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Студент

Группа	ФИО	Подпись	Дата
0AM1M	Фаустина Нтим Опоку		

Руководитель ВКР

Должность	ФИО	Ученая степень, звание	Подпись	Дата
Доцент НОЦ ЦМЯО ИЯТШ	Милойчикова И.А.	к.ф.-м.н.		

### КОНСУЛЬТАНТЫ ПО РАЗДЕЛАМ:

По разделу «Финансовый менеджмент, ресурсоэффективность и ресурсосбережение»

Должность	ФИО	Ученая степень, звание	Подпись	Дата
Доцент ОСГН ШИП	Меньшикова Е.В.	к.ф.н.		

По разделу «Социальная ответственность»

Должность	ФИО	Ученая степень, звание	Подпись	Дата
Доцент ОЯТЦ ИЯТШ	Передерин Ю.В.	К.Т.Н		

### ДОПУСТИТЬ К ЗАЩИТЕ:

Руководитель ООП	ФИО	Ученая степень, звание	Подпись	Дата
Nuclear medicine / Ядерная медицина	Верхотурова В.В.	к.и.н.		

School of Nuclear Science & Engineering

Field of training: 14.04.02 Nuclear Science and Technology

Specialization: Nuclear medicine

Research and Training Centre for International Nuclear Education and Career, School of Nuclear Engineering

### MASTER THESIS

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Student

Group	Full name	Signature	Date
0AM1M	Faustina N. Opoku		

Scientific supervisor

Position	Full name	Academic degree, academic rank	Signature	Date
Associate Professor	Irina A. Miloichikova	PhD		

### ADVISERS:

Section “Financial Management, Resource Efficiency and Resource Saving”

Position	Full name	Academic degree, academic rank	Signature	Date
Associate Professor	Ekaterina V. Menshikova	PhD		

Section “Social Responsibility”

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

### ADMITTED TO DEFENSE:

Programme Director	Full name	Academic degree, academic rank	Signature	Date
Nuclear medicine	Vera V. Verkhoturova	PhD		

## LEARNING OUTCOMES

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

<b>PC(U)-7</b>	Ability to develop reference books, tables and software containing data for clinical use in dosimetric planning of radiation therapy, radionuclide diagnostics and therapy.
<b>PC(U)-8</b>	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.
<b>PC(U)-9</b>	Ability to conduct training sessions and develop instructional materials for the training courses within the cycle of professional training programs (bachelor degree programs).

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

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Field of training (specialty): 14.04.02 Nuclear Science and Technology

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27.03.2023	5. Processing of received data	20
26.04.2023	6. Documentation of the work performed	15
01.06.2023	7. Preparing for defense	15

**COMPILED BY:**

**Scientific supervisor:**

Position	Full name	Academic degree, academic status	Signature	Date
Associate Professor	Irina A. Miloichikova	PhD		

**APPROVED BY:**

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

## **List of Abbreviations**

2D-conventional radiotherapy – Two dimensional conventional radiotherapy

3D-CRT – Three dimensional conformal radiotherapy

BCS – Breast conserving surgery

BRCA 1 – Breast cancer gene 1

BRCA 2 – Breast cancer gene 2

BED – Biologically effective dose

CT – Computed tomography

DCIS – Ductal carcinoma *in-situ*

DVH – Dose volume histogram

EBRT – External beam radiation therapy

EQD<sub>2</sub> – Equivalent dose in 2 Gy

ER – Estrogen receptor

ER- – Estrogen receptor negative

ER+ – Estrogen receptor positive

Gy – Gray

HER2 – Human epidermal growth factor receptor 2

HER2- – Human epidermal growth factor receptor 2 negative

HER2+ – Human epidermal growth factor receptor 2 positive

HR- – Hormone receptor negative

HR+ – Hormone receptor positive

IDCs – Invasive ductal carcinomas

IDCs -NST – Invasive ductal carcinomas of no special type

IDCs -ST – Invasive ductal carcinomas of special type

IGRT – Image guided radiation therapy

ILCs – Invasive lobular carcinomas

IMRT- Intensity modulated radiation therapy

IORT – Intraoperative radiation therapy

ILCs – Invasive lobular carcinomas  
LCIS – Lobular carcinoma *in-situ*  
MLC – MultiLeaf collimator  
NDCs – Non-communicable diseases  
OARs – Organs at risks  
RTOG – Radiation therapy oncology group  
SD – Standard deviation  
SEB – Sequential boost  
SIB – Simultaneous integrated boost  
TPS – Treatment planning system  
VMAT – Volumetric modulated arc therapy  
WBI – Whole breast irradiation

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# 1. Breast cancer

Breast cancer occurs when healthy cells coating the duct or lobules of the breast divides rapidly, grow out of control, and form tumors [8]. The human breast are paired structures located between the 2<sup>nd</sup> and 6<sup>th</sup> ribs below the subcutis on the muscles of the ventral thorax [8]. It include the duct and lobules, two types of epithelial cells (luminal and myoepithelial), and two types of stroma (interlobular and intralobular) as shown in Figure 1.1 [9]. The female breast consists of about 10–20 lobes, each containing lobules, and many terminal duct lobular units that constitute the milk duct system and drain to the nipple via the primary milk ducts and the lactiferous sinuses [8]. Each of these elements can be a site for both benign and malignant tumors (Figure 1.2).

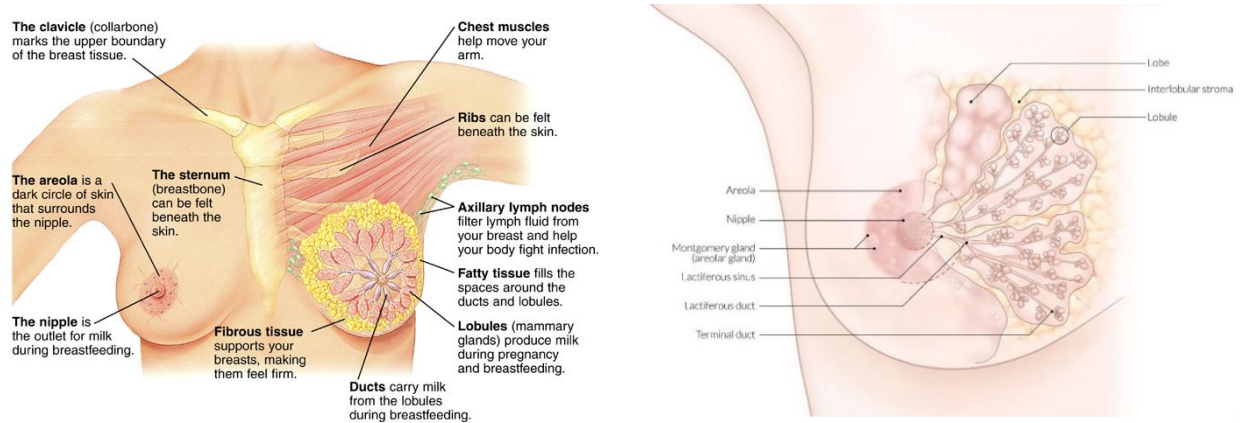


Figure 1.1 – Breast anatomy

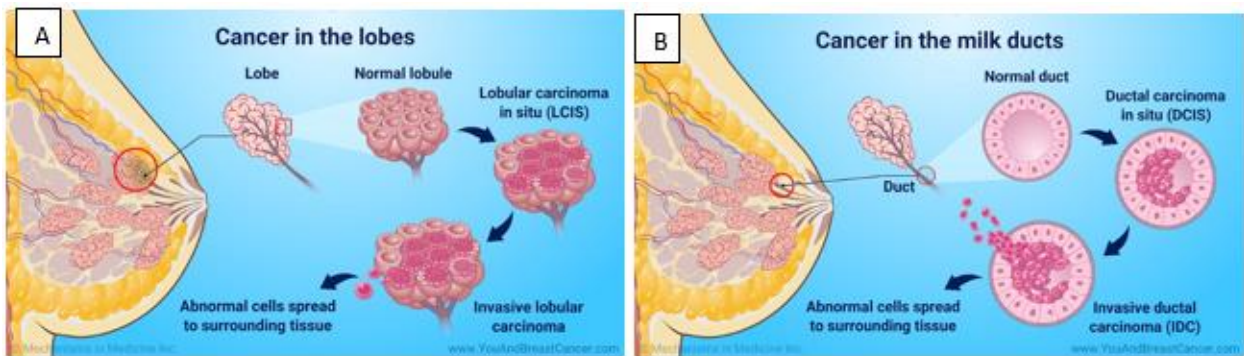


Figure 1.2 – An image of cancer in the breast. A- Cancer in the lobes; B- Cancer in the duct

Breast cancer can affect both men and women, but it is increasingly frequent in women. Being female, increasing age, history of breast conditions or breast cancer, closed relative with the disease, germline mutation of BRCA1 and BRCA2 genes, inherited genes that increase cancer risk, radiation exposure, obesity, little or no physical exercise, early period, later menopause, late childbirth, reduced breastfeeding, fewer children, having never been pregnant, postmenopausal hormone therapy, oral contraceptives and alcohol are some of the factors that increases the chance of getting this cancer as a woman [10,11]. Male breast cancer risk increases with age, BRCA1/2 gene mutations, and obesity just as female breast cancer does. Klinefelter syndrome, testicular diseases and tumors, diabetes, gynecomastia and obesity are some risk factors for men [12-14].

### **1.1 Incidence of breast cancer**

Breast cancer is a major public health issue worldwide with a high incidence rate in almost all countries [15]. This cancer affects approximately 1 in every 8 women, but only about 1 in 1,000 men. Annually, about 2.26 million cases are reported, representing 11.7% of total cancer cases and 24.5 % of cancers in female [16]. Indeed, population expansion and ageing populations are contributing to an increase in the worldwide burden of cancer among women in all nations. Approximately 49.5% of the people on earth are women, and they make up a higher share of people who are over 60 years of age. Breast cancer incidence varies by region and country [11]; hence, certain countries or regions have a higher incidence than others. Breast cancer cases are reported more in high-income regions than in low-income regions. For instance about 92 per 100,000 cases are reported in North America whereas about 27 per 100,000 are recorded in middle Africa and eastern Asia [11] In this regard, the highest incidence is in North America, Australia, New Zealand, northern and western Europe.

Breast cancer cases has been rising at a rate of 3.1% globally every year since 1980, reaching more than 1.6 million cases in 2010, and this trend is projected to

continue [11]. In 2012, about 1.7 million new cases and 521,900 deaths were reported globally [17]. Ferlay et al [18] reported in their studies that about 1.7 million new cases are recorded yearly making up twenty five percent of all cancer cases. In 2017, about 54,700 women and 390 men were diagnosed of this cancer in the United Kingdom as reported by Cancer Research UK[19]. About 2.09 million new cases and 630, 000 deaths were recorded globally in 2018 [20].

In the United States, it is the commonest cancer and the second largest cause of cancer-related deaths among women. In 2019, about 268,600 women were diagnosed of the disease which accounted for about 15.2% - 30% of all cancer cases recorded in US women [21]. Approximately, 42,000 US women die yearly from this cancer.

This cancer occurs in men as well, but it is rare, constituting less than one percent of all breast cancer [22]. In 1995, out of the 183,400 cases of breast cancer reported in the United States, 1400 was linked to breast cancer in men, and 240 died [23]. Unfortunately, male breast cancers are mostly discovered at the advanced stage due decreased awareness [23]. In a studies conducted by Seer [23], they observed a decrease in deaths from 0.4 deaths per 100 000 men in 1975-1979 to 0.3 deaths per 100 00 men in 2013-2017. This decrease was associated with advances in treatment as at that time. Male breast cancer globally is not more pronounced compared to women. However, in 2019, approximately 2,670 male breast cancer cases were recorded, representing < 1% of all male cancer cases that year [21].

About 2.3 million new cases were recorded globally in 2020 with 685, 000 deaths as illustrated in Figure 1.3 [24] . The 10 countries that recorded the highest breast cancer occurrences and fatalities in 2020 are presented in Table 1.1 [24].

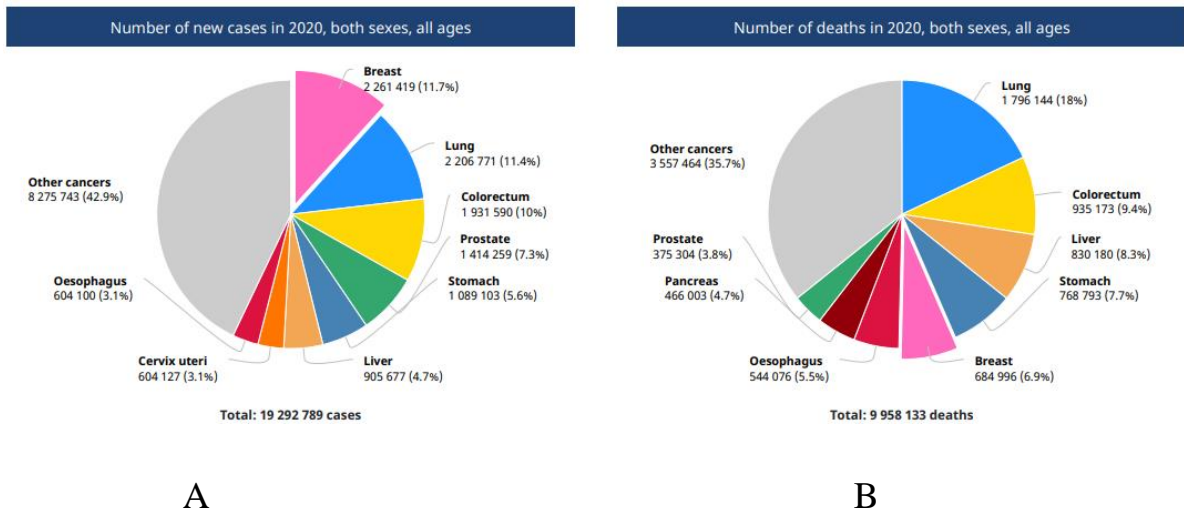


Figure 1.3 – Cancer incidence and mortality statistic worldwide. A- Number of new cases in 2020; B- Number of deaths in 2020. Source: Globocan 2020

Table 1.1 – Countries with highest rate of breast cancer incidence and mortality in women in 2020. A- Nation with largest incidence rate; B- Nations with the largest fatality rate.

