

# Reasons for Undergoing CT During Childhood: Can CT-Exposed and CT-Naive Populations Be Compared?

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## Abstract

Several epidemiological studies suggested an increased risk of cancer and other tumors in individuals undergoing computed tomography (CT) examination during childhood; however, it was questioned whether the group undergoing CT was comparable to that not undergoing CT. To address this issue, we investigated the reasons for undergoing CT in 763 children aged 0 to 19 years in 2013. Their medical records were fully evaluated and symptoms, underlying conditions, reasons for CT, and clinical courses after CT were investigated. Among the 763 children, 66.1% underwent repeat CT after the first examination, and 19.3% underwent CT 8 times or more. Among all the examined children, 8.8% had cancer and 4.7% had cancer-prone conditions such as Down syndrome, tuberous sclerosis, and cirrhosis. Only 11.4% of the 763 children underwent CT because of trauma, and 32.2% of the children had some types of congenital anomaly. The rate of trauma decreased with an increase in the frequency of CT examinations. Since the incidence of congenital anomalies is below 2.5% in the general population, it was concluded that the population of children undergoing CT is completely different from that not undergoing CT. The 2 groups should not be compared.

## Keywords

computed tomography, low-dose radiation, cancer risk, congenital anomaly

## Introduction

Computed tomography (CT) instruments, worldwide, have been under extreme pressure to reduce the dose of X-rays used to produce a scan. To lower the dose, manufacturers have had to increase costs of equipment or lower the quality images, or both. Computed tomography scans have also been reluctantly used or not used in many cases to decrease the X-ray exposure to individuals. This has been based on the belief that the radiation exposure at CT increases the risk of subsequent cancer, despite that the doses are very low.

Several epidemiological studies have been carried out to estimate the risk of developing cancer in children undergoing CT, and these reports have suggested increased risks of developing leukemia, solid cancer, and brain tumor.<sup>1-4</sup> Soon after their publication, these studies were heavily criticized; comparing 2 groups with or without CT during childhood was illogical because the CT groups contained cancer-prone individuals.<sup>5,6</sup> The CT groups in all studies are considered to have included patients with a predisposing factor for cancer. So, de Gonzalez et al<sup>7</sup> excluded patients with cancer-prone diseases such as Down syndrome and Noonan syndrome and reanalyzed their

data; they reported that the reanalysis still showed an increased risk of cancer. Even by excluding these syndromes, however, the biases between the CT and no-CT groups cannot be completely eliminated because healthy children never undergo CT.

As radiologists and clinicians actually involved in daily CT examinations at a radiology department, we considered that the population of children undergoing CT should be quite different from that not undergoing CT. There is no health screening using CT for children, and children with only a transient symptom such as headache would not be examined for CT.

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Therefore, we hypothesized that the 2 populations should be different and thus not compared. In this study, we examined the medical records of 763 children undergoing CT in 2013 to clarify the reasons for the children receiving CT examinations.

## Materials and Methods

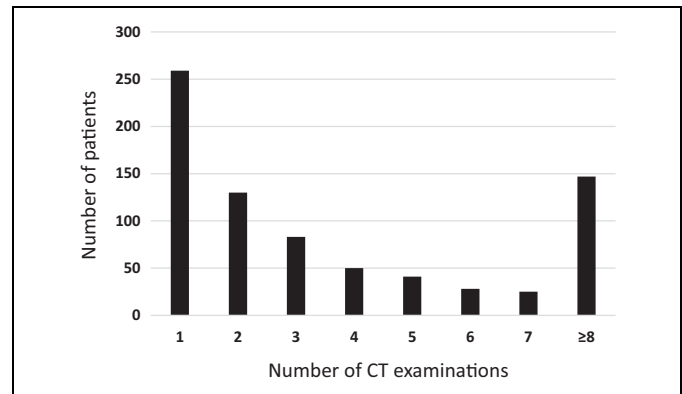
This study was approved by the institutional review board of our institute (approval number 60-19-0136). Informed consent for CT and the possible use of anonymous data for research purposes was obtained from all children or their parents. The study aimed to identify the reasons for undergoing CT during childhood. To limit the 95% confidence intervals (CIs) for 10% to  $\pm 2.5\%$ , 600 participants were considered necessary, and so we decided to investigate more than 600 patients. As 650 to 800 children undergo CT in a year in our hospital on average, we decided to investigate patients undergoing CT in 2013, because 5 years have already passed since then, and follow-up data were available in a proportion of patients.

