TITLE: Radiation Emissions from Computed Tomography: A Review of the Risk of Cancer and Guidelines

DATE: 04 June 2014

CONTEXT AND POLICY ISSUES

Computed tomography (CT) is a medical imaging technology used for the screening and diagnosis of medical conditions. It involves taking numerous X-ray images of a body area or organ and these images are reconstituted into computer-generated pictures.[1]

Radiation exposure is calculated in millisieverts (mSv) using effective dose (ED).[2] ED is a means of converting localized radiation dose to a dose that would be equivalent to a whole-body exposure in a reference patient. ED is defined as the total body absorbed dose required to achieve an adequate diagnostic image.[2] CT imaging exposes a person to 2 mSv of radiation (for example a head CT) to 30 mSv of radiation (for example a multiphase abdominal CT).[3] In contrast, it is estimated that a person is exposed to 3 mSv of radiation annually from background radiation.[4]

The use of CT has increased over the past decade. In 2011-2012, 4.4 million CT exams were performed in Canada, representing an annual increase of 2.7% since 2003.[5] The national rate for CT scans in 2011-2012 was 126 per 1,000 people. Provincial rates ranged from 209 per 1,000 people (New Brunswick) to 88 per 1,000 people (Alberta).[5] It has been suggested that 26% to 44% of CT scans are ordered inappropriately.[4] With an increase in the use of CT scans, radiation exposure is an important public health concern. The current evidence suggests that doses between 5 and 125 mSv may cause a small but statistically significant increase in cancer risk.[4] Furthermore, frequent radiation exposure leads to high cumulative doses of radiation.[4] The Canadian Nuclear Safety Commission recommends radiation dose limit for exposure to licensed sources of radiation of 1 mSv annually for the public, and 50 mSv annually or 100 mSv over five years for workers (for example nuclear power workers and medical personnel who work with sources of ionizing radiation).[6]

This report will review the evidence on the risk of cancer associated with CT exposure and recommended threshold of radiation doses.

RESEARCH QUESTIONS

1. What is the evidence for the risk of cancer associated with radiation emissions from computed tomography?

2. What are the evidence-based guidelines regarding an acceptable threshold of radiation emission from computed tomography?

KEY FINDINGS

There is some evidence that early life exposure (as children) to ionizing radiation through CT imaging increases the risk of cancer. This finding must be interpreted in light of the limitations of the studies. No guidelines explicitly make recommendations on radiation emission threshold above which there are safety concerns.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 4), ECRI (Health Devices Gold), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and May 6, 2014.

Rapid Response reports are organized so that the evidence for each research question is presented separately.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to the selection criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients requiring CT scans (for diagnosis or follow-up)
Intervention	CT scanning
Comparator	No CT scanning
Outcomes	· Clinical harm (cancer, malignancies) · Guidelines and recommendations – radiation emission threshold above which there are safety concerns (per exam or over a lifetime), radiation emission threshold below which there would be no safety concern

Study Designs	· Health technology assessments/ Systematic reviews/ Meta-analyses
	· Randomized controlled trials
	· Non-randomized controlled trials
	· Guidelines

Exclusion Criteria

Studies were excluded if they did not meet the selection criteria, were published prior to 2009, were modelling studies, or were included in a systematic review examined in this report.

Critical Appraisal of Individual Studies

The AMSTAR instrument[7] was used to guide the critical appraisal of the methodological quality of the systematic review (SR) included in this report. Non-randomized (non-RCTs) studies were assessed for validity using the JAMA User's Guide for articles about harm[8] and the Downs and Black checklist.[9] The quality of guidelines was evaluated using the AGREE II tool.[10]

Numeric scores for this evaluation are not reported and a narrative and tabular description of the strengths and limitations of each included study or guideline is presented instead.

SUMMARY OF EVIDENCE

Quantity of Research Available

The selection of studies is summarized in Appendix 1. The literature search yielded 466 citations. After screening of abstracts, 8 potentially relevant SRs, 29 potentially relevant trials and 7 potentially relevant guidelines were selected for full text review. Of these, one systematic review, three non-randomized trials, and three guidelines met the inclusion criteria. No health technology assessments or randomized controlled trials met the inclusion criteria.

Of note, 18 non-RCTs and one SR were excluded based on study design because the estimation of cancer risk was not based on observational data and follow-up of exposed and unexposed cases. The studies calculated average radiation doses in patients exposed to ionizing radiation and from these averages, the risk of cancer was estimated based on incidence data from atomic bomb survivors. Hence the risk is theoretical and not based on actual patient data. Excluded modelling studies which are of potential interest are listed in Appendix 2. Furthermore, three non-randomized studies were excluded (Pearce et al.,[11] van Walraven et al.,[12] and Davis et al.[13]) because they were already contained in the systematic review appraised in this report.

Summary of Study Characteristics

i) Systematic Reviews

Information on the characteristics of the included systematic review is provided in Appendix 3, Table A3.1.

One systematic review was retrieved.[14] Studies included in the SR were those in which CT scans or other ionizing radiation derived from medical imaging were used and for which cancer risks were reported. The studies were not limited by cancer type. Studies in which radiation risk was associated with occupational exposure were excluded. Also excluded were reviews, letters, and case reports. The literature review was conducted using PubMed and the Cochrane Library databases. Literature searching parameters included: English-only studies, from the previous 10 years up to 09 December 2012, and available as full-text.[14]

ii)   Non-RCTs

Two retrospective cohort studies[15,16] and one case control study[17] were retrieved. Information on the characteristics of the observational studies is provided in Appendix 3, Table A3.2.

Huang et al. examined the association between pediatric head CT scans and the risk of malignancy using the Taiwan National Health Insurance Research Database which contains de-identified medical claims from 99% of Taiwan's population.[15] From this database, 50% of children were randomly chosen for the purpose of the study. Children who had undergone a head CT scans from 1998 to 2006 were selected (n=28 185) as the exposed group. Children with disorders associated with an increased risk of cancer, children with a history of cancer, or children who developed cancer within the first two years of follow-up were excluded from the study (n=3,767). A lag period of two years was chosen. (A lag period is an exclusion period before a cancer diagnosis to avoid the possibility that the scan was part of a diagnostic procedure.) Children were followed until the diagnosis of any malignancy or benign brain tumour, withdrawal from the National Health Insurance system, or until the end of 2008. For each case identified, an unexposed group was randomly selected in a 1:4 ratio and matched with the exposed children for age, gender, year and month of index date. In the study population (both exposed and unexposed), 40.0% of children were between the ages of 0 to 6 years, followed by the 13 to 18 year old children (38.8%), and the 7 to 12 year old children (21.2%). Most of the study population consisted of boys (60.9%). In the exposed group, CT examination occurred only once during the study period in 93.4% of children, followed by twice (5.4% of children) and more than twice (1.2% of children). A total of 5% of the study participants were lost to follow-up at the end of 2008 due to various causes such as death and emigration.[15]