A			B		
Rank	Country	Number	Rank	Country	Number
	World	2,261,419		World	684,996
1	Belgium	11,734	1	Barbados	111
2	The Netherlands	15,725	2	Fiji	184
3	Luxembourg	497	3	Jamaica	637
4	France	58,083	4	Bahamas	80
5	France, New Caledonia	185	5	Papua New Guinea	847
6	Denmark	5,083	6	Somalia	1,189
7	Australia	19,617	7	Mali	1,425
8	New Zealand	3,660	8	Dominican Republic	1,577
9	Finland	5,228	9	Syria	1,946
10	US	253,465	10	Samoa	21

In the United States, about 287,850 incidences were recording in 2022 [16] In India, breast cancer is among the five leading cancers. In China, about 429,105 cases were recorded, which represent 8.9% of all cancer cases. In Chinese women, breast

cancer was the leading the cancer, representing 19.5 % of cancer cases in female in 2022 [16].

In Africa, breast cancer is among the 3 major cancer of concern. Similar to other countries, it is the most common cancer in women. And in 2022, 186, 598 new cases and 85,787 deaths were recorded in African women.

Despite the fact that the rate of occurrence in advanced countries is substantially higher than in less advanced countries, death rate is higher in less advanced countries due to enhanced screening and early detection of the cancer. In contrast, screening and healthcare are not as widely available in less developed countries where the disease is typically diagnosed at the advanced stage. Breast cancer burden is projected to increase to over 3 million with 1 million deaths yearly due to population growth and aging[24].

## **1.2 Clinical classification of breast cancer**

Breast cancer is a highly diverse disease because of its different morphological characteristics, and response to treatments [25]. Due to this diversity, the disease cannot be viewed as a whole clinic-pathological entity, and hence requires classification [25]. Accurate classification of breast cancers into clinically relevant subtypes is very important for therapeutic decision making, predicting survival, and informing preventive activities [26,27].

In a study conducted by De Ward et al [28], they discovered that female breast cancer mortality has a bimodal age distribution, with early and late age distributions at diagnoses. Based on these findings, they hypothesized that there are two types of breast cancer which are influenced by age and hormone. The first type of breast cancer is hormone-dependent, with a peak incidence around the age of 50, whereas the second type is hormone-independent, with a peak incidence around the age of 60 [28]. However, later studies revealed that these two age-related groupings of breast tumors had separate etiologies [29–31]. In view of this, breast cancer is grouped into classes by histological and molecular appearances, tumor grade, and tumor stage.



### **1.2.1 Molecular classification**

This classification is based on gene expression. Perou et al [32] in 2005 identified two groups of breast cancer which they further divided the groups into four molecular subtypes on the basis of gene expression profile similarity and or epithelial cell of origin (luminal or basal). There are two hormone receptor positive (HR+) breast cancers (Luminal A and Luminal B) and two hormone receptor negative (HR-) cancers (human growth factor receptor (HER2)-enriched and basal-like) with distinctive biological and clinical features [30,33]. They are Luminal A (HR+/HER2), Luminal B (HR+/HER2+), HER2-enriched (HR-/HER2+), and triple-negative (HR-/HER2-). The group of genes that influence these subtypes are genes related to the expression of estrogen receptors (ER), progesterone receptors (PR), human epidermal growth factor receptor 2 (HER2), and cell proliferation regulator (Ki-67) [32].

Luminal A is the commonest subtype making up about half of newly detected cases [32] with age adjusted rate of 88.1 new cases per 100,000 women [34]. The biomarkers associated with this subtype are estrogen receptor positive (ER+), progesterone receptor positive (PR+), human epidermal growth factor receptor 2 negative (HER2-) and low Ki67. It is more common in non-Hispanic white women than in non-hispanic black women [28]. Luminal B can be grouped into Luminal B (HER2-) or Luminal B (HER2+). HER2+ subtype is distinguished by high expression of HER2, estrogen and progesterone receptor negative (ER- and PR-), and high Ki-67 [32]. The least common subtype is triple negative. Patients with BRCA 1 mutations and young women are more likely to experience it [32]. An overview of the types of classification is presented in Table 1.2 [32].

Table 1.2 – Classification of molecules subtypes of breast cancer

Molecular Subtypes	Luminal A	Luminal B		HER2+	Tripple negative (TN)
		(HER2-)	HER2+)		
Biomarkers	ER+ PR+ HER2- Ki67 low	ER+ PR- HER2- Ki67 high	ER+ PR- HER2+ Ki67 low/ high	ER- PR- HER2+ Ki67 high	ER- PR- HER2- Ki67 high
Frequency of cases (%)	40-50	20-30		15-20	10-20
Histological grade	Well differentiated (Grade 1)	Moderately differentiated (Grade II)		Little differentiated (Grade III)	Little differentiated (Grade III)
Prognosis	Good	Intermediate		Poor	Poor

### 1.2.2. Histopathological classification

This type of classification is based on the diversity of the morphological features of the tumor. To understand the morphological features of breast cancer, it is important to understand the location of the tumor, that is whether it is limited to the epithelial component of the breast or has colonized surrounding stroma as well as whether it appeared in the mammary ducts or lobes [35]. Features such as cell type characteristics, number of cells, type and location of secretion, immunohistochemical profile and architectural are used to classify breast cancer in this classification. Generally, carcinoma in situ and invasive carcinoma are the two major type breast cancer under this classification.

Carcinoma in situ is a proliferation of cancer cells in the epithelial cells within the ductal and lobular system of the breast without invading surrounding tissues. There are two types of carcinoma in situ: ductal and lobular carcinoma in situ (DCIS and LCIS). LCIS is an early type and the most common form of carcinoma in situ breast cancer that occurs within the ductal system and has not yet invaded surrounding tissues whereas DCIS is the rarest type which typically does not develop into invasive cancer [32]. Invasive carcinoma is a group of epithelial cancer that invade adjacent tissues and have the tendency to metastasize [32]. In this type, the cancer arises from the mammary

epithelium mostly from the terminal duct lobular unit cells. Invasive ductal carcinomas (IDCs) and invasive lobular carcinomas (ILCs) are the two types of breast cancer under this type of breast cancer with IDCs been the most dominant cases representing about [35] representing about 50% to 80% of breast cancer cases [32].

Furthermore, invasive ductal carcinomas can be classified as no specific type (IDC-NST) if they present insufficient morphological characteristics to be determined as a characteristic histological type or special type (IDC-ST) if they present sufficient distinctive characteristics and particular cellular and molecular behavior [32]. The most common IDC-ST are medullary carcinoma, metaplastic carcinoma, apocrine carcinoma, mucinous carcinoma, cribriform carcinoma, tubular carcinoma, neuroendocrine carcinoma, classic lobular carcinoma and pleomorphic lobular carcinoma.

### **1.2.3 Staging of breast cancer**

Staging is the process of measuring the size and how far the cancer has disseminated [36]. It is an integral component of treatment optimization, as well as determining prognosis and cancer classification. Determining the stage of a cancer depend on the size or extent of the primary tumor. That is, it considers if the malignant has migrated to nearby lymph nodes or distant organs [36]. If the cancer cell is within and confined to its original layer, then the stage is in situ whereas if it has spread to surrounding tissue, it is considered invasive. Invasive tumors are further classified as local, region, or distant dependent on the degree of spread.

Clinically, cancer growth and spread are assessed by TNM staging system: size or extent of primary tumor (T), absence or presence of regional lymph node involvement (N), and absence or presence of distant metastases (M). This system uses the letter “T” and a number (0-4) to describe the size and location of the tumor [36]. T0 indicates no primary tumor whereas T1-4 indicate tumors of increasing size and/or involvement of lymphatic vessels or surrounding tissues. N0 indicates the existence or

non-existence of cancer in the lymph node; N1 indicates the spread of tumor to 1-3 axillary/internal mammary lymph nodes; N2 means that 4-9 axillary lymph nodes are involved; whereas N3 indicates that more than 10 lymph nodes are involved [36,37]. According to American Cancer Society [36], once the T, N, M is established, a stage of 0, I, II, III, or IV is assigned, with stage 0 being in situ, stage I being early, and stage IV being the most advanced disease as shown in Table 1.3[36]. Stage 0: This is a precancerous breast cancer and it is located only in the breast. This stage is called the non-invasive or in situ stage and there are two types: lobular and ductal carcinoma in situ (LCIS and DCIS). In both LCIS and DCIS, there are abnormal growth of cells in either the lobules or duct which are not yet cancerous. However, these abnormal growth increases the risk of one developing an invasive breast cancer [38] In contrast to DCIS, LCIS normally does not become invasive if not treated.

Stages I and II are considered the early stage of breast cancer. This stage means the cancer has spread beyond the lobes or duct to adjacent tissues, making it an invasive one. In stage I, tumor size is 2 cm and no lymph nodes are involved where as in Stage II, the tumor size is greater than 2 cm but less than 5 cm and may involve one to three lymph nodes.

Stages IIIA and IIIB are locally advanced stage of breast cancer. Here, the cancer involves at least four lymph nodes and or the tumor size is greater than 5 cm.

Table 1.3 – Stages of breast cancer

Stage	T	N	M
0	Tis	N0	M0
IA	T1	N0	M0
IB	T0	N1mi	M0
	T1	N1mi	M0
IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
IIB	T2	N1	M0
	T3	N0	M0
IIIA	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1	M0
	T3	N2	M0
IIIB	T4	N0	M0
	T4	N1	M0
	T4	N2	M0
IIIC	Any T	N3	M0
IV	Any T	Any N	M1

### 1.3 Breast cancer therapy

Different cancer treatments are available, depending on a variety of things including the type of cancer, where it is located, its biological traits, its stage, patient's health and treatments goals [39]. Most treatments are designed to either directly kill or remove cancer cells or deprive them of signals needed for their survival. Generally cancer treatments are classified into three groups: surgery, systemic and radiation therapy [40]. Systemic therapy includes chemotherapy, hormonal therapy, targeted drugs, and immunotherapy. In most cancer cases, one or two of these treatments are combined for best results and administered as adjuvant or neoadjuvant.

#### 1.3.1 Surgery

Standard surgical therapy for breast cancer has seen significantly improvement over the past three decades, leading to far better outcomes. Removal of cancer and staging of the disease are the two major objectives of breast cancer surgery. In this

treatment, either the whole breast tissue is removed which is referred to as mastectomy or only the tumor and a margin of surrounding normal tissue is removed and this termed as breast conserving surgery (BCS) or lumpectomy.

In early stage treatments (stage I and II), the later is the most recommended surgery since it offers survival comparable to complete mastectomy and axillary dissection while sparing the breast [41] BCS with radiotherapy is recommended as the preferred treatment option because it is a less invasive procedure, provides a better cosmetic outcome, and is associated with less morbidity [42] However, BCS is not recommended for patients with late stage breast cancer. Despite equivalent survival and advantages of BCS over mastectomy, there are some BCS-eligible patients who still opt for mastectomy due to fear of recurrence, aversion of radiation and desire for symmetry [42,43].

Mastectomy, on the other hand removes the whole breast tissue which includes the skin, nipple, areola, and pectoral muscles [44]. There are several types of mastectomy which includes radical, modified radical, skin-sparing, and nipple sparing mastectomy[45]. In comparison to BCS, most mastectomy patients have a significantly lower body image, poorer sexual function, a lower quality of life and lower rate of surgical satisfaction [46].

Sentinel lymph node biopsy (SLNB) is frequently used in both BCS and mastectomy to evaluate the extent of the tumor. It entails the removal of one or more regional lymph nodes from the armpit in order to determine the lymph node(s) to which the cancer is most likely to spread. Axillary lymph node dissection (ALND) is used in patient who need extensive lymph node dissection [47] yet, this type of procedure might induce swelling in the arm due to lymph fluid retention (lymphedema). Swelling occurs in SLNB patients as well; however, the number of SLNB patients who experience it is lower [47].

### **1.3.2 Chemotherapy**

Chemotherapy utilizes anticancer medicines to halt the growth and spread of cancer cells by targeting and destroying the cells, and preventing them from proliferating [48–50]. The medications can be taken either orally or intravenously, and they can be used alone or in combinations of two or more. Based on the features of the breast cancer, chemotherapy may be coupled with other treatments like surgery or radiation therapy [49]. The administration of chemotherapy prior to or post-surgery depend on some factors such as the stage of the disease, and presence or absence of hormone receptors [49].

In the metastatic stage of the disease, chemotherapy is regarded as an essential component of systemic therapy and it is used in treating most early breast cancers such as the luminal A and B, HER2 enriched, and triple negative cases [50] Adjuvant Chemotherapy are given after breast cancer surgery to destroy any undetected cancer cells during the surgery and also to prevent recurrence. On the other hand, neoadjuvant treatment is given before surgery to reduce the size of large cancer cells so that surgical removal will be easier and less extensive [50]. The classes of drugs which are mostly used to treat breast cancers are alkylating agents, antimetabolites, anthracyclines and mitotic inhibitors [40].

