ISSN 2689-8268 | Volume 2

American Journal of Surgery and Clinical Case Reports

Research Article Open Access

# Features of Radiation-Induced Thyroid Cancer

**Stojarov AN*and Khrustalev VV**

[1]Department of Radiation Medicine and Ecology, Belarusian State Medical University, Belarus

[2]Head of Department of General Chemistry, Belarusian State Medical University, Belarus

***Corresponding author:**

Alexander N. Stojarov,
Belarusian State Medical University,
pr. Dzerzhinskogo 83, 220116, Minsk,
Belarus, Phone:+375297560223,
E-mail: stojarov@mail.ru

Received: 03 Mar 2021
Accepted: 29 Mar 2021
Published: 03 Apr 2021



**Citation:**

Stojarov AN, Features of Radiation-Induced Thyroid Cancer. Ame J Surg Clin Case Rep. 2021; 2(8): 1-7.

**Keywords:**

Thyroid Cancer; Radioiodine; Chernobyl Accident; Radiation Risk

## 1. Features of Radiation-Induced Thyroid Cancer

A significant part of research on Thyroid Cancer (TC) incidence changes after nuclear disasters concerns mainly the dose effects on this oncopathology, as well as radiation epidemiology. Meanwhile, the features of this disease like gender characteristics of the stages and histological forms of cancer are of particular interest. The incidence and risks of various stages and forms of TC were analyzed in the present study. The analysis was carried out according to the data from the Belarusian Cancer Register. The control group of patients was taken from the Lepel and Chashniky districts of the Vitebsk region, which was not contaminated with iodine isotopes. In the territories contaminated after the accident at the Chernobyl nuclear power plant in 1986, cancer diagnostics took place mainly at the T1 stage, but in relatively "clean" regions of the republic – at T3 stage. In the population of the contaminated areas, the incidence was 2.5 – 3 times higher. In the age group 0 – 4 years at the moment of the accident, TC in women was more often detected at the T1 stage, while in men it was more often detected at T2. In the same group, there were frequent cases of detection of cancer at the stage T4, which was characterized by a latency period of 6 – 11 years. Basically, the patients had two forms of cancer: papillary tumor in the follicular variant (8340/3) and papillary adenocarcinoma (8260/3). In men, radiation genesis was mainly associated with papillary adenocarcinoma [18.24 (95% CI; 4.15..80.26)] and, to a lesser extent, with the second form of cancer. These data, as well as the high incidence of thyroid cancer in women, may be associated with the influence of other factors, including non-radiation nature.

## 2. Introduction

About 35 years have passed since the Chernobyl accident, which is considered the largest radiation disaster in the world. For many medical consequences of the radiation, the latency period has passed and therefore changes in the incidence in the affected population should be analyzed in detail. A significant part of the inhabitants of Belarus found themselves under the influence of a radioactive cloud ejected from the damaged reactor, continue to live in areas contaminated with radionuclides and consume contaminated food. All these factors contributed to the formation of effective doses for the population. Analysis of the influence of those factors on the incidence is of a great interest to scientists from around the world.

One of the main consequences of radiation that occurred very soon after the accident at nuclear power plant was thyroid pathology. This was due to the fact that one of the fission products of uranium nuclei is a mixture of iodine radionuclides, that was released in huge quantity into the environment. Iodine is a biogenic element that is required by the human thyroid gland for the synthesis of thyroid hormones. When radioactive iodine (I-131) was released in the environment, it accumulated in thyroid glands of residents of affected areas. Thyroid gland is quite radiosensitive, so the decay of I-131 forms the absorbed dose in this organ, that may be associated with the subsequent appearance of pathology, including cancer development. Actually, Thyroid Cancer (TC) is one of the main well-known diseases that make researchers and medical staff beware the consequences of radiation accidents. There is a large number of studies on to this problem [1,2,3]. However, a

significant part of them concerns mainly the dose effects on this oncopathology, as well as radiation epidemiology. There is a lack of information on the characteristics of TC caused by radiation, its morphological characteristics, forms and severity of the disease [4].

