TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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

School of Nuclear Science & Engineering
Field of training (specialty) 14.04.02 «Nuclear Physics and Technology»
Division for Nuclear-Fuel Cycle

MASTER'S GRADUATION THESIS

Topic of research work
Radionuclide diagnostics in the evaluation of the kidneys in patients with diabetic mellitus

UDC 616-07:616.379-008.64

Student

Group	Full name	Signature	Date
0AM8M	Kudaibergen Gibrat Bolatuly		

Scientific supervisor

Position	Full name	Academic degree, academic rank	Signature	Date
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Adviser

Position	Full name	Academic degree, academic rank	Signature	Date
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ADVISERS:

Section "Financial Management, Resource Efficiency and Resource Saving"

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Associate Professor	Menshikova E.V.	Ph.D		

Section "Social Responsibility"

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Associate Professor	Verigin D.A.	Ph.D		

ADMITTED TO DEFENSE:

Director of programme	Full name	Academic degree, academic rank	Signature	Date
Nuclear medicine	CherepennikovYu.M.	Ph.D		

Tomsk – 2020

Expected learning outcomes

Learning outcome (LO) code	Learning outcome (a graduate should be ready)	Requirements of the FSES HE, criteria and / or interested parties
Professional competencies		
LO1	To apply deep mathematical, scientific, socio-economic and professional knowledge for conducting theoretical and experimental research in the field of the use of nuclear science and technology.	FSES HE Requirements (BPC-1,2, PC-3, UC-1,3), Criterion 5 RAEE (p 1.1) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
LO2	To demonstrate ability to define, formulate, and solve interdisciplinary engineering tasks in the nuclear field using professional knowledge and modern research methods.	FSES HE Requirements (PC-9,10,13,14,15, BPC-1,3), Criterion 5 RAEE (p 1.2) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
LO3	To plan and conduct analytical, simulation and experimental studies in complex and uncertain conditions using modern technologies, and to evaluate critically research results.	FSES HE Requirements (PC-1,13,22, UC-2, BPC-1), Criterion 5 RAEE (p 1.3) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
LO4	To use basic and special approaches, skills and methods for identification, analysis, and solution of technical problems in the field of nuclear science and technology.	FSES HE Requirements (PC-2,4,6,8, UC-2, BPC-1), Criterion 5 RAEE (p 1.4) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
LO5	To operate modern physical equipment and instruments, to master technological processes in the course of preparation for the production of	FSES HE Requirements (PC-5,7,11,12, UC-2, BPC-1), Criterion 5 RAEE (p 1.4) requirements of the Ministry of Health and Social Development of the

	new materials, instruments, installations, and systems.	Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
LO6	To demonstrate ability to develop multioption schemes for achieving production goals with the effective use of available technical means and resources.	FSES HE Requirements (PC-16-21,23), Criterion 5 RAEE (p 1.5) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
Cultural competencies		
LO7	To demonstrate ability to use a creative approach to develop new ideas and methods for designing nuclear facilities, as well as to modernize and improve the applied technologies of nuclear production.	FSES HE Requirements (BPC-1,3, UC-3), Criterion 5 RAEE (p 2.4,2.5)
Basic professional competencies		
LO8	To demonstrate skills of independent learning and readiness for continuous self-development within the whole period of professional activity.	FSES HE Requirements (UC-3, PC-1, BPC-1), Criterion 5 RAEE (p 2.6) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
LO9	To use a foreign language at a level that enables a graduate to function successfully in the international environment, to develop documentation, and to introduce the results of their professional activity.	FSES HE Requirements (PC-11,16,17, BPC-3), Criterion 5 RAEE (p 2.2) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"
LO10	To demonstrate independent thinking, to function efficiently in command-oriented tasks and to have a high level of productivity in the professional (sectoral), ethical and social environments, to lead professional teams, to set tasks, to assign responsibilities and bear liability for the results of work.	FSES HE Requirements (PC-18,23, UC-2), Criterion 5 RAEE (p 1.6,2.3) requirements of the Ministry of Health and Social Development of the Russian Federation under the unified skills guide for positions of managers, specialists and non-manual workers for the position of "medical physicist"

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School of Nuclear Science & Engineering
Field of training (specialty) 14.04.02 «Nuclear Physics and Technology»
Division for Nuclear-Fuel Cycle

APPROVED BY:
Director of the programme
_____ _____ Cherepennikov Yu.M.
(Signature) (Date) (Full name)

ASSIGNMENT
for the Graduation Thesis completion

In the form:

Master's thesis

For a student:

Group	Full name
0AM8M	Kudaibergen Gibrat Bolatuly

Topic of research work:

Radionuclide diagnostics in the evaluation of the kidneys in patients with diabetic mellitus	
Approved by the order of the Director of School of Nuclear Science & Engineering (date, number):	

Deadline for completion of Master's Graduation Thesis:	

TERMS OF REFERENCE:

Initial data for research work:	1. Single-photon emission computer Philips BrightView tomograph; 2. Philips Jet Stream SoftwareWorkspace 3.0 and RView 9.06; 3. Statistica 6.

List of the issues to be investigated, designed and developed	1. Review and analysis of Russian and foreign literature on lung ventilation scintigraphy; 2. Data processing; 3. Development of diagnostic algorithm; 4. Financial management, resource efficiency sustainability and resource conservation; 5. Social responsibility.

Advisors to the sections of the Master's Graduation Thesis

Section	Advisor
Main sections of the graduate qualification work	Zavadovskaya V. D.
Financial Management, Resource Efficiency and Resource Saving	Menshikova E.V.
Social responsibility	Verigin D.A.

Date of issuance of the assignment for Master's Graduation Thesis completion according to the schedule	

Assignment issued by a scientific supervisor/advisor:

Position	Full name	Academic degree, academic status	Signature	Date
Associate Professor	Verigin D.A.	Ph.D		
Associate Professor	Zorkal'tsev M. A.	D.M.Sc.		

Assignment accepted for execution by a student:

Group	Full name	Signature	Date
0AM8M	Kudaibergen Gibrat Bolatuly		

TOMSK POLYTECHNIC UNIVERSITY ТОМСКИЙ ПОЛИТЕХНИЧЕСКИЙ УНИВЕРСИТЕТ

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School of Nuclear Science & Engineering
Field of training (specialty) 14.04.02 «Nuclear Physics and Technology»
Level of education Master Degree Program
Division for Nuclear-Fuel Cycle
Period of completion 2018/2019 and 2019/2020 academic years

Form of presenting the work:

Master's Thesis

SCHEDULED ASSESSMENT CALENDAR
for the Master's Graduation Thesis completion

Deadline for completion of Master's Graduation Thesis:	

Assessment date	**Title of section (module) / type of work (research)**	**Maximum score for the section (module)**
15.05.2019	1. Preparation of technical specifications and choice of research areas	10
30.06.2019	2. Development of a General research methodology	10
31.09.2019	3. Selection and study of materials on the topic	10
09.10.2019	4. Obtaining the necessary experimental data	20
14.11.2019	5. Checking the results	20
26.01.2019	6. Processing the received data	15
23.04.2020	7. Registration of completed work	15

COMPILED BY:
Scientific supervisor

Position	**Full name**	**Academic degree, academic rank**	**Signature**	**Date**
Associate Professor	Verigin D.A.	Ph.D		

Adviser

Position	**Full name**	**Academic degree, academic rank**	**Signature**	**Date**
Associate Professor	Zorkal'tsev M. A.	D.M.Sc.		

AGREED BY:
Director of the programme

Position	**Full name**	**Academic degree, academic rank**	**Signature**	**Date**
Associate Professor	CherepennikovYu.M.	Ph.D		

TASK FOR SECTION

«FINANCIAL MANAGEMENT, RESOURCE EFFICIENCY AND RESOURCE SAVING»

For a student:

Group	Full name
0AM8M	Kudaibergen Gibrat Bolatuly

School	School of Nuclear Science & Engineering	**Division**	Division for Nuclear-Fuel Cycle
Degree	Master Degree Program	**Field of training/programme**	14.04.02 Nuclear physics and technology / Nuclear medicine

Input data to the section «Financial management, resource efficiency, and resource-saving»:	
1. *The resource cost of scientific research (SR): material and technical, energetical, financial, informational and human* 2. *Expenditure rates and expenditure standards for resources* 3. *The current tax system, tax rates, charge rates, discount rates, and interest rates*	Working with information provided in Russian and foreign scientific publications, analytical materials, statistical bulletins and publications, and regulatory documents.
The list of subjects to study, design, and develop:	
1. *Assessment of the commercial and innovative potential of STR*	Ishikawa Diagram SWOT-analysis Project initiation
2. *Planning the STR management process: structure and schedule, budget, risks, and procurement organizationи формирование бюджета научных исследований*	Calendar schedule of project implementation
3. *Determination of resource, financial, and economic efficiency*	Determining the project's resource efficiency Project risk register
List of graphic material *(with exact indication of required drawings):*	
1. Ishikawa Diagram 2. SWOT-analysis 3. Project initiation 4. Deducation of the project 5. Calendar schedule of project implementation and budget STR 6. Determining the project's resource efficiency 7. Project risk register	

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

Task issued by adviser:

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

The student accepted the task:

Group	Full name	Signature	Date
0AM8M	Kudaibergen Gibrat Bolatuly		

Task for section
«Social responsibility»

To student:

Group	Full name
0AM8M	Kudaibergen Gibrat Bolatuly

School	School of Nuclear Science & Engineering	**Division**	Division for Nuclear-Fuel Cycle
Degree	Master Degree Program	**Field of training/programme**	14.04.02 Nuclear physics and technology / Nuclear medicine

Title of graduation thesis:

Radionuclide diagnostics in the evaluation of the kidneys in patients with diabetes mellitus	
Initial data for section «Social Responsibility»:	
1. Information about object of investigation (matter, material, device, algorithm, procedure, workplace) and area of its application	The dynamic renal scintigraphy method in the evaluation kidneys in patients with diabetes mellitus. Scope: nuclear medicine and radiation diagnostics.
List of items to be investigated and to be developed:	
1. Legal and organizational issues to provide safety: – Special (specific for operation of objects of investigation, designed workplace) legal rules of labor legislation; – Organizational activities for layout of workplace.	– Labour code of Russian Federation #197 from 30/12/2001 GOST 12.2.032-78 SSBT – Sanitary Rules 2.2.2/2.4.1340-03. Hygienic requirements for PC and work with it
2. Work Safety: 2.1. Analysis of identified harmful and dangerous factors 2.2. Justification of measures to reduce probability of harmful and dangerous factors	– Enhanced electromagnetic radiation level – Insufficient illumination of workplace – Excessive noise – Deviation of microclimate indicators – Electric shock – Ionizing radiation
3. Ecological safety:	– Indicate impact of radionuclides production on hydrosphere, atmosphere and lithosphere
4. Safety in emergency situations:	– Fire safety;

Assignment date for section according to schedule	

The task was issued by consultant:

Position	Full name	Scientific degree, rank	Signature	Date
Assistant professor	Verigin D.A.	Cand.of Sc.		

The task was accepted by the student:

Group	Full name	Signature	Date
0AM8M	Kudaibergen Gibrat Bolatuly		

ABSTRACT

The final qualification work contains 94 pages, 6 figures, 31 tables, and 72 references.

Keywords: nuclear medicine, medical physics, radionuclide diagnostics, single-photon emission computed tomography, renal scintigraphy, diabetic nephropathy, diabetes mellitus, glomerular filtration rate.

The object of research is outpatients of clinical departments of Siberian State Medical University's clinics with the established diagnosis of diabetic nephropathy in 91 patients with diabetes mellitus.

The purpose of this work is to evaluate the diagnostic capabilities of the dynamic scintigraphy method in determining the nature of kidney function disorders in patients with diabetes mellitus.

In the course of the study, we conducted: kidney scintigraphy in dynamic mode, the study of the possibilities of the method of dynamic kidney scintigraphy in assessing the state of the kidneys in patients with diabetes mellitus.

Scope: medical institutions.

Cost-effectiveness/significance of the work: solving a complex range of diagnostic problems should reduce the socio-economic burden on the population of various countries and significantly improve the quality of life of patients.

The master's thesis was performed at the department of radiation diagnostics and radiation therapy "Siberian State Medical University" in the Ministry of Health of Russia, Tomsk.

Scientific advisers: acting head of the department of radiation diagnostics and radiation therapy Zavadovskaya V. D. (doctor of medical Science, professor) and head of the department of radionuclide diagnostics in the department of radiation diagnostics and therapy Zorkal'tsev M. A. (doctor of medical Science, associate professor).

List definitions and abbreviations

DN - diabetic nephropathy

DRS – dynamic renal scintigraphy

MA – microalbuminuria

NA– normoalbuminuria

CBC – complete blood count

UA– urine analysis

SPECT – single-photon emission-computed tomography

PO – proteinuria

RP – radiopharmaceutical

DM – diabetic mellitus

GFR – glomerular filtration rate

ESRD – end - stage renal disease

CKD – chronic kidney disease

HbA1c – glycated hemoglobin

T_{max} – time to peak

$T_{1/2}$ – half time radiopharmaceuticals

^{99m}Tc – technetium, 99m

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Introduction

Backgrounds

Diabetes mellitus (DM) is a common socially significant disease that is characterized by multiple organ damage. According to experts from the World Health Organization (WHO) the total number of patients with all forms of diabetes nowadays is about 425 million people. Diabetes is anticipated to become the seventh leading cause of death in the world by 2030 [1].

