

# EFFICIENCY OF TOMOTHERAPY IN THE TREATMENT OF LUNG CANCER IN MALES WITH CONCOMITANT CARDIOVASCULAR PATHOLOGY (EXPERIENCE OF THE “UMIT” INTERNATIONAL ONCOLOGY CENTER OF TOMOTHERAPY)

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## ABSTRACT

**Relevance:** Non-small cell lung cancer (NSCLC) is frequently diagnosed in men with associated myocardial pathologies. Radiation therapy is one of the treatment methods for NSCLC; however, in Kazakhstan, there are virtually no studies on the efficacy and safety of tomotherapy in cancer patients with cardiac pathologies.

**The study aimed to** evaluate the clinical results of mono-tomotherapy in patients with NSCLC and concomitant cardiac pathologies at the International Oncology Center for Tomotherapy “UMIT” (Astana, Kazakhstan).

**Methods:** The study included 201 men with NSCLC who underwent spiral mono-tomotherapy at UMIT between 2020 and 2024. Patients were divided into Group 1 (n=139) – patients without cardiac pathologies- and Group 2 (n=62) – patients with severe associated cardiac pathologies. The average course duration was 32 days, the average treatment duration was 15 minutes, OD, 5 days a week. Treatment efficacy was assessed 8-12 weeks after completion of the course using PET-CT and CT data.

**Results:** Complete regression was more common in patients in Group 1, while disease progression was more common in patients in Group 2. Partial responses were more common in Group 1, and stabilization of the oncological process was more common in Group 2. In Group 2, the proportion of patients with positive dynamics was 49%; after accounting for the identified stabilization of the process, it was 84%. In Group 1, the one-year overall survival rate was 84%, and 74% for stages III and IV, respectively, with a median progression-free survival of 10.3 months. The two-year survival rate for stage III disease was 65%. In Group 2, the one-year overall survival rate was 76% and 63% for stages III and IV, respectively, with a median progression-free survival of 8.1 months and a two-year survival rate of 54% for stage III. No device malfunctions were observed in Group 2. Two patients undergoing coronary artery bypass grafting experienced decompensated heart failure requiring temporary hospitalization.

**Conclusion:** Tomotherapy demonstrates high clinical efficacy in the treatment of NSCLC with severe comorbid cardiac disease, although overall survival and treatment efficacy were lower than in patients without cardiac disease. Our experience confirms the feasibility of a relatively safe treatment in such patients when a personalized approach, strict dosimetric control, and multidisciplinary monitoring are employed.

**Keywords:** lung cancer, tomotherapy, cardiopathology, pacemaker, hypofractionation, high-precision radiation therapy.

**Introduction:** Malignant neoplasms of the lung remain one of the leading causes of cancer death worldwide. According to the Global Cancer Observatory international initiative, in 2022, lung cancer was the most common cancer diagnosed [1]. According to US cancer registries for 2020-2021, it ranked second (11% on average in men) in the number of diagnosed cases and first (20% in men) in estimated cancer deaths [2]. Globally, in 2022, the incidence of lung cancer reached 15.3% among other cancers (including unidentified ones), which amounted to more than 1,570,000 new cases per year. Moreover, the share of lung cancer in total cancer mortality, regardless of gender, was 22.7% or more than 1,233,000 deaths [1]. Lung cancer is usually diagnosed more often in men than in women, and the first detection in a significant number of cases occurs at late stages (III-IV), limiting the possibilities of radical treatment [1, 3-6].

Lung cancer occupies a leading position in the structure of oncological morbidity in the Republic of Kazakhstan. In 2010-2019, 36,916 cases of lung cancer were detected in the Republic of Kazakhstan, of which 80.5% were in men [4]. In a later study, covering the period from 2014 to 2022, the proportion of men in the total number of deaths from lung and respiratory tract cancer was more than 75% [5]. When using low-dose computed tomography, stage II and III lung cancer is detected in men on average 2 times more often than in women [6]. Despite a trend towards a slight decrease in the proportion of lung cancer (including trachea and bronchial cancer) in the total pool of oncological diseases in Kazakhstan from 2014 to 2022, it still constitutes about 16% of all types of cancer [5]. Moreover, according to recent national studies, the detection rate of asymptomatic patients with previously undiagnosed can-

cer may reach 2% among the population of regions with high background radiation levels, with more than half of them being diagnosed with lung cancer at stage III [6]. Similarly, regions with high levels of heavy metals (lead, cobalt, copper) also show a higher incidence of lung cancer [7]. As a result, lung cancer, along with other common cancers, makes a significant contribution to the total number of lost person-years, which negatively impacts the economy and social spectrum of the population of Kazakhstan [8]. This determines the relevance of assessing the effectiveness of new lung cancer treatments, including in men, as a significantly more vulnerable category of patients.

For patients with non-small cell lung cancer (NSCLC), when surgical intervention is not possible, conservative treatment, including chemotherapy, immunotherapy, and radiation therapy, becomes the priority. One of the modern approaches to radiation therapy is spiral tomotherapy with intensity-modulated tumor irradiation modes (Intensity-Modulated). Radiation Therapy (IMRT) with daily imaging during radiotherapy (Image-Guided Radiation Therapy (IGRT), which provides increased precision in planning and conducting sessions [9, 10]. As a result, it becomes possible to reduce the dose load on healthy tissues and organs surrounding the tumor (especially organs at risk) and to ensure a high level of control over tumor dynamics [11, 12].

Radiation therapy requires an individualized approach for all cancer patients. This is especially important for cancer patients with a complicated somatic background, particularly in the presence of severe cardiovascular diseases. Cardiovascular pathologies account for a significant part of the structure of comorbidities in cancer patients, occurring in approximately 22.6% of the total number of patients diagnosed with cancer of any type [13]. Concomitant congestive heart failure is detected in 16.5% of patients with lung cancer [14]. In patients with NSCLC, severe forms of cardiovascular pathology occur in 31.1% of cases, among which the most common are heart failure (47.7%), myocardial infarction (33.0%), and chronic arrhythmias (30.4%) [15]. These patients may also have implanted pacemakers (PMPs), cardioverter-defibrillators (ICDs), or may have a history of coronary artery bypass grafting (CABG).

