Geostatistical analysis of the relationship between heavy metals in drinking water and cancer incidence in residential areas in the Black Sea region of Turkey.

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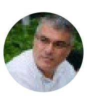

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INTERNATIONAL PERSPECTIVES

Geostatistical Analysis of the Relationship Between Heavy Metals in Drinking Water and Cancer Incidence in Residential Areas in the Black Sea Region of Turkey

Although most of the information presented in the Journal refers to situations within the United States, environmental health and protection know no boundaries. The Journal periodically runs International Perspectives to ensure that issues relevant to our international membership, representing over 25 countries worldwide, are addressed. Our goal is to raise diverse issues of interest to all our readers, irrespective of origin.

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Abstract **In the study described in this article, the authors examined the relationship between heavy metals in the drinking water and cancer densities in residential areas. The Turkish cities of Trabzon, Rize, and Giresun in the eastern Black Sea region were chosen as the study areas. Cancer registry data, population information, heavy metal chemical analysis results for drinking water, and other spatial information for the region were collected in a database designed in GIS. Information on a total of 13,012 registered cancer cases from the years 2000–2007 was obtained from a cancer record center and depicted spatially on a map. The incidence values explaining cancer density in residential units were calculated. Chemical analyses were then conducted to determine the presence of 17 different heavy metals by collecting a total of 541 drinking water samples. It was determined that among the 17 analyzed heavy metals, beryllium, nickel, antimony, and molybdenum had a significant relationship with cancer incidence values in the residential units.**

Introduction

Cancer is a significant community health care problem worldwide, and it is the second most common cause of death. Problems concerning recording cancer cases exist across Turkey. Cancer registry centers were established, however, to record the cases regionally. As a result, cancer incidence values have now been calculated across Turkey. Cancer incidence is the number of new cases arising in a given period in a specified population. The cancer incidence rate in Turkey for 2005 was 173.85 per 100,000 (Yilmaz et al., 2010). In European Union countries, the cancer incidence rate is 236.7 per 100,000 (GLOBACAN, 2008).

Cancer emerges gradually depending upon a variety of factors. Genetic features play a role in some types of cancer, while environmental factors such as people's lifestyle, eating habits, and exposure to chemicals play a role in most types of cancer (Boyle & Levin, 2008). Today, hundreds of chemicals that can lead to cancer have been identified. According to World Health Organization (WHO) data, environmental factors are responsible for more than 70% of cancer cases. A list of carcinogens published by the International Agency for Research on Cancer (IARC) includes 783 items. A small number of metals or metalloids was classified as carcinogenic by IARC/WHO, e.g., chromium, arsenic, nickel, cadmium, beryllium, lead, cobalt, mercury, and compounds (Dissanayake & Changrajith, 1999; International Agency for Research on Cancer [IARC], 2012). For example, the studies of people with high levels of arsenic in their drinking water have found higher risks of cancers of the bladder, kidney, lung, skin, and, less consistently, colon and liver (American Cancer Society, 2013). Cadmium is known to cause lung, prostate, and kidney cancer and aluminum is associated with lung and bladder cancer (IARC, 2012).

It is necessary to consider the environmental factors and genetic predispositions together when conducting studies that investigate the causes of cancer. As genetic studies are resource and labor intensive, not many

FIGURE **1**

Study Area Map

In our study, data including health, environment, chemistry, geography, and statistical parameters were investigated using an integrated approach. Our study was based on the TUBITAK project (Yomralioglu, 2008) and was aimed at investigating the relationship between cancer density in residential areas and heavy metals in drinking water. All data that have been used to conduct our study were collected in a geodatabase using GIS. Based upon cancer data with spot features and population size in residential areas, a cancer incidence map was created to determine cancer density in residential areas. Moreover, samples obtained from drinking water from the residential areas were used for chemical analyses to determine the presence of 17 heavy metals that are known to be carcinogenic. A linear regression statistical analysis was carried out to investigate the relationship between cancer incidence and the presence of 17 heavy metals in the drinking water of the studied regions. The influence of the heavy metals on incidence was also examined.

studies have been done in which cancer and its genetic features have been investigated. Most of the studies have been concerned with the environmental factors leading to cancer. In Turkey, epidemiological studies in different regions have been conducted on cancers that are a consequence of environmental impacts (Baris et al., 1987; Emri et al., 2002; Kadir et al., 2008; Taskin, Karavus, Topuzoglu, Hidiroglu, & Karahan, 2009; Tokmak, Capar, Dilek, & Yetis, 2004; Turkdogan, Kilicel, Kara, Tuncer, & Uygan, 2003).

