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Analysis of trace elements in the fingernails of breast cancer patients using instrumental neutron activation analysis

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Abstract

The aim of this study was to find trace elements that increase risk of breast cancer based on the deviation of the concentration of trace elements in the fingernail collected from the women with breast cancer and the normal women. The study was conducted with 10 elements (As, Au, Br, Co, Cr, Fe, Sb, Sc, Se, and Zn) using k_0-INAA and statistical analysis method. Significant differences ($P < 0.05$) were found for Cr, Fe, Sc and Zn between the case and the control groups. A significant correlation between Fe and Zn has found for the normal women, but this disappears in the women with breast cancer. On the contrary, a significant correlation between As and Cr has found in the case group, but no such correlation has noticed for the control group. The elements Cr, Fe, and Zn may be associated to the risk of breast cancer.

Keywords Trace elements in nails · Breast cancer · k_0-INAA · Correlation coefficient

Introduction

Trace elements play an important role for the body. It can affect to the functioning of organs or tissues, and lead to adverse health consequences. Trace elements enter the body through activities such as breathing, eating, drinking or skin contact with the environment. There is a real threat to health, when toxic trace elements that enter the body at low levels, it can lead to poisoning and illness, as well as exposure to accidentally elevated levels by promoting lethal health effects. There is ample evidence to show that if the human body is over-exposed or lacks certain trace elements, it can link to the risk of chronic diseases, including cancer and other diseases [1, 2].

Cancer is a multi-factorial disease and is one of the leading reasons that cause death in many countries. Various studies claimed that there is a relationship between trace elements and cancer risk [3–6]. In comparison with the healthy tissues, the changes in trace elements in cancerous tissues are probably evoked by a disease. Among various health testing, several essential and toxic elements in serum and tissues have been generally considered the best indicators of an individual's current exposure to pollution sources indicating the health of the body. For example, by studying the trace elements in colorectal cancer tumors, Arriola et al. [7] reported that the elements of Co, Fe, I, and Ba associated with the risk of colorectal cancer. While in studying on the concentration of trace elements in blood serum and colon tissues in colorectal cancer patients, Milde et al. [8] found that the concentration of Se and Zn were significantly different compared with those in the control group. Besides, Zaichick et al. [9] showed that there were considerable changes in the concentration of trace elements between the cancerous and normal thyroid tissues. Among all types

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of cancers, breast cancer is the third most common types worldwide and also the most common types among women [10]. Its incidence increases with age, with greater frequency at menopause. In the determination of some trace elements in breast cancer serum, Safaa Sabri Najim [11] found that the serum concentrations of Cr, Cd, Mn, Se, Fe, Cu, Mg, Co, and Zn were statistically significantly higher in the case group than the control group, while the concentration of Ni showed a lower level in the case.

In many studies, tissues or blood serum has been collected for analysis. The data obtained mirrored the current exposure of the trace elements in the human body only. Meanwhile, hair and nails are expected to be the indicators of the long-term exposure of the trace elements within the body. Therefore, they are recognized as biological tools for disease diagnosis. Trace elements accumulate in hair and nails at higher concentrations than other tissues throughout the body [12]. This suggests that hair and nails are one of the most reliable organs for determining the concentration of trace elements in the body [13, 14]. O'Brien et al. [15] have been measured the concentrations of 16 elements (As, Cd, Cr, Co, Cu, Fe, Hg, Mn, Mo, Ni, Pb, Sb, Se, Sn, V, and Zn) in the toenail samples of the women, who diagnosed with breast cancer, using inductive plasma mass spectrometry (ICP-MS). For the studied elements aside of nickel and antimony in toenail, they found that the post-diagnosis levels correlated with the pre-diagnostic levels. Janbabai et al. [16] measured the concentration of 11 elements (Cu, Fe, K, Li, Mg, Mn, Na, P, Se, Sr, and Zn) in hair and nail samples from patients with stomach cancer by atomic absorption spectrometry (AAS). They showed that the increase in concentration of Cu, K, Li, P, Se, and Fe have associated with the development of stomach cancer. In studying the trace elements in hair and nail samples of patients with cancer and type two diabetes using inductively coupled plasma optical emission spectrometry (ICP-OES), Salman et al. [17] indicated that the concentration of Se, Cr, Pb, and Cd in the hair and nails from cancer and diabetic patients was significantly different compared to those from the control group.

