

# [Evaluating the residual effects of chernobyl on thyroid cancer](https://assignbuster.com/evaluating-the-residual-effects-of-chernobyl-on-thyroid-cancer/)

## Introduction

### Papillary thyroid carcinoma is often observed in patients who were exposed to Chernobyl nuclear power accident. This paper will illustrate the connection between exposure and development of carcinoma as documented in peer-reviewed research articles. Research will focus on patients who under the age of 18 years old during exposure.

First, an informative background providing observations concluding that thyroid cancer has been linked to children is provided. Second, a general conclusions section outlines results collected through cohort and case-control studies. Next, synthesized findings of three studies conclude, exposure from radiation contributed to gene rearrangements or mutations to DNA, resulting in formation of papillary cancer. This is followed by findings predicting the prognosis for patients post thyroid cancer treatments and anticipated impacts for future generations. Finally, a gap is identified, thereby proposing a need for continued research in order to ensure proper researching includes appropriate participants for future cohort studies.

Background on Research on Topic

The Chernobyl nuclear power plant accident of 1986 has incurred health problems for those living nearby in Ukraine (Schneider & Sarne, 2005). Some of the vulnerable populations affected by this incident were children (Schneider &Sarne, 2005). These children have experienced increases in thyroid cancer, resulting from exposure to high levels of radioactive iodine (International Agency for Research on Cancer, 2005). This radioactive iodine was absorbed into the food and contaminated large areas of Belarus, Ukraine and the Russian Federation (WHO, 2006, para 17). According to the World Health Organization (2006), contact with elevated doses of radiation resulted in nearly 5, 000 reported cases of thyroid cancer in children under 18 years of age. Higher metabolic activity of the thyroid gland results in sensitivities to increased doses of radiation (Arndt et al., 2018).

Studies, including the case-control study conducted by Arndt et al. (2018) suggested that ionizing radiation contributed to gene rearrangements and mutations that prompted the growth and formation of papillary thyroid tumors. Additionally, Abend et al. (2013) performed a cohort study to determine gene differences in tissue taken from normal thyroid tissue exposed to radiation. Then, tissue was studied from individuals with thyroid cancer but were not exposed to radiation (Abend et al., 2013). Results concluded, radiation exposure made an impact by forming gene fusions to result in thyroid cancer (Abend et al., 2013). In addition, Efanov et al. (2017) conducted cohort studies monitoring patients over time to observe DNA breaks contributed by ionizing radiation that led to thyroid tumors. The goal of these studies was to observe the future outcomes of these effects. The following general conclusions from research describes these studies to evaluate residual effects of Chernobyl and thyroid cancer.

General Conclusions from Research

Multiple cohort and case-control studies have concluded that exposure at young ages to ionizing radiation has contributed to gene mutations resulting in the formation of thyroid cancer. Large sample sizes and monitoring individuals from the same age group over time, has allowed for reliable results supporting theories of radiation exposure contributing to cancer. Tissue samples taken from exposed individuals demonstrate differences in gene expressions compared to non-exposed individuals (Handkiewicz-Junak et al., 2016). Recurrences of cancer after treatment for thyroid tumors usually manifested within three years and had similar prognosis as those with thyroid tumors without radiation exposure (Shaha et al., 2017). Even though prognosis was insignificantly different than non-exposed individuals with thyroid cancers, exposed participants had greater odds of developing lymph node metastases post treatments (Fridman et al., 2018).

Synthesized Finding #1- Gene Mutations and Rearrangements Linked to Thyroid Cancer

Arndt et al. (2018) conducted a case-control study and compared genes and biopsied 96 of exposed and non-exposed participants 5. 5 years of age located in Ukraine and Belarus. Arndt et al. (2018) reported findings of gene rearrangements in 33. 3% of radiation exposed group versus only 11. 1% in non-exposed group. About 60% of rearrangements were in dose exposure ranges of > 100-500 mGy or > 60-300 mGy (Arndt et al., 2018). Illustrating rearrangements were statistically significant (p = 0. 047) and concluded as frequency of radiation increased, absorbed dose to thyroid increased (Arndt et al., 2018). Arndt et al. (2018) concluded no significant differences between genders. However, a weakness of this study was most of unexposed tissue samples were from female patients and results could be bias (2018). Also, sample size of non-exposed group was significantly smaller than the exposed group and may be an underestimation of the effected population (2018). Furthermore, strengths of the study included participants who were all of comparable ages. Methods included having two groups and a simple study that was able to confirm significant association between gene mutations occurring with increased radiation exposure. Ironically, the study performed by Arndt et al. (2018) is very similar in findings to those of Efanov et al. (2017).