A specific complication of diabetes mellitus is diabetic nephropathy (DN) and occupies a leading position in the structure of patients with end-stage renal disease (ESRD) which is required extracorporeal method of treatment (program hemodialysis, kidney transplantation) and is one of the most expensive areas of health care worldwide [2]. DN is usually associated with hypertension and increased cardiovascular morbidity and mortality. The statistics are significantly worse for people with type 1 or 2 diabetes who have developed DN than without it. In the structure of mortality of patients with DM in Russia, due to ESRD of DN is the third most common cause of passing in patients with type 1 diabetes (7.1%) and the seventh – in patients with type 2 diabetes (1.8%) [3].

The DN screening carried out within the framework of the Saint Vincent Declaration incorporates common clinical urine analysis, a study of urine for the presence of microalbuminuria (MA), and the determination of non–selective proteinuria [4]. This allows to diagnose DN at the MA stage. However, some of DM's patients with normoalbuminuria (NA) have progressive renal failure [5]. In this regard, the problem of determining the structural and functional changes of the kidney which are still reversible, becomes urgent.

Radiation diagnostic methods are broadly utilized in the research of uronephrology, such as X-ray, CT, and MRI [6]. These methods are less informative than radio-nuclide diagnostic methods and ultrasound. Ultrasound dopplerography is of-

ten used to evaluate kidney vessels, which is extremely important in DM [7]. However, when performing an ultrasound at the initial stages of DN development, structural and anatomical changes in the renal parenchyma may not be determined reliably [8]. However, radionuclide methods may reflect the functional state of organs by evaluating such parameters as the time of maximum accumulation of radiopharmaceutical RP (T_{max}), the half-time of RP ($T_{1/2}$) and the glomerular filtration rate (GFR), are regarded as methods of early registration of renal dysfunction, even at the preclinical stage of development of pathological changes. Meanwhile, only a small number of studies are devoted to the use of the scintigraphy method to assess the functional state of the kidneys in patients with DM.

In spite of the relevance of these studies in Nephrology, comparative data of radionuclide investigate methods in evaluating the state of the kidneys in patients with diabetes are not available.

Thus, at the moment, the problem of a single guide for different types of DM with DN is still not solved. One of the most urgent and vital issues of modern nuclear medicine, which has not been completely solved at the world level, is the study of the latest methodological approaches to DN with different types of DM.

The solution of a complex range of problems in the diagnosis of DN with DM should reduce the socio-economic burden on the population of various countries and essentially improve the quality of life of patients.

Purpose of research.

Evaluation of the diagnostic capabilities of the dynamic renal scintigraphy method for setting the nature of renal dysfunction in patients with DM

Task of research.

1. To study the results of dynamic renal scintigraphy in assessing the functional state of the kidneys in patients with DM depending on the severity of diabetic nephropathy;

2. Compare the results of dynamic renal scintigraphy with creatinine levels as a reference method for evaluating the glomerular filtration rate in a comparative aspect;
3. Improves the algorithm for diagnosing kidney status in patients with diabetes mellitus.

Scientific novelty.

1. For the first time, a comprehensive comparative clinical and instrumental appraisal of the kidney condition in patients with distinctive types of diabetes mellitus was performed.
2. For the first time, based on the assessment of the results of radiation investigate methods, an elective method of radiation diagnostics for assessing the functional state of the kidneys in patients with DM is proposed, including the use of dynamic renal scintigraphy to assess the filtration function of the kidneys.

Personal contribution of the author.

The author's personal contribution consists in setting research objectives, developing experimental methods to solve them, directly participating in all experimental and clinical studies, reviewing research results, and preparing for publication. All processing, analysis and interpretation of the obtained results is performed by the author personally.

Implementation of results in practice.

The results of the clinical study have been implemented in the practical work of the department of radionuclide diagnostics of the Federal State Budgetary Educational Institution of Higher professional education "Siberian State Medical University" of the Ministry of Health of the Russian Federation. It is used in the teaching process at the department of radionuclide diagnostics.

Annual stages.

1-st year – approval of the thesis topic with the head of the graduated qualifying work (GQW), the study of the necessary literature on the research topic, conducting radionuclide, and scintigraphy studies of patients, preparation of thesis chapters "Introduction" and "Literature review".

2-nd year – completion of a set of clinical materials, obtaining final results, processing, and analysis, formulation of research conclusions, implementation of results in clinical practice, the final design of the thesis. Thesis defense.

Chapter 1. Literature review

1.1 Diabetes Mellitus

According to the definition of the International Expert Committee (ICE) on the diagnosis and classification of diabetes mellitus (DM) from 1997, diabetes mellitus is a group of metabolic (exchange) diseases characterized by hyperglycemia, which is the result of damage to the secretion of insulin, the action of insulin, or a combination of these two factors [9, 10, 11, 12].

Diabetes mellitus occupies a dramatic role in world medicine as a disease associated with a high level of human and economic resources expenditure and will become the 7 main causes of death worldwide by 2030 [9, 10, 11, 14, 13]. Since chronic hyperglycemia, which develops in DM, is accompanied by the development of a large number of complications and multi-organ damage, primarily from kidneys, the heart, nerves, blood vessels, and eyes [15]. According to WHO experts, "diabetes mellitus is a problem of all peoples and ages", due to its wide geographical spread, an exceptionally rapid increase in morbidity, early disability in patients of working age and high mortality from complications that gradually progress after the occurrence, significantly reducing the quality of life and shortening its duration [16].

At present, the number of patients suffering from diabetes in the world is about 425 million people, and agreeable forecasts, the number of patients will grow to 629 million by 2045 [1]. According to the IDF (*International Diabetes Federation*), it is estimated that at least 212.4 million people worldwide, or half (50%) of all people with diabetes, are unaware of their illnesses [1, 11]. The study has shown that in 2012, additional health care costs due to undiagnosed diabetes amounted to $ 33 billion per year [17, 1]. And in 2017, 4 million people die worldwide due to DM, which is equivalent to one death every 8 seconds [1].

The age group of patients with DM ranges from 20 to 79 years [10, 1]. But also in 2017, there were more than 96,000 new cases of type 1 diabetes in children [1].

As of 01.01.2019, there were 4.58 million DM patients in Russia. Of these, 26,373 children, 9,972 adolescents, and 219,857 adults suffered from type 1 diabetes. And type 2 diabetes affected 913 children, 299 adolescents, and 4,237,291 adults [15]. In conformity with forecasts, the number of new patients with DM in the Russian Federation will increase to 4.4 million by 2030 [18].

As already mentioned, diabetes is a huge medical, social and economic problem [19, 20]. in 2017, the cost of health care due to diabetes reached 727 billion US dollars, and since 2013, it has increased by 32.6% of the total health care costs for treating the adult population in the world [1]. At the same time, costs in the United States of America amounted to 348 billion US dollars, that is, almost half of all costs for DM in the world, in China-110 billion US dollars [1]. In total, the patient's stay in the hospital for lower limb amputation totaled us $ 16.2 million [21].

1.2 Diabetic nephropathy

Diabetic kidney disease (DKD), or chronic kidney disease (CKD) in individuals with diabetes mellitus (DM), also called diabetic nephropathy (DN), is one of the most frequent and severe chronic complications of DM resulting from microvascular lesions in the renal glomeruli and tubules, the end stage of which is characterized by the development of chronic kidney disease (CKD) [22, 23, 1, 2]. However, due to the strong association between DN and cardiovascular diseases, the vast majority of patients with DN die even before the progression of ESRD, due to cardiovascular diseases [1, 2].

1.2.1 Epidemiology and frequency of DN development

Information on the frequency of diabetic nephropathy is variable and depends on the age and length of the illness in which it debuted. Recent epidemiological studies have shown that the frequency of DN ranges from 25 to 40% in patients with type 1 diabetes and from 5 to 40% in patients with type 2 diabetes. In addition, 20% to 30% of patients with type 1 diabetes have microalbuminuria (MA) on average after 5-10 years since DM is detected, but it can also be present in 20% of patients at the beginning of type 2 diabetes [24]. It is reported that the overall frequency of end-stage CKD is 4-17% in 20-30 years after the onset of type 1 diabetes [25, 26, 27]. Thus, in people with type 1 or type 2 diabetes, complications develop earlier, and, accordingly, screening should begin early in the course of diabetes [28]. Non-albuminuric diabetic nephropathy (NADN) has been less studied disease, but recently, Thorn et al. reported that 2% of patients with type 1 diabetes have NADN [29].

According to data from the UK, one fifth of people with diabetes and from the US, 40% of people with diabetes develop chronic kidney disease, while 19% show signs of stage 3 or higher [1]. Combined data from 54 countries show that

more than 80% of end-stage renal disease is caused by diabetes. The proportion of CKD caused by diabetes varies from 12 to 55%. The prevalence of CKD is also up to 10 times higher in people with DM than in people without it [1].

A study by Nichols G. A. et al. (2011) presented that the progression of diabetic nephropathy essentially increases the medical costs of treating patients diagnosed with diabetic nephropathy. The authors studied a sample of almost 8,000 patients with DN and found that restorative costs expanded by 37% when nephropathy advanced from normoalbuminuria to microalbuminuria, and by another 41% when it advanced from microalbuminuria to macroalbuminuria [30].

Thus, the long-term asymptomatic course of DN, the high mortality rate of patients with end-stage CKD, as well as the high financial costs of treating this category of patients make the advancement of methods for early determination of DN increasingly relevant in the present time [30, 31, 32].

1.2.2 Pathogenesis of DN

The development of diabetic kidney disease (DKD) depends on the duration of diabetes mellitus (DM), the severity of metabolic disorders, concomitant hypertension, and genetic factors. DN is caused by changes in the basement membrane, which lead to a decrease in its negative charge and an increase in the size of the pores. High blood glucose levels and blood pressure increase simultaneously with intra-glomerular pressure. As a result, albumin filtration increases, initially in the form of albuminuria (MA) from 30 to 300 mg / 24 hours, which is equivalent to 30 to 300 mg / g of creatinine in a random urine sample (albumin-to-creatinine ratio [A/CR], 3-30 mg/mmol), and then explicit proteinuria (PO)>300 mg/24 hours) [34]. Over time, this leads to glomerular hyalinosis (diffuse or nodular glomerulosclerosis), intra-tissue fibrosis, and the development of kidney failure. In addition, the presence of kidney failure increases the risk of heart disease and medical expenses in patients with DM [35, 35].

For diabetic kidney disease are significant certain risk factors in the prevention or delay of CKD and for personalized treatment strategies. Those factors divided on non-modified and modified are:

Non-modifiable

- Genetic factor
- Male sex
- Age the onset of diabetes from 5 to 15 years
- Long duration of diabetes
- Ethnicity
- Increasing age

Modifiable

- Poor glycemic control
- Hypertension
- Lipid abnormalities
- Obesity
- Metabolic syndrome
- Insulin resistances
- Low-grade inflammation
- Birth weight

1.2.3 Classification and formulation for the diagnosis of DN

According to the classification received in Russia, the taking after stages of DN have currently distinguished: the stage of chronic kidney disease, the stage of proteinuria, and the stage of microalbuminuria [37].

The stage of microalbuminuria is characterized by the appearance of a small amount of albumin in the urine: from 20-199 mcg/min in the morning portion and from 30-299 mg in the daily portion, undetectable during routine methods of urine testing. At this stage, the patient with DM does not have any clinical symptoms. The frequency of MA detection increases with the duration of the disease in both type 1 and type 2 diabetes [38].

The stage of proteinuria is determined by the preserved filtration function of the kidneys: urinary albumin excretion of more than 200 mg/min or more than 300 mg/day, normal GFR. The presence of proteinuria indicates the irreversibility of the process and sclerosis of 50-75% of the renal glomeruli [39].

The stage of chronic kidney failure is diagnosed in the presence of proteinuria and increased levels of creatinine and urea in the biochemical analysis of blood [40].

The diagnosis of diabetic nephropathy currently includes the stage of chronic kidney disease, according to the classification approved in 2005 by KDIGO (Kidney Disease: Improving Global Outcomes). CKD was divided into 5 stages depending on the GFR score calculated using the Cockcroft-Gault, MDRD, and CKD-EPI formulas (table 1).

Table 1 The stage of CKD by levels of estimated GFR

GFR (ml/min/1,73 m^2)	Determination	Stage
≥ 90	High and optimal	C1
60 – 89	Slightly reduced	C2
45 – 59	Moderately reduced	C3a
30 – 44	Significantly reduced	C3b
15 – 29	Sharply reduced	C4
< 15	End-stage renal disease	C5

Stage 3 of CKD is divided into 3a («moderately reduced» GFR– 45-59 ml/min/1,73 m²) and 3b stage («significantly reduced» GFR – 30-44 ml/min/1,73 m²) [15].