All the above mentioned characteristics of this radiation-induced pathology served as the basis for this study.

## 3. Methods

The incidence of TC in 1986 – 2016 was provided by the Belarusian Cancer Register. For the analysis, the data were taken on persons of different ages and both sexes, who lived in the territory of two districts of the Brest region (Stolin and Luninets) in April – May 1986. A radioactive cloud ejected from the damaged 4th unit of the Chernobyl nuclear power plant passed through these areas in the night of April 26, 1986. As a result, the territory was contaminated by iodine-131, cesium-137, strontium-90 and other radionuclides [5]. In the first period after the accident, radioactive iodine entered the body of residents through inhalation, a little later, the main route of its incorporation into the body was the alimentary one, mainly due to the consumption of whole milk. Protective measures (blockade of the thyroid gland with stable iodine, a ban on the use of whole milk, etc.), in general, were not carried out.

The analysis included residents of rural areas only due to their subsequent minimal migration from the "center" to the "periphery", i.e. in the direction of moving to the country. This allowed us to assume the presence of persons with a diagnosis of TC established in the next 30-year period in the same settlement where they had been at the time of the Chernobyl accident.

Since in the previous analysis of TC incidence among residents affected by the Chernobyl accident, which was carried out by UNSCEAR experts in 2016, age groups were identified, in this study we used this approach and in the studied cohort we identified the following age groups according to their ages at the moment of the accident at the Chernobyl nuclear power plant: 0 – 4 years, 5 – 9 years, 10 – 14 years, and 15 – 18 years [6]. In total, the cohort of residents of the Stolin and Luninets districts included 99,900 residents of rural settlements. Of these, 47,300 were males and 52,600 were females. The composition of age groups in the sample of two districts from the cancer register is shown in (Table 1).

As a control group, that is, persons who were not exposed to radiation due to the incorporation of radioactive iodine, we took the data on rural residents of two districts of the Vitebsk region (Lepel and Chashniky) from the cancer register for 1986 – 2016. Figure 1 shows a reconstructed map of the contamination of the territory of Belarus by I-131 and indicates the location of the above-mentioned areas. The number of rural residents in these two districts was 36,400, of which 16,900 were males and 19,500 were females. The distribution of age groups in the cancer register of residents of the Vitebsk region is also presented in (Table 1).

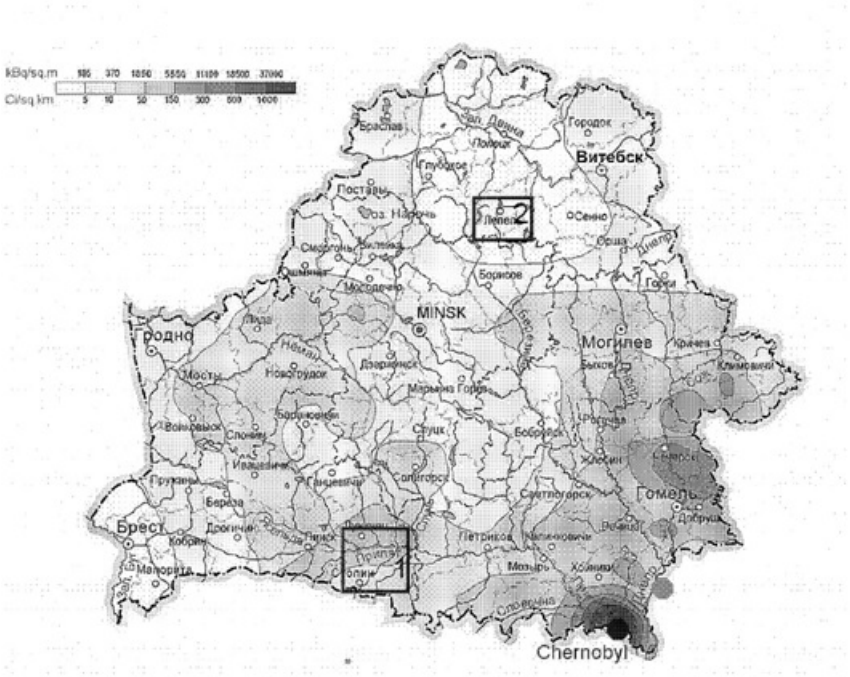


**Figure 1:** Reconstructed map of contamination of the territory of Belarus by I-131 (as of May 10, 1986). Note: 1 - the territory of the Stolin and Luninets districts of the Brest region; 2 - the territory of the Lepel and Chashniky district of the Vitebsk region