A second cohort study by Matthews et al. evaluated the cancer risk in Australians exposed to CT scans at ages 0 to 19 years.[16] The Australian Medicare database was used to identify persons born between 01 January 1985 and 31 December 2005. Records were linked to the Australian Cancer Database and the National Death Index. Each participant was categorized into of one of seven socioeconomic indexes. The exposed cohort (approximately 680,000 persons) was compared to unexposed persons of similar age (approximately 11 million persons). A lag period of one year was chosen, although additional analyses were conducted for five and 10 year periods. The study population was followed until 31 December 2007, death, or date of first cancer diagnosis. There were slightly more males (52.5%) than females in the exposed group. Age at first CT scan was 15 to 19 years old (48.5%), followed by the 10 to 14 year old group (29.8%), the 5 to 9 year olds (15.4%), and the 0 to 4 years old (6.3%). In the exposed group, 82% of children had received one scan, followed by 12.7% for two scans, 3.5% for three scans, and 1.8% for four or more scans. The most common site of first CT scan was the brain (59%) followed by facial bones (13%), and extremities (9%). Mean length of follow-up for the unexposed group was 17 years whereas the exposed group had a mean length of follow-up of 9.5 years, 7.3 years, and 5.5 years for the one, five, and 10 year lag periods, respectively.[16]

Behnampour et al. conducted a study to determine the predictors of gastric cancer in patients in Iran.[17] Cases of gastric cancer (n=156) were identified from diagnostic centres, medical clinics, hospitals, and health centres from March 2009 to March 2010. Controls consisted of one family member and one neighbor for each case and they were matched based on age, gender, and ethnicity. Data were collected through interviews using a questionnaire and a checklist which had been validated by an expert group (Cronbach's alpha=0.89 and Kuder-Richardson=0.82). Most of the cases were male (68%). Mean age at diagnosis in gastric patients was 62.9 years (standard deviation 13.8).[17]

iii)   Guidelines

Information on guideline characteristics is provided in Appendix 3, Table A3.3.

Three guidelines[18-20] were included in this review. One publication was a Position Statement by the American Academy of Oral and Maxillofacial Radiology[18] which included clinical guidelines for the use of cone beam CT in orthodontics. These were derived using information from the literature and recommendations were made by a Panel through consensus. The Panel developed grading criteria, but the recommendations were not graded.[18] Another guideline was developed by the Society of Cardiovascular Computed Tomography which provided recommendations on various CT radiation topics including radiation dose indices and dose optimization for cardiovascular conditions.[19] Recommendations were developed through consensus, based on the published literature, and these were not graded.[19] The third guideline was a Science Advisory from the American Heart Association which provided recommendations for the use of cardiac imaging that relies on ionizing radiation.[20] There was no information as to how the evidence was collected and how recommendations were made; each recommendation was graded using classes and levels of evidence (see footnote of Appendix 3, Table A3.3).[20]

Summary of Critical Appraisal

i)   Systematic Reviews

The strengths and limitations of the included SR are summarized in Appendix 4, Table A4.1.

The SR by Oh and Koea had clear objectives and inclusion / exclusion criteria. The literature search was well described however no hand searching of references and no searching of the grey literature was done. The articles were independently reviewed by two investigators but only for articles available as full-text. One table provided some of the included trials' characteristics; however some trials were described as 'retrospective' with no other information provided on study design. It was also unclear as to which studies were based on models and which ones were actual observational trials. One section in the text described the limitations of the trials (for example that most studies were based on models, most were retrospective, and case-control studies were prone to recall bias), but individual trial quality assessments and limitations were not provided. The major limitation was the lack of systematic reporting of results. A table of results was not provided and only selective reporting of results was conveyed in the narration. This made it challenging to summarize the SR's findings for the purpose of this report.

ii)   Non-RCTs

The strengths and limitations of the non-RCTs are summarized in Appendix 4, Table A4.2.

In all three studies, the groups were recruited from the same population and for the same time period. The time between exposure and disease was not reported in Behnampour et al. In the cohort studies, some children would have been followed for >6 years in one study and >15 years in the other, whereas other children would have been followed for only two years. There is uncertainty as to the latency period between radiation exposure and the development of cancer.[15] A follow-up of two years may not be long enough to develop and detect cancer.

A lag period of two years was chosen in one cohort study whereas the other chose one year. A one year lag period may be too short to ensure exclusion of patients who received a scan as part of a cancer diagnostic work-up; however the study included sensitivity analyses of 5 and 10 year lag periods.

All three studies provided limited information on patient demographics and it was impossible to determine whether or not the exposed and unexposed groups were comparable. This is somewhat mitigated by the fact that the sample sizes for the cohort studies were very large (regression to the mean) and controlling for confounders was done by statistical adjustment for age and sex in Huang et al., and by stratification of age, gender and year of birth in Matthews et al. Nevertheless, adjustments for other potential confounders such as diet and exposure to other sources of ionizing radiation were not done in the cohort studies and could be an issue if the risk factors were unequally distributed between groups. In Behnampour et al., all influential factors for gastric cancer were identified and entered into a regression model.

Huang included only patients exposed to brain CT scans; it was unclear if persons exposed to CT scans that were not brain scans were excluded from entering the study. If not, these persons would have been allocated to the unexposed group. In contrast, Matthews et al. included exposures to any type of CT scans.

Matthews et al. did not specify whether or not patients with a history of cancer or with diseases likely to increase the risk of cancer were excluded from the study. Furthermore, it did not provide a sub-group analysis by number of CT scans.

Behnampour et al. collected data through interviews and there is the potential for recall bias. In addition, it is unknown as to whether or not the investigators were blinded to disease status. The length of time between exposure and development of cancer was not reported. We don't know if this was a question asked in the interview and whether or not this was accounted for in the analysis. No information was provided on body area of CT scan and frequency of CT scan. The study was conducted in a Middle Eastern population and as such the results may not be generalizable to North America.

iii)   Guidelines

The strengths and limitations of the included guidelines are summarized in Appendix 4, Table A4.3.

For all reports, the objectives of the guidelines were well defined and clear recommendations were provided. One major limitation of the guidelines was the lack of information provided on the guidelines development process such as whether or not a systematic review of the literature was conducted. The view of patients was not solicited and although it appears that clinical experts were involved in the development of the recommendations, it was unclear if other types of experts (methodologists and policy-makers, for example) were involved. The source of

Radiation Emissions from Computed Tomography

funding was not stated although conflict of interest was disclosed. Only one guideline[20] graded the recommendations.

Summary of Findings

Risk of cancer associated with radiation emissions from computed tomography

The summary of results for the SR is available in Appendix 5, Tables A5.1.

Of the 36 included studies in the SR, most studies (exact number not clear) included CT imaging as the intervention. The majority of studies (N=34) found a positive association between ionizing radiation from medical imaging and an increased risk of cancer. One included study[12] reported a non-linear relationship between radiation and cancer risk. There was an age-dependent risk in children and young adults and the risk decreased as the patients became older. The risk of cancer from low dose exposure was uncertain.[14]

The summary of results for the cohort studies is available in Appendix 5, Tables A5.2a and A5.2b. Please note that selected data are shown in the tables.