We investigated individuals aged 0 to 19 years as children, considering the average ages of the previous publications on the cancer incidence after CT examinations.<sup>1-4</sup> First, all children undergoing CT were picked up, and their medical records were analyzed in detail to investigate the reasons for CT. The numbers and target sites of scans were recorded; the sites were classified into the brain/head and neck, thorax, abdomen, bone and soft tissues, and others. Examinations because of traumatic injuries were classified separately because many of the patients received CT for multiple sites. In addition, comorbidity and underlying conditions were recorded. Clinical information after CT to date was obtained to evaluate any disorder that was developed after CT.

## Results

In 2013, a total of 1033 CT examinations were performed in 763 children (424 boys and 339 girls). Of the 1033 examinations, the main target site was the brain/head and neck in 31.6%, followed by the thorax (17.6%), abdomen (16.9%), and bone/soft tissue (13.6%). Traumatic injuries were the reason for undergoing CT in 9.8% (101 of 1033 examinations; 95% CI, 8.0%-11.6%).

Figure 1 shows the number of CT examinations performed between January 2013 and January 2019 in the 763 children. Of them, 259 (33.9%) underwent CT only once, while 147 (19.3%) underwent CT 8 times or more. Of the 259 children undergoing CT only once, the main target site was the brain/head and neck in 35.9%, abdomen in 18.9%, bone/soft tissue in 10.4%, and thorax in 9.6%. Traumatic injuries were the reason for CT in 17.8% (46/259; 95% CI, 13.1%-22.5%). On the other hand, in 147 children undergoing CT 8 times or more by January 2019, a total of 313 CT examinations were performed during 2013. In the 2013 examinations, the main target site was the brain/head and neck in 36.4%, abdomen in 13.7%, bone/soft tissue in 6.4%, and thorax in 19.2%. Traumatic injuries were the reason for CT in 0%.



**Figure 1.** Number of CT examinations performed until January 2019 in children undergoing CT at least once during 2013. CT indicates computed tomography.

Table 1 summarizes diseases or conditions for which CT was performed. The number of patients who underwent CT because of trauma is shown in a separate column; 87 of the 763 children (11.4%, 95% CI, 9.1%-13.7%) underwent CT because of traumatic injury. Sixty-seven (8.8%) had cancer or other malignancy, including neuroblastoma, bone and soft tissue sarcoma, and leukemia/lymphoma, and 36 (4.7%) children had conditions associated with increased risks of cancer, including Down syndrome and tuberous sclerosis. Benign tumors were found in 47 (6.2%). Of the 763 children, 32.2% had congenital anomaly; frequently observed anomalies were skeletal anomalies (11.3%), cardiovascular anomalies (10.1%), neurological anomalies (3.5%), urogenital anomalies (2.5%), and multiple organ anomalies (3.1%). In 183 (24.0%) children, no definite disease was diagnosed; 75 of them had undergone CT because of trauma.

## Discussion

Previous studies on the cancer/tumor incidence after CT during childhood were large involving more than 160 000 children in 3 studies.<sup>1,2,4</sup> Because of this large population size, it was considered impossible to investigate the reasons for undergoing CT in individual children. The present study was a single-institutional study at a middle-sized university hospital with 800 beds, and it may be argued that the population of children undergoing CT in this study may not represent all children undergoing CT. However, pediatric CT is performed less frequently in small city hospitals, and so we consider that the results of this study would deviate little from those of the whole population, although the proportion of each reason may differ to some extent. Our study demonstrated that 32.2% of the children undergoing CT had a congenital anomaly. The incidence of these anomalies in neonates, all combined, is estimated to be less than 2.5% in Japan according to the National Institute of Radiological Sciences ([https://atomica.jaea.go.jp/data/fig/fig\\_pict\\_09-02-03-07-01.html](https://atomica.jaea.go.jp/data/fig/fig_pict_09-02-03-07-01.html)), so it is concluded that the population of children undergoing CT is completely different from that not undergoing CT. In