1.3 The laboratory method for evaluating filtration function of kidneys

There are several methods for evaluating the filtration function of the kidneys. To date, there is no method for studying GFR that is perfect in terms of accuracy, availability, and usability. The most accurate is the clearance methods. The volume of plasma that is completely cleared of any substance in a minute is called the clearance of this substance. To assess GFR, the clearance of such substances that

enter the urine only by glomerular filtration (not reabsorbed or secreted) is studied. In scientific research, GFR is calculated based on the clearance of exogenous substances that are injected into the blood. They remain the "gold standard" for measuring GFR, but their technical complexity and complexity, the need to inject a foreign substance into the blood, and high cost limit their use.

Glomerular filtration can also be measured by the clearance of endogenous substances. This substance can serve as creatinine, which enters the blood from muscle tissue at a roughly constant rate. Due to the fact that creatinine is not reabsorbed and is not released in the tubules, it enters the urine only by glomerular filtration, and its clearance is equal to the value of glomerular filtration. For its calculation, you can use the Rehberg test, which involves measuring the concentration of creatinine in plasma, the volume of daily urine, and the concentration of creatinine in the urine.

However, it requires a daily collection of urine, which is performed according to strict rules. Incorrect collection of urine and inaccurate measurement volume urine lead to significant distortions in the estimation of GFR.

Mathematical formulas are widely used for indirect estimation of GFR by the level of creatinine in the blood. The first was the Cockcroft– Gault formula that is enough to use an ordinary calculator. It is simple, but it is desirable to standardize the resulting value on the surface of the patient's body, which significantly complicates calculations [41]. When applying the Cockcroft-Gault formula, it should also be remembered that it was created to calculate creatinine clearance and does not take into account the creatinine channel secretion.

In the 90s, based on the data from the MDRD study, new equations were proposed that are more accurate than the Cockcroft-Gault formula and do not require additional standardization on the surface of the body [41]. To calculate using the MDRD formula, it is enough to know the serum creatinine level, gender, age, and race of the patient. Although the MDRD formula at stages 3-5 of CKD more accurately reflects the function than the Cockcroft-Gault formula, at true GFR above 60

ml / min/1.73 m^2, it gives understated results. In other words, the main limitation is an underestimation of GFR in normal kidney function.

In 2009-2011, the most universal and accurate method for calculating GFR was developed that works at any stage of CKD and in all three races – the CKD-EPI *equation* (collaboration in the epidemiology of chronic kidney disease).

CKD-EPI quations:

$$GFR\ (ml/min/1{,}73\ m^2) = 141 \times [min\ \text{plasma creatinine}(mcmol/l)/k\ \text{или}\ 1]^{\alpha} \times \times [max\ \text{plasma creatinine}\ (mcmol/l)\ /k\ \text{или}\ 1]^{-1{,}209} \times 0{,}993^{\text{Age}} \times 1{,}018\ \text{(for female)} \times 1{,}159\ \text{(for members of the black race)}$$

where k – 61,9 for female and 79,6 for male, α – (–0,329) for female and (–0,411) for male; creatinine (mcmol/l) = creatinine (md/dl) × 88,4

The CKD-EPI formula is better correlated with reference methods for determining GFR [41].

It is recommended to calculate GFR using the CKD-EPI equations when determining serum creatinine levels in each biochemical laboratory. However, modern markers recognize CKD when at least 50-70% of the nephrons in both kidneys are affected.

1.4 Method of radionuclide diagnostics

One of the types of radiation diagnostics is radionuclide diagnostics and its applications in urology and nephrology have made it able to help studying kidney function. Indications for radionuclide studies of kidneys are such diseases as acute or chronic renal failure, renal artery stenosis, obstructive uropathy, reflux nephropathy, congenital abnormalities, transplanted kidney, kidney injury or of the kidneys

and ureters [44].

Significant progress in the field of nuclear medicine, physics and technology are associated with the development of single-photon and positron-emission computed tomography, as well as radiopharmaceuticals (RP), which in the body allows you to register, capture and study extremely small amounts of radioactive radiation, which is practically harmless to the body of the subject.

Diagnostic RPs are administered to the patient in indicator quantities at which the radiation dose is minimal. Scintigraphy images are obtained based on the features of inclusion and distribution of RP registered with the help of radio-diagnostic equipment and the structural and functional state of the studied organs is evaluated depending on the functional state of their cellular system. The intensity of radiation from a radioactive indicator is used to quantify their viability or the degree of functional impairment, which later allows us to accurately compare studies in dynamics [44, 45].

Unlike contrast agents used in x-ray studies, isotope-labeled RP do not lead to side effects and are not nephrotoxic All isotopes used for radionuclide research are short-lived they quickly disintegrate, stopping irradiation, and RP is quickly removed from the body after the study. As a result, the radiation load is significantly lower than in radiography and computed tomography.

Radioisotope diagnostics makes it possible to detect abnormalities of kidney function already in the initial stages of the disease when other methods are still uninformative [46, 41, 42].

1.4.1 Dynamic renal scintigraphy

The main method of radionuclide study of kidneys is dynamic renal scintigraphy which provides an assessment of glomerular filtration, tubular secretion, urodynamics, the state of parenchyma and blood supply to the kidneys, the topography of the entire organ and its individual sections.

The most well-known RPs for kidney evaluation are ^{99m}Tc-DTPA (diethy-lenetriaminopentaacetic acid), ^{99m}Tc –MAG3 (mercaptoacetyltri-glycerol), and ^{99m}Tc-DMSA (3 - dimercaptoyantaric acid) [47, 48]. But in the world practice today, ^{99m}Tc-DTPA is mainly used for assessing kidney filtration.

The method of measuring gamma camera radiation using ^{99m}Tc-DTPA is a simple method for determining quantitative indicators:

1. T_{max} – time to peak, the time of maximum accumulation of RP when *this is the period of time RP from the vessels completely accumulates in the renal pelvis;*
2. $T_{1/2}$ – the half time, this is the time period for the removal of RP from the kidneys, which *the activity of the drug decreases by 2 times from the maximum*;
3. GFR – glomerular filtration rate, *reflecting the filtration capacity of the kidneys.*

The glomerular filtration rate during the radionuclide study of dynamic renal scintigraphy (DRS) was determined using a lattice algorithm, which is calculated using the formula [44]:$GFR = \frac{(C_l+C_r)}{P} \cdot 100\% \cdot 9{,}975621 - 6{,}19843$, meanwhile

$$C_l = K(2{,}3)_l \cdot \exp(0{,}153 \cdot D),$$
$$C_r = K(2{,}3)_r \cdot \exp(0{,}153 \cdot D).$$

where $K(2{,}3)_l$ and $K(2{,}3)_r$–the total savings for renographically curve in the interval from 2 to 3 min after the receipt of the drug (area renogram, indirectly reflecting the maximum amount of tracer that passed through the kidney for a specified period of time) for the left and right kidneys, respectively; P – the difference in the score of the syringe before and after injection; D – the depth of the kidney.

Separate GFR for left (GFR_l) or right (GFR_r) kidneys calculate as:

$$GFR_l = \frac{C_l}{C_l+C_r} \text{ or } GFR_r = \frac{C_r}{C_l+C_r}.$$

When performing dynamic renal scintigraphy, it is possible to determine the

initial changes in kidney function [43]. According to V.N. Slavnov et al., radionuclide research methods reveal significant changes in intrarenal hemodynamics and filtration-excretory kidney function in patients with type 2 diabetes already at the preclinical stages of DN [50]. Changes in the values of the filtration-excretory function of the kidneys indicate the bilateral nature of kidney damage in DM. Using radionuclide diagnostics methods, it is possible to determine the localization of the pathological process in the parenchyma, calyx, and pelvis of the kidneys, which is not always detected during clinical and laboratory examination.

Even though this method has been used for a long time – it has not lost its relevance to the present day, as evidenced by publications of the last decade [49, 52, 53, 54,55, 56, 57, 58]. However, only a small number of studies are devoted to the use of the scintigraphy method to assess the functional state of the kidneys in patients with type 2 diabetes [60, 59, 61,62]. This method requires less time than other methods, but the debate about its diagnostic accuracy continues. However, a common opinion on the diagnostic value of GFR indicators for various types of renal lesions from DM has not yet been formed [63, 64, 60].

1.5 The conclusion to the literature review

The development and implementation of prevention of DN progression are important both for preventing the development of CRF and subsequent dialysis treatment and for reducing the risk of cardiovascular complications since persistent albuminuria and reduced GFR are independent risk factors for high cardiovascular mortality in patients with DM. It is also important to remember that the prognosis of patients with DN is associated not only with a high risk of cardiovascular accidents, but also with the progression of other complications of DM: proliferative retinopathy, Autonomous, and peripheral neuropathy, diabetic foot syndrome, and largely depends on the timely diagnosis of this complication and correct treatment tactics at different stages [42].

Solving the problems of the diagnostic methods can help reduce the number of kidney transplants, which will reduce the socio-economic burden on society and improve the quality of life of patients

Chapter 2. Materials and methods of research

2.1 Design of research

A total of 91 patients admitted to the clinic for examination and treatment in the endocrinology clinic of the SSMU were studied, including: 48 patients with type 1 diabetes and 43 patients with type 2 diabetes in the period from 2015 to 2019.

All patients were examined according to modern diagnostic standards. They were given a clinical examination and follow-up, a resolution of the DM based on WHO criteria (1999), urine analysis for albuminuria (normoalbuminuria, microalbuminuria, proteinuria), determination of biochemical blood analysis (determination of creatinine, urea), including the level of glycated hemoglobin (HbA1c), radionuclide studies (DRS on the Philips BrightView gamma camera) were performed to calculate GFR renal function, maximum accumulation (T_{max}) and its half-time ($T_{1/2}$) of RP.

When analyzing each clinical observation of patients, various complaints were identified, information about kidney diseases was considered, attention was paid to the stage of the disease, as well as to the existing syndromes and symptoms.

The master's thesis performed at the department of radiation diagnostics and radiation therapy the Federal State Budgetary Educational Institution of Higher professional education "Siberian State Medical University" in the Ministry of Health the Russian Federation, c. Tomsk, the scientific adviser is head of the department of radiation diagnostics and radiation therapy V.D. Zavadovskaya (doctor medical science, professor), deputy chief doctor of clinics M.A.Zorkal’tsev (doctor medical science).

2.2 Object of research

The characteristics of patients by gender and age are presented in table 2.

The average age of patients with type 1 diabetes was 38.1 ±2.1 years, women predominated.

The average age of patients with type 2 diabetes was 61.1 ±1.4 years, men predominated.

Criteria for inclusion in the study group of patients with type 1 diabetes:

1. Absence of symptomatic arterial hypertension;
2. Age of the subjects is 18 years and older;
3. Consent patients for participation in ongoing research.

Criteria for exclusion from the study group of patients with type 1 diabetes:

1. Severe concomitant pathology (metastatic lesion, stage 4-5 CKD);
2. Viral hepatitis;
3. Pregnancy;
4. Voluntary refusal of patients to participate in the study.

Criteria for inclusion in the study group of patients with type 2 diabetes:

1. Control of hypertension;
2. Presence of a persistent increase in glucose levels;
3. Subjects aged 18 years or older;
4. Consent patients for participation in ongoing research.

Criteria for exclusion from the study group of patients with type 2 diabetes:

1. Viral hepatitis;
2. Presence of uncontrolled arterial hypertension;
3. Severe concomitant pathology (metastatic lesion, stage 4-5 CPN);
4. Pregnancy;
5. Voluntary refusal of patients to participate in the study.

Table 2 – Age and gender composition of the study groups

Characteristics		Patients (n=91)	
		n	%
Sex	Female with DM 1	25	27,5
	Male with DM 1	18	19,8
	Female with DM 2	23	25,3
	Male with DM 2	25	27,4
Av. age of patients DM 1	38,1 ±2,1 years	43	47,2
Av. age of patients DM 2	61,1 ± 1,4 years	48	52,8

In table 2, all patients were divided by age and gender under types of DM. Group of type 1 diabetes consisted of 18 men and 25 women aged 18 to 56 years (average age 38.1 ±2.1 years) and group of type 2 diabetes consisted of 25 men and 23 women aged 19 to 72 years (average age 61.1 ± 1.4 years).

Table 3 – Age-gender composition in the group of type 1 diabetes at various stages of diabetic nephropathy

Parameters		Statistic	NA (n=13)	MA (n=5)	PO (n=2)
Age		Me (Q1–Q3)	37 (33−43)	35 (26−36)	21 –
Duration of DM 1 type		Me (Q1–Q3)	19 (13−25)	16 (12 – 18)	15 (12−18)
Sex	m	N (%)	4 (30,8 %)	4 (80,0%)	1 (50,0%)
	f		9 (69,2%)	1 (20,0%)	1 (50,0%)
HbA1c, %		M±SE	8,0±0,6	8,5±1,5	12,5±2,6

Notes: M – average value; SE-standard error of the average; Me-median; Q1–Q3-quartiles (lower and upper); N (%) – number of people; p – level of statistical significance.

According to the revealed DN in patients with type 1 diabetes, patients were divided into the groups by the stage of normoalbuminuria (13 people), microalbuminuria (5 people) and proteinuria (2 people) shown in table 3. For the diagnosis of preclinical stages of diabetic nephropathy, urine analysis for microalbuminuria was used. Quantitative determination of albuminuria was performed by enzyme immunoassay using kits from ORGenTec Diagnostika.