Although chemotherapy is an effective treatment option, it has some side effects. These side effects depend on the type of drug and the quantity given, and how long the treatment last [40]. Some patients may experience hair loss, nail changes, mouth sores, loss of appetite or weight changes, nausea and vomiting, diarrhea, hot flashes and or vaginal dryness, and nerve damage [40].

### **1.3.3 Radiotherapy**

Radiotherapy is a type of treatment that uses high doses of radiation to destroy cancer cells and reduce tumor size [51] either by external beams and or by internal brachytherapy source. It entails the use of various types of radiation such as X-rays,

Gamma rays, particles to harm and eliminate tumors, either as a single modality or combined with surgery or chemotherapy [52]. At high doses, radiation kills or inhibits cancer cell division by damaging the DNA. External and internal radiotherapy are the two main types [53], and the type used for a patient depend on some factors such as type of cancer, tumor size and location, tumor proximity to radiosensitive normal tissues, health status and medical history of patient, and age. Radiotherapy can be used both intraoperatively and postoperatively, however it is most commonly employed postoperatively to eradicate undetected cancer cells after surgery in the breast, chest wall, or underarm, as well as to reduce the chance of the cancer occurring again.

Radiation applied after breast conserving surgery (BSC) has been found to decrease cancer relapse by about 50% after 10years and the probability of breast cancer fatality by about 20% after 15years [47]. On the other hand, it does not increase the survival chance for breast cancer patients of 70 years and above with small, lymph node- negative, HR+ cancers who are treated with hormonal therapy, despite reducing the probability of local relapse [47]. Radiation can also be applied in mastectomy patients whose tumor is larger than 5cm, and is spreading into surrounding tissues or if lymph nodes are included; as well as breast cancers that has expanded to the central nervous system or bones.

### **1.3.3.1 External beam radiotherapy**

External radiotherapy is more commonly used to treat breast cancer. This is a type of radiation therapy in which an external radiation source placed at a distance from the body is directed on the cancerous area [49, 53]. The therapy is delivered by a Cobalt unit which emits high-energy gamma rays, or a linear accelerator, which emits high-energy X-rays or electrons [52]. The radiation source is placed at a distance about 80-150cm from the patient in order to deliver an even dose of radiation to the target. Sometimes healthy tissues such as the skin surrounding the target are irradiated in the process which may cause reddening of the skin or partial superficial peeling. Higher-



energy beams are employed for deeper tumors to lessen this impact, and treatment is delivered from multiple angles to optimize the dose at the intersection [52]. Two-dimensional or conventional radiotherapy (2D), three-dimensional conformal radiotherapy (3D-CRT), intensity modulated radiotherapy (IMRT), volumetric modulated arc therapy (VMAT), and image guided radiotherapy (IGRT) are all forms of external radiotherapy.

2D-conventional radiotherapy is the oldest external radiotherapy technique, having been employed in cancer treatments for centuries before the introduction of modern techniques. This technology guides and positions radiation beams using 2D anatomical images and x-ray films [54]. Radiographs are utilized in this approach to outline anatomic landmarks, with a restricted number of beams to treat the target, which are either square or rectangular in shape [55]. Due to the low conformity of 2D conventional radiotherapy, healthy tissues surrounding the tumor frequently get excessive doses during irradiation. As a result, physical shielding or field shrinkage after a certain dose are used to protect organs at risk. In breast cancer treatment plans, wedges are used to compensate for this non-uniformity.

Conformal therapy is a general approach of maximizing dose to the target volume while sparing critical organs [56]. In comparison to 2D conventional therapy, this approach uses a large number of beams with varying weights, sizes, forms, and direction to treat the target. There are various types of conformal therapy, including 3DCRT, intensity-modulated radiation therapy (IMRT), and volumetric modulated arc therapy (VMAT), but 3DCRT was developed first. This therapy was developed based on 3D treatment with shaped fixed fields [56]. 3D-CRT entails the creation of 3-D computer images and the delivery of highly focused radiation to target while sparing surrounding healthy tissues [57]. This technique is dependent on precise anatomic delineation, particularly with regard to tumor site, as well as extensive knowledge of the mechanisms of likely infiltration and spread [56]. Furthermore, it employs a multileaf collimator (MLC) with 40-80 tungsten leaves in a step-and-shoot approach.

The MLC can move autonomously into the beam path to create an infinite number of beam shapes that are delivered from various angles to treat the target volume [58]. Through the tailoring of the MLC to adapt as much as feasible to the structure of the tumor, 3D-CRT maximizes dosage to the target volume while minimizing damage to essential organs without compromising dose uniformity and target volume coverage.

### **1.3.3.2 Brachytherapy**

Brachytherapy is a type of radiation therapy in which the source of radiation is placed near to or within the patient [59]. A radioactive substance is inserted into or near the tumor, where the dose is concentrated. And, because of the inverse square law, the dose falls off very quickly, with surrounding healthy tissues receiving substantially lower doses than the tumor. The location of the radioactive source within the patient (implant), type of loading, dose rate, duration of treatment, and type of emission all contribute to the classification of brachytherapy [59].

Moulds or plaques, interstitial, and intracavitary are the three most prevalent radioactive implant procedures used in brachytherapy. Moulds or plaques are used for superficial lesions, with the radioactive source inserted on the skin 1-2 cm from the lesion. It is most commonly used to treat ocular tumors. Interstitial implant entails temporarily inserting a radioactive source directly into the tumor volume, such as breast tissue [59]. In intracavity, radioactive source is positioned in a bodily cavity near or within the tissues to be treated. Breast brachytherapy has five approaches and these are shown in Figure 1.4 [61].

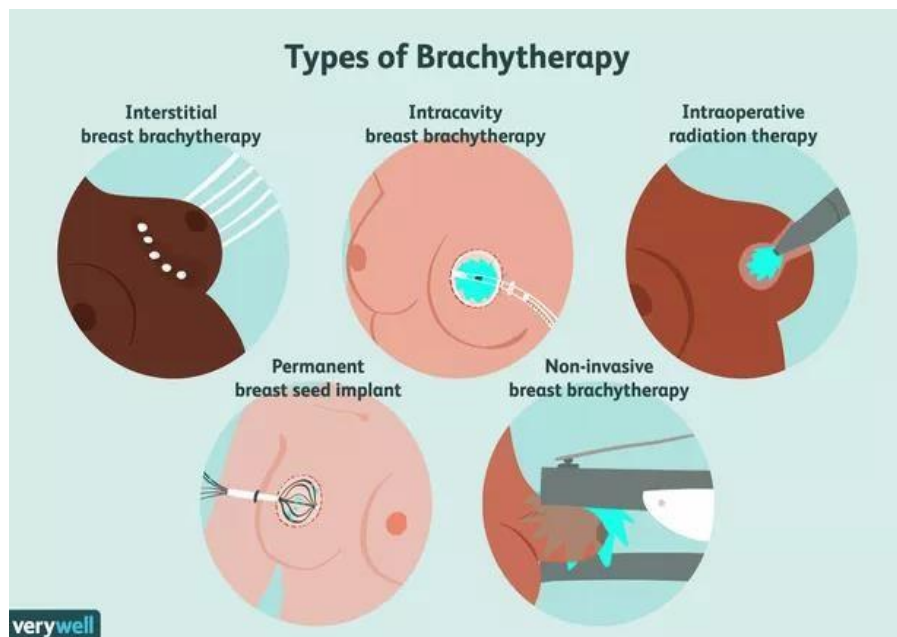


Figure 1.4 – Types of brachytherapy

Accelerated partial breast irradiation (ABPI), uses brachytherapy, to treat early-stage breast cancers that have not spread distant organs. This treatment is administered in conjunction with other therapies [61]. This technique is used to treat undetected cancer cells after lumpectomy, and occasionally maybe used to shrink tumors prior to surgery. In comparison to other treatments, brachytherapy damage surrounding healthy tissues less at high doses. During treatment, an imaging tool such as X-ray, ultrasound, or computed tomography is used to guide the placement of the radioactive source, and once the coordinated are established, one or more sources are carefully placed to the cancer [61].

### 1.3.3.3 Intraoperative radiotherapy

Intraoperative radiotherapy (IORT) is a type of radiation treatment that is used during surgery. In IORT, a substantial single dose of radiation, typically 10 Gy, is delivered to the tumor cavity, possibly the affected site and the lymphatic drainage area that are exposed during surgery in a single session [60,61]. This treatment is highly precise because it permits direct imaging of the tumor bed, thereby excluding normal tissues from the radiation field. As a result, damage to surrounding healthy tissues and

incidence of radiation related complications is greatly minimized. IORT delivered immediately after resection of the tumor shortens the time between surgery and radiation and decreases tumor cells proliferation [60].

#### **1.3.3.4 Boost technique in radiotherapy**

Postoperative radiotherapy has proven to reduce local recurrence and deaths due to breast cancer [62]. However, there is an additional increase in local control when boost is applied. Boost is the delivering of additional dose to the tumor bed following whole breast irradiation [62], Thus dose delivered to the tumor bed is always greater than the dose delivered to the whole breast in treatment plans with boost. In early stage breast where whole breast radiation after breast conserving surgery is recommended, boost is often applied to improve local control. In a study done by Kim et al. [63] they observed an anomalous increase in local recurrences in patient who omitted radiotherapy after their surgery. This is because tumor cell density is higher in a 4 cm area surrounding the macroscopic tumor edge, making that region more susceptible to recurrences.

Patients with higher risk of local recurrences are those with large tumor size, axillary lymph node involvement, young, high tumor grade, hormone receptor negative and positive margins [62]. These factors influence the addition of boost in a treatment as well. Adjuvant radiotherapy treatment include the use of external beam and intraoperative radiotherapy techniques, with the former being the most commonly used technique. Boost can be delivered by intraoperative technique and by external beam radiotherapy.

IORT is a technique that can be used either as a boost or full dose partial breast irradiation. IORT can be delivered by low-kV orthovolt systems and intraoperative electron radiation therapy (IOERT) [60].

In the former, a spherical applicator with the same size as the excision cavity is placed at the top of the source; giving the dose a spherical shape with a very steep dose

fall-off [60]. For X-ray IORT, usually 20 Gy per fraction is delivered as a boost to the tumor bed. IOERT is the application of electron radiation to directly to the tumor bed. The depth of the electrons can be controlled by the number of megavolts as they penetrate through tissues. The energies of the electrons used in IOERT ranges from 4-18 MeV. Usually dose of 10 Gy is applied to the tumor bed [60].

Boost dose can be divided into sequential (SEQ) and simultaneous integrated boost (SIB). SEQ is applied post WBI whereas SIB is delivered concurrently with WBI as shown in Figure 1.5. Simultaneous integrated boost compared to sequential integrated boost enables simultaneous delivery of varied dose per fraction to different target volumes while providing a high biologically effective dose to PTV. It reduces the treatment time and delivers a more homogenous and conformal dose than SEQ [63]. In both types, the dose usually of 10 Gy is delivered to tumor bed by photon beams. Boosting improves local control, reduces excess volumes of normal tissue irradiated, and decreases treatment course and dose per fraction for in breast cancer and this was confirmed by Katsochi [64] in his studies where boost of 16 Gy was delivered to the lumpectomy cavity after administration of 50 Gy to the whole breast. However, prior to the administration of boost, the chances of recurrences in the patient should be assessed as boost may worsen cosmetic outcome and increase the total cost of treatment [62]. Simply put, the benefits one is likely to enjoy from boost should outnumber the risks.

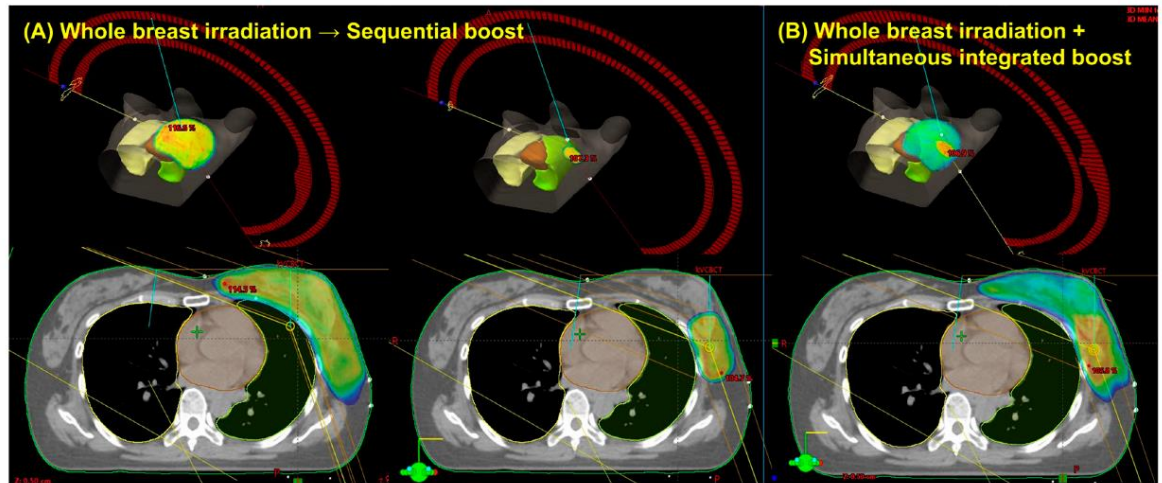


Figure 1.5 – Dose distribution and three dimensional view of a representative case using the sequential boost technique (A) versus the simultaneous integrated boost technique (B)

However, local control with boost is most pronounced in young patients who are less than or equal to 50 years than in older patients who are 50 years or above [62]. There are some controversies on the application of boost in adjuvant radiotherapy and who qualifies for boost. In view of this there are numerous recommendations but, in this research, the GEC-ESTRO Breast Cancer Working Group recommendation for boost was used.