In Huang et al.,[15] the risk of cancer was not statistically significantly higher in the exposed group compared with the unexposed group. The sub-groups for which there was a statistically significant difference included: increased risk in overall cancer in children who were between the ages of 0 to 6 years old when they had a CT scan (hazard ratio [HR] 1.96, 95% confidence interval [CI]: 1.06 to 3.63), increased risk in overall cancer in children who had a CT scan 4 to 5 years prior (HR 1.77 [95% CI: 1.07 to 2.92]), increased risk in overall cancer in children who had three or more head CT scans (HR 5.04 [95% CI: 1.25 to 20.4]), increased risk of leukemia in children who had three or more head CT scans (HR17.4 [95% CI: 2.32 to 131]), and increased risk of brain cancer in children who had two or more head CT scans (HR12.3 [95% CI: 2.72 to 55.4]).[15]

For all types of cancer, the incidence was 24% greater in the exposed group than in the unexposed group in Matthews et al., (Incidence rate ratio [IRR] 1.24 [95% CI: 1.20 to 1.29]) after stratification for age, gender and year of birth.[16] When the analyses were re-run based on 5- and 10-year lag periods, the incidence was also greater in the exposed group (IRR 1.21 [95% CI: 1.16 to 1.26] and IRR 1.18 [95% CI: 1.11 to 1.24], respectively). Considering risk for developing specific cancers, the IRR for the exposed group compared with the unexposed group was increased for brain cancer, cancer of the digestive system, melanoma, soft tissue, female genital organs, urinary tract, thyroid, Hodgkin's lymphoma and myeloid leukemia but not breast cancer and lymphoid leukemia. For all cancers combined, the incidence rate ratio decreased with increasing age at first exposure. Incidence rate ratio was the highest for children who were 0 to 4 years old at first CT exposure (IRR 1.72 [95% CI: 1.44 to 2.05]) compared with the 15 to 19 years old at first CT exposure (IRR 1.21 [95% CI: 1.16 to 1.27]). For all cancers combined, the proportional increase in incidence rate declined with years since first CT scan. However the differences between IRR were small and the excess risk highest after 15 years or more since first CT scan. The cancer risk by site of CT scan was considered. It was shown that there IRR was larger after CT scans of the chest (IRR 1.62 [95% CI: 1.22 to 2.14]), and abdomen / pelvis (IRR 1.61 [95% CI: 1.38 to 1.88]). The effect of exposure was not statistically significantly different based on socioeconomic status.[16]

Using a multivariate logistic regression model, Behnampour et al. showed that a history of exposure to CT was a risk factor for gastric cancer (OR 2.32 [95% CI: 1.21 to 4.45]).[17]

Three non-randomized studies were excluded (Pearce et al.,[11] van Walraven et al.,[12] and Davis et al.[13]) because they were already contained in the systematic review appraised in this report. Nonetheless, the results for these three studies are presented in Appendix 5, Table A5.2c. One non-RCT showed a statistically significant risk in developing leukemia and brain tumour for children and young adults exposed to CT. The results of two non-RCTs were not statistically significant for the risk of cancer after CT exposure.

Acceptable threshold of radiation emission from computed tomography according to clinical practice guidelines

Recommendations made with respect to radiation dose in the included guidelines are presented in Appendix 5, Table A5.3.

One guideline, the American Academy of Oral and Maxillofacial Radiology,[18] presented selected radiation dose thresholds based on published effective doses for various field of views for CT devices used in orthodontics. The table spans three pages in the publication and as such is not reproduced in this report. The other two guidelines did not provide threshold numbers but rather they stated that radiation dose optimization through algorithms or benchmarks should be established.[19,20] The Society of Cardiovascular Computed Tomography stated that radiation dose optimization should take into consideration various factors in developing algorithms including indication, scanner characteristics, and patient factors.[19] All three sets of guidelines supported the ALARA concept (as low as reasonably achievable) in determining patient dose.[20]

Limitations

The systematic review was not limited to studies of CT imaging but also included were all other ionizing radiation imaging devices.

The SR did not systematically appraise the quality of the included trials, nor did it systematically report their findings. Furthermore, it included modelling studies which determined theoretical cancer risk and not actual risk based on follow-up of patients from exposure to disease. These modelling studies determined the radiation burden associated with CT imaging conducted in various diseases and estimated the lifetime attributable risk of radiation-induced cancer from models. One such model that was used in some of these studies is the Biological Effects of Ionizing Radiation (BEIR) IV risk model developed by the US National Research Council to estimate the risk of cancer in an exposed person.[21] The model was developed from cancer incidence data of atomic bomb survivors who were exposed to high dose radiation and thus using this model to estimate the risk of cancer from a low LET radiation dose (<100 mSv) is done through extrapolation and this has limitations.[4,14,21]

Within the non-RCTs, it was unclear if cases and controls were similar with respect to important determinants and hence, it was impossible to determine the potential selection biases. Socioeconomic status (SES) could have had an impact on access to medical care and medical radiation exposure, but only one study categorized cases according to SES. Furthermore, it is unknown is patients exposed to other important sources of radiation, for example if X-rays and radiation therapy, were excluded. Whereas one cohort study included only CT head scans, the other included CT scans from all body areas.

One case-control study used self-reported information on CT exposure and it is unclear if the data were validated using medical records. The possibility of bias due to differential recall of exposures between cases and controls cannot be ruled out. If cases expended more effort than controls to remember exposures that may have contributed to their disease, this recall bias could overestimate the association between CT and cancer. Furthermore, if the investigators were not blinded to disease status, they may have expanded more efforts at the time of interview to get the information which could also overestimate the risk of cancer after CT examination.

The included guidelines did not provide a definite answer on radiation emission thresholds. This is not surprising as the determination of a radiation dose for a given patient is very much based on many factors such as patient gender, age, weight, organ to be imaged, type and brand of CT machine used, technique used, protocols, and radiologist desire for image quality.[3,22,23]

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

A CT scan is an important diagnostic tool. CT machines have become safer over the years, but due to its increased availability and frequency of scans, radiation exposure is an important public health concern. We identified one systematic review and three non-RCT studies that examined the association between exposure to CT and cancer. Three sets of guidelines considered radiation thresholds.

A SR of 36 studies found a positive association between ionizing radiation and cancer. However, the SR had many limitations and included modelling studies, and as such, it is challenging to draw conclusions. Furthermore, three non-randomized studies which were excluded from this report because they were already contained in the SR, showed a statistically significant risk in developing leukemia and brain tumour in one non-RCT, whereas the results of two non-RCTs were not statistically significant.

One included case-control study showed that a history of exposure to CT was a risk factor for gastric cancer. However this study had many limitations such as lack of information on number and timing of exposure.

In one cohort study, the risk of cancer following head CT was statistically significant in children aged 0 to 6 years at exposure, for those in the 4 to 5 year range since exposure, or when a child had been exposed to two or more CT scans. In another cohort study, the incidence of overall cancer was 24% greater in the exposed group than in the unexposed group. For all types of cancer, the incidence decreased with increasing age at first exposure. For both studies, it is unknown if patients exposed to other important sources of radiation, for example if X-rays and radiation therapy, were excluded.