The average age of DN patients with type 1 diabetes was 37 (33-43) years, in the 2nd – 35 (26-36) years, and in the third – 21 years. Patients of all three subgroups had different disease history (type 1 diabetes experience decreased from the NA subgroup to the PO subgroup), which is a consequence of the atypical course of diabetes before the onset of pronounced morphfunctional changes in the renal parenchyma. In the stage of NA, MA, The Hbalc level was 8.0±0.6% and 8.5±1.5 %, which indicates the decompensation of carbohydrate metabolism. Individuals in the PO group have marked decompensation of carbohydrate metabolism. If the difference available and would glycated hemoglobin less than 1.5% decompensation was seen as reasonable if the difference is more than 1.5% as severe.

Table 4 – Age-gender composition in the group of type 2 diabetes at various stages of diabetic nephropathy

Parameters		Statistic	NA (n=20)	MA (n=11)	PO (n=3)
Age		Me (Q1–Q3)	64 (59,5−70,3)	58 (54−60)	56 (56−62,5)
Duration of DM 2 type		Me (Q1–Q3)	17 (12,8−18,8)	9 (8−16)	21 (16−26,5)
Sex	m	N (%)	6 (30,0%)	5 (45,5%)	3 (100%)
	f		14 (70,0%)	6 (54,5 %)	0 (0%)

Continuation of table 4

HbA1c, %	M±SE	8,0±1,4	10,4±2,4	8,3±1,8

Notes: M – average value; SE-standard error of the average; Me-median; Q1–Q3-quartiles (lower and upper); N (%) – number of people; p – level of statistical significance.

And patients with type 2 diabetes were divided into the groups by the stages of normoalbuminuria (20 people), microalbuminuria (11 people), and proteinuria (3 people) shown in table 4. In which the average age in patients with DN with type 2 diabetes was 64 (59.5 – 70.3) years, in the 2nd -58 (54-60) years and in the third-56 (56-62,5) years. Patients of all three subgroups had different disease history (type 2 diabetes increased from the NA subgroup to the PO subgroup), which is a consequence of the typical course of diabetes before the onset of pronounced morphofunctional changes in the renal parenchyma. As in the subgroups of the norm - and microalbuminuria, the female sex prevailed over the male. In the stage of NA, PO, the HbAlc level was 8.0±1.4% and 8.3±1.8 %, which indicates the decompensation of carbohydrate metabolism. In individuals of the MA group, there is a marked decompensation of carbohydrate metabolism, which is the first mechanism of progression of kidney failure.

Research methods:

- Clinical and laboratory research methods;
- Instrumental radiation research methods.

Equipments:

- Calorimeters KvK-3;
- Goryaev's Camera;
- ORGenTec Diagnostica;
- SPECT Philips BrightView.

2.3 Clinical and laboratory research methods

Laboratory tests were performed in the clinical and diagnostic laboratory of the clinics of SSMU of the Ministry of the health of Russia. General urine analysis was performed using a unified method using colorimetric analysis on the colorimeter KvK-3, the specific weight of urine was measured using a hydrometer (durometer) with a scale range of 0.001-1.050. the Color, transparency of urine, the presence of sediment was evaluated visually. The pH of the urine was determined by a methylene blue indicator. The uniform elements were counted by Goryaev's camera.

Biochemical methods consisted of the determination of generally accepted indicators, including the determination of liver transaminases, glucose, creatinine, urea, and bilirubin.

The creatinine level was determined using the Popper method based on the Jaffe reaction. The urea level was determined by an enzymatic urease method using glutamate dehydrogenase as a catalyst. Reference values of creatinine and urea were the norms accepted by manufacturers of biochemical kits, taking into account age changes.

Quantitative determination of microalbuminuria was performed by enzyme immunoassay using kits from ORGenTec Diagnostika.

Then the true GFR in ml / min / 1, 73m^2 was calculated using the reduction of GFR obtained by the formula CKD-EPI. The stage of chronic kidney disease (CKD) was determined using the GFR index in patients according to the recommendations of the NKF K/DOQI (national initiative for quality of kidney disease outcomes of the national kidney Foundation) [49].

2.4 Instrumental radiation research methods

Dynamic renal scintigraphy (DRS) performs on a two-detector gamma camera (SPECT) Philips BrightView with using RP 99^{m}Tc-pentatech Russian analog ^{99m}Tc-DTPA (fabricated Ltd «DIAMED», Russia).

All patients were instructed in advance about the procedure. Preparation for the study included preliminary hydration (0.5 liters of water half an hour before the study) and emptying the bladder immediately before the study. Radiopharmaceutical (^{99m}Tc- pentatech) was administered intravenously at a dose of 74-111 MBq in the patient's supine position. Before and after the injection, the activity of the indicator in the syringe was recorded for 1 minute for subsequent calculation of GFR.

After the injecting of the RP, data was recorded in 1 frame/sec mode for 1 min to obtain angiograms, then the study was recorded in 2 frames/min mode for 20 minutes. In the course of the study, a series of scintigrams with images of the kidneys were obtained at various time intervals.

The data obtained during the DRS was processed using a software package on the Philips Medical system "JetStream Work-space 3.0" workstation and included:

- visual image analysis,
- building and analysis of angioscintigrams,

–building activity-time curves, the estimation of time and amplitude characteristics of renogram as indicators of filtration and excretory functions of the kidneys with the timing of maximum accumulation of the indicator (T_{max}) and half-life ($T_{1/2}$), the remainder of RP for 20-minute research, the contribution to filtration and determination of glomerular filtration rate (overall and separately for the left and right kidney normalized to the surface area of body 1.73m^2).

The result of renal scintigraphy is a series of scintigrams with images of the kidneys in different time intervals. Using native scintigraphy, we selected zones of

interest from the area of both kidneys, heart, and background, which were used to plot the "activity-time" curves (figure 1).

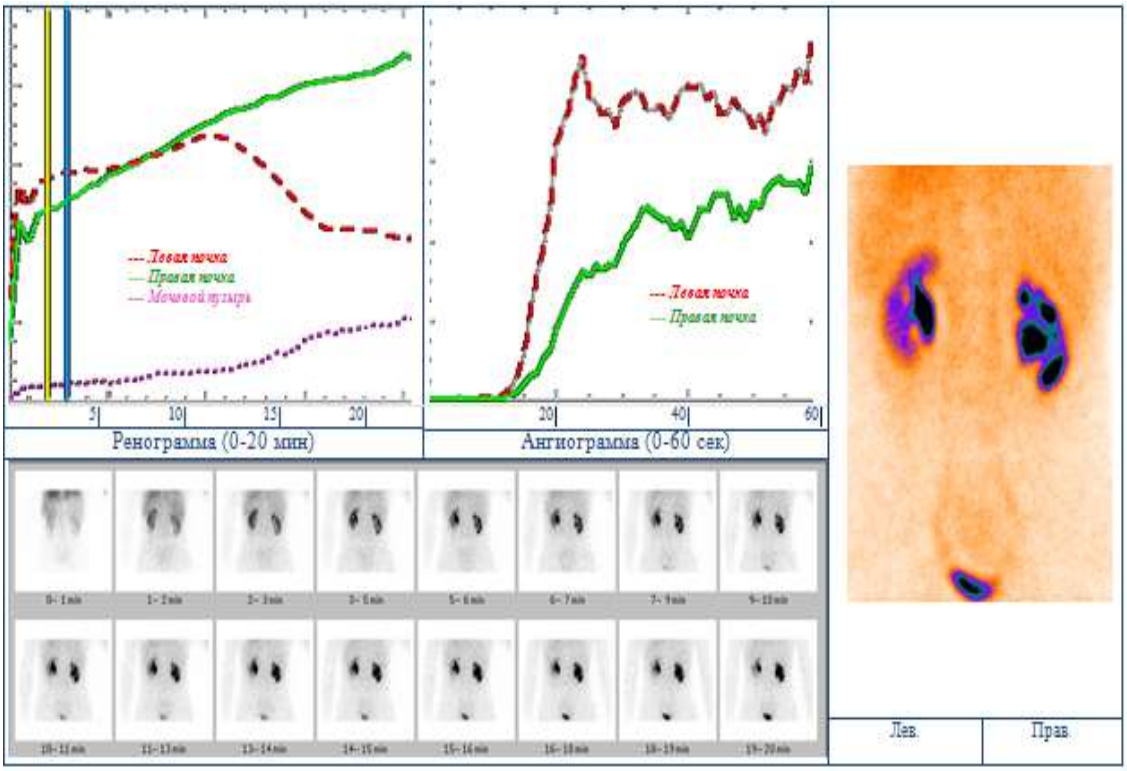

Figure 1 – Results of dynamic renal scintigraphy

2.5 Statistical processing of the material

The results of the study were processed in a special software STATISTICA-6 [65]. At the first stage of quantitative data analysis, the distribution law was checked using the Mann – Whitney test. Data obeying the normal distribution law were described using the mean and standard error of the mean. Quantitative data that do not follow the normal distribution law were described using median and quartiles. The choice of the method of comparison of the studied groups was also determined by the law of data distribution. Data obeying the normal distribution law were compared using the student's t-test. To assess the linear dependence of quantitative data, the Spearman coefficient (r) was calculated. The correlation was considered strong, with a coefficient value greater than 0.7 and less than -0.7; from 0.5 to 0.7 and from -0.5

to -0.7, the correlation was considered average; the correlation was considered weak, with a coefficient value less than 0.5 and more than -0.5. When the significance level of p is less than 0.05, it was assumed that the studied indicator in the compared groups had statistically significant differences.

Chapter 3. Results of research

3.1 Evaluation of dynamic renal scintigraphy parameters

The purpose of this section is to study the diagnostic capabilities of the dynamic renal scintigraphy method in identifying reliable parameters of DRS in patients DN with different types of DM.

At the first stage of the research in this section, the analysis of the relationship between clinical and laboratory data and the parameters of the DRS radionuclide study was performed. The obtained monitor values of GFR, T_{max}, and $T_{1/2}$ were used for comparison with clinical and laboratory data. In the study groups, the GFR level fluctuated within 26~140 ml/min, the maximum accumulation time of the T_{max} indicator fluctuated within 0.5 ~ 15.5 minutes, and the half-time of the $T_{1/2}$ indicator varied within 0 ~ 100 minutes.

When comparing the results of the daily protein level in urine, the volume of urine and the level of MA with the parameters of the DRS radionuclide study, no data were obtained on the presence of statistically significant correlations between the studied indicators, the data are shown below in tables 5, 6 and 7.

Table 5 – Searching results for the relationship between the level of daily protein in the urine and the main parameters of DRS

Parameters		Correlation coefficient, r	Student's criteria, t	Level of statistical significance, p
GFR	total	0,008	0,054	0,956
	left	0,027	0,171	0,864
	right	0,023	0,144	0,886
T_{max}	left	-0,004	-0,027	0,977
	right	0,028	0,178	0,859
$T_{1/2}$	left	0,200	1,296	0,202

Continuation of table 5

	right	-0,099	-0,629	0,532

Table 5 shows a statistically insignificant correlation between the level of daily protein in the urine, in which the GFR for the left kidney was r=0.027 (p=0.864), which differs slightly from the GFR for the right kidney and for the General, and is very weak and unreliable.

In the half-life of RP, there is a similar dynamic on the part of the kidneys. However, in the time of maximum accumulation of RP, the values for the right kidney were higher than for the left.

Table 6 – Searching results for the relationship between the volume urine and the main parameters of DRS

Parameters		Correlation coefficient, r	Student's criteria, t	Level of statistical significance, p
GFR	total	0,174	1,063	0,295
	left	0,135	0,809	0,424
	right	0,144	0,860	0,396
T_{max}	left	-0,129	-0,760	0,452
	right	0,059	0,352	0,727
$T_{1/2}$	left	0,092	0,547	0,588
	right	-0,002	-0,011	0,991

In this table, no statistically significant correlation was obtained by volume in the urine. The values of the total GFR were r=0.174 (p=0.295), which is slightly different from the GFR for the right kidney and for total, and are weak and unreliable

In the half-time and the time of maximum accumulation of RP, a similar dynamic was observed on the part of the kidneys.

Table 7 – Searching results for the relationship between the level of microalbuminuria and the main parameters of DRS

Parameters		Correlation coefficient, r	Student's criteria, t	Level of statistical significance, p
GFR	total	-0,197	-1,449	0,153
	left	-0,179	-1,303	0,198
	right	-0,281	-2,067	0,043
T_{max}	left	-0,070	-0,499	0,620
	right	-0,177	-1,269	0,210
$T_{1/2}$	left	0,265	1,961	0,055
	right	0,008	0,055	0,956

According to the results of table 7, a statistically insignificant correlation was obtained for the level of MA, in which the GFR for the left kidney is r= -0.179 (p=0.198), which differs in the direction of a slight decrease from the value of the total GFR and is weak and not reliable. However, the level of MA and GFR in the right kidney has a level of static significance p=0.043, but the correlation coefficient is very weak r= - 0.281.

In the half-time period of RP, there is also a level of static significance p=0.055 and is reliable, but the correlation coefficient is very weak r=0.265. the Values of the maximum accumulation time of RP for the right kidneys are higher than for the left kidneys.