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

To the student:

<b>Group</b>	<b>Full name</b>
0AM1M	Faustina N. Opoku

<b>School</b>	School of Nuclear Science & Engineering	<b>Division</b>	Research and Training Centre for International Nuclear Education and Career
<b>Degree</b>	Master	<b>Educational Program</b>	14.04.02 Nuclear Science and Technology / Nuclear medicine

**Input data to the section «Financial management, resource efficiency and resource saving»:**

<i>1. Resource cost of scientific and technical research (STR): material and technical, energetic, financial and human</i>	<ul style="list-style-type: none"> <li>– Material costs – 4250.00 rub.</li> <li>– Equipment costs – 18277.81 rub.</li> <li>– Salary costs – 265776.00 rub.</li> <li>– Labor tax – 72025.00 rub.</li> <li>– Overhead – 79733.00 rub.</li> <li>– Other direct costs – 1783.50 rub.</li> <li>– STR budget – 441845.31 rub.</li> </ul>
<i>2. Expenditure rates and expenditure standards for resources</i>	– Electricity costs – 5,8 rub per 1 kW
<i>3. Current tax system, tax rates, charges rates, discounting rates and interest rates</i>	<ul style="list-style-type: none"> <li>– Labor tax – 27,1 %;</li> <li>– Overhead costs – 30%;</li> </ul>

**The list of subjects to study, design and develop:**

<i>2. Assessment of commercial and innovative potential of STR</i>	– comparative analysis with other researches in this field;
<i>3. Development of charter for scientific-research project</i>	– SWOT-analysis;
<i>4. Scheduling of STR management process: structure and timeline, budget, risk management</i>	<ul style="list-style-type: none"> <li>– calculation of working hours for project;</li> <li>– creation of the time schedule of the project;</li> <li>– calculation of scientific and technical research budget;</li> </ul>
<i>5. Resource efficiency</i>	– integral indicator of resource efficiency for the developed project.

**A list of graphic material** (with list of mandatory blueprints):

<ol style="list-style-type: none"> <li>1. Competitiveness analysis</li> <li>2. SWOT- analysis</li> <li>3. Gantt chart and budget of scientific research</li> <li>4. Assessment of resource, financial and economic efficiency of STR</li> <li>5. Potential risks</li> </ol>	
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**Date of issue of the task for the section according to the schedule**

**Task issued by adviser:**

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

**The task was accepted by the student:**

Group	Full name	Signature	Date
0AM1M	Faustina N. Opoku		

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

$$C = \sum W_i \cdot P_i, \quad (4.1)$$

C – the competitiveness of research or a competitor;

W<sub>i</sub> – criterion weight;

P<sub>i</sub> – point of i-th criteria.

In order to attain the aim of radiotherapy, different techniques are used which also affect the outcome of a treatment plan. Over the years, the techniques for radiation treatments has evolved significantly from 2D-conventional to 3D-conformal radiotherapy.

For the competitive analysis of technical solution, two treatment techniques are considered and these are:

- 2D-Conventional radiotherapy – P<sub>i</sub>
- 3D-Conformal radiotherapy – P<sub>f</sub>

2D-conventional radiotherapy has been the traditional technique used in radiation treatment for years and it is still used in some institutions. However, this treatment technique as mentioned in Chapter 1, is based on 2D anatomical images and x-ray films which does not give details of the anatomy of the patients. Also the numbers of beams employed here are limited and are usually either square or rectangle in shape. This treatment technique has low conformity and as result healthy tissues surrounding the tumor are frequently exposed to excess dose.



3D-CRT on the other hand, allows the creation of 3D images of the tumor and surrounding tissues, hence the planner is able to focus the maximum dose to the target without exposing surrounding healthy tissues to unnecessary radiation. In comparison to 2D-conventional radiotherapy, these techniques employ MLC which shape the beam to conform to the shape of the tumor. Also, it allows target and normal tissues localization, and thus, organs at risk are exposed to less dose without compromising dose homogeneity and dose coverage in the target. Due to this, 3D-CRT is preferred over 2D-conventional radiotherapy.

In this research, both techniques are applied to compare the dose delivered to organs at risk by each technique.

Table 4.1 – Evaluation card for comparison of competitive technical solutions

Evaluation criteria <i>Example</i>	Criterion Weight $W_i$	Points		Competitiveness Taking into account weight coefficients	
		$P_f$	$P_{il}$	$C_f$	$C_{il}$
1	2	3	4	5	6
<b>Technical criteria for evaluating resource efficiency</b>					
1. Dose on critical organs	0.2	3	4	0.60	0.80
2. Dose homogeneity in the target volume	0.15	5	2	0.75	0.30
3. Ease of planning	0.14	5	2	0.7	0.28
4. Risk of radiotherapy side effects	0.17	3	4	0.51	0.68
5. Risk of recurrence	0.1	3	4	0.30	0.40
<b>Economic criteria for performance evaluation</b>					
1. Development cost	0.1	5	4	0.50	0.40
2. Competitive methods	0.08	5	4	0.40	0.32
3. Expected lifecycle	0.06	4	4	0.24	0.24
<b>Total</b>	<b>1</b>	<b>33</b>	<b>28</b>	<b>4.0</b>	<b>3.42</b>

This result shows that the use of 3D-CRT technique in radiotherapy is a better option in comparison to 2D-conventional radiotherapy.

#### 4.2 SWOT analysis

Complex analysis solution with the greatest competitiveness is carried out with the method of the SWOT analysis: Strengths, Weaknesses, Opportunities and Threats. The analysis has several stages. The first stage consists of describing the strengths and

weaknesses of the project, identifying opportunities and threats to the project that have emerged or may appear in its external environment. 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.

Table 4.2 – SWOT analysis

	<p><b>Strengths of the research project:</b></p> <p>S1. Decreased dose to critical organs without compromising dose to the target</p> <p>S2. Tumor control due to increase in dose to tumor</p> <p>S3. Shorter treatment time with better outcome</p>	<p><b>Weaknesses of the research project:</b></p> <p>W1. Lack of necessary software and equipment at oncology department in hospitals.</p> <p>W2. Difficulty in assessing late effects of radiation because it involves extended time of follow up.</p>
<p><b>Opportunities:</b></p> <p>O1. Treatment of breast cancer patients</p> <p>O2.Reduction in treatment time, thus reducing the cost of patients staying in the hospital.</p>	<p><i>Strategy which based on strengths and opportunities:</i></p> <p>1.Acceleration of the whole radiotherapy course.</p> <p>2.Since the treatment time is shorter, there is no risk of developing radioresistance due to decrease in patient treatment failure.</p> <p>3.Reduction in mortality, morbidity and risk of recurrence</p>	<p><i>Strategy which based on Weaknesses and opportunities:</i></p> <p>1. Equipping oncology departments with the necessary software</p> <p>2. Training medical physicists on how to work with the planning program</p> <p>3. Conducting long term researches to study late effects radiation in patients</p>

<p><b>Threats:</b></p> <p>T1. Lack of commercial interest in the project due to the availability of other conformal radiotherapy techniques</p> <p>T2. Affordability of 2D conventional radiotherapy treatment machines as compared to 3D-CRT machines</p> <p>T3. The complexity of funding from both the university and the state</p>	<p><i>Strategy which based on strengths and threats:</i></p> <p>Calculation of biological effective dose (BED) and equivalent dose in 2 Gy/fraction (EQD<sub>2</sub>) for 2D-conventional radiotherapy and 3D-CRT to choose the technique with better tumor control and less critical organs damage.</p>	<p><i>Strategy which based on weaknesses and threats:</i></p> <ol style="list-style-type: none"> <li>1. Creation of a statistical database showing the benefits of using 3D-CRT over 2D</li> <li>2. Evaluation of the five-year survival of patients with breast cancer who are treated with both techniques.</li> </ol>
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Based on the results of this analysis, it can be concluded that the interest in the use of 3D-CRT for breast cancer treatment can be increased due to decrease in dose to organs at risk without compromising dose homogeneity and PTV coverage.

### 4.3 Project initiation

The initiation process group consists of processes that are performed to define a new project or a new phase of an existing one. In the initiation processes, the initial purpose and content are determined and the initial financial resources are fixed. The internal and external stakeholders of the project who will interact and influence the overall result of the research project are determined.

Table 4.3 – Stakeholders of the project

<b>Project stakeholders</b>	<b>Stakeholder expectations</b>
Oncology hospitals/ clinics, and patients	Reduced patient mortality and morbidity; Reduced expenditure on treatment High efficiency of the procedure
Medical Physicists	Create treatment plans that maximize dose to the target while sparing organs at risk
Oncologist	Approve treatment plans.
Research Institutions	Better treatment outcome; Reduced overall expenditure on treatment

Tomsk Polytechnic University (TPU)	The results obtained could open more research opportunities in TPU.
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Table 4.4 – Purpose and results of the project

Purpose of project:	To optimize dose to critical organs in breast cancer radiotherapy, taking into account modern approaches to dosimetry planning.
Expected results of the project:	1. Dose reduction for critical organs 2. Increased local tumor control
Criteria for acceptance of the project result:	Maintenance of dose to organs at risk within the tolerance doses without compromising dose coverage in the target.
Requirements for the project result:	The project is completed on time.
	The efficiency of the equipment used.
	The results obtained must meet the acceptance criteria for the project result.

### 4.3.1 The organizational structure of the project

It is necessary to solve some questions: who will be part of the working group of this project, determine the role of each participant in this project, and prescribe the functions of the participants and their number of labor hours in the project.

Table 4.5 – Structure of the project

№	Participant	Role in the project	Functions	Labor time, hours (working days × 6 hours)
1	Irina Miloichikova	Scientific Supervisor	Coordination of work activities, guidance and assistance in project implementation. Verification of results obtained  Review of master's dissertation	237 (39 d x 6 h)
2	Faustina Ntim Opoku	Student	Work on project implementation. Analyzing data obtained. Writing of master's dissertation	492 (82 d x 6 h)
<b>Total:</b>				<b>850</b>

### 4.3.2 Project limitations

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

Table 4.6 – Project limitations

<b>Factors</b>	<b>Limitations / Assumptions</b>
3.1. Project's budget	441 845.31 Rubles
3.1.1. Source of financing	TPU
3.2. Project timeline:	1 February 2023 – 15 June 2023
3.2.1. Date of approval of plan of project	1 February 2023
3.2.2. Completion date	15 June 2023

### 4.3.3 Project schedule

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

Table 4.7 – Project Schedule


Job title	Duration, <b>working</b> days (without holidays and weekends)	Start date	Date of completion	Participants
Drawing up the technical assignment	3	1/02/2023	5/02/2023	Scientific supervisor
Literature review	11	6/02/2023	20/02/2023	Student
Calendar planning	2	21/02/2023	22/02/2023	Scientific supervisor, student
Research method/procedure	2	23/02/2023	25/02/2023	Scientific supervisor
Contouring	9	14/03/2023	24/03/2023	Student
Plan simulation	22	27/03/2023	25/04/2023	Scientific supervisor, student
Analysis of the data obtained	<b>7</b>	26/04/2023	3/05/2023	Scientific supervisor, student
Summary of results	2	4/05/2023	9/05/2023	Student
Evaluation of the effectiveness of the results	3	10/05/2023	12/05/2023	Scientific supervisor, Student
Model adjustment	5	13/05/2023	19/05/2023	Student
Making an explanatory note	8	20/05/2023	31/05/2023	Student
Defense preparation	11	1/06/2023	15/06/2023	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 4.8 – A Gantt chart

№	Activities	Participants	T <sub>c</sub> , days	Duration of the project													
				February			March			April			May				
				1	2	3	1	2	3	1	2	3	1	2	3		
1	Drawing up the technical assignment	Scientific supervisor	5														
2	Literature review	Student	15														
3	Calendar planning	Scientific supervisor, student	2														
4	Research method/procedure	Scientific supervisor	3														
5	Contouring	Student	9														
6	Planning	Scientific Supervisor, Student	26														
7	Analysis of the results	Supervisor, Student	7														
8	Summary of results	Student	3														
9	Evaluation of the effectiveness of the results	Scientific supervisor, student	3														
10	Drawing up a final report	Student	10														
	Defense Preparation	Student	8														

 - Scientific supervisor

 - Student

#### 4.4 Scientific and technical research budget

The amount of costs associated with the implementation of this work is the basis for the formation of the project budget. This budget will be presented as the lower limit of project costs when forming a contract with the customer.

To form the final cost value, all calculated costs for individual items related to the manager and the student are summed.

In the process of budgeting, the following grouping of costs by items is used:

- Material costs of scientific and technical research;
- costs of special equipment for scientific work (Depreciation of equipment used for design);
- basic salary;
- additional salary;
- labor tax;
- overhead.

