

Prevalence of COVID-19-associated pneumonia signs on chest computed tomography in cancer patients: the ARILUS study

Andrey A. Dyachenko^{1,✉}, Andrej M. Grjibovski^{1,2,3}, Maxim A. Bogdanov¹,
Dmitriy V. Bogdanov^{1,4}, Ekaterina A. Nazarova⁵, Anna A. Meldo¹, Valeria Yu. Chernina⁶,
Mikhail G. Belyaev⁶, Victor A. Gombolevsky^{6,7,8}, Mikhail Yu. Valkov^{1,4}

¹Northern State Medical University

51, Troitskiy Ave., Arkhangelsk, 163000, Russia

²North-Eastern Federal University

58, Belinsky str., Yakutsk, 677000, Russia

³Private University "REAVIZ"

8/2A, Kalinina str., Saint Petersburg, 198095, Russia

⁴Arkhangelsk Clinical Oncological Dispensary

145, bld. 1, Obvodny Ave., Arkhangelsk, 163045, Russia

⁵National Medical Research Center of Oncology

68, Leningradskaya str., St. Petersburg, 197758, Russia

⁶LLC "IRA Labs"

30, bld. 1, Bolshoy Boulevard, Moscow, 121205, Russia

⁷Artificial Intelligence Research Institute

32, bld. 1, Kutuzovskiy Ave., Moscow, 121170, Russia

⁸Sechenov First Moscow State Medical University (Sechenov University)

8/2, Trubetskaya str., Moscow, 119048, Russia

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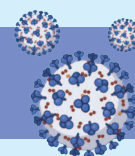
GRAPHICAL ABSTRACT



Prevalence of COVID-19-associated pneumonia signs on chest computed tomography in cancer patients: the ARILUS study

Summary

CT signs of COVID-19 pneumonia are detected in 48.4% of outpatient cancer patients and are associated with the localization of neoplasms in the lungs, head and neck, as well as with the presence of signs of pulmonary emphysema and coronary calcification.



Materials and methods

Time interval: from 01.04.2020 to 31.12.2021 (COVID-19 pandemic)



Outcomes

Factors associated with CT signs of COVID-19 pneumonia (aPR and 95%CI*)

Tumor Location		Emphysema		Coronary calcification	
Lungs	1.87 (1.40–2.49)	1.25 (1.09–1.45)		Agatston index:	
Head and neck	1.85 (1.32–2.58)			≥ 300	1.61 (1.36–1.90)
Upper GI tract	1.51 (1.12–2.04)			100–299	1.58 (1.33–1.87)
Breast	1.38 (1.00–1.90)			1–99	1.24 (1.05–1.47)
Reference group: tumors of female genital		Reference group: without emphysema		Reference group: Agatston index = 0	

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* adjusted prevalence ratio and 95% confidence intervals

Abstract

Aim. To study the prevalence of pneumonia features associated with 2019 coronavirus disease (COVID-19) in cancer patients based on chest computed tomography (CT) data using an artificial intelligence (AI) algorithm.

Materials and methods. A cross-sectional study was conducted as part of the ARILUS project. Using multitarget AI, CT images of 1148 patients examined at the Arkhangelsk Clinical Oncology Dispensary from 01.04.2020 to 31.12.2021 were analyzed. Patients were divided into groups: without signs of pneumonia ($n = 592$, 51.6%) and with signs of pneumonia ($n = 556$, 48.4%). In 95.3% of patients with pneumonia, the lesion volume was less than 25% (CT-1). Using multivariate Poisson regression, adjusted prevalence ratios (aPR) with 95% confidence intervals (CI) were calculated.

Results. For demographic characteristics such as gender, age, place of residence, no relationship with the presence of signs of COVID-19 pneumonia was established. Topography of neoplasm is associated with the presence of signs of COVID-19 pneumonia (reference group – cancers of the female genital organs): lung cancer – aPR 1.87; 95% CI: 1.40–2.49; head and neck cancers – aPR 1.85; 95% CI: 1.32–2.58; upper gastrointestinal tract – aPR 1.51; 95% CI: 1.12–2.04; breast cancer – aPR: 1.38; 95% CI: 1.00–1.90; $p < 0.01$. The presence of pulmonary emphysema is associated with signs of COVID-19 pneumonia: aPR 1.25; 95% CI: 1.09–1.45, $p = 0.002$. With an increase in the Agatston score (AS) reflecting coronary artery calcification (reference group absence of calcification), the association with the presence of signs of COVID-19 pneumonia increased – for AS 1–99: aPR 1.24; 95% CI: 1.05–1.47; AS 100–299: aPR 1.58; 95% CI: 1.33–1.87; AS 300 and above: aPR 1.61; 95% CI: 1.36–1.90; $p < 0.001$ for a linear trend.

Conclusion. Factors associated with the detection of COVID-19 pneumonia among cancer patients include the localization of neoplasms in the lungs, head and neck organs, upper gastrointestinal tract, breast, and as well as the presence of signs of emphysema and coronary calcification according to CT data.

Keywords: malignant neoplasms; pulmonary infiltration in COVID-19; artificial intelligence algorithm; population-based cancer registry

MeSH terms:

NEOPLASMS – COMPLICATIONS

COVID-19 – DIAGNOSTIC IMAGING

PNEUMONIA, VIRAL – DIAGNOSTIC IMAGING

ASSOCIATED DISEASES

THORAX – DIAGNOSTIC IMAGING

TOMOGRAPHY, X-RAY COMPUTED – METHODS

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CONTACT INFORMATION:

Andrey A. Dyachenko, Cand. of Sci. (Medicine), Associate Professor, Department of Radiation Diagnostics, Radiation Therapy and Oncology, Northern State Medical University.

Address: 51, Troitskiy Ave., Arkhangelsk, 163000, Russia

E-mail: andreydyachenko3@gmail.com

Ethics statements. The study was conducted in accordance with the permission of the Local Bioethics Committee of the Northern State Medical University, No 07/10-238, 2023.

Data availability. The data that support the findings of this study are available from the corresponding authors on reasonable request. Data and statistical methods used in the article were examined by a professional biostatistician on the Sechenov Medical Journal editorial staff.

Conflict of interests. Valeria Yu. Chernina – Head of the Clinical Evaluation Department of the LLC “IRA Labs”, Mikhail Yu. Belyaev – General Director of the LLC “IRA Labs”, Viktor A. Gombolevisky – Advisor of the LLC “IRA Labs”.