Efanov et al. (2017) recruited and assessed 65 cases of individuals who were under 18 years of age and resided in three of the most impacted areas during the Chernobyl accident. Criteria included participants to have dose measurements taken from thyroid glands at two months post exposure to radiation from Chernobyl accident. Participants were volunteers and guardians gave consent for minors to participate in the trial studies. Through the Efanov et al. (2017) study, findings established that gene fusions contribute to thyroid cancer more than point mutations. Point mutations may occur as a result of radiation exposure and result in a nucleotide base to be inserted or deleted from a DNA or RNA strand (Efanov et al., 2017). Results demonstrated driver mutations observed in 96. 9% of the cases, with 70. 8% being gene fusions and 26. 2% only being point mutations (Efanov et al., 2017). Unfortunately, a weakness of this study included, adding 70. 8% to 26. 2% equals 97%, not 96. 9%, which leads to inconsistent values possibly from miscalculation of results. Additional weaknesses of this study included, lack of accounting for uncertainties in dose estimates and only focusing on 62. 5% of reported cases due to strict guidelines of the testing (Efanov et al., 2017). On the other hand, strengths included a p-value analysis, illustrating a proper sample size was achieved (2017). Additionally, data was collected from populations in three different locations (2017).

Meanwhile, another study directed by Handkiewicz-Junak et al. (2016) further supported that differences in gene expression post- Chernobyl radiation due to low-dose exposure exist. Handkiewicz-Junak et al. (2016) conducted DNA microarray to examine 65 tissue samples collected from the Chernobyl Tissue Bank from patients born between 1987 and 1994. In doing so, Handkiewicz-Junak et al. (2016) evaluated samples on molecular levels and concluded small, however significant differences, between exposed and non-exposed tissue (p < 0. 01). This significance may be due to the inclusion of sporadic papillary thyroid cancers that occurred in absence of radiation exposure (Handkiewicz-Junak et al., 2016). Fortunately, this study provided strengths, which included results supporting the hypotheses that ionizing radiation increases thyroid cancer through gene alterations regardless of how low-dose the exposure is (2016). Unfortunately, a weakness of this study was the sample size was small (2016). Also, insufficient amounts of non-exposed tissue samples were available at the Chernobyl Tissue Bank, therefore Polish patients tissue samples were included (Handkiewicz-Junak et al., 2016).

Synthesized Finding #2- Prognosis of Future Metastasis in Patients Post Treatment

Other research has evaluated the prognosis of future recurrence of cancer in individuals exposed to radiation treatments. Shaha et al. (2017) produced a cohort study, which monitored 116 individuals exposed between 1986 and 2010 and then receive additional radiation as a form of treatment. Shaha et al. (2017) performed a five year follow up and recorded findings that found if individuals were going to have recurrences, they typically manifested within three years after treatment. After three years post treatment, no recurrences were noted. Non-exposed patients had a 98. 7% for no recurrence, whereas exposed patients had a 97. 4% for cancer metastasis, no significant differences were noted (Shaha et al., 2017). Meanwhile, a strength of the study included results providing strong evidence due to continued monitoring over 22 years. Another strength included observations that concluded recurrences usually manifest within three years, therefore a longer study is unlikely to produce a significant difference (Shaha et al., 2017). However, a weakness of Shaha et al. (2017) study, was age at exposure and measurement of dose received were undetermined and unable to illustrate representation of population. Shaha et al. (2017) concluded regardless of prior exposure to Chernobyl accident, similar outcomes post radiation therapy was observed.