**Table 1**: The age composition of person in selected districts from the Belarusian Cancer Register

| Age group | Stolin and Luninets districts | Lepel and Chashniky districts |
|---|---|---|
| 0 – 4 years | 44 | 0 |
| 5 – 9 years | 23 | 3 |
| 10 – 14 years | 23 | 1 |
| 15 – 18 years | 9 | 3 |
| > 18 years | 126 | 45 |
| Total | 235 | 52 |

Doses to the thyroid gland were calculated and provided by the head of the laboratory for reconstructing radiation doses on the population of the State Research Center of the Federal Medical Biophysical Center named after A.I. Burnazyan FMBA of Russia D.Sc. in Engineering Shinkarev S.M. Doses for children of various ages and adults were calculated using the 2004 semi-empirical model.

To analyze the contribution of the radiation component into the occurrence of TC, the calculation of the excess relative risk (ERR), ERR / 1 Gy, percent attributive risk (AR%) was performed [7]. These indices were expressed as risk value and 95% confidence interval (CI). As mentioned above, to estimate the risk, we took the data on people who were not exposed to radiation. Obviously, cases of TC were recorded among them as well.

Statistical data processing was performed using the Statistics 10.0 and Sigma Plot 13 programs.

This study was approved by the Ethics Commission of the Belarusian Association of Physicians (10.12.2020).

**4. Results**

According to the TNM classification of TC, there are 4 stages of this disease (symbol T), metastases to regional lymph nodes (symbol N) may be present or absent, and distant metastases (symbol M) may be present or absent. (Figure 2) shows the data on the diagnosis of TC for 1986 – 2016 at different stages in two districts of the Brest region (Figure 2a) and two control districts of the Vitebsk region not contaminated with radioactive iodine (Figure 2b). It is clearly seen that the level of morbidity among the population in the contaminated areas is higher than in the "clean" ones. Interestingly, in the districts of the contaminated Brest region, TC was diagnosed mainly at stage 1, when the tumor size did not exceed 2 cm and it was limited by the thyroid tissue. In contrast, in residents of the control Lepel and Chashniky districts, TC was detected mainly at the T3 stage, i.e. when the tumor was 2 times larger in size, but remained confined to the thyroid tissue or had minimal spread outside the capsule.

The study on the stages of cumulative incidence of TC in women and men in the studied districts of the Brest and Vitebsk regions without detailing the N and T indices showed that, in general, as expected, the incidence in women is several times higher than in men (Figure 3). In the contaminated districts of the Brest region (Stolin and Luninets), the incidence of diagnostics of TC at any stage is significantly (2.5 – 3 times higher) than in the control region of the Vitebsk region. From this figure, one can also confirm the prevalence of earlier diagnostics of TC at the initial stages of the disease in residents of the Stolin and Luninets districts, in contrast to the diagnostics of cancer at a later stage (T3) in the control districts of the Vitebsk region.

Analyzing the incidence of TC, it is of a great interest to assess the risk of the onset of the disease at one stage or another. In radiation medicine, an indicative criterion for radiation exposure is the calculation of excess relative risk (ERR) and especially ERR, expressed per unit of absorbed dose (ERR /1 Gy). (Table 2) shows the risk values for different stages of TC.

The initial stage of TC, stage T1 in the general group of victims is characterized by the highest risk value (for both ERR and ERR /1Gy). The same relationship can be traced in the group of women. However, in men at the T2 stage, very high values of these indices are revealed. Most likely, this index does not reflect the true state of affairs with the risk assessment. The fact is that in the data on the incidence of the control group, i.e. of persons who live in the Vitebsk region and were included in the Cancer Registry, only one case of TC at stage T2 was diagnosed among men in 30 years. Apparently, this value gave high risk values in the calculations However, the data below may support the true nature of this finding.