Three guidelines for the use of CT in orthodontics and cardiology with recommendations on radiation doses were reviewed. One guideline provided selected information on dose thresholds for various brands of cone beam CT scanners; the other two guidelines stated that there is a need to develop algorithms or benchmarks in this area. No guidelines explicitly reviewed the evidence of emission safety. Hence we could not determine, based on the available evidence, the radiation emission threshold above which there are safety concerns or the radiation emission threshold below which there would be no safety concern. There are models which estimate the lifetime attributable risk of cancer based on radiation dose, but these models are

theoretical and at doses less than 100 mSv, they may not be effective in determining cancer risk.

In conclusion, there is evidence that exposure to ionizing radiation from CT scan may increase the risk of cancer, particularly in persons for whom exposure occurred early in life and in persons exposed to multiple CT scans. However, all the studies reviewed had limitations. No guidelines provided information to determine the safety threshold. Clinicians were encouraged to adopt the ALARA principle.

PREPARED BY:
Canadian Agency for Drugs and Technologies in Health
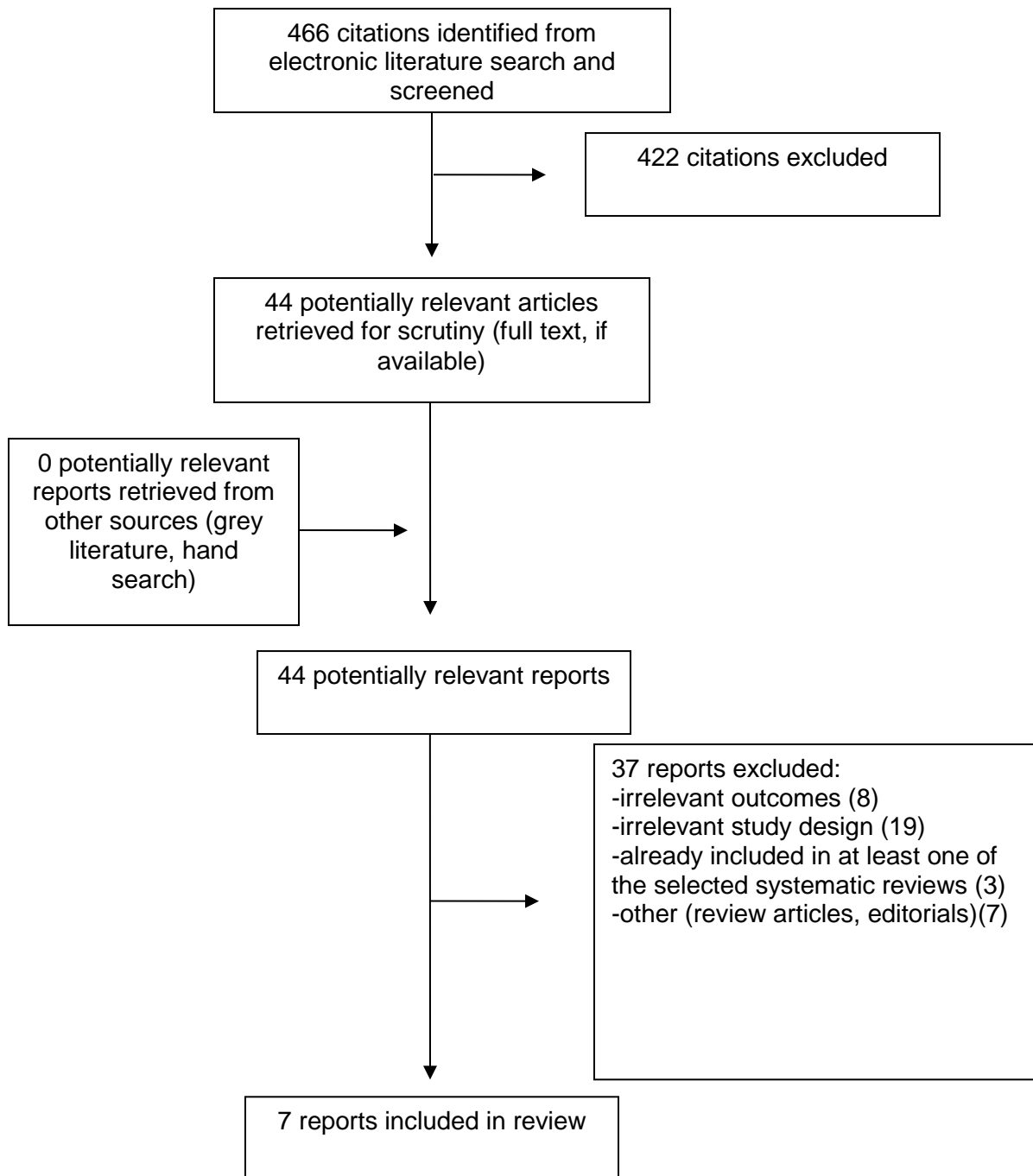Tel: 1-866-898-8439
www.cadth.ca

REFERENCES

1. Whole body screening using MRI or CT technology [Internet]. Ottawa: Health Canada; 2003 Nov. [cited 2014 May 14]. Available from: http://www.hc-sc.gc.ca/hl-vs/alt_formats/pacrb-dgapcr/pdf/iyh-vsv/med/mri-irm-eng.pdf

2. Battiwalla M, Fakhrejahani F, Jain NA, Klotz JK, Pophali PA, Draper D, et al. Radiation exposure from diagnostic procedures following allogeneic stem cell transplantation - how much is acceptable? Hematology. 2013 Nov 25.

3. Albert JM. Radiation risk from CT: implications for cancer screening. AJR Am J Roentgenol. 2013 Jul;201(1):W81-W87.

4. Sarma A, Heilbrun ME, Conner KE, Stevens SM, Woller SC, Elliott CG. Radiation and chest CT scan examinations: what do we know? Chest [Internet]. 2012 Sep [cited 2014 May 12];142(3):750-60. Available from: http://journal.publications.chestnet.org/data/Journals/CHEST/24838/750.pdf

5. Canadian Institute for Health Information. Medical imaging in Canada 2012: executive summary [Internet]. Ottawa: CIHI; 2013 Feb 12. [cited 2014 May 14]. Available from: http://www.cihi.ca/CIHI-ext-portal/pdf/internet/MIT_SUMMARY_2012_en

6. Health Canada [Internet]. Ottawa: Health Canada; 30 May 2014. Can you give details about radiation doses?; 2008 [cited 2014 Jun 2]. Available from: http://www.hc-sc.gc.ca/hc-ps/ed-ud/event-incident/radiolog/info/details-eng.php

7. Shea BJ, Grimshaw JM, Wells GA, Boers M, Andersson N, Hamel C, et al. Development of AMSTAR: a measurement tool to assess the methodological quality of systematic reviews. BMC Med Res Methodol [Internet]. 2007 [cited 2014 May 23];7:10. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1810543/pdf/1471-2288-7-10.pdf

8. Levine M, Walter S, Lee H, Haines T, Holbrook A, Moyer V. Users' guides to the medical literature. IV. How to use an article about harm. Evidence-Based Medicine Working Group. JAMA. 1994 May 25;271(20):1615-9.

9. Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health [Internet]. 1998 Jun [cited 2014 May 23];52(6):377-84. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1756728/pdf/v052p00377.pdf

10. Brouwers M, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, et al. AGREE II: advancing guideline development, reporting and evaluation in healthcare [Internet].The AGREE Research Trust; 2009 May; updated Sept 2013. [cited 2014 May 7]. Available from: http://www.agreetrust.org/wp-content/uploads/2013/10/AGREE-II-Users-Manual-and-23-item-Instrument_2009_UPDATE_2013.pdf

11. Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet [Internet]. 2012 Aug 4 [cited 2014 May

12];380(9840):499-505. Available from:
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3418594

12. van Walraven C, Fergusson D, Earle C, Baxter N, Alibhai S, MacDonald B, et al. Association of diagnostic radiation exposure and second abdominal-pelvic malignancies after testicular cancer. J Clin Oncol [Internet]. 2011 Jul 20 [cited 2014 May 12];29(21):2883-8. Available from: http://jco.ascopubs.org/content/29/21/2883.full.pdf+html

13. Davis F, Il'yasova D, Rankin K, McCarthy B, Bigner DD. Medical diagnostic radiation exposures and risk of gliomas. Radiat Res [Internet]. 2011 Jun [cited 2012 May 11];175(6):790-6. Available from: http://www.bioone.org/doi/pdf/10.1667/RR2186.1

14. Oh JS, Koea JB. Radiation risks associated with serial imaging in colorectal cancer patients: should we worry? World J Gastroenterol [Internet]. 2014 Jan 7 [cited 2014 May 12];20(1):100-9. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3885998

15. Huang WY, Muo CH, Lin CY, Jen YM, Yang MH, Lin JC, et al. Paediatric head CT scan and subsequent risk of malignancy and benign brain tumour: a nation-wide population-based cohort study. Br J Cancer. 2014 Apr 29;110(9):2354-60.

16. Mathews JD, Forsythe AV, Brady Z, Butler MW, Goergen SK, Byrnes GB, et al. Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. BMJ [Internet]. 2013 [cited 2014 May 12];346:f2360. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3660619

17. Behnampour N, Hajizadeh E, Zayeri F, Semnani S. Modeling of influential predictors of gastric cancer incidence rates in Golestan province, North Iran. Asian Pac J Cancer Prev. 2014;15(3):1111-7.

18. American Academy of Oral and Maxillofacial Radiology. Clinical recommendations regarding use of cone beam computed tomography in orthodontics. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013 Aug;116(2):238-57.

19. Halliburton SS, Abbara S, Chen MY, Gentry R, Mahesh M, Raff GL, et al. SCCT guidelines on radiation dose and dose-optimization strategies in cardiovascular CT. J Cardiovasc Comput Tomogr [Internet]. 2011 Jul [cited 2014 May 12];5(4):198-224. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3391026

20. Gerber TC, Carr JJ, Arai AE, Dixon RL, Ferrari VA, Gomes AS, et al. Ionizing radiation in cardiac imaging: a science advisory from the American Heart Association Committee on Cardiac Imaging of the Council on Clinical Cardiology and Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention. Circulation [Internet]. 2009 Feb 24;119(7):1056-65. Available from: http://circ.ahajournals.org/content/119/7/1056.full.pdf+html

21. National Research Council. Beir VII: health risks from exposure to low levels of ionizing radiation. Report in brief [Internet]. Washington (DC): The National Academies; 2011. [cited 2014 May 14]. Available from: http://dels.nas.edu/resources/static-assets/materials-based-on-reports/reports-in-brief/beir_vii_final.pdf

22. Colagrande S, Origgi D, Zatelli G, Giovagnoni A, Salerno S. CT exposure in adult and paediatric patients: a review of the mechanisms of damage, relative dose and consequent possible risks. Radiol Med. 2014 Mar 6.

23. Zondervan RL, Hahn PF, Sadow CA, Liu B, Lee SI. Body CT scanning in young adults: examination indications, patient outcomes, and risk of radiation-induced cancer. Radiology. 2013 May;267(2):460-9.

APPENDIX 1: Selection of Included Studies

```
          ┌─────────────────────────────┐
          │ 466 citations identified from│
          │ electronic literature search │
          │ and screened                 │
          └──────────────┬──────────────┘
                         │          ┌─────────────────────────┐
                         ├─────────▶│ 422 citations excluded   │
                         │          └─────────────────────────┘
                         ▼
          ┌─────────────────────────────┐
          │ 44 potentially relevant      │
          │ articles retrieved for       │
          │ scrutiny (full text, if      │
          │ available)                   │
          └──────────────┬──────────────┘
┌──────────────────────┐ │
│ 0 potentially relevant│ │
│ reports retrieved from│ │
│ other sources (grey   ├─┤
│ literature, hand      │ │
│ search)               │ │
└──────────────────────┘ ▼
          ┌─────────────────────────────┐
          │ 44 potentially relevant      │
          │ reports                      │
          └──────────────┬──────────────┘
                         │
                         │          ┌──────────────────────────────────┐
                         │          │ 37 reports excluded:             │
                         ├─────────▶│ -irrelevant outcomes (8)         │
                         │          │ -irrelevant study design (19)    │
                         │          │ -already included in at least one│
                         │          │ of the selected systematic       │
                         │          │ reviews (3)                      │
                         │          │ -other (review articles,         │
                         │          │ editorials)(7)                   │
                         ▼          └──────────────────────────────────┘
          ┌─────────────────────────────┐
          │ 7 reports included in review │
          └─────────────────────────────┘
```

Radiation Emissions from Computed Tomography

APPENDIX 2: EXCLUDED STUDIES ESTIMATING RISK OF RADIATION-INDUCED CANCER BASED ON MODELS

Brambilla M, De MA, Lizio D, Matheoud R, De LM, Carriero A. Estimated radiation risk of cancer from medical imaging in haemodialysis patients. Nephrol Dial Transplant. 2014 Apr 15.
PubMed: PM24737442

Meyer M, Klein SA, Brix G, Fink C, Pilz L, Jafarov H, et al. Whole-body CT for lymphoma staging: feasibility of halving radiation dose and risk by iterative image reconstruction. Eur J Radiol. 2014 Feb;83(2):315-21.
PubMed: PM24355659

Brix G, Berton M, Nekolla E, Lechel U, Schegerer A, Suselbeck T, et al. Cumulative radiation exposure and cancer risk of patients with ischemic heart diseases from diagnostic and therapeutic imaging procedures. Eur J Radiol. 2013 Nov;82(11):1926-32.
PubMed: PM23954016

Wen JC, Sai V, Straatsma BR, McCannel TA. Radiation-related cancer risk associated with surveillance imaging for metastasis from choroidal melanoma. JAMA Ophthalmol. 2013 Jan;131(1):56-61.
PubMed: PM23307209

Calandrino R, Ardu V, Corletto D, del VA, Origgi D, Signorotto P, et al. Evaluation of second cancer induction risk by CT follow-up in oncological long-surviving patients. Health Phys. 2013 Jan;104(1):1-8.
PubMed: PM23192082

Bach PB, Mirkin JN, Oliver TK, Azzoli CG, Berry DA, Brawley OW, et al. Benefits and harms of CT screening for lung cancer: a systematic review. JAMA. 2012 Jun 13;307(22):2418-29. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3709596
PubMed: PM22610500