##### 4.4.1 Calculation of material costs

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

$$C_m = (1 + k_T) \cdot \sum_{i=1}^m P_i \cdot N_{consi} \quad (4.2)$$

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<sup>2</sup>, 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<sup>2</sup>, 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 4.9 – Cost of materials and specialized equipment

Name	Unit per measurement	Quantity (units, amount)	Price per unit (rubles)	Sum (rubles)
Transportation	Unit	70	24	1680
Stationaries	Unit	1 each	1,000	1,000
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
Laptop	Unit	1	40000	898.63
Microsoft windows 10 professional RU x 64	Unit	1	5000	5000
Kaspersky anti-virus	Unit	1	2000	2000
XiO and Monaco TPS	Unit	2	300000	10379.18
Total costs of materials				22 527.81
Total transportation and purchasing costs (3-5%)				
Total costs per article, $C_m$				

#### 4.4.2 Calculation of 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:

$$N_D = \frac{1}{T} \cdot 100\% \quad (4.3)$$

where T is the expected lifetime in years.

In this project, the equipment used were already available in the radiology department.



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:

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

$$N_{Win10} = \frac{1}{4} \cdot 100\% = 25 \%,$$

$$N_{anti-virus} = \frac{1}{1} \cdot 100\% = 100 \%$$

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

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 82 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.

$$D_L = 40000 \cdot \frac{N_D}{100} \cdot \frac{T}{365} = 40000 \cdot \frac{10}{100} \cdot \frac{82}{365} = 898.63 \text{ RUB},$$

$$D_{TPS} = 600000 \cdot \frac{N_D}{100} \cdot \frac{T}{365} = 600000 \cdot \frac{7.7}{100} \cdot \frac{82}{365} = 10379.18 \text{ RUB},$$

The sum of depreciation for all equipment is:

$$D = 11277.81 \text{ RUB}$$

Table 4.10 – Costs of special equipment (+software)

№	Equipment identification	Quantity of equipment	Total cost of equipment, rub.	Life expectancy, year	Depreciation for the duration of the project, rub.
1.	Laptop	1	40 000	10	898.63
2	XiO and Monaco TPS	2	600 000	13	10379.18
<b>Total</b>					<b>11 277.81</b>

Depreciation is not calculated for equipment, which costs less than 40 thousand rubles.

#### 4.4.3 Basic salary

The basic salary includes the basic salary of participants directly involved in the implementation of work on this research. The value of salary costs is determined based on the labor intensity of the work performed and the current salary system

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

$$S_b = S_a \cdot T_w, \quad (4.4)$$

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 an participant, rub.

The average daily salary is calculated by the formula:

$$S_a = \frac{S_m \cdot M}{F_v}, \quad (4.5)$$

где  $S_m$  – monthly salary of an participant, rub. ;

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

at holiday in 48 days,  $M = 10.4$  months, 6 day per week;

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

Table 4.11 – The valid annual fund of working time

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

Monthly salary is calculated by formula:

$$S_{month} = S_{base} \cdot (k_{premium} + k_{bonus}) \cdot k_{reg}, \quad (4.6)$$

where  $S_{base}$  – base salary, rubles;

$k_{premium}$  – premium rate;

$k_{bonus}$  – bonus rate;

$k_{reg}$  – regional rate.

Table 4.12 – Calculation of the base salaries

Performers	$S_a$ , Rubles	$k_{premium}$	$k_{bonus}$	$k_{reg}$	$S_{month}$ , rub.	$S_d$ , rub.	$T_p$ , work days (from table 4.5)	$S_{base}$ , rub.
Scientific Supervisor (Senior Lecturer, Ph.D.)	34496	0.3	0.2	1.3	67267	2787	39	108693
Master student (low-skilled medical physicist)	20064				39125	1621	82	132922
<b>Total base salary, rub:</b>								<b>241615</b>

For Scientific Supervisor:

$$\begin{aligned}
 S_{month} &= S_a \times (k_{premium} + k_{bonus}) \times k_{reg} \\
 &= 34496 \times (1.3 + 0.2) \times 1.3 = 67267 \text{ rub} \\
 S_d &= \frac{S_{month} \times M}{F_v} = \frac{67267 \times 10.4}{251} = 2787 \text{ rub}
 \end{aligned}$$

$$S_{base} = S_d \times T_w = 2787 \times 39 = 108693 \text{ rub}$$

For the master student, the calculations are performed in a similar way.

#### 4.4.4 Additional salary

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

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

$$S_{add} = k_{extra} \times S_{base}, \quad (4.7)$$

where  $S_{add}$  – additional salary, rubles;

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

$S_{base}$  – base salary, rubles.

Table 4.13 shows the form for calculating the basic and additional wages.

Table 4.13 – Salaries of project executors

<b>Salary</b>	<b>Scientific Supervisor</b>	<b>Master</b>
Basic salary, rub	108693	132922
Additional salary, rub	10869	13292
<b>Total, rub:</b>	<b>265776</b>	

#### 4.4.5 Labor tax

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

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

$$P_{social} = k_b \times (S_{base} + S_{add}) \quad (4.8)$$

where  $k_b$  – coefficient of deductions for labor tax.

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

$$P_{social} = k_b \times (S_{base} + S_{add}) = 0.271 \times 265776 = \mathbf{72025\ rub}$$

Table 4.14 – Labor tax

	<b>Project leader</b>	<b>Engineer</b>
Coefficient of deductions	27.1	
Salary (basic and additional), rubles	119562	146214
Labor tax, rubles	32401.302	39623.99
<b>Total, rub</b>	<b>72025</b>	

#### 4.4.6 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 is calculated according to the formula:

$$C_{ov} = k_{ov} \times (S_{base} + S_{add}) \quad (4.9)$$

where  $k_{ov}$  – overhead rate (30%) .

$$C_{ov} = k_{ov} \times (S_{base} + S_{add}) = 0.3 \times 265776 = \mathbf{79733\ rub}$$

Table 4.15 – Overhead

	<b>Project leader</b>	<b>Engineer</b>
Overhead rate	30%	
Salary, rubles	119562	146214
Overhead, rubles	35868.6	43864.2
<b>Total</b>	<b>79733</b>	

#### 4.4.7 Other Direct Costs

Energy costs for equipment are calculated by the formula:

$$C = P_{el} \cdot P \cdot F_{eq}, \quad (4.10)$$

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

$P$  – power of equipment, kW;

$F_{eq}$  – equipment usage time, hours.

Table 4.16. – Other direct costs

	<b>Power rates, kWh</b>	<b>Power of equipment, kW</b>	<b>Equipment usage time, hr</b>	<b>Energy cost, rubles</b>
XiO TPS	5.8	0.5	123	356.70
Laptop	5.8	0.5	492	1426.80
<b>Total</b>				<b>1783.50</b>

#### 4.4.8 Formation of Budget Costs

The calculated cost of research is the basis for budgeting project costs.

Determining the budget for the scientific research is given in the Table 4.17 below.

Table 4.17 – Items expenses grouping

<b>Name</b>	<b>Cost, rubles</b>
1. Material costs	4 250
2. Equipment costs	18 277.81
3. Basic salary	241 615
4. Additional salary	24 161
5. Labor tax	72 025
6. Overhead	79 733
7. Other direct costs	1783.50
<b>Total planned costs</b>	<b>441 845.31</b>

#### 4.5 Evaluation of the comparative 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:

$$I_f^p = \frac{F_{pi}}{F_{max}}, \quad (4.11)$$

where  $I_f^p$  – integral financial measure of development;

$C_i$  – the cost of the i-th version;

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

In this project,  $C_i = 441\,845.31$ . It is assumed that,  $C_{max} = 450\,000.00$

Hence, the integral financial indicator is:

$$I_f^p = \frac{441845.31}{450000.00} = 0.98$$

The obtained value of the integral financial measure of development reflects the corresponding numerical increase in the budget of development costs in times (the value is greater than one), or the corresponding numerical reduction in the cost of development in times (the value is less than one, but greater than zero). The integral financial indicator is equal to 0.98. This means that, the corresponding numerical reduction in the cost of development times is 0.98.

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

$$I_m^a = \sum_{i=1}^n a_i b_i^a \quad I_m^p = \sum_{i=1}^n a_i b_i^p \quad (4.12)$$

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 4.18.

Table 4.18 – Evaluation of the performance of the project

Criteria	Weight criterion	Points	
		$I_m^p$	$I_m^a$
1. Reliability	0.15	5	4
2. Dose load on patient	0.1	3	4
3. Dose homogeneity in target volume	0.11	5	4
4. Dose on organs at risk	0.2	5	4
5. Ease of planning	0.1	4	4
6 Risk of recurrence	0.1	3	5
<b>Economic criteria for performance evaluation</b>			
1. Competitive methods	0.08	4	4
2. Expected lifecycle	0,06	5	5
3. Development cost	0.1	4	4
<b>Total</b>	<b>1</b>	<b>4.32</b>	<b>3.56</b>

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

$$I_m^p = (0.15 \times 5) + (0.1 \times 3) + (0.11 \times 5) + (0.2 \times 5) + (0.1 \times 4) + (0.1 \times 3) + (0.08 \times 4) + (0.06 \times 5) + (0.1 \times 4)$$

$$I_m^p = 4.32$$

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

$$I_m^a = (0.15 \times 4) + (0.1 \times 4) + (0.11 \times 4) + (0.2 \times 4) + (0.1 \times 4) + (0.1 \times 5) + (0.08 \times 4) + (0.06 \times 5) + (0.1 \times 4)$$

$$I_m^a = 3.56$$

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:

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

$$I_{fin}^a = \frac{3.56}{1} = 3.56; I_{fin}^p = \frac{4.32}{0.98} = 4.41$$

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.

$$E_{av} = \frac{4.41}{3.56} = 1.24$$

Thus, the effectiveness of the development is presented in Table 4.19.

Table 4.19 – Efficiency of development

№	Indicators	Points	
		Project	Analog (2D-conventional radiotherapy)
1	Integral financial indicator	0.98	1
2	Integral resource efficiency indicator	4.32	4.09
3	Integral efficiency indicator	4.41	4.09

Based on the values obtained for each indicator, we can conclude that the project is more competitive than the analog.

#### 4.6 Conclusion on the section “Financial management”

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

These stages include:

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

## TASK FOR SECTION "SOCIAL RESPONSIBILITY"

To the student:

<b>Group</b>	<b>Full name</b>
0AM1M	Faustina N. Opoku

<b>School</b>	School of Nuclear Science & Engineering	<b>Division</b>	Research and Training Centre for International Nuclear Education and Career
<b>Degree</b>	Master	<b>Educational Program</b>	14.04.02 Nuclear Science and Technology / Nuclear medicine

Subject FQW:

<b>Optimization of radiotherapy for patients with breast cancer</b>	
<b>Initial data for the section "Social responsibility":</b>	
1. Characteristics of the research object (substance, material, device, algorithm, technique, working area) and its scope	Object of study: Effect of exposure to ionizing radiation in radiation oncology centers on patients and health care workers due to exposure to radiation machines Scope: radiation therapy
List of questions to be researched, designed and developed:	
<b>1. Legal and organizational security issues:</b> - special (typical for the operation of the research object, the projected working area) legal norms of labor legislation; -organizational measures for the layout of the working area.	- SanPiN 2.6.1.2523-09 Radiation safety standards NRB-99/2009; - SanPiN 2.6.1.2573-10 Hygienic requirements for placement and operation of electron accelerators with energy up to 100 MeV. - SanPiN 1.2.3685-21 Hygienic standards and requirements for ensuring the safety and (or) harmlessness of environmental factors for humans; - other.
<b>2. Industrial safety:</b> <b>2.1. Analysis of the identified harmful and dangerous factors</b> <b>2.2. Rationale for mitigation measures</b>	Harmful and dangerous factors: - noise; - illumination; - microclimate; - electrical safety; - fire and explosion safety; - electromagnetic fields; - radiation safety.
<b>3. Safety in emergencies:</b>	- selection and description of a typical emergency; - justification of measures to prevent emergencies; - the order of actions in the event of an emergency.

<b>Date of issue of the task for the section on a line chart</b>	
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**The assignment was given by the consultant:**

<b>Position</b>	<b>Full name</b>	<b>Academic degree, title</b>	<b>Signature</b>	<b>date</b>
Associate Professor	Yuriy V. Perederin	PhD		

**The student accepted the assignment:**

<b>Group</b>	<b>Full name</b>	<b>Signature</b>	<b>Date</b>
0AM1M	Faustina N. Opoku		

when in close proximity to heat sources. Humidity also has a significant impact on human thermoregulation, so low humidity can lead to drying of the skin, mucous membranes and general dehydration of the body, and high humidity can lead to increased heat transfer and possible overheating of the body [95].

To maintain these sanitary standards, it is necessary to have a local air conditioning unit of a complete air conditioning unit that ensures a constant temperature, relative humidity, speed and air purity. A central water heating system is needed to provide a given temperature level in winter [95].

Table 5.1 shows the optimal values of microclimate indicators at workplaces, which are established by sanitary standards for various categories of work in different periods of the year. When working at a PC, the category of work is light (Ia), since there is no systematic physical activity [95].

Table 5.1 – Optimal values of microclimate indicators at workplaces of industrial premises

Period of the year	Category of work according to the level of energy consumption, W	Air temperature, °C	Surface temperature, °C	Relative humidity, %	Air speed, m/s
Cold	Ia (up to 139)	22-24	21-25	60-40	no more than 0.1
Warm	Ia (up to 139)	23-25	22-26	60-40	no more than 0.1

In the office of medical physicist No. 307 of the Research Institute of Oncology of the Tomsk National Research Medical Center, the microclimate standards are met.

To maintain sanitary standards, it is sufficient to have natural unorganized ventilation of the room and a local air conditioner of a full air conditioning unit, which ensures the constancy of temperature, relative humidity, speed of movement and air purity [98].

