Health Technol Assess Action 2026;10(2):65-70
doi:10.18502/htaa.v10i2.22223
https://htainaction.tums.ac.ir

Health Technology Assessment in Action

Original Article

Relationship between Blood Uranium Concentration and Tumor Size Using Contrast-enhanced Chest CT Scan in Patients with Lung Cancer

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Abstract

Introduction: Uranium has been known to pose a significant risk to human life, especially with increased serum concentrations. This study was conducted to investigate the relationship between blood uranium concentration and tumor size.

Methods: This case-control study with a convenience sampling technique was conducted at Specialized Oncology Center in Nasiriyah, Iraq, involving 40 lung cancer patients and 40 healthy individuals from February to August 2024. Pregnant females, participants under 40 years of age, and those with indeterminate imaging findings or no available follow-up data were excluded from the study. Venous blood samples of 3 mL were collected from each subject. Two techniques were used for analyzing blood samples using solid-state Nuclear track detectors (SSNTDs) named CR-39 detectors to determine serum uranium concentration in patients with lung cancer and healthy people. The serum isolation through centrifugation led to its deposition on CR-39 detectors before their subsequent drying. The samples were exposed to thermal neutrons for 6 days and an optical microscope was used to identify fission tracks. Computed Tomography (CT) was used for tumor staging and tumor size measurement. The materials used in the study included an Americium-Beryllium neutron source, etching solutions, a water bath, and an optical microscope. CT scans were performed on 40 lung cancer patients using a Siemens Somatom 64-slice CT Scanner. The statistical analysis was carried out using SPSS version 28.

Results: The results showed that patients with lung cancer were significantly older than healthy subjects, with males showing higher prevalence than females. The study shows that most of the patients with lung cancer were smokers. The study also found that patients with lung cancer had higher uranium concentrations in their blood than healthy subjects. The healthy subjects had higher uranium concentrations in Basrah than in Nasiriyah, and lung carcinoma patients had a higher concentration in blood serum in Al-Basrah than in Nasiriyah. Moreover, a strong significant positive correlation was found between the uranium level and tumor size.

Conclusion: There is a significant correlation between tumor growth and serum uranium levels, suggesting that uranium may have a role in the advancement of cancer.

Keywords: Uranium concentration, CA, Lung cancer, Tumor size, Nasiriyah, Basrah

Received: October 11, 2025, **Revised:** December 20, 2025, **Accepted:** February 5, 2026, **ePublished:** June 30, 2026

Introduction

Lung cancer is a major killer among cancer patients and is a major cause of morbidity worldwide, which presents a major health challenge (1). The etiology of the condition is not well understood, and the conditiosn is known to have various causes, including genetic predisposition, environmental factors, and lifestyle (2). Among these factors, contact with heavy metals, including uranium, has been proposed as a risk factor. Uranium is a naturally occurring radioactive chemical element that may be experienced through contact with minerals, workplace contact, water, or pollution. This substance is known to bioaccumulate in several organs and may have toxic and/or carcinogenic effects (3).

Researchers mentioned that the risk of lung cancer is associated with the level of exposure to uranium and pointed out that the issue has drawn rising concern in areas where higher geogenic uranium concentrations were reported (4). Biomarkers of uranium exposure are the level of uranium in whole blood and are associated with respiratory diseases and malignancies. However, the exact function of TGF-β in developing and staging cancer is not well explained (5).

Staging lung cancer is an important factor for assessing outcomes and planning management. It offers information about the prevalence of infection and aids in patient management (6). Contrast-enhanced chest computed tomography (CT) scans are essential tools for diagnostic and staging proposals and enable visualization of tumor characteristics, lymph node engagement, and metastatic patterns. Combining imaging data with functional biomarkers such as blood uranium level may help understand transportation and disequilibrium processes (7).

Serum uranium concentration and the extent of exposure are other factors that provide necessary information for health risk assessment (8). Technological development has provided new detector systems to better determine the concentration of uranium in different biological samples. This method includes using Solid State Nuclear Track Detectors (SSNTDs) focusing on the CR-39 nuclear track detector. This technique has the advantage of high sensitivity and reliability in determining alpha particles associated with uranium isotopes for environmental and biomedical applications (9).

This research aims to evaluate the correlation between blood uranium concentration and tumour size in patients with lung cancer using a CR-39 nuclear track detector and measuring tumor size.

