

Annotation

Tsoy Radmila Timsonovna

The dissertation thesis

«The value of brain absorptive capacity of gamma quanta of natural background radiation for evaluating human cognitive functions»

submitted for the degree of Doctor of Philosophy (PhD) by specialty

6D110100 – «Medicine»

Relevance of the research topic

In recent years, with the deterioration of the environmental situation in the world, environmental research has begun to be actively carried out, having medical and social significance. Warming, an increase in the intensity of solar radiation, a short increase in the average daily temperature, combined with an increased level of atmospheric air pollution with chemicals (nitrogen dioxide and sulfur) cause significant damage to public health in the form of increased mortality, hospitalization due to exacerbation of diseases of the cardiovascular system, respiratory organs, etc. Changing climate has an impact on the environmental, economic and social aspects of the country (Iskakova A.K., 2015).

Sensitive groups of the population: elderly people, children as well as people suffering from chronic diseases are mostly affected by such influences. In the epidemiological study conducted in Almaty, a group of scientists identified a tendency of the increasing incidence of malignant tumors under the influence of a multifactorial complex of environmental conditions. The average annual growth of oncological diseases in Almaty is 0.36%, this suggests the possible influence of small doses of natural background radiation (NBR) on the human body, since it is known that even low radiation exposures increase the risk of tumors (Kamhen V. B., Turbekova M.N., 2015).

The issue of the interaction of natural background radiation with the human body is still being studied. On the example of large megacities, work is underway on a comprehensive assessment of factors affecting human health and quality of life (Sobolev A.I. et al. 2005, Petrova T. B., 2010; Markelov D. A. et al., 2011; Oleinikov Yu.V., 2013; Omarova M.N. et al., 2015; Turuspekova S.T. et al., 2017; Karaev A.V., Inyukina T.A., 2018). According to the majority of the researchers, one of the important risk factor for the developing of mild cognitive impairment (MCI) is the environmental problem. The small doses of natural background radiation can be manifested primarily by cognitive impairment, and not other disorders (Kimeldorf DJ, Hunt EL, 1965; Mickley GA, 1987, Loganovsky K, 2009; Lowe XR, Bhattacharya S, Marchetti F, Wyrobek AJ, 2009; Manton KG, Volovik S, Kulminski A, 2004; Stefan J. Kempf, Omid Azimzadeh , Michael J. Atkinson & SoileTapio, 2012). Cognitive functions determine, first, the social and economic value of a person. Without cognitive support, human activity becomes fundamentally impossible. For the preservation and extension of adequate and active thinking, humankind spends huge funds and efforts.

Thus, the need to clarify the possible impact of natural background radiation on the cognitive functions of the population, together with determining the

prevalence of MCI and identifying risk factors for the development of MCI, is of particular relevance.

Mild cognitive impairment (MCI) was originally described as a single syndrome in which the individual appears: (a) subjective complaints on memory, confirmed by a reliable informant, (b) objective cognitive deficit when performing neuropsychological tests, (c) without impaired everyday life ; and, of course, (d) the absence of dementia.

According to Petersen, 2004; Winbland, 2004, World Alzheimer Report (World Alzheimer Report, 2016) 47 million people have dementia worldwide, a figure comparable to the population of Spain. By 2050, 131 million older people will suffer from dementia, 60% of people with dementia will live in Asia (World Alzheimer Report, 2016).

Kazakhstan occupies one of the leading place in terms of the diversity of climatic and geographical zones, in terms of the availability of natural resources and their extraction, the territory of Kazakhstan was Semipalatinsk nuclear test site, where nuclear tests were carried out for a long time; Baikonur is located - the place of launch of rockets (the influence of rocket and space activities). These factors played a large role in the current environmentally unfavorable environment and the possible negative impact of ionizing radiation of NBR on the human body.

Aging of the population and the associated cognitive impairment and dementia are, first, economic and medical - social losses affecting the development of society and the state.

Thus, due to the deterioration of the ecological situation of the environment in megacities (Ramachandran, TV, 2011; Brodskaya, 1998; Saldan, I.P. et al., 2017; Markova, O.I. et al., 2018), including an increase in the intensity of the natural background radiation, and rapid increase in the burden of noncommunicable diseases, mental disorders, there was a need to clarify new mechanisms for the development of cognitive impairment, to search for potential biomarkers for the early diagnosis of mild cognitive impairment at the stage of primary health care.

