Cancer Risks from Radiation Medical Imaging in Children: A Scoping Review

by

Danny Wong

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AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including required revisions, as accepted by my examiners. I understand that my thesis may be made available electronically to the public.

ABSTRACT

Background: radiation medical imaging is a valuable tool in detecting diseases. Biological Effects of Ionizing Radiation Report (BEIR VII Phase 2) suggested that radiation exposures, even at low dosages, may impose stochastic cancer risks. However, radiation medical imaging has yet been fully understood; further studies on this subject are much needed. Over several decades, there have been much research dedicated to studying the impact of low-dose diagnostic imaging on health, particularly in the children population. *Purpose:* This scoping review is to gather existing literature on the cancer risks associated with radiation medical imaging in children, and to identify gaps in the literature for future studies on this topic. *Methods:* Scopus and PubMed databases were selected for the literature search and the scoping review methodology was applied in this research. *Results:* The study has spanned over three thousand articles (N=3,191) and by applying the exclusion and inclusion criteria, twelve (12) articles have been chosen for this research. The research data suggested that exposure to (a) dental X-rays may be linked with thyroid cancer; due to limited research that had been conducted, more studies are needed to provide clearer understanding of the health impacts, (b) X-rays may not have any association with cancer, again, more research is required on this subject, (c) computed tomography scans may be linked to various cancers including thyroid, leukemia, solid cancer, and cancer mortality, and (d) angiography, based on mathematical cancer risk model, seems to suggest there are possible cancer risk. Today, there have been no studies performed on patient-level. *Conclusion*: The research indicates that there are potential cancer risks associated with dental x-ray, angiography (mathematical model), and CT scans; however, due to limited research that has been

performed up to this point, further studies are required on cancer risks from radiation medical imaging in children.

ACKNOWLEDGEMENTS

This thesis has been one of the most challenging projects undertaken. I would like to express my gratitude to all researchers, educators, health professionals, parents of patients, and patients for your contributions to this research. I also would like to send my sincere acknowledgements to the people who have fallen ill or deceased due to the unfortunate radiation exposures. Without your sacrifices, all this profound knowledge, theorem, hypotheses, and advancements in the field of medical imaging and health studies would not have been possible.

I am grateful for the opportunity to participate in this public health program at the University of Waterloo. I owe a huge debt of gratitude to my research committee members, Dr. David Koff, Dr. John Mielke, and Dr. Helen Chen, for your continuous support and valuable time. I also would like to send a special thank you to Dr. Chen for your endless encouragements and support.

I would like to sincerely thank my late mother and late aunt for your unconditional parental love. Your teachings, values, spirits, and work ethics have given me the courage and determination to overcome challenges and achieve my goals.

Lastly, to my family, I am grateful for your empowerment and sacrifices that enabled me to pursue my passion for learning and achieving my dreams. I would like to thank my three children (Ethan, Ellen, and Ava) for your laughter, playfulness, and enthusiasm. Your energies have helped me re-charge and focus when they were most needed. To my wife, Pamela, a sincere thank you for your endless encouragements, faith, patience, and sacrifices. Without

them, the completion of this project, and achieving such an academic milestone, would not have been possible.

My wishes are that the wisdom, skills, and experience that I gained on this journey will direct me to do valuable work that will potentially be beneficial to our society. I hope to make you proud.

Danny Wong

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CHAPTER 1: INTRODUCTION

Medical diagnostic imaging is a valuable tool in the diagnosis of illness and diseases. The tool is used to generate visuals of human bones, organs, and tissues; otherwise, it may be challenging to identify health issues. Commonly used medical imaging modalities include X-rays, fluoroscopy, angiography, mammography, computed tomography (CT) scan, magnetic resonance imaging (MRI), ultrasonography (ultrasound), positron emission tomography (PET), and single photon emission tomography (SPECT). Some modalities use ionizing radiation; therefore, they may have harmful effects on human health. X-rays, fluoroscopy, angiography, mammography, CT scans, PET, and SPECT all use energy sources such as X-rays and gamma-rays (Canadian Association of Radiologist, 2013).

Since the discovery of X-rays in 1895, radiography has been used in medical diagnosis and radiation therapy. Although there have been tremendous benefits in utilizing radiation in medical imaging, unfortunately, such irradiation exposures can be dangerous to human health (CRP, 2011). Early hypotheses indicated that irradiation may cause chromosome aberration and such aberration could lead to: 1) reconstitution of the chromosome, 2) rejoining with another broken chromosome, or 3) remaining broken (National Research Council, 2006). The illegitimate rejoining of chromosomes may lead to DNA mutation, which may occur in any person including adults and children; however, the greatest impact is on young children (Iacob, 2002). Due to the rapid cell changes in children, the probability of DNA mutation may be greater.

Figure 1. Pediatric Medical Imaging Usage Trend

(Repplinger, 2016)

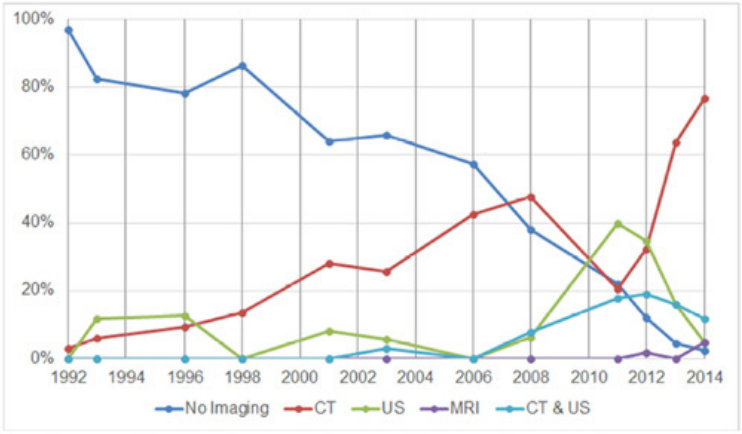


Figure 2. Pediatric CT Scan Usage Trend

(Inman 2015)

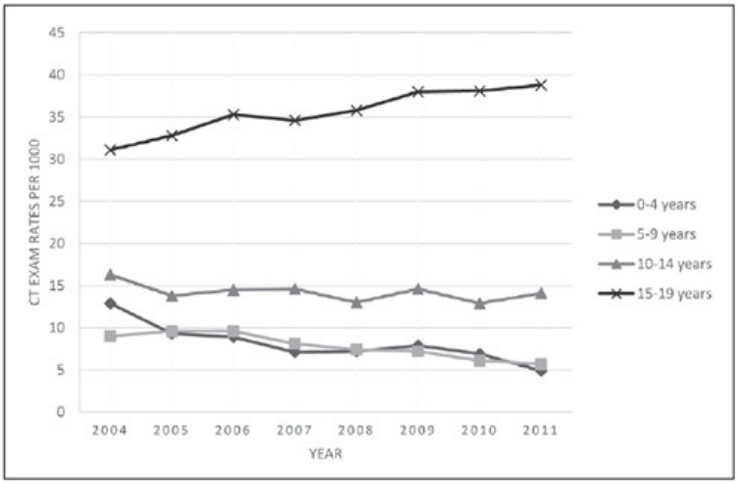


Figure 1 & 2 show examples of computed tomography usage trends in the United States and Canada (Mettler, 2009; Smith-Bindman, 2012; Miglioretti, 2013; Inman, 2015; and Repplinger, 2016). Depending on the studies, medical imaging usage trends may differ. Due to the potential risk of CT scans, particularly in children, much emphasis and effort were placed in minimizing CT scan usage and reducing radiation doses (Inman, 2015). Reported in BEIR VII (National Research Council U.S., 2006), studies of health effects of ionizing radiation

suggested that exposure to ionization may lead to the development of solid cancers, leukemia, and cancer mortality. Furthermore, the report indicated that females were more at risk for all solid cancer in contrast to males, 1300 versus 800 per 100,000 persons, respectively. Secondly, females were less at risk of developing leukemia compared to males, 70 versus 100 per 100,000 persons, respectively. Lastly, it was estimated that the lifetime attributable risk of developing solid cancer or leukemia was 1 in 100,000 persons in the general population, at an exposed dose of 100 milli-Sievert (mSv). From an epidemiological perspective, the report suggests that there might be associations between radiation exposures and cancer outcomes. With such concerns, the World Health Organization co-sponsored a medical radiation protection conference in Bonn Germany (WHO, 2012) and offered a list of recommendations (known as Bonn Call-for-Action). The recommendations include 1) raising awareness of potential health risks, 2) promoting patient radiation safely, and 3) implementing guidelines for appropriate radiation medical imaging usages.

Since the BEIR VII publication in 2006, there have been many studies on the possible association between ionizing radiation exposure and cancer risks. However, most of these investigations primarily focus on the overall population. As indicated earlier, radiation exposure, even at low doses, may be carcinogenic in children; thus, it is imperative that more investigations were conducted on such groups. Hence, the purpose of this scoping review is to gather patient-level studies that examined exposures to medical imaging and possible cancer risks in children. The goals are to identify the possible risks associated with diagnostic modalities that involve ionizing radiation and research gaps in this domain. Some of the key search concepts include diagnostic modalities, age at exposure, exposure doses, exposed

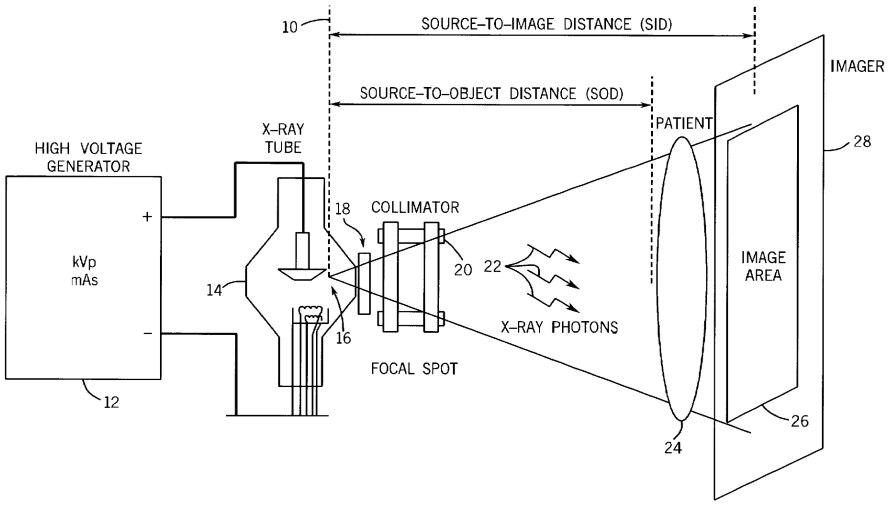
organs, cancer types, and possible cancer risks. These concepts are to be used for literature search and will be part of the data collection and analysis.

CHAPTER 2: LITERATURE REVIEW

Radiology Overview

X-rays were discovered in 1895 by Professor Wilhelm Conrad Roentgen at Wurzburg University in Germany. While working on his cathode-ray tube experiment, he observed a fluorescent glowing image on a nearby table. He then covered the tube with a solid black paper and noticed the light still protruded through the paper. His experiment revealed that X-rays passing through objects of lower absorption rate will project blackened figures of the objects; however, with objects of higher absorption rate, a whitened figure of the object is cast instead. Roentgen later captured the bone structure of his wife's hand on an x-ray film and that was the start of medical diagnostic imaging (Reed, 2011; and Iacob, 2002). Figure 3 provides the components of an irradiation machine such as the X-ray machine. The diagram shows that the X-ray tube emits X-ray photons toward the irradiant object, such as a patient's body. Behind the irradiant object is a detector such as a photographic film or digital detector, which is used to capture the studied images in two-dimensional views. There are other diagnostics tools that do not use radiation as an energy source and these will not be discussed in this study.

Figure 3. X-ray Machine



Source: Aufrichtig et al (2002)

Health professionals often use medical imaging as a tool to diagnose health issues by visualizing organs, tissues, and bones that are internal and/or beneath the skin. There are many types of medical imaging techniques and processes used to achieve specific results. Table 1 lists commonly used medical imaging techniques that involve ionizing radiation.

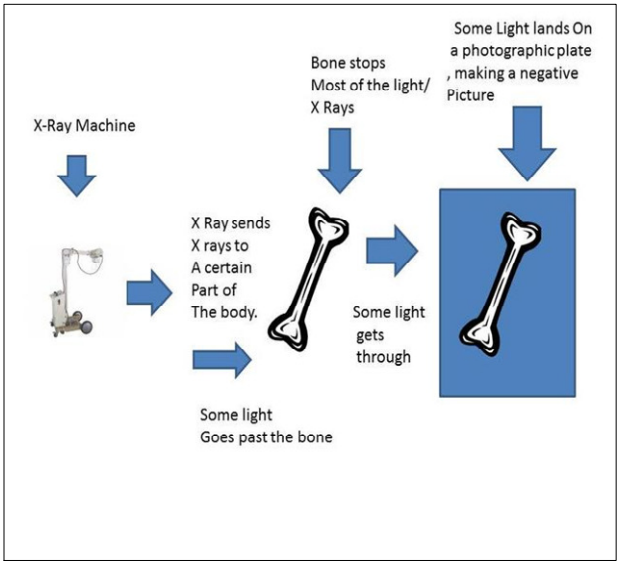
Table 1. Medical Imaging Techniques

Techniques	Description	Energy Source and Estimated Radiation Dose	Examples of Clinical Application
X-rays	use ionizing radiation to generate still images of human internal structures such as bones, organs, and tissues	X-rays Chest: 0.025 mSv Dental: 0.008 – 0.01 mSv	lung and bone pathologies, fractures, infections, abdomen air or fluid, or dental cavities
Fluoroscopy	produces continuous X-rays images of the body structure via passing an X-ray beam through the body. Can be done with contrast dye moving through the body during examinations or insertion of a catheter through blood vessels, bile ducts or urinary system	X-rays Chest ~1 mSv Cerebral Angiogram ~7 mSv	gastrointestinal tract or uterine cavity evaluations, Orthopedic surgery, Placement of devices within the body, vascular diseases, aneurysms, or bleeding vessels
Mammography	produces images of breast tissues	X-rays Breast screening: 0.1 - 0.4 mSv	breast cancer detection
Computed Tomography (CT) scans	produce a series of images; computer algorithms are then used to render the images into two- or three-dimensional views as required	X-rays Body: 6.9 – 14.2 mSv Head: 0.7 -2.6 mSv	e.g., brain, cranium, head or neck, chest, abdomen, or pelvis.
Positron Emission Tomography (PET), Single Photon Emission Tomography (SPECT)	PET and SPECT inject radioactive tracers into the body to detect cancerous tissues and cells. The difference between PET and SPECT modalities are the type of radioactive tracers being used	Gamma rays and X-rays 12 – 33 mSv	e.g. cancer tissues or cells

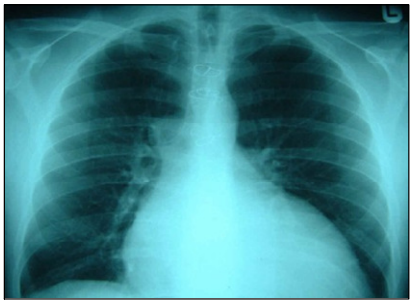
This study focuses specifically on low-dose ionizing radiation medical imaging exposures in children; hence, non-ionizing radiation medical imaging techniques such as MRI and ultrasound will be excluded. X-rays, which are a type of high energy light rays, consists of the shorter wavelength of 10^{-10} Hz that pass through non-metallic objects such as the human body. When X-rays project through a human body, they produce two different images depending on the objects' density. For softer tissues, such as a lung, a blackened figure on a photographic plate is generated when the X-rays pass through the organs. For higher density objects, such as bones and hearts, a whitened figure is produced instead (Figure 4).

In CT scans, computer-aided machines are used to capture multiple X-ray slices of the body parts and then reconstruct the images to produce two- or three-dimensional views of the body parts. Likewise, in mammography, these machines are designed to capture images of breast tissues and structure.

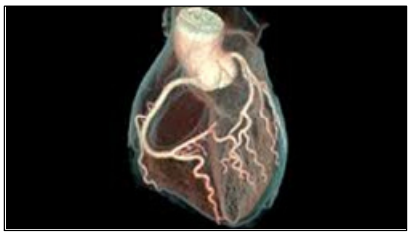
Figure 4. X-rays and CT Imaging



Source: https://researchthetopic.wikispaces.com/How+does+an+X-ray+machine+work%3F+Part+3



Source: http://www.heart-transplant.co.uk/images/xray5.jpg



Source: http://www3.gehealthcare.com

Dosimetry and Reporting

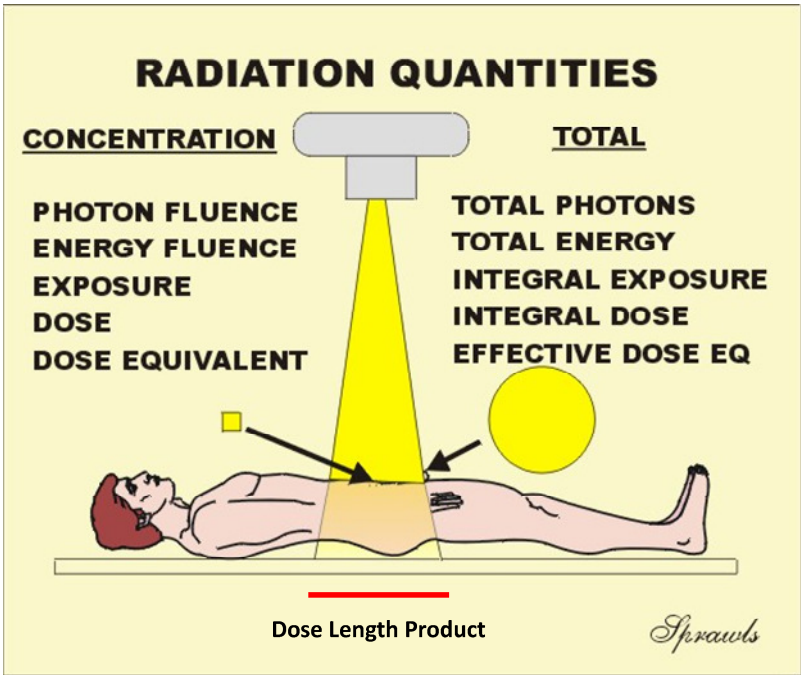
Depending on the examined body part, as discussed previously, there are various types of diagnostic modalities and machinery. The goal of irradiation medical imaging has always been to minimize the dosage to which the patient is exposed without misdiagnosis. This practice is commonly referred to As-Low-As-Reasonably-Achievable (ALARA).