Since childhood is characterized by a higher radiosensitivity of the thyroid gland, it was of interest to analyze the detection rate of different stages of cancer in different age groups. The groups were formed based on the age of the victims on April 26, 1986, i.e. at the time of the accident at the Chernobyl nuclear power plant and, therefore, at the time of irradiation of victims by radioactive iodine. Figure 4 shows data on the diagnosis of TC stages in different age groups of men and women.

As can be seen from the (Figure 4), in the age group from 0 to 4 years, TC in women was diagnosed mainly in the T1 stage, while in the male population, the tumor was more often detected in the second stage. It is interesting to note that among the female population, the tumor was often detected in the fourth stage. In the age group of 5 – 9 years, TC was detected with approximately the same frequency in women in stages T1 – T3. In men, diagnostics at the T1 stage dominated. The detection of a tumor at stage T4 was not observed in either women or men. The ratio of the stages of TC in the age group of 10 – 14 years is interesting. In women, the diagnosis of the disease occurred mainly in the first and third stages, which cannot be said about men. Roughly the same can be noted in the 15 – 18 years age group. The female population was

more likely to be diagnosed with stage T1 cancer. Analyzing these data, we can conclude that regardless of the age at which the exposure to radioactive iodine occurred, both the female and male part of the affected population warried about the state of their health. It is likely that this was facilitated by the system of dispensary observation existing in Belarus, as well as by the high qualifications of medical staffs. By virtue of this circumstance, it is obvious that in older age groups, a tumor in the fourth stage has almost never been found.

Analysis of histological forms of TC showed that the dominant forms in both cases are the follicular variant of the papillary tumor (8340/3) and papillary adenocarcinoma (8260/3) (Figure 5).

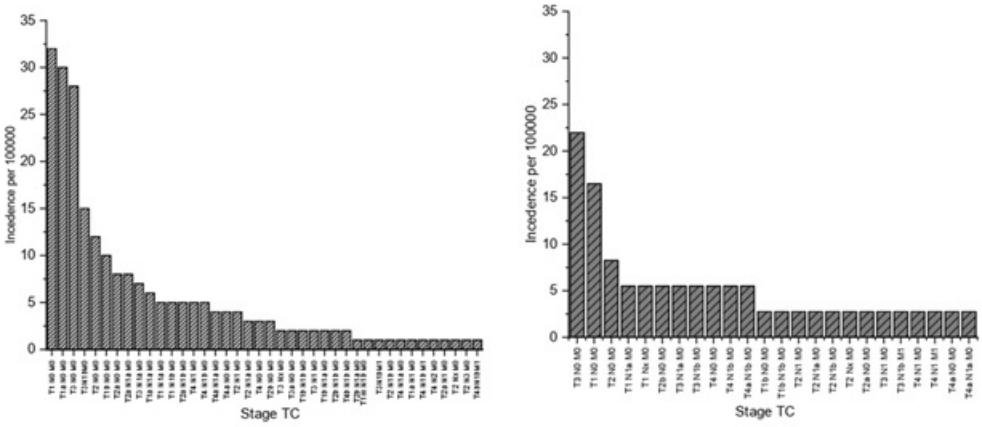


**Figure 2:** Distribution of the stages of TC in the population of the Stolin and Luninets districts (a), as well as of those from the Lepel and Chashniky districts (b) (1986-2016 years).

