Excess Lifetime Cancer Mortality Risk Attributable to Radiation Exposure from Computed Tomography Examinations in Children

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Abstract
Background: The use of computed tomography in Israel has been growing rapidly during recent decades. The major drawback of this important technology is the exposure to ionizing radiation, especially among children who have increased organ radiosensitivity and a long lifetime to potentially develop radiation-related cancer.

Objective: To estimate the number of excess lifetime cancer deaths related to annual CT scans performed in children in Israel.

Methods: We used CT scan utilization data from 1999 to 2003 obtained from the second largest health management organization in the country to project age and gender-specific CT scan use nationwide. Based on published organ doses for common CT examinations and radiation-related cancer mortality risk estimates from studies in survivors of the atomic bomb, we estimated the excess lifetime risks for cancer mortality attributed to use of CT in children and adolescents (up to 18 years old) in Israel.

Results: We estimated that 17,686 pediatric scans were conducted annually in Israel during 1999–2003. We project that 9.5 lifetime deaths would be associated with 1 year of pediatric CT scanning. This number represents an excess of 0.29% over the total number of patients who are eventually estimated to die from cancer in their lifetime.

Conclusions: Pediatric CT scans in Israel may result in a small but not negligible increased lifetime risk for cancer mortality. Because of the uncertainty regarding radiation effects at low doses, our estimates of CT-related cancer mortality should be considered with caution. Nevertheless, physicians, CT technologists, and health authorities should work together to minimize the radiation dose for children to as low as reasonably achievable and encourage responsible use of this essential diagnostic tool.

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Since its introduction in the early 1970s, computed tomography has become an essential tool for the diagnosis of many medical conditions and, more recently, for evaluation of treatment progress. Traditionally it was used in diagnosing cancer, conditions related to trauma, and inflammatory diseases. Improved technology and the development of helical and multidetector CT resulted in broader use, including the detection of pulmonary embolism, appendicitis and renal calculi [1]. The rapidly growing use of CT scans has been well documented in many countries, including Israel, where the number of scans per 1000 people increased from 52.1 in 1995 to 88.2 in 1999 with over half a million exams performed annually [2]. However, the growing use has raised concerns about potential risks. Surveys have shown that CT scans contribute significantly to the population collective radiation dose despite their constituting a relatively small proportion of all X-ray examinations [3]. One of the populations potentially vulnerable to adverse effects from CT is children. Previous studies have indicated that children are more sensitive than adults to the oncogenic effects of radiation, resulting in higher risks for acute leukemia and solid cancers [4]. In addition, the effective radiation doses received by children are about 50% higher than those received by adults due to their smaller body size and related attenuation [5]. Children also have a longer lifetime risk for developing radiation-induced cancers. To date there are no quantitative assessments of the potential risk of cancer associated with CT scans among children in Israel. The aim of the current study was to estimate the number of excess lifetime cancer deaths related to annual pediatric CT scans performed in Israel.

Methods
We used the methodology reported by Brenner and colleagues [6] to estimate the excess lifetime risks for cancer mortality attributed to CT exams in children and adolescents (≤18 years old) in Israel. We multiplied age, gender, and site-specific lifetime radiation-related cancer mortality risks (per unit dose) by the estimated age-dependent doses of ionizing radiation from abdominal and head pediatric CT scans [7]. We used the total lifetime risk of cancer mortality per unit dose [Figure 1] described by Brenner et al. [6], which was based on estimates from studies of the atomic bomb survivors [8], whereas the background lifetime risk of cancer mortality was based on the age-and-gender-specific mortality rates in Israel, published by the World Health Organization for 1999 [9].

We followed Brenner’s assumptions on the scan parameters of various types of CT machines, which were based on a previous British survey [10]. Since the reported mean CT scan parameters of the head (462 mAs, 12.5 slices, 9.1 mm slice width) were different from abdominal CT (404 mAs, 15.5 slices, 9.3 mm slice width) [10], we divided the risk calculations according to the sites scanned: head (cranial, face and neck) and the rest of the body (trunk and extremities).

