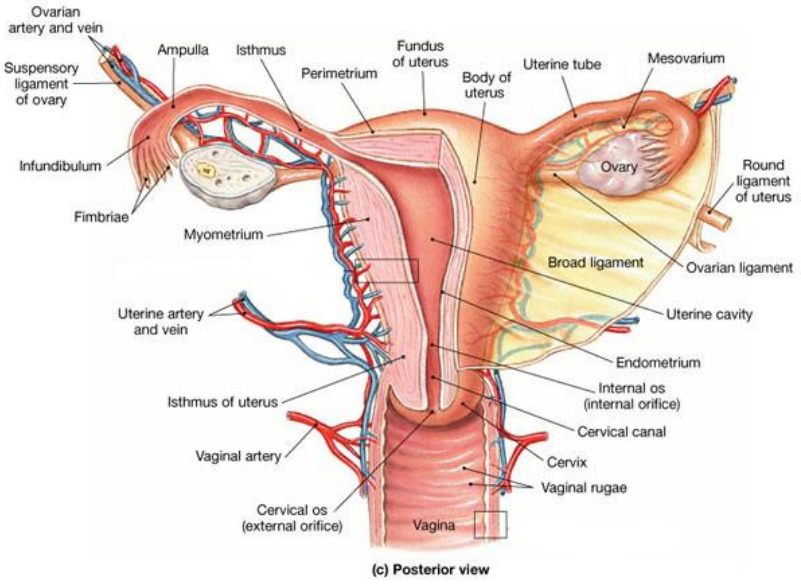

Figure 1.1 – Pelvic organs [9]

Epithelial cervical carcinoma is connected with the following risk factors: multiple sex partners, poor personal hygiene, low socioeconomic status, genetic factors, high usage of oral contraceptive, genetic factors, nutrient deficiency, tobacco usage, etc.

Cervical cancer is the only malignancy for which the causative agent is known. The etiologic agent resulting in cervical cancer has been identified as a sexually transmitted oncogenic virus, human papillomavirus (HPV). Cervical cancers caused by HPV can be avoided by abstaining from sexual activity, but a large population of women engage in sexual activity and are consequently at risk for contracting an HPV infection.

Early Detection and Screening of Cervical Cancer

Cervical dysplasia and cancer are slow to progress, able to be diagnosed early with current screening modalities, and almost always cured when diagnosed early.

Late diagnosis most frequently results in incurable disease and death.

Cytology (diagnosing diseases by looking at single cells and small clusters of cells), using the Papanicolaou (Pap) smear, and colposcopy (is a procedure to closely examine your cervix, vagina and vulva for signs of disease) are both valuable screening tools.

Signs and Symptoms Prevention, screening, and early treatment are imperative:

- Bleeding between or after menstrual cycles;
- The onset of menopausal hemorrhage;
- Abnormally heavy ad prolonged menstrual flow;
- Bleeding that occurs following pelvic examination, sexual intercourse, or douching;
- Persistent pain in the pelvis and/or at the back that cannot be explained;
- An increase in vaginal discharge;
- Painful sexual intercourse [10].

Stages of Cervical Cancer

- Stage 0 - Cancer is only on the surface of the cervix and has not spread to other parts of the reproductive system [11];
- Stage I – At this stage, the cancer has not progressed to the lymph nodes. It is localized in the cervix;
- Stage II – It has been established that the cancer has spread beyond the cervix and uterus. It is possible that, it got as far as the upper section of the vagina;
- Stage III – The malignancy has metastasized to either the pelvic walls or lower vagina. No lymph nodes in that area are affected at this stage;
- Stage IV – The most advances stage of development. The cancer has metastasized to other regions of the body [1], such as the liver, lungs, bladder or rectum.

1.2 Gynecological Cancer Therapy

Gynecological cancer can be treated in many ways. Some patients could have only one treatment, while others might require a combination of treatments, such as chemotherapy with radiotherapy and/or surgery. Some of the treatment options for cancer include surgery, where doctors/surgeons remove the cancer tissue in a surgical operation; chemotherapy, which makes use of special medications to kill or shrink the cancer cells and radiotherapy which uses doses of radiation to kill the cancer. There are a number of factors that go into choosing the type of treatment a patient receives. These factors include: the type and size of cancer tumors, their proximity to sensitive tissues, their general health, and whether or not they have had or would have other types of cancer treatment, etc. This information is recommended by the National Cancer Institute (NCI) [12].

In this chapter, different treatment options for cancer and the recommended treatment for various types of gynecological cancer would be discussed.

1.2.1 Surgery

During surgery, the cancer/tumor is removed from the body of the patient by a surgeon. Often, surgery requires cuts through the muscles, skin and sometimes the bone using sharp tools called scalpels. These cuts can be hurting; hence anesthesia is administered to patients before surgery. Anesthesia is a drug that causes loss of awareness temporarily. Anesthesia could be local, regional, or general. Local anesthesia causes loss of awareness in a minor area of the body; regional anesthesia induces loss of awareness in a part of the body, for instance the leg or arm; general anesthesia causes total loss of awareness and puts the patient in an unconscious state. Surgery may be open, in which the surgeon makes a large cut and removes the tumor and some healthy tissues; or minimally invasive [12].

Cancer surgery is performed for various reasons. It could be preventive, curative, staging, diagnostic, debulking, palliative, etc. Specialized surgeries such as cryosurgery, laser surgery, electrosurgery and microscopically controlled

surgeries are used during cancer treatment [13]. Some risks of surgery include severe pain, infection and in the worst case, death.

1.2.2 Chemotherapy

Chemotherapy may be recommended for early-stage cancers, recurrent cancers, or metastatic cancers. The most used agents in the treatment of gynecologic cancers are the platinums (carboplatin and cisplatin) and taxanes (paclitaxel and docetaxel). While these agents are used frequently, there are several other drugs employed in the recurrent setting and in the treatment of rare diseases [6]. Chemotherapy is commonly recommended in addition to radiation therapy, surgery, and other types of treatment. Chemotherapy could be used to shrink the tumor before surgery (neoadjuvant) or to kill the cancer cells that remain after surgery (adjuvant). It may be used to cure cancer, control its growth, or ease symptoms. Some common ways in which chemotherapy can be administered include:

- Oral – The patient ingests the chemotherapy medication which may come in the form of capsules, pills or liquids.
- Intravenous (IV) – Chemotherapy is administered by having the medication injected straight into the vein.
- Injection – Chemotherapy is administered in the form of a shot in a muscle in the hip, arm, or thigh, or directly under the skin in the fatty region of the belly, arm, or leg.
- Intrathecal – the chemotherapy is injected into the space between the layers of tissue that cover the brain and spinal cord.
- Intraperitoneal (IP) – in this form of treatment, the chemotherapy is administered directly into the peritoneal cavity. The peritoneal cavity is the region of the body that houses organs such as the liver, stomach, and stomach.
- Intra-arterial (IA) – the chemotherapy is injected directly into the artery that leads to the cancer.
- Topical – the chemotherapy comes in a cream that you rub onto the skin.

Chemotherapy not only kills fast-growing cancer cells, but also kills or slows the growth of healthy cells that grow and divide quickly. Examples are cells that line your mouth and intestines and those that cause your hair to grow. Damage to healthy cells may cause side effects, such as mouth sores, nausea, and hair loss. Side effects often get better or go away after you have finished chemotherapy. The most common side effect is fatigue, which is feeling exhausted and worn out [12].

1.2.3 Radiotherapy

Radiotherapy is a cancer treatment that involves exposing patients to high doses of radiation to destroy cancerous cells and reduce the size of tumors. Radiation is used in x-rays at low doses to see within the body of a patient. For example, an x-ray of the teeth or fractured bones uses radiation. Radiation therapy at high doses can kill or impede the growth of cancer cells by damaging their DNA. The ability of cancer cells to divide is compromised if their DNA is severely damaged beyond repair. The body breaks down damaged cells and eliminates them when they die [12].

Radiation therapy can be categorized into two types: external beam radiation therapy (teletherapy) and internal beam therapy (brachytherapy).

1.3.3.1 External Beam Radiotherapy

Radiation therapy that is administered by an external radiation source at a distance from the patient's body is referred to as external radiotherapy. It is a local treatment, which means that it only affects a particular area of the body. In order to deliver a homogenous radiation dose to the target, which may be several centimeters thick, the radiation source is placed at a distance from the patient (usually 80 cm for a Co-60 machine and 100 cm for a linear accelerator). It is usually given by a Cobalt unit or a linear accelerator, which can deliver high-energy photons and electrons. In the most common scheme, treatment is given daily for a period of 4-8 weeks. The more recent approaches, such as intensity modulated radiotherapy, image guided radiotherapy, and three-dimensional conformal radiotherapy, are able to get a precise shape of the target that is treated with the required amount of radiation with

incredible accuracy. These allow delivery of lower doses of radiation to healthy tissues, while at the same time delivering a higher dose to the tumor [14].