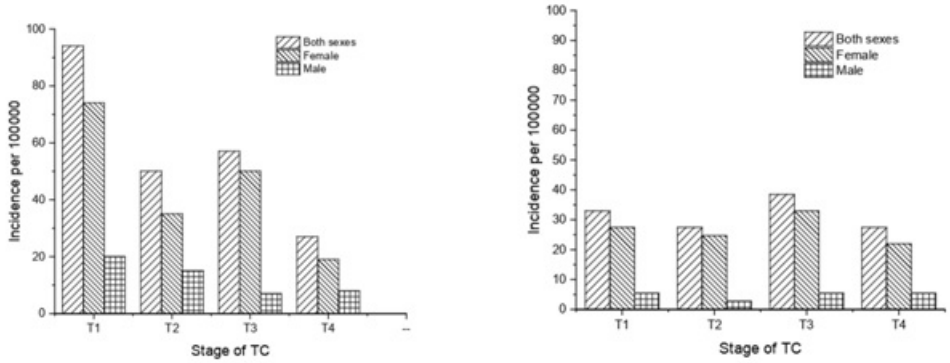


**Figure 3:** Gender differences in the cumulative incidence of TC in the contaminated districts of the Brest region (a) and control districts of the Vitebsk region (b) (1986-2016 years).

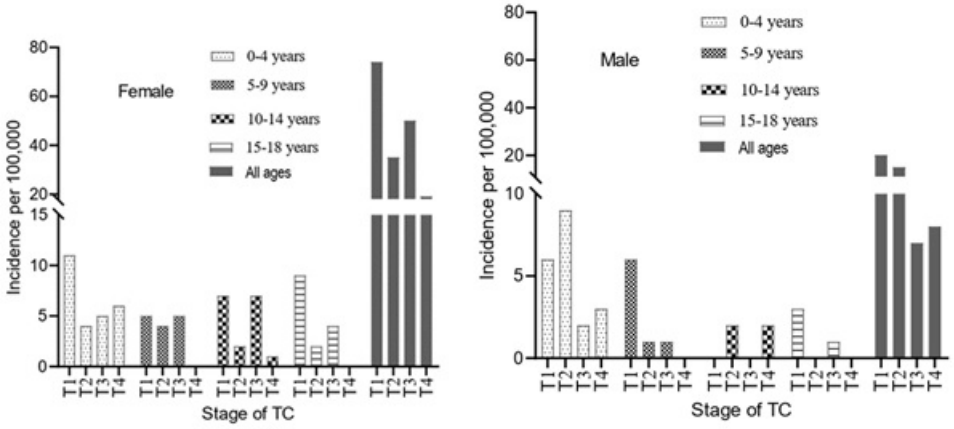


**Figure 4:** Data on the diagnosis of TC stages in different age groups of residents of the Stolin and Luninets districts (a - female, b - male).