The presence of severe concomitant cardiovascular diseases significantly influences the choice of treatment strategy, increases the risk of cardiotoxic complications during radiation therapy, and requires the use of both high-precision and gentle radiotherapy methods, such as tomotherapy. Furthermore, antitumor therapy itself can provoke the manifestation or exacerbation of cardiac pathology and/or malfunction of implanted devices. In such patients, there is a clear need to strictly limit the dose to critical structures, including the heart, coronary vessels, and the pulmonary artery trunk [12].

Kazakhstan has accumulated limited but promising experience using high-precision tomotherapy in this patient population. However, the domestic literature is virtually devoid of studies evaluating the efficacy and safety of this method in cancer patients with significant underlying cardiac pathology.

**The study aimed to** evaluate the clinical results of mono-tomotherapy in patients with NSCLC and concomitant cardiac pathologies at the International Oncology Center for Tomotherapy “UMIT” (Astana, Kazakhstan).

**Materials and Methods:** This retrospective study included 201 male patients diagnosed with non-small cell lung cancer (NSCLC). All patients underwent a course of mono-tomotherapy at the UMIT Tomotherapy Center between January 2020 and December 2024. The patients were divided into two groups: patients in Group 1 (n = 139) had no significant cardiovascular diseases, while patients in Group 2 (n = 62) were diagnosed with severe comorbid cardiovascular conditions prior to the start of tomotherapy, including ischemic heart disease, the presence of implanted pacemakers, and a history of coronary artery bypass grafting (Table 1).

**Inclusion criteria for Group 2 were:** reduced left ventricular ejection fraction (EF)  $\leq 50\%$ , history of coronary artery bypass grafting (CABG), presence of pacemakers (PM) or implantable cardioverter-defibrillators (ICD), post-infarction cardiosclerosis, and angina pectoris of functional class III–IV.

**Exclusion criteria for Group 2 included:** unstable angina, acute coronary syndrome, or inability to complete a full course of tomotherapy.

**Table 1 – Distribution of types of cardiovascular diseases and disorders in Group 2 patients**

Category of cardiovascular pathology	Absolute number of cases (n)	Share in Group 2 (%)
Post-coronary artery bypass grafting	24	38.7
Ejection fraction <40%	19	30.6
Ejection fraction between 40-50%	28	45.2
Implanted pacemakers	12	19.4
Implanted cardioverter-defibrillators	6	9.7
Post-infarction cardiosclerosis	16	25.8
Angina pectoris (class III-IV)	21	33.9

The mean age was 62.3 years in Group 1 and 68.5 years in Group 2.

The distribution of patients by cancer stage is presented in Figure 1: the relative distribution across differ-

ent stages was approximately equal in both groups, with a predominance of patients with stage III and IV NSCLC.

Spiral tomotherapy (Radixact X9, Accuray, Madison, WI, USA) was used in the study, combining the capabili-

ties of a computed tomography scanner and a linear accelerator. Adjustable parameters of the tomotherapy system were used, with an automatic correction system

that adjusts patient positioning and irradiation parameters, reducing the likelihood of erroneous dose delivery (Table 2).

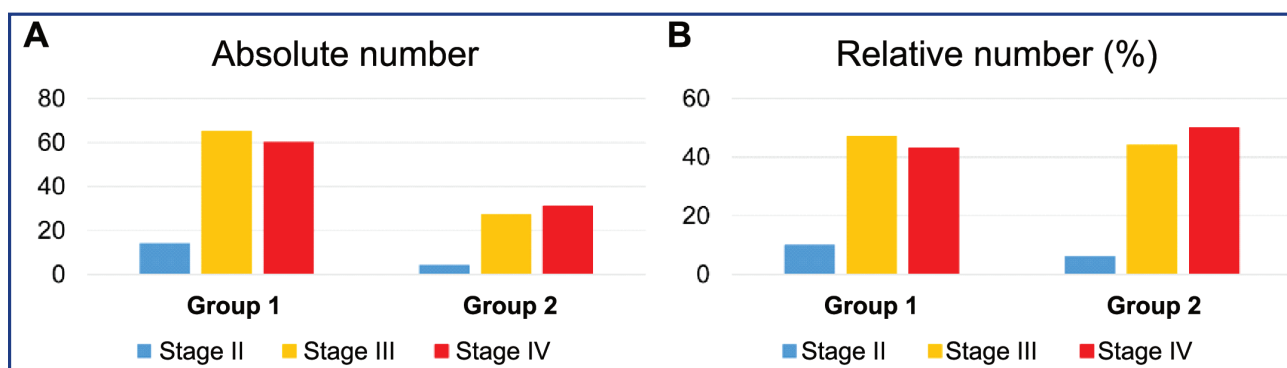


Figure 1 – Distribution of study participants by cancer stage: A – absolute number (n), B – relative number (%)

**Table 2 – Technical parameters of the computed tomography system used in the study**

Parameter	Description of the parameter
Accelerator power	6 MV (megavoltage) X-ray photons
Beam width (fan beam width)	Varies from 1 to 5 cm to adapt the treatment mode to individual anatomical features
Gantry rotation speed	Approximately 1 rotation every 15-30 seconds, depending on the selected mode
Dose intensity modulation	Achieved through real-time changes in the shape and intensity of the radiation beam
Tumor doses	Range from 50 to 60 Gy, distributed over 20-30 fractions, with daily monitoring and plan adaptation if needed
Exposure time	On average, 15-25 minutes per fraction

In some cases, multifocal irradiation modes were applied, in which several anatomical zones were irradiated simultaneously – both the primary tumor and regional lymph nodes – while providing maximal sparing of surrounding healthy tissues (average dosimetric exposure parameters are shown in Table 3, “Results” section).