By three-dimensional conformal radiotherapy (3-D CRT), it means treatments that are based on 3-D anatomic information and use treatment fields that conform as closely as possible to the target volume in to deliver adequate dose to the tumor and minimum possible dose to normal tissue. The concept of conformal dose distribution has also been extended to include clinical objectives such as maximizing tumor control probability (TCP) and minimizing normal tissue complication probability (NTCP) [15]. Thus, the 3-D CRT technique encompasses both the physical and biologic rationales in achieving the desired clinical results [16].

Intensity-modulated radiation therapy (IMRT) is a form of external beam radiotherapy which delivers inhomogeneous fluence from any given point of the treatment beam to the patient in order to optimize the composite dose distribution. Inverse planning is used to determine the ideal fluence profiles for a given set of beam directions and the planner defines the treatment criteria for plan optimization. As a result, the fluence files that are generated are transferred to a computer-controlled linear accelerator, which has the necessary software and technology to deliver the intensity-modulated beams as determined [16].

Figure 1.2 shows a picture of a linear accelerator received by the IAEA under partnership from manufacturer.

Figure 1.2 – Clinical linear accelerator [17]

There are different types of external beam radiation therapy based on delivery technique. In the early days of external beam radiation therapy, teletherapy machines

were used with orthovoltage and superficial beams with sealed radioactive sources. Megavoltage therapy matured in the 1950's with the development of the Cobalt-60 machines along with the clinical linear accelerator [18]. The methods of administering external beam radiotherapy have been improving since its discovery. In the following sections, different methods of administering EBRT is discussed.

2-D Conventional Radiation Therapy

Before the widespread availability of CT scanners, radiotherapy planning was based on 2D x-ray images. In these images, the projection of the target volume could be delineated, which lead to the design of 2D treatment fields.

Conventional radiation therapy, sometimes known as two-dimensional radiation therapy, refers to the older methods of radiation therapy, in which treatments were planned by designating a limited number of beams, with the limits of each beam being outlined on orthogonal x-rays of the patient. Other highly conformal forms of external beam radiation therapy, such as those that make use of CT scans in the treatment planning process, have now taken its place.

The ability to shape beams was restricted, and as a general rule, square or rectangular beams were utilized. The four-field box configuration is a common type of beam arrangement. Because these therapies have poor conformance, nearby tissues and organs frequently fall into the high dose region, which results in treatment side effects. In addition, the amount of radiation that is delivered to the targeted tumor is typically insufficient, which results in treatment that is less effective.

Despite the fact that, 2D-conventional radiotherapy is used infrequently lately, it nevertheless has a part to play in palliative treatments. These treatments make use of generous margins and, and the ease with which the planning procedure may be carried out enables same-day treatment [19].

3-D Conformal Radiation Therapy

3-D conformal radiation therapy is a common type of external beam radiotherapy technique. Target localization, treatment planning, and dose delivery are all done in three dimensions. CT, MRI, SPECT, PET, and ultrasound are some of the

imaging modalities used to pinpoint a target's exact location anatomically and functionally [20]. A computer program is used to obtain images from the above-mentioned imaging modalities. Figure 1.3 shows a typical visualization of tumor irradiation using conventional and conformal radiotherapy.

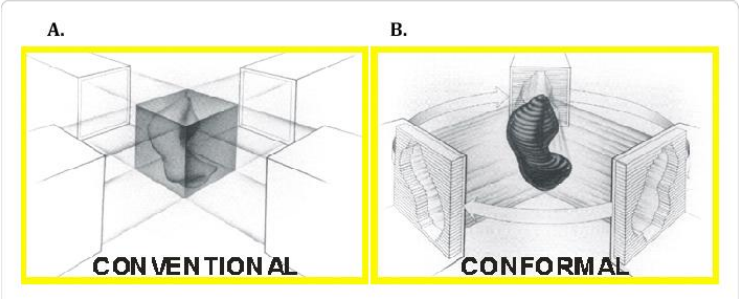

Figure 1.3 – Tumor irradiation using conventional (a) and conformal (b) radiotherapy [21]

The multi-leaf collimator (MLC) is shaped to conform as close as possible to the size of the tumor using the control console. The tumor is treated with one radiation field from each incident beam direction, where the shape of the radiation field is the projection of the target volume in beam's eye view. The incident fluence is homogeneous over the field [21]. This radiotherapy technique limits the irradiation of healthy tissues while ensuring maximum irradiation of the tumor. Figure 1.4 shows a MLC conformed to the shape and size of a tumor.

Figure 1.4 – Multi-leaf collimator shaped to the size of the tumor [22].

Intensity-Modulated Radiation Therapy

Intensity-Modulated Radiation Therapy (IMRT) is a form of conformal radiotherapy. Its technique and principle are similar to that of the 3D-CRT. The only difference is that, as the name suggests it is intensity modulated. The beams are conformed to be as close as possible to the tumor shape. IMRT requires for inhomogeneous and adjustable fluence distributions across the treatment field. While the use of fluence modulation does not remove radiation completely from critical

structures, it limits the dose to the structures directly within the beam's path. The resulting cold regions within the tumor are compensated by increasing the fluence from the other radiation beams [23]. This treatment modality is good for treating concave target volumes. The intensity of the beams is attuned at different points of the tumor to reach the required intensity at each point. Figure 1.5 shows typical isodose lines which represent the coverage and spillage of the prescribed dose in 3D-CRT and IMRT planning.

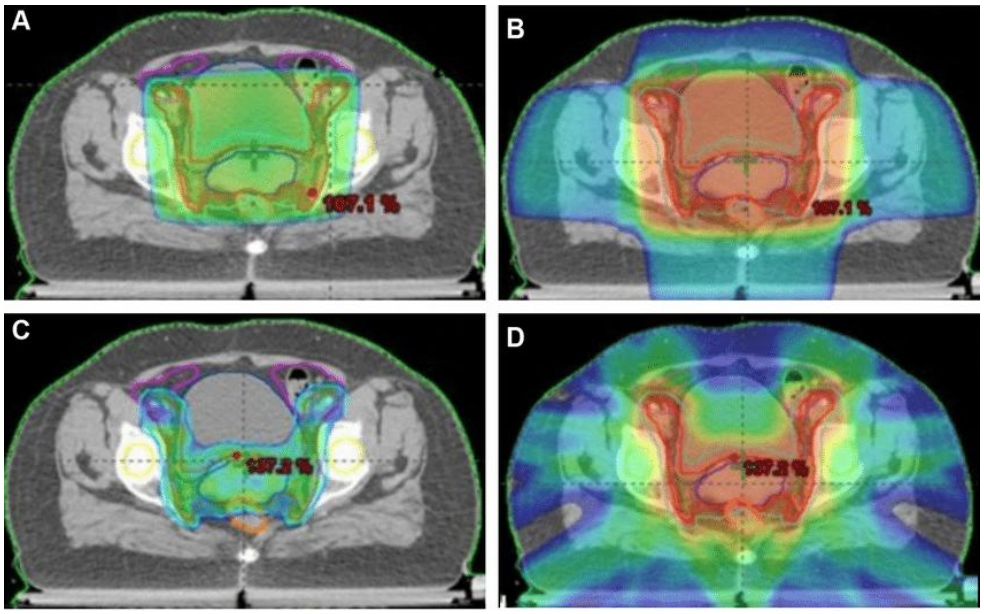

Figure 1.5.– Radiotherapy of cervix carcinoma. A, B: 3D conformal radiotherapy; C, D: intensity-modulated radiotherapy; A, C: planning target volume coverage with 99 % of the prescribed dose; B, D: dose spillage for 30 % of the prescribed dose [24].

Volumetric Modulated Arc Therapy

Volumetric Modulated Arc Therapy (VMAT) is a type of external beam radiation therapy that delivers radiation dose as the treatment machine continuously rotates around the patient. During the rotation, the gantry speed and dose rate are regulated to generate highly conformal dose distributions. Furthermore, the radiation beam is continually modulated by the multi-leaf collimator to conform to the size of the tumor at each rotation angle [25]. VMAT is used to effectively increase the number of beam angles and potentially decrease the treatment times for complex tumor treatments near critical structures [26]. Both VMAT and IMRT are equally

effective for normal tissue sparing. However, the treatment time for VMAT is significantly shorter, thus benefits patients who require longer (30 minutes or more) treatment time [25].