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Распространенность признаков пневмонии, ассоциированной с инфекцией COVID-19, на компьютерных томограммах органов грудной клетки у онкологических больных: исследование АРИЛИС

А.А. Дяченко^{1,✉}, А.М. Гржибовский^{1,2,3}, М.А. Богданов¹, Д.В. Богданов^{1,4}, Е.А. Назарова⁵,
А.А. Мелдо¹, В.Ю. Чернина⁶, М.Г. Беляев⁶, В.А. Гомболевский^{6,7,8}, М.Ю. Вальков^{1,4}

¹ФГБОУ ВО «Северный государственный медицинский университет»

Министерства здравоохранения Российской Федерации

пр-т Троицкий, д. 51, г. Архангельск, 163000, Россия

²ФГАОУ ВО «Северо-Восточный федеральный университет им. М.К. Аммосова»

ул. Белинского, д. 58, г. Якутск, 677000, Россия

³ЧУОО ВО «Университет «РЕАВИЗ»»

ул. Калинина, д. 8, корп. 2А, г. Санкт-Петербург, 198095, Россия

⁴ГБУЗ АО «Архангельский клинический онкологический диспансер»

пр-т Обводный, д. 145, корп. 1, г. Архангельск, 163045, Россия

⁵ФГБУ «Национальный медицинский исследовательский центр онкологии имени Н.Н. Петрова»

Министерства здравоохранения Российской Федерации

ул. Ленинградская, д. 68, пос. Песочный, г. Санкт-Петербург, 197758, Россия

⁶ООО «АЙРА Лабс»

бульвар Большой, д. 30, стр. 1, г. Москва, 121205, Россия

⁷АНО «Институт искусственного интеллекта»

пр-т Кутузовский, д. 32, корп. 1, г. Москва, 121170, Россия

⁸ФГАОУ ВО «Первый Московский государственный медицинский университет имени И.М. Сеченова»

Министерства здравоохранения Российской Федерации (Сеченовский Университет)

ул. Трубецкая, д. 8, стр. 2, г. Москва, 119048, Россия

Аннотация

Цель. Изучить распространенность признаков пневмонии, ассоциированной с коронавирусной инфекцией 2019 года (Coronavirus Disease 2019, COVID-19), у онкологических пациентов по данным компьютерной томографии (КТ) органов грудной клетки с помощью алгоритма искусственного интеллекта (ИИ).

Материалы и методы. Проведено поперечное исследование в рамках проекта АРИЛИС. С помощью мультитаргетного ИИ проанализированы изображения КТ 1148 пациентов, проходивших обследование в Архангельском клиническом онкологическом диспансере за период с 01.04.2020 по 31.12.2021. Пациенты разделены на группы: без признаков пневмонии ($n = 592$, 51,6%) и с признаками пневмонии ($n = 556$, 48,4%). У 95,3% пациентов с пневмонией объем поражения составил менее 25% (КТ-1). С помощью многомерной регрессии Пуассона рассчитывали скорректированные отношения распространенностей (сОР, adjusted prevalence ratio) с 95% доверительными интервалами (ДИ).

Результаты. Для демографических признаков: пол, возраст, место жительства связи с наличием признаков пневмонии COVID-19 не установлено. Локализация опухоли ассоциирована с наличием признаков пневмонии COVID-19 (референтная группа – опухоли женских половых органов): рак легкого – сОР 1,87; 95% ДИ: 1,40–2,49; опухоли головы и шеи – сОР 1,85; 95% ДИ: 1,32–2,58; верхние отделы желудочно-кишечного тракта – сОР 1,51; 95% ДИ: 1,12–2,04; рак молочной железы – сОР 1,38; 95% ДИ: 1,00–1,90; $p < 0,01$. Наличие эмфиземы легких ассоциировано с признаками пневмонии COVID-19: сОР 1,25; 95% ДИ: 1,09–1,45, $p = 0,002$. С увеличением индекса Агатстона (Agatston score, AS) кальциноза коронарных артерий (референтная группа без кальциноза) увеличивалась ассоциация с наличием признаков пневмонии COVID-19 – для AS 1–99: сОР

1,24; 95% ДИ: 1,05–1,47; AS 100–299: cOP 1,58; 95% ДИ: 1,33–1,87; AS 300 и выше: cOP 1,61; 95% ДИ: 1,36–1,90; $p < 0,001$ для линейного тренда.

Заключение. Факторами, ассоциированными с выявлением пневмонии COVID-19, являются локализация новообразований в легком, органах головы и шеи, верхних отделах желудочно-кишечного тракта, молочной железе, а также наличие признаков эмфиземы и коронарного кальциноза по данным КТ.

Ключевые слова: злокачественные новообразования; легочная инфильтрация при COVID-19; алгоритм искусственного интеллекта; популяционный регистр рака

Рубрики MeSH:

НОВООБРАЗОВАНИЯ – ОСЛОЖНЕНИЯ

COVID-19 – ДИАГНОСТИЧЕСКОЕ ИЗОБРАЖЕНИЕ

ПНЕВМОНИЯ ВИРУСНАЯ – ДИАГНОСТИЧЕСКОЕ ИЗОБРАЖЕНИЕ

БОЛЕЗНИ СОПУТСТВУЮЩИЕ

ГРУДНАЯ КЛЕТКА – ДИАГНОСТИЧЕСКОЕ ИЗОБРАЖЕНИЕ

ТОМОГРАФИЯ РЕНТГЕНОВСКАЯ КОМПЬЮТЕРНАЯ – МЕТОДЫ

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КОНТАКТНАЯ ИНФОРМАЦИЯ:

Дяченко Андрей Андреевич, кандидат медицинских наук, доцент кафедры лучевой диагностики, лучевой терапии и онкологии ФГБОУ ВО «Северный государственный медицинский университет» Министерства здравоохранения Российской Федерации.

Адрес: пр-т Троицкий, д. 51, г. Архангельск, 163000, Россия

E-mail: andreydyachenko3@gmail.com

Соответствие принципам этики. Исследование проведено в соответствии с разрешением Локального этического комитета Северного государственного медицинского университета (№ 07/10-238, 2023 г.).

Доступ к данным исследования. Данные, подтверждающие выводы этого исследования, можно получить у авторов по обоснованному запросу. Данные и статистические методы, представленные в статье, прошли статистическое рецензирование редактором журнала – сертифицированным специалистом по биостатистике.

Конфликт интересов. Чернина В.Ю. – руководитель отдела клинической оценки компании ООО «АЙРА Лабс», Беляев М.Ю. – генеральный директор компании ООО «АЙРА Лабс», Гомболевский В.А. – советник компании ООО «АЙРА Лабс».