Determining the amount of radiation exposure and its biological effects is a highly complex process. The amount of ionizing radiation emitted to the organs depends on many factors, see Figure 5 and Table 2. For example, when a patient receives a CT scan, the following attributes will need to be considered: (a) the amount of energy emitted (Computed Tomography Dose Index - CTDI), as denoted by the yellow square box, (b) the surface area of the human body exposed (Dose Length Product - DLP) as denoted by the yellow circle, (c) the number of slices per scan, (d) the organ and tissue radiosensitivity (tissue-weighting factors), and (e) the radiation-weighting factor such as X-rays, gamma rays, beta rays, or positron. All these variables need to be assessed in determining the dose equivalent and effective dose of the CT medical imaging procedure (Sprawls, 1993; and Sprawls and Duong, 2013).

Depending on the patient's age, gender, irradiated body parts, and radiation weight factor, the effective dose may vary (Deak, 2010; and ICRP, 2011). The effective dose is normally adjusted for the age of the patient and the radiosensitivity of the organs being examined. Hence, the effective dose for children is less than those for adults. Similarly, the effective doses for girls are reported slightly lower than for boys (Shi, 2016). Furthermore, cumulative dosages are used to measure the amount of radiation being administered over a

patient's lifetime. Cumulative dose measurements are an important aspect in determining the stochastic effects of re-occurring exposures.

Figure 5. Diagnostic Imaging Dose Measurements



Source: Sprawls and Duong (2013)

Table 2. Ionizing Radiation Dose Measurements

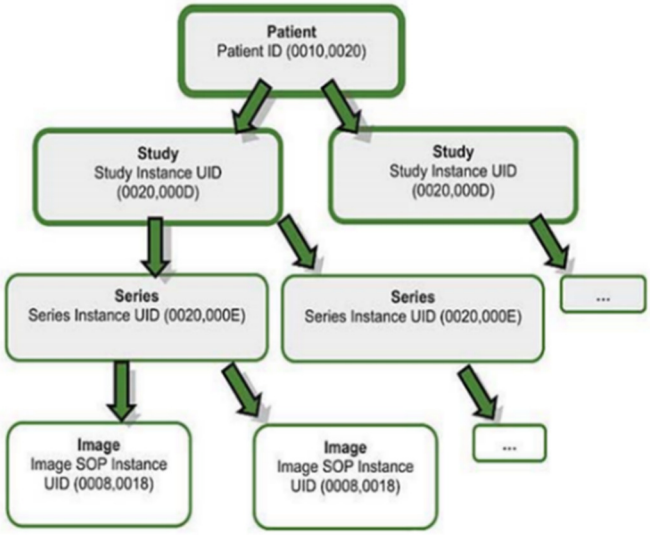
Measurement	Description and Formula
Photon (Curies or Becquerel)	Small units of energy that are presented in electromagnetic radiation (light, X-ray, gamma, etc.) are called photons. The total emitted photons are then used to determine the amount of radioactivity
Exposure (Roentgen – old unit)	A concentrated quantity of radiation (measured in Roentgen unit) that is emitted by the medical imaging machine, 1 R = 2.58 x 10 exp-4 C/Kg of air
Dose Area Product (DAP) (Gy-cm^2)	Measurements of the total amount of radiation energy that is delivered to the irradiated area (body) in Gy-cm^2 per series. DAP = absorbed dose * radiated area
Dose Length Product (DLP)	Measurements of the total radiation energy that is deposited in the human body per series DLP = CTDIvol (mGy) X length of scan (cm)
Absorbed Dose (Gray or Rad)	Measurements of the amount of irradiation energy (in Roentgen) deposited onto an object *Absorbed Dose = Energy / mass (kg)* 1 rad = 100 ergs/g; 1 Gy = 1 Joule per Kg = 100 rads Absorbed Dose Measurement Units: X-rays = kVp; CT = CTDI (CT Dose Index)
Equivalent Dose (Sievert or Rem)	Measurements of the amount of energy absorbed by the irradiated tissues based on specified radiation types (e.g., alpha, beta, gamma, X-ray, neutron, etc.) Equivalent dose is the absorbed dose multiply by the radiation weighting factor (wR) *Equivalent Dose (Sv) = Absorbed Dose (Gy) x wR* e.g. of radiation weighting factor (wR): X and Y rays =1 Electros = 1 Neutrons = varies (5 to 20) Protons = 2-5

Measurement	Description and Formula
Effective Dose (Sievert)	Measurements of the total amount of energy that is absorbed by the organs which included the weighting factor of organ radiation sensitivity 1 Gray (Gy) = 1 Sievert (Sv) Effective dose is the sum of (equivalent doses) multiply by the radiation sensitivity weighting factor *Effective Dose (Gy) = sum (Equivalent Dose (Gy)) x wT* e.g., of radiation sensitivity weighting factor (wT) lung = 0.12, stomach =0.12, liver = 0.05, skin = 0.01 …
Cumulative Dose (Sievert)	Measurements of the total amount of radiation that is exposed to the organs or body over a period or series of radiation treatments

Most medical imaging equipment and Picture Archiving and Communication Systems (PACS) comply with ISO standards for data collection and transmission called Digital Imaging and Communications in Medicine (DICOM). A DICOM consists of two parts, DICOM Core (which consists of file format and networking protocol) and DICOM Objects (which contains clinical information). Since DICOM Core focuses mainly on the machinery aspect, it will not be discussed in this document. The DICOM Objects (Figure 5) store the following information: patient profile, study details, study series, equipment details, and instances (medical images). For patient health studies, the patient profile, study details, and equipment information contain the most important details (DICOM Standards Committee, 1999 and 2005). Radiology imaging details are stored in the DICOM Objects and the data is used for clinical purpose and health research. As shown in Figure 6, a patient may have many diagnostic imaging studies. A single study may contain multiple series, and a series may contain multiple images. For dose measurements (as mentioned in Table 2), doses were collected at the study-level and is

typically reported in the Radiation Dose Structure Report (Dose SR). The Dose SR contains the patient profiles (such as patient ID, name, date of birth, sex, weight, height, and location), medical imaging device information, and most importantly, the dose measurement details. Depending on the medical devices, they may capture information such as modality types, modality calibration information (photom sizes, computed tomography dose index (CTDI), etc.), dose length product, number of slice per series, etc. All these radiology data are critical in determining the absorbed, effective, equivalent, and/or cumulative doses of the radiology procedures.

Figure 6. DICOM Structure & Radiation Dose Structure Report

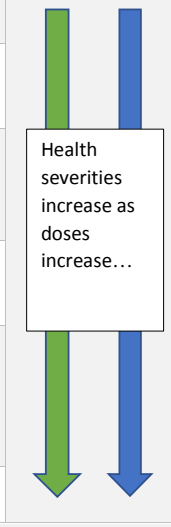


Dose-Responses (Deterministic and Stochastic)

Deterministic or *stochastic* biological effects are measurements used in studies of ionizing radiation exposures and cancer outcomes on human (UNSEAR, 2008). Deterministic effects occur when a certain level of radiation (dose threshold) is exceeded and are mainly associated with higher radiation dose exposures (i.e., approximately above 200 mSv equivalent dose). In some cases, the deterministic effects can be observed within hours, and

in others; they can take months to emerge. Table 3 (Health Physics, 2004) demonstrates the effects such as skin erythema, cataracts, sterility, radiation sickness, and death. However, the carcinogenic effects of low dose exposures (less than 200 mSv effective doses) may or may not have a latency period of up to 20 years (stochastic effect). The focus of this research will be on low-dose medical imaging modalities. High ionizing radiation dose exposures are beyond the scope of this research.

Table 3. Deterministic Health Effects

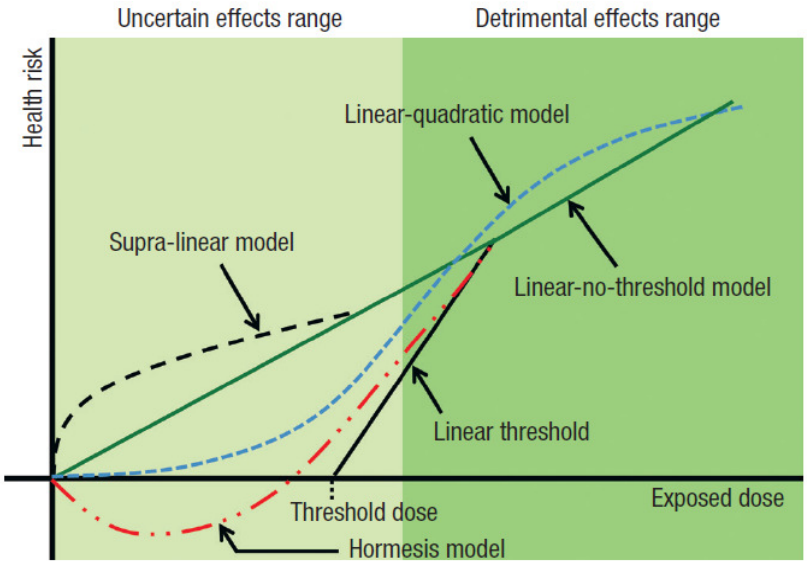
Dose (mSv)	Health Impacts	Health effects
0 - 200		No detectable immediate effects.
200 - 1000		Blood-bone marrow effects, temporary decrease in white blood cell count
1000 – 2000		Eye effects (cataracts), skin effects (Skin Erythema), acute radiation sickness - nausea, vomiting, longer-term of a decrease in white blood cells.
2000 – 3000		Sterility, hair loss, vomiting, diarrhea, loss of appetite, listlessness, death in some cases.
3000 – 6000		Gastrointestinal effects, immune system effects, vomiting, diarrhea, hemorrhaging, deaths are occurring in 50% of the cases at 350 rad or above without medical treatment.
Above 6000		Thyroid effects, eventual death in almost all cases.
Units of measurements: 1 rad = 1 rem = 1 cGy = 10 mGy = 10 mSv		

Radiation Exposure Risk Models and Risk Measures

Over past decades, nuclear research organizations proposed a risk model based on the atomic bombs Life Span Studies (LSS) as shown in Figure 7. The model shows five different dose-response scenarios: 1) Supra-Linear, this model suggests that the exposure initially imposes a high level of risk; there is no threshold limit. However, the lifetime risk may be marginal. For example, children who have been exposed to CT scans may have a risk of

developing leukemia within the first five years following the exposure; however, the risk may be reduced thereafter. 2) Linear-Quadratic, this model suggests that the exposure imposes a marginal level of risk; there is no threshold limit as well. However, repetitive exposures may elevate the risk exponentially. For example, a single CT scan may impose a relatively low level of solid cancer risk; however, repetitive CT scans may increase the level of developing solid cancer. 3) Linear No-Threshold, this model suggests that exposure will linearly increase the risk of cancer. Again, this model has no threshold limit. For example, children who have been exposed to a CT scan will have the odds ratio of 1.4 in developing thyroid cancer. The odds will increase in proportion to the increase of exposure dose. (4) Hormesis, this model suggests that a small exposure dose may reduce the risk of developing cancer. However, beyond a threshold dose, the risk will begin to increase. For example, a single x-ray procedure may lead to a negative risk of developing solid cancer (e.g., Relative Risk is 0.70). However, if exposed to five X-ray procedures will increase the risk (e.g., Relative Risk is 1.3). (5) Linear threshold, this model suggests that exposure to a low amount of radiation is considered risk-free; however, beyond a threshold, the risk will increase linearly. X-ray procedures may follow the pattern of the linear threshold model. These 5 risk models have been adopted in many cancer risk studies.

Figure 7. Radiation Exposure Risk Models



In addition, estimating cancer risk may be determined by different statistical methods (see Table 4). Depending on the studied objectives and desired results, the following cancer risk methods may be reported. The two most common indications for cancer risk estimates are cancer incidence rates and cancer risk probabilities (National Research Council, 2006). Depending on the research objectives, other risk and incidence indicators (e.g., Incidence Rate Ratio, Excess Relative Risk, etc.) can be derived from these two cancer estimates.

Table 4. Cancer Risk Assessments

Measurement	Type	Descriptions
Lifetime Attributable Risk (LAR)	Risk	LAR is an estimated probability of death or develops cancer from radiation exposure. It is a percent difference between an exposed person (A) and an unexposed person (B). $AR = (A - B)/A * 100$ A = incidence in the exposed person B = incidence in unexposed person The results are reported in the form of incidence rate per 10,000 or 100, 000 persons. The higher incidence values the higher cancer risk.
Excess Lifetime Death (ELD)	Excess Risk	The radiation-induced cancer death that is above the normal rate of death. $ELD = n/N (u - u^*)$ n= cancer patient population N= total population u= mortality in cancer patient population u*= mortality in the total population The results are expressed as excess cancer-related death in their lifetime in the percentage format. A high value implies a higher cancer risk.
Excess Relative Risk (ERR)	Excess Risk	ERR is the risk of developing cancer from medical imaging exposure above the cancer risk from background radiation exposure. $RR = (RR-1)$ The ERR is expressed as a positive figure which represents a value above the normal risk. A high value implies a higher cancer risk.
Excess Incidence Rate (EIR)	Excess Incidence	EIR presents the number of the incident above the normal incident rate of cancer.

Measurement	Type	Descriptions
		The results are expressed in the number of cases per 100,000 persons. A high value implies a higher cancer risk.
Standardized Incidence Ratio (SIR)	Incidence Ratio	SIR is the ratio of the observed number of cancer cases to the expected number of cases. The observed number of cases refer to several cancer cases in the cohort studies. The expected number of cases is a statistic computed reference study population (e.g., weighted age-specific data). For SIR>1, the results show the cancer incidence is greater for the observed than the expected cases. If the SIR<1 the results show the cancer incidence is greater for the expected than the observed cases. If the SIR=1.0 or approximately, there is no significant difference between the observed and expected cases. A value greater than 1 implies that there is a higher risk.
Incidence Rate Ratio (IRR)	Incidence Ratio	IRR is the incidence rate ratio of the exposed versus unexposed, after stratification for age, sex, and year of birth. For IRR>1, the results show the cancer incidence is greater for the exposed than the unexpected groups. If the IRR<1 the results show the cancer incidence is greater for the unexposed than the exposed groups. If the IRR=1.0 or approximately, there is no significant difference between the two groups. A value greater than 1 implies that there is a higher risk.
Relative Risk (RR)	Risk Ratio	RR measures the probability that an exposed population will develop cancer relative to the probability of an unexposed population that will also develop cancer. *RR = P (cancer /exposed) / P(cancer/unexposed)* For RR>1, there is an increased risk of developing cancer among those that have been exposed. If the RR<1, the exposure may decrease the risk of developing cancer. In this case, exposure to radiation may provide health benefits (hormesis cancer model). If the RR=1 or approximately to 1, it implies that there is no association between exposure and cancer risk.

Measurement	Type	Descriptions
Odds Ratio (OR)	Risk Ratio	OR measures the odds of cancer in the exposed population over the odds of cancer in the unexposed population. OR is used to describe the association between the exposure and outcome. *OR = [P (cancer/exposed) / (1 - P(cancer/exposed)] / [P (cancer/unexposed) / (1 - P(cancer/unexposed)]* For OR>1, there are chances of developing cancer among those that have been exposed. If the OR<1, there are no possible chances of developing cancer amongst those that have been exposed. If the OR=1 or approximately to 1, it implies that there are no differences between the exposed and unexposed.
Hazard Ratio (HR)	Risk Ratio	The hazard ratio is the radiation hazard in the exposed population over the radiation hazard in the unexposed population. Cox regression statistical method is commonly used for determining the HR. For HR>1, the results show the cancer incidence is greater for the exposed than the unexpected populations. If the HR<1, the results show the cancer incidence is greater for the unexposed than the exposed groups. If the HR=1.0 or approximately, there is no significant difference between the populations. A value greater than 1 implies that there is a higher risk.

Radiation Medical Imaging Exposures and Cancer Risks

A study of child radiography in Romania (Iacob,2002) showed that chest, spine, pelvis, head, abdomen, limb, and joint X-rays were frequently prescribed to young children (from birth to age 15). Chest X-ray procedures have been one of the most common procedures, accounted for 60 percent of annual occurrences, with an average effective dose of 0.74 mSv annually (with a range of 0.53 mSv to 1.08 mSv). The benefits of X-ray procedures provide a

quick method for detection of abnormalities of the heart, lung diseases, rib fractures, airway obstructions, or fluid in the lungs. Young children are often prescribed X-rays as a diagnostic method for detecting health issues; otherwise, they may not be detectable by other means. Although X-rays (0.02 mSv – 8.0 mSv) and dental X-rays (0.005 to 0.01 mSv) emit very low radiation doses, according to the Linear-No-Threshold model, there are no amounts of radiation exposures that are considered as safe.

Fluoroscopy is a diagnostic imaging method that continuously gathers X-ray images of internal organ studies. Fluoroscopy procedures include studies of the respiratory, gastrointestinal, and urinary tracts. Given that these procedures capture multiple X-ray images and have a longer examination time, fluoroscopy dose measurements may be higher, with the effective dosages ranging from 11.81 mSv to 16.45 mSv. The lifetime attribute risk from fluoroscopy procedures ranges from 0.2% to 0.8% (Huang, 2008).