The purpose of the study is to study the significance of the absorption of natural background radiation for assessing cognitive functions.

Research objectives

1. To study the features of the absorption of gamma quanta of natural background radiation (NBR) by the brain in people 60 years of age and older;
2. To study the features of the influence of gamma quanta of NBR on the functional ability of the brain in people 60 years of age and older;
3. To assess the prevalence of mild cognitive impairment (MCI) and find an association with significant risk factors that cause MCI in people 60 years of age and older in Almaty City;
4. To improve the algorithm for the preventive diagnostics of MCI in people 60 years of age and older;

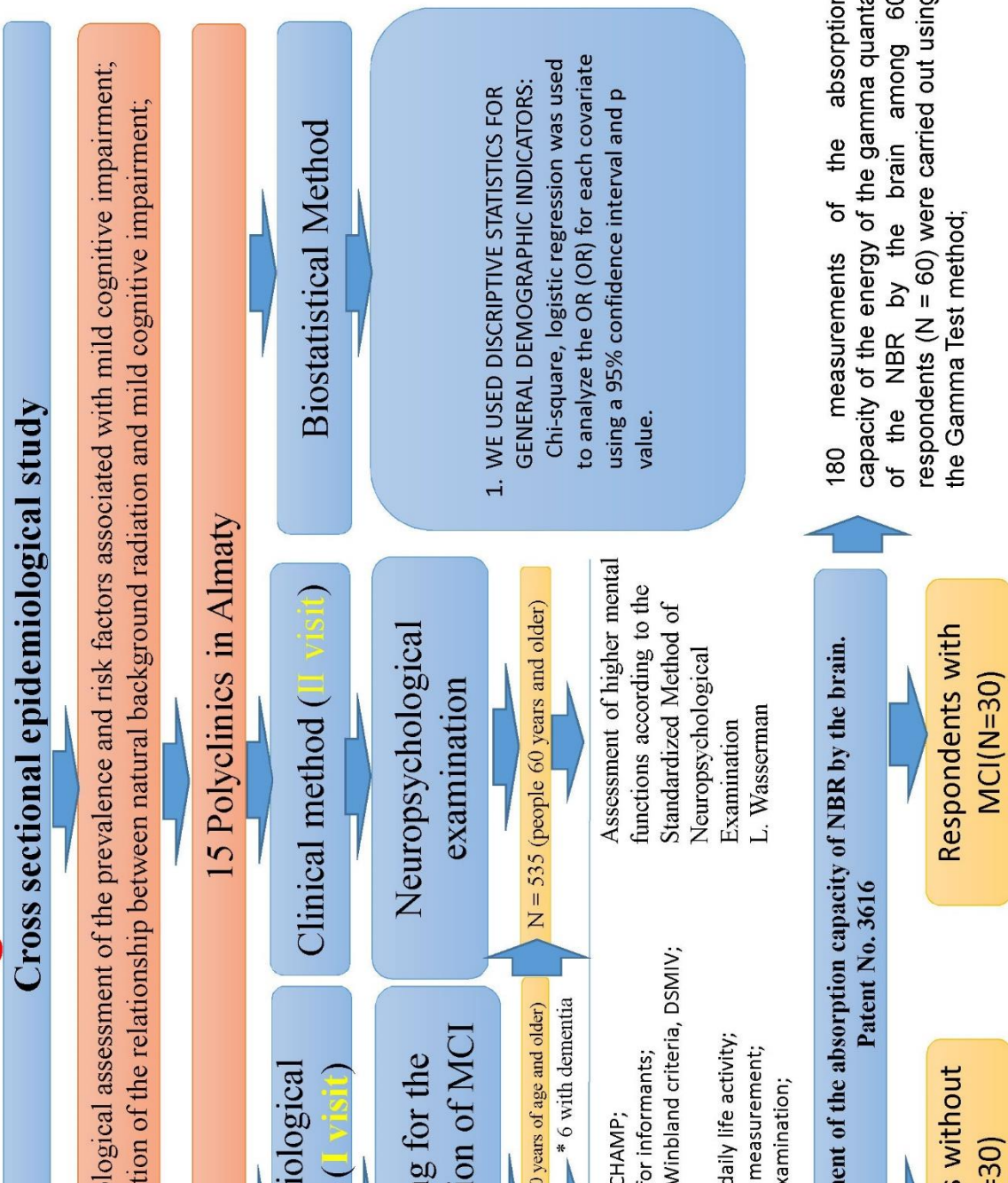
Scientific novelty

1. For the first time, the effect of the energy of gamma rays on the brain is shown and the functional ability of the brain is analyzed taking into account the effects of natural background radiation.

2. The first proposed method ("Gamma Test") for measuring the absorption capacity of brain tissue.
3. Cognitive impairments have been identified taking into account the influence of gamma-ray energy, and among them the modal-specific mnemonic and neurodynamic disorders are most clearly distinguished.
4. The prevalence of mild cognitive impairment in Almaty was established;

Design of the research

LEC, protocol №421 of 22.02.2017



The practical significance:

1. A useful model has been developed for measuring the absorption capacity of brain tissue of ionizing radiation of gamma quanta of natural background radiation (patent application filed with registration No. 2019 / 0851.1 of 11/20/2019), which can be used for further research, objectification of functional ability brain, taking into account radiation exposure, to assess the prediction of cognitive deficit, to obtain additional objective diagnostic criteria.
2. Knowing the most significant risk factors for MCI will allow to timely develop a program of corrective measures and prevent the occurrence and exacerbation of a cognitive deficit;
3. Identifying the prevalence of mild cognitive impairment in the Almaty City among the elderly population will allow to predict the level of disability and optimize the algorithms for the provision of qualified assistance;
4. The algorithm for diagnosing mild cognitive impairment (MCI) at the PHC stage has been improved to prevent cognitive impairment and dementia (methodological recommendations were considered and approved at a meeting of the Academic Council of NKSC KazNMU, meeting minutes No. 4 dated February 12, 2019). The research results have been introduced into the office of a general practitioner, a general practitioner physician in city polyclinics No 3,17,27,29,19 and in a city clinical hospital No. 1 in Almaty.