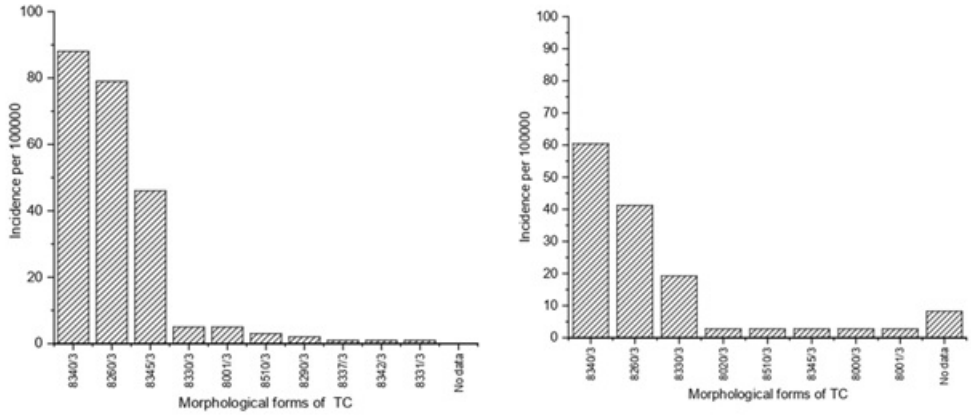


**Figure 5:** Histological forms of TC in Exposed (a) and non-Exposed (b) residents of Belarus (1986-2016 years).

**Table 2**: ERR and ERR/1Gy of TC diagnosed at different stages of the pathological process

| TC stage | Population category | RR | ERR | ERR/1Gy |
|---|---|---|---|---|
| T1 | Both sexes | 2,9 | 1,85(95%CI;1,02..3,38) | 8,06(95%CI;4,42..14,70) |
| | Female | 2,7 | 1,75(95%CI;0,9..3,38) | 8,69(95%CI;4,49..16,82) |
| | Male | 3,6 | 2,57(95%CI;0,60..11,01) | 7,83(85%CI;1,83..33,48) |
| T2 | Both sexes | 1,8 | 0,82(95%CI;0,42..1,62) | 3,56(95%CI;1,81..7,02) |
| | Female | 1,4 | 0,44(95%CI;0,21..0,92) | 2,21(95%CI;1,06..4,59) |
| | Male | 5,4 | 4,36(95%CI;0,58..33,02) | 13,26(95%CI;1,75..100,36) |
| T3 | Both sexes | 1,5 | 0,48(95%CI;0,27..0,87) | 2,10(95%CI;1,17..3,77) |
| | Female | 1,5 | 0,55(95%CI;0,29..1,03) | 2,72(95%CI;1,45..5,11) |
| | Male | 1,3 | 0,25(95%CI;0,05..1,21) | 0,76(95%CI;0,16..3,67) |
| T4 | Both sexes | 1,0 | 0,02(95%CI;0,01..0,03) | 0,07(95%CI;0,03..0,15) |
| | Female | 0,9 | 0,12(95%CI;0,05..0,27) | 0,59(95%CI;0,26..1,34) |
| | Male | 1,4 | 0,43(95%CI;0,09..2,02) | 1,31(95%CI;0,28,..6,15) |

As expected, in the contaminated districts of the Brest region (Stolin and Luninets districts), these forms of cancer had 1.5-2 times higher incidence than in the control Vitebsk region. The third place according to histological characteristics was taken by different types of cancer in different regions. In two districts of the Brest region, medullary cancer was diagnosed in third place in terms of detection rate (8345/3), while in the uncontaminated Vitebsk region it was follicular adenocarcinoma (8330/3). Other types of TC were detected at the level of several percent.

Calculation of the risks for the two main histological forms of TC among victims living in the Brest region and included in the Cancer Registry showed that the incidence in men can definitely be associated with radiation exposure due to the incorporation of I-131 (Table 3). This is especially true for papillary adenocarcinoma 8260/3 [18.24 (95% CI; 4.15… 80.26)]. In women, the risk was several times lower [4.26

**Table 3**: Assessment of the risk of various histological forms of TC in residents of contaminated areas

| TC form | Population category | RR | ERR | ERR/1Gy | AR% |
|---|---|---|---|---|---|
| **Follicular variant of papillary tumor 8340/3** | Both sexes | 0,8 | 0,22(95%CI;0,15..0,32) | 0,95(95%CI;0,65..1,37) | -27,9 (95%CI;14..-69,9) |
| | Female | 1,3 | 0,34(95%CI;0,20..0,57) | 1,7(95%CI;1,01..2,86) | 25,4(95%CI;-19,6..70,5) |
| | Male | 2,1 | 1,06(95%CI;0,37..3,05) | 3,21(95%CI;1,11..9,27) | 51,3(95%CI;-22,7..125,4) |
| **Papillary adenocarcinoma 8260/3** | Both sexes | 1,9 | 0,92(9%CI;0,53..1,60) | 4,0(95%CI;2,3..6,94) | 47,9(95%CI;8,1,,87,7) |
| | Female | 1,9 | 0,86(95%CI;0,47..1,55) | 4,26(95%CI;2,35..7,73) | 46,1(95%CI;2,5..89,8) |
| | Male | 7,0 | 6,0(95%CI;1,36..26,4) | 18,24(95%CI;4,15..80,26) | 85,7(95%CI;29,7..141,7) |
| **Lymph node metastases** | Both sexes | 1,8 | 0,76(95%CI;0,47..1,25) | 3,32(95%CI;2,03..5,44) | 43,3(95%CI;6,2..80,5) |
| | Female | 1,6 | 0,56(95%CI;0,32..0,99) | 2,8(95%CI;1,59..4,91) | 36,0(95%CI;-9,0..81,0) |
| | Male | 2,5 | 1,5(95%CI;0,53..4,28) | 4,57(95%CI;1,6..13.01) | 60,0(95%CI;-6,2..126,2) |