At the same time, there is a statistically significant correlation between creatinine levels and total GFR (figure 2), as well as separate GFR for the left and right kidneys. The weak and medium level of correlation is consistent with the data on the influence of various pathological processes on the creatinine level that are not directly related to the filtration function of the kidneys in table 8.

Table 8 – Searching results for the relationship between the creatinine and the main parameters of DRS

Parameters		Correlation coefficient, r	Student's criteria, t	Level of statistical significance, p
GFR	total	-0,609	-5,480	0,000001
	left	-0,491	-3,988	0,000217
	right	-0,582	-5,016	0,000007
T_{max}	left	-0,023	-0,162	0,872
	right	-0,210	-1,506	0,138
$T_{1/2}$	left	0,243	1,770	0,083
	right	0,123	0,874	0,386

Special attention should be paid to the fact that there is no static relationship between such an indicator of renal filtration function as T_{max} and creatinine level, which indicates its limited use at the current level of diagnosis.

Also noteworthy is the lack of a reliable relationship between the level of creatinine and radionuclide indicators of excretory kidney function $T_{1/2}$. On the left excretory kidney, the significance level almost reached a reliable p=0.083.

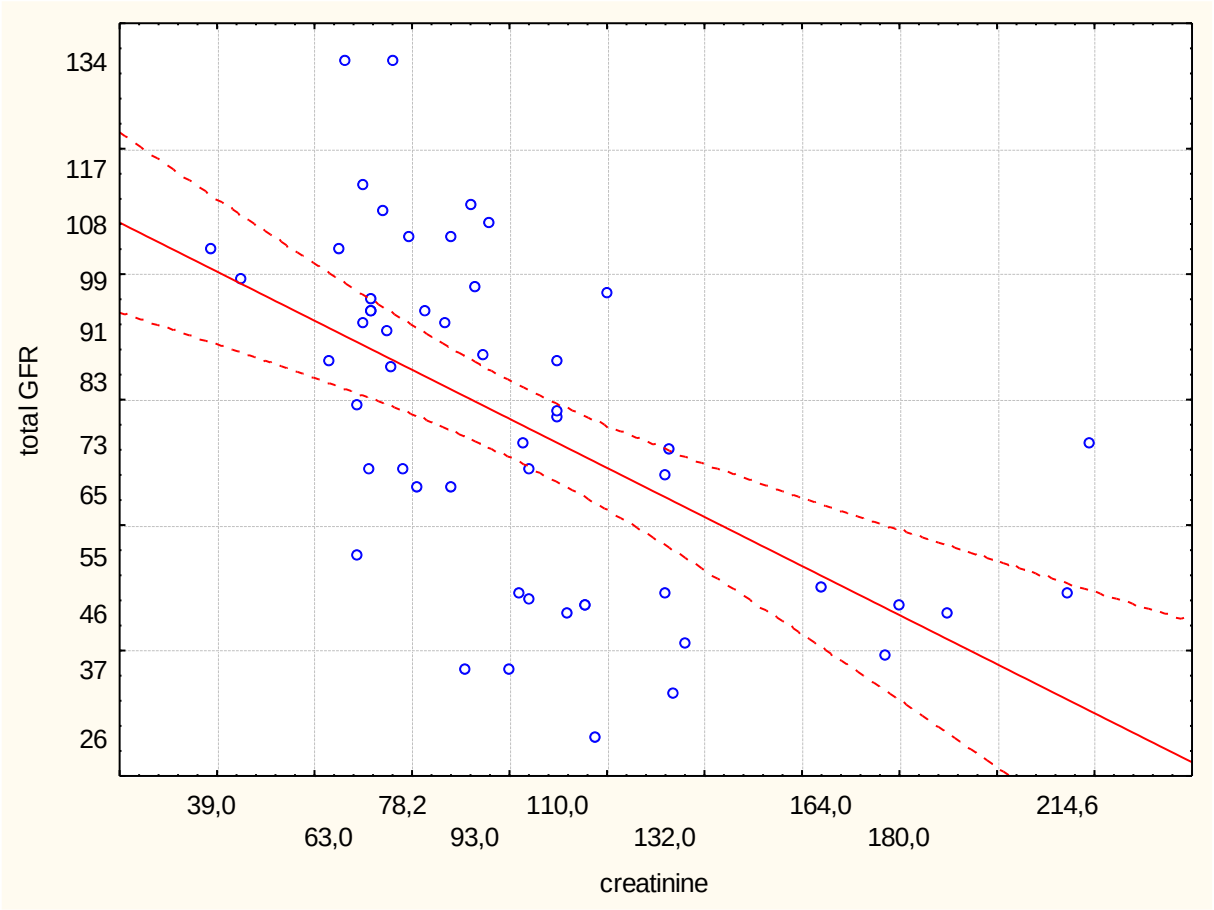

Figure 2. Comparison of total GFR for creatinine

When searching for the relationship between the age of patients and radionuclide indicators of GFR, attention was drawn to the presence of an average inverse correlation between the studied indicators with an absolute level of static significance Age did not correlate with data on excretory kidney function. On the left kidneys $T_{1/2}$, there is a high level of static significance p=0.019 with a weak correlation coefficient r = 0.276.

Table 9 – Searching results for the relationship between age of patients and the main parameters of DRS

Parameters		Correlation coefficient, r	Student's criteria, t	Level of statistical significance, p
GFR	total	-0,626	-6,709	0

Continuation of table 9

	left	-0,608	-6,363	0
	right	-0,504	-4,808	0,000009
T_{max}	left	0,103	0,855	0,396
	right	-0,105	-0,876	0,384
$T_{1/2}$	left	0,276	2,396	0,019
	right	0,165	1,400	0,166

According to table 9, the average inverse correlation with GFR indicators demonstrates how kidney function decreases depending on the patient's lifetime.

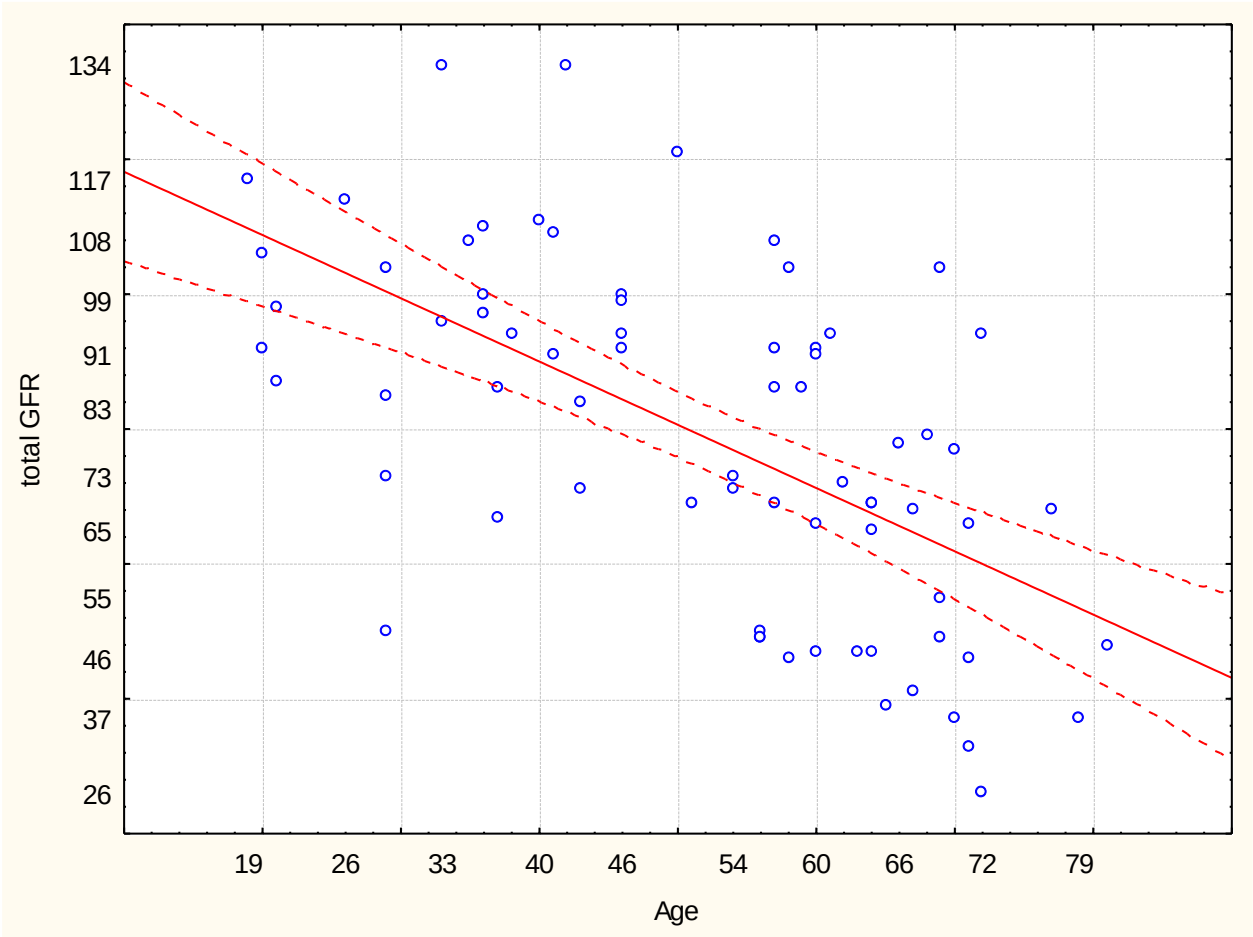

Figure 3 Comparison of total GFR for age of patients

However, the duration of the disease and the results of radionuclide assessment of kidney function were not interrelated, which may be due to the effectiveness of the therapy.

There was also no correlation between the level of glycated hemoglobin and the results of radionuclide research. That is, glycated hemoglobin does not affect the kidney directly, due to the fact that it is the main initiating metabolic factor in the development of diabetic kidney damage.

Table 10 – Searching results for the relationship between duration of DM and the main parameters of DRS

Parameters		Correlation coefficient, r	Student's criteria, t	Level of statistical significance, p
GFR	total	-0,039	-0,330	0,742
	left	-0,082	-0,679	0,499
	right	-0,095	-0,783	0,437
T_{max}	left	-0,025	-0,203	0,839
	right	-0,125	-1,034	0,303
$T_{1/2}$	left	0,103	0,864	0,391
	right	0,146	1,223	0,226

According to table 10, in general, the inverse correlation of the GFR relationship was found to be very weak for both the total and the divided (right and left kidney) with an unreliable level of significance.

According to the time of maximum accumulation of RP for the right kidney, the level of significance is more significant than the left one with weak correlation relationships.

According to the data of excretory kidney function, the values for both kidneys did not differ significantly, also with a weak correlation relationship.

Table 11 – Searching results for the relationship between glycated hemoglobin and the main parameters of DRS

Parameters		Correlation coefficient, r	Student's criteria, t	Level of statistical significance, p
GFR	total	-0,065	-0,539	0,592
	left	0,002	0,018	0,985
	right	-0,064	-0,533	0,596
T_{max}	left	0,022	0,183	0,855
	right	-0,240	-2,043	0,045
$T_{1/2}$	left	0,049	0,408	0,685
	right	-0,132	-1,111	0,270

According to table 11, a statistically insignificant correlation was obtained for HbA1c glycerol hemoglobin, in which the GFR for the left and right kidneys was r= -0.065 (p=0.592) and r= -0.064 (p=0.596), respectively, and differs in the direction of insignificant entrainment from the GFR value for the left kidney and are weak and incomplete.

According to the time of maximum accumulation of RP for the right kidney, there is a reliable level of static significance p= 0.45 with a weak inverse correlation.

According to the data of excretory kidney function, the values for both kidneys did not differ significantly, also with a weak correlation relationship.

Further, we compared the total glomerular filtration rate of a radiopharmaceutical against types of diabetes mellitus. Special attention should be paid to the influence of the type of diabetes on the indicators of kidney function.

In a pairwise comparison, there is a statistically significant difference between the type of diabetes and the level of total GFR (figure 4).

