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Running Title: Risk Estimation of Thyroid Cancer for Children

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Risk Estimation of Thyroid Cancer for Children Undergoing Brain CT Examinations

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Abstract

Background: Despite significant diagnosis benefits, the usage of ionizing radiation is not risk-free. The aim of this study was to determine the risk of thyroid cancer for children who exposed from brain computed tomography (CT) scan.

Method: In this a cross-sectional study, 90 patients under 20 years of age who underwent brain CT-scan were selected. Parameters such as age, sex, imaging technique, imaging characteristics, and thyroid absorbed dose were considered. We used SPSS software, version 21, at 95% confidence interval to analyze the absorbed dose and risk for each individual.

Results: The mean and standard deviation of absorbed the dose for girls and boys for the spiral technique were 3.954 ± 0.393 and 4.72 ± 0.000 mGy and in sequential technique, they were 2.282 ± 0.461 and 1.985 ± 0.431 mGy, respectively. The mean and standard deviation of the absorbed dose in <5 years age group was 5.65 ± 2.00 , 3.03 ± 1.34 in 6 to 10 years, 2.63 ± 0.98 in 11 to 15 years, and in 16 to 20 years was 2.57 ± 1.04 mGy ($P < 0.001$). There was a significant negative correlation between the absorbed dose and field dimensions ($r = -0.604$, $P < 0.001$) and slice thickness ($r = -0.777$, $P < 0.001$). The mean and standard deviation of Lifetime risk for thyroid cancer induction ($\times 10^5$) in <5 years age group in spiral technique was 158.79 ± 322.50 for female subjects and 16.5 ± 42.90 for male patients, which was significantly more than those of other groups and techniques ($P < 0.001$).

Conclusion: The rate of thyroid absorbed dose during brain CT-scan was found to be noticeable, especially in spiral CT imaging, for female patients < 5 years. Based on our results, it was associated with an increased risk of thyroid cancer in this age group.

Keywords: Computed tomography, Thyroid dose, Cancer risk, Children

Introduction

Computed tomography (CT) is one of the most common methods of ionizing radiation imaging, accounting for 11% of the total diagnostic radiology and 67% of the total effective dose of human society.¹ Overall, about 30% of the total helical CT-scans was performed for the head and neck region.²

Although it has been stated that most of the imaging modalities are necessary for diagnostic purposes, the ionizing nature of these rays can increase the risk of complications, such as cancer or genetic mutations. Such disorders are less likely to occur in the elderly patients, but can be significantly evident in children and young people.³

Thyroid is the largest and the most important endocrine gland in the human body, secreting two major hormones of triiodothyronine (T3) and thyroxine or Tetraiodothyronine (T4). Thyroid is located in the anterior part of the front trunk neck and just below the larynx and is surrounded by the trachea protrusion.⁴ Thyroid cancer was the first malignant tumor to have increased dramatically among Japanese survivors of the atomic bomb blast and other radiation events, including Chernobyl and Marshall Island.⁵⁻⁷ During the human growth period, due to the increasing growth of thyroid cells, the sensitivity to radiation increases considerably.⁸ Therefore, it is important to measure the dose received by thyroid during imaging, specifically in children under medical radiation procedures.

Considering the high incidence of cancer among people of different ages in Iran, determining the effective factors and their contribution to the spread of the disease in society is of great importance. This study aimed to estimate the thyroid dose in brain imaging by CT scan in children using thyroid absorption dose and estimating the risk of cancer using models presented by ICRP103 and BEIR VII.

Materials and Methods

Patients

This cross-sectional study was performed in the CT scan section of Be'sat medical center of Hamadan University of Medical Sciences.

The sample consisted of 90 children and adolescents under the age of 20 who underwent brain CT-scan. A checklist as well as a consent form was completed for each patient. This study was supported by the Student Research Committee contract under the number 9704192093 and ethical number of IR.UMSHA.REC.1397.197 of Hamadan University of Medical Sciences, Hamadan, Iran.