The main thesis of the dissertation

1. With age, there is a tendency of delay increase of the energy of gamma rays of NBR. A statistically significant association was found between the level of cognitive abilities and the delay increase of the energy of gamma quanta of natural background radiation (NBR) (95% CI 0.086; 0.005) ($p \leq 0.01$ *);
2. The relationship between the reduced score in the following samples was established: orientation in time and in place ($r = 0.49$; 95% CI 0.094; 0.0096); visual - spatial ($r = 0.38$; 95% ID 0.093; 0.09); Test "Drawing watch" ($r = 0.36$; 95% CI 0.09; 0.005); a short-term memory subtest ($r = 0.37$; 95% CI 0.07; 0.009) at $p \leq 0.01$ * and increased absorption of NBR in respondents with MCI;
3. The cognitive disorders indicates the dominance of the following syndromes: the lesion of the temporoparietal occipital cortex area and the damage of the median nonspecific brain structures among respondents with MCI;
4. The use of standardized methods of MCI and confirmation by clinical examination can improve the diagnosis of MCI at the stage of primary health care in order to prevent the development of dementia;

Conclusions

1. An association was established between the low value of cognitive function assessment and the delay increase of the energy of gamma quanta of NBR by the brain among respondents with MCI (95% CI (0.08; 0.09), $p \leq 0.05$);
2. Dominant syndromes of the lesion of the temporoparietal occipital cortex (45,10%) and the syndrome of damage of the median nonspecific brain structures (39,15%) were found among respondents with MCI;

3. It has been established that with age, there is a tendency of delay increase of the energy of gamma rays of the NBR ($p \leq 0.05$) (95% CI 0.08; 0.099);

4. The prevalence of mild cognitive impairment (MCI) among old people in Almaty City is constituted 30,21% (OR 1.65 (95% ДИ 0.98, 2.79)); age, low level of education correlated with higher risk of developing MCI; the proposed algorithm is able to improve the diagnostics of cognitive impairment at the PHC stage in order to prevent the development of dementia;

Personal contribution of the author

The author spent 3 years diagnosing, directly participating in identifying, prescribing treatment, and transferring patients with mild cognitive impairment to local to clinics.