The atomic spectrometric methods provide several advantages in trace element analysis such as low detection limit, multi-element measurement, high sample throughput, relatively low investment, and running cost. However, these methods require very complicated sample processing, which increases the risk of loss or contamination, especially for trace and ultra-trace elements. Instrumental neutron activation analysis (INAA) can also carry out multi-element measurements without or very simple sample processing. Therefore, this method has been applied to the analysis of trace elements on hair, nails and other tissues in the human body [7, 18–20]. In particular, the k_0-standardization method of INAA is one that provides high sensitivity and precision, and especially no standard samples are required [21, 22].

In harmonizing with the previous investigation, an extra study on the correlation of the concentration of trace elements in nail samples of breast cancer patients to normal group may provide useful information to predict breast cancer. The aim of this study is to investigate the concentration of trace elements in the fingernails of the women with breast cancer and to find the trace elements that could link to a woman's risk of breast cancer.

In the present study, the k_0-standardization method of INAA (k_0-INAA) was applied to determine the concentrations of the desired trace elements in fingernail samples. The study was conducted the two groups of Vietnamese women living in Dong Nai province, southeast of Vietnam, where located many large industrial zones. One of which was normal (control group), and the other was in first-stage breast cancer (case group). The data were evaluated using some statistical analysis for the correlation of trace elements in the fingernails of both groups.

Experimental

This study was approved by the ethics committee of Dong Nai General Hospital, and an informed consent was signed by each participant.

Sample collection

The study involved a group of breast cancer females (case group) and a group of normal women as reference (control group). The case group included thirty-four female patients whose ages were between 45 and 60, and treated breast cancer at the Oncology Department of the General Hospital Dong Nai. The control group consisted of thirty-five normal women whose ages were similar to those of the first group and living also in Dong Nai province. All the patients in the study were in first-stage breast cancer and had not treated by chemical or radiation. The mean age was 47.28 for both studied groups. The fingernail samples were collected from August 2017 to February 2018 on the persons who had been aware of the investigation.

The nail donors were asked to clean their hands with fresh water, then with distilled water. The free edge of the nail from 10 fingers has taken by a stainless-steel nail clipper, kept in a pre-cleaned plastic bag and stored in ambient laboratory conditions. The information on the nail donors, including name, ages, place of living, health conditions, etc., was recorded.

Sample preparation

For neutron activation analysis, the fingernail samples were treated as described elsewhere [18, 23–25]. Briefly, the treatment procedure for fingernail based on 5 steps as follows: (1) the fingernail samples were first kept soaked in distilled water for 10 min, followed by another 5 min in rubbing alcohol with slight shaking. This step was to reduce the risks of microbiological activities from fungi and bacteria. (2) The fingernail samples were soaked in triplicate in acetone with ultrasonic agitation (B2510-DTH, Branson, USA) for 1 min. For each replicate, the acetone was discarded, and new acetone was added to the nail sample. (3) The fingernail samples were treated in the same manner with step 2, using 2% Triton X100 (Merck, Germany) instead of acetone. (4) The fingernail samples were cleaned in triplicate by soaking in distilled water and ultrasonic agitation for 1 min. (5) The cleaned fingernail samples pre-dried by placing on a filter paper for 12 h at ambient temperature.

For neutron activation analysis, approximately 30–70 mg of each sample was placed in a cleaned polyethylene bag and sealed before irradiation. The certified reference materials, namely, NIST 1566b (Oyster Tissue) and NIST 1577a (Bovine Liver) were also used as quality control samples. For dry based calculation, the moisture of fingernail samples and certified reference materials—NIST 1566b, and NIST 1577a were measured (MB45, Ohaus, USA). For this determination, approximately 80 mg of NIST 1566b and 130 mg of NIST 1577a were dried in an oven (UFB 500, Memmert, Australia) at 80 °C for 12 h. The moisture content was 4.1% and 11% for NIST 1566b and NIST 1577a, respectively. For the fingernail samples, the moisture content was between 8.2% and 10.7%.