1.3.3.2 Brachytherapy

Brachytherapy is an internal radiation therapy in which substances/materials such as seeds, ribbons or capsules that contain a radiation source are placed in the body of a patient, either inside or near the tumor. It is sometimes referred to as internal radiation therapy. There are various techniques used in brachytherapy, and they can be classified according to different characteristics. To gain an overall perspective of the field of brachytherapy physics, it is important to understand the terminology used to classify brachytherapy treatment.

Brachytherapy is classified according to how the radioactive sources are placed within the patient, known as the implant technique. This is often governed by the anatomical treatment site. Interstitial brachytherapy is treatment with sources placed directly in tissue. Brachytherapy treatments for prostate cancer, head and neck cancer, soft tissue sarcomas, and other types of tumors are typically achieved using an interstitial technique. Intracavitary brachytherapy uses sources that are placed in a body cavity, which is near or within the tissue to be treated. Treatments in which radioactive sources are placed within the vagina or uterus for gynecological disease are classified as intracavitary. Intraluminal brachytherapy involves the placement of sources within lumen, such as the esophagus or trachea. Surface mold or plaque brachytherapy uses sources placed on the surface of the tissue, such as the skin or the globe of the eye. Finally, the use of radiation sources placed in blood vessels is classified as intravascular brachytherapy [27].

Also, brachytherapy is classified according to how long the radiation remains in the patient. Permanent brachytherapy uses sources that are permanently placed in the patient, never to be removed. Temporary brachytherapy uses sources that are placed for a specified amount of time and are removed at the completion of treatment [27].

Brachytherapy is classified according to dose rate or how quickly dose is delivered to the patient. Low-dose rate (LDR) brachytherapy is defined as the delivery of dose at rates between 0.4 and 2 Gy/h. It may be performed either on an inpatient or outpatient basis. High-dose rate (HDR) brachytherapy is defined as the delivery of dose greater than 12 Gy/h. Using modern HDR delivery equipment, treatment can be delivered at dose rates as high as 7 Gy/min. Due to the short treatment times, HDR treatment can be performed on an outpatient basis. Medium dose rate (MDR) brachytherapy delivers dose at rates between 2 Gy/h and 12 Gy/h. Pulsed dose rate (PDR) involves short pulses of high-intensity radiation that are delivered typically once per hour to simulate LDR treatment [27].

Brachytherapy is classified according to the technique in which sources are placed within the patient. Intracavitary brachytherapy is a type in which the sources are placed in body cavities close to the tumor volume. In interstitial brachytherapy, the sources are implanted within the tumor volume. There are other types under this classification. Intracavitary brachytherapy has largely been developed for the treatment of gynecologic cancers [27].

In summary, gynecological brachytherapy carried out by placing into the vagina a high strength source for a short period of time using a remote afterloading machine is classified as intracavitary, temporary, HDR, or remotely afterloaded brachytherapy. Each classification can have a different impact on the dose distribution, radiobiological effects, treatment delivery accuracy, and staff exposure [27].

Most common brachytherapy sources emit photons; however, in a few specialized situations β or neutron emitting sources are used [20]. Examples of brachytherapy sources which are normally used include Cobalt-60, Iridium-192 and Iodine-125. The choice of source depends mainly on the type and energy of radiation emitted by the source. The development of different brachytherapy sources and constructions has evolved over time, as have various methods of quantifying source strength. The dose deposited in a patient using brachytherapy has unique properties compared with external-beam radiation therapy [27].

Brachytherapy is classified into different ways based on various techniques and different characteristics used in delivering the treatment. It can be classified with respect to implant technique, treatment duration, dose rate and source loading technique. These techniques are described in the sections below.

Implant Technique

Brachytherapy can be classified by the implant technique. That is, the process of placing the source in the body. It could be intracavitary, interstitial, intraluminal, intraoperative, surface/mould, intraoperative or intravascular [28].

In intracavitary brachytherapy, a radioactive source is placed in a body cavity which is located within or close to the tissue with the tumor. Gynecological cancers often make use of intracavitary technique as sources are placed within the uterus or vagina for treatment. Interstitial brachytherapy uses sources that placed directly in the tumor volume. Interstitial brachytherapy is commonly used to treat sarcomas of the prostate, head and neck and soft tissues. Interstitial therapies could be short-term or permanent whereas intracavitary treatments are always short-term. Remote afterloading or manual methods are used to place temporary implants. Photons are typically emitted by intracavitary and interstitial brachytherapy sources [20].

Treatment Duration

Brachytherapy can be classified by the duration of treatment. Sources could be placed permanently or temporarily. Temporary treatment/afterloaders deliver a dose in a short time and remove the source after the prescribed dose is attained, whereas permanent treatment delivers the dose for the life of the source until the decay is complete. The source is never removed in permanent treatment. The radionuclides used for permanent implant brachytherapy have relatively shorter half-lives than those used for afterloader-brachytherapy.

Dose Rate

Brachytherapy may be classified by the quantity/amount of radiation dose administered per duration. It could be pulsed-dose rate (PDR), medium-dose rate (MDR), high-dose rate (HDR) or low-dose rate (LDR). In PDR, short pulses of high-

intensity radiation are delivered typically once per hour to simulate LDR treatment. HDR delivers doses greater than 12 Gy/h. It uses modern HDR equipment to deliver maximum dose of 7 Gy/min. HDR is usually delivered on an outpatient basis, due to the short treatment duration compared to LDR. In LDR, dose is delivered at rates between 0.4 Gy/h to 2 Gy/h. Doses could be delivered on outpatient or inpatient basis. MDR brachytherapy is defined as the delivery of dose at rates between 2 Gy/h and 12 Gy/h. [27].

Source Loading Technique

Source loading technique can be defined as the method which is used to place a brachytherapy source within a patient. Brachytherapy sources can be placed within patients in different ways. The equipment used for loading a source varies according to the source loading technique being applied. This equipment is known as an applicator. The design of applicators is unique to specific treatment sites.

The use of applicators with the sources already loaded first, then placed within the patient is known as preloaded brachytherapy. The technique in which the applicator is first positioned in the patient [29], after which the clinician manually places sources into the applicator is called manually afterloaded brachytherapy. A more advanced technique called remote afterloaded brachytherapy reduces radiation exposure to the staff [30]. During remotely afterloaded brachytherapy, the applicators are positioned within the patient, after which an equipment is controlled remotely (usually from another room) to load the source into the applicator.

Uniform loading is the use of all sources either having the same activity or staying within the patient for the same period of time. Nonuniform loading is the use of sources either having different strengths with respect to each other or staying within the patient for variable amounts of time. Uniform and nonuniform loading have different effects on the dose distribution [27].

1.4 Direct and indirect effects to organs at risk of the female pelvis

With contemporary 3D conformal radiation therapy and its technological advances, a prescribed radiation dose is delivered to the target volume and a dose

escalation rule is applied to limit the dose to healthy organs. Modern radiation techniques have increased the need for greater accuracy in determining the organs at risk (OAR), gross tumor volume (GTV) and clinical target volume (CTV), and for more accurate quantification of the dose delivered to the organs at risk (OARs) [15] and clinical target volume (CTV). As a result of these, GTV, CTV and OARs delineation plays an elementary role in the planning of radiation therapy. Radiographic imaging is essential to determine clinical volumes, from radiation therapy planning to delivery [31]. Although the planning phase is primarily based on CT, which is usually performed without contrast, this method is quite limited in defining some organs at risk, principally structures with comparable electron density to nearby structures.

Negligence on the part of radiation oncologists to accurately delineate GTV, CTV and organs at risk, could result in some unwanted negative effects especially on the healthy tissues. Organs at risk of the female pelvis include the rectum, bladder, femoral heads and ovaries. In this chapter, the effects of radiation on organs at risk of the female pelvis are discussed.

Rectum

The rectum, located at the end of the large intestine, is about 5 cm long [32] and includes the pelvic region and perineum. The anatomical boundary between the two parts is the intersection of the levator muscle of the anus. At the origin, the rectum usually correlates with the third sacral vertebrae, descending to the anterior surfaces of the sacrum and coccyx [32]. It also forms an anterior hollow curve (sacral curve) which transforms into a convex curve corresponding to the apex of the prostate gland in men and mid-vagina in women. The rectal wall is composed of three layers: the mucosa, the submucosa and the muscle. Knowledge of the anatomical structure of the rectal wall is important in understanding the complex pathophysiology and physiology of rectal destruction following the completion of radiotherapy.