As part of the dissertation, the author carried out clinical (examination of patients, history taking, screening, assessment of higher mental functions, assessment of neurological status) and instrumental (measuring the absorption capacity of energy of gamma quanta of NBR by the brain) research methods with interpretation of data, treatment and recommendations to patients.

A literature search was carried out for a given problem, a useful gamma-test model was developed, a database was collected, primary processing of the material, statistical analysis, interpretation of the results obtained with the development of an algorithm for diagnosing MCI at the PHC stage.

Implementation in practical healthcare and training

The developed algorithm for the early diagnosis of MCI at the PHC stage is based on the results of the study and is intended to be introduced into clinical practice by physicians, general practitioners at the PHC stage.

Approbation of the thesis

The main results of the dissertation were reported at the following conferences:

XIII International scientific-practical conference “Ecology. Radiation. Health”, named after Academician B. Atchabarov”, Semey, Kazakhstan, 2017 (oral report);

II International Conference of the Caspian littoral states “Actual issues of modern medicine” Astrakhan, Russia, 2017 (oral report);

“XIX International Congress “Health and Education in the XXI Century ” “Problems of integrating healthcare into the world system of education, economics and the information space ”(Moscow, Russia, 2017) - awarded with a diploma (oral report);

International Neurology Summit on Brain Disorders, Sydney, Australia. The International Summit on Neurology and Brain Disorders (Sydney, Australia, 2017) (oral report);

The 12th World Congress on Controversies in Neurology (CONy), Warsaw, Poland, 2018 (poster report);

XV International scientific and practical environmental conference (Belgorod, Russia, 2018) (oral report);

International scientific-practical conference "Innovations in the field of

medical science and education" dedicated to the 25th anniversary of the International University of Kyrgyzstan, the 15th anniversary of the International Higher School of Medicine and the 70th anniversary of the first rector of the Higher School of Medicine, Doctor of Medical Sciences, Professor Chyngyshpaev Shamil Mukashevich (Bishkek , Kyrgyzstan, 2018) - was awarded a diploma of the II degree (oral report);

XIII scientific and practical conference of young scientists and students with international participation dedicated to the "Year of the development of tourism and folk crafts", April 27, 2018, Dushanbe, Tajikistan (oral report);

AD/PD™2019 The 14th International Conference on Alzheimer's & Parkinson's Diseases (Lisbon, Portugal, 2019) (Poster report);

International scientific and practical conference "Akanov readings: the role of primary health care in achieving universal health care coverage" (Almaty, Kazakhstan, 2019) - was awarded a degree III diploma (oral report);

International scientific and practical conference of students and young scientists "Apsatar readings: The future of medicine. Challenges and decisions"(Almaty, Kazakhstan, 2019) (oral report);

The anniversary scientific-practical conference with international participation "Actual problems of clinical, experimental neurology, neurosurgery, neurophysiology" dedicated to the 85th anniversary of the Department of Nervous Diseases with a course of neurosurgery at JSC NMU (Almaty, Kazakhstan 2019) - was awarded a diploma of I degree (oral report).

Scientific and practical conference with international participation "Innovative technologies in the field of neurology and related specialties", 11/06/2019, Moscow, Russia;

XXIV World Congress of Neurology, Dubai, 2019, (Journal of the Neurological Sciences (IF1.97)), page 122

Publications on the topic of the dissertation

Based on the materials of the thesis, 22 works were published. Of these, 6 articles were in journals recommended by the Committee for Control in the Sphere of Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan and 1 article in the RSCI.

One publication in a journal indexed in the Scopus database and Web of science (Alzheimer disease and associated disorders. - 2019. (IF 2.44, category - Q1, percentile - 87%)),

One article in a peer-reviewed scientific and practical journal recommended by the Higher Attestation Commission of the Russian Federation, indexed in RSCI (Table 1). Thirteen abstracts are submitted to foreign international conferences (3 in English) (Table 2).