The checklist included specifications of the device model, imaging type and technique, kV, milli Amper seconds (mAs), open field dimensions, pitch, feed rotation, and irradiation time in addition to age and sex of the patients. The Patients were divided into four age groups, including <5, 6-10, 11-15, and 16-20 years.

Thermoluminescent dosimeters

50 TLD tablets of GR-200 type were used for external dosimetry of the patients, mainly due to its small size and proper structure which does not cause any harm to the patient. The tablets were purchased and calibrated using a 137-Cesium and read by TLD reader (model 7103, Iran).⁹⁻¹⁰

Skin surface dose and absorbed dose

The superficial dose of skin in the thyroid site was measured using TLD tablets placed on the patient's body. Three dosimeter tablets were used for each patient, which were averaged from their readings. The absorbed dosage was also considered equivalent to the dose on the patients' trunk surface.¹¹

Estimating the risk of cancer

The National Academies' Biological Effects of Ionizing Radiation (BEIR VII) had used a Life Time Attributable Risk (LAR) model to estimate the risk of radiation-driven cancer in a population of 100,000. This model is more specifically described for thyroid cancer as formula 1:¹²

$$LAR(D, e) = \sum M(D, e, a) \cdot \frac{S(a)}{S(e)} \quad (1)$$

$$M(D, e, a) = ERR(D, e, a) \cdot \lambda_7^e(a)$$

For men, formula 2 is used:

$$ERR(D, e, a) = 0.53 \exp(-0.83(e - 30)/10) \quad (2)$$

and for women, formula 3 is used:

$$ERR(D, e, a) = 1.05 \exp(-0.83 (e - 30)/10) \quad (3)$$

$M(D, e, a)$ is the absolute risk estimated for the incidence of cancer. e is the age of irradiation by year and a is the incidence of cancer, and often $a=e+5$ is used for all types of cancers, except for leukemia. $S(a)$ is the survival probability up to age a and $S(a)/S(e)$ is the survival probability up to age a compared to survival up to age e . D represents the dosage of received thyroid and is calculated based on Gray.

To calculate the risk of thyroid cancer due to radiation, it is necessary to determine the radiation age of each individual, given by parameter e in the formula. Coefficient $\lambda_1^e(a)$ in Table 2-12 of the BEIR VII report is an indicator of cancer incidence as a function of sex and age, which was reported 230 for men and 550 for women.

Coefficient value $\frac{S(a)}{S(e)}$ is calculated based on Table 12D-1 in the BEIR report for different ages by multiplying the absorbed thyroid dosage by the number of each age in the table and then dividing the dose by 0.1 Gy .¹² This number is computed and divided by $S(a)$ and $S(e)$.

It must be noted that the numbers reported in the table for the ages 0, 10, 15, 20, 30, 40, 50, and 60 are expressed by sex. Patients' ages are amongst these numbers. To calculate the exact number for each patient, the Graph was drawn by age and then the corresponding equation was obtained and this equation was used to calculate the number for each age.

Data analysis methods

The obtained data were analyzed by SPSS16 software. We used central and dispersion indices to analyze the data. The student t-test (Mann-Whitney U-test) was utilized to compare the means in the two groups.

Results

Results of device imaging information

Out of the total brain imaging performed, 65.5% were boys and 34.5% were girls. Among them, 50% were spiral and 50% were

sequential. It must be noted that all imaging were done spirally for the age group <5 years in this center and therefore, the data for this age group were not obtained in sequential technique.

Tables 1 and 2 present the data obtained by sex for the two spiral and sequential techniques.

Based on the results of Spearman correlation coefficient analysis, to determine the relationship between the absorbed dosage and kilovoltage rate used for each patient (Table 3), although increasing the kilovoltage resulted to an increase in thyroid absorbed dose, this trend was not significant ($P > 0.05$). Moreover, Table 3 indicates a significant and negative correlation between the amount of the absorbed dose and the amount of mAs, field dimensions, and slice thickness ($P < 0.001$).