The tomotherapy protocol included mandatory CT-based planning with a 2-3 mm slice thickness at the preliminary stage, with the patient in the supine position and fixed. The scan duration was 15 minutes. Irradiation was performed daily (5 times a week, on working days) with one session per day; in exceptional cases (<2% of patients), alternate-day regimens were used based on clinical indications, such as decompensation of chronic somatic pathology. The course duration ranged from 20 to 40 days, depending on the protocol (normo- or hypofractionation, radiation volume, individual tolerability, and treatment regimens). Hypofractionated regimens were used in 22% of cases (n = 44); however, the distribution across the groups was uneven: in Group 2, hypofractionated irradiation was used in 59.7% of cases (37 out of 62) vs. only 5% of cases in Group 1 (7 out of 139).

CT data were processed using MIM Maestro software and the TomoTherapy Precision® planning system. Statistical data analysis was performed using SPSS v.26 and Microsoft Excel. Student’s t-test was used for normally distributed data and the Mann-Whitney U test for non-nor-

mally distributed data to compare quantitative variables between groups. Differences were considered statistically significant at  $p < 0.05$ .

Overall survival was defined as the time from the start date of the tomotherapy course to death from any cause or the date of the last follow-up. Progression-free survival was defined as the time from the start of treatment to the first documented disease progression (according to RECIST 1.1) or death. Comparison of survival values between groups was performed using the log-rank test. Median overall and progression-free survival were calculated for the entire cohort and for each study group, with 95% confidence intervals (95% CI) reported.

**Results:** Table 3 presents the recommended and actual average dose parameters to critical organs in the patients included in the study, used to assess the quality of treatment planning and radiation safety. In Group 2 patients (with cardiopathology), the mean heart dose was significantly higher than in Group 1 patients (without cardiopathology), whereas no significant differences were observed in other organs. At the same time, the mean dose in Group 2 did not exceed the recommended threshold, and the mean doses differed by no more than 1.4 Gy between the groups. Based on this, we assume that the observed statistically significant difference in myocardial dose between the study groups did not influence the effectiveness of the tomotherapy course.

**Table 3 – Recommended and actual mean dose parameters to critical organs in patients included in the study**

Organ / Risk zone	Planning constraint (recommendation)	Actual mean dose		p-value
		Group 1	Group 2	
Lungs ( $V_{20}$ )	≤30%	27.1±2.8%	28.4±3.1%	0.08
Heart ( $D_{mean}$ )	<15 Гр	11.2±2.1 Gy	12.6±2.4 Gy	0.04*
Esophagus ( $D_{max}$ )	≤50 Гр	41.5±5.3 Gy	43.1±4.8 Gy	0.21
Spinal cord ( $D_{max}$ )	≤45 Гр	34.7±3.6 Gy	35.9±3.9 Gy	0.15

Note: The symbol "\*" indicates a statistically significant difference between the study groups (at a significance level of  $p < 0.05$ ).

Treatment efficacy was evaluated based on PET-CT and CT data obtained 8-12 weeks after completion of the course. The results on cancer disease dynamics are presented in Table 4. Complete regression was observed significantly more often in Group 1 patients, whereas disease progression was more frequent in Group 2. There was a trend toward a higher partial response rate in Group 1, whereas stabilization of the oncological process occurred more often in Group 2. A comparison of the relative frequency of complete regression, partial

response, stabilization, or disease progression between the study groups indicates that tomotherapy was less effective in Group 2 than in Group 1. Nevertheless, in Group 2, positive dynamics were observed in nearly half of the participants (49%; complete regression + partial response), and, among patients with oncological process stabilization, in 84%. This suggests a fairly high effectiveness of mono-tomotherapy in patients with NS-CLC and concomitant severe cardiopathology of various etiologies.

**Table 4 – Outcomes in patients included in the study following tomotherapy**

Outcome	Group 1	Group 2	p-value
Complete regression (%)	10% (14)	3% (2)	0.03*
Partial response (%)	58% (81)	46% (29)	0.10
Stable disease (%)	28% (39)	35% (22)	0.25
Oncological disease progression (%)	4% (5)	16% (9)	0.01*

Note: The symbol "\*" indicates a statistically significant difference between the study groups (at a significance level of  $p < 0.05$ ).

The median overall survival in the entire patient cohort was 18.6 months (95% CI: 16.9-20.3); Group 1 – 19.8 months (95% CI: 18.2-21.4); Group 2 – 16.2 months (95% CI: 14.1-18.3) (significantly lower in Group 2; log-rank  $p=0.04$ ). The median progression-free survival was 9.7 months (95% CI: 8.5-10.9); Group 1 – 10.3 months (95% CI: 9.2-11.4); Group 2 – 8.1 months (95% CI: 6.9-9.3) (log-rank  $p=0.03$ ). The one-year overall survival rate was 82% for the entire cohort, 84% for Group 1, and 76% for Group 2. The two-year overall survival rate was 62% for the entire cohort (65% in Group 1 vs. 54% in Group 2). Depending on the stage of the disease, the median overall survival in the entire cohort was: Stage III – 20.4 months (95% CI: 18.5-22.3); Stage IV – 16.3 months (95% CI: 14.5-18.1). The median progression-free survival was 10.8 months (95% CI: 9.4-12.2) for stage III and 8.3 months (95% CI: 7.1-9.5) for stage IV. Both indicators showed a statistically significant difference between stages (log-rank  $p<0.01$ ).

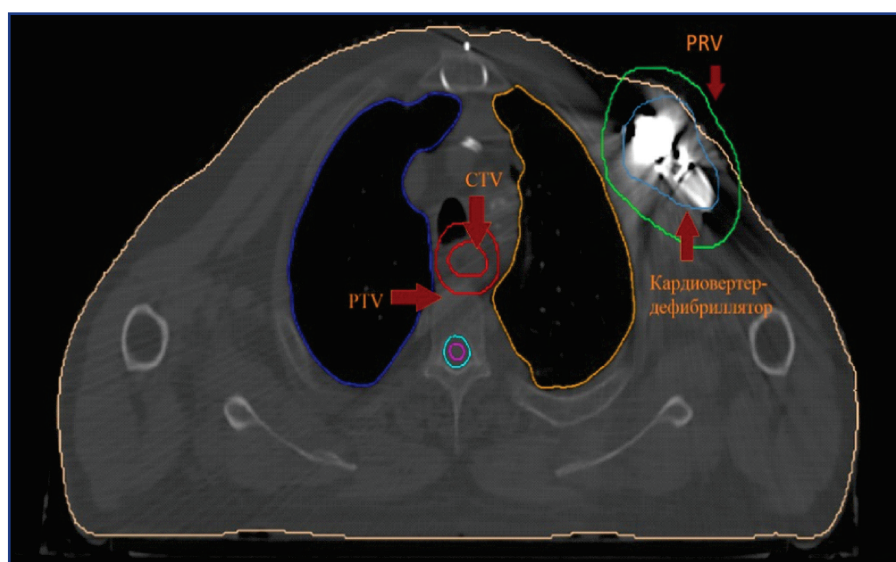
Comparative safety analysis showed that patients with significant cardiopathology had a higher risk of cardiovascular complications; however, the overall tolerability profile of tomotherapy remained acceptable. Other radiation-induced complications (esophagitis, pneumonitis) did not exceed grade II according to