The rectum is a mixed structure organ at risk [32]. It is composed mainly of parallel subunits but may also include serial subunits. Its radiation tolerance is

dependent on the dose received as a percentage of its volume, as well as the maximum dose at a particular point. Radiation therapy can cause acute and late rectal damages. In the acute stage, it lessens the number of crypts and induces the infiltration of inflammatory cells in the wall of the rectum. However, there is no clear distinction between the symptoms of acute and late damage, and it is unclear when acute destruction resolution occurs and when late destruction begins. Alternatively, it remains unclear whether symptoms and accompanying acute destruction can coexist with symptoms of late destruction. Acute effects have been proven to predict late effects (urinary and fecal incontinence, bleeding, tenesmus, urgency, proctitis, mucorrhea), despite the fact that patient factors and prior surgery can independently affect the rectal tolerance. Fecal and urinal incontinence is a possible result of radiation therapy, and sphincter effects can identify changes in sphincter pressure at rest and during exercise 4 to 6 weeks after radiotherapy and may persist for two years after the end of radiation therapy. Decreased rectal volume at the borderline level of stimulus perception may suggest possible destruction at the neuronal level, related with myenteric plexus hypertrophy.

Lastly, fibrosis associated with decreased elastic fibers and increased overall sphincter stiffness may be related to decreased rectal capacity. No morphological changes occur at the internal sphincter level and the Meissner plexus, indicating that post-radiation injury mainly occurred in the outermost layers of the rectal wall [32].

Bladder

The bladder is a muscular, hollow membranous organ that changes in shape, size and position as it fills and empties. An empty bladder is confined completely in the small pelvis, behind the pubic junction, in front of the uterus [32] in women, and in the rectum in men. The upper part is hollow, and covered with peritoneum and the lower part is located on the posterior surface of the pubic joint and is convex. During filling, the walls of the bladder expand and the most expandable part rises and becomes convex, giving the bladder an ovoid shape. When fully-filled, the bladder imbricates the upper edge to reach the region of the lower abdomen. An expanded

bladder can be detailed as: the base, or lower portion; the corpus (with a rear, anterior and two lateral parts); and the peak all representing distinct anatomical relations.

The occurrence of urination, due to bladder expansion is in three stages: the filling, pre-urinary and emptying stages [32]. At each stage, the sphincter system, nerve structures, the muscles of the urethra, the detrusor muscle, and the pelvic plane are involved differently. The rectitude of this method and related structures is essential for maintaining urinary continence. The urinary continence mechanism is not involved in urination itself, but creates sufficient urethral resistance to prevent leakage of urine through the urethra except while urinating. In the pathophysiology of bladder destruction, the bladder should be considered as a serial organ because it lacks traceable functional units. Nevertheless, each layer of the bladder can exhibit its own unique radiation sensitivity.

Subepithelial microvascular changes following protein migration and large-scale beta production are early changes induced by ionizing radiation; a continuous accumulation of type I and III [32] collagen fibers in the wall of the bladder occur. An acute effect of bladder irradiation is that the epithelium is excessively exfoliated which results in urothelium ruptures, leaving the bladder vulnerable to infection and damage as a result. Acute symptoms are daytime and nocturia pollakiuria, dysuria, hematuria, cystalgia and urgent urination. These symptoms transpire in about 40 % of patients and usually withdraw 6 weeks after completion of radiation therapy. In the chronic phase, the late effects appear to be as a result of detrusor muscle degeneration and collagen-type fibrosis of the muscle layer. Endoarteritis obliterans associated with ischemia of the bladder wall causes hematuria and/or fistulas. The clinical outcome is loss of bladder function. Late effects normally arise within a period of two years after the completion of radiation therapy, but sometimes 10 years later. The frequency and severity of acute and late effects on the bladder depend on the site being treated and the dose [32].

Femoral Heads

The femoral head stands for the proximal end of the femur that forms the femur skeleton. It has a rounded shape and is located in the articulated acetabulum. At its

center is the fovea capitis femoris, to which the round ligament of the femur attaches and connects to the base of the acetabulum. It is supported by a bony part called the anatomical neck, at the base of which there are two femoral trochanters [32]. The head of the femur usually consists of spongy tissue formed by thin trabeculae, or spicules [32], that border communicating cavities filled with hematopoietic bone marrow.

Trabeculae is made up of bones, which are small tubular structures that contain the intramedullary cavities. These cavities are covered by unorganized plates of tissue or concentric layers of bone called endosteum. The femoral head is an organ at risk from radiation therapy to pelvic tumors. Ionizing radiation induces both direct and indirect consequences on bones. These consequences are related to vascular changes.

Ovaries

The ovaries are the female gonads and perform a dual function; the gametogenic function to produce gametes or oocytes and the endocrine function to release steroid hormones. The ovaries are a pair of organs, each located on either side of the uterus close to the side wall of the small pelvis. It is similar in shape and size to the large almond, with a large vertical axis in the sagittal plane. The ovaries are not covered by the visceral peritoneum, but by a special epithelium called the germinal epithelium [32].

The ovaries have the ability to follow uterine displacements and as such can vary their position. However, in a normal position, the ovaries are positioned so that its lateral surface corresponds to a depression (the ovarian groove) in the posterolateral wall of the small pelvis [32].

The ovaries start their hematogenic and endocrine responsibilities during puberty. These activities that characterize a woman’s period of physical maturity have a cycle of 28 days according to the pituitary gonadotropins. Irradiation of the abdomen, pelvis and spinal cord is related with an increased risk of ovarian insufficiency and infertility, principally when the ovaries in the area exposed to radiation. The first target of exposure damage is represented by the granulosa cells that cover the ovarian follicles during growth. These follicles support oocyte function

during maturation. Ovarian transposition (ovariopexy) outside the field of treatment can preserve ovarian function and may be considered for women under childbearing age [32].

1.5 GEC-ESTRO recommendations for target volume definition for brachytherapy of gynecological cancer

It is no doubt that the precise contouring of gross tumor volume (GTV), clinical target volume (CTV) and planning target volume (PTV) [33], and determination and delineation of critical organs have a direct impact on brachytherapy procedures, especially when optimization can adjust the pear-shaped iso-dose, fixed dose and /or allow for DVH analysis in a fixed volume. It is agreeable that a common language is needed to apply these terms [34] to utero-vaginal brachytherapy. In this regard, a group by name Gynecological (GYN) GEC-ESTRO working group [35] was founded in the year 2000. This group was made of physicists and physicians originating from distinct cancer centers but working in the field of gynecological cancer brachytherapy. The goal of the group was to work together to describe fundamental concepts and expressions for the 3D imaging-based 3D treatment planning approach to enable the communication of results of various groups working in this field with a common language [34]. The GYN GEC-ESTRO working group [35] represented two approaches. One by Insitut Gustave Roussy (IGR) and the other by the Vienna group. The approach by the IGR was based on CTV delineation according to clinical examination of the GTV during diagnosis. The approach by the Vienna group was based on CTV delineation according to GTV at time of brachytherapy, considering the extent of the tumor during diagnosis. The dose specification was at a point A with standard dose distribution as well as standard applicators usage was considered [36].

It was clear that, it was almost impossible to overcome the difficulties in the concept and terminologies employed in the above approaches through discussions of theory. Therefore, a questionnaire was designed by applying the distinct concepts to define the parameters. The concepts are newly defined parameters that were assessed in patients who were treated per the 3D evaluation and clinical treatment strategies

used at the various within the working group (Southampton, Olso, IGR, Leuven, Vienna). Some necessary information collected in the questionnaire include:

- GTV, CTV size and volume as defined in Clinical examination and MRI:
- At the time of diagnosis [34];
- Using BT (after external investigation).
- Size and volume of the reference volume (60, 75, 90 and 120 Gy) [34];
- Volume of isodose passing through point A;
- Therapeutic dose (prescribed dose);
- Ratio ranges related to CTV and GTV;
- DVH analysis for fixed dose and specific coverage GTV and CTV ratios;
- Dose at points B and A, left and right, mean;
- Dose parameters for organs at risk.