According to the findings of Table 4 and the result of a one-way analysis of variance, there was a statistically significant difference among boys in terms of absorbed dosages. The post hoc test results showed that the average thyroid absorbed dose in the boys of <5 age groups was significantly higher than in the age group of 6 to 10 years ($P = 0.001$), 11-15 years ($P < 0.001$), and 16-20 years ($P < 0.001$). Meanwhile there were no significant differences in the average thyroid absorbed dose between the age groups of 6-10 years, 11-15 years, and 16-20 years old. Additionally, the results of the one-way ANOVA test showed a statistically significant difference in terms of absorbed dosage in the girls. The post hoc test results indicated that the average thyroid absorption dose in the girls of 0-5 years old was significantly higher than that of the age group of 6-10 years ($P = 0.001$), 11-15 years ($P = 0.001$), and 16-20 years ($P = 0.001$). However there were no significant differences in the average thyroid absorption dose between 6-10, 11-15, and 16-20 years ($P < 0.001$).

The results of calculating cancer risk for different groups for both sexes were calculated based on sex and age (Table 5).

Discussion

In this study, the absorbed dose of patients with different age groups during CT imaging of the patients' brains was measured. Different imaging parameters of each individual were also studied. The results showed that although the increase in kV voltage led to an increase in thyroid dosage, this difference was not significant. Nonetheless, the mAs, field dimensions, and slice thickness had the opposite effect. Comparing the thyroid-absorbed dose in the spiral and sequential techniques showed that thyroid dose in the spiral technique was significantly higher than that in the sequential technique. The results of calculating Lifetime risk for thyroid cancer showed that the risk was notably higher in <5 years age group in spiral technique than other groups and techniques.

Some studies have shown that in addition to the length of the scan area, the amount of mAs can also have a significant effect on the absorbed dose,¹³⁻¹⁵ but this effect was been significant in the present study. Comparing the results of this study to those of Mazonakis et al., the use of spiral method leads to a significantly higher thyroid absorbed dose than the sequential method and the results, which is consistent with our study.¹⁶ This increase in the absorbed dose in the spiral method might be the result of the radiation dose increase along the z-scan axis and due to the high pitch parameter value used during spiral imaging. In addition, factors such as radiation beam collimation or image reconstruction techniques may have impact on this increase of dosage.¹⁷

Furthermore, comparing the estimated absorbed dosage of this study to that in the paper by Mazonakis indicated that the absorbed dose for the sequential method was not significantly different from the absorbed dose calculated by the Monte Carlo method. However, the reported dose of the spiral method in that study was significantly different from the obtained data of this paper, which is due to the lower age of the samples studied in their work. By comparing the thyroid absorption dosage of this study to the study conducted by Su et al. (2014), it is

evident that the sequential thyroid absorption rate in this study is consistent with the reported rate in the Su study but no data have been reported for the spiral method.¹⁸

The results of calculating cancer risk for women and men in the paper by Su paper and our study showed that the risk of thyroid cancer for women is several times higher than that for men; is due to the higher coefficients used in computational models, which is because of the differences in physical and biological parameters and higher thyroid sensitivity of women than men.¹⁸

In addition, comparing the obtained results to those by Vafaie et al.'s study showed that by using the model employed in this study to estimate the risk, the calculated absorbed dose and risk were lower than the results obtained in this study and that is due to the higher age of the samples studied. The results also indicated that two highly sensitive organs of thyroid and eye received high doses during CT imaging, especially head and neck CT.¹⁹

The provided proposals to reduce the absorbed dose of organs during CT imaging were investigated in various studies. Several studies have shown that changes in imaging parameters can reduce the received dose in patients, but there are some concerns about the diminished image quality. Certain manufacturing companies have shown that patient's dose can be reduced by up to 15% by optimizing protocols or using advanced software and algorithms to optimize image processing, without decreasing the image quality.^{20, 21} If it is not necessary to take images from eyes, it is also recommended to minimize the imaging field during the cervical region imaging. Considering the method on minimizing the field, it is crucial to use a shield to prevent radiation from reaching these critical organs.²²

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Conflict of Interest

None declared.