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Abbreviations:

ACOD – Arkhangelsk Clinical Oncology Dispensary

AI – artificial intelligence

COVID-19 – CoronaVirus Disease 2019

CI – Confidence Interval

CT – Computed Tomography

ICD-10 – International Classification of Diseases, 10th Revision

INIPA – insurance number of individual personal account

GIT – Gastrointestinal Tract

MN – Malignant Neoplasm

NAO – Nenets Autonomous Okrug

OR – Odds Ratio

PR – Prevalence Ratio

PBCR – Population-Based Cancer Registry

HIGHLIGHTS

Gender, age, and place of residence are not associated with the risk of detecting signs of COVID-19 pneumonia in patients with malignant neoplasms.

In lung, head and neck, upper gastrointestinal tract, and breast cancer, the frequency of detecting signs of COVID-19 pneumonia is 38–87% higher compared with the reference group – tumors of the female genital organs.

The presence of pulmonary emphysema in patients with malignant neoplasms increases the risk of detecting signs of COVID-19 pneumonia by 25%.

The presence of coronary artery calcification in patients with malignant neoplasms increases the risk of detecting signs of COVID-19 pneumonia by 24–61%.

The 2019 coronavirus disease (COVID-19) pandemic significantly affected the diagnosis and treatment of malignant neoplasms (MN). During the pandemic, a substantial decline in global MN incidence rates was observed [1, 2], including in the Russian Federation [3], primarily due to quarantine measures. Breast and cervical cancer screening programs, along with other cancer screenings, were suspended during the pandemic and later gradually resumed with scheduled visit intervals to reduce staff density and enhance infection control protocols [4]. In the Arkhangelsk region, the decrease in MN incidence during the COVID-19 pandemic was largely attributed to reduced detection of early-stage cervical, lung, and colorectal cancers [5].

Compared to other visualization methods, chest computed tomography (CT) has one of the highest sensitivity rates in detecting lung abnormalities associated with COVID-19 pneumonia. CT can identify characteristic lung changes in COVID-19 patients even before positive laboratory test results are obtained [6]. Meanwhile, artificial intelligence (AI) algorithms enable highly accurate detection of minimal lung changes on CT scans in asymptomatic and mild COVID-19 cases that do not require hospitalization. An independent evaluation of one such algorithm, developed by IRA Labs LLC (Moscow, Russia), demonstrated high diagnostic performance in detecting COVID-19 pneumonia signs: Receiver Operating Characteristic Area Under the Curve (ROC AUC) – 0.98, sensitivity – 0.95, specificity – 0.94, and accuracy – 0.94 [7].

During the COVID-19 pandemic, population-based cancer registries (PBCRs), with their large sample sizes and broad population coverage, were well-suited for monitoring shifts in cancer stage distribution at initial diagnosis and survival analysis. However, challenges arose in determining the exact stage at diagnosis due to delays in surgical interventions and pathological assessments. Given that chest CT scans were frequently performed for MN patients during outpatient visits and hospitalizations in the COVID-19 era, signs of pneumonia—including clinically silent cases – could also be tracked.

The Arkhangelsk Regional and Nenets Autonomous Okrug (NAO) Cancer Registry was established in 1998 and has maintained satisfactory completeness in recording and tracking MN patients from initial diagnosis

to outcome since 2000. Data on deceased MN patients are updated monthly by cross-referencing mortality records from the Arkhangelsk Regional Medical Information and Analytical Center with the registry database. The registry's completeness, accuracy, and timeliness have undergone multiple international audits, including within the "Cancer on Five Continents", CONCORD, and VENUSCANCER programs [8–10]. The registry also contains codes for the immediate causes of death in cancer patients, enabling the estimation of cancer-specific survival and non-cancer mortality rates.

Study objective: to assess the prevalence of COVID-19-associated pneumonia signs in a population-based cohort of MN patients using AI-assisted chest CT analysis.

MATERIALS AND METHODS

A cross-sectional study was conducted as part of the Arkhangelsk Research on the Impact of Multitarget Artificial Intelligence for Computed Tomography on Reducing Non-Cancer Lethal Outcomes in Patients with Malignant Neoplasms (ARILUS) project [11].

Data Collection

To achieve the study's objective, all chest CT scan series from the central medical imaging archive of the Arkhangelsk Clinical Oncology Dispensary (ACOD) were extracted for the period from April 1, 2020, to December 31, 2021, corresponding to the COVID-19 pandemic.

Chest CT scans during this period were performed for two main indications: routine diagnostic workup and staging of MN; exclusion of viral pneumonia signs in hospitalized patients who developed COVID-19 symptoms (at admission, all patients were required to have no respiratory symptoms and a negative nasopharyngeal/oropharyngeal swab test for COVID-19). A total of 11,173 CT scans were performed during this period, of which 3533 were conducted for healthcare workers or private-pay patients without MN.

Selection of valid images for processing was performed considering AI algorithm limitations, specifically excluding cases with lung atelectasis based on radiologists' interpretation reports, contrast-enhanced CT series based on DICOM tag analysis (ProtocolName Tag 0018,1030).

After deidentification, all valid CT series were sent for analysis by IRA Labs LLC (Moscow, Russia) AI system. At this stage, cases with severe motion artifacts, slice thickness >1.5 mm and incomplete lung scanning area were excluded. The total number of patients with valid CT studies was 1542.

After processing all images by the AI algorithm, they were sent via secure channel to ACOD using the key – insurance number of individual personal account (INIPA), and merged with the database of PBCR of Arkhangelsk Region and NAO, extracted on 15.04.2024. The total PBCR database contained information on 137,773 patients registered with MN diagnosis at the data extraction date, with INIPA data available for 62,988 patients. INIPA data in PBCR of Arkhangelsk Region and NAO have been recorded since January 1, 2021 for all newly registered patients, and during 2021 INIPA numbers were added for follow-up category patients. For the entire registration period (01.01.2000–15.04.2024), completeness of INIPA data was 45.7%. Data extraction from PBCR was necessary to establish causes of death in patients with available INIPA data. Among patients with valid CT studies, 394 had cancer but their INIPA data were unavailable, making outcome

assessment impossible (the ARILIS study part on outcome assessment is considered separately and will be presented independently). Patients without INIPA data were excluded from the study.

The final analysis included 1148 patients (Fig. 1).

The combined database for analysis included the following variables: patient identification code, INIPA, age at the time of CT scan, sex, type of residential locality (urban/rural), MN diagnosis code under the International Classification of Diseases, 10th Revision (ICD-10). The data for all the variables for the study period were 100 per cent complete.