Irradiation, measurement, and calculation

The samples were divided into two groups. The first group was included with 29 fingernail samples from the case group, NIST 1566b, cleaning blank (~ 123 mg) and Al-0.1%Au (wire form, ~ 3.6 mg) as a neutron flux monitor. The second group was included with 30 fingernail samples of the control group and NIST 1577a. Samples from each group were placed together, wrapped with aluminum foil and placed in an aluminum irradiation device called "rabbit". The neutron irradiations were performed for 10 h on Rotary Rack at a thermal neutron flux of approximately 3.59×10^{12} n cm^{-2} s^{-1} of Dalat Nuclear Research Reactor, Vietnam. At this position, the deviation of the epithermal neutron spectrum and the ratio of thermal/epithermal neutron fluxes were $\alpha = 0.073 \pm 0.001$, and $f = 37.3 \pm 0.4$, respectively [26].

The irradiated sample was measured using a gamma-ray spectrometer with HPGe detector (Canberra, USA) which its resolution (FWHM) of 1.8 keV at 1332.5 keV peak of ^{60}Co. Each sample was subjected into a two-stage measurement. The first one was carried out after a decay time of 4–5 days followed by the second one after 12 days of decay. At the full energy peak of radioisotopes, the net area was obtained using software GENIE 2000. In the fingernail samples, 10 elements were identified, including As, Au, Br, Co, Cr, Fe, Sb, Sc, Se, and Zn. For the blank, 10 elements were detected, including As, Br, Ca, Cr, K, La, Na, Sb, Sc, and Zn; however, all of them were at low levels (μg kg^{-1}). The k_0-INAA was used to calculate the concentration of elements [21, 22].

Data and statistical analysis

The element concentrations obtained in this study were subtracted to those which also presented in the blank, as follow

$$\rho = \frac{\rho_0 w - \rho_B w_B}{w}$$

where ρ_0 is the concentration of measured element, w is the weight of the sample which corrected for humidity, ρ_B is the concentration of element obtained in the blank, and w_B is the weight of the blank.

The uncertainty of concentrations of trace elements obtained was calculated using the propagation of error [27]. The *Z*-score index was used to evaluate the accuracy of the analytical measurements using the results obtained from the analysis of certified reference materials [28, 29].

The concentrations of the desired trace elements in the fingernail samples were expressed as arithmetic mean (Mean), standard deviation (SD), minimum and maximum values (Range), and median which were calculated using Microsoft Office Excel. The difference between the mean values of the cancerous and normal groups was statistically assessed by Student's *t* test and *T* critical at two tails. When a probability value (*P* value) is smaller than 0.05, the difference was considered to be significant. Besides, the compositional relationships among the elements in the fingernails were evaluated using a correlation matrix. Any estimated correlation coefficient values of zero were considered "no correlation" while those (absolute) values in range of $0.1 \le |R| < 0.3$, of $0.3 \le |R| \le 0.5$, of $0.5 < |R| < 0.8$, and of $0.8 \le |R| < 1.0$ were stated "poor correlation", "fair correlation", "moderate correlation", and "very strong correlation", respectively [30, 31].

Results and discussion

Analytical quality control

Table 1 showed the results obtained from the analysis of NIST 1566b Oyster Tissue and NIST 1577a Bovine Liver, respectively. The relative deviation between measured and certified values for NIST 1566b Oyster Tissue and NIST 1577a Bovine Liver were lower than 7% and 9%, respectively. In this work, the Z-score values obtained in both reference materials were less than 2, it means that the

Table 1 Concentrations of elements (μg g^{-1}) in certified reference materials

Element	NIST 1566b Oyster Tissue			NIST 1577a Bovine Liver		
	Measured value	Certified value	|Z-score|	Measured value	Certified value	|Z-score|
Ag	0.712 ± 0.021	0.666 ± 0.009	2.01	–	–	–
As	7.29 ± 0.47	7.65 ± 0.65	0.45	–	–	–
Co	0.347 ± 0.040	0.371 ± 0.009	0.59	0.23 ± 0.02	0.21 ± 0.05	0.37
Fe	219.5 ± 17.8	205.8 ± 6.8	0.72	204 ± 22	194 ± 20	0.34
K	6229 ± 498	6520 ± 90	0.58	–	–	–
Na	3237 ± 162	3297 ± 53	0.35	2442 ± 140	2430 ± 130	0.06
Rb	3.23 ± 1.06	3.26 ± 0.14	0.03	13.1 ± 0.8	12.5 ± 0.1	0.74
Se	1.99 ± 0.21	2.06 ± 0.15	0.27	0.69 ± 0.12	0.71 ± 0.07	0.14
Zn	1376 ± 59	1424 ± 46	0.64	121 ± 4	123 ± 8	0.22

results obtained are within the range of certified values at a confidence level of 95% [29]. As a result, all the elements obtained in the analysis of the certified reference materials were satisfactory. It indicated that the analytical method used in this work was reliable and applicable.