The environmental factors causing cancer have been investigated in many scientific studies. In particular, the relationship between heavy metals and cancer risk has been investigated in a number of epidemiological small-area studies (Chhabra et al., 2012; Hinwood, Jolley, & Sim, 1999; Karagas et al., 1998; Kuo, Wong, Lin, Lai, & Lee, 2006; Lang et al., 2009; Linos et al., 2011; Liu, Ni, & Xia, 2011; Matthew, 1992; McElroy, Shafer, Trentham-Dietz, Hampton, & Newcomb, 2006; Wongsasuluk, Chotpantarat, Siriwong, & Robson, 2014; Yenugadhati, Birkett, Momoli, & Krewski, 2009; You, Harvey, & Harvey, 2003). Georeferenced health and environmental data are often used in conjunction with GIS to conduct spatial epidemiology (Bailony et al., 2011; Katayama, 2012). In many public health and epidemiology studies, GIS has emerged as an innovative component (Blanco & Cooper, 2004; Brewer, 2006; Cromley & McLafferty, 2002; Elliott, Wakefield, Best, & Briggs, 2000). GIS technology has already become a powerful tool for the epidemiologic investigation of the effects of environmental factors on diseases (Birmingham & McLaughlin, 2006; Colak, 2010; Craig et al., 2008; Jerrett et al., 2003; Poulstrup & Hansen, 2004; Yeganeh et al., 2013; Yomralioglu, Colak, & Aydinoglu, 2009). Health events that are spatially referenced allow the exploration of the causes of these events. Therefore, GIS technology is important for such investigations because it allows both spatial and statistical analyses to be performed. The data, methodology, spatial queries, and statistical analysis change depending on the features of the investigated hypothesis. Modeling the relationship between disease rates and other spatially referenced data requires spatial regression or generalized linear models for statistical analysis.

Methods

Overview of the Study Area

Turkey has a total area of 785,562 km^2 and comprises seven geographical regions. According to an address-based population registration system in 2011, Turkey has a population of 74,724,269 people (Turkish Statistical Institute [TurkStat], 2012). The study area was composed of three cities in the eastern Black Sea region in Turkey. These cities are Giresun, Trabzon, and Rize (Figure 1).

Trabzon is a central city located in the eastern Black Sea region. The population of Trabzon in 2011 was 757,353. The population of Rize in 2011 was 323,012, and the population of Giresun was 419,498 (TurkStat, 2012). Trabzon, Rize, and Giresun cover areas of 4,685 km^2, 3,920 km^2, and 6,934 km^2, respectively.

Cancer Data

Statistical cancer data belonging to the study area were obtained from a Trabzon population-based cancer registration center. This center records the information of cancer patients who were diagnosed in the cities of the Black Sea region in Turkey in accordance with ICD-100 disease registry standards.

In this study, during the years 2000–2007, 13,012 cancer cases were registered in the three cities within the study area. First, the cancer case registry obtained from the cancer registry center was added to a map based on the address information of the patients. Furthermore, the cancer incidence values in a total of 1,526 residential units were calculated by using population information from the Turkish Statistical Institute from between these dates. The residential units were evaluated on the basis of village/district for small area studies. The cancer incidence values calculated for the residential units were calculated by standardizing against a population size of 100,000. GIS were used to provide cancer incidence values based on geography. The cancer incidence values in the residential units were added to a specially designed geodatabase and were mapped with ArcGIS 10 software using the Kriging geostatistics technique. Geostatistics is often used for spatial prediction modeling of the spatial variability of cancer. In particular, Kriging produces output surfaces from point-based cancer data, including predictions, prediction standard errors, probabilities, and quartiles (Buzzelli & Jerrett, 2003; ESRI, 2001; Figueira, Sérgio, Lopes, & Sousa, 2007; Sloan et al., 2012). On the map created by the GIS, it is possible to see the range of the cancer incidence value densities (Figure 2).