AI Algorithm for COVID-19-Associated Pneumonia Diagnosis

To detect qualitative and quantitative (percentage of lung involvement) infiltrative changes characteristic of COVID-19 viral pneumonia (classified as U07 under ICD-10) [12], we used a medical AI-based software developed by IRA Labs LLC (Moscow, Russia): “Software for CT Scan Analysis Using AI Technology ‘Intelligent Radiology Assistants’”, Technical Specifications (TU): 58.29.32-001-44270315-2021, Registration Certificate (Roszdravnadzor): No. RZN 2024/22895¹ (Fig. 2).

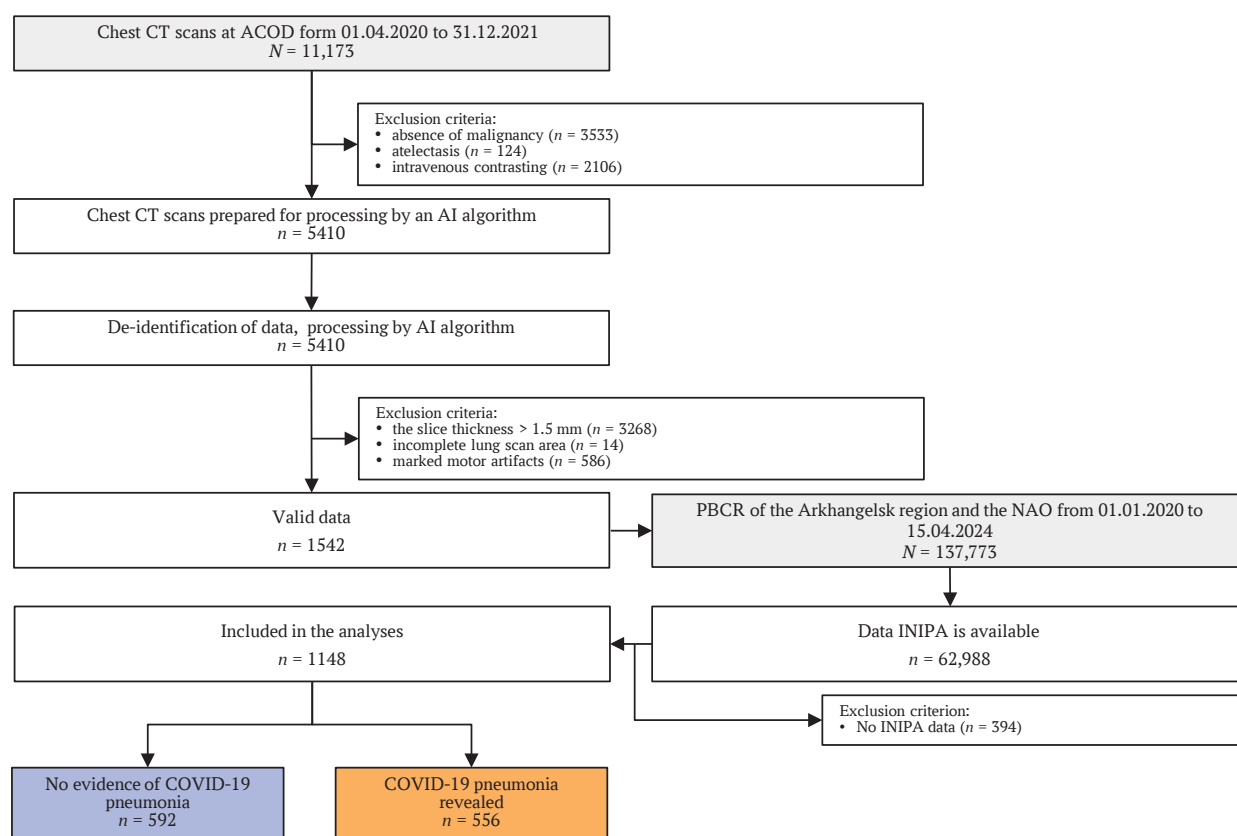


FIG. 1. Flowchart of the study.

Note: ACOD – Arkhangelsk Clinical Oncological Dispensary; AI – artificial intelligence; CT – computed tomography; INIPA – insurance number of individual personal account; NAO – Nenets Autonomous Okrug; PBCR – population-based cancer registry.

¹ Website of the Federal Service for Surveillance in Healthcare (Roszdravnadzor). State Register of Medical Devices and Organizations (Individual. Entrepreneurs), Engaged in the Production and Manufacturing of Medical Devices <https://roszdravnadzor.gov.ru/services/misearch> (access date: 10.12.2024).

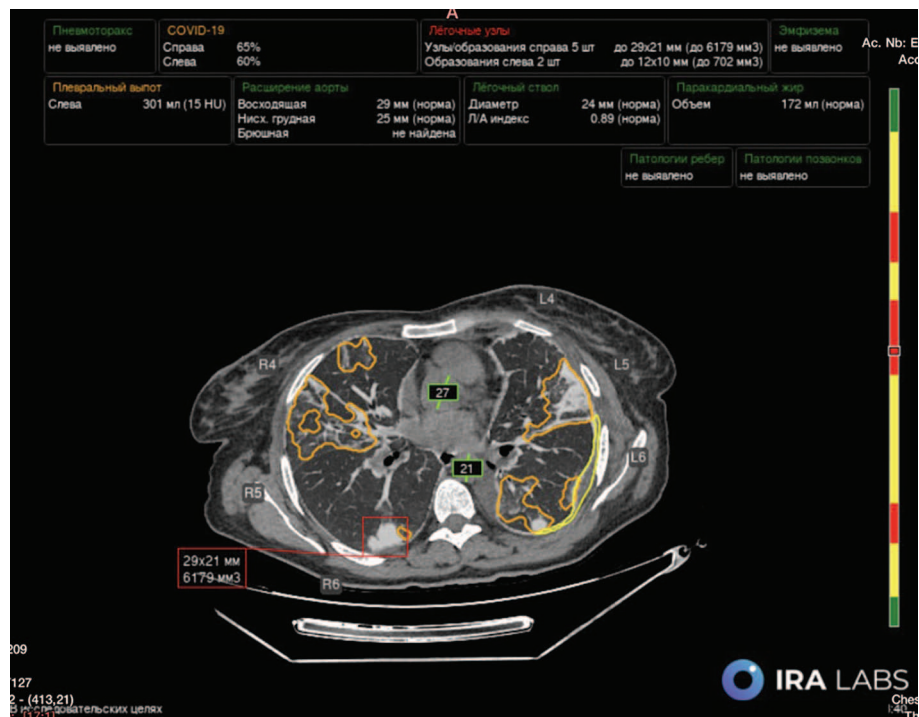


FIG. 2. Processing of chest computed tomography images using multi-target artificial intelligence technology.
Note: Lung tissue lesions of COVID-19 – associated pneumonia (orange) are presented as percentages for each lung. Also highlighted are lung nodules (red), their size and volume, fluid in the pleural cavity (yellow), its volume and densitometric density units, and vessel diameters (green).