Concentrations of trace elements in the fingernails

In the fingernails of both groups, the concentration of eight elements, including As, Au, Br, Co, Cr, Sb, Sc, and Se, were found at sub part per million (μg g^{-1}) levels, while the other elements, including Fe and Zn, were ranging between some ten and hundreds μg g^{-1} (Table 2).

Table 3 shows a comprehensive comparison of the desired elemental concentrations in the fingernails of the control group in our study with those reported by others [20, 32–34]. For six comparable elements (As, Co, Cr, Sb, Se, and Zn), the concentrations were in good agreement with those obtained by Goulle et al. [32]. With few exceptions, some deviation in the values of geometric mean between the control group, and of those reported by Chaudhary et al. [33], Vance et al. [34], and Wee et al. [20] were observed. The difference could probably be due to fingernail samples analyzed by these authors could have been collected from both genders. For the desired trace elements of the case group, a comparison with other studies was impossible because we had not found any literature reporting such data for breast cancer patients. However, the observed trace element concentrations in the fingernails of the case group (Table 2) were in good agreement with values reported by Xiao et al. [19] in the fingernails of esophageal cancer patients.

The correlation of elemental constituents with breast cancer

Statistical analysis showed that there were significant differences in concentrations of Cr, Fe, Sc, and Zn between two groups ($P < 0.05$), while no difference for other elements has found (Table 4). In this study, selenium (Se) is observed at the high P value, and positive correlation has found for Zn with the low P value. Both Se and Zn are essential elements in the human body. However, the difference between the case group and the control group has not found for Se; while, there was a significant difference for Zn. This is necessary to have a discussion of the correlation between these two elements and other observed elements in the fingernails.

Table 2 The concentration of elements (μg g^{-1}) in the fingernail of both groups

Element	Case group ($n = 34$)				Control group ($n = 35$)			
	Mean	Median	SD	Range[a]	Mean	Median	SD	Range[a]
As	0.37	0.35	0.12	0.02–0.98	0.40	0.34	0.13	0.03–0.95
Au	0.87	0.91	0.33	0.19–1.35	0.74	0.72	0.32	0.32–1.47
Br	1.07	1.07	0.43	0.26–2.22	0.92	0.92	0.39	0.30–1.98
Co	0.15	0.12	0.09	0.03–0.49	0.12	0.10	0.07	0.02–0.27
Cr	0.87	0.91	0.38	0.04–1.57	0.62	0.58	0.28	0.12–1.17
Fe	103.80	97.92	40.60	50.76–188.75	68.56	68.88	23.40	27.78–141.0
Sb	0.069	0.063	0.032	0.01–0.20	0.068	0.060	0.032	0.020–0.200
Sc	0.034	0.016	0.015	0.009–0.109	0.012	0.010	0.006	0.002–0.030
Se	0.77	0.84	0.30	0.32–1.34	0.80	0.79	0.40	0.16–1.95
Zn	70.06	77.50	24.12	23.23–103.81	103.24	101.56	38.96	33.23–204.0

[a]First values of range = limit of detection (LOD)

Table 3 Concentration of elements (μg g^{-1}) of control group from this work and literature values

Element	This work[a] Avg. age (47.6 years)	Chaudhary[a] Mukaka [31] Avg. age (30.3 years)	Vance[a] Goulle et al. [32] Avg. age (59 years)	Wee[a] Wee and Ebihara [20] Avg. age (27.7 years)	Goulle[b] Akoglu [30]
As	0.321	0.0545	0.0318	0.0993	0.024–0.404
Au	0.640	0.0299	0.0233		
Br	0.832	2.11	2.09		
Co	0.010	0.0421	0.0275	0.0191	0.008–0.043
Cr	0.535	0.898	1.65		0.18–0.76
Fe	64.39	19.5	13.5	17.7	
Sb	0.058	0.0366	0.0245	0.0073	0.014–0.086
Sc	0.010	0.0027	0.0084		
Se	0.688	1.003	1.002	0.998	0.47–1.06
Zn	103.23	147	149	104	83–143