The results of the second attempt were assessed and deliberated over a meeting in Paris. GTVs at the time of diagnosis and reference volumes were similar. CTV evaluation at the time of diagnosis and brachytherapy, was however different and incomparable. The same applied to the scope of application of the induced dose. Parameters related to point A could not be compared because the IGR did not have point A assessment. Remarkably, irrespective of the significant contrasts in the approaches used for planning, the outcomes were comparable in terms of reference volumes for clinical circumstances which are comparable. However, to understand and compare 3D imaging approaches to treatment planning, these results were considered insufficient because key pertinent parameters, that is, CTV assessment and CTV coverage were not available and could not be compared.

A joint decision was therefore made in the year 2002/3 to work more thoroughly on GTV and CTV assessments and to further develop methodologies unique to distinct clinical approaches. It was again decided to test these approaches based on a multi-center case comparison using a modern version of the previous protocol. CTV was further defined in an attempt to standardize specific clinical situations according to the spread of the disease: the quantity and topography of peri-

uterine, vaginal and intrauterine spread at different stages. The margin of safety was determined. This approach mainly targeted the GTV extents at diagnosis and the CTVs associated with those extents. When making a diagnosis on images obtained during BT with an installed applicator, changes in the composition and topography of the tumor during treatment and the process of superimposing this information in the images have not been well studied and described. X-ray anatomy was also not detailed.

A resident from Paris/Vienna examined two patients at separate institutions by the use of the joint protocol version. Results showed large differences in target assessment for alike clinical circumstances as a result of protocol ambiguity. From the images on MRI and CT, it was clear that the main anatomical and pathological features were not well understood. For example, what is the topography and parameter expansion of MRI and CT during brachytherapy and diagnosis? What is vaginal dilation with tomography? What is the pelvic wall? The clinical circumstance was not accurately defined as the need for a detailed description of the process was provided, only a qualitative description and some parameters (e.g., width in cm).

It was realized that the experience so far was related to some drawbacks in defining protocols for CTV and evaluating parameters relating to CTV. It was hence recommended to hold expert meetings (seminars on boundary definition/delineation in practical and theoretical aspects) through joint practice in the process of delineation based on similar clinical cases. Based on this, the protocol had to be further specified and retested in a joint assessment.

Proceedings during the first workshop is as follows. Comprehensive clinical explanations based on extended 3D diagrams during brachytherapy and diagnosis were requested. Also, during brachytherapy and diagnosis, MRI-based evaluations of the CTV and GTV had to be performed in sagittal, lateral and coronal planes. No special orientation with respect to the axis of the applicator was required. A seminar was held in this workshop with intricate lectures on normal and pathological anatomy, surgical anatomy and radiation anatomy from the perspective of a therapeutic and diagnostic radiologist. These lectures were aimed at addressing the

issues of presentation during brachytherapy and diagnosis. The protocol was modified upon discussion and a decision was made on which two CTVs to define based on the varying clinical approaches used by the GYN GEC-ESTRO working group.

It turned out that the processes involved in the new protocol were possible, hence the two CTVs (high-dose and intermediate-dose) and GTV could be delineated. Comparisons were made for different volumes. The results were analyzed by comparing the contours prepared by different experts for the three cases, calculating smallest common volumes (SCV), and adding additional volumes as contoured by the experts respectively.

During the next joint debate of these results with image evaluation (in a meeting in December, 2003 at Vienna), it was realized that the largest differences were found for the situations as described below:

- The classical orientation (sagittal, coronal, axial) of the image slices made it difficult to delineate due to the oblique presentation of the applicator and topography of the vaginal extension;
- Overlaying the anatomical and pathological information of parameters from images acquired during diagnosis to images acquired during brachytherapy for CTV intermediate-dose (ID) delineation;
- Understanding and identification of parametric boundaries (lateral, superior, posterior, inferior, anterior): contouring of potential microscopic residual disease (CTV ID) on MRI had proven difficult and irreproducible;
- Clinical information was not accurate enough;
- Image results interpretation was ambiguous.

Workshop II was organized for the delineation of CTV and GTV. Treatment planning was done at different centers for three patients with similar clinical characteristics (stage IIb, width of tumor 5 – 6 cm, width of tumor at time of brachytherapy 1 – 2 cm), using the above parameters for treatment planning based on exhaustive MRI and clinical information during diagnosis and brachytherapy. They

were orderly assessed according to the modified protocol for delineation of GTV and CTV, and also a modified protocol for dose volume parameters. Dose comparisons included biological modeling using linear-quadratic models. The size and volume of dose at point A, high-risk CTV, intermediate-risk CTV, reference volume, and isodose volume through point A were similar within limited limits, mostly for access to treatment. Comparable results were found for vital organs. Based on these results, the current GYN GEC-ESTRO working group protocol is the first to allow a repeatable comparison of 3D image-based parameters (CTV, GTV, dose-to-volume ratio) and various existing parametric-based (point A, reference volume 60 Gy) cervical cancer treatment strategies, which is applicable to anatomically defined critical organs and target volumes. A more detailed protocol was written based on this process. Some of them are shown below.

These target definitions were made based on the clinical experience and dosimetric concepts at various institutions (Vienna, IGR, Leuven). They take into consideration differences between clinical traditions which are based on disease evaluation during diagnosis and others based on the severity of the disease during brachytherapy:

- The point A as a reference point approach begins primarily with tumor spread (GTV) during brachytherapy, considering the spread at diagnosis, and defines the CTV for brachytherapy, for cervical-restricted primary response and adjacent organs with suspected residual disease (w30 – 60 cc). The intention is to provide a notable overall dose to this CTV depending on the stage and risk. For example, 80 – 90 cGy for definitive radiation therapy in advanced tumor. This dose is similar to the dose of point A;
- The approach based on ICRU 38 guidelines begins with GTV at diagnosis to define CTV during brachytherapy, and arrives at CTV with an anatomical target safety margin for GTV dimensions (w150 – 300cc) at diagnosis. The total prescribed dose to this CTV is 60 Gy at a dose rate of 50 cGy per hour. This dose is incomparable to the dose at point A, which is much larger.

Two CTVs have been proposed in order to consider these key concepts that are fundamentally different but have significant clinical relevance:

- "High-risk" CTV (HR CTV) has a higher risk of local recurrence due to residual macroscopic disease. The goal is to administer the highest possible and accurate total dose suitable for eradication of all residual macroscopic tumors;
- "Intermediate risk" CTV (IR CTV) has a greater risk of local reappearance in areas that correlate to the initial macroscopic spread of the tumor, leaving only microscopically visible disease during brachytherapy. The goal is to deliver a total radiation dose of at least 60 Gy equivalent to the dose suitable to cure the microscopic disease of cervical cancer.

These guidelines were adopted for target volume and OARs definition for brachytherapy for cervical cancer.

oncology. The results of this research would be useful for oncology departments of hospitals in choosing the optimal technique of radiotherapy for patients with cervical cancer.

Segmentation is the division of buyers into homogeneous groups, each of which may require a specific product (service). It is possible to apply geographic, demographic, behavioral and other criteria for segmenting the consumer market.

The category of these groups of consumers is commercial organizations. The segmentation criteria are: user rate, benefits sought, readiness state, attitude towards product, etc. Figure 3.1 shows the market segmentation map of services.

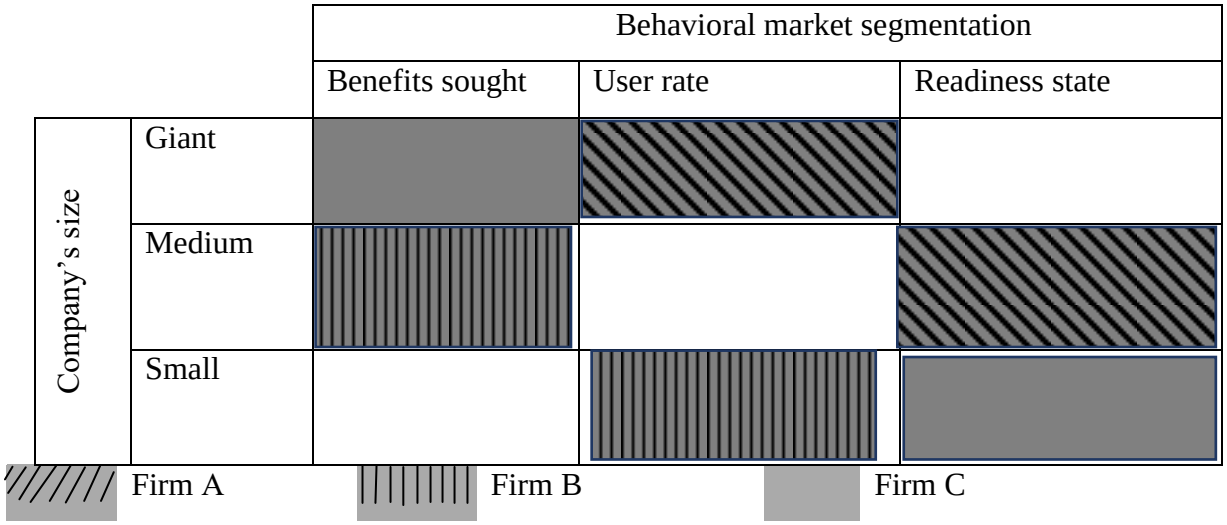

Figure 3.1. – Market segmentation map of services for the web design:

Firm A – Tomsk Institute of Oncology, Russia

Firm B – Sweden-Ghana Medical Center, Ghana

Firm C – Tomsk Oncology Dispensary, Russia

Firm A and C are more suitable for using this research results because the results provide benefits sought by these firms. In addition, firm C has a high user-rate hence these results may be helpful to them.