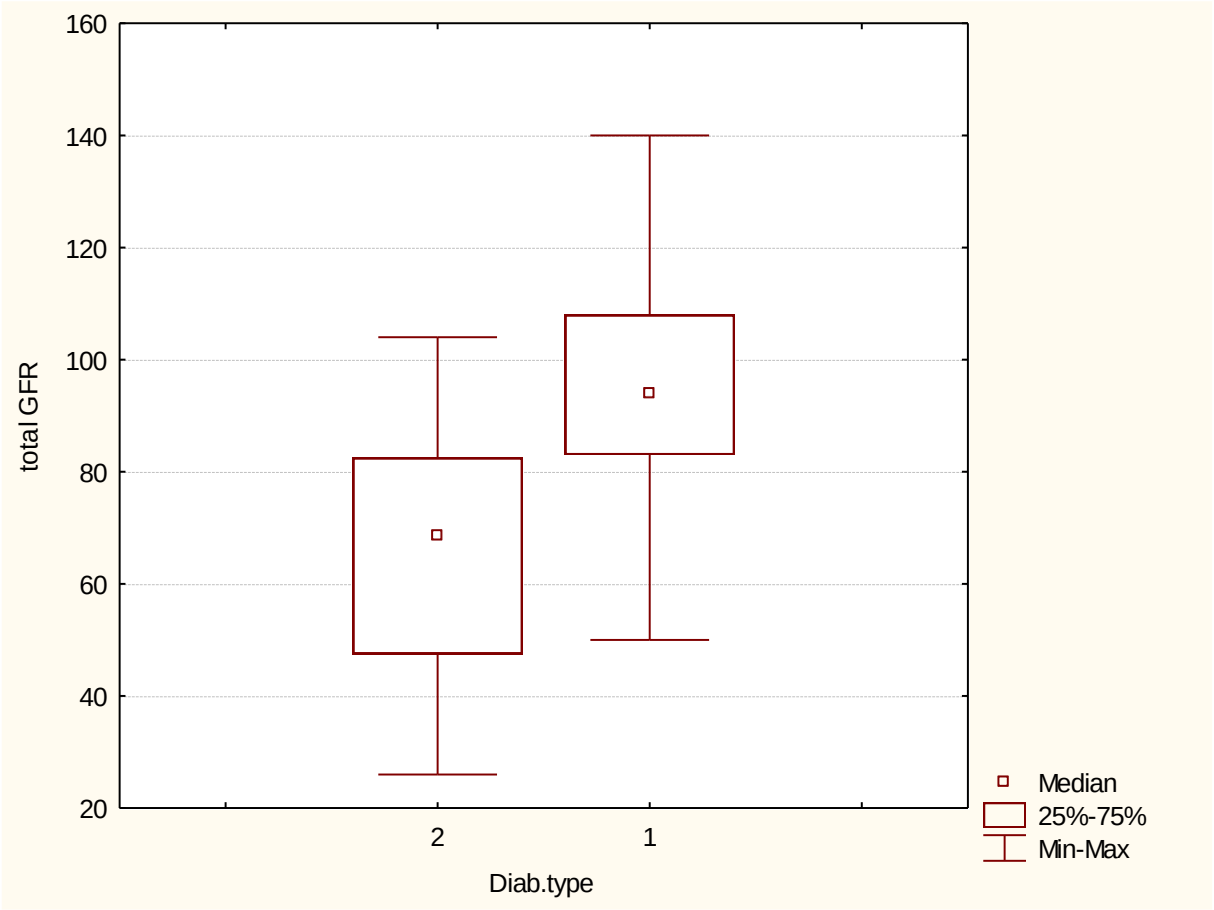

Figure 4 – Indicators of the total glomerular filtration rate of a radiopharmaceutical (total GFR) for type DM (1 and 2) according to dynamic renal scintigraphy

At the same time, the median values of total GFR in patients with type 2 diabetes are lower than in type 1 diabetes and are 68.5 and 94.0 ml / min/ 1.73 m^2, respectively (table 10). And this difference is due to the greater severity of the progression of renal failure (inflammation of the interstitial tissue with a decrease in the tone of the pelvicalyceal system).

It can be assumed that the delayed evacuation of the radiopharmaceutical from the calico-pelvic system is based on the inflammatory infiltration of interstitial tissue with a decrease in the tone of the calico-pelvic system of the kidneys. Inflammation is one of the main factors contributing to the development of diabetes complications.

Table 12 – Indicators of the total glomerular filtration rate in the kidneys depending on the types of diabetes according to dynamic renal scintigraphy

№	Type of DM	n	Total GFR Me (Q1–Q3)	Level of statistical significance, p
1	1 type	43	94 (83.0-108.0)	$p_{1-2}<0,001$
2	2 type	48	68.5 (47.5-85.5)	

Notes: Me – median; Q_1–Q_3 – quartile (lower and upper); p – level of statistical significance.

Thus, the DRS reflects the main pathological changes in the kidneys in patients with diabetes mellitus. At the same time, more attention should be paid to the GFR indicator in terms of reliability, in contrast to T_{max} and $T_{1/2}$, which did not show themselves to be reliable indicators in all comparisons.

3.2 Building an algorithm based on the result

According to results, the confidence parameters for the diagnosis of kidneys in patients with diabetes mellitus is the glomerular filtration rate in comparison with others. But other parameters give no less important information about the state of the kidneys, such as vascular diseases, reflux, and retention in the renal pelvis.

When constructing the screening algorithm, risk factors for chronic kidney disease and cardiovascular disease in patients with diabetes mellitus were taken into account.

Although albuminuria was not correlated and was not static when looking for a relationship with GFR. It is an important risk factor for cardiovascular disease. The value of the phenotype as a marker of nephropathy progression changed after demonstrating that a significant proportion regressed to normal albumin excretion (normoalbuminuria) in both type 1 and type 2 diabetes mellitus [34, 68]. This is due to the filtration capacity of the kidneys of different ages of patients with different stages of renal insufficiency on the background of diabetes mellitus.

Thus, GFR and Albuminuria are indeed associated with renal and cardiovascular diseases in people with diabetes.

For the early diagnosis of kidney damage or prevention of the development of chronic kidney disease, we have provided a single diagnostic guide for various types of DM with DN, and the algorithm is shown in figure 5.

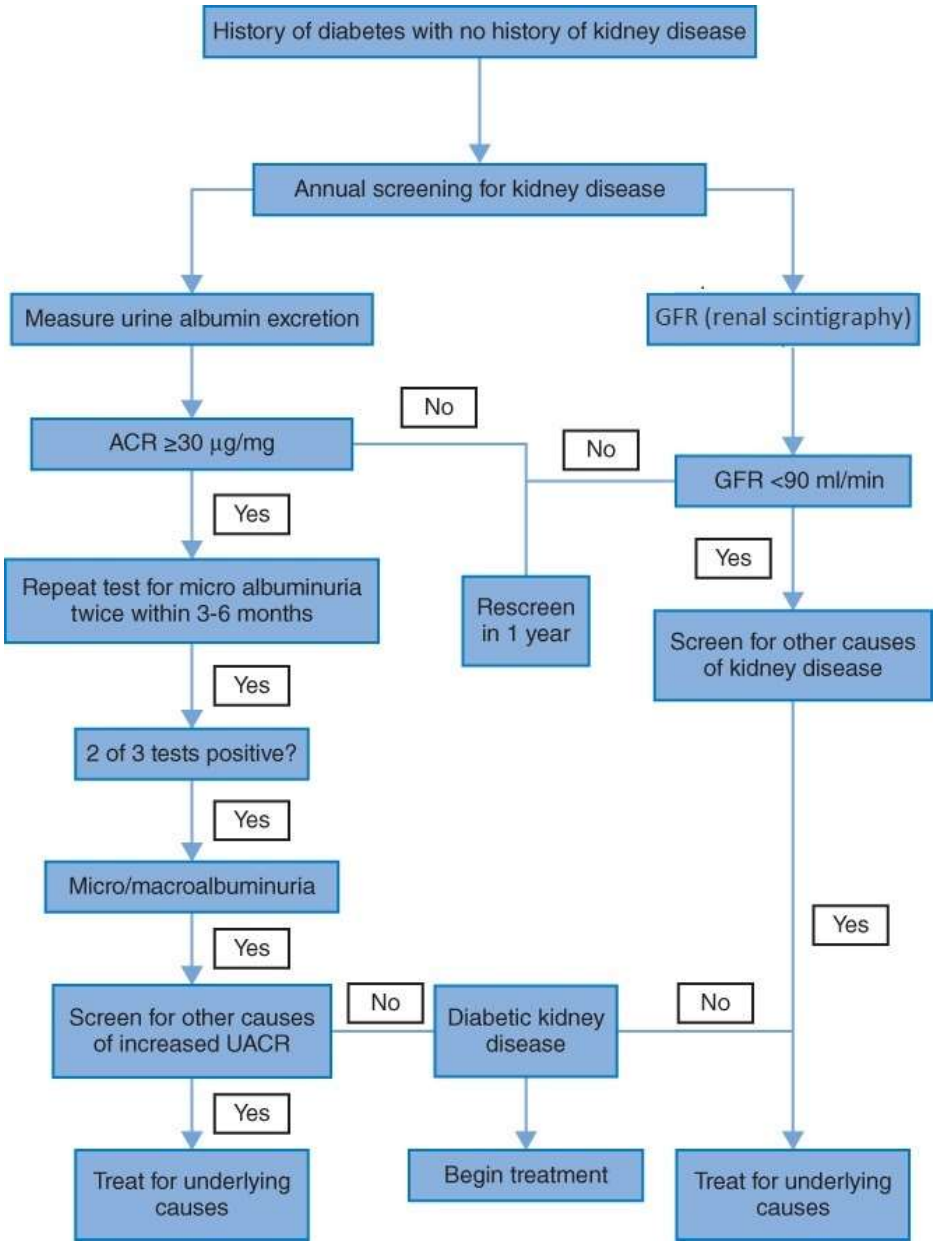

Figure 5 – Algorithm for evaluating kidney function in people with diabetes

Chapter 4. Financial management, resource efficiency, and resource-saving

Research master's thesis is a scientific work related to scientific research, conducting research in order to obtain scientific generalizations, finding principles, and ways to create (modernize) products.

Currently, the prospect scientific research isn't determined to scale of the discovery that in the early stages of the life cycle of high-tech and the resource-efficient product is hard enough to reach. Therefore, commercial value is as important as development research.

Evaluation of the commercial value (potential) of the development is a necessary condition when searching for sources of funding for scientific research and commercialization of its results. The commercial value is essential for developers who need to understand the state and prospects of ongoing research.

The purpose of this Chapter is to determine the prospects and success of a scientific research project, develop a mechanism for managing and supporting specific project solutions at the implementation stage.

Currently, the demand for new technologies in the diagnosis of various diseases is significantly increasing. The largest markets for the production of these technologies are GE, Siemens, Toshiba, Philips, which is directly related to the state interest in this area, as well as the quality of treatment in clinics where those technologies used. But the above companies are world-class companies, and therefore the target group of consumers includes medical centers and hospitals, the terms of use of which are undoubtedly dictated by people who diagnose with diseases of various etiologies.

4.1 Ishikawa diagram

Ishikawa diagram (also called fishbone diagrams, herringbone diagrams,

cause-and-effect diagrams, or Fishikaw) is a graphical method for analyzing and forming a cause-effect link, a tool for systematically determining the causes of the problem and subsequent visual representation.

Scope of the diagram:

– Identify the causes of the problem;

– Analysis and structuring of processes in the enterprise;

– Assessment of cause-and-effect links.

Figure 6 shows the use of the Ishikawa scheme (one of the seven classical methods for analyzing the quality management system), which allows you to identify and to group the conditions and factors that affect the process of making a diagnosis in a patient, and analyze the cause-and-effect link (a means of object decomposition) in this process.

Diagnostic tests performed in all patients to establish a clinical diagnosis include central and concomitant diseases. As a rule, this diagnostic mechanism includes medical examinations, blood and urine tests, a minimum list of biochemical indicators, taking into account compliance with the requirements for the standard of medical care –quality indicators for significant diseases.

The list of diagnostic and therapeutic measures for the patient must be scientifically justified.

Medical care measures should define at all the main stages of treatment and the location of the disease. Indications for additional methods of diagnosis and treatment should be clearly and shortly formulated. It is necessary to include the minimum clinical information for decision-making and choice of tactics.

It is vital to use the Ishikawa scheme to reduce document flow, eliminate duplication of information and its concentration. Using this scheme for a rational consultation algorithm in the process of diagnosis will avoid repetitions in the examination. So, we are reducing the personal time of both the attending doctor and consultants, improve contact with the patient (his relatives) and, most importantly, carry out an objective assessment and analysis of the work of various employees.