[a]Geometric mean, except Zn = arithmetic mean

[b]Range of values

Table 4 The statistical parameters of concentration of elements in the fingernails

Element	*t* test	T critical	*P* value	Sign. difference
As	0.758	1.998	0.660	No
Au	1.661	1.997	0.128	No
Br	1.516	1.997	0.134	No
Co	1.624	2.002	0.192	No
Cr	3.104	2.000	0.002	Yes
Fe	4.401	2.005	8.4×10^{-5}	Yes
Sb	0.132	1.996	0.901	No
Sc	7.862	2.026	2.8×10^{-5}	Yes
Se	0.353	1.998	0.602	No
Zn	4.267	2.002	7.6×10^{-5}	Yes

For the case group, positive correlations at fair-moderate levels between Cr and As, Fe and Co, Sc and Fe, Sc and Sb, Se and Co, Se and Sb, Zn and Se were observed (Table 5). For the control group, positive correlations at fair-moderate levels were found between Sc and Fe, Zn and Fe, Zn and Se, while negative correlation at moderate level was noticed between Fe and Co. In contrast, weak correlation among Au and Br with other elements was observed in both groups.

Weak correlations between As and Cr, Se and Sb, Sb and Sc were recognized in the control group, while the elements in each pair were significantly correlated for the case group. In addition, Zn and Fe were realized to be correlated for the control group, but this correlation was not observed in the case group. Particularly, in this work, a reversed correlation was found between Fe and Co for the case group and control group.

The trace elements have diversified biological functions from essential elements to toxic elements, and it is considered as one of the reasons that possibly cause cancer or other diseases. The essential elements, such as Cr, Co, Fe, Se, Zn, etc., are particularly important in the process of metabolism, respiration, growing up and death of the cells [35–37]. The change in the concentration of trace elements may associate with the disorder of processes of the body [35, 38, 39].

As one know, Zn does activate the gene transcription and cell proliferation. The increasing of Zn concentration in cells has contributed to the processes of multiplies cell, even cells of tumors [40]; while, Se is to prevent for development of cancer cells, and it provides protection and avoids chromosome injury, which may cause cancer [41]. Therefore, Zn and Se are always to correlate with the human body. This judgment was completely confirmed via the correlation between Se and Zn in our study (Table 5). This correlation was also found in non-cancerous and cancerous breast tissues [42]. In the fingernails of the case group, the concentration of Zn was lower than that of the control group, while the concentration of Se was still not significantly different (Table 4). Hence, for the case group, the correlation between Zn and Se has a slight decrease in comparison to the control group. However, the change in concentration of Zn did not disrupt their correlation.

In this study, the obtained result of the correlation between Zn and Fe was quite interesting. In a study on the correlation between Zn and Fe in the breast tissues of normal and cancer women, Ebrahim et al. [43] showed that, no correlation between Zn and Fe in the breast tissues of cancer women, but the two elements had found to be correlated in breast tissues of healthy women with the R-value of 0.44. This result was in good agreement with our study for the fingernails. Thus, it can be said that the correlation between Zn and Fe in the fingernails was similar to that in

Table 5 Correlation coefficients between elements in the fingernails

	As	Au	Br	Co	Cr	Fe	Sb	Sc	Se	Zn
Case group										
As	1.000									
Au	0.072	1.000								
Br	−0.117	0.126	1.000							
Co	−0.100	−0.182	0.227	1.000						
Cr	**0.512**	0.067	−0.174	0.057	1.000					
Fe	−0.248	−0.208	0.139	**0.401**	−0.046	1.000				
Sb	−0.038	0.198	0.182	0.178	0.165	0.298	1.000			
Sc	−0.172	0.237	0.058	0.233	−0.100	**0.429**	**0.442**	1.000		
Se	−0.045	−0.126	0.201	**0.421**	0.000	0.231	**0.520**	0.343	1.000	
Zn	−0.102	−0.232	0.249	0.302	−0.303	0.195	0.084	0.324	**0.569**	1.000
Control group										
As	1.000									
Au	0.194	1.000								
Br	−0.236	0.268	1.000							
Co	0.032	−0.079	0.224	1.000						
Cr	−0.142	−0.328	0.083	0.097	1.000					
Fe	−0.122	−0.119	−0.207	**−0.480**	0.024	1.000				
Sb	−0.197	0.203	0.014	−0.174	0.137	0.155	1.000			
Sc	0.259	−0.172	−0.251	−0.202	0.070	**0.506**	0.081	1.000		
Se	−0.053	−0.249	0.003	−0.086	−0.011	0.207	0.171	0.085	1.000	
Zn	−0.099	−0.245	−0.213	−0.209	−0.194	**0.519**	0.220	0.277	**0.667**	1.000