To calculate the air exchange performance of the ventilator in the office of a medical physicist at the Oncology Research Institute of the Tomsk National Research Medical Center, we use the formula:

$$W = V \cdot K, \quad (5.1)$$

where  $V = 124.6 \text{ m}^3$ ; air exchange rate in the room  $K = 3 \text{ h}^{-1}$ , which corresponds to the norm according to [98]. Substituting the known values into the formula, we get  $W = 373.8 \text{ m}^3\text{h}^{-1}$ . Based on the available criteria, a vortex blower is suitable Becker SV 400/1 5.5, with maximum performance  $390 \text{ m}^3\text{h}^{-1}$  [98].

### 5.1.2 Ionizing radiation

Laboratory No. 307, where the work was carried out, was tested in the radiation monitoring laboratory accredited by the State Standard of Russia in terms of the parameter: determination of the radiation situation and complies with regulatory requirements.

It is necessary to ensure the radiation safety of personnel at the Oncology Research Institute of the Tomsk National Research Medical Center in connection with the radiation generated by the SL75-5-MT and Elekta synergy linear accelerators.

Table 5.2 shows the main dose limits. The main dose limits, like all other permissible exposure levels for group B personnel, are equal to 1/4 of the values for group A personnel [96].

Table 5.2 – Basic limits of doses of ionizing radiation for personnel of group A and the public.

Normalized values	Dose limits	
	Personnel (Group A)	Population
Effective dose	20 mSv per year on average for any consecutive 5 years, but not more than 50 mSv per year	1 mSv per year on average for any consecutive 5 years, but not more than 5 mSv per year
equivalent dose per year in		
– lens of the eye	150 mSv	15 mSv
– skin	500 mSv	50 mSv
– hands and feet	500 mSv	50 mSv

To protect against the effects of ionizing radiation on the body, the following three methods are used: protection by quantity, time and distance. The main preventive measures include the correct choice of the layout of premises, equipment, interior

decoration, technological regimes, the rational organization of workplaces, the observance of personal hygiene measures by workers, rational ventilation systems, protection against external and internal radiation, collection and disposal of radioactive waste, as well as the use personal protective equipment [96].

When ionizing radiation interacts with air, a number of toxic substances are formed, the excess of which can pose a danger to human health. To reduce the concentration of toxic substances, special exhaust ventilation is calculated and installed. It should be taken into account that during the operation of the electron accelerator, ozone is mainly formed, respectively, ventilation is calculated based on ozone emissions [96].

When working on a CT scanner, the main hazards are:

- high voltage;
- X-ray radiation when monitoring the position of organs;
- noise generated by equipment;
- heat release from equipment and communications;

When working on the SL75-5-MT and the Elekta Synergy linear accelerator, the main hazards are:

- high radiation background near the source storage;
- high radiation background when the source exits during a treatment session;
- high voltage;
- heat release from equipment and communications;

Persons who do not have medical contraindications, classified as group A personnel or group B personnel, accompanied by group A personnel, who have been trained in the rules of operation of the device and in radiation safety, and who have been instructed in radiation safety [97], are allowed to work.

During operation, warning light and sound signals are mandatory on the control panel and above the entrance to the working chamber.

Also, the apparatus is located in a special bunker, the design of radiation protection of which provides the necessary protection for personnel and the public. Before switching on, it is necessary to urgently leave the bunker, and then make sure that the doors are tightly closed and all conditions meet the requirements. In addition, it is necessary to carry an individual dosimeter in a breast pocket. The internal radiation safety service regularly conducts dosimetric control of all premises, checks the readings of individual dosimeters, and controls the use of personal protective equipment [97].

### **5.1.3 Noise and vibration**

Noise worsens working conditions, has a harmful effect on the human body, namely, on the hearing organs and on the whole body through the central nervous system. As a result, attention is weakened, memory deteriorates, reaction decreases, and the number of errors during work increases. Noise can be generated by equipment in operation, air conditioning units, daylight lighting fixtures, and can also come in from outside.

To assess the noise environment, it is allowed to use a numerical characteristic called the sound level (measured in dB). The permissible noise level during work that requires concentration, work with increased requirements for the processes of monitoring and remote control of production cycles at workplaces in rooms with noisy equipment is 75 dB [99].

Behind the working surface, the noise level from the computer reaches 30 dB, which is within the normal range. The noise level from the vortex blower is 53 dB, which complies with the standards [100].

### **5.1.4 Illumination**

Workplace lighting is the most important factor in creating normal working conditions. Lighting should be given special attention, since the eyes get the most stress

during work. Insufficient illumination of the working area is also considered one of the factors affecting human performance. For industrial enterprises, the optimal illumination of the territory and premises is an important and difficult technical task, the solution of which provides normal hygienic conditions for working personnel. Properly selected light sources and their design create conditions for production work, the correct execution of technological operations, compliance with rules and safety precautions.

Lighting is divided into natural, artificial and combined. Combined combines both types of lighting.

The reasons for the insufficiency of natural and artificial lighting are the remoteness of the workplace from light sources, insufficient power and poor quality of light sources, inappropriate weather factors or time of day. Insufficient lighting reduces labor productivity, increases fatigue and the number of mistakes made, and can also lead to occupational eye diseases [101].

The necessary illumination in the workplace is achieved by artificial lighting with fluorescent lamps. We calculate the required number of fixtures using the formula:

$$n = \frac{E \cdot S \cdot Z \cdot K}{F \cdot U \cdot m}, \quad (5.2)$$

where  $E$  – normalized illumination,  $E = 300$  lx;

$S$  – room area,  $S = 35.6$  m<sup>2</sup>;

$Z$  – luminaire correction factor,  $Z = 1.2$ ;

$K$  – safety factor taking into account the decrease in illumination during operation,  $K = 1.2$ ;

$F$  – luminous flux of one lamp, LD 40,  $F = 2130$  lx;

$U$  – utilization factor,  $U = 0.55$ ;

$m$  – number of lamps in the lamp,  $m = 2$ .



Substituting the values, we get  $n = 6.56$  pcs. But since an integer is needed, rounding up, we get 7 lamps, which corresponds to the number of lamps in the office of a medical physicist No. 307.

### **5.1.5 Electrical safety**

Depending on the conditions in the room, the risk of electric shock to a person increases or decreases. You should not work with a computer in conditions of high humidity (relative air humidity exceeds 75% for a long time), high temperature (more than 35 ° C), the presence of conductive dust, conductive floors and the possibility of simultaneous contact with ground-connected metal elements and the metal case of electrical equipment. The operator works with electrical appliances: a computer (display, system unit, etc.) and peripheral devices. The danger of electric shock exists in the following cases [102]:

- with direct contact with live parts during repair;
- when touching non-current-carrying parts that are energized (in case of violation of the insulation of current-carrying parts);
- when touching the floor, walls that are energized;
- in case of a short circuit in high-voltage units: power supply unit and display scanner unit.

Electric current, passing through the human body, has a thermal, chemical and biological effect.

Thermal (thermal) effect is manifested in the form of burns of the skin area, overheating of various organs, as well as ruptures of blood vessels and nerve fibers resulting from overheating.

Chemical (electrolytic) action leads to electrolysis of blood and other solutions contained in the human body, which leads to a change in their physico-chemical composition, and hence to disruption of the normal functioning of the body.

Measures to ensure the electrical safety of electrical installations:

- disconnection of voltage from current-carrying parts on which or near which work will be carried out, and taking measures to ensure that it is impossible to supply voltage to the place of work;
- hanging posters indicating the place of work;
- grounding of housings of all installations through a neutral wire;
- coating of metal surfaces of tools with reliable insulation;
- inaccessibility of current-carrying parts of the equipment (conclusion in cases of electro-shocking elements, conclusion of current-carrying parts in a case) [103].

The room in which the work took place is suitable for class 1 rooms, in which the operating voltages do not exceed 1000 V [102].

#### **5.1.6 Electromagnetic fields**

The main harmful factor in the use of computers is electromagnetic radiation from the constituent parts of devices. An increased level of electromagnetic radiation can negatively affect the human body, namely, lead to nervous disorders, sleep disturbance, a significant deterioration in visual activity, a weakened immune system, and disorders of the cardiovascular system.

Electromagnetic fields are controlled in the following ranges: 50 Hz (power frequency) and from 30 kHz to 300 GHz. Measurements are carried out at the workplaces of users of stationary and portable personal computers. The following parameters are controlled: the strength of the electric and magnetic fields, the strength of the electrostatic field.

The norms of maximum permissible levels (MPL) of electromagnetic radiation, established in the document [99], are shown in tables 5.3 and 5.4.

Table 5.3 – Maximum permissible levels of electric and magnetic fields of industrial frequency 50 Hz

No.	Impact type	Electric field strength, kV/m	Induction (magnetic field strength), $\mu\text{T}$ (A/m)
1	In residential buildings, children's, preschool, school, educational institutions	0.5	5.0 (4.0)
2	In public buildings	0.5	10.0 (8.0)
3	On the residential area	1.0	10.0 (8.0)

Table 5.4 – Maximum permissible levels of EMF in the frequency range 30 kHz-300 GHz

Frequency range	30-300 kHz	0.3-3 MHz	3-30 MHz	30-300 MHz	0.3-300 GHz
Normalized parameter	Electric field strength, E (V/m)				Energy flux density, ( $\mu\text{W}/\text{cm}$ )
Limit-acceptable levels	25	15	10	3	10 25 for cases of exposure from antennas operating in the circular view or scanning mode

The computer, located in the office of medical physicist No. 307 of the Research Institute of Oncology of the Tomsk National Medical Research Center, creates electromagnetic radiation with a frequency of 130 Hz, which is not controlled [99].

### 5.1.7 Fire and explosion safety

Depending on the characteristics of the substances used in the production and their quantity, according to fire and explosion hazard, the premises are divided into categories А, Б, В, Г, Д . Since the room belongs to category В in terms of fire and explosion hazard, i.e. to rooms with solid combustible substances, it is necessary to provide a number of preventive measures [104].

Possible causes of fire:

- malfunction of current-carrying parts of installations;
- work with open electrical equipment;
- short circuits in the power supply;
- non-compliance with fire safety rules;

– the presence of combustible components: documents, doors, tables, cable insulation, etc.

Measures for fire prevention are divided into: organizational, technical, operational and regime.

Organizational measures include the correct operation of equipment, the correct maintenance of buildings and territories, fire safety briefing for workers and employees, training of production personnel in fire safety rules, publication of instructions, posters, and an evacuation plan.

Technical measures include: compliance with fire regulations, standards in the design of buildings, in the installation of electrical wires and equipment, heating, ventilation, lighting, proper placement of equipment.

Regime measures include the following: the establishment of rules for the organization of work, and compliance with fire prevention measures. To prevent a fire from short circuits, overloads, etc., the following fire safety rules must be observed [104]:

- exclusion of the formation of a combustible environment (sealing of equipment, air control, working and emergency ventilation);
- correct operation of the equipment (correct connection of the equipment to the power supply network, control of equipment heating);
- correct maintenance of buildings, territories (exclusion of the formation of an ignition source - prevention of spontaneous combustion of substances, restriction of hot work);
- training of production personnel in fire safety rules;
- publication of instructions, posters, availability of an evacuation plan;
- compliance with fire safety rules and regulations in the design of buildings, in the installation of electrical wires and equipment, heating, ventilation, lighting;
- correct placement of equipment;
- timely preventive inspection, repair and testing of equipment.

In the event of an emergency, you must:

- inform the manager;
- call the emergency service or the Ministry of Emergency Situations - tel. 112;
- take measures in accordance with [105].

## **5.2 Safety in accident situation and emergencies**

An emergency (accident) situation is a situation in a certain territory that has developed as a result of an accident, a dangerous natural phenomenon, a catastrophe, the spread of a disease that poses a danger to others, a natural or other disaster that may or have caused loss of life, damage to human health or environment, significant material losses and violation of the living conditions of people. There are two types of emergencies:

- technogenic;
- natural.

Man-made emergencies include fires, explosions, sabotage, and releases of toxic substances. Natural disasters are natural disasters. The most probable technogenic emergencies are fires.

Accidental hazards include a sudden and uncontrolled source of energy: a moving object, uncontrolled movement or energy [105].

Let's consider possible accidents and emergencies in the office of medical physicist No. 307 at the Oncology Research Institute of the Tomsk National Research Medical Center, namely:

- fall from the height of one's own height;
- electric shock;
- the occurrence of a fire.

Measures to prevent the above accidents and emergency situations and measures to eliminate their consequences are presented in Table 5.5.