Methodological recommendations "Early diagnosis and prevention of mild cognitive impairment in the elderly" were published - reviewed and approved at a meeting of the Academic Council of NJSC NMU: No. 4 dated February 12, 2019 (Table 3).

The patent application for the invention "A method for determining brain

disorders by measuring the absorption of gamma quanta by the brain” has been filed. An application has been filed for a patent for the invention with registration No. 2019 / 0851.1 of 11/20/2019 (Table 4).

Table 1 – List of published articles based on the results of dissertation research

№	Article	Publisher, magazine (name, year, country, city) or copyright certificate number
1	An aging brain and natural background radiation: New mechanisms of interaction?	Clinical Gerontology. - 2017. - T. 23. - No. 9-10. - S. 66-68. Moscow, Russia ISSN 1607-2499 eISSN: 1607-2499
2	A modern view on the question of the effect of natural background radiation on human cognitive functions	Publisher "Health of Kazakhstan." The journal "Medicine". - 2018. - No. 2/188.- C.39 - 45. Almaty, Kazakhstan. ISSN-1728-452X
3	The effect of small doses of natural background radiation on the neuropsychological functions of a person in the conditions of the Almaty City	Vestnik of KazNMU. No. 2-2018. - S.172 - 174 Almaty, Kazakhstan. ISSN 2524 - 0684 (print) ISSN 2524 - 0692 (online)
4	The first results of a cross-sectional study of mild cognitive impairment and dementia of people 60 years and older, conducted on the basis of nine city polyclinics in Almaty	The journal "Neurosurgery and Neurology of Kazakhstan" No. 1 (50), 2018. P.17 - 21. Almaty, Kazakhstan. ISSN 1813-3908 (print) ISSN 2409-44-98 (online)
5	Current status of the prevalence of moderate cognitive impairment and dementia	The journal "Neurosurgery and Neurology of Kazakhstan" No. 1 (50), 2018. P.17 - 21. Almaty, Kazakhstan. ISSN 1813-3908 (print) ISSN 2409-44-98 (online)
6	The interaction of natural background radiation with human brain	Publishing house "Health of Kazakhstan". The journal "Medicine". - 2019. - No. 4/202. - C.25 - 32. Almaty, Kazakhstan. ISSN-1728-452 X (print) & ISSN 2518-1009 (online). Journal DOI 10.31082 / 1728 - 452X DOI 10.31082 / 1728 - 452X - 2019 - 202 - 4.
7	The results of the second stage of a	Vestnik of KazNMU. No. 3-2019. -

	cross-sectional study of moderate cognitive impairment and dementia of people 60 years and older, conducted on the basis of six city clinics in Almaty	S.334 - 335 Almaty, Kazakhstan. ISSN 2524 - 0684 (print) ISSN 2524 - 0692 (online)
8	Prevalence of mild cognitive impairment among older people in Kazakhstan and potential	Alzheimer disease and associated disorders. – April - June 2019. Volume 33, Number 2, page 136 - 141 ISSN:0893-0341 E-ISSN:1546-4156
9	The impact of the background radiation on the Health	“Proceedings of the NAS RK. Biological and Medical Science Series ”. ISSN 2518-1629 (Online), ISSN 2224-5308 (Print) Volume 3, Number 333 (2019), 5 – 10 https://doi.org/10.32014/2019.2519-1629.24

Table 2 – List of published abstracts based on the results of dissertation research

№	Title of thesis	Published in
1	The prevalence of mild cognitive impairment and dementia in Almaty.	Materials of the conference "XIX International Congress" Health and Education in the XXI Century "" Problems of integrating healthcare into the world system of education, the economy and the information space ". - 2017. - P.303 Moscow, Russia
2	Screening Results for Mild Cognitive Impairment and Dementia in Almaty	Materials of the conference “22nd Interregional Scientific and Practical Conference. ACTUAL QUESTIONS OF NEUROLOGY, dedicated to the 80th anniversary of the creation of the Department of Neurology, FSBEI HE NGMU of the Ministry of Health of Russia. " Scientific and practical peer-reviewed journal "Neurology of Siberia" - 2017. - No. 2 (2) 2017. C121. Novosibirsk, Russia.