Bold values are defined as values with a fair–moderate or higher correlation

breast tissues for breast cancer patients. However, there are significant differences in the average concentration of Zn and Fe between fingernails and breast tissues. For the breast tissue of the women with breast cancer, the concentration of Zn was higher than that of normal women [43, 44]. It is likely that the development of the tumor led to the increasing in the quantity of cells so that they need to Zn in the transformation and metabolism. In the cancerous cells, the trend of increase in concentration of Zn was also occurred for other cancer types, such as prostate cancer [45], and gastric cancer [40, 46]. It seemed that the cancer tissue enriched Zn leading to the deficiency in other tissues in the body, including nails and hair. This was in good agreement with the obtained results in this work. Theoretically, cancer cells need more blood than normal cells; the concentration of Fe was, therefore, to be increased in cancer tissues. However, earlier studies showed that the concentration of Fe in breast cancer tissues was no significant difference from normal breast tissues [43, 44]. In our study, in comparison to normal women, the concentration of Zn in the fingernails decreased, while the concentration of Fe increased (Table 2). It was shown that the correlation between Zn and Fe in breast tissues has reversed in comparison to the fingernail. In our study, no correlation between Zn and Fe in the fingernails has found in the case group (Table 5). This result can be interpreted as follows: when cancer cells develop, the biological function of breast tissue will be broken down. This will result in the cancer cells no longer absorbing Fe for the growth up. Therefore, when the amount of Fe gets into the body through diet, medicine, etc., it will be partly absorbed by the breast tissues, largely get out through other tissues of the body, including hair and nails. In a study on metal exposure in the nails of the population at Punjab, India, Blaurock-Busch et al. [12] found that the concentration of Fe in nails of breast cancer patients was higher compared to normal people, and Fe as well as some other metals had entered into the human body from water, soil, and phosphate fertilizers.

Until now, no report on the evaluation of the concentration of Zn in nails from the women with breast cancer and normal women was found. However, Choudhury et al. [47] showed that, for the persons who experienced a chronic arsenic exposure, the concentration of Zn in hair has strongly decreased in comparison with the normal ones. Furthermore, the concentration of Zn has found to be increased in tissues of stomach cancer patients [40, 46]. Campos et al. [48, 49] presented a reverse correlation between the concentration of Zn in nails and stomach cancer. In our study, the concentration of Zn in fingernails of the case group was lower than that in the control group. It was likely that the increase in the concentration of Zn in cancerous cells leads to its deficiency in other organs in the body.

Cobalt (Co) has a great biological role that exists in form of coenzyme (vitamin B12) in blood, liver, gastric, and ileum. The deficiency of this vitamin will result in anemic. In a study on trace elements in breast tissues, Ebrahim et al. [43] showed that no difference in Co and Sc between the cancerous and the normal breast tissues. In our study, Co in the fingernails was not different between the two groups, while the Sc did. However, the biological roles of such elements within the body had been still unclear with no scientific evidence [37]. The correlation between Co and Sc was not assessed for both groups in this study. Particularly, in the current study we observed that the correlation between Co and Fe has an opposite tendency in the case group and the control group. This could be explained that since both Co and Fe are essential trace elements for the growth of blood cells and tissues in the body, for normal women, once the concentration of Fe increased, the concentration of Co decreased, or vice versa, to achieve balance on the biological system in the body. Meanwhile, for women with breast cancer, when both the Fe and Co levels were increased, it may predict that the biological balance system in the body could be broken, resulting in disease or cancer.