the Common Terminology Criteria for Adverse Events (CTCAE) and occurred in less than 10% of patients in both groups. Thus, helical tomotherapy demonstrated high efficacy and satisfactory tolerability in patients with cardiopathology. Key safety factors included contouring cardiac devices and bypass grafts as critical structures, strict dose control, IMRT, and daily IGRT.

*Safety in patients with pacemakers (PMs) or implantable cardioverter-defibrillators (ICDs):* In patients with implanted PMs or ICDs ( $n=18$ ), irradiation was performed using adaptive planning, with the implanted devices contoured as critical organs (Figure 2). The mean distance from the tumor to the device was 4.3 cm. The maximum dose to the PM or ICD did not exceed 2 Gy. As a result of treatment, no cases of device malfunction or need for replacement were recorded (0/18 patients).

*Treatment of patients after CABG and with low EF:* In patients with prior CABG ( $n=24$ ), the radiation dose to the graft region was limited to 15 Gy or less (Figure 3). Patients with  $EF<40\%$  received standard irradiation regimens (2-2.5 Gy per fraction). In two patients, decompensated heart failure was observed, requiring temporary hospitalization, but the full course of tomotherapy was completed in both cases.





Legend: Кардиовертер-дефибрилятор – Implantable cardioverter-defibrillator

Figure 2 – Implanted devices (PM/ICD) were contoured as critical structures (the device is indicated by the arrow in the upper right corner). Average distance to the tumor: 4.3 cm; maximum dose to the device:  $\leq 2$  Gy. Notes: PRV (Planning Organ at Risk Volume) – region defined for an organ at risk; PTV (Planning Target Volume) – target irradiation area; CTV (Computed Tomography Venography) – region used for CT venography

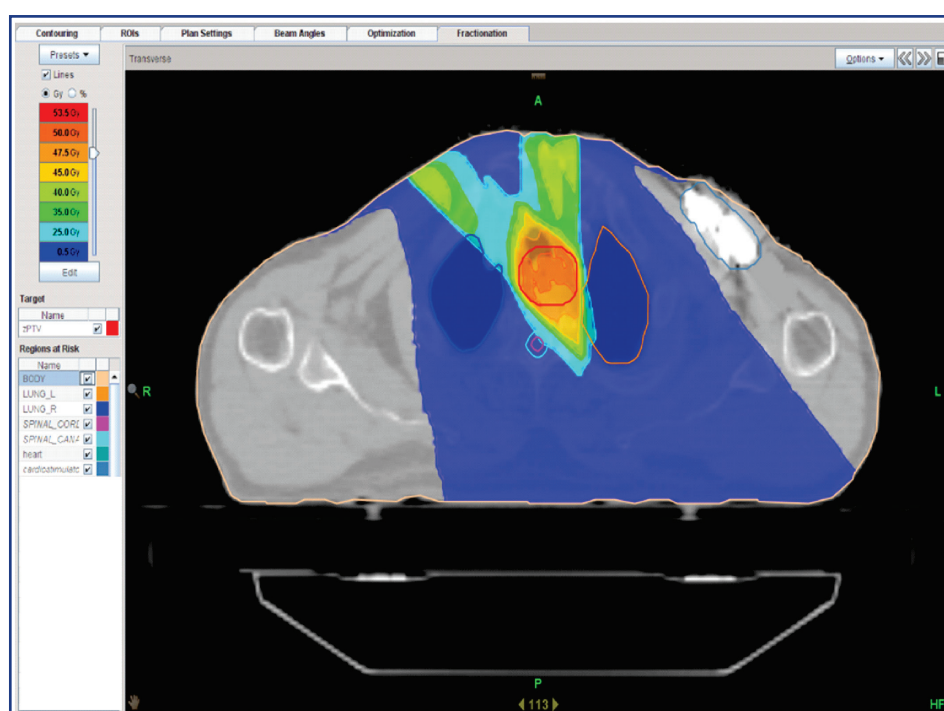


Figure 3 – Example of dose distribution to the target volume and critical organs in a patient with concomitant cardiopathy, demonstrating target coverage with minimal irradiation of adjacent structures. Color-coded regions represent different radiation dose levels, and different organs are delineated with predefined contour colors

**Discussion:** Tomotherapy continues to evolve as an approach to cancer treatment, including by reducing the risk of harmful radiation exposure [16]. This leads to a decrease in the incidence of radiation-induced toxic effects, as demonstrated in numerous studies on tomotherapy for prostate cancer [17], breast cancer [11, 18], metastatic liver cancer [19], grade II gliomas [20], craniospinal tumors [21], skin neoplasms [22], and other types of cancer. Advancements in particle accelerators across different tomother-

apy systems have led to more effective spatial distribution of radiation doses, as demonstrated in a study involving patients with six cancer types, including lung cancer [23].

IGRT provides additional benefits by preventing or significantly reducing exposure to tissues and organs adjacent to the target, while simultaneously enhancing the irradiation efficacy of the target itself through respiratory motion management [24]. This approach is recommended by radiological associations for many types of cancer [9, 25].