The competitor is the 2D-conventional radiotherapy technique. Suppliers of technology for this technique may have an advantage, because it is less expensive and if the results prove to deliver less dose to the critical organs, it would be a preferred option.

3.2 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 3.1. 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:

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

C - the competitiveness of research or a competitor;

W_i– criterion weight;

P_i – point of i-th criteria.

The type of radiotherapy treatment a patient receives depends on several factors. Various processes are involved before treatment is finally delivered. These include; diagnoses, treatment simulation, image contouring, and others. A treatment plan is dependent on the type of machine that would be used to deliver the dose.

For the competitive analysis of technical solution, two treatment techniques are considered. These are:

- 2D-Conventional radiotherapy – P_i
- 3D-Conformal radiotherapy – P_f

As discussed in previous chapters, 2D-conventional radiotherapy is based on treatment plans by defining a limited number of beams with the boundaries delineated on orthogonal x-rays of the patient. Beam shaping was limited and typically simple square or rectangular beams were used. A typical beam arrangement

is the four-field box. Due to the low conformity of these treatments, adjacent tissues/organs often fall into the high dose region resulting in treatment side effects. Also, the amount of radiation delivered to the targeted tumor is usually not adequate resulting in less effective treatment.

3D-conformal radiotherapy, on the other hand is a more localized technique applied for external beam radiation therapy. It is based on 3-D target localization, 3-D treatment planning and 3-D dose delivery techniques. It ensures maximum dose to the target volume while minimizing dose to the surrounding organs.

The competitor is the 2D-conventional radiotherapy technique. This is because it is less expensive and if the results prove to deliver less dose to the critical organs, it would be a preferred option.

In this research project, 3D-conformal radiotherapy is applied.

Table 3.1 - Evaluation card for comparison of competitive technical solutions

Evaluation criteria ***example***	**Criterion weight**	**Points**		**Competitiveness** Taking into account weight coefficients	
		P_f	P_i	C_f	C_i
1	2	3	4	7	8
Technical criteria for evaluating resource efficiency					
1. Risk of radiotherapy side effects	0,18	4	3	0,62	0,3
2. Dose homogeneity	0,13	5	4	0,56	0,5
3. Dose on organs at risk	0,2	4	3	0,8	0,39
4. Ease of planning	0,14	3	4	0,5	0,6
5. Risk of treatment failure	0,1	5	4	0,8	0,56
Economic criteria for performance evaluation					
1. Competitive methods	0,08	5	4	0,5	0,4
2. Expected lifecycle	0,07	4	4	0,35	0,35
3. Development cost	0,1	5	4	0,6	0,34
Total	**1**	**35**	**30**	**4,73**	**3,44**

This analysis suggests that the study is effective because it provides acceptable quality results. Further investment in this development can be considered reasonable. Hence, 3D-conformal radiotherapy can be considered a better option compared to 2D-conventional radiotherapy.

3.3 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 3.2.

Table 3.2 - SWOT analysis

	Strengths: S1. Increases dose to tumor lead to increase tumor control. S2. Shorter treatment time	**Weaknesses:** W1. Lack of necessary software at oncology department of hospitals.
Opportunities: O1. Treatment of patients with cervical cancer. O2. Reduction in patient's treatment time	***Strategy which based on strengths and opportunities:*** 1. Acceleration of the entire course of Radiotherapy.	***Strategy which based on weaknesses and opportunities:*** 1. Training of medical physicists to work with the planning program.
Threats: T1. Lack of commercial interest in the project due to the availability of	***Strategy which based on strengths and threats:*** 1. Calculation of biological effective dose (BED) and	***Strategy which based on weaknesses and threats:*** 1. Creation of a statistical database showing the

other 3D-CRT techniques	equivalent dose in 2 Gy/fr (EQD2) for 3D-CRT and brachytherapy boost.	comparison between 3D-CRT and brachytherapy boost.

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.

3.4 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.

3.4.1 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 3.3 - Stakeholders of the project

Stakeholders of the project	**Stakeholders of the project expectations**
Cancer hospitals/clinics	Less procedure time; Convenient in usage; High efficiency of the procedure
Research Institutions	Less procedure time; Convenient in usage; High efficiency of the procedure
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 3.4.

Table 3.4 - Project goals and results

Project goals	Optimize combined course radiotherapy for patients with cervical cancer to reduce doses to critical organs, taking into account modern approached to topometry and dosimetry planning.
Expected results of the project	Based on the conducted research, the results of the treatment plans are analyzed for the different. Efficiency of various treatment machines are

	compared.
Acceptance criteria of the project result	Efficiency in relation to the proposed measures to improve the quality of radiotherapy treatment and ensure maximum dose to the target tumor.
Requirements to the project results	The project is completed on time.
	Stability of technological equipment.
	The efficiency of the equipment used.
	The results are used to improve treatment planning for cancer patients. That is, to reduce doses to critical organs while ensuring maximum dose to the target volume.

3.4.2 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 table 3.5.

Table 3.5 - Project Working Group

№	**Name**	**Role in the Project**	**Functions**	**Hours spent** (working days (from table 3.7) × 6 hours)
1	Irina Miloichikova	Scientific Supervisor	Coordination of work activities, guidance and assistance in project implementation. Verification of results obtained.	100
2	Esther Kwashie	Student	Work on project implementation.	750
Total:				850

Assumptions and constraints

Limitations and assumptions are summarized in table below.

Table 3.6 - Limitations and assumptions

Factor	**Limitations/assumptions**
1. Project budget - for design	1 112 819,65 RUB
1.1 Source of budgeting	Own funds / bank loan
2. Project timeline:	1 February 2022 – 20 May 2022
2.1 Date of approval of the project management plan	12 February 2022
2.2 Project completion date	20 May 2022
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.

3.5 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.

3.5.1 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.

3.6 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 3.7 - Project duration and timeline for various processes.

Job title	Duration, working days	Start date	Date of completion	Participants
Drawing up the technical assignment	5	1/02/2022	5/02/2022	Scientific supervisor
Literature review	15	6/02/2022	20/02/2022	Student
Calendar planning	2	21/02/2022	22/02/2022	Scientific supervisor, student
Research method/procedure	3	23/02/2022	25/02/2022	Scientific supervisor
Contouring	9	14/03/2022	24/03/2022	Student
Plan simulation	26	25/03/2022	29/04/2022	Scientific supervisor, Student
Analysis of the results	7	30/04/2022	06/05/2022	Scientific supervisor, Student
Summary of results	3	09/05/2022	11/05/2022	Student
Evaluation of the	3	11/05/2022	13/05/2022	Scientific

effectiveness of the results				supervisor, student
Ph.Dawing up a final report	10	14/05/2022	23/05/2022	Student
Defense Preparation	8	24/05/2022	31/05/2022	Student

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 3.8 - Gantt chart showing the timeline of the project

	Activities	Participants	T_c, days	Duration of the project: February	March	April	May
	Ph.Dawing up the technical assignment	Scientific supervisor	**5**				
	Literature review	Student	**15**				
	Calendar planning	Scientific supervisor, student	**2**				
	Research method/ procedure	Scientific supervisor	**3**				
	Contouring	Student	**9**				
	Planning	Scientific Supervisor, Student	**26**				
	Analysis of the results	Scientific supervisor, Student	**7**				
	Summary of results	Student	**3**				
	Evaluation of the effectiveness of the results	Scientific supervisor, student	**3**				
0	Ph.Dawing up a final report	Student	**10**				
	Defense Preparation	Student	**8**				

- 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 46 days. The total number of working days is 91.

3.7 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 table 3.9.