The age and gender-specific distributions and the frequency of pediatric patients in Israel undergoing CT scans were estimated by extrapolating data from Maccabi Healthcare Services, the second largest health management organization in Israel. About 26%
of 2.2 million people under age 18 in Israel are members of Maccabi from which they receive comprehensive health care services [11]. Data were obtained from Maccabi’s computerized database of members. The database includes patients’ demographic information and all billing records of CT examinations performed on members between January 1999 and December 2003. For each CT exam the body site of the examination is recorded.

**Results**

Based on the annual rate of pediatric CT scans performed in Maccabi from 1999 to 2003, we estimated that 17,686 scans (8256 in girls and 9430 in boys) were performed annually in Israel during this 4 year period. Table 1 shows the distribution of site of CT exam by age and gender. It also shows approximate doses to the brain (for head CT) and stomach (for abdominal CT), which decline from 130 mGy and 51 mGy in children under 3 years old to 30 mGy and 24 mGy in adolescents aged 15–18 years, respectively.

The projected annual number of pediatric CT-related lifetime cancer deaths by site of CT scan, age and gender is shown in Table 2. The number of lifetime deaths associated with 1 year of CT scans performed on persons under 18 years old is estimated to be about 9.5 and about 7.25 for persons scanned before age 15. Following Brenner and co-authors [6], we estimated 4.42 cancers from CT scans of head or neck (mostly brain and thyroid cancers) and 5.08 cancers due to all other CT scans. The approximate dose to the brain (for head CT) and stomach (for abdominal CT), which decline from 130 mGy and 51 mGy in children under 3 years old to 30 mGy and 24 mGy in adolescents aged 15–18 years, respectively. The total number of expected deaths represents an excess of 0.29% over the total number of patients who are estimated to die from cancer in their lifetime. The highest excess risk was calculated for CT of children under 3 years old (0.52%) and the risk declined steadily with increasing age. In men, more excess cancer deaths are attributable to scans of the head (55%) compared to only 38% in women.

**Discussion**

Our analysis suggests that current annual pediatric CT use in Israel increases the lifetime risk of cancer mortality by 0.29%. While there are large uncertainties related to this estimate, it is concordant with a previous estimation of 0.35% excess in lifetime cancer mortality for 1 year of CT scans in children (< 15 years old) in the United States [6].

Despite the frequent use of this technology we could not find any published study to assess the risk of pediatric and young

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**Table 1. Distribution of site of pediatric CT scans in Israel by age and gender**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Girls</th>
<th>Boys</th>
<th>Head‡</th>
<th>Rest of body§</th>
<th>Head‡</th>
<th>Rest of body§</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 3</td>
<td>213.7</td>
<td>203.3</td>
<td>810</td>
<td>949</td>
<td>85%</td>
<td>15%</td>
</tr>
<tr>
<td>4–6</td>
<td>205.6</td>
<td>195.0</td>
<td>610</td>
<td>768</td>
<td>84%</td>
<td>16%</td>
</tr>
<tr>
<td>7–9</td>
<td>192.8</td>
<td>182.9</td>
<td>1,005</td>
<td>1,129</td>
<td>85%</td>
<td>15%</td>
</tr>
<tr>
<td>10–12</td>
<td>183.6</td>
<td>174.6</td>
<td>1,384</td>
<td>1,538</td>
<td>77%</td>
<td>23%</td>
</tr>
<tr>
<td>13–15</td>
<td>176.8</td>
<td>168.3</td>
<td>1,868</td>
<td>1,942</td>
<td>71%</td>
<td>29%</td>
</tr>
<tr>
<td>16–18</td>
<td>174.0</td>
<td>165.9</td>
<td>2,589</td>
<td>3,103</td>
<td>65%</td>
<td>35%</td>
</tr>
<tr>
<td>Total</td>
<td>1,146.5</td>
<td>1,090.0</td>
<td>8,256</td>
<td>9,430</td>
<td>74%</td>
<td>26%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Site of scan</th>
<th>Estimated dose to organ† (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head CT (brain)</td>
<td>130</td>
</tr>
<tr>
<td>Abdominal CT (stomach)</td>
<td>51</td>
</tr>
</tbody>
</table>