Numerous publications have demonstrated the high efficacy and safety of helical tomotherapy in cancer treatment [16, 20-22], including head and neck cancers [26, 27], gastrointestinal malignancies [26], breast cancer (without regional lymph node metastasis) [18], inoperable stage III NSCLC [28], and localized prostate cancer in elderly patients [29, 30]. On the other hand, the presence of comorbidities increases the risk of developing toxic conditions during tomotherapy. For example, in patients with compromised immune status, the risk of pulmonary complications (e.g., pneumonia) increases during craniospinal irradiation with helical tomotherapy [31]. The same applies to the risk of complications in patients with comorbid cardiovascular conditions. Specifically, the risk of cardiotoxicity is directly related to the absorbed radiation dose delivered to the heart or its structures [32]. Helical tomotherapy, when combined with IMRT/IGRT, reduces this risk by minimizing the dose to the left ventricle and the left anterior descending artery compared with 3D-conformal radiation therapy [12, 33].

The role of computed tomography in the treatment and diagnostics of oncology patients (with or without cardiopathology) is evident. In particular, regarding myocardial pathophysiology, this method enables visualization and assessment of calcium accumulation, facilitating earlier detection of atherosclerotic lesions in cardiac vessels [34]. On the other hand, further clarification and continued data accumulation are required to conduct a more detailed analysis of the short- and long-term outcomes in patients with comorbidities. The results presented in this article are generally consistent with previously published data on the efficacy and safety of tomotherapy in oncology patients with cardiovascular disorders. Our quantitative assessments demonstrate that tomotherapy is an effective and safe treatment option for NSCLC, even in patients with significant cardiac pathology. However, to ensure the necessary level of safety and to reduce the risk of complications, at least three conditions must be met: 1) incorporation of PMs, ICDs, and bypass grafts into the treatment plan as risk structures, in order to minimize radiation exposure to these devices; 2) use of the IMRT mode to achieve the most uniform radiation dose distribution to the target, taking into account its anatomical and morphological features; 3) application of IGRT to ensure high precision in beam positioning and to monitor tumor and adjacent structure dynamics during each treatment session. In addition, the more frequent use of hypofractionated regimens in patients with cardiopathology may have contributed to the lower rates of complete tumor regression and higher incidence of oncological process progression observed in this group. Nevertheless, reduced radiation intensity is necessary in such patients to preserve the heart's functional characteristics and minimize the risk of interference with implanted cardiac devices.

**Conclusion:** Helical tomotherapy in patients with NSCLC and coexisting cardiopathology demonstrated a fairly high efficacy, albeit lower than in patients without cardiac condi-

tions, in terms of complete regression and disease progression. One- and two-year overall survival rates were lower in patients with cardiopathology, although this may have been due to causes of death unrelated to cancer, such as complications arising from cardiovascular disease. Tomotherapy showed high safety and satisfactory tolerability, with infrequent side effects, in patients with cardiopathology. Key safety factors included contouring cardiac devices and bypass grafts as critical structures, strict dose control, IMRT, and daily IGRT. The experience of the UMIT International Tomotherapy Oncology Center confirms the feasibility of delivering relatively safe treatment in this patient population, provided that a personalized approach, rigorous dosimetric control, and interdisciplinary monitoring are implemented.

### References:

1. Bray F., Laversanne M., Sung H., Ferlay J., Siegel R.L., Soerjomataram I., Jemal A. *Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries // CA Cancer J. Clin.* – 2024. – Vol. 74(3). – P. 229-263. <https://doi.org/10.3322/caac.21834>
2. Siegel R.L., Giaquinto A.N., Jemal A. *Cancer statistics, 2024 // CA Cancer J Clin.* – 2024. – Vol. 74(1). – P. 12-49. <https://doi.org/10.3322/caac.21820>
3. Kratzer T.B., Bandi P., Freedman N.D., Smith R.A., Travis W.D., Jemal A., Siegel R.L. *Lung cancer statistics, 2023 // Cancer.* – 2024. – Vol. 130(8). – P. 1330-1348. <https://doi.org/10.1002/cncr.35128>
4. Yessenbayev D., Khamidullina Z., Tarzhanova D., Orazova G., Zhakupova T., Kassenova D., Bilyalova Z., Igissinova G., Sayakov U., Dzhumabayeva F., Imankulova A., Idrissov K., Urazova S., Omarbekov A., Turebayev D., Adabayev K., Kozhakhmetov S., Rustemova K., Telmanova Z., Kudaibergenova I., Igissinov N. *Epidemiology of Lung Cancer in Kazakhstan: Trends and Geographic Distribution // Asian Pac J Cancer Prev.* – 2023. – Vol. 24(5). – P. 1521-1532. <https://doi.org/10.31557/APJCP.2023.24.5.1521>
5. Akhmedullin R., Aimyshev T., Zhakhina G., Yerdessov S., Beyembetova A., Ablayeva A., Biniyazova A., Seyil T., Abdulkhakimova D., Segizbayeva A., Semenova Y., Gaipov A. *In-depth analysis and trends of cancer mortality in Kazakhstan: a joinpoint analysis of nationwide healthcare data 2014-2022 // BMC Cancer.* – 2024. – Vol. 24(1). – P. 1340. <https://doi.org/10.1186/s12885-024-13128-2>
6. Panina A., Kaidarova D., Zholdybay Z., Ainakulova A., Amankulov J., Toleshbayev D., Zhakenova Z., Khozhayev A. *Lung Cancer Screening With Low-dose Chest Computed Tomography: Experience From Radon-contaminated Regions in Kazakhstan // J Prev Med Public Health.* – 2022. – Vol. 55(3). – P. 273-279. <https://doi.org/10.3961/jpmph.21.600>
7. Rakhimbekova F., Kaidarova D.R., Orazgalieva M., Ryspambetov Z., Buzdin A., Anapiyayev B. *Cancer Incidence Relation to Heavy Metals in Soils of Kyzylorda Region of Kazakhstan // Asian Pac J Cancer Prev.* – 2024. – Vol. 25(6). – P. 1987-1995. <https://doi.org/10.31557/APJCP.2024.25.6.1987>
8. Kassymbekova F., Glushkova N., Dunenova G., Kaidarova D., Kissimova-Skarbek K., Wengler A., Zhetpisbayeva I., Shatkovskaya O., Andreyeva O., Davletov K., Auyezova A., Rommel A. *Burden of major cancer types in Almaty, Kazakhstan // Sci Rep.* – 2024. – Vol. 14(1). – P. 20536. <https://doi.org/10.1038/s41598-024-71449-5>
9. de Crevoisier R., Lafond C., Mervoyer A., Hulot C., Jaksic N., Bessières I., Delpont G. *Image-guided radiotherapy // Cancer Radiother.* – 2022. – Vol. 26(1-2). – P. 34-49. <https://doi.org/10.1016/j.canrad.2021.08.002>
10. Dennis K., Linden K., Gaudet M. *A shift from simple to sophisticated: using intensity-modulated radiation therapy in conventional nonstereotactic palliative radiotherapy // Curr Opin Support Palliat Care.* – 2023. – Vol. 17(1). – P. 70-76. <https://doi.org/10.1097/SPC.0000000000000639>
11. Duma M.N., Heinrich C., Schönknecht C., Chizzali B., Mayinger M., Devecka M., Kampfer S., Combs S.E. *Helical Tomotherapy for locally advanced or recurrent breast cancer // Radiat Oncol.* – 2017. – Vol. 12(1). – P. 31. <https://doi.org/10.1186/s13014-016-0736-1>
12. Palumbo I., Marcantonini M., Scialpi M., Bini V., Di Benedetto M., Nucciarelli S., Fulcheri C., Perrucci E., Aristei C. *Heart and Coronary Artery*