Materials and Methods

The present case-control study with a convenience sampling technique was done in Dhiqar Specialized Oncology Center at Al-Haboubi Teaching Hospital from February 2024 to August 2024. The study included 40 patients with lung cancer and 40 healthy individuals. Participants were asked questions related to basic demographic information, smoking behaviors, and medical history. Pregnant women, patients less than 40 years of age, and those with indeterminate imaging or no available follow-up data were excluded from the study.

The study was undertaken in Basrah and Nasiriyah governorates in Southern Iraq, which suffered the impacts of the 1991 and 2003 Gulf Wars. These areas have shown high concentrations of uranium, leading to environmental pollution and increased cancer incidences.

Briefly, a blood sample of 3 mL was collected from each patient and healthy control subject. It was collected into a heparinized tube and was centrifuged to obtain serum, which was kept at 4°C until assayed. Two methods were employed: microchemical analysis using Solid-State Nuclear Track Detectors (SSNTDs) for analysis of concentrations of uranium in blood serum and Computed Tomography (CT) for tumor staging and tumor size following the TNM classification. The materials employed in the study included CR-39 detectors, an Americium-Beryllium neutron source, etching solutions, a water bath, and an optical microscope. Additionally, micropipettes, centrifuges, and syringes were used for sample preparation and measurement.

The serum samples were deposited on the surface of CR-39 detectors by the drop method, allowed to dry and then formed in a "sandwich" structure for irradiation. Standard samples were prepared by adding uranium into the sample solutions, which was recommended by the International Atomic Energy Agency (IAEA) for calibration standards. A total of 20 samples were exposed to thermal neutrons for 7 days, and uranium concentrations were determined using the optical microscope. Computed tomography scans of 40 patients with lung cancer were done with Siemens Somatom 64-slice CT scanner.

Standard samples were prepared using uranium concentrations provided by the IAEA for measurement calibration. Samples were exposed to the neutron thermal flux for a week, and fission tracks were observed with an optical microscope to determine uranium concentrations using standard curves.

Low-dose CT scans were taken from 40 lung cancer patients using a Siemens Somatom 64-slice CT Scanner. Patients were placed in a supine position with an MDCT scan performed with and without contrast material (Omnipaque 350 mg/mL). Tumor size and the T, N and M stages were quantified regarding CT images using the TNM staging system.

The statistical analysis was performed using SPSS version 28. Chi-square was used to show patients' characteristics. A paired *t*-test was used to explore the significance of the correlation between two dependent variables, while an unpaired *t*-test was used for independent variables. The Pearson correlation test was used to check the correlation between two variables. A regression analysis curve was used to evaluate the linear correlation between the two variables. The difference between two variables was considered significant if the *P*-value was equal to or less than 0.05.

Results

The characteristics of healthy subjects and patients with lung carcinoma included in this study are shown in Table 1. The analysis showed that the age of patients with lung cancer was significantly higher than that of the healthy subjects. Males showed higher prevalence than females without any significant difference. The subjects selected for this study were collected from two states: Nasiriyah and Basrah. Based on the results, 50% of the healthy subjects were recruited from Basrah, and the other 50% were recruited from Nasiriyah.

Additionally, 42.5% of the patients with lung carcinoma were from Nasiriyah and 57.5% from Basrah. Most healthy subjects were classified as housewives, followed by retired employees, military personnel, taxi drivers, and teachers, respectively. On the other hand, most of the patients with lung cancer were military personnel, followed by housewives, farmers, petroleum engineers, teachers, ceramic workers, and retired employees, respectively. Most subjects, whether healthy or patients with lung cancer, were smokers.

Table 2 shows the comparison between healthy subjects and Lung cancer patients in terms of overall serum uranium concentration. The statistical analysis shows that the patients with lung carcinoma have a significantly higher uranium concentration in their blood than the healthy subjects, as shown in Figure 1.