CT scans are another type of X-ray diagnostic imaging procedures, whereby cross-sectional images are taken to provide three-dimensional images of the organs, tissues, bones, or blood vessels. Complementary to fluoroscopy or angiography, the purpose of CT scans is to detect internal organs and structure abnormalities, the growth of tumours, and injuries and traumas. The effective dose of a full-body spinal CT scan may range from 0.03 mSv to 70 mSv. The cancer risks from CT scans may impose non-cancer health issues as well as lifetime risks of developing solid cancer and leukemia. The next section will discuss cancer and non-cancer impacts in more detail.

From the Life Span Study of Japanese atomic bomb survivors and nuclear accidents (Samartizis,2011; Kusunoki, 2008; Wang, 2016; Neriishi, 2007; Johnson, 2014; Rahu, 2014; and

Ivanov, 2000), there has been evidence of cancer and non-cancer adverse health effects. For non-cancer health effects, some of the illnesses may include diseases (e.g., blood, circulatory, respiratory, and digestive) and disorders (e.g., genitourinary, musculoskeletal, and mental). Many of non-cancer health effects may be linked to high-dose exposures, as in the case of exposures to atomic bombs, nuclear accidents, and radiation therapies. In addition, low-dose exposures may induce non-cancer health issues such as cardiovascular and respiratory diseases. For this research, non-cancer health impacts are also beyond the scope.

Types of Childhood Cancers

Our bodies are constantly exposed to the background and different types of radiations. During such exposures, some cells are damaged and destroyed; however, these cells are automatic repaired. During the repair process, sometimes the DNA stands are improperly formed, and the cells became defective. Consequently, DNA mutations may develop which potentially lead to the development of cancers (Iacob, 2002). Given that children are in a constant state of growth, there is a higher probability of DNA mutations. Second, children have more years of life; therefore, it is expected that the probability of lifetime cancer risk would be greater. According to the American Childhood Cancer Organization and Healthy Children, ‘‘Childhood cancer is the number one disease killer and the second overall leading cause of death of children in the United States. More than 10,000 children under the age of 15 in the United States are diagnosed with cancer annually’’. Table 5 provides a list of childhood cancers and their statistics (American Childhood Cancer Organization, 2018).

Table 5. Types of Childhood Cancer

Cancer Type	Descriptions	Childhood cancer ranking & incidence percentages
Leukemias	Leukemia is defined as the abnormal amount of white blood cells that are produced in the bone marrow. There are different types of leukemia: acute lymphoblastic leukemia (75%), acute myeloid leukemia (20%), juvenile myelomonocytic (rare), acute promyelocytic (rare), chronic lymphoblastic (rare) and chronic myeloid (rare). Leukemia is one of the most common types of childhood cancers (ages 2 to 20 years).	Rank 1st acute lymphoblastic leukemia – 26% Rank 5th acute myeloid leukemia – 5%
Brain Cancers	Brain cancer is defined as a form of a tumour in the brain area. There are different types of brain tumours, such as astrocytomas medulloblastomas and ependymomas. Brain cancers often occur in children ages 2 to 6 years.	Rank 2nd Brain and central nervous system – 21%
Neuroblastoma	Neuroblastoma is defined as solid cancer that forms in the nervous system. This cancer occurs from birth to 5 years old.	Rank 3rd Neuroblastoma – 7%
Lymphomas (Thyroid Cancer)	Lymphoma is defined as cancer where abnormal white blood cells are found in the lymph system. There are two types of lymphoma cancers: Hodgkin and Non-Hodgkin. Lymphoma cancers are common in children ages 10-20 years. Non-Hodgkin is the most common type of cancer.	Rank 4th Non-Hodgkin Lymphoma – 6% Rank 7th Hodgkin Lymphoma – 4%
Wilms Tumor	Wilms is defined as a form of kidney cancer. It usually appears at 3 to 4 years old.	Rank 5th Wilms tumor 5%
Bone Cancers	Bone tumours are commonly found at the skull, shoulders, arms, knees, or	Rank 6th Bone tumours – 4%

Cancer Type	Descriptions	Childhood cancer ranking & incidence percentages
	pelvis. A common type of bone cancer is osteosarcoma. Bone cancers typically occur during teenage years.	
Sarcomas (Rhabdomyosarcoma)	Sarcomas are abnormal growth of tumours (soft tissues in muscle, fat, fibrous tissue, blood vessels, tendons, etc.). Rhabdomyosarcoma appears in children from birth to 10 years old.	Rank 8th Rhabdomyosarcoma – 3%
Retinoblastoma	Retinoblastoma is defined as a form of tumour, typically on the retinal layer of the eyes. It is typically found in children under the ages of 15.	Rank 9th Retinoblastoma – 3%
Hepatoblastoma	Hepatoblastoma is a solid cancer of the liver. This cancer typically occurs in children under 4 years of age.	Rank 10th Hepatoblastoma – 1%
Rhabdoid Tumors (Atypical Teratoid)	Rhabdoid is defined as a rare form of a tumour. It is usually found in the cerebellum (near the brain region). Although this cancer is rare, it is a highly aggressive form of tumours. It can be found in children of ages 2 to 13 years.	Rank 11th Rhabdoid Tumors - Rare

Sex differences in cancer susceptibility

Dorak and Karpuzoglu studied the possibilities of sex differences in cancer susceptibility. Although the reasons remain enigmatic, Dorak and Karpuzoglu cited that there are several possible causes of cancer susceptibilities: chromosomes, hormones, and environmental factors. In childhood cancer, the study indicated that boys are at a higher lifetime attributable risk than girls; moreover, boys and girls are prone to different cancer

types. Due to the sex physiological variations, certain cancers have higher incidence rates between the sexes. For example, the incidence rate of Hodgkin Lymphoma (HL) is greater in girls than in boys, with a ratio of 4 males: 5 females. Sex chromosomes are another key sex difference as males carry a single X-chromosome whereas females carry a double XX-chromosome. In females, only one X-chromosome is used while the second X-chromosome is randomly inactivated. If an X-chromosome gene becomes damaged, females would have an advantage of having a second X-chromosome. This extra X-chromosome enables females to continue with normal functions such as protein production. Hormones are another key sex difference such that the body generates a greater amount of androgen in males, whereas it generates a greater amount of estrogen in females. Both androgen and estrogen fulfill a major function in the immune system, which leads to the capacity for protecting the body against cancer progression. For example, estrogen has been identified as a protection against colorectal cancer. In some cases, hormone therapy has been used for cancer treatments. Dorak and Karpuzoglu also cited that environmental factors play a greater role in cancer susceptibilities than that of genetics. Genetics may not be the primary factors "…genetic factors are more likely to be modifiers of susceptibility rather than primary determinants of susceptibility". Although there have been advancements in the studies of sex-specific and associations in diseases and cancers; the results may not be conclusive at this time.

CHAPTER 3: STUDY RATIONALE

Radiation medical imaging is an effective technique in detecting health issues; however, radiation exposure may elevate the risk of developing cancer. It has been reported that the use of diagnostic imaging is on the rise in the last few decades (Mettler, 2009; Smith-Bindman, 2012; Migliorettti, 2013; Inman, 2015; and Repplinger, 2016). Although (Inman, 2015) indicated that, in recent years, the usage of CT scans and the exposure dose may have been reduced.

There were many studies that have been performed on cancer risks associated with radiation medical imaging (National Research Council, 2006); it is unclear how many studies were based on children. Evidence from the literature indicates that there have been deterministic cancer effects in high-dose irradiation exposures (above 200 mSv) and stochastic cancer effects in low-dose irradiation exposures (below 200 mSv). As indicated earlier, children's bodies undergo continuous development and rapid growth, and children of ages less than five years are the group with the highest cancer risks.

The purpose of this scoping review is to explore studies that have been conducted on radiation diagnostic imaging and cancer risks in children and to identify gaps in current literature. Depending on the available literature, this research will gather intelligence on this subject such as: what modalities may be associated with cancer, what factors are contributing to cancer risks, what are cancer incidence and risk probabilities, and are there possibly gender differences? These findings will help pave the path for future research.

CHAPTER 4: METHODOLOGY

Research Methodology

Scoping Review methodology has been applied to this research (Arksey and O'Malley, 2005). Upon formulating the search concepts and MeSH terms, they were used to query the search databases. The results of the literature search and triage are presented in the PRISMA diagram (Liberati, 2009). Sections below provide the details of literature search concepts, MeSH terms, exclusion and inclusion, data collection, and synthesis analysis.

In achieving the research objectives, the following key concepts (see Appendix A) were used for literature searches: 1) Radiation-induced medical imaging (i.e., X-rays, dental X-rays, fluoroscopy, angiography, and computed tomography) are the exposures. 2) The target study population includes those up to 18 years of age. The following terms were to be used in the query: pediatrics, children, young age, and childhood. 3) Low- dose exposures were also included as a key concept as some of the procedures involved higher radiation doses. 4) Lastly, cancers are the health outcomes; the following types of cancer are of interest: all cancer types, solid cancer, tumour, or leukemia.

PubMed and Scopus were the electronic databases used for the searches; other databases such as Cochrane, CINAHL and EMBASE have been intentionally omitted as this literature will have been included in the PubMed and/or Scopus databases. All four concepts were joined as one string for the databases (see Appendix A). The search syntaxes have been modified to fulfill the databases' search requirements. The two search results were combined, and duplicate and non-English articles were then removed before the screening was performed.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were used for triage of the search literature. Tables 6 and 7 provide a list of the inclusion and exclusion conditions. The key inclusion parameters are children, non-cancer patients prior to the first irradiation medical imaging procedure, low-dose medical imaging exposures, patient-level cohort studies, and all cancer types health outcomes. The exclusion parameters include prenatal or adult patients, high-dose exposures, and non-ionizing imaging procedures.

Table 6. Inclusion Criteria

Categories	Criteria	Description
Patient	Age	Newborn up to 18 years
	Sex	Female and male
	Medical conditions	No cancer, prior to first irradiation medical imaging procedure
Modality	Irradiation imaging procedures	X-ray, dental X-ray, fluoroscopy, angiography, and computed tomography scan
	Exposed organs	All body parts
	Exposed doses	Low dose (below 200 mSv), for single and/or multiple procedures
Health studies	Cancer type	All cancers, solid cancer, tumours, and/or leukemia
	Study design	Patient-level health studies Observational studies (e.g., retrospective, prospective, case-control, cross-sectional,ecological, etc.)
	Exposure period	All dates
	Origin	All countries
Document	Date	All documents, up to the date of document search (May 28th, 2018)
	Sources	PubMed and Scopus
	Availability	Electronic format, including scanned documents

Table 7. Exclusion Criteria

Categories	Criteria	Description
Patient	Age	Prenatal (pre-birth) or adults (age >19-year-old)
	Medical conditions	Patients who developed cancers prior to radiation medical imaging
Modality	Imaging procedures	Non-ionizing radiation (e.g., MRI, Ultrasound) Mammography procedures are typical administer in adult population (Radhakrishnan, 2017)
	Dose	High dose (above 200 mSv)
Health studies	Exposures	Radiotherapy, occupational, environmental radiation exposures, or atomic bomb survivors
	Study	Mathematical cancer risk studies
Document	Date	None
	Language	Non-English articles
	Sources	Non-peer review (e.g., commentaries, editorial, etc.)

Data Collection

From the selected articles, the following attributes/data have been gathered (see Table 8).

Table 8. Journal Evaluation Criteria

Categories	Attribute	Description
Study	Date of studies	The study dates and ages of exposures are key factors for this investigation. The exposed doses may have been reduced over the years; thus, the results of the studies may have been affected
	Studies' objectives	The focus of the investigation
	Age of patients	Ages of subjects for the studies from birth to 18 years; grouped by birth to 1-year-old, 1 to 5-year-old, 6 to 10-year-old, 11 to 15-year-old, and over 16-year-old
	Cancer risks	Record the cancer type, incidence rate and risks due to ionizing radiation exposure
	Modality	Record the type of radiation medical imaging procedures that were used
	Dosages	For the studies, observe the type of doses (e.g., absorb, equivalent, effective, or cumulative) that were applied
	Exposure frequency	Observe the frequency of exposures for the studies
	Latency /Follow-up	Record the latency, since the first exposure
Data Analysis	Study designs	Identify the type of epidemiology study design of the studies
	Strengths/Limitations	Observe the strengths and limitations of the investigations
	Risk calculations	Identify the types of risks that were reported, such as Lifetime Attributable Risk, Relative Risk, Odds Ratio, Incidence Rate, etc.

Categories	Attribute	Description
	Size of population	Identify the studies population size
	Statistical method	Observe the data analysis method, confidence level, and variances
	Inclusions/exclusions	Observe the inclusion and exclusion criteria of the studies
Research Results	References	Review the references that were used for the analysis, discussions, and conclusions
	Results	Analyze the results present, the margin of errors, and statistical significance
	Conclusion statements	Observe the conclusion statements, such as definitive and inconclusive

Upon collecting the data (see Appendix B), the next steps were to organize and standardize the data into categories. Table 9 provides the information of interest for data analysis and synthesis.

Table 9. Data Organization

Categories	Description
Study timelines	Group together the year of the cohort and the year of the studies
Age	Categorized by: 1) Less than 1-year-old, 2) 1 to 5-year-old, 3) 6 to 10-year-old, 4) 11 to 15-year-old, and 5) 15 to 18-year-old
Sex	Categorized by: 1) females, and 2) males
Dosages /exposure	If possible, categorize the dosages: 1) absorbed dose, 2) equivalent dose, 3) effective dose, and 4) cumulative dose If possible, categorize the exposed organs: 1) head, 2) chest, 3) abdomen, and 4) extremities

Categories	Description
Health effects, radioactive sensitivity, and latency periods	Report on the evidence of all cancers, solid cancer, tumour, or leukemia based on the radiation-induced on the exposed organs. Also, report on the latency period when evidence of cancer first appears
Cancer risk estimations	Reported on different levels of cancer risks, incidence rate, and ratios *Risks & Incidence Rates:* Lifetime Attributable Risk (LAR), Excess Lifetime Death (ELD), Excess Relative Risk (ERR), Excess Incidence Rate (EIR), *Ratios*: Relative Risk (RR), Odds Ratio (OR) Standardized Incidence Ratio (SIR), Incidence Rate Ratio (IRR), or Hazard Ratio (HR)

Data Synthesis, Harmonization, and Reporting

After data collection and organization of the data, the next steps were to perform data synthesis, evaluations, and comparisons. Table 10 provides a list of possible techniques and approaches that may be used for data synthesis and reporting.

Table 10. Reporting Techniques

Approaches	Description	Data Synthesis
Classification	Conversion/standardization of data • Exposure age groups (0-1, 1-5, 6-10, 11-15, and 16-20) • Dosages (absorbed, equivalent, effective, and cumulative) • Expose organs (head, chest, abdomen and extremities) • Cancer risks	• Convert and standardize the exposed age groups • Group the cohorts into age categories • Convert/translation risk nomenclatures into a standard risk indicator, if possible • Resolve data quality issues and remove outliers and non-resolvable datasets, of possible

Approaches	Description	Data Synthesis
		• Align the data sets so that they present exposure, outcomes, and risks
Comparative	Data evaluations: • Modalities • Exposed age groups • Exposed gender • Exposed organs • Frequency of exposures	Upon standardizing the data sets, the next steps were to use different statistical and epidemiological methods for calculations, comparisons, clustering, and associating, if applicable. The goals were to detect patterns, associations, and/or probabilities of the data sets
Assessment	Review of research methodologies: • Study design • Data collections • Bias and limitations • Results/conclusions • Narratives - key discoveries/outcomes	Furthermore, each research report will be assessed for the quality of study design, data selection/ collection, bias, limitation, etc. Lastly, an overall assessment of the data collected will be conducted
Reporting	Cancer outcomes • Risks (positive, undetermined, negative) • Excess risks • Incidence rate (No. per 10,000 or 100,000 persons) • Risk ratio	As indicated in BEIR VII, the estimation of cancer risks can be expressed as an incidence rate/probability. Hence, the cancer risks in this research are to be harmonized as one of following risks: 1) probability of cancer development, 2) probability of developing cancer beyond the normal risks, 3) incidence cancer incident rates, and 4) cancer ratio comparison

CHAPTER 5: FINDINGS

Literature Search Results

Four concepts (i.e., pediatrics, low dosage, irradiation diagnostic procedures, and cancer risks) were used for the literature search in the PubMed and Scopus databases. The details of the search terms and results were captured in (Appendix A). After conducting literature screening (see Figure 8), ten (10) articles were selected and two (2) manual search articles found to be eligible for this study. Of the twelve (12) eligible articles, there was one (1) for dental X-rays, three (3) for X-rays, zero (0) for fluoroscopy or angiography, and eight (8) for CT scans.

Study Demographics

As shown in Table 11, the twelve selected studies included in this review covered over one million patients cumulatively. The genders in most studies were evenly divided between females and males except for the study of dental X-ray exposure where the male to female ratio is 1:3 (Memon, 2010). CT scans studies provided the greatest number of participants. On population age, most of the diagnostic procedures performed were at ages zero to one and one to five years. Chodick noted that the use of diagnostic imaging reduced as the age of patients increased. He stipulated that this irregular CT scan usage pattern may be due to the greater cases of injuries and head trauma among those at the younger ages. With the increase in exposure, particularly higher doses of irradiation procedures such as CT scans, the lifetime attributable risk would increase correspondingly.