Another study conducted by Abend et al. (2013) sought to evaluate whether gene mutations developed due to exposure would be passed on to future generations. Abend et al. (2013) designed a cohort study composed of 71 volunteers diagnosed with cases of thyroid cancer between the years 1998 and 2008. Tissue RNA samples from volunteers were collected from the Chernobyl Tissue Bank. However, of the 73 samples, only 63 could be assessed (Abend et al., 2013). Abend et al. (2013) observed a multistep process in cancer formation, which begins in normal tissue but can be exacerbated by gene alterations brought on by radiation exposure. Finally, strengths of this study were doses were measured shortly after exposure and cancers observed were identified in screened participants of the cohort study following standardized protocols. Regrettably the study weaknesses include, small sample size and not accounting for uncertainties in dose (Abend et al., 2013).

Lastly, a cohort study produced by Fridman et al. (2018) compared two groups. Group A had been exposed to radiation on several occasions, meanwhile group B was exposed to radiation and received surgery for papillary thyroid cancer. Patient volunteers gave consent at the time of surgery to share findings. Group A, or the “ post-Chernobyl group” was comprised of 373 participants, and group B, or the “ sporadic” was composed of 136 participants (Fridman et al., 2018). Data was collected following patients that had surgery for tumor/node removal. Follow up screening of patients continued for 6-26 years (Fridman et al., 2018). The “ Post-Chernobyl” group had greater findings for nodal burden than the “ sporadic” group. Children and adolescences with nodal involvement had greater odds of metastases (Fridman et al., 2018). However, no significant difference between the two groups for lymph node metastases. Presumably a weakness was some patients stopped following up and lost interest in the study (Fridman et al., 2018). As a consequence, the length of the study made it expensive. All things considered strengths still included a detailed long-term follow up and large sample size (Fridman et al., 2018).

Need for Further Research

Radiation exposure has been identified as a contributor to thyroid cancer in children throughout these studies. However, a gap in research fails to include evidence regarding the geographic extent of Chernobyl radiation exposure to individuals. Arndt et al. (2018) conducted a case- control study assessing tissue from groups deemed as “ non-exposed” to radiation from the Chernobyl accident. Unfortunately, researchers failed to identify the location of these individuals. Efanov et al. (2017) also focused findings on areas that were considered the most irradiated, radiation was not contained or limited to small areas. The extent that radiation geographically covered needs to be addressed. A study is necessary to be conducted to measure this distance so samples being studied are accurate when identifying them as “ non-exposed”. If samples are taken from participants who are still within proximity to the radiation accident, they may still be irradiated to a lesser extent and should not be labeled as “ non-exposed”. This undermines the internal validity of these studies and the findings of the research.  The following proposed study should be conducted to further conclude more accurately the impact of Chernobyl causing thyroid cancer in children.

This proposed cohort study will build upon the Efanov et al. (2017) research. Efanov et al. (2017) observed a connection between dose and gene fusions by measuring radiation exposure to thyroid glands. Similarly, this study would also assess radiation dose measurements from thyroid glands of individuals throughout effected areas to conclude a connection to the distance of the affected area. A cohort study recruiting of 100 participants who have been diagnosed as children under the age of 18 years old with papillary cancer will be utilized. Two groups will be compared with 25 male and 25 female participants in each group. Group A will include participants exposed to Chernobyl, while group B will include the non-exposed. Samples from the participants may be obtained through tissue banks just as Arndt et al. (2018) and Efanov et al. (2017) did through their studies. Informed consent will be required and if participant is under the age of 18, guardians must give consent. Group A, tissue samples will be from Chernobyl Tissue Bank. Group B, the non-exposed group should come from the U. S. A. and allow for a substantial distance from affected site. Samples will be collected from a tissue bank located in Washington D. C. which is 4, 835 miles away. Tissue samples representing group A should be collected from specific pre-determined areas equally spaced throughout the affected areas of Belarus, Russia and Ukraine. In addition to less exposed areas identified such as France and Belgium (Dadiverina, A., 2016). This will allow for a more accurate sample and illustrate the distance the radiation has reached.

Duration of the group monitoring will continue for 20 years to produce evidence. This replicates Fridman et al. (2018) cohort study which successfully observed cancer recurrences in individuals after treatments. Routine evaluations and screening for any new cancer conditions will be performed yearly. Participants will be provided with informed consent and that their identities and health information will remain anonymous. Study will be performed in accordance with the rules and regulations of HIPPA. Participants will be informed that they may withdraw from the study at any time. For each year that participants remain in the study, they will be compensated fifty dollars. Educating the participants on the importance of the study, as well as the benefits of having their health monitored may motivate them to continue through the entire study duration. Then, results will be analyzed to conclude if radiation caused the incident of thyroid cancer to increase in children and where these effects were seen geographically.