Healthy subjects and patients with lung cancer were compared regarding their smoking habits and serum uranium concentration, as shown in Table 3. The mean serum uranium concentration of smokers was 1.17 ± 0.22 μg/L in healthy subjects and it was 1.44 ± 0.31 μg/L in

Table 1. Characteristics of Subjects Included in this Study

Characteristics	Healthy subjects	Lung cancer patients	*P*-value
Age (Years)	52.32 ± 8.61	60.3 ± 8.68	≤0.0001*
Gender			
Male	24 (60%)	27 (67%)	0.485351
Female	16 (40%)	13 (33%)	
Province			
Nasiriyah	20 (50%)	17 42.5 %)	
Basrah	20 (50%)	23(57.5%)	
Work			
Housewife	17 (43%)	7 (17%)	
Military personnel	8 (20%)	11 (28%)	
Teacher	3 (7%)	4 (10%)	
Farmer	0	6 (15%)	
Petroleum engineer	0	5 (12%)	
Ceramic worker	0	3 (8%)	
Taxi driver	3 (7%)	0	
Retried employee	9 (23%)	4 (10%)	
Smoking habits			
Smoker	24 (60%)	27 (67%)	
Non-smoker	16 (40%)	13 (33%)	

* Significant difference at $P \leq 0.05$

Table 2. Overall Serum Uranium Concentration

	Healthy subjects	Lung cancer patients	*P*-value
Serum uranium concentration (µg/L)	1.02 ± 0.07	1.31 ± 0.106	≤0.0001*

* Significant difference at $P \leq 0.05$

Table 3. The Effects of Smoking Habits on Serum Uranium Concentration

	Healthy subjects	Lung cancer patients	*P*-value
Smoker	1.17 ± 0.22	1.44 ± 0.31	0.00270*
Non-Smoker	0.92 ± 0.15	1.05 ± 0.23	0.10700
P-value	0.00015*	0.000802*	

* Significant difference at $P \leq 0.05$

patients with lung cancer, indicating a highly significant difference between healthy smokers and smokers with lung cancer ($P = 0.00270$). On the other hand, the mean concentration of uranium in non-smokers was 0.92 ± 0.15 µg/L among the healthy women and 1.05 ± 0.23 µg/L among women with lung cancer, without a statistically significant difference ($P = 00.10700$). The results showed that smokers and non-smokers had significantly different concentrations of serum uranium, with lung cancer patients having a relatively higher *P*-value (0.000802) than the other group (0.00015). These post-implementation outcomes provided more information on smoking and its possible effects on serum uranium concentration, as shown in Figure 2.

Table 4 shows the distribution of healthy subjects and patients with lung carcinoma in two provinces: Nasiriyah and Basrah. The results showed that uranium concentrations of healthy subjects were significantly higher in Basrah than in Nasiriyah. Additionally, a

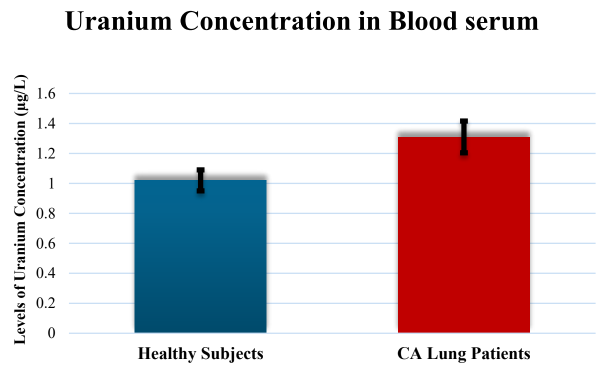

Figure 1. Comparison between the Healthy Subjects and Lung Cancer Patients in Terms of Overall Serum Uranium Concentration

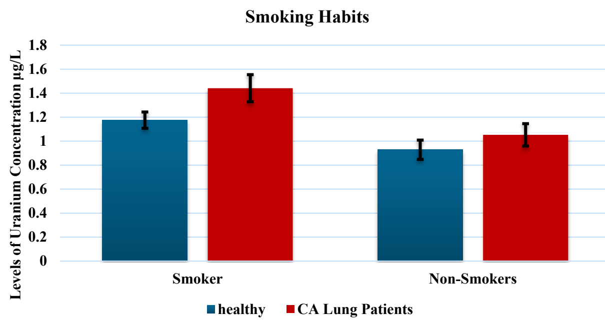

Figure 2. Comparison between Healthy Subjects and Patients with Lung Cancer in Terms of Smoking Habits and Serum Uranium Concentration

significantly higher serum uranium concentration was found in lung carcinoma patients who lived in Al-Basrah, followed by Nasiriyah, as shown in Figure 3. The results also showed that lung cancer patients had significantly higher serum concentrations of uranium than healthy participants.

A correlation statistical test was used to evaluate the relationship between the tumor size of patients with lung carcinoma and their serum uranium concentration, the results of which are shown in Table 5. A significant strong positive correlation was found between the tumor size and the serum uranium concentration, as shown in Figure 4.