FIGURE **2**

Cancer Incidence Map Created Using the Ordinary Kriging Technique

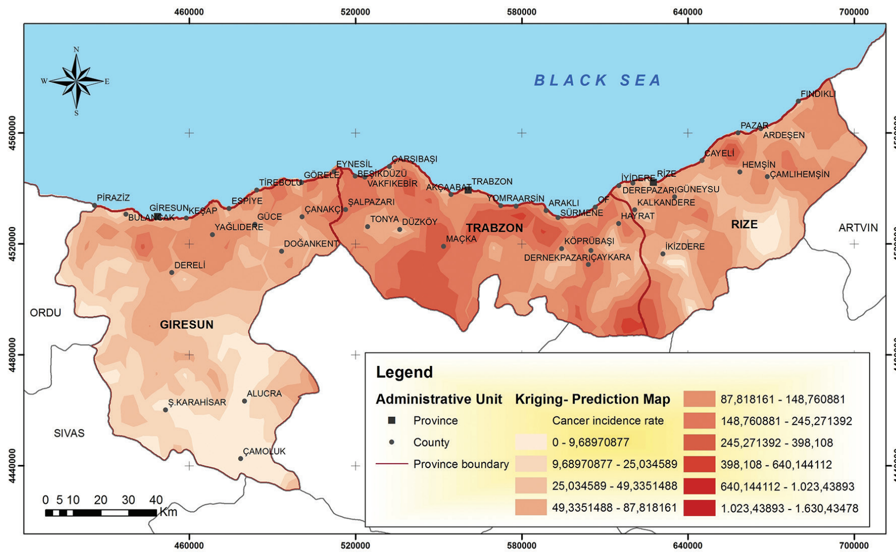
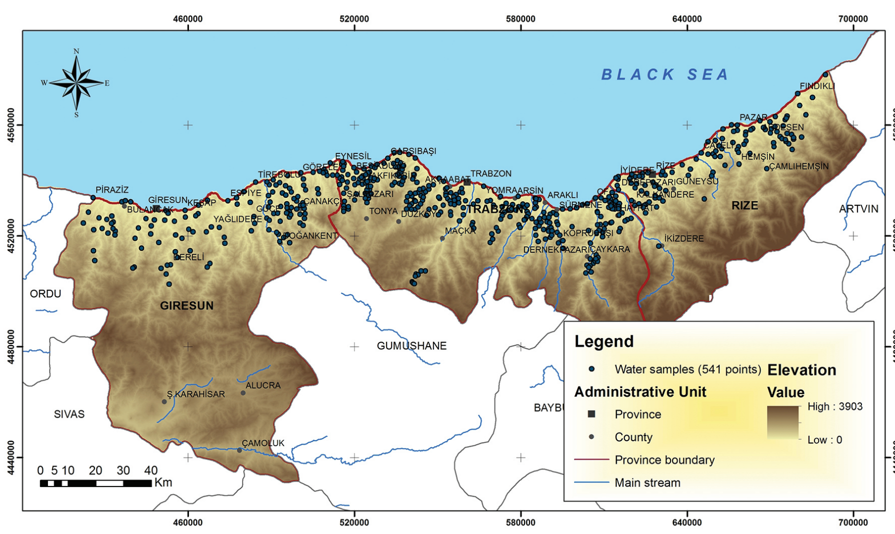


FIGURE **3**

Map Showing the Distribution of the Water Sampling Points



Collection and Chemical Analysis of Water Samples

A water values map was created for the study area by putting water samples that were provided by the water supply networks and taken from different sources in the study area for chemical analysis. In our study, to determine the carcinogenic elements that might exist in the water samples in the area, preliminary studies were carried out to establish the presence and concentration of the carcinogenic elements arsenic, beryllium, cadmium, cobalt, chromium, mercury, nickel, lead, selenium, vanadium, antimony, barium, strontium, copper, bismuth, molybdenum, and aluminum.

For this purpose, stations where samples were to be collected were designated. Overall, 541 water samples were collected in the area at a 95% confidence interval. The map in Figure 3 shows the stations where water samples were taken. The number of samples and stations for collection in all areas and residential units were determined. Determining the stations where samples would be taken also benefited the cancer incidence map. The points where water samples were taken were designated on the map of the study area (Figure 3).