(95% CI; 2.35 ... 7.73)]. To a lesser extent, the risk was expressed in men in relation to the occurrence of another form of TC – the follicular variant of papillary tumor 8340/3 [3.21 (95% CI; 1.11...9.27)], but exceeded this value in women. The values of excess relative risk greater than one, as it is known, may indicate the influence of a specific factor that causes a certain effect. In this case, we are talking about the radiation factor. The findings may indicate that papillary adenocarcinoma is a more radiation-induced form of TC in men due to exposure to radioactive iodine. To a lesser extent, this is expressed in the female population.

When assessing risk factors for the occurrence of various histological forms of cancer, it is very important to know the specific contribution of the radiation factor, since there may be other reasons that can lead to similar results. Calculation of the attributive risk percentage (AR%) can be of a great help. As follows from the data in (Table 3), it is obvious that 86% of cases of papillary adenocarcinoma (8260/3) in men in the study cohort are due to radiation exposure [85.7 (95% CI; 29.7 ... 141.7)]. In women, its contribution is also great, but half as much [46.1 (95% CI; 2.5 ... 89.8)]. Almost the same contribution of the radiation factor to the induction of the follicular variant of a papillary tumor (8340/3) was found in men and slightly less in women 51.3 (95% CI; -22.7 ... 125.4) and 25.4 (95% CI; -19.6 ... 70.5), respectively. But nevertheless, this types of cancer also have a fairly high probability of radiation genesis.

It is known that metastases are one of the signs of the late stages of the oncological process. The calculation of the risks of metastases to regional lymph nodes showed similar results to the above written ones. It is found that metastasis is typical for men [4.57 (95% CI; 1.6… 13.01)] and the contribution of the radiation factor correlates with the dominance of papillary adenocarcinoma in men.

From the risk assessment data, it becomes obvious that the male population of the studied areas of the Brest region is more likely to develop thyroid tumors due to exposure to radiation from the incorporation of I-131. This is evidenced by the AR% value, especially when diagnosing papillary adenocarcinoma. One might assume that among the male population a higher incidence should be recorded. However, data on the incidence of the affected population indicate the opposite, i.e. prevalence of TC incidence is observed in women (Figure 3). The question arises about how to compare this data? The only explanation for this phenomenon may be the following. In women, due to a number of characteristics, other factors may play a role in the occurrence of cancer. These can be menopause, a deficiency of stable iodine in the environment, an excess of nitrates in food, the presence of xenobiotics in them, even the effect of the electromagnetic field of a mobile phone [8]. And the features of the female body with its characteristic hormonal characteristics can be of decisive importance and the implementation of certain processes, including pathological ones.

**5. Discussion**

The detection of TC among residents of the affected areas (Stolin and Luninets) at the early stages of the pathological process, mainly at the stage T1, can be explained as follows. These areas are referred to as the so-called controlled areas of Belarus, where a system of medical examination is established. Annual medical examinations of the population, including those with the use of ultrasound of the thyroid gland, make it possible to identify pathology at an earlier stage. In the uncontrolled areas of the Vitebsk region, there is no such medical examination. A certain role can be played by the alertness and awareness of the radiation factor by the population who have suffered from the accident at the Chernobyl nuclear power plant.

The process of carcinogenesis has a complexed and sometimes not completely clear mechanism. Various processes are involved at different stages. It is very interesting to trace the values of TC risk at different stages to the effect of ionizing radiation. The high ERR and ERR /1Gy values associated with the initial stages of TC are quite understandable. Similar high risk values have already been reported for residents of Belarus and Ukraine [9]. The development of cancer is associated with the molecular genetic mechanisms of cell transformation, which will result in the onset of tumor growth, i.e. initial stages of TC. The action of radiation will modify precisely these stages of the process, which, due to the probabilistic effect, are capable of leading to the development of a tumor.