Discussion

The study established that elevated bloodstream uranium levels affect tumour size in lung cancer patients in uranium-tainted areas. Blood serum uranium measurements demonstrated statistically higher levels among patients with lung cancer versus healthy participants ($P = 0.0001$). The lung cancer patients from Al-Nasiriyah had a mean uranium concentration of 1.34 ± 0.10 µg/L while healthy subjects had a mean uranium concentration of 1.02 ± 0.09 µg/L ($P = 0.0069$). Blood tests conducted in Basrah revealed a significant difference between the patients (1.75 ± 0.15 µg/L) and the control group (1.03 ± 0.06 µg/L) ($P = 0.0022$). Results showed that residents of Basrah had higher uranium concentration than residents of Al-Nasiriyah ($P = 0.0168$) because Basrah had more industrial activities and environmental contamination from the Gulf Wars.

Table 4. Serum Uranium Concentration in Healthy Individuals and Patients with Lung Cancer Based on the Place of Residence

	Healthy subjects	Lung cancer patients	*P*-value
Nasiriyah	1.02 ± 0.09	1.34 ± 0.10	0.0069*
Basrah	1.03 ± 0.06	1.75 ± 0.15	0.0022*
P-value	0.921	0.016849*	

* Significant difference at $P \leq 0.05$

Table 5. Correlation between Tumor Size and Serum Uranium Concentration in Patients with Lung Cancer Considering the Maximum Diameter of the Tumor

	Max.diameter (mm)	Uranium concentration	r	*P*-value
Mean	48.15	1.31	0.9351	≤0.0001*
Standard deviation (SD)	25.04	0.34		
Minimum	10	0.8		
Maximum	120	2.51		

* Significant difference at $P \leq 0.05$

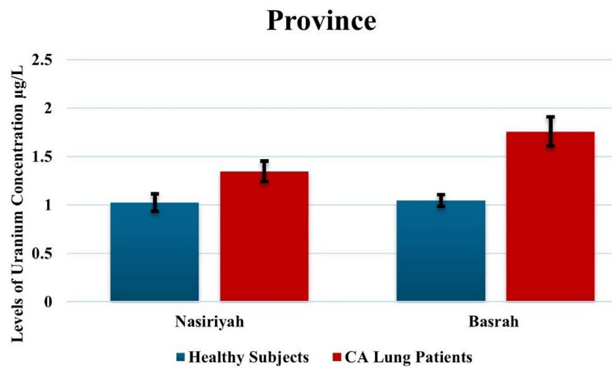

Figure 3. Serum Uranium Concentration among Healthy Subjects and Patients with Lung Cancer Based on the Place of Residence

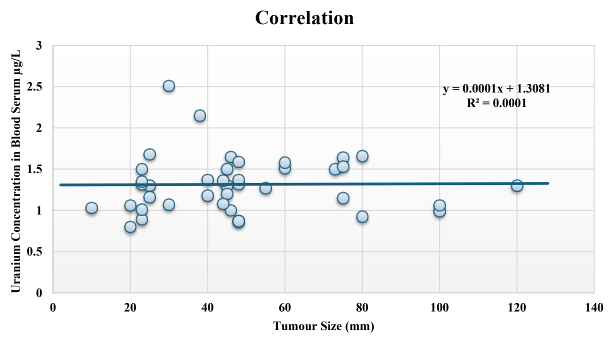

Figure 4. Correlation of the Maximum Diameter (mm) of the Tumor with Serum Uranium Concentration among Lung Cancer Patients

Smoking increased existing uranium levels in patients with lung cancer. Smokers diagnosed with lung cancer presented with a mean serum uranium level of 1.44 ± 0.31 µg/L, but non-smokers showed a lower mean uranium concentration (1.05 ± 0.23 µg/L) ($P = 0.0008$). Uranium values showed a robust statistical correlation with cancer tumour dimensions in the study ($P \leq 0.0001$). Lung tumors 10 mm in diameter showed a serum uranium level of 0.8 µg/L, and the uranium measurements in tumors 120 mm in diameter reached 2.51 µg/L, demonstrating a link between tumor dimensions and uranium concentrations.