Water samples were taken from mostly drinking water supplies. The water samples were collected in accordance with standards of TS ISO 5667-6 and TS ISO 5667-14. The station coordinates of the samples were recorded with the aid of mobile GPS. The samples were filtered through a 0.45-µm cellulose nitrate porous filter and were also soured by nitric acid and kept in sea-cap polyethylene covers. Ultra-pure chemicals

TABLE **1**

Number of Samples of Chemical Analysis That Were Higher Than World Health Organization (WHO) Recommended Limits

Heavy Metal Elements	WHO Recommended Limits	# of Samples Above the Limit
Beryllium, bismuth	No guideline	–
Mercury, antimony, molybdenum	6 µg/L, 20 µg/L, 0.07 µg/L	under WHO limits
Chromium, barium, copper	50 µg/L, 700 µg/L, 2000 µg/L	under WHO limits
Cadmium	1 µg/L	5
Arsenic	10 µg/L	103
Lead	10 µg/L	290
Selenium	10 µg/L	306
Aluminum	200 µg/L	21
Nickel	70 µg/L	5
Strontium	10 µg/L	8
Cobalt	10 µg/L	1

(Trace SELECT) and ultra-pure water (bidistilled, deionized) were used.

The analysis of the collected water samples was conducted using a Spectro GENESIS model horizontal plasma inductively coupled plasma-atomic emission spectrometer. Chemical analyses to determine the presence of the 17 heavy metals identified above were conducted. The results of these heavy metal chemical analyses were added to the GIS database. International water quality standards, as defined by WHO, were used when evaluating the analysis results.

GIS-Based Mapping Chemical Analyses

A spatial database in GIS was designed to map the results of the chemical analyses. After the analyses of the water samples were conducted, the results were added to a database and associated with points that were represented spatially on the map and were also integrated with a cancer-based geographical database. Thus, the heavy metals presence and concentration in the water sources were associated with the map data. GIS-based mapping chemical analysis used ArcGIS 10 software extensions such as ArcGIS spatial analyst and ArcGIS geostatistical analyst. ArcGIS spatial analyst provides a wide range of powerful analysis tools and queries. ArcGIS geostatistical analyst allows you to create a statistically valid prediction surface, along with prediction uncertainties, from a limited number of data measurements. With the aid of spatial analyses and an investigation conducted in GIS, the drinking water heavy metal analysis results for the residential units and the cancer incidence values were arranged in a table for statistical analysis. By using spatial analyses and statistical mapping, maps were created based on the heavy metal analyses. Especially the Kriging method was used for statistical mapping in ArcGIS geostatistical analyst.

Statistical Analysis

The potential relationship between heavy metals in the drinking water of residential units and cancer incidence was examined using a statistical analysis. To test the hypothesis, “Do heavy metals in water samples collected in residential units have an impact on cancer incidence values in residential units?”, a linear regression analysis was conducted. A regression analysis is a method to investigate the impact of one or multiple independent variables on a dependent variable. This statistical analysis technique is also used in studies that investigate the impact of environmental factors on health (Hinwood et al., 1999; Lang et al., 2009; Sloan et al., 2012; Yenugadhati et al., 2009).

The regression analysis revealed to what extent heavy metals in the drinking water explained the observed cancer incidence values in residential units. In conducting this analysis, the analysis values associated with the presence in water samples of the 17 tested heavy metals were considered independent variables, while the cancer incidence calculated for the residential units was considered the dependent variable.

The data obtained with the spatial queries and analysis in ArcGIS also evaluated statistical software. A linear regression analysis of the data was conducted using the SPSS v. 10 statistical package. The square roots of the cancer incidence values were used in the analysis to reduce the effect of extreme values (SPSS, 2004). The values of beta (normalized coefficient) and p (significance) for each factor, and the adjusted R^2, F (F-test statistic) and p were given for the model was examined in the table of the results of the analysis (Grand & Garland, 2006).

Results

Chemical Analysis Results

The results of chemical analysis for the water samples in the study area were evaluated based on WHO international standards. In the study area, 541 drinking water samples were collected, and chemical analyses were carried out to evaluate the presence of 17 heavy metals. Drinking water samples were size based on a 95% confidence level with a margin of error of ±10%. The evaluation for each metal was conducted separately after entry into the geographical database.