- Dose Sparing in Left-sided Breast Cancer: 3D-Conformal Radiotherapy vs. Helical Tomotherapy // *In Vivo*. – 2023. – Vol. 37(6). – P. 2760-2767. <https://doi.org/10.21873/invivo.13387>
13. O'Neill C., Donnelly D.W., Harbinson M., Kearney T., Fox C.R., Walls G., Gavin A. Survival of cancer patients with pre-existing heart disease // *BMC Cancer*. – 2022. – Vol. 22(1). – P. 847. <https://doi.org/10.1186/s12885-022-09944-z>
14. Hernandez D., Cheng C.Y., Hernandez-Villafuerte K., Schlander M. Survival and comorbidities in lung cancer patients: Evidence from administrative claims data in Germany // *Oncol. Res.* – 2023. – Vol. 30(4). – P. 173-185. <https://doi.org/10.32604/or.2022.027262>
15. Batra A., Sheka D., Kong S., Cheung W.Y. Impact of pre-existing cardiovascular disease on treatment patterns and survival outcomes in patients with lung cancer // *BMC Cancer*. – 2020. – Vol. 20(1). – P. 1004. <https://doi.org/10.1186/s12885-020-07487-9>
16. Lin B., Gao F., Yang Y., Wu D., Zhang Y., Feng G., Dai T., Du X. FLASH Radiotherapy: History and Future // *Front Oncol.* – 2021. – Vol. 11. – Art. no. 644400. <https://doi.org/10.3389/fonc.2021.644400>
17. Hatano K., Tohyama N., Kodama T., Okabe N., Sakai M., Konoeda K. Current status of intensity-modulated radiation therapy for prostate cancer: History, clinical results and future directions // *Int J Urol.* – 2019. – Vol. 26(8). – P. 775-784. <https://doi.org/10.1111/iju.14011>
18. Zwicker F., Klepper R., Hauswald H., Hoefel S., Raether L., Huber P.E., Debus J., Schempp M. Helical Tomotherapy of Lymph Node-negative Early-stage Breast Cancer After Breast-conserving Surgery: Long-term Results // *Anticancer Res.* – 2023. – Vol. 43(5). – P. 2041-2053. <https://doi.org/10.21873/anticancerres.16365>
19. Takaoka T., Shibamoto Y., Murai T., Kobayashi M., Sugie C., Manabe Y., Kondo T., Okazaki D., Yamada Y., Torii A. Helical tomotherapy for chemo-refractory multiple liver metastases // *Cancer Med.* – 2019. – Vol. 8(18). – P. 7594-7602. <https://doi.org/10.1002/cam4.2651>
20. Sun M., Wang L.L., Wang S.Q., Lin X., Zhou W. Dosimetry comparison with helical tomotherapy, volumetric modulated arc therapy, and intensity-modulated radiotherapy for grade II gliomas: A single-institution case series // *Open Life Sci.* – 2023. – Vol. 18(1). – P. 20220550. <https://doi.org/10.1515/biol-2022-0550>
21. Turcas A., Kelly S.M., Clementel E., Cernea D. Tomotherapy for cranio-spinal irradiation // *Clin Transl Radiat Oncol.* – 2022. – Vol. 38. – P. 96-103. <https://doi.org/10.1016/j.ctro.2022.11.003>
22. Nien H.H., Hsieh C.H., Shueng P.W., Tien H.J. Total Skin Treatment with Helical Arc Radiotherapy // *Int J Mol Sci.* – 2023. – Vol. 24(5). – P. 4492. <https://doi.org/10.3390/ijms24054492>
23. Gallio E., Sardo A., Badellino S., Mantovani C., Levis M., Fiandra C., Guarneri A., Arcadipane F., Richetto V., Ricardi U., Giglioli F.R. Helical tomotherapy and two types of volumetric modulated arc therapy: dosimetric and clinical comparison for several cancer sites // *Radiol Phys Technol.* – 2023. – Vol. 16(2). – P. 272-283. <https://doi.org/10.1007/s12194-023-00716-3>
24. Ferris W.S., Kissick M.W., Bayouth J.E., Culbertson W.S., Smilowitz J.B. Evaluation of radixact motion synchrony for 3D respiratory motion: Modeling accuracy and dosimetric fidelity // *J Appl Clin Med Phys.* – 2020. – Vol. 21(9). – P. 96-106. <https://doi.org/10.1002/acm2.12978>
25. Bertholet J., Vinogradskiy Y., Hu Y., Carlson D.J. Advances in Image-Guided Adaptive Radiation Therapy // *Int J Radiat Oncol Biol Phys.* – 2021. – Vol. 110(3). – P. 625-628. <https://doi.org/10.1016/j.ijrobp.2021.02.047>
26. Shaukat F., Ahmed Y., Tahseen R., Mahmood T. Clinical Outcomes of Definitive Radiotherapy Delivered by Helical Tomotherapy // *J Coll Physicians Surg Pak.* – 2025. – Vol. 35(1). – P. 66-70. <https://doi.org/10.29271/jcpsp.2025.01.66>
27. Mayo Z.S., Ileri E.O., Matia B., Smile T.D., Fleming C.W., Reddy C.A., Scharpf J., Lamarre E.D., Prendes B.L., Ku J., Burkey B.B., Joshi N.P., Woody N.M., Koyfman S.A., Campbell S.R. Limited Toxicity of Hypofractionated Intensity Modulated Radiation Therapy for Head and Neck Cancer // *Anticancer Res.* – 2022. – Vol. 42(4). – P. 1845-1849. <https://doi.org/10.21873/anticancerres.15660>
28. Zhang Q., Fan S., Xu X., Du S., Zhu G., Jiang C., Xia S.A., Li Q., Wang Q., Qian D., Zhang M., Xiao H., Chen G., Zeng Z., He J. Efficacy and Toxicity of Moderately Hypofractionated Radiation Therapy with Helical Tomotherapy Versus Conventional Radiation Therapy in Patients with Unresectable Stage III Non-Small Cell Lung Cancer Receiving Concurrent Chemotherapy: A Multicenter, Randomized Phase 3 Trial // *Int J Radiat Oncol Biol Phys.* – 2024. – Vol. 120(2). – P. 422-431. <https://doi.org/10.1016/j.ijrobp.2024.03.030>
29. Cui D., Du L., Yu W., Cai B., Meng L., Yang J., Luo Y., Chen J., Ma L. Moderate hypofractionated helical tomotherapy for older patients with localized prostate cancer: long-term outcomes of a phase-II trial // *Radiol Oncol.* – 2022. – Vol. 56(2). – P. 216-227. <https://doi.org/10.2478/raon-2022-0011>
30. Cozzi S., Ruggieri M.P., Ali E., Ghersi S.F., Vigo F., Augugliaro M., Giaccherini L., Iori F., Najafi M., Bardoscia L., Botti A., Trojani V., Ciammella P., Iotti C. Moderately Hypofractionated Helical Tomotherapy for Prostate Cancer: Ten-year Experience of a Mono-institutional Series of 415 Patients // *In Vivo*. – 2023. – Vol. 37(2). – P. 777-785. <https://doi.org/10.21873/invivo.13141>
31. Lee J., Kim E., Kim N., Suh C.O., Chung Y., Yoon H.I. Pulmonary toxicity of craniospinal irradiation using helical tomotherapy // *Sci Rep.* – 2022. – Vol. 12(1). – P. 3221. <https://doi.org/10.1038/s41598-022-07224-1>
32. Ratosa I., Ivanetic Pantar M. Cardiotoxicity of mediastinal radiotherapy // *Rep Pract Oncol Radiother.* – 2019. – Vol. 24(6). – P. 629-643. <https://doi.org/10.1016/j.rpor.2019.09.002>
33. Alshabanah M.O., Hegazy M.W., Moftah B., Shehadeh M. Helical Tomotherapy versus Conventional Technique for Post Mastectomy Left Sided Breast Cancer; Dosimetric Study // *Rev Recent Clin Trials.* – 2017. – Vol. 12(2). – P. 143-146. <https://doi.org/10.2174/1574887112666170201125913>
34. Lopez-Mattei J.C., Yang E.H., Ferencik M., Baldassarre L.A., Dent S., Budoff M.J. Cardiac Computed Tomography in Cardio-Oncology: JACC: CardioOncology Primer // *JACC CardioOncol.* – 2021. – Vol. 3(5). – P. 635-649. <https://doi.org/10.1016/j.jacc.2021.09.010>