Zondervan RL, Hahn PF, Sadow CA, Liu B, Lee SI. Body CT scanning in young adults: examination indications, patient outcomes, and risk of radiation-induced cancer. Radiology. 2013 May;267(2):460-9.
PubMed: PM23386731

Meer AB, Basu PA, Baker LC, Atlas SW. Exposure to ionizing radiation and estimate of secondary cancers in the era of high-speed CT scanning: projections from the Medicare population. J am coll radiol. 2012 Apr;9(4):245-50.
PubMed: PM22469374

Motaganahalli R, Martin A, Feliciano B, Murphy MP, Slaven J, Dalsing MC. Estimating the risk of solid organ malignancy in patients undergoing routine computed tomography scans after endovascular aneurysm repair. J Vasc Surg. 2012 Oct;56(4):929-37.
PubMed: PM22784414

Perisinakis K, Seimenis I, Tzedakis A, Papadakis AE, Kourinou KM, Damilakis J. Screening computed tomography colonography with 256-slice scanning: should patient radiation burden and associated cancer risk constitute a major concern? Invest Radiol. 2012 Aug;47(8):451-6.
PubMed: PM22766908

Mahajan A, Starker LF, Ghita M, Udelsman R, Brink JA, Carling T. Parathyroid four-dimensional computed tomography: evaluation of radiation dose exposure during preoperative localization of parathyroid tumors in primary hyperparathyroidism. World J Surg. 2012 Jun;36(6):1335-9.
PubMed: PM22146947

Berrington de GA, Kim KP, Knudsen AB, Lansdorp-Vogelaar I, Rutter CM, Smith-Bindman R, et al. Radiation-related cancer risks from CT colonography screening: a risk-benefit analysis. AJR Am J Roentgenol. 2011 Apr;196(4):816-23. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3470483
PubMed: PM21427330

Kim S, Yoshizumi TT, Frush DP, Toncheva G, Yin FF. Radiation dose from cone beam CT in a pediatric phantom: risk estimation of cancer incidence. AJR Am J Roentgenol. 2010 Jan;194(1):186-90.
PubMed: PM20028922

Smith-Bindman R, Lipson J, Marcus R, Kim KP, Mahesh M, Gould R, et al. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. Arch Intern Med. 2009 Dec 14;169(22):2078-86.
PubMed: PM20008690

Theocharopoulos N, Chatzakis G, Damilakis J. Is radiography justified for the evaluation of patients presenting with cervical spine trauma? Med Phys. 2009 Oct;36(10):4461-70.
PubMed: PM19928077

Kim KP, Einstein AJ, Berrington de GA. Coronary artery calcification screening: estimated radiation dose and cancer risk. Arch Intern Med. 2009 Jul 13;169(13):1188-94. Available from: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2765044
PubMed: PM19597067

Tarin TV, Sonn G, Shinghal R. Estimating the risk of cancer associated with imaging related radiation during surveillance for stage I testicular cancer using computerized tomography. J Urol. 2009 Feb;181(2):627-32.
PubMed: PM19091344

Weustink AC, Mollet NR, Neefjes LA, van SM, Neoh E, Kyrzopoulos S, et al. Preserved diagnostic performance of dual-source CT coronary angiography with reduced radiation exposure and cancer risk. Radiology. 2009 Jul;252(1):53-60.
PubMed: PM19451542

Griffey RT, Sodickson A. Cumulative radiation exposure and cancer risk estimates in emergency department patients undergoing repeat or multiple CT. AJR Am J Roentgenol. 2009 Apr;192(4):887-92.
PubMed: PM19304691

APPENDIX 3: Summary of Study Characteristics

Table A3.1 Systematic Reviews

Author, year, country	Key inclusion criteria, Methods, N studies	Types of Included studies	Outcomes
Oh 2013[14] New Zealand	Studies in which CT scans or other ionizing radiation derived from medical imaging were used and risks reported All cancer types Studies from previous last 10 years to December 2012; English only articles available as full-text PubMed and Cochrane library were searched; N=36 studies	Modelling Case-control Cohort Retrospective (no other description provided in SR) No RCTs identified	Narrative description Relative risk and LAR of cancer

CT=computed tomography, LAR=lifetime attributable risk, RCTs=randomized controlled trials, SR=systematic review

Table A3.2 Non-RCTs

Cohort studies				
Author, year, country	Objective	Characteristics of exposed cases, N	Characteristics of unexposed cases, N	Other
Leukemia, brain tumour and other cancer				
Huang, 2014[15] Taiwan	To evaluate the association between pediatric head CT and subsequent risk of malignancy	Children (<18 years old) who underwent head CT examination from 1998 to 2006, identified from the Taiwan National Health Insurance Research Database N=24,418	Children not treated with head CT before the index date randomly selected from the Database in 4:1 ratio, matched for sex, age, year/ month of index N=97,668	Followed until diagnosis of malignancy or benign brain tumour, withdrawal from the National Health Insurance system, or end of 2008 Lag period: 2 years
Any malignancy				
Matthews, 2013[16] Australia	To assess the cancer risk following exposure to low dose ionizing radiation from diagnostic CT	Children (0 to 19 years old) exposed to CT scan, identified from the Australian Medicare System, born 01 January 1985 to 31 December 2005	Children (0 to 19 years old) not exposed to CT scan N~11 million	Followed until date of first cancer, date of death, or end of 2007. Lag period: 1

Cohort studies				
Author, year, country	**Objective**	**Characteristics of exposed cases, N**	**Characteristics of unexposed cases, N**	**Other**
		N=680,211		year,5 years and 10 years
Case control study				
Gastric cancer				
Behnampour, 2014[17] Iran	To determine the predictors of gastric cancer in Golestan Province	Patients with gastric cancer. Cancer data obtained from diagnostic centres, clinics and health centres from March 2009 to March 2010 N=156	One family member and one neighbor (two controls) matched for age, gender, and ethnicity N=312	

CT=computed tomography
*Lag period is an exclusion period before a cancer diagnosis to exclude the possibility of reverse causation (i.e., scan was part of a cancer diagnostic procedure)

Table A3.3: Clinical Practice Guidelines

Author, year, country	**Intervention and Practice Considered**	**Evidence collection, selection and synthesis**	**Recommendations development and evaluation**
American Academy of Oral and Maxillofacial Radiology			
American Academy of Oral and Maxillofacial Radiology, 2013[18] US	Cone beam CT Maxillofacial/ Orthodontics	Literature and consensus	Used panel with consensus and previously published criteria to develop 3 possibility of recommendations: · Likely indicated · Possibly indicated · Likely not indicated Recommendations not graded
Society of Cardiovascular Computed Tomography			
Halliburton, 2011[19] US	Cardiovascular CT Cardiac	Published literature and consensus about best practices	Recommendations not graded
American Heart Association			
Gerber, 2009[20] US	CT and fluoroscopy Cardiac	Not described	See table footnote* for class and levels of evidence

*Classification of Recommendations
Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is beneficial, useful, and effective.
Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
Class IIb: Usefulness/efficacy is less well established by evidence/opinion.
Class III: Conditions for which there is evidence and/or general agreement that a procedure/treatment is not useful/ effective and in some cases may be harmful.
*Levels of Evidence
Level of Evidence A: Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B: Data derived from a single randomized trial or nonrandomized studies.
Level of Evidence C: Only consensus opinion of experts, case studies, or standard of care.