Figure 8. PRISMA Flowchart

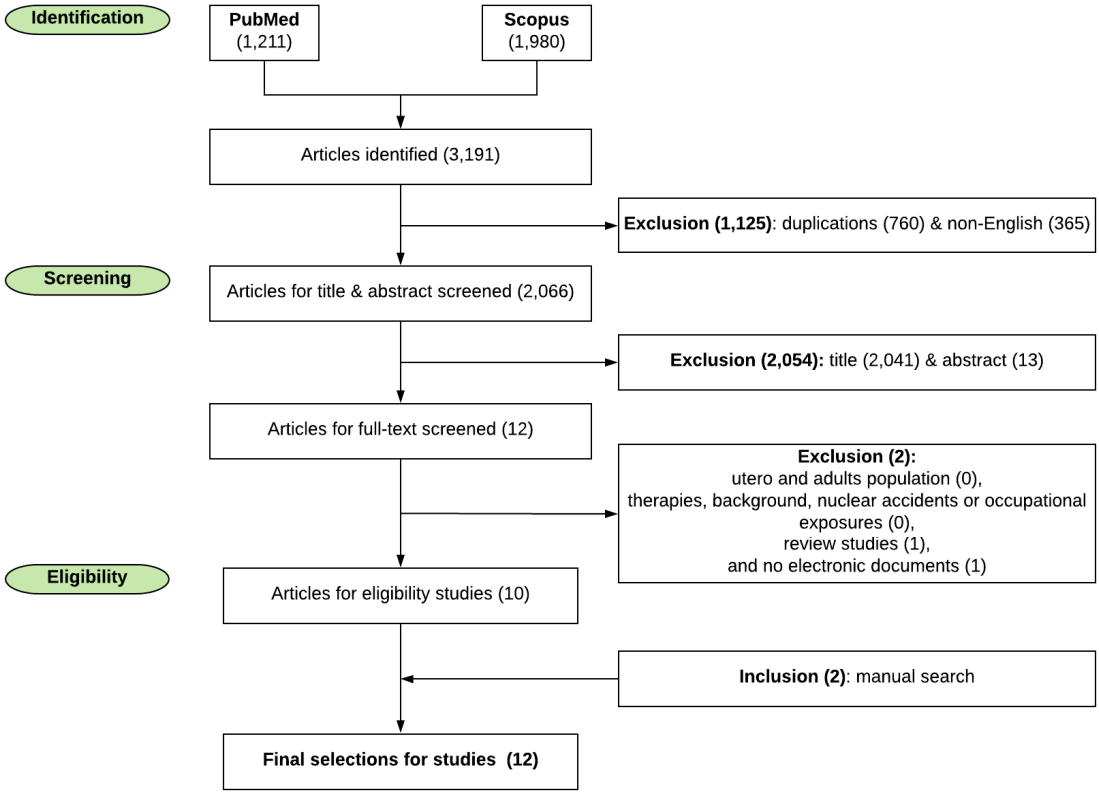


Table 11. Study Populations

		Studies populations			Ages of exposures				
No.	**Author**	**Population**	**Male**	**Female**	**Ages (0-1)**	**Ages (1-5)**	**Ages (6-10)**	**Ages (11-15)**	**Ages (16-20)**
1	Memon et al., (2010)	313	75	238	No data	No data	6		51
2	Inskip et al., (1995)	484	113	371	No data				
3	Hammer et al., (2009)	92,957	50,005	41,432	20,546	22,243	6,387	2,489	No data
4	Hammer et al., (2011)	78,527	42,436	34,829	No data				
5	Chodick et al., (2007)	17,686	9,430	8,256	No data				
6	Pearce et al., (2012)	178,604 leukemia 176,587 brain tumors			No data				
7	Mathews et al., (2013)	680,211	357,119	323,092	42,798	N/A	104,618	202,420	330,375
8	Miglioretti et al., (2013)	744	372	372	No data	232	219	293	No data
9	Su et al., (2014)	926	633	293	13	148	346	419	No data
10	Huang et al., (2014)	24,418	No data		9,767		5,177	9,474	No data
11	Niemann et al., (2015)	522	291	231	110	201	130	73	No data
12	Krille et al., (2015)	44,584	26,146	18,387	16,496		12,929	15,159	No data

Radiation Medical Diagnostics

A. Dental X-rays

Dental X-rays are routine procedures that are used for the detection of teeth issues such as decay, cavities, bone loss, wisdom teeth, or abnormal bone structures. Often, these teeth issues are not vividly visible to the dental professionals. Therefore, most patients undertake dental X-rays every one or two years as part of their routine dental checkups. Due to the proximity of the thyroid gland, dental X-rays may impose thyroid cancer risks. The Atomic Bomb Survivor Life-Span Studies (LSS) indicated that the thyroid gland is a highly radiation-sensitive organ. Memon and colleagues suggested that there is a possible

association between dental X-rays and thyroid cancer. The case-control study consisted of patients aged 5 to 70 years with a sample size of 313; however, the children cohort size was n=57 (ages 5-14 (n=6) and 15-24 (n=51)). The overall study showed an Odds Ratio (OR) of 2.1 (95% CI=1.4 – 3.1, and p-value of 0.001). The study also showed that 1-4 exposures had an OR of 2.2 (95% CI=1.4 – 3.5, p-value of 0.001), 5-9 exposures had an OR of 4.6 (95% CI=1.4 – 14.7, p-value of 0.01), and 10 or more exposures had an OR of 5.4 (95% CI=1.1 – 26.7, p-value of 0.037). For gender-specific (females and males), the results showed an OR of 2.0 (95% CI=1.2 – 3.3, p-value < 0.01) and 2.4 (95% CI=1.0 – 5.1, p-value of 0.05), respectively. This study did not disclose information on the exposed dosages (i.e., effective dose and cumulative dose). Overall, although the sample size was small (n=57), the study data showed an increasing risk associating dental X-rays with thyroid cancer, where the OR is significantly above the equilibrium point (OR=1.0). The study also indicated that there is an elevated risk with the increase of dental X-ray exposures. The data suggested that males and females are equally at risk. The study noted that protective lead collars were commonly used during the period of this dental X-ray study (1998-2002).

B. X-rays

X-rays are common procedures used in detecting fractures and abnormalities of organs, tissues, and bones. Possible body regions include head and neck, chest and shoulders, spine and pelvis, upper and lower extremities, abdomen, and more. From LSS, human organs (such as red bone marrow, lungs, breasts, the thyroid, skin, and eyes) and children (including fetuses to ages 18 years) are highly susceptible to carcinogenesis. Due to the small sample size, further research is required.

Inskip and colleagues examined the risk of thyroid cancer from X-ray exposures to different parts of the body, during the period from 1980 to 1992. They conducted a case-control study of 484 cases and 484 control subjects; females (n=371) and males (n=113,); and ages of <20 to >60. Overall, there were 2235 (female) and 682 (male) subject cases, and 2457 (female) and 754 (male) control cases. For the group aged <20 years, there were 272 subject cases and 237 control cases. The results showed that with exposures of one to five times to the upper body regions (i.e., head, neck, and upper spine), the relative risk (RR) of developing thyroid cancer was 1.02 (95% CI= 0.76 -1.38). With exposures greater than six times to the same exposed body regions, the RR was 1.22 (95% CI= 0.46 – 3.34). Note, the doses applied to this region were indicated as the highest relative radiation dose to the thyroid gland in comparison to other exposed regions. Similarly, with one to five exposures to the upper-middle body regions (i.e., chest, shoulders, and upper gastrointestinal tract), the RR was 1.06 (95% CI= 0.78 -1.46). With exposures of six to ten times to the same body region, the RR was 1.11 (95% CI= 0.67 - 1.87), and with exposures of >10 times, the RR was 0.99 (95% CI= 0.47 – 2.08). Note, the doses applied to this region were indicated as the medium relative dose to the thyroid. Lastly, exposures of one to five times toward the lower middle body regions (i.e., abdomen, pelvis, and legs), the RR was 0.75 (95% CI=0.56 – 1.00), with exposures of six to ten times, the RR was 0.99 (95% CI= 0.60 - 1.62), and exposure of >10 times, the RR was 0.75 (95% CI= 0.42 – 1.35). Note, the doses applied to this region were indicated as the lowest relative dose to the thyroid. The effective doses range from 0.03 mGy (for small intestine) to 13 mGy (for thoracic spine). The study also investigated the risks of cumulative doses: 0.08 mSv, 0.32 mSv, and 1.95 mSv, the relative risks were 1.05 (95% CI=0.73-1.52), 1.04 (95% CI=0.70-1.55) and 1.05 (95% CI=0.73-1.52), respectively. Based on the relative risks shown in this study

(ranges between 0.75 to 1.22), Inskip suggested the following: 1) there was no evidence linking thyroid cancer with X-rays, 2) there was no evidence that increasing the number of X-ray exposures will elevate thyroid cancer risks, and 3) there was no evidence of elevated risks with the increase of cumulative doses. Due to the small pediatric study size, additional studies on this subject are required.

Hammer and colleagues, published in 2009, investigated the childhood cancer risk from X-ray diagnostic imaging. This study comprised of 92, 957 children from a German hospital between 1976 – 2003. There were 50,005 boys and 41,432 girls, and their ages of exposure were less than 20 years. More than half of patients (59%) received only one examination, 19% and 8% received two and three procedures, respectively. Only 14% received four or more examinations. The Standardized Incidence Ratio (SIR) of all cancer risk was 0.99 (95% CI=0.79 – 1.22), leukemia risk was 1.09 (95% CI=0.74 – 1.52), lymphoma risk was 0.97 (95% CI=0.52 – 1.66), tumor (CNS) risk was 0.52 (95% CI=0.25 – 0.95), and other tumor risk was 1.25 (95% CI=0.85 – 1.77). The SIR on gender-specific was relatively equal; boys were 0.99 (95% CI=0.74 – 1.29) and girls were 1.00 (95% CI=0.69 – 1.38). Similarly, the SIRs based on the number of X-ray examinations were relatively the same: one scan was 0.97 (95% CI=0.73 – 1.27), two scans were 0.91 (95% CI=0.50 – 1.52), and three or more scans were 1.10 (95% CI=0.67 – 1.70). Furthermore, the Incidence Rate Ratio (IRR) on different exposed doses (0.0-9.9 μSv, 10-49.9 μSv, and 50+ μSv) for all cancers were 1.00, 1.02, and 1.01, respectively. For leukemia and lymphoma, they were 1.00, 1.00, and 1.04, respectively while solid tumours were 1.00, 1.05, and 0.98, respectively. The SIR ranges from 0.97 to 1.25 which was close to 1.0 and the results seem to suggest that there are no evaluated cancer incidence rates between the exposed and unexposed populations.

Hammer and colleagues studied the childhood cancer risk from X-ray diagnostics. The cohort composed of 78,527 patients who received X-ray procedures from 1980 to 2006 where 42,438 were boys, 34,829 were girls, and 1,263 were unknown. Most patients received only one examination (63%); the rest received two (19%), three (8%), and four or more examinations (11%). The median cumulative effective dose in all patients was 5 μSv. The SIR in all patients for all cancers risk was 0.97 (95% CI=0.75 – 1.23), solid tumors were 0.88 (95% CI=0.60 – 1.25), and leukemia and lymphoma were 1.05 (95% CI=0.74 – 1.45). The IRR in all patients with <10 μSv was 1.00 (reference point); 10-49.9 μSv was 1.08 (95% CI=0.62 – 1.90, p-value=0.78), and >=50 μSv was 1.05 (95% CI=0.56 – 1.98, p-value = 0.88). In both of Hammer and colleagues' studies (2009 and 2011), the results also indicated that there was no evidence linking X-rays to cancer (i.e., all cancers, leukemia, lymphoma, or tumours). Likewise, there was no evidence linking multiple exposures or the increase of cumulative dose exposures to elevated cancer risks.

The studies of X-rays (Inskip and Hammer) showed that the RRs are closely 1.0 which suggests that there is a very small cancer risk with normal X-ray procedures. The studies also showed that a single exposure has an RR<1.0 (e.g., RR=0.75 95% CI: 0.56-1.00) which hypothetically, may act as a cancer protection. According to the BEIR hormesis model, a small radiation dose exposure may help to initiate the cell repair mechanisms, which subsequently, the cell repair seems to offer better protection against cancer.

C. Fluoroscope and angiography

The literature search did not find a patient-level study on fluoroscopy; however, there was a mathematical study on angiography and cancer risks of a 5-year-old child. Huang and colleagues, 2008, conducted on four retrospective ECG-gated CT coronary angiography protocols (40, 60, 70 and 90 bpm) in the United States and Hong Kong (China). The effective doses for the four protocols were 16.45, 12.17, 11.97, and 11.81 mSv. The results of the mathematical study indicated that the LAR of the 5-year-old boys and girls in the United States were 0.14% to 20% and 0.43% to 0.60%, respectively; and in Hong Kong were 0.22% to 0.33% and 0.61% to 0.85%, respectively. Furthermore, Huang discovered that the risks were 2.5-3.3 times higher in girls compared to boys, and Hong Kong children were 1.4-1.6 times higher than United States children. The mathematical study, conducted in the United States and Hong Kong children, suggested that there were associations of angiography and cancer risks.

D. CT Scans

CT scans provide cross-sectional images, or slices, of human organs, tissues, blood vessels, and bones. Similar to X-rays, they are used to detect bone fractures, diseases (organ diseases, disorders, or infections), blood clots, or cancer. Unlike X-rays, they emit high cumulative radiation doses to the examined organs to capture cross-sectional slices or images. The most common types of CT scans are brain, chest, abdomen or pelvis, spine, or neck. Due to higher radiation dose exposures, CT scans are considered high cancer risk procedures and they should only be prescribed if the medical benefits exceed the risks.

Chodick and colleagues studied cancer risks from CT scans in Israel between 1999 to 2003. The cohort was comprised of 17, 686 children (males – 9,430 and females - 8,256), ages from birth to 18 years. The effective doses were 130 mGy (head CT) and 51 mGy (abdomen) at the age of < 3 years old; however, the effective doses reportedly decreased to 30 mGy (head CT) and 24 mGy (abdomen) as the ages of patients increased. The final results showed that the excess lifetime death (ELD) for this study was 0.29%. The study reported that the ELD was higher in males than those of females (e.g., 0.78 vs. 0.48 for children ages <3, respectively). The investigator noted that a possible rationale for this result was that boys were more prone to head injuries and trauma than girls; and therefore, they required more CT scans. Ultimately, the excessive CT scans may lead to a higher excess in death rates.

Pearce and colleagues investigated the association of CT scans with leukemia and brain tumours. The cohort encompassed 178,604 leukemia and 176,587 tumour patients from the National Health Service (United Kingdom) during the period of 1985 to 2002. The administered effective doses (mGy) to the brain was (28 – 43 mGy), the chest was (0.2 - 0.4 mGy), the abdomen was (0.0 – 0.2 mGy), and extremities was (0.0 mGy). In both cases, males and females had been prescribed similar effective dosages. The study noted that the prescribed effective doses were proportional to the children's ages. The results showed that there was an associated risk of leukemia when CT scans are directly at the bone marrow. The excess relative risk (ERR) per mGy for leukemia was (0.042, p-value=0.6300) in females and (0.031, p-value=0.6300) in males; and for brain tumors was (0.016, p-value=0.0850) in females and (0.028, p-value=0.0850) in males. The data also showed that the increase in the number of CT scan procedures will lead to higher ERRs of leukemia (i.e., 1 CT scan, ERR of 0.013; 2-4 CT scans, ERR of 0.028; and >5 CT scan, ERR of 0.035; p-value of 0.8013) and higher ERRs of brain

tumors (i.e., 1 CT scan, ERR of 0.007; 2-4 CT scans, ERR of 0.021; and >5 CT scan, ERR of 0.018; p-value of 0.1213). Leukemia appears to be more prominent in the first few years after CT scan exposure; however, the ERRs decrease as the number of years since the exposure increases. The ERRs for Leukemia was 0.055 (2 to 5 years or less), 0.021 (5 to 10 years or less), 0.005 (10 to 15 years or less) and 0.026 (15 years or more); p-value of 0.5357. The ERRs for brain tumours was 0.026 (5 to 10 years or less), 0.023 (10 to 15 years or less) and 0.005 (15 years or more); p-value of 0.2399. In both cases, the younger the age when exposed, the higher leukemia and brain tumours cancer risks. Overall, this study showed how CT scans impose elevated risks of leukemia and brain tumour, more evidently in early ages of exposure and in repeated procedures. However, the risks seem to subside as the latency period since the first exposure increases.

Mathews and colleagues studied the relationship between CT scans and cancer incidence rates. This study consisted of 680,000 participants, ages of 0-19 years, who were born between 1985 and 2005. There were 357,119 (52.5%) males and 323,092 (47.5%) females. The percentages of CT scan procedures to the brain was 59.4%, facial bones were 13.1%, extremities were 9.5%, the spine was 8.6%, the abdomen was 5%, the chest was 1.7%, and others was 2.7%. The overall incidence rate ratio (IRR) for 1-year, 5-year, and 10-year lag periods were 1.24 (95% CI=1.20 to 1.29), 1.21 (95% CI=1.16 to 1.26), and 1.18 (95% CI=1.11 to 1.24), respectively. The absolute excess incidence rate (EIR) per 100,000 for all solid cancers, thyroid cancers, leukemia, and all cancers were 7.76 (95%, CI=6.24 to 9.27), 1.10 (95% CI=0.62 to 1.59), 0.53 (95% CI=0.09 to 0.97), and 9.38 (95%, CI=7.68 to 11.08), respectively. Furthermore, the study showed that excess rate ratio per mSv of all cancers were 0.035 (95% CI=0.026 to 0.042) – 1-year lag period, 0.031 (0.022 to 0.040) – 5-year lag period, and 0.027

(95% CI=0.017 to 0.037) – 10-year leg period. Likewise, the excess rate ratio per mSv of brain cancer was 0.029 (95% CI=0.023 to 0.037) – 1-year lag period, 0.021 (0.014 to 0.029) – 5 years lag period, and 0.015 (95% CI=0.007 to 0.026) – 10 years leg period. Similarly, the excess rate ratio per mSv of leukemia was 0.039 (95% CI=0.014 to 0.070) – 1-year lag period, 0.042 (0.010 to 0.080) – 5 years lag period, and 0.017 (95% CI=0.029 to 0.078) – 10 years leg period. The study illustrated that there was an excess of cancer incidence comparing the exposed and unexposed groups. However, the incidence rate seems to reduce as the latency period of the first exposure increases.