Table 3.9 – Grouping costs by articles

Name	Cost, rubles
1. Material costs	6070,00
2. Equipment costs	647000,00
3. Basic salary	235083,49
4. Additional salary	23508,35
5. Labor tax	70078,39
6. Overhead	129295,92
7. Other direct costs	1783,50
Total planned costs	1 112 819,65

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.

The calculation of material costs may be also 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 3.10 shows the costs of specialized equipment. This point includes the costs associated with the acquirement of special equipment necessary to perform tasks of the research.

Table 3.10 – Costs of specialized equipment

Name	Unit per measurement	Quantity (units, amount)	Price per unit (rubles)	Sum (rubles)
Laptop	Unit	1	40000	40000
Microsoft windows 10 professional RU x 64	Unit	1	5000	5000
Kaspersky anti-virus	Unit	1	2000	2000
XiO and HDRplus TPS	Unit	2	300000	600000

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

Table 3.11 - Costs of other materials resources

Name	Unit per measurement	Quantity (units, amount)	Price per unit (rubles)	Sum (rubles)
Stationaries	Unit	1	1,000	1,000
Transportation	Unit	70	50	3,500
Printing	Page	200	5	1,000
Folder	Unit	2	10	20
Stapler	Unit	1	200	200
Staples	Pack	1	50	50
Hole puncher	Unit	1	300	300
Total costs for materials Total transportation and purchasing costs (3-5%) Total costs per article, C_m				

3.8 Calculation of the Depreciation

The cost of specialized equipment is recorded in the form of depreciation charges. Depreciation is a reduction in the value of an asset over time, due in particular to wear or tear. To calculate the total depreciation of the specialized equipment, the annual depreciation is calculated first, then the monthly depreciation, according the number of working days the equipment was used. The annual depreciation is calculated using the following formula:

$N_D = \frac{1}{T} \cdot 100\%$, where T is the expected lifetime in years.

The life time of the laptop is approximately 10 years, the Microsoft Windows 10 license is 4 years, the anti-virus software is 1 year, and the Xio TPS is 13 years. Then the annual depreciation rate for each of them respectively, is:

$$N_D = \frac{1}{10} \cdot 100\% = 10\ \%,$$

$$N_D = \frac{1}{4} \cdot 100\% = 25\ \%,$$

$$N_D = \frac{1}{1} \cdot 100\% = 100\ \%$$

$$N_D = \frac{1}{13} \cdot 100\% = 7.7\ \%$$

The daily depreciation is estimated based on the number of days the equipment is used. In this project, it is assumed that each specialized equipment is used for a period of 5 months, which is 150 days. Hence, the depreciation is calculated as such:

$D_L = P \cdot \frac{N_D}{100} \cdot \frac{T}{365}$, where P is the cost of the equipment, N_D is the annual depreciation and T is the period of use in months.

$$D_L = 40000 \cdot \frac{N_D}{100} \cdot \frac{T}{365} = 40000 \cdot \frac{10}{100} \cdot \frac{150}{365} = 1643{,}84 \text{ RUB},$$

$$D_{Win10} = 5000 \cdot \frac{N_D}{100} \cdot \frac{T}{365} = 5000 \cdot \frac{25}{100} \cdot \frac{150}{365} = 513{,}7\ RUB,$$

$$D_{SS} = 2000 \cdot \frac{N_D}{100} \cdot \frac{T}{365} = 2000 \cdot \frac{100}{100} \cdot \frac{150}{365} = 821{,}92 \text{ RUB},$$

$$D_{TPS} = 600000 \cdot \frac{N_D}{100} \cdot \frac{T}{365} = 600000 \cdot \frac{7.7}{100} \cdot \frac{150}{365} = 18986{,}3 \text{ RUB},$$

The sum of depreciation for all equipment is:

$$D = 21965{,}76\ RUB$$

3.9 Basic Salary

The basic salary includes the basic salary of scientific and engineering workers, and all other participants directly involved in the performance of this project. The amount of salary expenses is determined based on the labor intensity of the work performed and the current system of remuneration. The basic salary includes a bonus paid monthly from the salary fund (the amount is determined by the Regulations on Remuneration of Labor).

The basic salary (S_b) is calculated according to the following formula:

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

where S_b – basic salary per participant;

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

S_a - the average daily salary of a participant, rub.

The average daily salary for a 5-day working week is calculated by the formula:

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

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 = 11.2 months, 6 day per week;

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

Table 3.12 - 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	48

- sick absence	
The valid annual fund of working time	251

Monthly salary is calculated by formula:

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

where S_{base} – base salary, rubles;

$k_{premium}$ – premium rate;

k_{bonus} – bonus rate;

k_{reg} – regional rate.

Assuming, an associate professor of technical sciences, working at TPU has a salary equal to 40000 rubles and a medical physicist with no experience in Tomsk has an average salary of 20000 rubles. With this in mind, the total salary of the project manager and project executor is calculated

Monthly salaries:

For scientific supervisor:

$$S_{month} = S_{base} \cdot (k_{\text{premium}} + k_{bonus}) \cdot k_{reg} = 40000 \cdot (1{,}3 + 0{,}25) \cdot 1{,}3 = 80600 \text{ RUB}$$

For student:

$$S_{month} = S_{base} \cdot (k_{\text{premium}} + k_{bonus}) \cdot k_{reg} = 20000 \cdot (1{,}3 + 0{,}25) \cdot 1{,}3 = 40300 \text{ RUB}$$

Table 3.13 - Calculation of the base salaries

Performers	S_{base}, rubles	$k_{premium}$	k_{bonus}	k_{reg}	S_{month}, rub.	W_d, rub.	T_p, work days (from table 3.7)	W_{base}, rub.
Scientific supervisor	40000	1,3	0,25	1,3	80600	2686,67	46	123586,82
Student	20000				40300	1343,33	83	111496,67
Total								235083,49

3.9.1 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:

$$W_{add} = k_{extra} \cdot W_{base},$$

where W_{add} – additional salary, rubles;

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

W_{base} – base salary, rubles.

Table 3.14 - Additional Salary

Participant	Additional Salary, rubles
Scientific supervisor	12358,68
Student	11149,67
Total	23508,35

3.9.2 Social Security Pays (Labor Tax)

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

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

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%.

Table 3.15 - Labor tax

	Scientific supervisor	Student
Coefficient of deductions	30 %	
Salary (basic and additional), rubles	135945,5	122646,34
Labor tax, rubles	40783,65	36793,90
Total		77577,55

3.9.3 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 formula:

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

where k_{ov} – overhead rate.

Table 3.16 - Overhead cost

	Scientific supervisor	**Student**
Overhead rate	50%	
Salary, rubles	135945,5	122 646,34
Overhead, rubles	67972,75	61 323.17
Total		129 295,92

3.9.4 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 3.17 - Other direct costs

	Power rates, kWh	Power of equipment, kW	Equipment usage time, hr	Energy cost, rubles
Computer for TPS	5.8	0.5	123	356,70
Laptop	5.8	0.5	492	1426,80
Total				1783,50

3.10 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.

3.10.1 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 3.18.

Table 3.18 – Evaluation of the performance of the project

Criteria	Weight criterion	Points	
		I_m^p	I_m^a
1. Risk of radiotherapy side effects	0,18	5	3
2. Dose homogeneity	0,13	4	4
3. Dose on organs at risk	0,2	5	5
4. Ease of planning	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_{fin}^p) and of the analog (I_{fin}^a) is determined according to the formula of the integral basis of the financial integral resource efficiency:

$$I_{fin}^a = \frac{I_m^a}{I_f^a};\ I_{fin}^p = \frac{I_m^p}{I_f^p};$$

$$I_{fin}^a = \frac{4{,}09}{1} = 4{,}09;\ I_{fin}^p = \frac{4{,}55}{0{,}93} = 4{,}89$$

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

$$E_{av} = \frac{I_{fin}^{p}}{I_{fin}^{a}}$$

Where E_{av} - is the comparative project efficiency; I_{fin}^{p} - integral indicator of project; I_{fin}^{a} - integral indicator of the analog.

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

Thus, the effectiveness of the development is presented in table 3.19.

Table 3.19 – Efficiency of development

Indicators	**Points**	Analog
	Project	2D-conventional radiotherapy
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 is the 2D-conventional radiotherapy.

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.

The legal basis for organizing work in emergency situations and mitigating their consequences is provided by the laws of the Russian Federation «On Protection of the Population and Territory from Natural and Man-Caused Emergencies» (1994), «On Fire Safety» (1994), and «On the Use of Atomic Energy» (1995).

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 [45].

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 [46].

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 [45].

4.2 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.