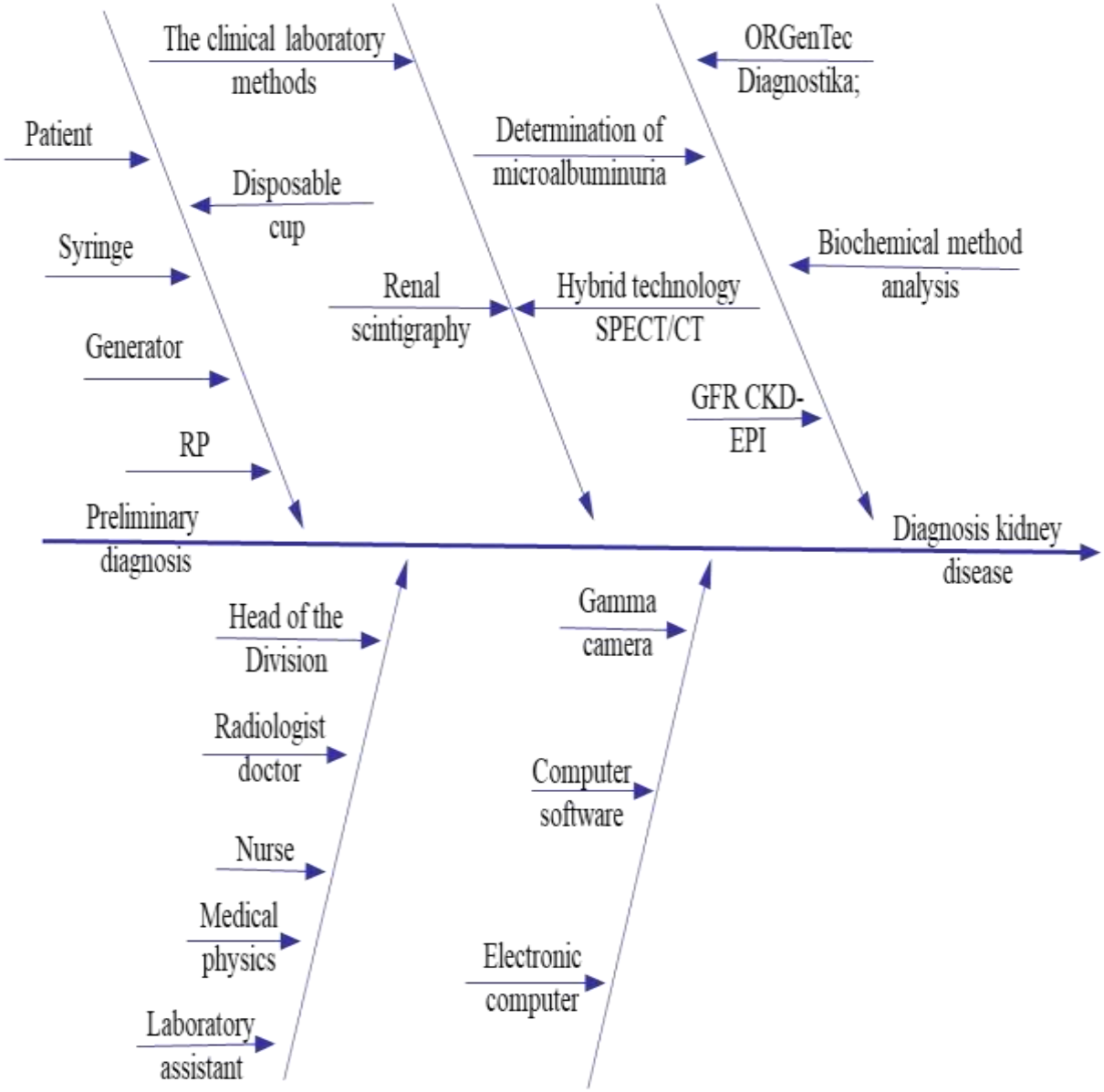

Figure 6 – Cause-and-effect diagrams during the diagnosis process

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. SWOT analysis is used to study the external and internal environment of the project (Table 13)

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.

An interpretation of each of these concepts:

1. Strengths are factors that characterize the competitive side of a research project. Strengths indicate that the project has a distinctive advantage or special resources that are special in terms of competition. In other words, strengths are resources or capabilities which is available to the project management that can be effectively used to achieve the goals set. At the same time, it is important to consider the strengths both side from the point of view of the project management and who involved in it.

2. Weaknesses are a lack, omission, or limitation of a scientific research project that hinder the achievement of its goals. This is something that does not work well within the project or where it has insufficient capabilities or resources compared to competitors.

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

4. A threat is any undesirable situation, trend or change in the project environment that is disruptive or threatening to its competitiveness in the present or future. A threat can be a barrier, restriction, or anything else that can cause problems, destruction, harm, or damage to the project. To identify project threats, we recommend answering the following questions:

Table 13 – SWOT analysis

	Strengths: S1. The important advantages of the procedure include accuracy and speed. Scintigraphy is also highly informative: it allows not only to exclude or confirm the disease, but also, if the diagnosis is confirmed, to obtain qualitative and quantitative data on the localization, size, and extent of damage to the structures of the body at the earliest stages. S2. Technetium is foreign to human biochemistry, so it does not interfere in any way with metabolic processes and is completely eliminated from the body without causing harm S3. The cost of conducting research is lower than other types due to the simplicity of the method and the low cost of the technology. S4. The damage caused by radioactive substances is minimal, much lower compared to computed tomography	**Weaknesses:** W1. The absence of hybrid technology. W2. It is contraindicated to conduct an examination of pregnant and nursing women, as well as children. W3. Possible allergic reactions.
Opportunities: O1. The use of the infrastructure of Siberian State Medical University O2. The use of the infrastructure of The Scientific Research Institute of Cardiology O3. Optimization of master's degree programs in the specialists of " Nuclear medicine»	Results for the interactive matrix of the project «Strengths and Opportunities»: 1) Development of new RP with a shorter half-life and lower radiation load to reduce the negative effects of ionizing radiation on patients. 2) Development of a methodological guide to improving the process training of specialists in the sphere of nuclear medicine.	Results for the interactive matrix of the project «Weaknesses and Opportunities»: 1) The possibility of combining radiation hybrid technology due to the development of additional software for the best results.

Continuation of table 13

Threats: T1. Absence of funding from the state and private organizations T2. Threat of gamma camera failure T3. Threat of electronic computer failure T4. Delays in delivery of the RP generators	Results for the interactive matrix of the project «Strengths and Threats»: 1) Publication of the obtained data in the scientific community. 2) A strategy to reduce threats through timely maintenance and installation of modern software.	Results for the interactive matrix of the project «Weaknesses and Threats»: 1) Getting research grants. 2) Development of new methods and protocols for medical equipment. 3) Professional development of staff

The results of SWOT analysis are taken into account when developing the structure of work performed within the framework of a research project.

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. This information is provided in the Project Charter.

The Project Charter documents the business needs, current understanding of the project customer's needs, and a new product, service, or result that is planned to be created.

Charter research project master's thesis the following structure:

1. The purpose and results of the project. This section provides information about project stakeholders, the hierarchy of project purposes, and criteria for achieving purposes.

Project stakeholders are defined as individuals or organizations that are actively involved in the project or whose interests may be affected either positively or negatively during the execution or completion of the project (Table 14).

Table 14 – Stakeholders of the project

Project stakeholders	Stakeholder expectations
Medical institutions (scientific research institutes, laboratories, universities)	–The results of the research allow us to expand the existing possibilities of radionuclide research methods in the assessment of renal insufficiency against diabetes mellitus, to give a comprehensive assessment of the state of the calyx-pelvis and urinary system in this category of patients.
SI TPU	–Development of bilateral relations with partner universities in the sphere of nuclear medicine. –Publications in international and national journals, conferences to improve the quality rating of the University, citation index

Table 15 provides information about the hierarchy of project purposes and criteria for achieving goals.

Table 15 – Purpose and results of the project

Purpose of project:	Improving radiological diagnostics of kidney condition in patients with diabetic nephropathy and diabetes mellitus using renal scintigraphy.
Expected results of the project:	The obtained data significantly complement and expand the existing capabilities of radionuclide research methods (SPECT/CT) in assessing the severity of diabetic nephropathy (DN) against the background of diabetes mellitus (DM); The revealed features of renal disorders indicate the need for early scintigraphy examination of patients with clinical manifestations of these types of pathologies.

Continuation of table 15

Criteria for acceptance of the project result:	For the first time, a comprehensive comparative clinical and instrumental assessment of the state of the calico-pelvic system in patients with DN in DM; The role of renal scintigraphy in determining the severity of General and regional lesions in patients with DN on the background of DM is argued, and criteria for assessing the severity of this condition based on the results of radionuclide methods are developed.
Requirements for the project result:	To study the nature and severity of kidney function using scintigraphy in patients with diabetic nephropathy (DN) for DM; Development of a method for calculating glomerular filtration rate in patients using radionuclide studies To evaluate in a comparative aspect the features (degree of reduction) of GFR in DN patients with type 1 and type 2 diabetes.

2. 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. This information is represented in table form (Table 16).

Table 16 – Project workgroup

№	**Participant**	**Role in the project**	**Functions**	**Labor time, hours.**
1	Zavadovskaya V.D.	Supervisor	Project activity controlling	2460
2	Zorkal'tsev M.A.	Head of Division	Controlling the activities of the division's staff	3450
3	Udodov V.M	Radiologist Doctor	Conducting research	1010

Continuation of table 16

4	Kudaibergen G.B.	Medical Physicist	Processing of results	4480
Total:				11 400

3. Project limitations and assumptions. Project limitations are all factors that can be as a restriction on the degree of freedom of the project team members. This information is represented in table 17.

Table 17 – Project limitations

Factors	**Limitations / Assumptions**
Project's budget	405 711,1 rub
Source of financing	State budget
Project timeline:	2 years
Date of approval of plan of project	November 2018
Completion date	June 2020

4.4 Project plan

As part of planning a science project, you need to build a project timeline and a Gantt Chart. The schedule is presented in table 18.

Table 18 – Project Schedule (working days)

Job title	**Duration, working days**	**Start date**	**Date of completion**	**Participants**
Preparation of technical specifications and choice of research direction	41	November 1, 2018.	December 28, 2018.	Radiologist Doctor/Supervisor
Selection and study of materials on the topic	198	January 9, 2019.	December 27, 2019.	Medical Physicist

Continuation of table 18

Calendar planning of work on the topic	345	November 1, 2018.	June 7, 2020.	Head of Division
Development of a General research methodology	60	March 1, 2019.	May 31, 2019.	Radiologist Doctor/Medical Physicist
Obtaining the necessary experimental data and checking the results	205	June 1, 2019	March 27,2020.	Supervisor/Medical Physicist
Processing the received data	140	September 2, 2019.	March 27, 2019.	Medical Physicist
Writing a master's thesis	96	December 2, 2020.	May 29, 2020.	Medical Physicist
Master's thesis defense	14	June 1, 2020.	June 19, 2020.	Medical Physicist

4.5 Formation budget costs

When planning the budget of scientific research, it should be provided with a complete and reliable reflection of all types of planned expenditures necessary for its implementation. In the process of budgeting, planned expenditures are grouped by the items, which are shown in table 19.

Table 19 – Items expenses grouping

Items							
Name	Material costs	Costs of special equipment	Basic salary	Additional salary	Deductions on social needs	Overhead	Total cost
Cost, rubles	405789	1022725	3580383	537058	1235232	139200	6920310

Material costs of scientific and technical research

In this article are included the cost of purchasing all types of materials, components and semi-finished products necessary for the execution of works on the subject. The amount of required material values is determined by the consumption rate in the amount of 91 patients

Table 20 – Raw materials, supplies, purchased products, and semi-finished products

Name	**Mark, size**	**Quantity, pc**	**Price per unit, rub.**	**Sum, rub.**
Syringes	19G, 20ml	91	18	1638
Gloves	L	91	2,7	245,7
Masks	AMC-Med	91	4,4	400,4
RP Generator	Generator Technetium-99m	4	96000	384000
Cups	FLO ART. 18/20, 6 PS	91	2	182
For materials				386466
Transport and purchasing expenses (3-5%)				405789
Total by item				405789

Special equipment for scientific (experimental) work

This article includes all costs associated with the purchase of special equipment (devices, instrumentation, stands, devices and mechanisms) necessary for carrying out work on a specific topic. The cost of special equipment is determined according to the current price lists, and in some cases at the contract price (table 21).

Table 21 – Calculating costs by item «Special equipment for scientific work»

Name of the equipment	Number of equipment units	The price of the equipment, M. rub.	Total cost of equipment, M. rub.
Philips BrightView	1	27M. rub.	27M. rub.

The cost of equipment used in the implementation of a specific scientific project and available in this scientific and technical organization is taken into account in the form of depreciation charges:

$$C = 27M.rub.$$

$$A = \frac{100\%}{11} = 9{,}09\% \ \ per \ \ year$$

$$\sum A = \frac{27 \cdot 9{,}09}{100} = 2{,}45M.rub.per \ \ year$$

$$A_m = \frac{2{,}45}{12} = 204545rub.per \ \ month$$

$$A_{m.j} = 204545 \cdot 5 = 1022725 \ \ rub$$

where A – amortization rate, %;

∑A – the sum of amortization, rub. per year;

A_m – the sum of amortization, rub per month;

$A_{m.j}$ – the sum of amortization for the period of scientific research work , rub.

Basic salary

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

The item includes the basic salary of employees directly involved in the project (including bonuses, surcharges) and additional wages:

$$C_s = S_{basic} + S_{add}$$

where:

S_{basic} – basic salary;

S_{add} – additional salary.

The basic salary (S_{basic}) of the head (laboratory assistant, engineer) from the enterprise (if there is a head from the enterprise) is calculated by the following formula:

$$S_{basic} = S_{av} \cdot \mathrm{T}_w$$

where:

S_{basic}– basic salary per employee;

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

S_{av}– the average daily salary of an employee, rub.

The average daily salary is calculated by the formula:

$$S_{av} = \frac{S_m \cdot \mathrm{M}}{F_v}$$

where:

S_m – monthly salary of an employee, rub;

M – the number of work months without vacation for a year:

–at holiday in 24 working days. M =11,2 months, 5 days per week;

–at holidaye in 48 working days, M=10,4 months, 6 days per week;

F_v– valid annual Fund of working hours of scientific and technical personnel, working days (table 22).

Table 22 – Working time balance for working group of the project

Parameters	**Working group of the project**
Calendar number of days	365
The number of non-working days -weekend -holidays	 104 14
Loss of working time -vacation -absences due to illness	 53
Valid annual working time (F_v)	195

Monthly salary of an employee:

$$S_m = S_b \cdot (k_{pr} + k_b) \cdot k_d$$

where:

S_b – base salary, rub.;

k_{pr} –premium coefficient;

k_b – bonus coefficient;

k_d – district coefficient, equals 1,3 (for Tomsk).