Depending on the presence or absence of signs of pneumonia associated with COVID-19, all patients included in the database ($n = 1148$) were divided into two groups: without signs of pneumonia ($n = 592$, 51.6%) and with signs of pneumonia ($n = 556$, 48.4%). Notably, in most patients in the second group – 530 (95.3%) – the lesion volume was less than 25% (CT-1), signs of moderate (CT-2) and moderate (CT-3) pneumonia were found in 22 (4%) and 4 (0.7%) patients.

The AI-based software utilized in this study features a multitarget algorithm, enabling concurrent assessment of pulmonary emphysema, aortic and pulmonary trunk diameters, coronary artery calcification, bone mineral density of thoracic vertebrae (Fig. 2).

Statistical Methods

For ease of analysis and interpretation, all variables were categorized as ordinal (age, coronary artery calcification, bone mineral density), nominal (ICD-10 diagnosis codes/MN groups), binomial (sex, pulmonary emphysema, aortic aneurysm/dilation, pulmonary trunk dilation). Frequency distribution comparisons were performed using Pearson’s chi-square test.

Association strength was quantified through unadjusted (univariate) and adjusted (multivariate) prevalence ratios (PR) with 95% confidence intervals (CI). PR was calculated using Poisson regression (both univariate and multivariate forms) with the standard

formula. This approach was selected over logistic regression to avoid overestimation of effect measures given the high prevalence of the outcome variable. Only predictor variables showing an association with CT-detectable pneumonia signs at significance level (p) less than 0.15 in preliminary analyses were retained in the final adjusted model.

Prevalence ratio	The prevalence of identified cases of the phenomenon under study among people with a risk factor ^a
	The prevalence of identified cases of the phenomenon under study among people without a risk factor ^a

^a The presence of signs of COVID-19 pneumonia on CT was taken as a risk factor.

The reference categories included age below 40 years, urban residence, absence of signs of pulmonary emphysema, aortic dilation and osteoporosis, MNs of the female genital organs (ICD-10 codes C51–58), as well as absence of signs of coronary artery calcification. For the rank variables, the significance level for the linear trend was calculated by including the categories listed in the table as continuous variables.

In all statistical procedures, the critical significance level (p) was set at 0.05.

Statistical analysis was performed using Stata v.18 (Stata Corp., TX, USA).

RESULTS

The distribution of characteristics by study groups is presented in Table 1.

In the analyzed cohort, sex distribution was approximately equal, while CT signs of pneumonia were detected significantly more frequently in men than

Table 1. Characteristics of the groups

Feature	Total (n = 1148)	No evidence of COVID-19 pneumonia (n = 592)	COVID-19 pneumonia (n = 556)	p-value
Sex				
female	634 (55.2)	374 (63.2)	260 (46.8)	<0.001
male	514 (44.8)	218 (36.8)	296 (53.2)	
Age, years				
0–39	43 (3.8)	27 (4.6)	16 (2.9)	0.002
40–49	115 (10)	72 (12.2)	43 (7.7)	
50–59	236 (20.6)	126 (21.3)	110 (19.8)	
60–69	456 (39.7)	238 (40.2)	218 (39.2)	
70–79	250 (21.8)	113 (19.1)	137 (24.6)	
80 and older	48 (4.1)	16 (2.6)	32 (5.8)	
Place of residence				
urban	860 (74)	457 (72.5)	403 (74.9)	n.s.
rural	288 (26)	135 (27.5)	153 (25.1)	
ICD-10 codes, cancers				
C51–58, Malignant neoplasms of female genital organs	122 (10.6)	80 (13.5)	42 (7.6)	<0.001
C0–14, C30–32, Head and neck cancers	47 (4.1)	19 (3.2)	28 (5.0)	
C15, C16, Upper GIT cancers	140 (12.2)	60 (10.1)	80 (14.4)	
C18–25, Lower GIT cancers	238 (20.7)	148 (25.0)	90 (16.2)	
C34, Lung cancer	185 (16.1)	55 (9.3)	130 (23.4)	
C43–49, Skin and soft tissues cancer	74 (6.5)	37 (6.3)	37 (6.6)	
C50, Breast cancer	151 (13.2)	79 (13.3)	72 (13.0)	
C61, Prostate cancer	50 (4.4)	29 (4.9)	21 (3.7)	
C64–68, Urinary system cancers	76 (6.6)	39 (6.6)	37 (6.7)	
other neoplasms	65 (5.6)	46 (7.8)	19 (3.4)	
Lung emphysema				
no	1064 (92.7)	574 (97.0)	490 (88.1)	<0.001
revealed	84 (7.3)	18 (3.0)	66 (11.9)	
Aortal aneurism				
no	1125 (98.4)	581 (98.6)	544 (98.2)	n.s.
revealed	18 (1.6)	8 (1.4)	10 (1.8)	
Aortal dilation				
no	777 (68.0)	426 (72.3)	351 (63.4)	0.001
revealed	366 (32.0)	163 (27.7)	203 (36.6)	
Pulmonary trunk dilation				
no	627 (65.8)	305 (67.8)	322 (64.0)	n.s.
revealed	326 (34.2)	145 (32.2)	181 (36.0)	
Coronary artery calcification, Agatston index				
0	518 (47.3)	321 (57.6)	197 (36.5)	<0.001
1–99	264 (24.1)	133 (23.9)	131 (24.3)	
100–299	139 (12.7)	48 (8.6)	91 (16.9)	
300 and more	175 (16.0)	55 (9.9)	120 (22.3)	
Osteoporosis, osteopenia				
no	355 (32.3)	201 (35.5)	154 (28.8)	<0.05
osteopenia	428 (38.9)	214 (37.9)	214 (40.0)	
osteoporosis	317 (28.8)	150 (26.6)	167 (31.2)	

Notes: Data are presented as the absolute number of patients with the symptom and the proportion in the group expressed as a percentage (in parentheses). Pathological signs of aortic aneurysm/dilation, pulmonary trunk dilation, coronary calcification, and osteopenia were not assessed in all CT series due to either incomplete organ visualization or algorithm limitations.