Radiation Emissions from Computed Tomography

APPENDIX 4: Summary of Critical Appraisal

Table A4.1: Systematic Reviews

Author, year	Strengths	Limitations
Oh 2013[14]	· Objectives and inclusion/ exclusion criteria established a priori · Literature search described · Articles independently reviewed by two investigators · Some characteristics of included studies provided · Global overview of quality of studies provided	· No hand searching of references; no description if grey literature was searched · Studies not available as full-text excluded · List of excluded studies not provided · Difficult to determine which included studies were simulation studies vs. case-control/ cohort studies · Some studies described as retrospective, but study design not stated · No table of results provided · Selective reporting of study results in narration · Conflict of interest not declared · Funding source not provided

Table A4.2: Non-RCTs

	Huang, 2014[15]	Matthews, 2013[16]	Behnampour, 2014[17]
Groups comparable with regards to important determinants	Unclear – baseline characteristics of the exposed/ unexposed cohorts not described although it is stated that these were compared using statistical methods.	Data drawn from the general population. No other information provided.	Demographic information collected but not presented.
Differences adjusted for in analysis	Age and sex adjusted. Children were excluded from study if they had a disorder which increased their cancer risk.	Results stratified by age, gender and year of birth.	Not reported
Exposures measured in the same way in the groups	Groups recruited from same population and same time period. Both exposed/ unexposed cohorts identified from the Taiwan National Health Insurance Research Database.	Groups recruited from same population and same time period. Both exposed/ unexposed cohorts identified from the Australian Medicare System.	Data collected through interviews of both groups.
Follow up sufficiently long and complete	Results provided for >6 years since first exposure.	Results provided for >15 years since first exposure.	Not reported

Radiation Emissions from Computed Tomography

	Huang, 2014[15]	Matthews, 2013[16]	Behnampour, 2014[17]
Temporal relationship correct	Yes	Yes	Yes
Dose response gradient present	Dose-response relationship not measured but the risk related to number of CT scans examined.	Dose-response relationship based on average effective dose obtained from published literature + risk related to number of CT scans were measured.	Not measured
Other	Very large sample size. Limited to brain CT. Potential confounders not identified.	Sample size is the whole Medicare population. All CT scans included. Cancer risk by body area of CT scan provided. Each person categorized in one of seven groups according to socioeconomic index. Other potential confounders such as smoking and alcohol were unknown and hence unaccounted for.	No information on body area of CT scan, frequency of CT scan, and time between exposure and development of cancer. Not specified whether or not investigators blinded to cases vs. controls. Potential for recall bias All influential factors for gastric cancer were identified and entered into a regression model. Limited external validity

Table A4.3: Clinical Practice Guidelines

Guideline	Strengths	Limitations
American Academy of Oral and Maxillofacial Radiology[18]	· Scope and purpose of guidelines well defined · Panel members included orthodontists and maxillofacial radiologists as content experts · Methods for formulating recommendations described · Clear recommendations provided	· Unclear if methodologist, policy-makers, and other relevant experts were part of the panel · Did not include or seek the views of patients/ public · Guideline development process unclear · Not clear if a systematic review of the literature was conducted · No grading done of the recommendations · Conflict of interest not reported · Source of funding not explicit
Society of Cardiovascular Computed Tomography[19]	· Scope and purpose of guidelines well defined · Methods for formulating recommendations described · Clear recommendations provided · Guidelines externally reviewed · Conflict of interest disclosed	· Unclear as to the types of experts involved in preparing the guidelines · Did not include or seek the views of patients/ public · Guideline development process unclear · Not clear if a systematic review of the literature was conducted

Radiation Emissions from Computed Tomography

Guideline	Strengths	Limitations
		· No grading done of the recommendations · Source of funding not explicit
American Heart Association[20]	· Scope and purpose of guidelines well defined · Methods for formulating recommendations described · Clear recommendations with grading of the evidence provided · Guidelines externally reviewed · Conflict of interest disclosed	· Unclear as to the types of experts involved in preparing the guidelines · Did not include or seek the views of patients/ public · Guideline development process unclear · Not clear if a systematic review of the literature was conducted · Source of funding not explicit

Radiation Emissions from Computed Tomography

APPENDIX 5: Summary of Findings

Table A5.1: Systematic Reviews

Author, year	Results and conclusions
Oh 2013[14]	· 34/ 36 studies found a positive association between ionizing radiation from medical imaging and increased risk of cancer · Risk is age dependent (risk greater for children and young adults) · Using conservative estimates and worst case scenarios, cancer risk is low in the elderly · Risk of low dose exposure (<50 mSV) is uncertain · Potential benefits of CT imaging must be weighed against harms of radiation

Table A5.2a: Non-RCTs, Results for Huang, 2014[15]

Incidence and adjusted hazard ratio of cancer type compared with the unexposed group						
Cancer type	**Unexposed group N=97 668**			**Exposed group N=24 418**		**HR* (95%CI)**
	# cancers	**# person-years**	**IR per 100,000 PY**	**# cases**	**# person-years**	**IR per 100,000 PY**	
Overall	122	428 381	28.5	39	106 216	36.7	1.3 (0.9,1.9)
Brain cancer	11	428 381	2.6	5	106 216	4.7	1.8 (0.6,5.3)
Leukemia	17	428 381	4.0	8	106 216	7.5	1.9 (0.8,4.4)
Other cancer	75	428 381	17.5	12	106 216	11.3	0.7 (0.4,1.2)
Incidence and adjusted hazard ratio of cancer type, ≥6 years since first exposure						
Cancer type	**Unexposed group**			**Exposed group**		**HR* (95%CI)**
	# cancers	**# person-years**	**IR per 100,000 PY**	**# cases**	**# person-years**	**IR per 100,000 PY**	
Overall	53	188 934	28.0	11	46 615	23.6	0.8 (0.4, 1.6)
Brain cancer	5	188 934	2.7	2	46 615	4.3	1.6 (0.3, 8.4)
Leukemia	4	188 934	2.1	2	46 615	4.3	2.0 (0.4, 11.1)
Other cancer	35	188 934	18.5	3	46 615	6.4	0.4 (0.1, 1.1)

Incidence and adjusted hazard ratio of cancer type by frequency of CT during F/U period						
Head CT frequency	**Overall**			**Brain cancer**		
	# cancers # PY	**IR per 100,000 PY**	**HR* (95%CI)**	**# cancers**	**IR per 100,000 PY**	**HR* (95%CI)**
None	122 428 391	28.5	reference	11	2.6	reference
1	34 98 994	34.5	1.2 (0.8, 1.8)	3	3.0	1.2 (0.3, 4.3)

2	3 6116	49.1	1.7 (0.5, 5.3)	2	32.7	12.3 (2.7, 55.4)
≥3	2 1406	142.2	5.0 (1.3, 20.4)	0	0	--