According to the data described earlier, it follows that in the age group of 0 – 4 years, especially in women, diagnosis of TC often occurred at stage T4. This fact looks very strange. Obviously, of all the studied age groups, the representatives of this sample are the youngest. At the current moment, they are between 35 and 40 years old. A more detailed analysis showed that the time to diagnosis in this group is from 6 to 11 years (mean value 8 years), their age at the time of diagnosis was from 8 to 11 years. At other stages of cancer, the latency period was significantly longer (13 – 28 years). The absorbed thyroid doses in all diagnosed stages of cancer in this group were high and relatively comparable. In this regard, the appearance of this form of TC can be explained by its aggressiveness, which has already been reported earlier [4]. Nevertheless, other factors, including those of a non-radiation nature, may play role in the induction of this oncological pathology.

This assumption is supported by the results of calculating the risks of histological types of TC. An additional calculation of the attributive risk showed significantly higher values of the risk of developing papillary thyroid tumors in men, as well as the risk of tumor metastasis. At the same time, papillary adenocarcinoma is highly likely to occur due to radiation genesis (8260/3). These data may indicate a greater likelihood of tumors in the male population. An-

other form of TC has almost the same contribution to morbidity (Figure 5a). In the group of women, the mentioned histological forms occur with the same frequency (data not shown). And due to the fact that the incidence, as shown above, is higher in women, it can be concluded that TC in the affected residents of Belarus can be caused not only by the radiation factor, but by other reasons, for example, gender, as well as physical and chemical factors of the external environment.

Indeed, according to the data from American Cancer Society, the incidence of TC among women in USA is about 3 times higher than in men. In 2021, 32,130 cases were revealed in women, and just 12,150 were revealed in men (https://www.cancer.org/, date of access 14.03.2021). So, the overall high incidence of TC in women is indeed determined by a gender and, probably, by some associated confounders. According to the current study, accumulation of I-131 in thyroid gland does lead to the increased risk of CT development in both genders. However, this risk is significantly higher in men, than in women. Moreover, the rate of tumor progression might be faster in males who were at the age of 0 – 4 years at the moment of Chernobyl accident.

## References


1. UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) 2008 . Sources and effects of ionizing radiation. Report Vol. II, 2011, 219.
2. Cardis E., Hatch M. The Chernobyl accident — an epidemiological perspective. Clin Oncol (R Coll Radiol). 2011, 23: 251–60
3. Beresford N, Fesenko S, Konoplev A, L Skuterud, J T Smith, G Voigt. Thirty years after the Chernobyl accident: What lessons have we learnt? J Environ Radioact. 2016;157:77-89.
4. Williams E, Abrosimov A, T Bogdanova T, E P Demidchik, Ito M, V LiVolsi, et al. Thyroid carcinoma after Chernobyl latent period, morphology and aggressiveness. Br J Cancer. 2004;90: 2219 – 24.
5. Germenchuck M. (2000) PhD thesis. Reconstruction of radioactive contamination of the territory of Belarus by Iodine-131 after the catastrophe on Chernobyl NPP. Minsk. URL: http://rad.org.by/public/I_1986.jpg (date accessed: 17.11.2020).
6. UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) (2018). New York: Evaluation of data on TC in regions affected by the Chernobyl accident: A white paper to guide the Scientific Committee's future programme of work. 20.
7. Calculating and Interpreting Attributable Risk and Population Attributable Risk.
8. Family Health Outcomes Project. Appendices III-b, URL: https://fhop.ucsf.edu/planning-guide (date accessed:15.03.2021).
9. Luo J, Deziel N, Huang H, Chen Y, Ni X, Ma S, et al. Cell phone use and risk of thyroid cancer: a population-based case-control study in Connecticut. Ann Epidemiol. 2019;29: 39–45.
10. Jacob P, Bogdanova T, Buglova E, Chepurniy M, Demidchik Y, Gavrilin Y, et al. Thyroid cancer risk in areas of Ukraine and Belarus affected by the Chernobyl accident. Radiat Res. 2006; 165:1–8.