COVID-19 – Coronavirus Disease 2019; CT – computed tomography; GIT – gastrointestinal tract; ICD-10 – International Classification of Diseases 10th Revision; n.s. – not significant.

women. The distribution of age categories was skewed towards older age groups in patients with COVID-19 pneumonia (Table 1).

In the study population, the most common tumor sites were the lower gastrointestinal tract (GIT) (20.7%), lung cancer (16.1%), breast cancer (13.2%), and upper GIT cancer (12.2%). The frequency of pneumonia detection varied significantly depending on cancer location: the highest rate was observed in lung cancer patients (70.3%), followed by head and neck malignancies (59.6%) and upper GIT cancers (57.1%). In patients with skin and soft tissue malignancies, the frequency of COVID-19 pneumonia was 50%; breast cancer (47.7%), urinary tract (48.7%), prostate cancer (42%), lower GIT (37.8%), female genital tract (34.4%), and other sites (29.2%) (Table 1).

Indicators of cardiovascular and pulmonary pathology, as well as signs of osteoporosis detected by AI-based multitarget CT analysis, were unevenly distributed. Signs of pulmonary emphysema, aortic dilation, presence and severity of coronary artery calcification, and osteoporosis were more prevalent in the group with COVID-19 pneumonia. However, no significant differences were found between the two groups in the distribution of aortic aneurysm/dilation and pulmonary trunk dilation.

The results of univariate and multivariate Poisson regression analyses are presented in Table 2.

In the unadjusted model, pneumonia sign prevalence was significantly higher in men (by 40%) than women, but after adjustment for other factors, gender differences became insignificant. Prevalence of COVID-19 signs on CT progressively increased with age (p for trend <0.001), but intergroup differences reached statistical significance only for age group ≥ 80 years, where COVID-19 signs were recorded 1.8 times more frequently than in reference group (<40 years). However, after including other variables in the multivariate model, all age differences in COVID-19 sign prevalence disappeared.

Rural residents had 13% higher prevalence of COVID-19 signs on CT in univariate analysis, but differences did not reach statistical significance ($p = 0.058$). The multivariate model showed no differences between urban and rural cancer patients in COVID-19 sign prevalence.

In the multivariate model, prevalence of COVID-19-associated pneumonia signs was 51–87% higher in lung cancer, head and neck tumors, and upper GIT tumors compared to female genital tumors. It was also significantly higher in breast cancer. For lower GIT tumors and prostate cancer, pneumonia sign prevalence did not differ significantly from the reference group.

Pulmonary emphysema signs were significantly associated with COVID-19 in both univariate and multivariate analyses. In patients with emphysema, after adjustment for all available factors, prevalence of

COVID-19-associated pneumonia signs was 25% higher than in those without emphysema.

Radiological signs of aortic aneurysm or dilation were significantly associated with COVID-19 in univariate analysis, but no independent associations between this sign and pneumonia signs on CT were found. Another potential predictor of increased cardiovascular mortality – coronary artery calcification level measured by Agatston score – was associated with higher probability of COVID-19 pneumonia in both univariate and multivariate models. Adjusted PRs for pneumonia signs increased from 1.24 (95% CI 1.05–1.47) to 1.61 (95% CI 1.36–1.90) for scores 1–99 to ≥ 300 compared to the no-calcification reference group. Aortic aneurysm and pulmonary trunk dilation were associated with pneumonia signs on CT at significance level >0.15 in univariate modeling and were not included in the multivariate model.

Prevalence of COVID-19 signs progressively increased with osteoporosis severity ($p = 0.015$ for trend) in univariate analysis. After including other factors in the model, PRs decreased to statistically insignificant levels.

DISCUSSION

Our study found that half of MN patients admitted to ACOD in 2020–2021 for specialized treatment had signs of COVID-19-associated pneumonia, with most cases showing $\leq 25\%$ lung involvement. We identified independent factors associated with COVID-19 pneumonia detection: cancer topography in lungs, head/neck, upper GIT, and breast, as well as presence of emphysema and coronary calcification on CT.

The COVID-19 pandemic significantly impacted cancer diagnosis and treatment organization: mortality reached 23.4% in hospitalized patients [13], mainly from pneumonia against 3–15-fold increased thrombosis rates [14]. Approximately 15–30% of hospitalized patients developed acute respiratory distress syndrome, increasing mortality risk [15]. Lung involvement volume on CT predicts COVID-19-associated pneumonia mortality [16]. COVID-19-associated pneumonia can be asymptomatic in 50% of patients [17, 18], which is consistent with our findings.

Risk factors for severe disease include older age, male sex and comorbidities. In our study, age and male sex were not independent pneumonia risk factors. However, older patients and men in general population have higher risk of coronary vessel atherosclerosis and emphysema – factors that showed independent effects on pneumonia risk in our study. This highlights the need for comprehensive risk assessment.

Our analysis showed substantially higher pneumonia prevalence in lung, upper GIT, and head/neck cancer patients versus cohort average. Smoking is the most important modifiable risk factor for these MNs. While some early studies suggested protective association