* Ref 25  
** Extrapolated from CT examination rates in Maccabi Healthcare Services during 1999–2003 [13]  
† Including face and neck  
§ Including pelvis, spine, extremities, and chest  
‡ Adopted from ref 6

**Table 2. Estimated cancer mortality attributable to annual CT examinations in patients aged ≤18 years in Israel**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>From CT to head **</th>
<th>From CT to rest of body†</th>
<th>From CT to head **</th>
<th>From CT to rest of body†</th>
<th>Total no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 3</td>
<td>0.48</td>
<td>0.33</td>
<td>0.78</td>
<td>0.13</td>
<td>1.72 (0.52%)</td>
</tr>
<tr>
<td>4–6</td>
<td>0.30</td>
<td>0.29</td>
<td>0.51</td>
<td>0.17</td>
<td>1.21 (0.48%)</td>
</tr>
<tr>
<td>7–9</td>
<td>0.34</td>
<td>0.25</td>
<td>0.48</td>
<td>0.16</td>
<td>1.24 (0.31%)</td>
</tr>
<tr>
<td>10–12</td>
<td>0.32</td>
<td>0.48</td>
<td>0.36</td>
<td>0.28</td>
<td>1.43 (0.26%)</td>
</tr>
<tr>
<td>13–15</td>
<td>0.20</td>
<td>0.70</td>
<td>0.25</td>
<td>0.50</td>
<td>1.65 (0.22%)</td>
</tr>
<tr>
<td>16–18</td>
<td>0.17</td>
<td>0.91</td>
<td>0.23</td>
<td>0.94</td>
<td>2.25 (0.21%)</td>
</tr>
<tr>
<td>Total</td>
<td>1.81</td>
<td>2.90</td>
<td>2.61</td>
<td>2.18</td>
<td>9.49 (0.29%)</td>
</tr>
</tbody>
</table>

* Estimated risks based on lifetime cancer mortality reported in ref 6, see Figure 1.  
** Including face and neck  
† Including pelvis, spine, extremities, and chest  
‡ Excess increased risk cancer mortality over the age-specific background risk.
adult cancer associated with CT scanning during childhood in Israel. A historic cohort study of conventional diagnostic X-ray exams performed primarily during adolescence [12] with individual dose assessment (mean exposure dose to the breast = 110 mSv) reported a significant linear dose-response trend for breast cancer. Previous case-control studies of childhood cancers also showed a significant association with diagnostic X-ray scans [13,14]. However, these studies may have been affected by recall bias and, therefore, overestimation of the actual risks. The present report underlines the need for follow-up studies of large cohorts of children undergoing CT scans.

The comparatively high number of estimated cancer deaths attributable to head CT scans in men is probably a result of two factors: more exams for conditions related to trauma and a higher excess attributable risk of brain tumors, which were calculated in the Life Span Study on the atomic bomb survivors [15] and are mainly explained by considerably lower background rates in males.

The number of estimated cancer deaths attributable to head CT scans was calculated based on the linear non-threshold hypothesis, which assumes that any given increment in dose is directly proportionate to an increase in the probability of incurring radiation-related cancer. This hypothesis is a fundamental element in the practical system of radiological protection and is commonly used by leading advisory organizations such as the International Commission on Radiological Protection (ICRP) [16] and the National Council on Radiation Protection and Measurements (NCRP) [17]. Because of the uncertainty regarding radiation effects at low doses, our estimates of CT-related cancer mortality should be considered with caution. Since the ICRP warns that this is not appropriate, for the purpose of public health, to calculate the hypothetical number of cases of cancer that might be associated with very small radiation doses received by numbers of people over very long periods [18], we are presenting these data to highlight the potential long-term radiation risks for children undergoing CT and to encourage more active reduction of CT exposure settings in the pediatric context.