## АҢДАТПА

## ЖҮРЕК-ҚАНТАМЫРЛАРЫНЫҢ ҚАТАРЛАС ПАТОЛОГИЯСЫ БАР ЕРЛЕРДЕ ӨКПЕ ОНЫҢ ЕМДЕУДЕГІ ТОМОТЕРАПИЯНЫҢ ТИІМДІЛІГІ («UMIT» ХАЛЫҚАРАЛЫҚ ОНКОЛОГИЯЛЫҚ ТОМОТЕРАПИЯЛЫҚ ОРТАЛЫҒЫНЫҢ ТӘЖІРИБЕСІ)

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**Өзектілігі:** Өкпенің ұсақ жасушалы емес қатерлі ісігі (NSCLC) көбінесе ер адамдарда миокард патологиясымен қатар диагноз қойылады. НМРЛ емдеу әдістерінің бірі сәулелік терапия болып табылады, алайда Қазақстанда кардиопатологиясы бар онкопациенттерде томотерапияның тиімділігі мен қауіпсіздігі бойынша зерттеулер іс жүзінде жүргізілген жайттар жоқ.

**Зерттеудің мақсаты:** Халықаралық онкологиялық Томотерапия «UMIT» орталығында (Астана, Қазақстан) NSCLC және ілеспе кардиопатологиясы бар пациенттерде моно-томотерапияны қолдануың клиникалық нәтижелерін бағалау болып табылады.

**Әдістері:** Зерттеуге «UMIT» орталығында 2020-2024 жылдары спиральды моно-Томотерапия курсынан өткен NSCLC бар 201 ер адам кіреді. Пациенттер 1-топқа бөлінеді-кардиопатологиясыз (N=139) және 2 – топ-ауыр ілеспе кардиопатологиямен (N=62). Курстың орташа ұзақтығы - 32 күн, процедураның орташа ұзақтығы – 15 минут, күніне бір рет, аптасына 5 күн. Емдеу тиімділігі ПЭТ-КТ және КТ деректері бойынша курс аяқталғаннан кейін 8-12 аптадан кейін бағаланды.