Unfortunately, this study has limitations. First, this study will be costly due to the compensation paid to the participants and length of 20 years of observation. However, the evidence produced from this cohort study will be strong and credible. This study will be feasible especially if conducted through adjoining tissue banks from the same company or work together for other projects.

Analyzed researched outlined in this paper supports the hypothesis that exposure of radiation to children under the age of 18 years old, has led to an increase in papillary thyroid cancer. Through further research findings may conclude how far Chernobyl radiation has reached. Knowledge of its impact will allow for better observations and unbiased results. Improved longevity of the individuals affected may be achieved and prevention of continued exposure after another incident may be avoided.

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Appendix- Study Analysis Table

| Citation Information  | Arndt, A., Steinestel, K., Rump, A., Sroya, M., Bogdanova, T., Kovgan, L., &… Eder, S. (2018). Anaplastic lymphoma kinase (ALK) gene rearrangements in radiation-related human papillary thyroid carcinoma after the Chernobyl accident. The journal of pathology. Clinical research , 4 (3), 175-183.  | Efanov, A. A., Brenner, A. V., Bogdanova, T. I., Kelly, L. M., Liu, P., Little, M. P., &…  Drozdovitch, V. (2017). Investigation of the relationship between radiation dose and gene mutations and fusions in post-Chernobyl thyroid cancer. JNCI: Journal of the National Cancer Institute , 110 (4), 371-378.  | Fridman, M., Krasko, O., & King-yin Lam, A. (2018). Optimizing treatment for children and adolescents with papillary thyroid carcinoma in post-Chernobyl exposed regions: The roles of lymph node dissections in the central and lateral neck compartments. European Journal of Surgical Oncology, 44 (6), 733-743.  |
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| Permalink  | https://www-ncbi-nlm-nih-gov. libproxy. boisestate. edu/pmc/articles/PMC6065115/  | https://academic-oup-com. libproxy. boisestate. edu/jnci/article/110/4/371/4641728  | https://www-sciencedirect-com. libproxy. boisestate. edu/science/article/pii/S0748798318300052  |
| Purpose  | To illustrate that there is a tie between an increase in thyroid cancer due to gene mutations in people exposed as children during Chernobyl.  | To establish a connection between the dose of radiation received and two common fusions of genes vs. point mutations.  | The purpose is was to find the best way to deal with PTC and to help avoid recurrence.  |
| Study Design  | Case-control study compared two different groups with thyroid cancer, one was exposed to radiation and the other was not.  | Cohort study that monitored patients who were exposed to see if they developed thyroid cancer.  | Cohort study compared two groups one that was exposed to radiation on several occasions. The other group was exposed and had surgery for PTC were the controls.  |
| Participants  | There were 77 exposed volunteer participants who were approximately 5. 5yrs of age and exposed to Chernobyl. This included 53 women and 24 men. Then, there is 19 unexposed to Chernobyl participants who were around 5. 2 yrs. but developed thyroid cancer that included 18 women and 1 man.  | The researchers recruited 65 cases of individuals who were under 18yrs of age and resided in three of the heaviest areas hit during Chernobyl. Criteria was participants had to have dose measurements taken from thyroids at two months post exposure. Participants were volunteers and if minor guardians gave consent.  | Patient volunteers gave consent at the time of surgery to share findings. Study had two groups the “ post-Chernobyl group” of 373, and the “ sporadic” group of 136.  |
| Data Collection  | Data was collected from tissue samples from Ukrainian patients diagnosed with thyroid cancer post Chernobyl to screen for gene mutations or rearrangements vs. the tissue from non-exposed patients diagnosed with thyroid cancer.  | Radioactivity measurements of the thyroid were collected 2 months post exposure. Along with the use of ecological and biokinetic models to evaluate the change in radioactivity over time. Also, noted the behavioral and dietary habits of the volunteers. RNA was extracted from tumor samples and tested for detection of gene fusions and point mutations.  | Data was collected following the patients that had surgery for tumor/node removal ipsilaterally. Then, the other group had bilateral surgery. Follow up screening of patients continued for 6-26 yrs.  |
| Results  | Findings showed that radiation exposure may increase gene fusions that increase the risks of developing thyroid cancer.  | Gene fusions were found to be more invasive and more likely to spread than the point mutations. Point mutations were more prominent in the older volunteers of the study. Males had greater odds of gene fusions and those who were younger during the event. Gene fusions are proportional to absorbed thyroid dose.  | “ Post-Chernobyl” group had greater findings for nodal burden than the “ sporadic” group. Children and adolescences with nodal involvement had greater odds of metastases. However, no significant difference between the two groups for lymph node metastases.  |
| Weaknesses  | * Some samples were not useable/missing from the exposed individuals resulting in an under-estimation of radiation effects.
* The non-exposed group was significantly smaller and contained less men, than the exposed group.
 | * Study was only able to focus on 62. 5% of PTC cases due to strict guidelines of the testing.
* Did not account for uncertainties in dose estimates.
 | * Long study and some patients lost interest and stopped following up.
* Expensive due to the length of the study.
 |
| Strengths  | * Individuals were all of comparable ages at surgery.
* Testing confirmed a significant association between gene mutations.
 | * P-values illustrated that proper sample size was achieved.
* Collected data from populations in three different locations.
 | * Large sample size
* Detailed long-term follow-up
 |
| Relevance to Topic  | This points to an increase in occurrences of thyroid cancer in people exposed to Chernobyl. Also, supports the idea that future generations could be affected by gene mutations.  | It presented the link between Chernobyl exposure causing a generation of cancer-causing gene fusions.  | Shows the impact of developing PTC and the effects it can have from recurrences.  |