Table 5.5 – Accident and emergency situations, measures to prevent accidents and emergencies, measures to eliminate the consequences of accidents and emergencies

No.	Accidents and emergencies	Measures to prevent accidents and emergencies	Measures to eliminate the consequences of accidents and emergencies
1	Injury from a fall from a height of appropriate height	<ol style="list-style-type: none"> <li>1. Keeping the premises in proper order.</li> <li>2. Restriction of the working space.</li> <li>3. Timely briefing.</li> </ol>	<ol style="list-style-type: none"> <li>1. Examine or interrogate the victim;</li> <li>2. if necessary - call an ambulance - tel. 112;</li> <li>3. stop bleeding, if any;</li> <li>4. if there is a suspicion that the victim has a broken spine (sharp pain in the spine at the slightest movement), it is necessary to provide the victim with complete rest in the supine position until qualified medical assistance is provided.</li> <li>5. call the emergency service or the Ministry of Emergency Situations - tel. 112;</li> </ol>
2	Electrical shock	<ol style="list-style-type: none"> <li>1. Grounding of all electrical installations.</li> <li>2. Restriction of the working space.</li> <li>3. Ensuring the inaccessibility of current-carrying parts of the equipment.</li> <li>4. Timely briefing.</li> </ol>	<ol style="list-style-type: none"> <li>1. Quickly release the victim from the action of electric current;</li> <li>2. call an ambulance - tel. 112;</li> <li>3. if the victim has lost consciousness, but breathing is preserved, he should be comfortably laid down, unbuttoned tight clothes, create an influx of fresh air and ensure complete rest;</li> <li>4. the victim should be allowed to smell ammonia, sprinkle his face with water, rub and warm the body;</li> <li>5. in the absence of breathing, artificial respiration and heart massage should be done immediately.</li> <li>6. call the emergency service or the Ministry of Emergency Situations - tel. 112;</li> </ol>
3	Fire	<ol style="list-style-type: none"> <li>1. Timely briefing.</li> <li>2. Installation of automatic fire extinguishing equipment in the premises.</li> <li>3. Installation of smoke and fire detectors.</li> <li>4. Ensuring escape routes and maintaining them in proper condition.</li> <li>4. Control of the operation of electrical appliances.</li> </ol>	<ol style="list-style-type: none"> <li>1. De-energize the room, stop the air supply;</li> <li>2. immediately report the fire to the person on duty or to the security post;</li> <li>3. if possible, take measures to evacuate people, extinguish a fire and save material assets.</li> <li>4. call the emergency service or the Ministry of Emergency Situations - tel. 112;</li> </ol>

This subsection discusses potential emergencies and accidents that may arise when working in the office of medical physicist No. 307 at the Oncology Research Institute of the Tomsk National Research Medical Center. Measures to prevent and eliminate the consequences of these situations are considered according to [105].

### **5.3 Conclusions on the section "Social responsibility"**

The section discusses the organizational issues of ensuring the safety of workers, identifies possible harmful and dangerous factors (microclimate, ionizing radiation, ventilation, vibration, noise, lighting, electrical safety, fire hazard), also analyzes them and substantiates a number of measures to reduce their impact on the researcher.

Regular work at the Oncology Research Institute of the Tomsk National Research Medical Center will not harm the employee. The room is classified as class B for fire hazard [104], category 1 for electrical safety (up to 1000 V) [102], category IV for radiation exposure [96].

Possible accidents and emergencies are analyzed, measures to prevent accidents and emergencies, as well as measures to eliminate the consequences of accidents and emergencies are described. The most probable emergency is the occurrence of a fire in the workplace due to the ignition of equipment.

## References

1. Ghoncheh M., Pournamdar Z., Salehiniya H. Incidence and Mortality and Epidemiology of Breast Cancer in the World // *Asian Pac J Cancer Prev*. 2016. Vol. 17, № S3. P. 43–46.
2. Zahedi A. et al. Incidence, Trends and Epidemiology of Cancers in North West of Iran // *Asian Pac J Cancer Prev*. 2015. Vol. 16, № 16. P. 7189–7193.
3. Noncommunicable diseases [Electronic resource]. URL: <https://www.who.int/health-topics/noncommunicable-diseases> (accessed: 26.05.2023).
4. Devi R., Anandhamala G., Sundhar R. Recent Trends in Medical Imaging Modalities and Challenges For Diagnosing Breast Cancer // *Biomedical and Pharmacology Journal*. 2018. Vol. 11. P. 1649–1658.
5. Breast cancer [Electronic resource]. URL: <https://www.who.int/news-room/fact-sheets/detail/breast-cancer> (accessed: 26.05.2023).
6. What Are the Symptoms of Breast Cancer? [Electronic resource] // Centers for Disease Control and Prevention. 2022. URL: [https://www.cdc.gov/cancer/breast/basic\\_info/symptoms.htm](https://www.cdc.gov/cancer/breast/basic_info/symptoms.htm) (accessed: 26.05.2023).
7. Möller T.R. et al. A prospective survey of radiotherapy practice 2001 in Sweden // *Acta Oncol*. 2003. Vol. 42, № 5–6. P. 387–410.
8. The breasts - Knowledge @ AMBOSS [Electronic resource]. URL: [https://www.amboss.com/us/knowledge/The\\_breasts](https://www.amboss.com/us/knowledge/The_breasts) (accessed: 27.05.2023).
9. Health Library - Menopause, Fertility Problems, Vaginal Infections, Pregnancy: Tests & Procedures [Electronic resource]. URL: <https://www.nevadawomenscare.com/health-library/anatomy-and-physiology/382194/breast-anatomy.html> (accessed: 27.05.2023).



10. Breast cancer - Symptoms and causes [Electronic resource] // Mayo Clinic. URL: <https://www.mayoclinic.org/diseases-conditions/breast-cancer/symptoms-causes/syc-20352470> (accessed: 27.05.2023).
11. Epidemiology of Breast Cancer [Electronic resource]. URL: [https://www.researchgate.net/publication/366826374\\_Epidemiology\\_of\\_Breast\\_Cancer](https://www.researchgate.net/publication/366826374_Epidemiology_of_Breast_Cancer) (accessed: 27.05.2023).
12. Brinton L.A. et al. Anthropometric and hormonal risk factors for male breast cancer: male breast cancer pooling project results // J Natl Cancer Inst. 2014. Vol. 106, № 3. P. djt465.
13. Ruddy K.J., Winer E.P. Male breast cancer: risk factors, biology, diagnosis, treatment, and survivorship // Ann Oncol. 2013. Vol. 24, № 6. P. 1434–1443.
14. Fox S., Speirs V., Shaaban A.M. Male breast cancer: an update // Virchows Arch. 2022. Vol. 480, № 1. P. 85–93.
15. Clegg L.X. et al. Impact of socioeconomic status on cancer incidence and stage at diagnosis: selected findings from the surveillance, epidemiology, and end results: National Longitudinal Mortality Study // Cancer Causes Control. 2009. Vol. 20, № 4. P. 417–435.
16. Global Cancer Statistics 2022: The Trends Projection Analysis [Electronic resource]. URL: [https://www.researchgate.net/publication/364185741\\_Global\\_Cancer\\_Statistics\\_2022\\_the\\_trends\\_projection\\_analysis](https://www.researchgate.net/publication/364185741_Global_Cancer_Statistics_2022_the_trends_projection_analysis) (accessed: 27.05.2023).
17. Desantis C. et al. International Variation in Female Breast Cancer Incidence and Mortality Rates // Cancer Epidemiology Biomarkers & Prevention. 2015. Vol. 24.
18. Ferlay J. et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012 // Int J Cancer. 2015. Vol. 136, № 5. P. E359-386.

19. Risk factors [Electronic resource]. URL: <https://www.cancerresearchuk.org/about-cancer/breast-cancer/risks-causes/risk-factors> (accessed: 27.05.2023).
20. The 2021 China report of the Lancet Countdown on health and climate change: seizing the window of opportunity [Electronic resource]. URL: [https://www.researchgate.net/publication/355997425\\_The\\_2021\\_China\\_report\\_of\\_the\\_Lancet\\_Countdown\\_on\\_health\\_and\\_climate\\_change\\_seizing\\_the\\_window\\_of\\_opportunity](https://www.researchgate.net/publication/355997425_The_2021_China_report_of_the_Lancet_Countdown_on_health_and_climate_change_seizing_the_window_of_opportunity) (accessed: 27.05.2023).
21. Breast Cancer Epidemiology and Risk Factors: Epidemiology, Reproductive Factors, Endogenous Sex Hormones and Risk of Breast Cancer [Electronic resource]. URL: <https://emedicine.medscape.com/article/1697353-overview> (accessed: 27.05.2023).
22. Leon-Ferre R.A. et al. A contemporary review of male breast cancer: current evidence and unanswered questions // *Cancer Metastasis Rev.* 2018. Vol. 37, № 4. P. 599–614.
23. Street W. Breast Cancer Facts & Figures 2019-2020.
24. Arnold M. et al. Current and future burden of breast cancer: Global statistics for 2020 and 2040 // *The Breast.* Elsevier, 2022. Vol. 66. P. 15–23.
25. Viale G. The current state of breast cancer classification // *Ann Oncol.* 2012. Vol. 23 Suppl 10. P. x207-210.
26. Dai X. et al. Breast cancer intrinsic subtype classification, clinical use and future trends // *Am J Cancer Res.* 2015. Vol. 5, № 10. P. 2929–2943.
27. Kohler B.A. et al. Annual Report to the Nation on the Status of Cancer, 1975-2011, Featuring Incidence of Breast Cancer Subtypes by Race/Ethnicity, Poverty, and State // *J Natl Cancer Inst.* 2015. Vol. 107, № 6. P. djv048.
28. De Waard F., Baanders-Vanhalewijn E.A., Huizinga J. The bimodal age distribution of patients with mammary carcinoma; evidence for the existence of 2 types of human breast cancer // *Cancer.* 1964. Vol. 17. P. 141–151.

29. Anderson W.F., Rosenberg P.S., Katki H.A. Tracking and evaluating molecular tumor markers with cancer registry data: HER2 and breast cancer // J Natl Cancer Inst. 2014. Vol. 106, № 5. P. dju093.
30. Anderson W.F. et al. How many etiological subtypes of breast cancer: two, three, four, or more? // J Natl Cancer Inst. 2014. Vol. 106, № 8. P. dju165.
31. Anderson W.F. et al. Human epidermal growth factor receptor-2 and estrogen receptor expression, a demonstration project using the residual tissue repository of the Surveillance, Epidemiology, and End Results (SEER) program // Breast Cancer Res Treat. 2009. Vol. 113, № 1. P. 189–196.
32. Nascimento R.G.D., Otoni K.M. Histological and molecular classification of breast cancer: what do we know? // Mastology. 2020. Vol. 30. P. e20200024.
33. Rouzier R. et al. Breast cancer molecular subtypes respond differently to preoperative chemotherapy // Clin Cancer Res. 2005. Vol. 11, № 16. P. 5678–5685.
34. Female Breast Cancer Subtypes - Cancer Stat Facts [Electronic resource] // SEER. URL: <https://seer.cancer.gov/statfacts/html/breast-subtypes.html> (accessed: 27.05.2023).
35. Vuong D. et al. Molecular classification of breast cancer // Virchows Arch. 2014. Vol. 465, № 1. P. 1–14.
36. Cancer Staging | Has Cancer Spread | Cancer Prognosis [Electronic resource]. URL: <https://www.cancer.org/cancer/diagnosis-staging/staging.html> (accessed: 28.05.2023).
37. Barrett A., Ma J.D. Practical Radiotherapy Planning.
38. Lobular Carcinoma in Situ | LCIS | American Cancer Society [Electronic resource]. URL: <https://www.cancer.org/cancer/types/breast-cancer/non-cancerous-breast-conditions/lobular-carcinoma-in-situ.html> (accessed: 28.05.2023).
39. Cancer Treatments [Electronic resource] // CancerQuest. URL: <https://www.cancerquest.org/patients/treatments> (accessed: 28.05.2023).

40. (4) (PDF) Toxicity and Pharmacogenomic Biomarkers in Breast Cancer Chemotherapy [Electronic resource]. URL: [https://www.researchgate.net/publication/340660312\\_Toxicity\\_and\\_Pharmacogenomic\\_Biomarkers\\_in\\_Breast\\_Cancer\\_Chemotherapy](https://www.researchgate.net/publication/340660312_Toxicity_and_Pharmacogenomic_Biomarkers_in_Breast_Cancer_Chemotherapy) (accessed: 28.05.2023).
41. Bilateral Mastectomy versus Breast-Conserving Surgery for Early-Stage Breast Cancer: The Role of Breast Reconstruction - PubMed [Electronic resource]. URL: <https://pubmed.ncbi.nlm.nih.gov/26017588/> (accessed: 28.05.2023).
42. NIH consensus conference. Treatment of early-stage breast cancer // JAMA. 1991. Vol. 265, № 3. P. 391–395.
43. Breast-conserving surgery followed by whole-breast irradiation offers survival benefits over mastectomy without irradiation: Breast-conserving surgery and irradiation versus mastectomy without irradiation [Electronic resource]. URL: [https://www.researchgate.net/publication/325907465\\_Breast-conserving\\_surgery\\_followed\\_by\\_whole-breast\\_irradiation\\_offers\\_survival\\_benefits\\_over\\_mastectomy\\_without\\_irradiation\\_Breast-conserving\\_surgery\\_and\\_irradiation\\_versus\\_mastectomy\\_without\\_irradiation](https://www.researchgate.net/publication/325907465_Breast-conserving_surgery_followed_by_whole-breast_irradiation_offers_survival_benefits_over_mastectomy_without_irradiation_Breast-conserving_surgery_and_irradiation_versus_mastectomy_without_irradiation) (accessed: 28.05.2023).
44. Breast Cancer Surgery: New Issues [Electronic resource]. URL: [https://www.researchgate.net/publication/355277020\\_Breast\\_Cancer\\_Surgery\\_New\\_Issues](https://www.researchgate.net/publication/355277020_Breast_Cancer_Surgery_New_Issues) (accessed: 28.05.2023).
45. Understanding Breast Cancer Surgery Options [Electronic resource] // Verywell Health. URL: <https://www.verywellhealth.com/breast-cancer-surgery-options-430561> (accessed: 28.05.2023).
46. Aly M.M.O.M. et al. Comparison of breast simultaneous integrated boost (SIB) radiotherapy techniques // Radiation Oncology. 2015. Vol. 10, № 1. P. 139.
47. Lymph Node Surgery for Breast Cancer | American Cancer Society [Electronic resource]. URL: <https://www.cancer.org/cancer/types/breast->