Miglioretti and colleagues studied the cancer risks from all CT scans. The cohort was comprised of six integrated healthcare systems in the United States. The data gathered was from 1996 to 2010, with 4,857,736 being child-years observed. The effective doses ranged from 0.03 to 60.2 mSv. Given that the ages of exposure were under five years, the lifetime attributable risk (LAR) per 10,000 of head CT scans was 17.5 for girls and LAR per 10,000 was 7.4 for boys. The LAR for leukemia was 1.9 for both genders. For abdomen CT scans, girls had a LAR of 33.9 and boys had a LAR of 14.8 per 10,000 persons. As for leukemia, the LAR for both genders was 0.8. For chest CT scans, girls had a LAR of 28.4 and boys had a LAR of 8.4 per 10,000 persons. The LAR for leukemia was 0.6 for both genders. Lastly, for spine scans, girls had a LAR of 37.7 and boys had a LAR of 5.3 per 10,000 persons. For leukemia risk, the LAR was 0.7 for both genders. However, the LARs of cancer were reduced when the patients' ages increased (i.e., 5 to 9 years and ages 10 to 14 years). These declining trends apply to both boys and girls. The study seems to suggest that girls are more at risk compared to boys. Second, receiving CT scans at a younger age increases the LAR of cancer in both genders. Last, the incidence rate of solid cancer and leukemia reported increases as the number of CT scan

increases. For example (Miglioretti, 2013), the numbers of Head CT scans leading to 1 case of cancer were: ages <5 (570 CT scans), ages 5-9 (6,130 CT scans), and ages 10-14 (9,020 CT scans) in girls and ages <5 (1,350 CT scans), 5-9 (4,150 CT scans), and ages 10-14 (4,660 CT scans) in boys. The results showed similar patterns for abdomen, chest, and spine CT scans.

Su and colleagues studied the thyroid cancer risk from CT scan procedures of 922 children from China between January to December of 2012. The cohort comprised of 68% females and 32% males. The cohort ages were between 0 to 15 years. The CT scans in the study included paranasal sinus (10.4%), head (53.3%), chest (10.6%), abdomen/pelvis (18.5%), spine (3.1%), and extremities (4.1%). The applied doses to the sinus, head, and chest ranged from (0.61- 0.92 mGy), (1.10 -2.45 mGy), and (2.63 – 5.76 mGy), respectively. The results of this study showed that girls had a lifetime attributable risk (LAR) of thyroid cancer incidence per 100,000 children for sinus, head, and chest scans were 2.7 (95% CI=1.7-4.2), 8.7 (95% CI=2.8-48.5), 14.1 (95% CI=7.0-65.4), respectively. Moreover, the highest LARs for children aged less than one year was 23.6 (head scans) and 55.5 (chest scans) per 100,000 persons. As for boys, the LAR of sinus scans was 0.4 (95% CI=0.2-1.1), LAR of head scans was 1.1 (95% CI=0.4-3.6), and LAR of chest scans was 2.1 (95% CI=1.0-8.5) per 100,00 persons. Likewise, boys ages less than one year had LARs of 3.3 (head scans) and 7.8 (chest scans) per 100,000 persons. The study suggested that chest CT scans imposed a higher LAR for developing thyroid cancer than CT scans of other parts of the body. Second, females seem to report a higher LAR relative to boys. Last, those children exposed at an early age exhibited a higher LAR of thyroid cancer than those who were exposed at later ages.

Huang and colleagues studied the association of head CT scans with possible risks of malignancy and benign brain tumours. The cohort comprised of 24,418 patients between 1998 to 2006. The median effective dose was 2 mSv for regular head CT examinations to 14 mSv for stroke CT scan procedures. The study showed that for CT scan exposure, it had an overall Hazard Ratio (HR) of 1.29 (95% CI=0.90 – 1.85). Specifically, for a single CT scan exposure, the HR of brain tumours of malignant and benign, malignant, and benign were 2.56, 1.84, and 2.97, respectively. The HR for leukemia was 1.90. The study also found that children who had CT scans at the ages of 4-5, the HR of brain tumours and malignancy were at the highest level. The appearances of cancer were seen in some children three years after the first CT scan procedure. Moreover, the HRs increase for every additional CT scan procedures.

Neimann and colleagues studied the lifetime attributable risk and mortality risk of a single chest CT scan on a cohort of 522 pediatric patients. The effective doses were: newborn (1.93 mSv), 5 years old (1.4 mSv), 10 years old (1.3 mSv), and 15 years old (0.85 mSv) respectively. The study indicated that there was be a positive association of CT chest scans with stomach, colon, liver, lung, breast, uterine, ovarian, bladder, thyroid, and leukemia cancers. For females, ages of zero to one, the LAR per 100,000 persons, for the cancers as indicated above, were 3.04, 1.34, 0.93, 28.72, 47.58, 0.07, 0.19, 26.22, and 2.05, respectively. For males ages, zero to one, the LAR of cancer, for the cancers as indicated above, were 2.73, 2.56, 2.42, 14.36, 0.23, 5.76, and 3.07, respectively. Based on the results, they suggested that lung, breast, and thyroid cancers scored the highest LAR for both genders. As the ages of exposure increased, the LARs gradually decreased. These trends seem to apply to both boys and girls.

Krille and colleagues studied the risks of solid cancer, leukemia, and tumours from exposure to CT scans in children under the age of fifteen who were born between 1966 and 2010. The study comprised of 44,584 patients (26,146 were boys, 18,387 were girls, and 51 were unknown). However, the effective doses in this study were not provided. The results from this study showed that the Standardized Incidence Ratio (SIR) for all cancers, leukemia, lymphomas, CNS tumours, and solid cancer were 1.87 (95% CI=1.33-2.55), 1.72 (95% CI=0.89-3.01), 3.26 (95% CI=1.63-5.83), 1.35 (95% CI=0.54-2.78), and 1.68 (95% CI=0.77-3.19), respectively. The study also showed that with the increase in the number of examinations (two or more), the SIRs also increase. For example, in all cancer for one CT scan, the SIR is 1.71 (95% CI=1.12-2.25), and for two CT scans or more, the SIR is 2.29 (95% CI=1.22 to 3.91). These patterns were also shown for leukemia, lymphomas, CNS tumours, and solid cancers.

Overall, the studies of CT scans showed elevated incidences and risks of leukemia and cancers. These risks and incidences are dependent on exposed ages, exposed organs, repetitive procedures, and latency period. Sections below will address the cancer risks and incidence, and the dependant factors.

Cancer Risks

Linet and colleagues indicated that irradiation medical imaging dose in 2006 per capita in the United States was 3.0 mSv, compared to 0.53 mSv per capita in 1980. Secondly, as noted by Miglioretti, CT scan procedures had increased from 10 per 1000 children in 1996 to 15 per 1000 children ages up to 5 years and 25 per 1000 children ages 5 to 14 years by 2015. Diagnostic medical imaging has been a valuable instrument for saving lives. The study seems to indicate that dental X-rays, X-rays, and CT scans impose moderate to high risks of thyroid

cancer, leukemia and lymphomas, tumours, solid cancer, and all cancers, and even cancer mortality. The trend of increasing irradiation diagnostic doses and frequent usages of medical imaging, especially on children, may provide reasons to be alarmed. Sections below will describe the findings in more detailed.

A. Thyroid Cancer

Biomedical radiation studies such as BIER and LSS indicated that thyroid is one of the most common types of cancer in both children and adults; however, the biological sensitive reasons have yet been fully explained at this time. The results from this study indicated that dental X-rays, X-rays, and CT scans may have positive associations with thyroid cancer, particularly irradiation exposures near the thyroid gland region (Table 12). The incidence rate ratio, relative risk, and odds ratio, as shown in Table 12, above 1.0 indicated that there were elevated risks of thyroid cancer seen for Dental X-rays and CT scans. Also, the positive values of LAR indicated that there are probabilities of cancer risk. Due to the proximity of the thyroid in dental X-rays and due to higher doses prescribed in CT head scans, perhaps these may be causation for thyroid cancer. Memon indicated that the use of thyroid lead protective gear was not a common practice during the studied period between 1998-2002. Most dental X-ray protocols today required patients and dental practitioners to arm themselves with protective gears. Hopefully, this practice may help to protect the adverse effect of cancer risks. Thyroid cancer from chest X-rays to the abdomen and extremities regions appear to impose low risk; where RR is below 1.0 ratio. Moreover, X-rays to different body parts, such as head, chest, or abdomen, again demonstrated very low thyroid cancer risk (Hammer, 2009). The results of X-rays studies showed that repetitive X-rays exposures, up to 10 procedures, do not seem to

elevate thyroid cancer risk. Furthermore, the latency of thyroid cancer development in various radiation diagnostics has not yet been clearly defined. Due to limited research that is available today; further studies are required in determining the potential risks.

B. Leukemia and Lymphomas

Based on the literature of this research, leukemia and lymphomas may be associated with CT scan exposures (see Table 13). These cancer cells seem to illustrate a short latency period (Mathew, 2013 and Huang, 2014). A formation of cancer within the first five years after being exposed. Pearce suggested an excess relative risk (ERR) of 0.031 per mGy for males and 0.042 per mGy for females. Furthermore, Miglioretti suggested that exposures to the abdomen compared to other body parts pose the highest risks (1 case per 10,000 scans), and the younger the ages of exposure, the higher the lifetime attributable risk (e.g., at age <5 females, 33.9 per 10, 000 persons (Pearce, 2002). The cancer risks and medical benefits of CT scans have been appropriately documented and communicated to patients and medical professionals.

Table 12. Thyroid Cancer Associations

Study	Modality	Exposure	Thyroid Cancer Risk	Elevated Risk
Mathews et al. (2013)	CT scan	Head	IRR = 1.33 (95% CI=1.13 - 1.57)	Yes, since the IRR is above 1.0
Memon et al. (2010)	Dental X-ray	Dental	OR = 2.10	Yes, since the OR is significantly above 1.0
Inskip et al. (1995)	X-ray	Head	RR = 1.00 to 1.22	Yes, since the RR is above 1.0
Su et al. (2014)	CT scan	Head	Girls: LAR = 1.1 (95% CI=0.4 - 3.6) * Boys: LAR = 8.7 (95% CI=2.8 - 48.5) *	Yes, since the LAR is a positive value
Su et al. (2014)	CT scan	Sinus	Girls: LAR = 2.7 (95% CI=1.7 – 4.2) * Boys: LAR = 0.4 (95% CI=0.2 – 1.1) *	Yes, since the LAR is a positive value
Mathews et al. (2013)	CT scan	Spine	IRR = 1.78 (95% CI=1.24 – 2.58)	Yes, since the IRR is above 1.0
Inskip et al. (1995)	X-ray	Chest	RR = 0.99 to 1.11	Yes, since the RR is above 1.0. However, the risk may not be significantly high.
Mathews et al. (2013)	CT scan	Chest	IRR = 1.41 (95% CI=0.45 – 4.38)	Yes, since the IRR is above 1.0
Su et al. (2014)	CT scan	Chest	Girls: LAR = 14.1 (95% CI=7.0 - 65.4) * Boys: LAR = 2.1 (95% CI=1.0 – 8.5) *	Yes, since the LAR is a positive value
Inskip et al. (1995)	X-ray	Abdomen	RR = 0.75 to 1.10	Yes, since RR is above 1.0. However, the risk may not be significantly high.
Mathews et al. (2013)	CT scan	Abdomen	IRR = 1.47 (95% CI=0.83 – 2.59)	Yes, since the IRR is above 1.0
Mathews et al. (2013)	CT scan	Extremity	IRR = 1.19 (95% CI=0.73 – 1.94)	Yes, since the IRR is above 1.0. However, the risk may not be significantly high.

IRR=incidence rate ratio, OR = odds ratio, RR = relative risk, LAR= lifetime attributable risk, *per 100,000 persons, ** per 10,000 persons

Table 13. Leukemia and Lymphomas Associations

Study	Modality	Exposure	Leukemia and Lymphomas	Elevated Risk
Mathews et al. (2013)	CT scan	Head	IRR = 1.16 (95% CI=0.99 - 1.37)	Yes, since the IRR is above 1.0. However, the risk may not be significantly high.
Mathews et al. (2013)	CT scan	Spine	IRR = 1.31 (95% CI=0.85 - 2.04)	Yes, since the IRR is above 1.0
Miglioretti et al. (2013)	CT scan	Head	LAR = 1.9 **, ages <5 LAR = 0.9 **, ages 5-9 LAR = 0.45 **, ages 10-14	Yes, since the LAR is a positive value.
Miglioretti et al. (2013)	CT scan	Spine	LAR = 0.7 **, ages <5 LAR = 0.4 **, ages 5-9 LAR = 0.5 **, ages 10-14	Yes, since the LAR is positive value.
Mathews et al. (2013)	CT scan	Chest	IRR = 0.74 (95% CI=0.18 - 2.95)	No, since the IRR is below 1.0
Miglioretti et al. (2013)	CT scan	Chest	LAR = 0.6 **, ages <5 LAR = 0.5 **, ages 5-9 LAR = 0.4 **, ages 10-14	Yes, since the LAR is a positive value
Mathews et al. (2013)	CT scan	Abdomen	IRR = 3.24 (95% CI=2.17 – 4.84)	Yes, since the IRR is above 1.0
Miglioretti et al. (2013)	CT scan	Abdomen	LAR = 0.8 **, ages <5 LAR = 0.5 **, ages 5-9 LAR = 0.4 **, ages 10-14	Yes, since the LAR is a positive value
Mathews et al. (2013)	CT scan	Extremity	IRR = 1.42 (95% CI=0.93 - 2.16)	Yes, since the IRR is above 1.0
Hammer et al. (2009)	X-ray	All body	IRR = 1.00 (reference) – 0 cGy to IRR =1.05 (95% CI=0.73 – 1.52) with 1.95 cGy cumulative exposure	Yes, since the IRR is above 1.0. However, the risk may not be significantly high.
Hammer et al. (2011)	X-ray	All body	SIR = 1.04 (95% CI=0.51 – 2.12)	Yes, since the SIR is above 1.0. However, the risk may not be significantly high.
Pearce et al. (2012)	CT scan	All body	Male, ERR = 0.031 per mGy Female, ERR = 0.042 per mGy	Yes, since the ERR is a positive value

Study	Modality	Exposure	Leukemia and Lymphomas	Elevated Risk
Huang et al. (2014)	CT scan	All body	HR =1.90 (95% CI=0.82 - 4.40) *	Yes, since the HR is above 1.0
Krille et al. (2015)	CT scan	All body	Leukemia SIR = 1.72 (95% CI=0.89 – 3.01)	Yes, since SIR is above 1.0
Krille et al. (2015)	CT scan	All body	Lymphomas SIR = 3.26 (95% CI=1.63 – 5.83)	Yes, since SIR is above 1.0
Krille et al. (2015)	CT scan	All body	CNS tumours SIR = 1.35 (95% CI=0.54 – 2.78)	Yes, since SIR is above 1.0
Krille et al. (2015)	CT scan	All body	Solid cancers SIR = 1.68 (95% CI=0.77 – 3.19)	Yes, since SIR is above 1.0

IRR = incidence rate ratio, OR = odds ratio, RR = relative risk, LAR = lifetime attributable risk, SIR = Standardized Incidence Ratio, ERR = excess relative risk, HR = hazard ratio
*per 100,000 persons, ** per 10,000 persons

C. All Cancers

Benign and malignant tumours, solid cancer, and all cancers are considered as rare health diseases, especially in the children population. The studies showed that these risks may be closely associated with CT scans than with X-rays (see Table 14). For example, the data indicated that the excess relative risk was 0.016 per mGy for males and 0.028 per mGy for females (Mathews, 2013). The cancer latency studies (Matthew, 2013) indicated that the incidence rate ratios were 1.24 (95% CI=1.20-1.29, p<0.001)- 1-year lag period), 1.21 (95% CI=1.16-1.26, p<0.001) - 5-year lag period, and 1.18 (95% CI=1.11-1.24, p<0.001) - 10-year lag period. It has also been documented in BEIR and LSS studies that lag periods may extend to 15 years after the first exposure. The complexity of studying the linkages of irradiation medical

imaging and solid cancers may be contributed to many factors: 1) cancer is considered as a rare disease in children, 2) cancer may have long latency periods, possibly 15 years period, 3) cancer risks are dependent on the exposed organs and exposed doses; and of equal importance, 4) cancer may be based on the patients' genetically predisposed conditions, as well as medical conditions genetical, and/or lifestyles. One of the challenges is the long latency in cancer development, where the report of cancer incidents is not complete or accurate due to patients dropping out of the studies or lack to follow up. If the patients develop cancer beyond the studies, the outcomes may be unreported.