Incidence and adjusted hazard ratio of cancer type by frequency of CT during F/U period						
	Leukemia			**Other cancer**		
Head CT frequency	**# cancers**	**IR per 100,000 PY**	**HR* (95%CI)**	**# cancers**	**IR per 100,000 PY**	**HR* (95%CI)**
None	17	3.4	reference	75	17.5	reference
1	7	7.1	1.8 (0.7, 4.3)	11	11.2	0.6 (0.3, 1.2)
2	0	0	--	1	16.4	0.9 (0.1, 6.4)
≥3	1	71.1	17.4 (2,3, 131)	0	0	--

CT=computed tomography, CI=confidence interval, F/U=follow-up, HR=hazard ratio, IR=incidence rate, PY=person-years

 *HR adjusted for age and sex

Table A5.2b: Non-RCTs, Results for Matthews, 2013[16]

Incidence rate ratios, exposed vs. unexposed, for various lag periods							
Cancer type	**Unexposed group**		**Exposed group**				**IRR† (95%CI)**
	# cancers	**# person-years**	**# cancers**	**# person-years**	**# expected cancer***	**# excess cancer***	
Lag period 1 year							
All cancers	57 524	177 million	3 150	6.5 million	2 542	608	1.24 (1.20,1.29)
Lag period 5 years							
All cancers	58 309	180 million	2 365	3.9 million	1 963	402	1.21 (1.16,1.26)
Lag period 10 years							
All cancers	59 269	182 million	1 405	1.8 million	1 196	209	1.18 (1.11,1.24)

Outcomes for the exposed group by years since first CT exposure, based on a one year lag period (all cancers)							
IRR* (95% CI)				**EIR* per 100 000 PY (95%CI)**			
1 - 4 years	**5 - 9 years**	**10 - 14 years**	**≥15 years**	**1 - 4 years**	**5 - 9 years**	**10 - 14 years**	**≥15 years**
1.35 (1.25, 1.45)	1.25 (1.17, 1.34)	1.14 (1.06, 1.22)	1.24 (1.14, 1.34)	8.0 (5.8, 10.2)	8.9 (6.1, 11.7)	7.7 (3.2, 12.2)	20.4 (12.1, 28.6)

Outcomes for the exposed group by age at first CT exposure, based on a one year lag period (all cancers)							
IRR* (95% CI)				**EIR* per 100 000 PY (95%CI)**			
0 - 4 years	**5 - 9 years**	**10 - 14 years**	**15-19 years**	**0 - 4 years**	**5 - 9 years**	**10 - 14 years**	**15-19 years**
1.72 (1.44, 2.05)	1.40 (1.25, 1.58)	1.21 (1.13, 1.30)	1.21 (1.16, 1.27)	11.1 (6.5, 15.7)	8.1 (4.9, 11.4)	7.1 (4.3, 10.0)	10.9 (8.1, 13.7)

CI=confidence interval, EIR=absolute excess incidence rate, IRR=incidence rate ratios, PY=person-years

* calculated from rates in unexposed group after stratification for age, sex, year of birth

†exposed vs. unexposed

Radiation Emissions from Computed Tomography

Table A5.2c: Non-RCTs* Included in the SR by Oh and Koea[14]

Retrospective cohort studies			
Author, year, country	**Objective, N**	**Methods**	**Results**
Pearce et al. 2012[11] UK	To assess the excess risk of leukemia and brain tumour from CT scans in children and young adults N=178,604 (leukemia analysis) N=176 587 (brain tumour analysis)	Patients without previous malignant disease with CT between 1985 and 2002, and younger than 22 years old. Data obtained from historical data from electronic radiology information systems linked to NHS Central Registry from 1985 to 2008. F/U for leukemia and brain tumour began 2 and 5 years after CT, respectively	Compared with patients who received radiation doses of < 5 mGy: RR for leukemia in patients who received doses of 30 mGy 3.2 (95%CI:1.5, 6.9) RR for brain tumour in patients who received doses of 50-74 mGy 2.8 (95%CI:1.3, 6.0)
Van Walraven, 2001[12] Canada	To determine whether the risk of second abdominal-pelvic cancer is associated with radiation received for testicular cancer N=2,569	Men treated for low grade testicular cancer diagnosed between 01 July 1991 and 31 December 2004. Data obtained from various health care databases in Ontario, including the Ontario Cancer Registry. Median F/U=11.2 years Lag period: 5 years	HR per 10 mSv radiation dose increase 0.87 (95%CI:0.45, 1.67)
Case-control study			
Author, year, country	**Objective, N**	**Methods**	**Results**
Davis 2011[13] US	To determine the association between medical diagnostic radiation exposure and gliomas Cases N=205 Controls N=333	Diagnostic radiation exposure as an adult including CT of head and neck Adults (≥18 years old) newly diagnosed with glioma between 2003 and 2007, recruited from two referral centers Friend(s) of cases used as controls	OR in patients with 1-2 CT scans compared to no CT scans 1.10 (95%CI:0.69, 1.76) OR in patients with ≥3 CT scans compared to no CT scans 1.97 (95%CI:0.92, 4.23)

CI=confidence interval, CT=computed tomography, F/U=follow-up, HR=hazard ratio, OR=odds ratio, RR=relative risk
*Non-randomized studies retrieved in literature search and excluded because they were already contained in the systematic review appraised in this report.

Radiation Emissions from Computed Tomography

Table A5.3: Recommendations from Clinical Practice Guidelines

Guideline	Recommendations
American Academy of Oral and Maxillofacial Radiology[18]	**Recommendation 2.1**. "*Consider the Relative Radiation Level when assessing the imaging risk for imaging procedures over a course of orthodontic treatment.*" (page 243) Table V presents selected <u>published effective doses</u> for various field of view of cone beam computed tomography devices used in orthodontics. (pages 244 to 246)
Society of Cardiovascular Computed Tomography[19]	"*… the ALARA principle, which states that the radiation dose to a patient should be As Low As Reasonably Achievable, is generally accepted. However, a radiation dose level exists below which certain scans may become uninterpretable, which would remove the potential benefit from the test and significantly alter the benefit–risk ratio for patients.*" (page 3) "*Individual sites should consider developing site-specific algorithms for radiation dose optimization that take into account the cardiovascular indication, scanner characteristics and capabilities, patient heart rate and variability, and patient body habitus. These settings should be tailored to individual patients, but a standardized algorithm may be helpful as a starting point in formulating dose-appropriate protocols.*" (page 18) **Recommendations** (page 56) <u>Radiation dose standards and measurements</u> "*The volume CT dose index should be used for optimizing cardiovascular CT protocols.*" "*The dose-length-product should be used for comparing radiation doses and characterizing radiation dose from a cardiovascular CT study.*" <u>Applying algorithms for dose optimization in clinical practice</u> "*Individual sites should consider developing site-specific algorithms for radiation dose optimization, which should be reviewed and revised if needed at least annually.*"
American Heart Association[20]	"*Even though the accuracy of radiation-dose estimates and the relationship between the radiation dose received from cardiac imaging and the risk of malignancies may be uncertain, this Writing Group supports the concept of keeping patient doses as low as reasonably achievable but consistent with obtaining the desired medical information.*" *(page 1061)* **Recommendation** (page 1061) "*The imaging community should actively participate in the voluntary determination of diagnostic reference levels for radiation doses from cardiac radiographic imaging procedures to establish radiation doses as benchmarks for comparisons between practices on a national level*" *(Class I, Level of Evidence B).*