Antimony (Sb) was found at low levels for both groups, in this study (Table 2). However, a significant difference between the case group and the control group for this element was noticed (Table 5). Sb is a toxic element causing chronic diseases i.e. respiratory irritation, pneumoconiosis, antimony spots on the skin and gastrointestinal symptoms [50] after a long exposure with various sources, such as industrial materials, soil, water, and food [51]. In addition, antimony trioxide is considered carcinogenic to humans, and in particular of the risk of lung cancer [52]. In this study, very weak correlation between Sb and other elements for the control group was noticed, but a fairly correlation between Sb (toxic element) and Se (essential element) was found for the case group (Table 5). As a result, the obtained concentration of Sb in the fingernails of the case group was much lower than those of the control group.

Scandium (Sc) was also found at quite low levels with a significant difference for both groups. The correlation between Sc and Fe was found at both groups. Sc has not been described as the essential element for human because no biochemical function was directly connected to it [41]. The fact that the concentration of Sc in fingernails of the case group is higher compared to the control group and how Sc was interacted on Fe is still to be uncleared.

In this study, no significant difference in arsenic (As) concentrations between two groups was seen. This result did agree with the results reported by Jouybari et al. [53] for breast tissues and Blaurock-Busch et al. [12] for nails confirming that As was unlikely related to the risk of breast cancer. A significant correlation between As and Cr was found for the case group, but little correlation between As and other elements was found in the fingernails of the control group. This result was also agreement with studied result in breast tissue [43]. It is very difficult to satisfactorily explain in this case, except the intake from environment.

At cell levels, chromium (Cr) exposure might lead to a break in the cell cycle and cause cancer [54]. The concentration of Cr in the cancerous breast tissues was higher compared to the normal breast tissues [43, 55]. Garland et al. [3] found the relationship between the risk of cancer in menopausal women and the concentration of Cr in toenails. In our study, the concentration of Cr obtained in the fingernails from the case group was higher compared to those from the control group (Table 2). Our results revealed a significant difference between the case group and the control group (Table 4) for the concentration of Cr in the fingernails. These results are in good agreement with literatures [3, 15, 43].

Bromine (Br) and gold (Au) in the fingernails showed no significant difference between the case group and the control group. Moreover, these elements also showed no significant correlation with any other elements that detected in this study. Chaudhary et al. [33] had shown that, Au analysed in the nail samples had a significant correlation with gender. Au was found to be higher in females compared to males (possibly due to the frequent use of Au jewelry). Therefore, we thought that Au did not associate with the risk of breast cancer. In this study, a higher concentration of Br was found in the fingernails of the case group in comparison to the control group, which agreed with those of Magalhaes et al. [44] in the cancer breast tissues.

Conclusions

The k_0-INAA was the appropriate method for determination of trace element in nails. The concentrations of Cr, Fe, and Sc in the fingernail of the women with breast cancer were much higher in comparison to those of the normal women, while the Zn concentration was in reverse tendency. The elements As, Au, Br, Co, Sb, and Se were the same level for both groups.

Significant differences ($P < 0.05$) between the women with breast cancer and the normal women were found for the elements Cr, Fe, Sc, and Zn. The positive at moderate level correlation between Zn and Se was found for both groups. A similar correlation was found for Fe and Zn in normal women, but no significant correlation was noticed for the women with breast cancer. In contrast, a significant correlation between As and Cr was found in the women with breast cancer, but this did not occur in the normal women.

From our findings, it could be concluded that the elements Cr, Fe, and Zn were likely associated with the risk of breast cancer. However, due to limited sample size, the results in this paper might be insufficient to provide a reliable statement on the use of concentration of trace elements in fingernails as an indicator of breast cancer. Further investigation conducting a larger scale of sampling should be needed for reliable conclusion on the association of trace elements in nails with breast cancer.

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Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Huynh Truc Phuong, Tran Tuan Anh, Tran Pham Ngoc Trinh, and Nguyen Thi Truc Linh. The first draft of the manuscript was written by Huynh Truc Phuong and all authors commented on previous versions of the manuscript. The manuscript was edited and revised by Nguyen Van Dong. All authors read and approved the final manuscript.

Compliance with ethical standards

Conflict of interest We have no conflict of interest.

Research involving human participants and/or animals Research has carried out on the fingernail of breast cancer patients.

Informed consent This study was approved by the ethics committee of Dong Nai General Hospital and participants.

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