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Table 1. Mean of scanning parameters in spiral technique for different age and gender groups

Age group	gender	Age(year)	Field size (mm)	KV	mAs	Slice thickness(mm)	pitch	Rotation time(s)
1	Male	3.73±1.33	212.73±22.1 1	110.00	102.53±37.6 4	4.40±0.82	0.65±0.19	0.92±0.1 6
	Female	2.32±1.56	205.58±13.6 9	110.00	85.41±23.39	4.42±0.51	0.58±0.13	0.97±0.1 1
2	Male	6.71±0.76	211.57±5.85	110.00	102.43±30.3 8	4.43±0.97	0.68±0.22	0.88±0.1 9
	Female	7.00	215.00	110.00	129.00	5.00	0.55	1.00
3	Male	12.50±1.29	239.00±16.0 0	125.00±10.0 0	135.00±5.35	5.00	0.89±0.22	0.70±0.2 0
	Female							
4	Male	16.60±0.55	218.20±43.2 2	126.00±8.94	105.40±39.8 9	4.20±1.30	0.96±0.09	0.76±0.2 2
	Female	19.00	247.00	130.00	125.00	5.00	1.00	0.60

KV: Kilo Voltage of the X-Ray tube

MaS: mili Amper second of the X-Ray tube

Table 2. Mean of scanning parameters in sequential technique for different age and gender groups

Age group	gender	Age(year)	Field size(mm)	KV	mAs	Slice thickness(mm)	Feed rotation(m m)	Rotation time(s)
2	Male	7.90±1.51	236.00	110.00	125.40±28.56	9.60	19.20	2.70±1.17
	Female	8.00±1.41	236.00	110.00	100.00	9.60	19.20	2.40±1.68
3	Male	13.30±1.16	236.00	110.00	100.00	9.60	19.20	1.17±1.22
	Female	13.75±0.50	234.00±4.00	110.00	118.75±37.50	9.60	19.20	1.20±1.20
4	Male	17.87±0.99	236.00±2.83	110.00	100.00	9.60	19.20	1.70±1.54
	Female	18.62±1.41	235.00±2.83	110.00	100.00	9.60	19.20	1.10±0.99

KV: Kilo Voltage of the X-Ray tube

mAs: mili Amper second of the X-Ray tube

Table 3. Spearman Correlation Coefficient between the absorbed dose and KV, mAs, field size, and slice thickness

Correlation	r ¹	P Value
Absorbed dose and KV	0.119	0.265
Absorbed dose and mAs	-0.268	0.011
Absorbed dose and field size	-0.604	<0.001
Absorbed dose and slice thickness	-0.774	<0.001

¹ Spearman Correlation Coefficient

Table 4. Frequency distribution of thyroid absorbed dose in different gender and age groups

Age group(year)	Number of patients	mean absorbed \pm SD dose (mGy)	gender	P Value
0-5	15	4.85 \pm 1.17	Male	<0.001
	12	6.64 \pm 2.41	Female	
6-10	17	3.15 \pm 1.34	Male	
	6	2.66 \pm 1.41	Female	
11-15	14	2.60 \pm 1.11	Male	
	4	2.28 \pm 0.17	Female	
16-20	13	2.77 \pm 1.36	Male	
	9	2.29 \pm 1.00	Female	
Total	59	3.37 \pm 1.46	Male	
	31	4.04 \pm 2.68	Female	

SD: Standard deviation

Table 5. Lifetime risk for thyroid cancer induction from brain CT examinations in different gender and age groups of children

Imaging technique	Age group (year)	gender	Lifetime risk for thyroid cancer induction ($\times 10^5$)
Spiral	0-5	Male	42.90 \pm 16.52
		Female	322.50 \pm 158.79
Spiral	6-10	Male	29.85 \pm 2.65
		Female	148.65 \pm 0.00
sequential	6-10	Male	12.53 \pm 4.35
		Female	58.54 \pm 21.31
Spiral	11-15	Male	15.06 \pm 3.23
		Female	-
sequential	11-15	Male	6.67 \pm 2.43
		Female	32.83 \pm 3.18
Spiral	16-20	Male	8.35 \pm 1.04
		Female	29.49 \pm 0.00
sequential	16-20	Male	3.45 \pm 0.80
		Female	13.81 \pm 6.27