Table 2. Association between COVID-19 pneumonia and studied characteristics

Feature	cPR with 95% CI	p-value	aPR with 95% CI	p-value
Sex				
female	1.00 (ref.)	<0.001 ^a	1.00 (ref.)	n.s.
male	1.40 (1.25–1.58)		1.15 (0.98–1.35)	
Age, years				
0–39	1.00 (ref.)	<0.001	1.00 (ref.)	n.s. ^a
40–49	1.00 (0.64–1.58)		0.87 (0.56–1.36)	
50–59	1.25 (0.83–1.89)		0.86 (0.56–1.30)	
60–69	1.28 (0.86–1.92)		0.80 (0.53–1.21)	
70–79	1.47 (0.98–2.21)		0.95 (0.63–1.45)	
80 and older	1.79 (1.16–2.77)		1.09 (0.69–1.71)	
Place of residence				
urban	1.00 (ref.)	n.s.	1.00 (ref.)	n.s.
rural	1.13 (1.00–1.29)		1.06 (0.93–1.20)	
ICD-10 codes, cancers				
C51–58, Malignant neoplasms of female genital organs	1.00 (ref.)	<0.001	1.00 (ref.)	<0.001
C0–14, C30–32, Head and neck cancers	1.73 (1.23–2.43)		1.85 (1.32–2.58)	
C15, C16, Upper GIT cancers	1.66 (1.25–2.20)		1.51 (1.12–2.04)	
C18–25, Lower GIT cancers	1.10 (0.82–2.47)		1.06 (0.78–1.45)	
C34, Lung cancer	2.04 (1.57–2.65)		1.87 (1.40–2.49)	
C43–49, Skin and soft tissues cancer	1.45 (1.04–2.03)		1.40 (0.99–1.93)	
C50, Breast cancer	1.39 (1.03–1.86)		1.38 (1.00–1.90)	
C61, Prostate cancer	1.22 (0.81–1.83)		1.07 (0.70–1.63)	
C64–68, Urinary system cancers	1.41 (1.01–1.98)		1.39 (0.98–1.98)	
other neoplasms	0.85 (0.54–1.33)		0.78 (0.48–1.25)	
Lung emphysema				
no	1.00 (ref.)	<0.001	1.00 (ref.)	0.002
revealed	1.71 (1.50–1.94)		1.25 (1.09–1.45)	
Aortal dilation				
no	1.00 (ref.)	<0.001	1.00 (ref.)	n.s.
revealed	1.23 (1.09–1.38)		0.96 (0.85–1.10)	
Coronary artery calcification, Agatston index				
0	1.00 (ref.)	<0.001 ^a	1.00 (ref.)	<0.001 ^a
1–99	1.30 (1.11–1.54)		1.24 (1.05–1.47)	
100–299	1.72 (1.46–2.03)		1.58 (1.33–1.87)	
300 and more	1.80 (1.55–2.09)		1.61 (1.36–1.90)	
Osteoporosis, osteopenia				
no	1.00 (ref.)	0.015 ^a	1.00 (ref.)	n.s. ^a
osteopenia	1.15 (1.00–1.33)		1.11 (0.95–1.27)	
osteoporosis	1.21 (1.05–1.39)		1.10 (0.93–1.29)	

Notes: ^a *p* for linear trend.

aPR – adjusted prevalence ratio; CI – confidence interval; cPR – crude prevalence ratio; n.s. – not significant; Ref – reference category.

between smoking and COVID-19 severity (“smoker’s paradox” [19]), most authors link tobacco smoking with increased risk of symptomatic SARS-CoV-2 infection and disease progression [20, 21]. A recent US analysis found current tobacco smoking significantly associated with increased hospitalization (Odds Ratio (OR) 1.72; 95% CI: 1.62–1.82; $p < 0.001$), ICU admission (OR

1.22; 95% CI: 1.10–1.34; $p < 0.001$) and all-cause mortality (OR 1.37; 95% CI: 1.20–1.57; $p < 0.001$) after adjustment [22]. Our assumption about smoking and CT opacity probability is further supported by more frequent pneumonia signs in men, who smoke more.

Among healthcare AI services, radiology has the most products. Russia’s largest AI radiology project is

the Experiment on Using Innovative Computer Vision Technologies for Medical Image Analysis in Moscow Healthcare System, which processed >12 million radiological studies. In this project, IRA Labs LLC leads the maturity matrix for comprehensive chest CT AI by performance quality (ROC AUC) [7]. Using this algorithm detects pneumonia signs more frequently than unaided interpretation.

Study strengths include population-based design, using all available CTs for analysis. PBCR data completeness was previously validated at high levels. For example, the mortality/incidence ratio in Arkhangelsk Region and NAO PBCR for 2008–2017 is 0.58, comparable to Eastern European registries. Death certificate only (DCO) rate is 4.5%, higher than in European countries, but this can be explained by high autopsy rates (>60% in MN patients) and, subsequently, a high rate of accident postmortem cancers. The difference between cases registered in PBCR during 2008–2017 and annual reports versus 5-year updated data is <3% [10].

Reliable PBCR patient data enabled assessment of lung infection prevalence in a representative MN patient cohort and provided high statistical power. Another key advantage is using objective AI-derived radiological criteria, revealing higher viral pneumonia probability with chronic lung (emphysema) and coronary vessel diseases.

Study Limitations

Chest CT was used both for routine MN staging/diagnosis and COVID-19 symptom evaluation. Separating these streams was impossible in this design. However, hospitalization rules during pandemic required

AUTHORS CONTRIBUTION

Andrey A. Dyachenko – development of the research concept, development of the methodology, analysis of the work, drafting the manuscript, critical revision of the text, interpretation of the research results, final approval of the manuscript. Andrej M. Grjibovski – development of the methodology, statistical analysis and its interpretation, critical revision of the text, interpretation of the research results. Maxim A. Bogdanov, Dmitriy V. Bogdanov, Valeria Yu. Chernina – analysis of the work, critical revision of the text, interpretation of the research results. Ekaterina A. Nazarova – analysis of the work, critical revision of the text, interpretation of the research results. Anna A. Meldo, Mikhail G. Belyaev – critical revision of the text, interpretation of the research results. Victor A. Gombolevsky, Mikhail Yu. Valkov – scientific supervision, development of the research concept, development of the methodology, critical revision of the text, interpretation of the research results. All authors approved the final version of the article.

baseline disease exclusion, making hospital-acquired infection risk random and dependent only on analyzed factors.

Correlation of CT pneumonia signs with SARS-CoV-2 PCR results was impossible. However, during the pandemic, other viral infections rarely caused pneumonia [23]. Moreover, many cases with clear clinical manifestations had initial negative nasopharyngeal PCR, with COVID-19 later confirmed by repeat PCR or seroconversion [24].

Incomplete INIPA data in PBCR. However, we assume most patients undergoing chest CT during 04/2020–12/2021 were in follow-up category by 2021. Among 1542 patients with validated CTs and AI analysis, 74.4% matched PBCR records.

The cancer registry doesn't collect smoking data, preventing independent assessment of this factor's impact on CT pneumonia sign risk.

Future Research Directions

Clinical significance of incidentally detected CT pneumonia signs in MN patients will be assessed in survival and cause-of-death analyses. Since age was an independent mortality risk factor in some COVID-19 pneumonia studies [25, 26], we plan to analyze the overall cohort survival by age.

CONCLUSION

In this analysis, half of the patients admitted to Arkhangelsk oncology center during COVID-19 pandemic showed CT signs of pneumonia. Independent factors associated with COVID-19 pneumonia detection include tumor location (lung, head/neck, upper GIT, breast) and CT signs of emphysema and coronary calcification.