The investigations of mercury, antimony, and molybdenum indicated levels under the quantification limit of 6 µg/L, 20 µg/L, and 0.07 µg/L, respectively, and no WHO guideline for beryllium and bismuth is available. Cadmium was detected at five stations at a level higher than the values recommended by WHO (1 µg/L). It was determined that new and detailed studies are necessary to gather more water samples in these areas. The values of chromium, barium, and copper were found to be under the WHO recommended limits, which are 50 µg/L, 700 µg/L, and 2,000 µg/L, respectively.

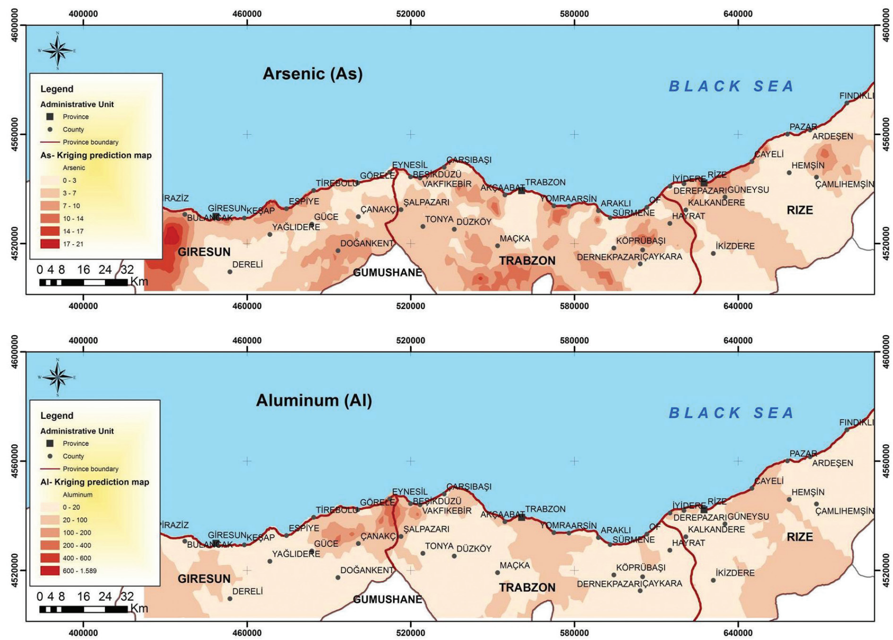
When examining the arsenic data from 103 stations, arsenic levels were discovered to be higher than the WHO recommended limit (10 µg/L), but the levels were in accordance with TS 266 recommended limits (50 µg/L). Lead levels were higher than the WHO recommended limit (10 µg/L) in samples from 290 stations and were higher than the TS 266 recommended limits (50 µg/L) at 23 stations. Selenium values were higher than the WHO recommended limit (10 µg/L) in samples from 306 stations. In samples from 46 out of 306 stations, however, the selenium values were discovered to be higher than the limit of quantification (60 µg/L). Aluminum values were higher than the WHO recommended limit (200 µg/L) in samples from 21 stations.

Nickel values were higher than the WHO recommended limit (70 µg/L) in samples from five stations. Strontium values were found to be higher than the limit of quantification (10 µg/L) in samples from eight stations. Cobalt values were found to exceed WHO recommend limits (10 µg/L) in samples from one station. The number of samples of chemical analysis that were higher than the WHO recommended limits are shown in Table 1.

Seventeen heavy metals were examined via chemical analyses conducted on 541 water samples from the study areas, and it was determined that eight chemical elements (cadmium, arsenic, lead, nickel, selenium, strontium, cobalt, and aluminum) were present at levels higher than the recommended human health and safety–related WHO limits. The Kriging prediction maps of arsenic, lead, aluminum, and selenium values of drinking water using geostatistical analyst of GIS are presented in Figures 4 and 5.

FIGURE **4**

The Prediction Map of Arsenic and Aluminum Values of Drinking Water by Ordinary Kriging Techniques



Statistical Analysis

A statistical evaluation of the relationship between the chemical analysis and the cancer densities in the residential units was conducted via linear regression. In this analysis, the dependent variable was residential unit cancer incidence, and 17 independent variables represented the 17 different heavy metals in the water samples.

Linear regression analyses were performed (at the 95% confidence level). The 17 heavy metal variables were significantly associated with cancer incidence. Cancer incidence values in the residential units were associated with beryllium, nickel, antimony, and molybdenum (*RR* = 2.798). The level of significance was set at $p < .01$. The linear regression had a regression ratio of $R = 0.287$ and $R^2 = 8.2\%$. The effect of the 17 independent variables over the model is 8.2%.