Table 14. Tumours, Solid Cancer, and All Cancers Associations

Study	Modality	Exposure	All Cancer Risk	Elevated Risk
Mathews et al. (2013)	CT scan	Head	IRR = 1.23 (95% CI=1.18 – 1.29)	Yes, since the IRR is above 1.0
Miglioretti et al. (2013)	CT scan	Head	Girls LAR = 17.5 **, ages <5 LAR = 1.6 **, ages 5-9 LAR = 1.1 **, ages 10-14 Boys LAR = 7.4 **, ages <5 LAR = 2.4 **, ages 5-9 LAR = 2.1 **, ages 10-14	Yes, since the LAR is a positive value
Mathews et al. (2013)	CT scan	Chest	IRR = 1.62 (95% CI=1.22 – 2.14)	Yes, since the IRR is above 1.0
Miglioretti et al. (2013)	CT scan	Chest	Girls LAR = 28.4 **, ages <5 LAR = 30.5 **, ages 5-9 LAR = 20.9 **, ages 10-14 Boys LAR = 8.4 **, ages <5 LAR = 9.2 **, ages 5-9 LAR = 6.1 **, ages 10-14	Yes, since the LAR is positive value
Niemann et al. (2015)	CT scan	Chest	LAR of Cancer Incidence * Exposed age 0, males Stomach (2.73), Colon (2.56), Liver (2.42), Lung (14.36), and Bladder (0.23) Exposed age 0, females Stomach (3.04), Colon (1.34), Liver (0.93), Lung (28.72), Breast (47.58) and Bladder (0.19) LAR of Cancer Incidence * Exposed age 5, males Stomach (1.41), Colon (0.51), Liver (1.30), Lung (9.73), and Bladder (0.04) Exposed age 5, females	Yes, since the LAR is a positive value

Study	Modality	Exposure	All Cancer Risk	Elevated Risk
			Stomach (1.74), Colon (0.34), Liver (0.56), Lung (19.19), Breast (31.24) and Bladder (0.05) LAR of Cancer Incidence * Exposed age 15, males Stomach (.38), Colon (0.04), Liver (0.41), Lung (4.53), and Bladder (0.00) Exposed age 15, females Stomach (0.61), Colon (0.04), Liver (0.20), Lung (9.23), Breast (12.73) and Bladder (0.01)	
Mathews et al. (2013)	CT scan	Abdomen	IRR = 1.45 (95% CI=1.10 – 1.92)	Yes, since the IRR is above 1.0
Mathews et al. (2013)	CT scan	Abdomen	IRR = 1.61 (95% CI=1.38 – 1.88)	Yes, since the IRR is above 1.0
Miglioretti et al. (2013)	CT scan	Abdomen	Girls LAR = 33.9 **, ages <5 LAR = 25.8 **, ages 5-9 LAR = 27.2 **, ages 10-14 Boys LAR = 14.8 **, ages <5 LAR = 13.7 **, ages 5-9 LAR = 13.1 **, ages 10-14	Yes, since the LAR is positive value
Mathews et al. (2013)	CT scan	Extremity	IRR = 1.36 (95% CI=1.11 – 1.67)	Yes, since the IRR is above 1.0
Mathews et al. (2013)	CT scan	Extremity	IRR = 1.33 (95% CI=1.18 – 1.50)	Yes, since the IRR is above 1.0
Hammer et al. (2009)	X-ray	All body	IRR = 1.00 (reference) – 0 cGy to IRR =1.05 (95% CI=0.73 - 1.52) with 1.95 cGy cumulative exposure	Yes, since the IRR is above 1.0. However, the risk may not be significantly high.
Hammer et al. (2011)	X-ray	All body	SIR = 1.01 (95% CI=0.60 – 1.71) – all cancer SIR = 0.98 (95% CI=0.46 – 2.12) – solid tumors	Yes, if the SIR is above 1.0. However, the risk may not be

Study	Modality	Exposure	All Cancer Risk	Elevated Risk
				significantly high.
Pearce et al. (2012)	CT scan	All body	Male, ERR = 0.016 per mGy Female, ERR = 0.028 per mGy	Yes, since the ERR is a positive value
Huang et al. (2014)	CT scan	All body	HR =2.56 * (95% CI=1.44 – 4.54)	Yes, since the HR is a positive value
Huang et al. (2014)	CT scan	All body	HR =0.65 * (95% CI=0.35 - 1.19)	Yes, since the HR is a positive value
Huang et al. (2014)	CT scan	All body	HR =1.29 * (95% CI=0.90 – 1.85)	Yes, since the HR is a positive value
Krille et al. (2015)	CT scan	All body	SIR = 1.87 (95% CI=1.33 – 2.55)	Yes, since the HR is a positive value

IRR = incidence rate ratio, OR = odds ratio, RR = relative risk, LAR = lifetime attributable risk, SIR = Standardized Incidence Ratio, ERR = excess relative risk, HR = hazard ratio
*per 100,000 persons, ** per 10,000 persons

D. Cancer Mortality

Chodick and colleagues studied the cancer excess lifetime death (ELD). This study suggested that the overall patient lifetime excess death was 0.29% and that children aged less than three years have the highest mortality rate (0.52%). The ELD showed a trend of decline as the patients' age increased. Males' excessive cancer death from head CT scans appear to be higher than females at 55% and 38%, respectively. The study also noted that most medical examinations were due to forehead trauma, particularly in boys. It is possible that due to the patients' medical conditions and circumstances, there was an elevated need for frequent CT

scans. It is possible that head trauma may be a confounding factor in the excess cancer death rate in boys. More studies are needed on this specific subject.

Niemann also indicated that a chest CT scan may result in LAR of cancer incidence, mortality per 100,000 persons, of thyroid (1.8), stomach (0.45), lung (0.45), and breast (0.39). Furthermore, females have a mortal risk of 0.31, compared to males of 0.16 per 100, 000 persons. However, the risks appear to decrease as the children's ages increase.

A few findings in this study seem to align with BEIR reports: 1) In a few studies, they showed girls are more radiosensitive than boys (see Appendix B, Table 19); however, the trends may be reversed in adulthood. The reasons for such changes may be due to environmental factors, occupational hazards, and/or differences in lifestyle (Dorak, 2102), 2) exposure to irradiation at early ages seemed to increase the lifetime cancer risks for both genders (Chodick, 2012, Miglioretti, 2013, Su, 2002, and Huang, 2014), 3) the frequent exposures tended to increase the lifetime cancer risks (Memon, 2010; Pearce, 2012; and Huang 2014), and 4) higher administered radiation doses seemed to increase the likelihood of cancer risks (Chodick, 2012). This study also suggested that radiation exposure to the thyroid gland, lungs, and bone marrow are most likely to increase the cancer risk, possibly due to higher radiosensitivity in organs. However, this study reported that X-rays procedures to all body parts and repetitive exposures, up to ten occurrences, have not shown evaluated cancer risks. Due to limited studies available today on X-rays, this subject requires further investigation. Last, although only one study is available today and the studied population comprised of a very small sample size, Memon suggested that dental X-rays are highly correlated with thyroid cancer.

Appendix B provides a series of tables which map the exposures, outcomes, and risk levels. These tables show that dental X-rays are highly associated with thyroid cancer, whereas general X-rays are less associated with thyroid, leukemia, or solid cancer. CT scans, however, are prone to cancer and cancer mortality risks.

CHAPTER 6: DISCUSSION

Prior radiation exposure intelligence

Much of radiation carcinogenesis intelligence had been gathered from BEIR III (1980), V (1990), and VII (Phase 1 - 1998 and Phase 2 - 2006) reports. BEIR VII suggested that "one individual in 100 persons would be expected to develop cancer (solid cancer or leukemia) from a dose of 100 mSv". The research further indicated that the excess cases from 100 mSv exposures yielded 800 male and 1300 female cases of all solid cancer per 100,000 persons. Likewise, for 100 mSv irradiation exposure, it resulted in 100 male and 70 female cases of leukemia per 100,000 persons. From the patient demographic perspective, the studies suggested that children (of all genders) were more radiosensitive than adults and that females were more radiosensitive than males. As for exposures, for every additional radiation exposure, the lifetime cancer risk would also elevate. Furthermore, the earlier the ages of exposure, independent of gender, the lifetime cancer risk would also be elevated. With the increase in exposed irradiation dosages (i.e., absorbed, equivalent, effective, or cumulative dosages), the lifetime cancer risk would also increase. In most cases, the lifetime cancer risks exhibit a linear no-threshold risk pattern; however, there were possible cases of hormesis. Furthermore, in some cases, cancer development may have a long latency period, possibly be extended to five, ten, or fifteen years. It appears that lymphoid, bone marrow, blood, lung, thyroid, breast, skin, and eyes are considered relatively higher radiosensitive organs (Rubin and Casarett, 1968), the reasons for this radiosensitivity remained unclear at this point. It is important to note that the datasets for these studies were based primarily on the atomic bomb, radon, and nuclear accident cohorts, and not from irradiation medical imaging. The question is, then, how do the data from the BEIR reports corollate with this research?

Research Gaps

The scoping review showed that there are limited studies on patient-level health for modalities such as dental x-rays, x-rays, and CT scans. The results indicated that there are elevated cancer risks associated with CT scans for thyroid and leukemia cancers, and high risk associated with dental X-rays and thyroid cancer. Due to the limited data available, the review's results cannot be simply declared as conclusive at this time. As mentioned earlier, there are several factors contributing to the elevated risks. The scoping review unveiled several literature gaps. As illustrated in Appendix B, Table 17, the data points from the studies are quite diverse and are measured in different risk measurement units. In addition, there is only one study on dental X-rays, three studies on X-rays, and eight studies on CT scans. Furthermore, although there are eight studies on CT scans, the studied topics and objectives are quite different from each other. It would not be feasible to perform quantitative or meta-analysis at this time. It should be noted that there are no patient studies on fluoroscopy or angiography imaging in children. However, there is a mathematical study on angiography based on a 5-year-old patient phantom analysis (Huang, 2008). Huang indicated that with an effective dose of ranging from 11.81 mSv to 16.46 mSv, the mathematical model shows a LAR of 0.14% to 0.20% (boys) and 0.43% to 0.60% (girls) in the United States and 0.22% to 0.33% (boys) and 0.61% to 0.85% (girls) in Hong Kong. Fluoroscopy and angiography modalities typically emit greater radiation doses than those of x-rays (e.g., 0.025 mSv per procedure). Due to higher exposed doses, this indeed highlights the urgent need for research on patient health studies. Secondly, the scoping review did not find studies that address the cancer risks on cumulative dose exposures. The cancer risk on cumulative exposure may be different depending on the length of time between the exposures (i.e., 3 exposures within a year or 1

exposure per year for 3 years). Based on the stochastic principle, some cancers may not be truly identifiable until the child patients become adults. Su, Pearce, and Huang suggested that early ages of exposures lead to higher lifetime cancer risk based on the LSS risk models. On the contrary, Mathews' study indicated that ERR and IRR for all cancers and tumours will decline as the latency period increase since 1, 5, and 10 years after the first exposure. Based on the literature gathered, there are no longitudinal studies on radiation exposure and cancer. Although the research offered good insight into radiation medical imaging and cancer risk in children, much research is required.

Patient-Level Risks

On patient cancer risks, Huang (2014) highlighted that a young child of ages 0 to 6 scored the highest cancer hazard risk (HR=1.96 per 100, 000 persons); however, the hazard risks seemed to gradually decrease as the ages of exposure increase (HR=0.93 per 100, 000 persons at ages 7 to 13). This finding has been confirmed by other studies (Su, 2002; Chodick, 2012; Pearce, 2012; Niemann, 2015; and Miglioretti, 2013) that the lifetime risks, incidence rates, and risks ratio were reduced as the ages increase; the lowest risks of exposure were the adolescent ages (see Appendix B, Table 17). Due to rapid growth in younger children, the possibility of illegitimately rejoining of the chromosomes may cause DNA mutations; hence, may elevate the risk of cancer. As indicated in Matthews, the latency period may extend to 15-years and beyond. For this reason, the recommendations are to limit the amount of radiation medical imaging procedures in younger children; and if these procedures are necessary, the exposed doses should be as low as possible.

On gender differences and cancer risks, are females more radiosensitive than males? The results from most studies offered different results between genders (see Appendix B, Table 19). Huang (2014) indicated that males (HR=1.29 per 100,000 persons) may be at a slightly higher risk than females (HR=1.28 per 100,000 persons). Although the delta seems to be marginal which suggested the possibility of no gender differences. In other studies, Su, Chodick, and Niemann showed that the ERRs and LARs of CT Scans between genders were drastically different. For example, the ERR per mGy for females of 0.042 versus males of 0.031 and LARs of 2.7 (females) and 0.4 (males) per 100,000 persons. Based on these comparisons, the results showed that there is a gender cancer susceptibility difference. As mentioned in the earlier chapter, Dorak and Karpuzoglu studied the physiological variations and cancer susceptibilities in the gender. This study suggested that the susceptibilities may change as the children became adults. However, there are no studies that have been conducted on gender differences and cancer susceptibility for children and following into adulthood. This could be a valuable topic for future studies.

Overall, the findings on patient-level risk seem to match the BEIR report on age and cancer risk. Children, at early ages of exposure, exhibit a higher lifetime cancer risk independent of gender. Due to the children's ongoing cell development, the risks of DNA mutations from radiation are greater in younger children. As for gender differences, the results showed that females were more vulnerable in CT Scans. However, there are no gender-specific studies on this subject.

Contributing Risk Factors

The research showed that elevated cancer risk may be attributed to the following factors: age at exposure, the frequency of exposures, and the latency period of cancer development. The research found that the age of exposure as one of the key factors for elevated cancer risk. The studies suggested that children at ages less than 1-year-old is grouped with the highest LAR (Miglioretti, 2013). Furthermore, the LAR seems to decline as the ages of exposure increased. Younger children are anticipated to have a longer number of years to live; therefore, they have been predicted to have more chance of developing cancer. This risk model has been based on the LSS; based on the literature gathered, there are not radiation medical imaging longitudinal studies that have been conducted. Further studies are required to confirm such results.

On the frequency of exposures, Pearce showed the ERR per mGy of developing leukemia on 1 CT scan is 0.013, 2 to 4 CT scans is 0.028, and 5 or more CT scan is 0.035. Likewise, Huang (2014) showed an overall cancer Hazard Risk of 1.21 per 100, 000 persons for one CT procedure, 1.68 for two CT procedures, and 5.04 for three or more CT procedures. Memon also showed that for one to four dental X-ray exposures, he reported one to four exposures had an OR=2.2, five to nine exposures had an OR=4.6, and ten or more exposures had an OR=5.4. For X-rays, the SIR of one exposure was 0.97, SIR of two exposures was 0.91, and SIR of three or more exposures was 1.10 in Hammer. Currently, there are no longitudinal studies that follow the pediatric patients into adulthood. With the increase in the number of medical imaging procedures, it is anticipated that the cumulative exposure dose would also be increased.

Although the cancer risk for X-rays is low, the SIRs also increase as the number of exposures increase. Hammer (2009) was the only study that captured the cumulative exposed doses and the relative risk of developing cancer. It showed that a cumulative dose of 0 µSv to 9.9 µSv has a relative risk (RR) of 1.00, 10 µSv to 49.9 µSv has an RR of 1.02, and 50+ µSv has an RR of 1.01. According to the data, additional exposures, although the changes are quite small, they do suggest an elevated risk.

On latency effect, Matthews and Huang indicated that in some cancers, the cancer development may have long latency periods, extending to five years (IRR=1.21), ten years (IRR=1.18), and possibly beyond. Notably, some cancers (e.g., Brain) seems to be elevated in the fourth and fifth years and then decline thereafter (Huang, 2014). Contrary to the theory of LAR, cancer risks may possibly decline as the years since first exposure increase. Therefore, the development of cancers may be elevated due to other factors and not solely on radiation medical imaging (Dorak, 2012). Again, there are no radiation medical imaging longitudinal studies that have been performed on this subject; the risks were based on LSS studies. The risk factors found in this research seem to be consistent with the BEIR VII report.

Modalities and Cancers Association

Memon, Su and Matthews suggested that dental x-ray (OR=2.10) and CT scans (LAR = 2.1 and IRR=1.78) may induce thyroid cancer. Due to the proximity of the thyroid gland and the examined region, this may result in thyroid cancer risks. Another possible theory is that the thyroid gland is more radiosensitive in children than anticipated. At this point, there is insufficient data to draw a conclusion.

American Childhood Cancer Organization, published on their website, suggested that acute lymphoblast leukemia ranked first in childhood cancer (26% percent rate). Pearce, Matthews, and Miglioretti found that CT scans may induce leukemia (as demonstrated by ERR= 0.031 per mGy, IRR=3.24, and LAR= 0.7 per 100,000 persons). As Rubin and Casarett indicated, bone marrow is found to be one of the most radiosensitive organs. Due to the highly radiosensitive nature, leukemia can be fully developed within the first five years of exposure. Therefore, leukemia is highly associated with CT Scan in children.

Huang showed that angiography (mathematical study) may impose cancer risk in children. The research has indicated that there could be significant risks with this modality. This modality typically emits higher radiation doses than those of X-ray procedures as indicated in Huang (16.45, 12.17, 11.97, and 11.81 mSv). At this point, there are no patient-level studies that have been performed. Further studies on patient-level may offer better insight of the cancer risks.

Inskip and Hammer suggested that at minimal X-ray exposures, they do not seem to impose cancer risks (RR<1.0). However, increase exposures up to ten occurrences seem to elevate the cancer risks. It is unclear as to which types of cancer may be developed. Based on the three studies, the cancer risks appeared to be marginal. It is possible that the exposure doses and exposure organs were considered as low radiosensitivity. Due to the limited research at this point, it would be challenging to conclude the cancer risks. More studies are required to better understand the true health impact of X-rays. Prospective longitudinal studies will provide insight into the stochastic effect of this modality.

CHAPTER 7: STRENGTHS AND LIMITATIONS

The strengths of this research included repeatable methodology, data collection strategy, and peer reviews. This research utilized a standard scoping review methodology and the results were carefully screened for eligibility. The data were then categorized, summarized, and compared with similar studies. The study utilized the knowledge and results of radiation health studies in the last decade (BEIR and LSS). Last, the search strategy and results have been peer-reviewed by associate graduate students and library specialists. The limitations of this research included search strategy limitations, screening and evaluation errors, publication bias, exclusion of non-English studies, and limited study sample size.