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| Purpose  | The purpose was to see if patients with thyroid cancer and a history of exposure had the same outcomes as those without prior exposure to radiation.  | The study was to establish an association between childhood irradiation and subsequent thyroid cancer.  | To evaluate if the molecular biology of thyroid cancers were different from those brought on from radiation exposure.  |
| Study Design  | Cohort study compared patients exposed to radiation vs. not exposed and measure recurrences over time.  | Cohort study evaluated genes altered post Chernobyl.  | Case- control study evaluated samples from exposed and non-exposed individuals with thyroid cancer.  |
| Participants  | Patients were selected from an institutional database and consisted of 116 individuals who were exposed between 1986 and 2010.  | Volunteers included were 71 individuals diagnosed with cases of thyroid cancer between 1998 and 2008.  | Volunteers were recruited, and informed consent was received from parents/guardians for a total sample size of 65.  |
| Data Collection  | Data collection consisted of follow up exams post five year and continued for 22-plus years for any recurrences for either groups.  | Tissue samples were collected from these individuals from the Chernobyl Tissue Bank.  | Chernobyl Tissue Bank provided tissue samples from patients born between 1987 and 1994.  |
| Results  | The five year follow up show no difference in rates between exposed and non-exposed. Males were the more dominant group to be exposed.  | RNA extraction of the tissue samples showed a strong and consistent association linking childhood exposure to thyroid cancer.  | Observed excellent correlation between the incidence of thyroid cancer post Chernobyl.  |
| Weaknesses  | * Results may have been affected had the study been longer
* Study was unable to determine the age at exposure/ measurement of dose received and may not be good representation of population.
 | * Didn’t account for uncertainties in dose
* Small sample size
 | * Small sample size
* Not enough non- exposed samples were available at the Chernobyl tissue bank, so Polish patients were included in to sample.
 |
| Strengths  | * Recurrences that were observed showed up within three years after treatment, unlikely a longer study would show much difference.
* Long study able to collect more data
 | * Doses were taken shortly after exposure
* Cancers seen were identified in well screened individuals in the cohort study following standardized protocols.
 | * Results support claim that ionizing radiation increases thyroid cancer through gene alterations.
* Concluded two separate groups and simple study design
 |
| Relevance to Topic  | Prognosis for patients regardless of prior history of radiation exposure are good.  | Shows significant findings of thyroid cancer in young exposure.  | Gene mutations are found to be greater in those exposed increasing risk for tumor growth.  |