The findings of the present study indicated higher serum uranium levels in subjects with lung carcinoma than in the control group, suggesting a possible link between uranium levels and presence or progression of lung cancer. Similarly, Shankar et al (2019) (10) revealed increased concentrations of uranium in cancer patients and attributed those high levels to environmental risks in areas with intense uranium mining activities. Moreover, Ma et al (2020) (3) observed that uranium affects total health by contributing to respiratory diseases and elevating the risk of cancer; therefore, uranium is considered dangerous to human health. The growing airborne uranium levels result from environmental contamination, including military operations, industrial waste dumps, and natural uranium concentrations in geological structures. The Gulf Wars produced considerable uranium contamination that lasted as an ongoing pollution threat for Basrah from abandoned uranium-based weapons. Based on these findings, uranium could be another area often overlooked but strongly related to cancer promotion. Moreover, epidemiological studies of Tomasek et al (2008) (11) provided consistent and convincing evidence of the increased risk of lung cancer among uranium miners. These studies proved that lung cancer risk is associated with alpha particle exposure from 222Rn and its decay products, which arise from the decay of 238U.

Smoking causes an increase in the accumulation of uranium because uranium-isotope-bearing toxins, as well as carcinogens in tobacco smoke, cause elevated DNA mutations while increasing oxidative stress. This finding supports the result presented by Richardson et al (2022) (12) who found an additive effect between smoking and uranium on developing lung cancer. In their case, they observed that the risk of developing lung carcinoma was high among smokers who had been exposed to uranium as compared to non-smokers. Rostron et al (2021) (13) also realized that smoking history and uranium have biomarkers that trigger lung damage, supporting earlier findings that have established the dangerous prospect of smoking and uranium exposure to the health of the lungs.

A strong relationship exists between tumor dimensions and uranium concentration because cancer cells with elevated metabolism tend to absorb more uranium. Metabolic disturbances from chronic inflammation and altered metal metabolism in cancer patients may contribute to increased uranium levels in their bodies. These findings are consistent with the results of the study done by Coradduzza et al (2024) (14). They discovered that patients with increased tumor size were exposed to environmentally toxic substances, including uranium, and had more advanced diseases. Kelly-Reif et al (2020) (15) also reinforced these findings by stating that uranium was detected at high concentrations in the serum of advanced-stage lung cancer patients compared to the controls, pointing to uranium exposure as one way of enhancing tumor growth.

For strengthening this study, the observational results backed by significant statistics showcase how exposure to uranium impacts lung cancer progression according to this study. The research offers a complete comparison based on uranium examinations between lung cancer patients and healthy people throughout the industrialized Basrah area versus the less industrialized Al-Nasiriyah region. Additional depth in the analysis comes from studying how smoking acts as an independent risk factor. Tumor size measurements alongside uranium analyses in this study give researchers fresh perspectives on the potential of uranium as a marker for cancer development. The study adds to prior research by presenting its results using benchmark data from existing scientific publications.

The weaknesses of this study include inadequate reporting regarding the duration and intensity of uranium exposure among participants, which leads to uncertainties about the definitive accuracy of key findings in this research. Serum uranium testing as a singular measure to detect exposure fails to account for all environmental and lifestyle factors which contribute to the development of lung cancer. A complete investigation of confounding factors, including occupational hazards, genetic predisposition, and dietary habits, failed to occur in this study.

The limitation of this study is that the observational setup of this study prevents investigators from using data to prove that uranium exposure directly triggers lung cancer formation. The research lacks information about varying uranium exposure pathways from water, air, and food, and it does not assess enduring health repercussions from minimal uranium intake.

The present study proves that uranium contamination stands out as a primary cause of lung cancer advancement, combined with environmental contamination patterns along with tobacco use habits. Research has shown that above-average serum uranium concentrations have the potential to be used as both a biomarker for tumor progression and an environmental hazard assessment tool.

Conclusion

The study validated the associations between uranium concentration in test samples and tumor size, indicating that uranium exposure potentially drives cancer advancement. The discovered relationship demonstrates the capacity of uranium to grow lung cancer cells in environments where contamination occurs and among smokers. Evidence shows that toxic uranium exposure leads to cancer development while also demonstrating how air contamination combines with smoking behavior risks. The research findings match earlier studies demonstrating that uranium clean-up operations must be treated as fundamental public health issues. Based on the findings presented in this research, areas affected by military operations and industrial pollution need greater long-term health risk awareness.

Authors' Contribution

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Project administration: Nada Fadhil Twafiq
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Validation: Nada Fadhil Twafiq
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Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

This study was approved by Institution Review Board (IRB) of College of Medicine at Al-Nahrain University (20231130 at 24/12/2023).

Funding

Self-funding.

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