- cancer/treatment/surgery-for-breast-cancer/lymph-node-surgery-for-breast-cancer.html (accessed: 28.05.2023).
48. Chemotherapy for Breast Cancer | Breast Cancer Treatment [Electronic resource]. URL: <https://www.cancer.org/cancer/types/breast-cancer/treatment/chemotherapy-for-breast-cancer.html> (accessed: 28.05.2023).
  49. Chemotherapy for Breast Cancer [Electronic resource]. URL: <https://www.breastcancer.org/treatment/chemotherapy> (accessed: 28.05.2023).
  50. Chemotherapy for breast cancer - Mayo Clinic [Electronic resource]. URL: <https://www.mayoclinic.org/tests-procedures/chemotherapy-for-breast-cancer/about/pac-20384931> (accessed: 28.05.2023).
  51. Gong L. et al. Application of Radiosensitizers in Cancer Radiotherapy // Int J Nanomedicine. 2021. Vol. 16. P. 1083–1102.
  52. Cancer treatment: Radiotherapy [Electronic resource]: Text. IAEA, 2016. URL: <https://www.iaea.org/topics/cancer-treatment-radiotherapy> (accessed: 28.05.2023).
  53. Radiation Therapy for Cancer - NCI [Electronic resource]: cgvArticle. 2015. URL: <https://www.cancer.gov/about-cancer/treatment/types/radiation-therapy> (accessed: 28.05.2023).
  54. Conventional radiation therapy | Radiology Reference Article | Radiopaedia.org [Electronic resource]. URL: <https://radiopaedia.org/articles/conventional-radiation-therapy> (accessed: 28.05.2023).
  55. Benveniste M.F. et al. Recognizing Radiation Therapy-related Complications in the Chest // Radiographics. 2019. Vol. 39, № 2. P. 344–366.
  56. Themes U.F.O. Three-Dimensional Conformal Radiation Therapy [Electronic resource] // Radiology Key. 2016. URL: <https://radiologykey.com/three-dimensional-conformal-radiation-therapy/> (accessed: 28.05.2023).
  57. Ismael D.K., Hassan F.F. 3D-Conformal Radiation Therapy and IntensityModulated Radiation Therapy Techniques for Laryngeal Cancer Taking Parotid Glands as Organ at Risk // Hosp Pract Res. 2020. Vol. 5, № 1. P. 10–16.

58. 3D conformal radiation therapy | Radiology Reference Article | Radiopaedia.org [Electronic resource]. URL: <https://radiopaedia.org/articles/3d-conformal-radiation-therapy?lang=gb> (accessed: 28.05.2023).
59. Brachytherapy: An International Perspective | SpringerLink [Electronic resource]. URL: <https://link.springer.com/book/10.1007/978-3-319-26791-3> (accessed: 28.05.2023).
60. Safety and efficacy of INTRABEAM intraoperative radiotherapy... : Medicine [Electronic resource]. URL: [https://journals.lww.com/md-journal/fulltext/2020/07020/safety\\_and\\_efficacy\\_of\\_intrabeam\\_intraoperative.84.aspx](https://journals.lww.com/md-journal/fulltext/2020/07020/safety_and_efficacy_of_intrabeam_intraoperative.84.aspx) (accessed: 28.05.2023).
61. Sedlmayer F. et al. Intraoperative radiotherapy (IORT) as boost in breast cancer // Radiat Oncol. 2017. Vol. 12, № 1. P. 23.
62. Gulstene S., Raziee H. Radiation Boost After Adjuvant Whole Breast Radiotherapy: Does Evidence Support Practice for Close Margin and Altered Fractionation? // Front Oncol. 2020. Vol. 10. P. 772.
63. Kim M. et al. Comparison of Heart and Lung Doses According to Tumor Bed Boost Techniques in Early-Stage Left-Sided Breast Cancer: Simultaneous Integrated Boost versus Sequential Boost // Medicina (Kaunas). 2022. Vol. 58, № 7. P. 873.
64. Katsochi D. Radiation Therapy with a Simultaneous Integrated Boost // Radiotherapy. IntechOpen, 2017.
65. Computed Tomography (CT) Scan [Electronic resource]. 2021. URL: <https://www.hopkinsmedicine.org/health/treatment-tests-and-therapies/computed-tomography-ct-scan> (accessed: 28.05.2023).
66. What Are CT Scans and How Do They Work? [Electronic resource] // livescience.com. 2018. URL: <https://www.livescience.com/64093-ct-scan.html> (accessed: 28.05.2023).

67. Khan's treatment planning in radiation oncology. Fourth edition / ed. Khan F.M., Gibbons J.P., Sperduto P.W. Philadelphia Baltimore New York London Buenos Aires Hong Kong Sydney Tokyo: Wolters Kluwer, 2016. 662 p.
68. Lam B. Commissioning for Treatment Planning System // JCPCR. 2016. Vol. 6, № 2.
69. Computerised Medical Systems. Inc. [Electronic source]. 2003. URL: [https://www.accessdata.fda.gov/cdrh\\_docs/pdf3/K032762.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf3/K032762.pdf) (accessed: 28.05.2023)
70. Clements M. et al. Monaco treatment planning system tools and optimization processes // Med Dosim. 2018. Vol. 43, № 2. P. 106–117.
71. Elekta to showcase Monaco 5.11 treatment planning system at AAPM [Electronic resource] // dotmed.com. URL: <https://www.dotmed.com/news/story/32143> (accessed: 01.06.2023).
72. Elekta. Monaco 5.11 comprehensive treatment planning. [Electronic source] // jnciltd.com. URL: <https://www.jnciltd.com/uploads/products/monaco.pdf> (accessed: 01.06.2023)
73. Ahmed S. et al. Prediction of Dose Calculation of Breast and Chest Tumors using Different Algorithms // Biosciences Biotechnology Research Asia. 2016. Vol. 13, № 4. P. 2379–2385.
74. Hardcastle N., Oborn B.M., Haworth A. On the use of a convolution-superposition algorithm for plan checking in lung stereotactic body radiation therapy // J Appl Clin Med Phys. 2016. Vol. 17, № 5. P. 99–110.
75. Drzymala R.E. et al. Dose-volume histograms // Int J Radiat Oncol Biol Phys. 1991. Vol. 21, № 1. P. 71–78.
76. Generation of Dose Volume Histograms Using Voxel Structure and the Monte Carlo Method in Low Dose Rate Brachytherapy [Electronic resource]. URL: [https://www.researchgate.net/publication/309463741\\_Generation\\_of\\_Dose\\_V](https://www.researchgate.net/publication/309463741_Generation_of_Dose_V)

- olume\_Histograms\_Using\_Voxel\_Structure\_and\_the\_Monte\_Carlo\_Method\_in\_Low\_Dose\_Rate\_Brachytherapy (accessed: 28.05.2023).
77. Dose volume histogram analysis and comparison of different radiobiological models using in-house developed software [Electronic resource]. URL: [https://www.researchgate.net/publication/221732765\\_Dose\\_volume\\_histogram\\_analysis\\_and\\_comparison\\_of\\_different\\_radiobiological\\_models\\_using\\_in-house\\_developed\\_software](https://www.researchgate.net/publication/221732765_Dose_volume_histogram_analysis_and_comparison_of_different_radiobiological_models_using_in-house_developed_software) (accessed: 28.05.2023).
78. RadOnc: An R Package for Analysis of Dose-Volume Histogram and Three-Dimensional Structural Data [Electronic resource]. URL: [https://www.researchgate.net/publication/268147620\\_RadOnc\\_An\\_R\\_Package\\_for\\_Analysis\\_of\\_Dose-Volume\\_Histogram\\_and\\_Three-Dimensional\\_Structural\\_Data](https://www.researchgate.net/publication/268147620_RadOnc_An_R_Package_for_Analysis_of_Dose-Volume_Histogram_and_Three-Dimensional_Structural_Data) (accessed: 28.05.2023).
79. Opisane uskoritelja jelektronov SL75-5 MT i analizatora dozy TLD Victoreen 2800M, Linejnyj uskoritel' jelektronov SL-75-5MT - Total'noe obluchenie tela cheloveka [Electronic resource]. URL: [https://studwood.net/2041894/bzhd/opisanie\\_uskoritelya\\_elektronov\\_sl75\\_analizatora\\_dozy\\_victoreen\\_2800m](https://studwood.net/2041894/bzhd/opisanie_uskoritelya_elektronov_sl75_analizatora_dozy_victoreen_2800m) (accessed: 28.05.2023).
80. Linear Accelerator (LINAC) [Electronic resource]. URL: <https://www.medindia.net/patients/patientinfo/linear-accelerator.htm> (accessed: 28.05.2023).
81. Elekta Synergy | Radiation Therapy Cancer Care | Elekta [Electronic resource]. 2022. URL: <https://www.elekta.com/products/radiation-therapy/synergy/> (accessed: 28.05.2023).
82. Intraoperacionnaja luchevejaja terapija - B.N. Zyrjanov, S.G. Afanas'ev, A.A. Zav'jalov, L.I. Musabaeva; Ros. akad. med. nauk. NII onkologii TNC SO RAMN. 1999.
83. Novikov V.A. et al. Intraoperacionnaja luchevejaja terapija: real'nost' i perspektiva // Zlokač. opuholi. 2017. № 3s1. P. 35–40.



84. Fifteen years of experience with intraoperative radiotherapy [Electronic resource]. URL: <https://cyberleninka.ru/article/n/pyatnadtsatiletniy-opyt-primeneniya-intraoperatsionnoy-luchevoj-terapii/viewer> (accessed: 01.06.2023).
85. Novaja tehnologija intraoperacionnoj luchevoj terapii v sochetanii s distancionnoj gamma-terapij pri kombinirovannom lechenii onkologicheskikh bol'nyh [Electronic resource]. URL: <https://www.elibrary.ru/item.asp?edn=qcshub> (accessed: 01.06.2023).
86. Jelektronnaja biblioteka dvgmu :: intraoperacionnaja luchevoj terapija pri kombinirovannom lechenii nemelkokletochnogo raka legkogo iii stadii: predel'no dopustimaja doza odnokratnogo obluchenija, chastota luchevyh reakcij i oslozhnenij [Electronic resource]. URL: <http://elib.fesmu.ru/elib/Article.aspx?id=226655> (accessed: 01.06.2023).
87. Lisin v.a. ocenka predel'no dopustimoj odnokratnoj dozy dlja nekotoryh tkanej cheloveka v intraoperacionnoj luchevoj terapii // radiacionnaja biologija. Radiojekologija. 2015. Vol. 55, № 2.
88. Statistical Radiobiology | Oncology Medical Physics [Electronic resource]. URL: <https://oncologymedicalphysics.com/statistical-radiobiology/> (accessed: 28.05.2023).
89. Themes U.F.O. Time, Dose, and Fractionation in Radiotherapy [Electronic resource] // Radiology Key. 2016. URL: <https://radiologykey.com/time-dose-and-fractionation-in-radiotherapy/> (accessed: 28.05.2023).
90. Frometa-Castillo T. et al. Biologically Effective Dose (BED) or Radiation Biological Effect (RBEf)? // Recent Techniques and Applications in Ionizing Radiation Research. IntechOpen, 2020.
91. Zwicker F. et al. Hypofractionated Radiotherapy With Simultaneous-integrated Boost After Breast-conserving Surgery Compared to Standard Boost-applications Using Helical Tomotherapy With TomoEdge // Anticancer Res. 2021. Vol. 41, № 4. P. 1909–1920.

92. Yeung S.Y. et al. EP-1187: Comparing simultaneous integrated boost and sequential electron boost technique in radiotherapy for breast cancer // Radiotherapy and Oncology. 2015. Vol. 115. P. S644.
93. Aly M.M.O.M. et al. Comparison of breast sequential and simultaneous integrated boost using the biologically effective dose volume histogram (BEDVH) // Radiation Oncology. 2016. Vol. 11, № 1. P. 16.
94. GOST 12.0.003-2015 System of labor safety standards. Dangerous and harmful production factors. Classification: introduction date 2017-03-01.
95. GOST 30494-2011 Residential and public buildings. Indoor microclimate parameters: introduction date 2013-01-01.
96. SanPiN 2.6.1.2523-09 Radiation safety standards - 99/2009.
97. SanPiN 2.6.1.2573-10 Hygienic requirements for placement and operation of electron accelerators with energy up to 100 MeV.
98. GOST 32548 - 2013. Ventilation of buildings. Air distribution devices. General specifications.
99. SanPiN 1.2.3685-21 Hygienic standards and requirements for ensuring the safety and (or) harmlessness of environmental factors for humans: introduction date 2021-01-28.
100. SP 51.13330.2011 Noise protection. Updated version of SNiP 23-03-2003: introduction date 2011-05-20.
101. SP 52.13330.2016 Natural and artificial lighting. Updated edition of SNiP 23-05-95\*.
102. GOST 12.1.019-2017 System of labor safety standards. Electrical safety. General requirements and nomenclature of types of protection: introduction date 2019-01-01.
103. GOST R 58698-2019 (IEC 61140:2016). Protection against electric shock. General provisions for electrical installations and electrical equipment: introduction date 2020-06-01.

104. SP 12.13130.2009. Definition of categories of premises, buildings and outdoor installations in terms of explosion and fire hazard (as amended by No. 1, approved by order No. 643 of the Russian Emergencies Ministry of 09.12.2010): introduction date 2009-05-01.
105. GOST 12.1.004-91 Occupational safety standards system. Fire safety. General requirements.