**Table 1.** Diseases or Conditions for Which CT Was Performed in 763 Children.

Condition/Disease	n	%	Trauma (n = 87)
Cancer/malignancy	<b>67</b>	8.8 (6.8-10.8)	
Neuroblastoma	13	1.7	
Osteosarcoma/soft tissue sarcoma	11	1.4	
Leukemia/lymphoma	10	1.3	
Brain tumor	8	1.0	
Cancer-prone condition	<b>36</b>	4.7 (3.2-6.2)	
Down syndrome	10	1.3	
Tuberous sclerosis	5	0.7	
Liver cirrhosis	4	0.5	
Inflammatory bowel disease	4	0.5	
Infectious mononucleosis	3	0.4	
Benign tumor	<b>47</b>	6.2 (4.5-7.9)	
Benign bone tumor	16	2.1	
Cervical cyst	4	0.5	
Ovarian tumor	3	0.4	
Congenital anomaly	<b>246</b>	32.2 (28.9-35.5)	5
Skeletal	86	11.3	2
Thoracic anomaly	33	4.3	
Hip joint anomaly	17	2.2	
Vertebral anomaly	10	1.3	
Cardiovascular	77	10.1	1
Complex cardiac anomaly	48	6.3	
Ventricular septal defect	7	0.9	
Valvular disease	6	0.8	
Neurological	27	3.5	1
Meningo/encephalocele	8	1.0	
Hydrocephalus	7	0.9	
Urogenital	19	2.5	
Pyeloureteral junction stenosis	10	1.3	
Uterine anomaly	2	0.3	
Urethral anomaly	2	0.3	
Other organ	13	1.7	
Multiple organ	24	3.1	1
Other	<b>184</b>	24.1 (21.1-27.1)	7
Cholesteatomatous otitis media	21	2.8	
Epilepsy	19	2.5	
Appendicitis	16	2.1	
No proven disease	<b>183</b>	24 (21.0-27.0)	75

Abbreviation: CT, computed tomography.

The values in parenthesis represents 95% confidence interval. Only 2 to 5 diseases with large patient numbers in each category/subcategory are listed.

addition, it was reported that children with birth defects have a higher risk of cancer compared with children without birth defects, and the relative risk was estimated to be 3.05 (95% CI, 2.65-3.50).<sup>8</sup> This study included chromosomal congenital anomalies like Down syndrome, but a recent report demonstrated that the cancer risk was also higher in patients with a nonchromosomal anomaly.<sup>9</sup> Such a high relative risk may not result from radiation at diagnostic imaging and probably is inherent to the disease condition. So, the increased risk of cancer/tumor in previous studies may be largely explained by our observation.

A few studies investigated the effects of radiation doses used for CT in mice. Miller et al<sup>10</sup> investigated the issue in mice exposed to a tobacco-specific carcinogen. A/J mice

received 0, 10, 30, and 50 mGy of whole-body irradiation 4 times at 1-week interval. Irradiated mice exhibited 1.8- to 2-fold increases in tumor multiplicity, but no dose-effect relationship was observed among the 3 dose groups. However, contradictory data were reported more recently. Lemon et al<sup>11</sup> investigated cancer development and longevity of cancer-prone *Trp53*<sup>+/-</sup> mice exposed to a single 10-mGy CT scan or  $\gamma$  irradiation. Computed tomography-exposed mice lived longer than the control mice, and the low-dose radiation caused a significant increase in the latency of sarcoma and carcinoma. In another experiment by the same group, 4 Gy was administered first to the same mice and weekly CT was repeated 10 times.<sup>12</sup> The overall life span was about 8% longer in mice exposed to multiple CT scans after 4-Gy irradiation than the control mice receiving 4 Gy alone. Increased latency periods for lymphoma and sarcoma progression were observed again. Thus, these data are conflicting; however, it should be noted that the former study suggesting the carcinogenic effect used only 20 mice per group, whereas the latter 2 studies used about 100 or 200 mice per group. Prolongation of the latency period for tumor development in mice was also observed by single or continuous low-dose irradiation.<sup>13,14</sup> Our group also demonstrated other beneficial effects of low-dose radiation, including growth promotion of silkworm larvae<sup>14,15</sup> and the radioadaptive response of mice<sup>16</sup> and cultured cells.<sup>17</sup> These beneficial effects may be based on biopositive responses to low-dose radiation at molecular, cellular, and tissue levels.<sup>18</sup>

The concept that low-dose radiation from CT may increase the cancer incidence is based on the linear no-threshold (LNT) hypothesis, but recently, much criticism has been focused on the LNT hypothesis first put forward more than a half-century ago.<sup>19-22</sup> Based on historical data, the LNT theory might have not been founded on scientific data. To support or refute the theory would have marked influences on many aspects of human life. Data on CT-exposed children can never support the LNT hypothesis. To conclude, the 2 groups undergoing and not undergoing CT during childhood should never be compared.


## Declaration of Conflicting Interests

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