**Нәтижелері:** Толькерегрессия 1-топтағы пациенттерде, аурудың өрісуі 2-топтағы пациенттерде жиі байқалды. Көбінесе жауап 1-топта, онкологиялық процестің тұрақтануы 2-топта жиі кездеседі. 2-топта оң динамикасы бар пациенттердің үлесі 49% – 8 құрады, процестің анықталған тұрақтануын ескере отырып-84% - құрады. 1-топта жыл сайынғы жалты өмір

сүру деңгейі ІІІ және ІV кезеңдерде 84% және 74% құрады, сәйкесінше прогрессиясыз орташа ұзақтығы – 10,3 ай, ІІІ кезеңдегі екі жылдық өмір сүру деңгейі – 65%. 2-топта жыл сайынғы жалты өмір сүру деңгейі ІІІ және ІV кезеңдерде 76% және 63% құрады, сәйкесінше прогресс 8,1 прогрессиясыз орташа ұзақтығы, ІІІ кезеңдегі екі жылдық өмір сүру деңгейі 54%. 2-топта имплантацияланған құрылғы функциясының бұзылу жағдайлары тіркелмеген, коронарлық артерияны айналып өтуі бар екі пациентте уақытша ауруханаға жатқызууды қажет ететін жүрек жеткіліксіздігінің декомпенсациясы болған.

**Қорытынды:** Томотерапия ауыр қатар жүретін кардиопатологияда NSCLC емдеуде жоғары клиникалық тиімділікті көрсетеді, дегенмен жалты өмір сүру және емдеу тиімділігі кардиопатологиясы жоқ науқастарға қарағанда төмен көрсеткіштер байқалды. Біздің тәжірибеміз жекелендірілген тәсіл, қатаң дозиметриялық бақылау және пәнаралық бақылау принциптерін сақтай отырып, мұндай пациенттерде салыстырмалы түрде қауіпсіз емдеу мүмкіндігі бар екенін растайды.

**Түйінді сөздер:** өкпе рагы, томотерапия, кардиопатология, кардиостимулятор, гипофракция, жоғары дәлдіктегі сәулелік терапия.

## АННОТАЦИЯ

# ЭФФЕКТИВНОСТЬ ТОМОТЕРАПИИ В ЛЕЧЕНИИ РАКА ЛЁГКИХ У МУЖЧИН С СОПУТСТВУЮЩЕЙ СЕРДЕЧНО-СОСУДИСТОЙ ПАТОЛОГИЕЙ (ОПЫТ МЕЖДУНАРОДНОГО ОНКОЛОГИЧЕСКОГО ЦЕНТРА ТОМОТЕРАПИИ «UMIT»)

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**Актуальность:** Немелкоклеточный рак лёгкого (НМРЛ) часто диагностируется у мужчин в сочетании с патологиями миокарда. Одним из методов лечения НМРЛ является лучевая терапия, однако в Казахстане практически отсутствуют исследования эффективности и безопасности томотерапии у онкопациентов с кардиопатологиями.

**Цель исследования** – оценить клинические результаты применения моно-томотерапии у пациентов с НМРЛ и сопутствующими кардиопатологиями в Международном онкологическом центре томотерапии «UMIT» (Астана, Казахстан).

**Методы:** В исследование включен 201 мужчина с НМРЛ, прошедший курс спиральной моно-томотерапии в 2020-2024 годах в центре «UMIT». Пациенты разделены на Группу 1 – без кардиопатологий (n=139) и Группу 2 – с тяжёлыми сопутствующими кардиопатологиями (n=62). Средняя длительность курса – 32 дня, средняя продолжительность процедуры – 15 минут, один раз в день, 5 дней в неделю. Эффективность лечения оценивали через 8-12 недель после завершения курса по данным ПЭТ-КТ и КТ.

**Результаты:** Полный регресс чаще отмечался у пациентов Группы 1, прогрессирование заболевания – чаще у пациентов Группы 2. Частичный ответ чаще встречался в Группе 1, стабилизация онкологического процесса – чаще в Группе 2. В Группе 2 доля пациентов с положительной динамикой составила 49%, с учетом выявленной стабилизацией процесса – 84%. В Группе 1 одностепенная общая выживаемость составила 84% и 74% при ІІІ и ІV стадиях, соответственно, медианная продолжительность без прогрессирования – 10,3 месяцев, двухлетняя выживаемость при ІІІ стадии – 65%. В Группе 2 одностепенная общая выживаемость составила 76% и 63% при ІІІ и ІV стадиях, соответственно, медианная продолжительность без прогрессирования – 8,1 месяца, двухлетняя выживаемость при ІІІ стадии – 54%. В Группе 2 не зафиксировано случаев нарушения функции имплантированного устройства, у двух пациентов с аортокоронарным шунтированием была декомпенсация сердечной недостаточности, потребовавшая временной госпитализации.

**Заключение:** Томотерапия демонстрирует высокую клиническую эффективность при лечении НМРЛ при тяжёлой сопутствующей кардиопатологии, хотя общая выживаемость и эффективность лечения были ниже, чем у пациентов без кардиопатологий. Наш опыт подтверждает возможность сравнительно безопасного лечения у таких пациентов при соблюдении принципов персонализированного подхода, строгого дозиметрического контроля и междисциплинарного наблюдения.

**Ключевые слова:** рак лёгкого, томотерапия, кардиопатология, кардиостимулятор, гипофракционирование, высокоточная лучевая терапия.

**Transparency of the study:** Authors take full responsibility for the content of this manuscript.

**Conflict of Interests:** The authors declare no conflict of interest.

**Funding:** The study was conducted with the financial support of the Science Committee of the Ministry of Science and Higher Education of the Republic of Kazakhstan (IRN AP19680098).

**Authors Contribution:** Conceptualization, Study Design – D.K. Berikbol, A.M. Ganina, E.M. Shayakhmetov; Investigation, Validation – all authors; Writing – Original Draft Preparation – D.K. Berikbol, A.M. Ganina, E.M. Shayakhmetov, D.N. Idrissova.

**Acknowledgements:** The authors express their gratitude to the Candidate of Biological Sciences O.N. Lukin (National Scientific Medical Center, JSC) for assistance with scientific expertise and manuscript preparation.

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