The regression equation is as follows:

Incidence = 252,214 – 31,690*Be – 0,850*Ni + 15,770*Sb – 16,286*Mo

According to this analysis, the elements beryllium (Be), nickel (Ni), antimony (Sb), and molybdenum (Mo) have an effect on incidence. A negative relationship exists between beryllium, nickel, and molybdenum and cancer incidence and a positive relationship exists between antimony and cancer incidence ($p < .01$).

Discussion

Studies on the effect of heavy metals on cancer are available. An examination of existing studies, however, indicates that the studies primarily examine the relationship of one or more heavy metals and their influence on a particular type of cancer. Our study utilized both GIS and geostatistical analyses to assess cancer incidence and the influence of environmental factors. Furthermore, ours is also a general study in which densities of all types of cancer in residential units were evaluated rather than the densities of particular types of cancer. The residential units were evaluated in terms of village/districts for the small-area study, which included populations from three cities. That is, the cancer incidence ratios were calculated on village/district scale.

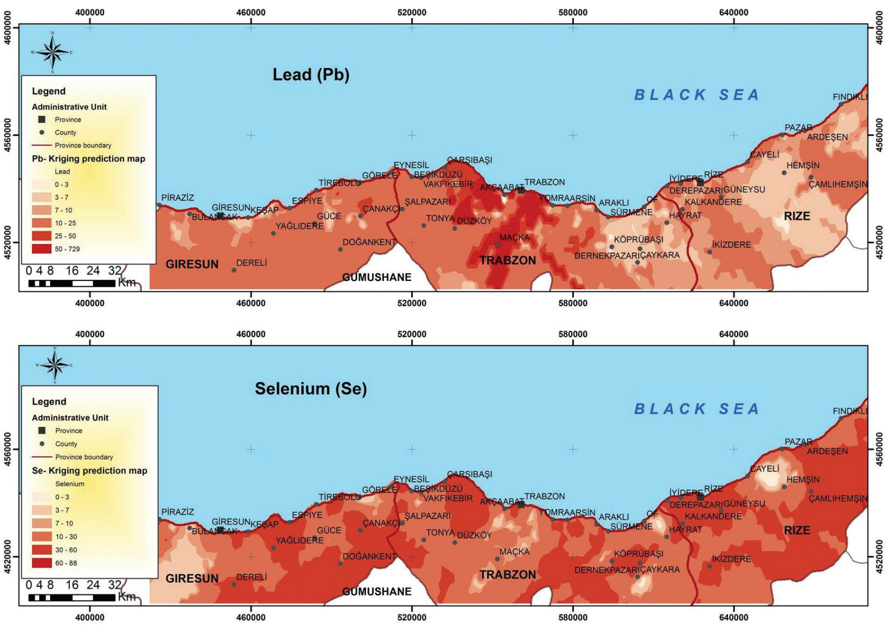
Seventeen different heavy metals were examined in 541 water samples. The relationship of these metals with cancer densities in the residential units was examined statistically. The statistical analyses were performed at the 95% confidence level. The results of the statistical analysis indicate the drinking water values of the 17 heavy metals explain an 8.2% incidence change in the residential units. The reason why this percentage is so low is that many environmental factors lead to cancer. In addition, genetic factors were ignored for our study. A negative relationship existed between beryllium, nickel, and molybdenum and cancer incidence and a positive relationship existed between antimony and cancer incidence ($p < .01$). Considering the chemical analysis results in the context of the recommended WHO limits, beryllium, molybdenum, and antimony were under the limit in the samples from all stations, and nickel was over the recommended limit in samples from only five stations.

Conclusion

The results of our study are products of a general study conducted on a fairly broad scale. It would be quite difficult to conduct a study

FIGURE **5**

The Prediction Map of Lead and Selenium Values of Drinking Water by Ordinary Kriging Techniques



that investigated the relationship between all of the cancer types and heavy metals. In our study, multiple types of cancer and multiple heavy metals have not been addressed. These results can serve as a useful guide in the future for more locally directed studies and for studies focused on specific types of cancer. Our study is distinctive in that the chemical analyses and cancer data were evaluated via both spatial and statistical analyses.

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