Calculation for salaries are on table. 23

Table 23 – Calculation of salaries

Executors	S_b**, rub**	k_{pr}	k_b	k_d	S_m**,rub**	S_{av}**, rub.**	T_w**, working days.**	S_{basic}**, rub.**
Supervisor	50000	0,3	1,28	1,3	102700	5477	246	1347342
Head of Division	30000				61620	3286	345	1133670
Radiologist Doctor	20000				41080	2191	101	221291
Medical physicist	17890				36746	1960	448	878080

Additional salary of research and production personnel

This article includes the amount of payments stipulated by the legislation on labor, for example, payment of regular and additional holidays; payment of time associated with the performance of state and public duties; remuneration of service, etc. (on average - 12% of the amount of the basic salary).

Additional salary is calculated on the basis of 10-15% of the basic salary, workers directly involved in the implementation of the topic

$$S_{add} = k_{add} \cdot S_{basic}$$

where:

S_{add} – additional salary, rub.;

k_{add}– additional salary coefficient;

S_{basic} – basic salary, rub.

There are calculations for salaries in table 24.

Table 24 – Salary calculation

Salary	**Supervisor**	**Head of Division**	**Radiologist doctor**	**Medical physicist**
Basic salary	1347342	1133670	221291	878080

Continuation of table 24

Additional salary	202101	170051	33194	131712
Salary of maker	1549443	1303721	254485	1 009792
Total C_S	4117441			

Deductions for social needs.

This item includes deductions to extra-budgetary funds (table 25)

$$C_{ex} = k_{ex} \cdot (S_{basic} + S_{add}) = k_{ex} \cdot C_s$$

where k_{ex} – coefficient of deductions for payment to extra-budgetary funds (pension fund, compulsory medical insurance fund, etc.), equal 0,3.

Table 25 – Deductions for social needs

Name	**Sum**
Salary of maker of a supervisor, rub.	1549443
Coefficient of deductions	0,3
Sum of the supervisor's deductions, rub.	464833
Sum of the head of division's deductions, rub.	391116
Sum of the radiologist doctor's deductions, rub.	76346
Sum of the medical physicist's deductions, rub.	302937
Total	1235232

Overhead costs

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

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

Overhead is calculated according to the formula:

$$C = T_{el} \cdot P \cdot t_{eq}$$

where:

T_{el} –tariff for electricity (5,8 rub per 1 kW*h);

P – equipment capacity kW;

t_{eq} – equipment usage time, h.

Electricity costs were 139200 rub.

Table 26 – Electricity costs

Name	**Measure unit**	**Number of days**	**Working hours per day for equipment, hour**	**Price per unit, rub.**	**Electricity costs, rub.**
Electricity	kW*h	240	10	5,8	139200
Total:					139200

4.6 Project risk register

The identified risks of the project include possible uncertain events that may occur in the project and cause consequences that will entail undesirable effects. All information is in table 27.

Table 27 – Risk register

№	**Risk**	**Potential impact**	**Probability of occurrence (1 - 5)**	**Influence (1 - 5)**	**Level of risk**	**Ways to mitigate risk**	**Condition of occurrence**
1	Failure of gamma camera	Suspension of the radioisotope diagnostics	3	5	High	Regular maintenance and quality control	Absence of quality control and maintenance

Continuation of table 27

2	A failure in the supply of the RP generator	Suspension of the radioisotope diagnostics	2	5	High	Absent	Failure of the nuclear reactor; absence of fuel for the aircraft; termination of the license for the production of generators

Chapter 5. Social responsibility

5.1 Introduction

This section discusses issues related to safety in the workplace, its rules of operation in the event of possible dangerous situations.

In the final qualifying work, the task was to develop renal scintigraphy criteria for affected kidneys using radionuclide technology (SPECT)in patients with diabetic nephropathy with various types of diabetes mellitus. To perform this work, a diagnostic device of the SPECT was required, which is currently in the department of radionuclide diagnostics of the Federal State Budgetary Educational Institution of Higher professional education "Siberian State Medical University" of the Ministry of Health of the Russian Federation. And the main part of the work was on processing the received images and data on a PC.

This section will cover dangerous and harmful factors that may arise during research, legal and organizational issues, as well as emergency measures.

5.2 Legal and organizational items in providing safety

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

Occupational safety is a system of legislative, socio-economic, organizational, technological, hygienic and therapeutic and prophylactic measures and tools that ensure the safety, preservation of health and human performance in the work process [69].

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

- to have a workplace that meets Occupational safety requirements;

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

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

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

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

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

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

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

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

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

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

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

The workplace when working with a PC should be at least 6 square meters. The legroom should correspond to the following parameters: the legroom height is at least 600 mm, the seat distance to the lower edge of the working surface is at least 150 mm, and the seat height is 420 mm. It is worth noting that the height of the table should depend on the growth of the operator.

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

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

5.4 Occupational safety

A dangerous factor or industrial hazard is a factor whose impact under certain conditions leads to trauma or other sudden, severe deterioration of health of the worker [69].

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

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

The object of the study is "diagnostics of kidneys by radionuclide diagnostics in the SPECT devices". Therefore, the object of research of dangerous and harmful factors has, during the work, you need to observe safety regulations. In addition, you need to do a lot of work on processing the received images on a PC.

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

The working conditions in the workplace are characterized by the presence of hazardous and harmful factors, which are classified by groups of elements: physical, chemical, biological, psychophysiological. The main elements of the production process that form dangerous and harmful factors are presented in Table 28.

Table 28 – Possible hazardous and harmful factors

Factors (GOST 12.0.003-2015)	Work stages			Legal documents
	Development	Manufacture	Exploitation	
1. Deviation of microclimate indicators	+	+	+	Sanitary rules 2.2.2 / 2.4.1340–03.

Continuation of table 28

2. Excessive noise		+	+	Sanitary and epidemiological rules and regulations "Hygienic requirements for personal electronic computers and work organization." Sanitary rules 2.2.1 / 2.1.1.1278–03. Hygienic requirements for natural, artificial and combined lighting of residential and public buildings. Sanitary rules 2.2.4 / 2.1.8.562–96. Noise at workplaces, in premises of residential, public buildings and in the construction area. Sanitary rules 2.2.4.548–96. Hygienic requirements for the microclimate
3.Increased level of electromagnetic radiation	+	+	+	
4.Insufficient illumination of the working area		+	+	

Continuation of table 28

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

The following factors effect on person working on a computer:

- physical:
    - temperature and humidity;
    - noise;
    - static electricity;
    - electromagnetic field of low purity;
    - illumination;
    - presence of radiation;
- psychophysiological:

- psychophysiological dangerous and harmful factors are divided into:
  - physical overload (static, dynamic)
  - mental stress (mental overstrain, monotony of work, emotional overload).

Deviation of microclimate indicators

The air of the working area (microclimate) is determined by the following parameters: temperature, relative humidity, air speed. The optimum and permissible values of the microclimate characteristics are established in accordance with [**70**] and are given in Table 29.

To create optimal weather conditions used an air conditioner that maintains optimal microclimate parameters automatically, regardless of changing circumstances. In the cold season, heating is used to maintain the optimal air temperature in the room (table 29).

Table 29 – Optimal and permissible parameters of the microclimate

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

Excessive noise

Noise and vibration worsen working conditions, have a harmful effect on the human body, namely, the organs of hearing and the whole body through the central nervous system. It results in weakened attention, deteriorated memory, decreased response, and increased number of errors in work. Noise can be generated by operating equipment, air conditioning units, daylight illuminating devices, as well as

spread from the outside. When working on a PC, the noise level in the workplace should not exceed 50 dB.

Increased level of electromagnetic radiation

The screen and system blocks produce electromagnetic radiation. Its main part comes from the system unit and the video cable. According to [**70**], the intensity of the electromagnetic field at a distance of 50 cm around the screen along the electrical component should be no more than:

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

The magnetic flux density should be no more than:

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

Abnormally high voltage value in the circuit

Depending on the conditions in the room, the risk of electric shock to a person increases or decreases. Do not operate the electronic device in conditions of high humidity (relative air humidity exceeds 75% for a long time), high temperature (more than 35 ° C), the presence of conductive dust, conductive floors and the possibility of simultaneous contact with metal components connected to the ground and the metal casing of electrical equipment.

The computer operator works with electrical devices: a computer (display, system unit, etc.) and peripheral devices.

There is a risk of electric shock in the following cases:

− with direct with current-carrying parts during computer 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 or walls that are energized;

− in case of short-circuit in high-voltage units: power supply unit and display scanner unit.

Table 30 – Upper limits for values of contact current and voltage

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

Insufficient illumination of the working area

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

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

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

Increased levels of ionizing radiation

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

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

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

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

Table 31– The basic dose limits

Quantity	Dose limits	
	Personnel (group A)	Population
Effective dose	20 mSv per year in average during 5 years, but not higher than 50 mSv per year	1 mSv per year in average during 5 years, but not higher than 5 mSv per year
Equivalent dose per year in eye's lens	150 mSv	15 mSv
Equivalent dose per year in skin	500 mSv	50 mSv
Equivalent dose per year in hands and feet	500 mSv	50 mSv

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

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

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

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

Deviation of microclimate indicators

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

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

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

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

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

Excessive noise

In research audiences, there are various kinds of noises that are generated by both internal and external noise sources. The internal sources of noise are working

equipment, personal computer, printer, ventilation system, as well as computer equipment of other engineers in the audience. If the maximum permissible conditions are exceeded, it is sufficient to use sound-absorbing materials in the room (sound-absorbing wall and ceiling cladding, window curtains). To reduce the noise penetrating outside the premises, install seals around the perimeter of the doors and windows.

Increased level of electromagnetic radiation

There are the following ways to protect against EMF:

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

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

When working with a computer, the ionizing radiation source is a display. Under the influence of ionizing radiation in the body, there may be a violation of normal blood coagulability, an increase in the fragility of blood vessels, a decrease in immunity, etc. The dose of irradiation at a distance of 20 cm to the display is 50 μrem / hr. According to the norms [70], the design of the computer should provide the power of the exposure dose of x-rays at any point at a distance of 0.05 m from the screen no more than 100 μR / h.

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

Increased levels of ionizing radiation

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

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

The radiation control is control of:

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

The main controlled parameters are:

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

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

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

- characteristics of radioactive contamination of the environment;

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

Abnormally high voltage value in the circuit

The mechanical action of current on the body is the cause of electrical injuries. Typical types of electric injuries are burns, electric signs, skin metallization, tissue tears, dislocations of joints and bone fractures.

The following protective equipment can be used as measures to ensure the safety of working with electrical equipment:

- disconnection of voltage from live parts, on which or near to which work will be carried out, and taking measures to ensure the impossibility of applying voltage to the workplace;
- posting of posters indicating the place of work;
- electrical grounding of the housings of all installations through a neutral wire;
- coating of metal surfaces of tools with reliable insulation;
- inaccessibility of current-carrying parts of equipment (the conclusion in the case of electroporation elements, the conclusion in the body of current-carrying parts) [71].

Insufficient illumination of the working area

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

Also, as a means of protection to minimize the impact of the factor, local lighting should be installed due to insufficient lighting, window openings should be equipped with adjustable devices such as blinds, curtains, external visors, etc.

5.5 Ecological safety

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

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

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

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

5.5.2 Analysis of the environmental impact of the research process

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

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

metals and other materials; melting; refining and processing of metals. Thus, there is an effective disposal of computer devices.

5.5.3 Justification of environmental protection measures

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

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

5.6 Safety in emergency

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

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

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

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

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

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

Organizational measures provide for correct operation of equipment, proper maintenance of buildings and territories, fire instruction for workers and employees, training of production personnel for fire safety rules, issuing instructions, posters, and the existence of an evacuation plan [72].

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

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

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

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

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

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

Conclusion

This Master's thesis is the first to investigate the possibilities of the method of dynamic renal scintigraphy in determining the nature of kidney disarranges in patients with diabetic nephropathy with diabetes mellitus

To develop scintigraphy criteria for evaluating the functional state of the kidneys based on radionuclide technology (SPECT) in patients with diabetic nephropathy with diabetes mellitus, the confidential relationship between the parameters of the device and clinical and laboratory data was studied and differences in patients were evaluated.

Solving a complex set of problems in the diagnosis of diabetic nephropathy in diabetes mellitus should reduce the socio-economic burden on the population of various countries and significantly improve the quality of life of patients.

Inferences

1. Dynamic renal scintigraphy reflects the main pathological changes in the kidneys in patients with diabetes mellitus.

2. At the same time, the doctor should pay attention to the values of the GFR indicator in terms of reliability, in contrast to T_{max} and $T_{1/2}$, which did not show themselves as reliable indicators in all comparisons.

3. Static significant inversely correlated relationship between the total glomerular filtration rate and separate for the left and right kidneys with indicators of clinical and laboratory data reflects the development of chronic renal failure in patients with diabetes mellitus.

4. Decreasing glomerular filtration rate in patients of both groups is due to the reaction of the pelvicalyceal system, which compensates for the violation of protein metabolism.

5. Compensatory capabilities in patients with type 2 diabetes in combination with type 1 diabetes pathology are more pronounced in hyperfiltration, and may even be absent in some patients.

6. Dynamic renal scintigraphy can be used in the algorithm of radiation diagnostics of kidney condition in patients with type 1 and 2 diabetes

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