CHAPTER 8: CONCLUSION

The results from this scoping review indicate that there is possible cancer association with radiation medical imaging in children. This study suggested that there is a possible strong association between dental X-rays and thyroid cancers. The study also suggested a possible link between leukemia and CT scans. The study found that X-rays were considered low-risk when prescribed under normal conditions. Although the results suggested possible risks, however, due to the small sample data, it is not possible to reach more conclusive statements at this time. Furthermore, the scoping review found several research gaps: 1) the review did not find patient-level studies on fluoroscopy or angiography, 2) dental X-ray is linked to evaluated thyroid cancer; however, the studied children population was relatively small, 3) due to stochastic cancer risk of low dose exposures, based on the literature gathered, there are no studies that follow-up the child patients into adulthood, and 4) there are no studies that address the cancer risks on cumulative dose exposures.

Today, medical diagnostic imaging health professional and patients are more aware and better educated on the risks and benefits of radiation diagnostic procedures. However, there are gaps in understanding the differences in gender, organs radiosensitivity, and long-term cancer effects. As precautions, many dental x-rays required patients to wear chest and neck lead vest. In addition, many organizations such as the World Health Organization and Canada Safe Imaging have established to provide guidelines, tools, and education on patient radiation safety. As a general recommendation on patient radiation safety, many practitioners follow the radiation practice principle known as ‘‘As-Low-As-Reasonably-Achievable (ALARA)’’ while balancing the risk of misdiagnosis. Due to the limited radiation medical imaging studies in children that are available today, more studies are much needed. As for suggestions for

future research, more investigation is needed on cancer risks associated with dental x-rays and angiography as insufficient evidence are shown in the current studies. In addition, the current lifetime attributable risk is based on Life-Span Study (LSS), and retrospective longitudinal studies may help to validate the lifetime cancer risk in children. The LSS, BEIR and this research found that exposure to radiation elevates the lifetime risk. Therefore, it is important that patient safety, particularly in younger children, must always be a priority.

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APPENDICIES

APPENDIX A – SEARCH CONCEPTS/TERMS & RESULTS

Table 15. Appendix A - Literature Search Terms & Results

Concepts / Mesh Terms	
1	Population: (paediatric* OR pediatric* OR children OR child* OR childhood OR young-age OR juvenile OR youth* OR adolescent* OR toddler* OR post-natal)
2	Exposure: ("low-dose ionising radiation" OR low-dose OR radiation-induced OR Low-LET OR low-level OR "radiation effect")
3	Modality: ("diagnostic imaging" OR X-ray* OR "dental X-ray" OR "CT Scan" OR "computed tomography" OR fluoroscopy OR radiography)
4	Cancer risk: (cancer* OR neoplasm* OR "solid cancer" OR "all cancers" OR leukemia OR leukaemia OR "thyroid cancer" OR tumor* OR lesion* OR benign* OR malignant* OR "cancer mortality")

Search results	User Query	Count
PubMed	Best matches for (("paediatric"[All Fields] OR "pediatric"[All Fields] OR "children"[All Fields] OR "child"[All Fields] OR "childhood"[All Fields] OR "young-age"[All Fields] OR "juvenile"[All Fields] OR "youth"[All Fields] OR "adolescent"[All Fields] OR "toddler"[All Fields] OR "post-natal"[All Fields]) AND ("low-dose ionising radiation"[All Fields] OR "low-dose"[All Fields] OR "radiation-induced"[All Fields] OR "Low-LET"[All Fields] OR "low-level"[All Fields] OR "radiation effect"[All Fields]) AND ("diagnostic imaging"[All Fields] OR "X-ray"[All Fields] OR "dental X-ray"[All Fields] OR "CT Scan"[All Fields] OR "computed tomography"[All Fields] OR "fluoroscopy"[All Fields] OR "angiography"[All Fields] OR "radiography"[All Fields]) AND ("cancer"[All Fields] OR "neoplasm"[All Fields] OR "solid cancer"[All Fields] OR "all cancers"[All Fields] OR "leukemia"[All Fields] OR "leukaemia"[All Fields] OR "thyroid"[All	**1,211**

Search results	User Query	Count
	Fields] OR "tumors"[All Fields] OR "lesions"[All Fields] OR "benign"[All Fields] OR "malignant" OR "cancer mortality"[All Fields])) Search performed on May 28, 2018	
Scopus	(TITLE-ABS-KEY ((paediatric* OR pediatric* OR children OR child* OR childhood OR young-age OR juvenile OR youth* OR adolescent* OR toddler* OR post-natal)) AND TITLE-ABS-KEY (("low-dose ionising radiation" OR low-dose OR radiation-induced OR low-let OR low-level OR "radiation effect")) AND TITLE-ABS-KEY (("diagnostic imaging" OR X-ray* OR "dental X-ray" OR "CT Scan*" OR "computed tomography" OR fluoroscopy OR radiography)) AND TITLE-ABS-KEY ((cancer* OR neoplasm* OR "solid cancer" OR "all cancers" OR leukemia OR leukaemia OR "thyroid cancer" OR tumor* OR lesion* OR benign* OR malignant* OR "cancer mortality"))) Search performed on Aug 14, 2018	**1,980**
	Total	**3,191**

Table 16. Appendix A - Studies Selection

Title, Author, and Year	Study Design & Period	Population	Age at Examination	Body Part Exposed	Cancer Association	Risk Type
1. Dental X-rays Dental X-rays and the risk of thyroid cancer: a case control study Anjum Memon et al., 2010, Kuwait	Case Control 1998 to 2002	N=313	ages 5 to 70	Head	Thyroid cancer	Odds Ratio

Title, Author, and Year	Study Design & Period	Population	Age at Examination	Body Part Exposed	Cancer Association	Risk Type
2. X-ray Medical Diagnostic X rays and Thyroid Cancer Peter Inskip et al, 1995, Sweden	Case Control Jan 1, 1980 to Dec 31, 1992	N=484	<20, 20-39, 40-59, >=60	Lungs, chest, ribs, head, all types	Thyroid cancer	Relative Risk
3. X-ray A cohort study of childhood cancer incidence after postnatal diagnostic X-ray exposure Gael Hammer et al., 2009, Germany	Retrospective 1976-2003	N=92,957	from 6 months old to less than 14.5 years old	Unknown	All cancer, leukemia, solid cancer	Standard Incidence Ratio
4. X-ray Childhood Cancer Risk from Conventional Radiographic Examinations for Selected Referral Criteria: Results from a Large Cohort Study Gael Hammer et al., 2011, Germany	Retrospective, 1976-2003	N=78,527	from 6 months old to less than 14.5 years old	Unknown	All cancer, leukemia, lymphoma, solid tumors	Standard Incidence Ratio
5. CT Scan Excess lifetime cancer mortality risk attributable to radiation exposure from computed tomography examinations in children Gabriel Chodick et al., 2012, Israel	Retrospective 1999-2003	N=17,686	<=3 to 18 years of age	Head, rest of body, abdominal	Lifetime cancer death	Excess Relative Risk
6. CT Scan Radiation exposure from CT Scans in childhood and subsequent risk of leukemia and brain tumors: a retrospective cohort study Mark Pearce et al., 2012, United Kingdom	Retrospective, Jan 1, 1985 - Dec 31, 2008	N= 178, 604 (leukemia); N=176, 587 (brain tumor)	younger than 22 years of age	Head, chest, abdominal, extremity	Leukemia, brain tumors	Excess Relative Risk

Title, Author, and Year	Study Design & Period	Population	Age at Examination	Body Part Exposed	Cancer Association	Risk Type
7. CT Scan Cancer risk in 680,000 people exposed to CT Scan in childhood or adolescence: data linkage study of 11 million Australians John Mathews et al., 2013, Australia	Case control Jan 1, 1985 - Dec 31, 2005	N= 680,211	from 0 - 19 years old	Brain, chest, facial bones, extremities, abdomen, spine, neck	All cancers	Incidence Rate Ratio
8. CT Scan The use of Computed Tomography in Pediatrics and the associated radiation exposure and estimated cancer risk Diana Miglioretti et al., 2013, United States	Retrospective 1996 to 2010	N=744	children younger than 15 years of age	Head, abdomen/pelvis, chest, spine, or other/unknown	Solid cancer, leukemia	Lifetime Attributable Risk
9. CT Scan Radiation Dose in the Thyroid and the Thyroid Cancer Risk Attributable to CT Scans for Pediatric Patients in One General Hospital of China Yin-Ping Su et al, 2014, China	Retrospective, Jan 1, 2012 to Dec 31, 2012	N=926	age groups 1-5, 5-10, 10-15 for sinus, head, and chest CT Scans	Thyroid	Thyroid cancer	Lifetime Attributable Risk
10. CT Scan Paediatric head CT Scan and subsequent risk of malignancy and benign brain tumor: a nation-wide population-based cohort study W-Y Huang et al., 2014, Taiwan	Case Control Jan 1996 – Dec 2008	N=24,418	under 18 years of age, (0-6 YO, 40%), (7-12 YO, 21.2%), (13-18 YO, 38.8%)	Head CT Scan	Malignancy and benign brain tumor	Hazard Ratio
11. CT Scan Estimated risk of radiation-induced cancer from paediatric chest CT: two-year cohort study Tilo Niemann et al., 2015, United States	Retrospective Sept 2009 - Sept 2011	N=522	under 18 years of age	Helical chest CT	All Cancers	Lifetime Attributable Risk

Title, Author, and Year	Study Design & Period	Population	Age at Examination	Body Part Exposed	Cancer Association	Risk Type
12. CT Scan Risk of cancer incidence before the age of 15 years after exposure to ionizing radiation from CT: results from a German cohort study Lucian Krille et al., 2015, Germany	Case control Jan 1, 1980 - Dec 31, 2010	N=44,584	under 15 years	head, neck, chest, abdomen, pelvis, extremities, multiple regions	All cancers	Standard Incidence Ratio

APPENDIX B – STUDIED DATA

Table 17. Appendix B - Exposures and Outcomes

No.	Author	Dosages	Head/ Brain/ Neck	Chest	Abdomen/ Pelvis	Rest of body	All Cancer	Solid Cancer	Leukemia	Thyroid	Mortality
1	Memon et al.	No data	Dental	N/A	N/A	N/A	N/A	N/A	N/A	OR = 2.1 95% CI: 1.4, 3.1 (p=0.001); statistically highly significant	N/A
2	Inskip et al.	Cumulative doses: Cat 1 (0.00 mGy) Cat 2 (0.08 mGy) Cat 3 (0.32 mGy) Gat 4 (1.95 mGy)	110	320	20	859	N/A	N/A	N/A	Head/neck/ upper spine X-rays (highest risk), RR = 1.0 to 1.22 Chest, shoulder, upper gastro tract X-rays (medium risk), RR = 0.99 to 1.11 Abdomen, pelvis, arms, legs X-rays (lowest risk), RR = 0.75 to 1.10	N/A

No.	Author	Dosages	Head/ Brain/ Neck	Chest	Abdomen/ Pelvis	Rest of body	All Cancer	Solid Cancer	Leukemia	Thyroid	Mortality
3	Hammer et al.	Cumulative dose = 134.7 µSv (0.1347 mSv)	No data	No data	No data	No data	IRR = 1.00 to 1.01	IRR = 0.98 to 1.05	IRR = 1.00 to 1.04	N/A	N/A
4	Hammer et al.	Cumulative effective dose = 5 µSv (0.0005 mSv)	No data	No data	No data	No data	SIR = 0.97	SIR = 0.88	SIR = 1.05	N/A	N/A
5	Chodick et al.	Absorbed doses: Head = 30-130 mGy Abdominal = 24-51 mGy	12,333	N/A	N/A	5,353	N/A	N/A	N/A	N/A	Excess lifetime deaths: Ages <3: 0.52%, Ages 4-6: 0.48% Ages 7-9: 0.31% Ages 10-12: 0.26%, Ages 13-15: 0.23% Ages 16-18: 0.21% Head, no. of excess lifetime death = 1.81 to 2.61 Rest of body, no. of excess

No.	Author	Dosages	Head/ Brain/ Neck	Chest	Abdomen/ Pelvis	Rest of body	All Cancer	Solid Cancer	Leukemia	Thyroid	Mortality
											lifetime death = 2.18 to 2.90
6	Pearce et al.	Absorbed doses: Brain = 28 to 44 mGy Chest = 2 to 4 mGy Abdomen = 1 to 2 mGy Extremity = 0 mGy	No data	No data	No data	No data	N/A	Brain tumors: Male ERR per mGy = 0.016 Female ERR per mGy = 0.028	Male ERR per mGy = 0.031 Female ERR per mGy = 0.042	N/A	N/A
7	Mathews et al.	Absorbed doses: Brain cancer: 1-year lag (40 mGy), 10 years lag (40 mGy), 15 years lag (40 mGy); Leukaemia: 1-year lag (4.6 mGy), 10 years lag (4.7 mGy), 15 years lag (4.2 mGy)	493,238	11,381	33,970	141,722	EIR = 9.38 per 100,000	EIR = 7.76 per 100,000	EIR = 0.53 per 100,000	EIR = 1.1 per 100,000	N/A
8	Miglioretti et al.	Effective doses:	279	147	276	42	N/A	Head scan: LAR age<5= 17.5/7.4;	Head scan: LAR Age<5= 1.9;	N/A	N/A

No.	Author	Dosages	Head/ Brain/ Neck	Chest	Abdomen/ Pelvis	Rest of body	All Cancer	Solid Cancer	Leukemia	Thyroid	Mortality
		Ages (<5) mean dose = 10.6 mSv Ages (>=5) mean dose = 14.8 mSv						Age 5-9=1.6/2.4; Age 10-14=1.1/2.1 Chest scan: LAR age<5= 28.4/8.4; Age 5-9=30.5/9.2; Age10-14=20.9/6.1 Pelvis scan: LAR Age<5= 33.9/14.8; Age 5-9=25.8/13.7; Age10-14=27.2/13.1	Age5-9=0.9; Age10-14=0.5 Chest scan: LAR Age<5= 0.6; Age 5-9=0.5; Age10-14=0.4 Pelvis scan: LAR Age <5= 0.8; Age5-9=0.7; Age10-14=1.0		
10	Su et al.	Absorbed doses: Head = 1.10 - 2.45 mGy; Chest = 2.62 - 5.76 mGy; Other = 0.61 - 0.92 mGy	696	139	242	230	N/A	N/A	N/A	LAR of incidence: Sinus CT LAR = 1.4 per 100,000 boys; 2.7 per 100,000 girls	N/A

No.	Author	Dosages	Head/ Brain/ Neck	Chest	Abdo men/ Pelvis	Rest of body	All Cancer	Solid Cancer	Leukemia	Thyroid	Mortality
										Head CT LAR = 1.1 per 100,000 boys; 8.7 per 100,000 girls Chest CT LAR = 2.1 per 100,000 boys; 14.1 per 100,000 girls Birth to age: LAR = 100 per 100,000 5 Years: LAR = 31 per 100,000 10 Years: LAR = 20 per 100,000	
11	Huang et al.	N/A	N/A	N/A	N/A	N/A	HR = 1.29 per 100,000	HR = 1.84 to 2.97 per 100,000	HR = 1.90 per 100,000	N/A	N/A

No.	Author	Dosages	Head/ Brain/ Neck	Chest	Abdomen/ Pelvis	Rest of body	All Cancer	Solid Cancer	Leukemia	Thyroid	Mortality
12	Nieman n et al.	Effective doses: Newborns = 1.93 mSv, 5 years = 1.4 mSv, 10 years = 1.3 mSv, 15 years = 0.85 mSv	No data	N/A	N/A	N/A	No data	No data - Breasts and lungs	No data	No data - Thyroid	LAR Stomach:0.28 to 2.05; Colon:0.01 to 0.78, Liver:0.16 to 0.95; Lungs:4.58 to 14.54; Breasts:5.35 to 11.13; Uterus:0.0 to 0.02; Ovaries:0.01 to 0.10; Bladders:0.0 to 0.05; Leukemia:0.31 to 0.92
12	Krille et al.	No data	29,281	4,110	1,956	10,000	SIR = 1.71	SIR = 1.54	SIR = 1.18	N/A	N/A

Table 18. Appendix B - Studied Results Summary

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
1	Dental X-rays	Memon et al. (2010)	Dental	Thyroid	OR = 2.10, 95% CI: 1.4-3.1	Yes
2	X-rays	Inskip et al. (1995)	Head	Thyroid	RR = 1.00 (reference) – no exposure to 1.22, 95% CI: 0.46-3.34 – 6 exposures	No
3	X-rays	Inskip et al. (1995)	Chest	Thyroid	RR = 1.00 (reference) – no exposure to 0.99, 95% CI: 0.47- 2.08 - 6 exposures	No
4	X-rays	Inskip et al. (1995)	Abdomen	Thyroid	RR = 1.00 (reference) – no exposure to 0.75, 95% CI: 0.42- 1.35 - 6 exposures	No
5	X-rays	Hammer et al. (2009)	All body	All Cancer	IRR = 1.00 (reference) to 1.01, 95% CI: 0.60-1.71	No
6	X-rays	Hammer et al. (2009)	All body	Leukemia and lymphoma	IRR = 1.00 (reference) to 1.04, 95% CI: 0.51-2.12	No
7	X-rays	Hammer et al. (2009)	All body	Solid tumors	IRR = 1.00 reference to 0.98, 95% CI: 0.46-2.12	No
8	X-rays	Hammer et al. (2011)	All body	All Cancer	SIR = 0.97, 95% CI: 0.75-1.23	No
9	X-rays	Hammer et al. (2011)	All body	Leukemia and lymphoma	SIR = 1.05, 95% CI: 0.74-1.45	No