3	The prevalence of moderate cognitive impairment and dementia in Almaty: A comparative analysis.	Materials of the conference "II International Conference of the Caspian littoral states" Actual issues of modern medicine ". - 2017. - P.181. Astrakhan, Russia. ISBN 978-5-4424-0277-3
4	Features of the influence of natural radiation background on cognitive functions.	Conference materials "VI International Scientific and Practical Conference "Actual issues of medicine." - 2017. - Conferenceabstractbook. S. 159. Baku, Azerbaijan.
5	The features absorption of gamma-quanta of natural background radiation under physiological aging of the central nervous system.	The International Summit on Neurology and Brain Disorders. – 2017. – Sydney, Australia.
6	Age-related features of the absorption of gamma-quanta of natural background radiation during physiological aging of the central nervous system	Materials of the conference "XIII International scientific-practical conference" Ecology. Radiation. Health "named after Academician B. Atchabarov." Semey, Kazakhstan. - 2017. - S.169 ISBN: 601-248-823-4
7	Preliminary results of screening of the mild cognitive impairment and dementia in Almaty	The 12th World Congress on Controversies in Neurology (CONy). 25 – 22 мапта, 2018. Warsaw, Poland. Abstract Journal - PolskiPrzeglądNeurologiczny, 2018, vol. 14, supplement A.p.102. (опубл. http://www.comtecmed.com/cony/2018/)
8	The results of the first cross-sectional study of the prevalence of mild cognitive impairment among people 60 years and older in Almaty: the main risk factors	XIII scientific and practical conference of young scientists and students with international participation dedicated to the “Year of the development of tourism and folk crafts”, April 27, 2018, 113 pages. Dushanbe, Tajikistan
9	The effect of small doses of natural background radiation on the neuropsychological functions of a person in the conditions of the city of Almaty	XV International Scientific and Practical Environmental Conference. October 8–12, 2018, Belgorod, Russia. Biological view in the structural and functional hierarchy of the Biosphere: a collection of materials of the XV International Scientific and Practical Environmental Conference. October 8-12, 2018 / open. for the release of A.V. Sacred. - Belgorod: Publishing House

		"Belgorod" NRU "BelSU", 2018. - 190 p. Page 87. ISBN 978-5-9571-2608-9 P.87
10	Prevalence of moderate cognitive impairment and possible risk factors among people 60 years of age and older	An International scientific and practical conference "Akanov readings: the role of PHC in achieving universal health coverage." April 25 - 26, 2019, Almaty, Kazakhstan, p247.
11	The interaction between natural ionizing radiation with human brain	International scientific and practical conference of students and young scientists "Apsatar readings: The future of medicine. Challenges and solutions." April 24, 2019, Almaty, Kazakhstan
12	Natural radiation background and cognitive functions: to the issues of interaction	Scientific and practical conference with international participation "Innovative technologies in the field of neurology and related specialties", 11/06/2019, Moscow, Russia
13	Preliminary results of cross – sectional research for moderate cognitive impairments among persons over 60 years in the Kazakh population	XXIV World Congress of Neurology, Dubai, 2019, (Journal of the Neurological Sciences (IF1.97)), page 122

Table 3. List of teaching aids on the topic of dissertation research

1	Early diagnostics and prevention of mild cognitive impairment among the elderly people	Guidelines // Almaty: National Medical University Joint Stock Company, 2019, p.40 UDC: 616.8 (075.8) BBK: 56.12ya73 ISBN 978-601-305-328-8
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Table 4. List of intellectual property

№	Name	By whom and when issued
1	An application has been filed - a patent for the invention "A method for determining brain disorders by measuring the absorption of gamma quanta by the brain"	Registration No. 2019 / 0851.1 dated 11/20/2019

Volume and structure of the dissertation

The dissertation is presented on 125 pages of typewritten text and consists of a list of abbreviations and notation, normative references, introduction, literature review, description of materials and methods, results of our own research,

conclusions, including conclusions, practical recommendations and a list of references. The work is illustrated by 21 figures, 11 tables, 20 applications. The bibliographic index includes 312 sources.