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 [47].

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 3D-conformal radiation therapy (3D-CRT) using the Elekta Synergy medical linear accelerator and Theratron Equinox Cobalt-60 machine (for external beam radiotherapy), and the Bebig multi-source Co-60 HDR machine (for brachytherapy). The 3D-CRT plans represent the delivery pattern of ionizing radiation to the tumor. Consequently, the object of study may create a detriment of elevated levels of ionizing radiation when implementing 3D-CRT plans, thus delivering the dose to the tumor.

The dangerous and harmful factors are presented in Table 4.1.

Table 4.1 - 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” [4].
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” [4].
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” [4].
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” [4].
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” [5].
6. Increased levels of ionizing radiation	+	+	+	Sanitary rules 2.6.1.2523-09. Radiation Safety Standards (NRB-99/2009) [6].

A student working at a computer is exposed to physical factors: temperature and humidity, noise, static electricity, electromagnetic fields of low purity, illumination; presence of radiation. Psychophysiological dangerous and harmful factors are divided into: physical overload (static, dynamic) and mental stress (mental overstain, monotony of work, emotional overload) [47].

4.2.1 Analysis of Hazardous and Harmful Production Factors

The main parameters that characterize working conditions are the microclimate, noise, vibration, 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.

4.2.2 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 [48] and given in table 4.2 below.

Table 4.2 - Optimal parameters of the microclimate [48]

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 [49] 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.

4.2.3 Excessive Noise

Noise and vibration worsen working conditions, have a harmful effect on the human body, namely, the organs of hearing and the whole body through the central nervous system. It results in weakened attention, deteriorated memory, decreased response, and increased number of errors in work. Noise can be generated by operating equipment, air conditioning units, daylight illuminating devices, as well as spread from the outside. When working on a PC, the noise level in the workplace should not exceed 50 dB [48]. Noise levels did not exceed 50 dB in the medical physicists' room of the Tomsk Oncology Institute, where this research work was conducted.

4.2.4 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 [48], 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 4.3 – Permissible levels of intensity and density of the electromagnetic field [48]

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

4.2.5 Insufficient Illumination of the Working Area

Light sources can be both natural and artificial. The natural source of the light in the room is the sun, artificial light are lamps. With long work in low illumination

conditions and in violation of other parameters of the illumination, visual perception decreases, myopia, eye disease develops, and headaches appear.

According to the standard, the illumination on the table surface in the area of the working 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% [50].

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 [50].

The work was conducted in the medical physicists' room of the Tomsk Oncology Institute. 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 [50].

Calculation of the general fluorescent lighting system. Distance of luminaires from ceiling (overhang) h_{ov} – 0.5 m [50]. 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).

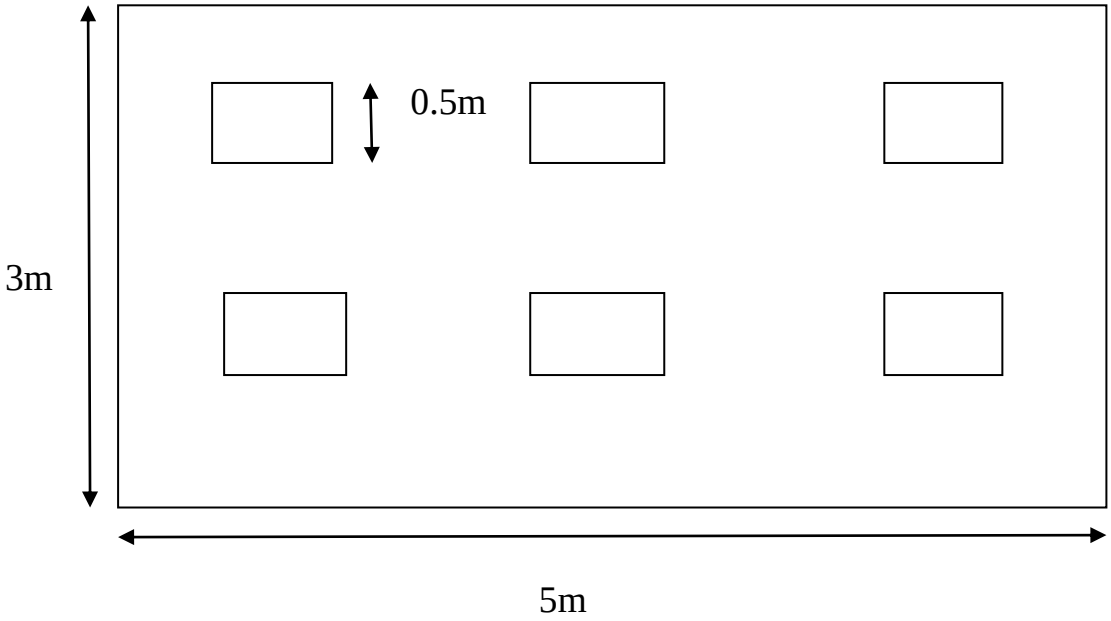

Figure 4.1 – Downlights positions in the working room

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 [48]; 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. Hence, the lighting system of the operating room corresponds to the standard.

4.2.6 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 [48]. 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 [48].

The upper limits for values of contact current and voltage are shown in Table 4.4 below.

Table 4.4 – Upper limits for values of contact current and voltage [48]

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

4.2.7 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) [20]. 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 [51], 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 [51].

Table 4.5 shows dose limits for all three groups of people.

Table 4.5 – Basic dose limits [51]

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.			

For women below the age of 45 years there is a limit of 1 mSv per month of equivalent dose on lower abdomen. During gestation and breastfeeding woman must not work with radiation sources [51].

4.3 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 [47]. 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 [52].

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 [53].

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 [47].

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 [54].

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 [54].

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 [55].

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 [56].

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 [51].

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 [51].

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 [51].

4.4 Ecological Safety

Sources of ionizing radiation used in medicine could be divided into two groups: radioactive substances and radiation generators. The difference is that radiation generators like accelerators and x-ray tubes emit ionizing radiation only when they are turned on. In ordinary work with necessary safety precautions, there are insignificant impact of using sources of ionizing radiation on environment. The immediate effect of ionizing radiation is ionization of air in room, but after a specified time the ionization disappears.

For the implementation of the work, special therapeutic installations of radiation therapy are required. Two types of equipment can be used, the first of which is an electron accelerator. The danger of such in devices is minimized and work on such equipment does not have a significant impact on the environment. The second type of equipment, it is device with a radioactive source. In case of using radioactive

materials, the danger could occur only in accidents with stealing and loosing such materials due to high radioactivity.

Process of investigation itself in the thesis do not have essential effect on environment. In this research, the impact on the environment can occur in the case of disposal of a personal computer, which contains both organic materials and a large number of metallic chemical elements. All these components are not dangerous during the operation of the product.

Technogenic waste in the form of computer monitors that have served their time cannot be destroyed by nature itself. Moreover, their bulkiness and the presence of toxic chemicals inside do not allow this technique to be destroyed by incineration. Metals such as lead, antimony, mercury, cadmium, arsenic, which are part of electronic components, are transformed under the influence of external conditions into organic and soluble compounds and become the strongest poisons [20].

Therefore, burial and disposal of high-tech waste should be carried out in specially prepared landfills. Landfills for storage and disposal must provide reliable protection against penetration of waste into the lithosphere, atmosphere and hydrosphere [57].

4.5 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 [58].

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 4.6 below.

Table 4.6 – Categories of premises for explosion and fire hazard [58]

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 [59]. The room where the research was conducted is in category B4.

4.5.1 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 [60].

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, 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 [59].

The most likely emergencies that may occur at the workplace are fire, electrocution and falling from a height with their proposed prevention and emergency plan. Possible emergency situations, their preventions and emergency plan are presented in Table 4.7 below.

Table 4.7 – 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	An object falling from a height onto a person in the room	– making sure objects lying low; – correct placement of equipment	– Inform management and supervisor; – call the emergency service – telephone 112; – take measures to mitigate the consequence of the accident
3	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

Conclusion

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

- deviation of microclimate indicators [48];
- excessive noise [48];
- increased level of electromagnetic radiation [48];

- insufficient illumination of the working area [48];
- abnormally high voltage value in the circuit, the closure which may occur through the human body [61];
- increased levels of ionizing radiation [51].

All relevant safety measures and precautions to lower the likelihood of accidents and traumas during investigation were brought to light. Attention was given to the potential negative effect on environment due to the study and is not significant. The most likely emergencies that could have occur at the workplace are fire, electrocution and falling from a height. 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.

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