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
10	X-rays	Hammer et al. (2011)	All body	Solid tumors	SIR = 0.88, 95% CI: 0.60-1.25	No
11	CT Scan	Chodick et al. (2007)	Head	Mortality	ELD (boys) = 0.78 to 2.61; ELD (girls) = 0.48 to 1.81	Yes
12	CT Scan	Chodick et al. (2007)	Rest of body	Mortality	ELD (boys) = 0.13 to 2.18; ELD (girls) = 0.33 to 2.90	Yes
13	CT Scan	Pearce et al. (2012)	Brain, Chest, Abdomen, and Extremity	Leukemia	ERR = 0.031 (male) per mGy and 0.042 (female) per mGy	Yes
14	CT Scan	Pearce et al. (2012)	Brain, Chest, Abdomen, and Extremity	Brain tumors	ERR = 0.016 (male) per mGy and 0.028 (female) per mGy	Yes
15	CT Scan	Mathews et al. (2013)	Brain	Thyroid	IRR = 1.33, 95% CI: 1.13-1.57	Yes
16	CT Scan	Mathews et al. (2013)	Brain	Leukemia	IRR = 1.16, 95% CI: 0.99-1.37	Yes
17	CT Scan	Mathews et al. (2013)	Brain	Solid cancer	IRR = 1.13, 95% CI: 1.05-1.23	Yes
18	CT Scan	Mathews et al. (2013)	Brain	All Cancer	IRR = 1.23, 95% CI: 1.18-1.29	Yes
19	CT Scan	Mathews et al. (2013)	Chest	Thyroid	IRR = 1.41, 95% CI: 0.45-4.38	Yes

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
20	CT Scan	Mathews et al. (2013)	Chest	Leukemia	IRR = 0.74, 95% CI: 0.18-2.95	Yes
21	CT Scan	Mathews et al. (2013)	Chest	Solid cancer	IRR = 1.96, 95% CI: 1.26-3.04	Yes
22	CT Scan	Mathews et al. (2013)	Chest	All Cancer	IRR = 1.62, 95% CI: 1.22-2.14	Yes
23	CT Scan	Mathews et al. (2013)	Extremity	Thyroid	IRR = 1.19, 95% CI: 0.73-1.94	Yes
24	CT Scan	Mathews et al. (2013)	Extremity	Leukemia	IRR = 1.42, 95% CI: 0.93-2.16	Yes
25	CT Scan	Mathews et al. (2013)	Extremity	Solid cancer	IRR = 1.36, 95% CI; 1.11-1.67	Yes
26	CT Scan	Mathews et al. (2013)	Extremity	All Cancer	IRR = 1.33, 95% CI: 1.18-1.50	Yes
27	CT Scan	Mathews et al. (2013)	Abdomen	Thyroid	IRR = 1.47, 95% CI: 0.83-2.59	Yes
28	CT Scan	Mathews et al. (2013)	Abdomen	Leukemia	IRR = 3.24, 95% CI: 2.17-4.84	Yes
29	CT Scan	Mathews et al. (2013)	Abdomen	Solid cancer	IRR = 1.45, 95% CI: 1.10-1.92	Yes
30	CT Scan	Mathews et al. (2013)	Abdomen	All Cancer	IRR = 1.61, 95% CI: 1.38-1.88	Yes
31	CT Scan	Mathews et al. (2013)	Spine	Thyroid	IRR = 1.78, 95% CI: 1.24-2.58	Yes

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
32	CT Scan	Mathews et al. (2013)	Spine	Leukemia	IRR = 1.31, 95% CI: 0.85-2.04	Yes
33	CT Scan	Mathews et al. (2013)	Spine	Solid cancer	IRR = 1.02, 95% CI: 0.82-1.27	Yes
34	CT Scan	Mathews et al. (2013)	Spine	All Cancer	IRR = 1.13, 95% CI:1.00-1.28	Yes
35	CT Scan	Miglioretti et al. (2013)	Head	Solid cancer	LAR = 1.1 to 17.5 per 10,000 persons	Yes
36	CT Scan	Miglioretti et al. (2013)	Head	Leukemia	LAR = 0.5 to 1.9 per 10,000 persons	Yes
37	CT Scan	Miglioretti et al. (2013)	Abdomen	Solid cancer	LAR = 13.1 to 33.9 per 10,000 persons	Yes
38	CT Scan	Miglioretti et al. (2013)	Abdomen	Leukemia	LAR = 0.7 to 0.8 per 10,000 persons	Yes
39	CT Scan	Miglioretti et al. (2013)	Chest	Solid cancer	LAR = 6.1 to 30.5 per 10,000 persons	Yes
40	CT Scan	Miglioretti et al. (2013)	Chest	Leukemia	LAR = 0.4 to 0.6 per 10,000 persons	Yes
41	CT Scan	Miglioretti et al. (2013)	Spine	Solid cancer	LAR = 5.3 to 37.5 per 10,000 persons	Yes
42	CT Scan	Miglioretti et al. (2013)	Spine	Leukemia	LAR = 0.4 to 0.7 per 10,000 persons	Yes

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
43	CT Scan	Su et al. (2014)	Sinus	Thyroid	LAR (girls)= 2.7, 95% CI: 1.7-4.2 per 100,000 persons LAR (boys)= 0.4, 95% CI: 0.2-1.1 per 100,000 persons	Yes
44	CT Scan	Su et al. (2014)	Head	Thyroid	LAR (girls)= 8.7, 95% CI: 2.8-48.5 per 100,000 persons LAR (boys)= 1.1, 95% CI: 0.4-3.6 per 100,000 persons	Yes
45	CT Scan	Su et al. (2014)	Chest	Thyroid	LAR (girls)= 14.1, 95% CI: 7.0-65.4 per 100,000 persons LAR (boys)= 2.1, 95% CI: 1.0-8.5 per 100,000 persons	Yes
46	CT Scan	Huang et al. (2014)	All body	Brain tumors	HR =2.56, 95% CI: 1.44-4.54 per 100,000 persons	Yes
47	CT Scan	Huang et al. (2014)	All body	Leukemia	HR =1.90, 95% CI: 0.82-4.40 per 100,000 persons	Yes
48	CT Scan	Huang et al. (2014)	All body	Solid cancer	HR =0.65, 95% CI:0.35-1.19 per 100,000 persons	Yes

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
49	CT Scan	Huang et al. (2014)	All body	All Cancer	HR =1.29, 95% CI: 0.90-1.85 per 100,000 persons	Yes
50	CT Scan	Niemann et al. (2015)	Chest	All Cancer	Exposed age of 0, LAR (males) = 5.76 (thyroid), 3.07 (leukemia), and 14.36 (lung) incidence per 100,000 persons LAR (females) = 26.22 (thyroid), 2.05 (leukemia), and 28.72 (lung) incidence per 100,000 persons	Yes
51	CT Scan	Niemann et al. (2015)	Chest	All Cancer	Exposed age of 5, LAR (males) = 2.92 (thyroid), 1.30 (leukemia), and 9.73 (lung) incidence per 100,000 persons LAR (females) = 13.32 (thyroid), 0.84 (leukemia), and 19.19 (lung) incidence per 100,000 persons	Yes
52	CT Scan	Niemann et al. (2015)	Chest	All Cancer	Exposed age of 10, LAR (males) = 1.78 (thyroid), 1.05 (leukemia), and 7.79 (lung) incidence per 100,000 persons	Yes

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
					LAR (females) = 8.24 (thyroid), 0.62 (leukemia), and 15.02 (lung) incidence per 100,000 persons	
53	CT Scan	Niemann et al. (2015)	Chest	All Cancer	Exposed age of 15, LAR (males) = 0.81 (thyroid), 0.67 (leukemia), and 4.53 (lung) incidence per 100,000 persons LAR (females) = 3.61 (thyroid), 0.45 (leukemia), and 9.23 (lung) incidence per 100,000 persons	Yes
54	CT Scan	Niemann et al. (2015)	Chest	Mortality	Exposed age of 0, LAR (males) =0.92 (leukemia), and 14.54 (lung) mortality incidence per 100,000 persons Exposed age of 0, LAR (females) =0.59 (leukemia), and 25.19 (lung) mortality incidence per 100,000 persons	Yes
55	CT Scan	Niemann et al. (2015)	Chest	Mortality	Exposed age of 5, LAR (males) =0.62 (leukemia), and 9.84 (lung) mortality	Yes

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
					incidence per 100,000 persons Exposed age of 5, LAR (females) =0.39 (leukemia), and 16.85 (lung) mortality incidence per 100,000 persons	
56	CT Scan	Niemann et al. (2015)	Chest	Mortality	Exposed age of 10, LAR (males) =0.62 (leukemia), and 7.90 (lung) mortality incidence per 100,000 persons Exposed age of 10, LAR (females) =0.38 (leukemia), and 13.17 (lung) mortality incidence per 100,000 persons	Yes
57	CT Scan	Niemann et al. (2015)	Chest	Mortality	Exposed age of 15, LAR (males) =0.45 (leukemia), and 4.58 (lung) mortality incidence per 100,000 persons Exposed age of 15, LAR (females) =0.31 (leukemia), and 8.12 (lung) mortality incidence per 100,000 persons	Yes

No.	Modality	Author	Exposure	Outcome	Result	Elevated Risk
58	CT Scan	Krille et al. (2015)	All body	All Cancer	SIR = 1.87, 95% CI: 1.33-2.55	Yes
59	CT Scan	Krille et al. (2015)	All body	Leukemia	SIR = 1.72, 95% CI: 0.89-3.01	Yes
60	CT Scan	Krille et al. (2015)	All body	Lymphomas	SIR = 3.26, 95% CI:1.63-5.83	Yes
61	CT Scan	Krille et al. (2015)	All body	Lymphomas	SIR = 1.35, 95% CI:0.54-2.78	Yes
62	CT Scan	Krille et al. (2015)	All body	Lymphomas	SIR = 1.68, 95% CI:0.77-3.19	Yes

Table 19. Appendix B - Sex Differences

Modality	Author	Exposure	Outcome	Result (Overall)	Female	Male
Dental	Memon et al. (2010)	Dental	Thyroid	OR = 2.10, 95% CI: 1.4-3.1	OR = 2.00	OR = 2.4
X-rays	Inskip et al. (1995)	Head	Thyroid	RR = 1.00 to 1.22	N/A	N/A
X-rays	Inskip et al. (1995)	Chest	Thyroid	RR = 0.99 to 1.11	N/A	N/A
X-rays	Inskip et al. (1995)	Abdomen	Thyroid	RR = 0.75 to 1.10	N/A	N/A
X-rays	Hammer et al. (2009)	All body	All Cancer	IRR = 1.00 (reference) to 1.01, 95% CI: 0.60- 1.71	SIR = 1.00	SIR = 0.99
X-rays	Hammer et al. (2009)	All body	Leukemia and lymphoma	IRR = 1.00 to 1.04	N/A	N/A
X-rays	Hammer et al. (2009)	All body	Solid tumors	IRR = 0.98 to 1.05	N/A	N/A
X-rays	Hammer et al. (2011)	All body	All Cancer	SIR = 0.97	N/A	N/A
X-rays	Hammer et al. (2011)	All body	Leukemia and lymphoma	SIR = 1.05	N/A	N/A
X-rays	Hammer et al. (2011)	All body	Solid tumors	SIR = 0.88	N/A	N/A

Modality	Author	Exposure	Outcome	Result (Overall)	Female	Male
CT Scan	Su et al. (2002)	Sinus	Thyroid	LAR (girls)= 2.7, 95% CI: 1.7-4.2 per 100,000 persons LAR (boys)= 0.4, 95% CI: 0.2-1.1 per 100,000 persons	LAR = 2.7	LAR = 0.4
CT Scan	Su et al. (2002)	Head	Thyroid	LAR (girls)= 8.7, 95% CI: 2.8-48.5 per 100,000 persons LAR (boys)= 1.1, 95% CI: 0.4-3.6 per 100,000 persons	LAR = 8.8	LAR = 1.1
CT Scan	Su et al. (2002)	Chest	Thyroid	LAR (girls)= 14.1, 95% CI: 7.0-65.4 per 100,000 persons LAR (boys)= 2.1, 95% CI: 1.0-8.5 per 100,000 persons	LAR = 14.1	LAR = 2.1
CT Scan	Chodick et al. (2007)	Head	Mortality	ELD (boys) = 0.78 to 2.61; ELD (girls) = 0.48 to 1.81	ELD = 1.81	ELD = 2.61
CT Scan	Chodick et al. (2007)	Rest of body	Mortality	ELD (boys) = 0.13 to 2.18; ELD (girls) = 0.33 to 2.90	ELD = 2.90	ELD = 2.18
CT Scan	Pearce et al. (2012)	Brain, Chest, Abdomen, and Extremity	Leukemia	ERR = 0.031 (male) per mGy and 0.042 (female) per mGy	ERR = 0.042 per mGy	ERR = 0.031 per mGy
CT Scan	Pearce et al. (2012)	Brain, Chest, Abdomen, and Extremity	Brain tumours	ERR = 0.016 (male) per mGy and 0.028 (female) per mGy	ERR = 0.028 per mGy	ERR = 0.016 per mGy

Modality	Author	Exposure	Outcome	Result (Overall)	Female	Male
CT Scan	Mathews et al. (2013)	Brain	Thyroid	IRR = 1.33	N/A	N/A
CT Scan	Mathews et al. (2013)	Brain	Leukemia	IRR = 1.16	N/A	N/A
CT Scan	Mathews et al. (2013)	Brain	Solid cancer	IRR = 1.13	N/A	N/A
CT Scan	Mathews et al. (2013)	Brain	All Cancer	IRR = 1.23	N/A	N/A
CT Scan	Mathews et al. (2013)	Chest	Thyroid	IRR = 1.41	N/A	N/A
CT Scan	Mathews et al. (2013)	Chest	Leukemia	IRR = 0.74	N/A	N/A
CT Scan	Mathews et al. (2013)	Chest	Solid cancer	IRR = 1.96	N/A	N/A
CT Scan	Mathews et al. (2013)	Chest	All Cancer	IRR = 1.62	N/A	N/A
CT Scan	Mathews et al. (2013)	Extremity	Thyroid	IRR = 1.19	N/A	N/A
CT Scan	Mathews et al. (2013)	Extremity	Leukemia	IRR = 1.42	N/A	N/A
CT Scan	Mathews et al. (2013)	Extremity	Solid cancer	IRR = 1.36	N/A	N/A
CT Scan	Mathews et al. (2013)	Extremity	All Cancer	IRR = 1.33	N/A	N/A
CT Scan	Mathews et al. (2013)	Abdomen	Thyroid	IRR = 1.47	N/A	N/A
CT Scan	Mathews et al. (2013)	Abdomen	Leukemia	IRR = 3.24	N/A	N/A
CT Scan	Mathews et al. (2013)	Abdomen	Solid cancer	IRR = 1.45	N/A	N/A
CT Scan	Mathews et al. (2013)	Abdomen	All Cancer	IRR = 1.61	N/A	N/A
CT Scan	Mathews et al. (2013)	Spine	Thyroid	IRR = 1.78	N/A	N/A
CT Scan	Mathews et al. (2013)	Spine	Leukemia	IRR = 1.31	N/A	N/A
CT Scan	Mathews et al. (2013)	Spine	Solid cancer	IRR = 1.02	N/A	N/A
CT Scan	Mathews et al. (2013)	Spine	All Cancer	IRR = 1.13	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Head	Solid cancer	LAR = 1.1 to 17.5	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Head	Leukemia	LAR = 0.5 to 1.9	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Abdomen	Solid cancer	LAR = 13.1 to 33.9	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Abdomen	Leukemia	LAR = 0.7 to 0.8	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Chest	Solid cancer	LAR = 6.1 to 30.5	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Chest	Leukemia	LAR = 0.4 to 0.6	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Spine	Solid cancer	LAR = 5.3 to 37.5	N/A	N/A
CT Scan	Miglioretti et al. (2013)	Spine	Leukemia	LAR = 0.4 to 0.7	N/A	N/A
CT Scan	Huang et al. (2014)	All body	Brain tumours	HR =2.56	HR = 2.48	HR = 2.62
CT Scan	Huang et al. (2014)	All body	Leukemia	HR =1.90	HR = 1.62	HR = 2.02
CT Scan	Huang et al. (2014)	All body	Solid cancer	HR =0.65	HR = 0.69	HR = 0.62
CT Scan	Huang et al. (2014)	All body	All Cancer	HR =1.29	HR = 1.28	HR = 1.29

Modality	Author	Exposure	Outcome	Result (Overall)	Female	Male
CT Scan	Niemann et al. (2015)	Chest	All Cancer	Exposed age of 0, LAR (males) = 14.36 (lung) incidence per 100,000 persons LAR (females) = 28.72 (lung) incidence per 100,000 persons	(At age=0) LAR = 28.72	(At age=0) LAR = 14.36
CT Scan	Niemann et al. (2015)	Chest	Mortality	Exposed age of 0, LAR (males) = 14.54 (lung) mortality incidence per 100,000 persons Exposed age of 0, LAR (females) = 25.19 (lung) mortality incidence per 100,000 persons	(At age=0) LAR = 25.19	(At age=0) LAR = 14.54
CT Scan	Krille et al. (2015)	All body	All Cancer	SIR = 1.87	N/A	N/A
CT Scan	Krille et al. (2015)	All body	Leukemia	SIR = 1.72	N/A	N/A
CT Scan	Krille et al. (2015)	All body	Lymphomas	SIR = 3.26	N/A	N/A
CT Scan	Krille et al. (2015)	All body	Lymphomas	SIR = 1.35	N/A	N/A
CT Scan	Krille et al. (2015)	All body	Lymphomas	SIR = 1.68	N/A	N/A