In evaluating potential risk from pediatric CT, non-cancer effects also deserve attention. A recently published study in Sweden [19] showed that radiation to infants’ cranium with doses similar to those in CT scans of the head may impair intellectual development. In addition, studies on the A-bomb survivors [20] suggest a significant relationship between ionizing radiation and cardiovascular diseases. Additional studies and further analyses of existing studies are needed to determine the lifetime risks for cancer and non-cancer morbidity and mortality, as was recently recommended by the National Academy of Sciences’ last report on biological effects of ionizing radiation (BEIR VII) [21].

The number of cancer deaths attributable to annual CT use in children under the age of 15 calculated in our analysis (7.25 cases) is of the same order of magnitude as previously [22] calculated (nine cases) for the entire United Kingdom, which has a tenfold larger population. This difference in risk estimates can be explained by the fourfold higher frequency of CT scans in Israel [23] and by the use of data from the late 1980s and early 1990s in the UK study when CT use was less frequent. Our findings stress that while CT remains a crucial tool for pediatric diagnosis and its benefits far outweigh any potential risks for an individual, it is necessary that physicians, radiological technologists and health authorities work together to minimize the radiation dose to children to as low as reasonably achievable (ALARA) [7]. This includes better adjustment of the CT exposure parameters when scanning children, taking appropriate measures to ensure that CT is used only when clinically justified, and considering the use of other diagnostic modalities that do not involve ionizing radiation. Long-term strategies also may include the development of pediatric CT protocols and the dissemination of information regarding the protocols and potential risks through public and professional organizations [24].

References
17. NCRP (National Council on Radiation Protection and Measure-

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Capsule

Genetics of heart disease

Certain lifestyle factors, such as smoking, greatly increase the risk of developing heart disease, but genetic factors also contribute. In independent studies, McPherson and colleagues (Science 2007;316:1488) and Helgadottir et al. (p. 1491) used genome-wide association scanning to identify DNA sequence variants at chromosome 9p21 that increase the risk of heart disease in Caucasian populations. The 20–25% of Caucasians with two copies of the so-called risk allele had a 30–40% higher risk of heart disease compared with individuals with no copies of this allele. The genomic region of interest falls outside the boundaries of annotated protein-coding genes, so the mechanism by which it influences heart disease remains mysterious. Intriguingly, DNA sequence variants within the same general region of chromosome 9p21 have recently been shown to increase the risk of type 2 diabetes.

Eitan Israeli

Capsule

Practice

The Practice section of the British Medical Journal recently had a trio of interesting and useful articles. Lauria and Lombardi review recent advances in the use of skin biopsy to diagnose and monitor peripheral neuropathy (Br Med J 2007;334:1159). An easy to perform 3 mm punch biopsy can make the diagnosis of small nerve fiber neuropathies, which can be associated with diabetes and other metabolic disorders, sarcoidosis and other immune-mediated disorders, and viral and hereditary diseases. Commonly recommended nerve conduction studies only evaluate large myelinated fibers. Sural nerve biopsies, used to diagnose peripheral neuropathies, are invasive and sometimes dangerous procedures. Punch biopsy is worth thinking about in patients – especially those with chronic diseases – who complain of burning, prickling sensations or deep and aching foot pains. In a 10 minute consultation on sinusitis, Neil Chadha and Rashmi Chadha emphasize that the diagnosis of rhinosinusitis is a clinical one, at least in primary care (p. 1165). Characteristic signs and symptoms include nasal congestion and discharge, facial pain, and decreased sense of smell. Sinus X-rays are not indicated. Bacterial etiology, and thus antibiotic treatment, is more likely if the condition has lasted more than a week, purulent discharge is present, and there are systemic symptoms (fever and malaise). Referral is indicated for chronic or recurrent cases or if complications are suspected. The UK National Institute for Health and Clinical Excellence (NICE) has released guidance on the assessment and initial management of young children with feverish illness (p. 1163). Based on evidence when it is available and consensus when it is not, the recommendations follow a “traffic light” system that directs management decisions based on whether the risk of serious illness is low (green), intermediate (amber), or high (red). High risk children should receive a face-to-face assessment within 2 hours and urgent referral to specialty care. Children at intermediate risk should be followed closely. Low risk children may be managed at home.

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