ВКЛАД АВТОРОВ


А.А. Дяченко – разработка концепции исследования, разработка методологии, анализ работы, составление черновика рукописи, критический пересмотр текста, интерпретация результатов исследования, окончательное утверждение рукописи. А.М. Гржибовский – разработка методологии, статистический анализ и его интерпретация, критический пересмотр текста, интерпретация результатов исследования. М.А. Богданов, Д.В. Богданов, В.Ю. Чернина – анализ работы, критический пересмотр текста, интерпретация результатов исследования. Е.А. Назарова – анализ работы, критический пересмотр текста, интерпретация результатов исследования. А.А. Мелдо, М.Г. Беляев – критический пересмотр текста, интерпретация результатов исследования. В.А. Гомболевский, М.Ю. Вальков – научное руководство, разработка концепции исследования, развитие методологии, критический пересмотр текста, интерпретация результатов исследования. Все авторы утвердили окончательную версию статьи.

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INFORMATION ABOUT THE AUTHORS / ИНФОРМАЦИЯ ОБ АВТОРАХ

Andrey A. Dyachenko , Cand. of Sci. (Medicine), Associate Professor, Department of Radiology, Radiation Therapy and Oncology, Northern State Medical University.
ORCID: <https://orcid.org/0000-0001-8421-5305>

Andrej M. Grjibovski, Dr. of Sci. (Medicine), Head of the Directorate for Scientific and Innovation Work, Northern State Medical University; Professor, Department of Healthcare Organization and Preventive Medicine, Medical Institute of the North-Eastern Federal University; Adviser to the Rector of the REAVIZ University.
ORCID: <https://orcid.org/0000-0002-5464-0498>

Maxim A. Bogdanov, Assistant Professor, Department of Radiation Diagnostics, Radiation Therapy and Oncology, Northern State Medical University.
ORCID: <https://orcid.org/0009-0002-3469-658X>

Dmitrii V. Bogdanov, Assistant Professor, Department of Public Health, Healthcare and Social Work, Northern State Medical University; Chief Physician, Arkhangelsk Clinical Oncology Dispensary.
ORCID: <https://orcid.org/0000-0002-4105-326X>

Дяченко Андрей Андреевич , канд. мед. наук., доцент кафедры лучевой диагностики, лучевой терапии и онкологии ФГБОУ ВО «Северный государственный медицинский университет» Минздрава России.
ORCID: <https://orcid.org/0000-0001-8421-5305>

Гржибовский Андрей Мечиславович, д-р медицины (PhD), начальник управления по научной и инновационной работе ФГБОУ ВО «Северный государственный медицинский университет» Минздрава России; профессор кафедры организации здравоохранения и профилактической медицины Медицинского института ФГАОУ ВО «Северо-Восточный федеральный университет им. М.К. Аммосова»; советник ректора университета «РЕАВИЗ».
ORCID: <https://orcid.org/0000-0002-5464-0498>

Богданов Максим Андреевич, ассистент кафедры лучевой диагностики, лучевой терапии и онкологии ФГБОУ ВО «Северный государственный медицинский университет» Минздрава России.
ORCID: <https://orcid.org/0009-0002-3469-658X>

Богданов Дмитрий Васильевич, ассистент кафедры общественного здоровья, здравоохранения и социальной работы ФГБОУ ВО «Северный государственный медицинский университет» Минздрава России; главный врач ГБУЗ АО «Архангельский клинический онкологический диспансер».
ORCID: <https://orcid.org/0000-0002-4105-326X>

Ekaterina A. Nazarova, physician-methodologist, National Medical Research Center of Oncology.

ORCID: <https://orcid.org/0009-0006-0634-528X>

Anna A. Meldo, Dr. of Sci. (Medicine), Professor, Department of Radiology, Radiation Therapy and Oncology, Northern State Medical University.

ORCID: <https://orcid.org/0000-0002-4906-9901>

Valeria Yu. Chernina, Assistant Professor, Department of Radiation Diagnostics, Radiation Therapy and Oncology, Northern State Medical University; Head of the Department of Clinical Evaluation of AI, IRA Labs.

ORCID: <https://orcid.org/0000-0002-0302-293X>

Mikhail G. Belyaev, Cand. of Sci. (Physics and Mathematics), Professor, General Director, IRA Labs.

ORCID: <https://orcid.org/0000-0001-9906-6453>

Victor A. Gomboleviskiy, Cand. of Sci. (Medicine), Advisor, Radiologist, IRA Labs; Leading Researcher, Artificial Intelligence Research Institute; Senior Researcher, Institute of Personalized Oncology, Sechenov First Moscow State Medical University (Sechenov University).

ORCID: <https://orcid.org/0000-0003-1816-1315>

Mikhail Yu. Valkov, Dr. of Sci. (Medicine), Professor, Head of the Department of Radiology, Radiation Therapy and Oncology, Northern State Medical University.

ORCID: <https://orcid.org/0000-0003-3230-9638>

Назарова Екатерина Александровна, врач-методист ФГБУ «Национальный медицинский исследовательский центр онкологии имени Н.Н. Петрова» Минздрава России.

ORCID: <https://orcid.org/0009-0006-0634-528X>

Мелдо Анна Александровна, д-р мед. наук, профессор кафедры лучевой диагностики, лучевой терапии и онкологии ФГБОУ ВО «Северный государственный медицинский университет» Минздрава России.

ORCID: <https://orcid.org/0000-0002-4906-9901>

Чернина Валерия Юрьевна, ассистент кафедры лучевой диагностики, лучевой терапии и онкологии ФГБОУ ВО «Северный государственный медицинский университет» Минздрава России; руководитель отдела клинической оценки ИИ ООО «АЙРА Лабс».

ORCID: <https://orcid.org/0000-0002-0302-293X>

Беляев Михаил Геннадьевич, канд. физ.-мат. наук, профессор, генеральный директор ООО «АЙРА Лабс».

ORCID: <https://orcid.org/0000-0001-9906-6453>

Гомболеviskiy Виктор Александрович, канд. мед. наук, советник, врач-рентгенолог ООО «АЙРА Лабс»; ведущий научный сотрудник АНО «Институт искусственного интеллекта»; старший научный сотрудник Института персонализированной онкологии ФГАОУ ВО «Первый Московский государственный медицинский университет имени И.М. Сеченова» Минздрава России (Сеченовский Университет).

ORCID: <https://orcid.org/0000-0003-1816-1315>

Вальков Михаил Юрьевич, д-р мед. наук, профессор, заведующий кафедрой лучевой диагностики, лучевой терапии и онкологии ФГБОУ ВО «Северный государственный медицинский университет» Минздрава России.

ORCID: <https://orcid.org/0000-0003-3230-9638>