ESTIMATION OF CUMULATIVE EFFECTIVE DOSE AND POTENTIAL RISKS OF RADIATION EXPOSURE FROM MULTIPLE SCANS OF CT HEAD

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by

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LIST OF SYMBOLS

λ	Wavelength
€	Velocity
3-D	Three Dimensional
eVs^{-1}	electronVolt per second
f	Frequency
Hz	Hertz
Js^{-1}	Joule per second
kVp	kiloVolt Peak
M	Mean
m	Meter
mAs	milliAmpere second
mGy	milliGray
ms^{-1}	meter per second
mSv	milli-Sievert
s^{-1}	Per second
W_T	Weighting Factors

LIST OF ABBREVIATIONS

ACR	American College of Radiology
ALARP	As Low as Reasonably Practicable
AMDI	Advanced Medical and Dental Institutes
AT	Ataxia Telangiectasia
ATM	Ataxia Telangiectasia Mutated
BEIR	Biological Effects of Ionising Radiation
CSV	Comma-Separated Value
CT	Computed Tomography
CTDI	CT dose Index
DLP	Dose Length Product.
DSCT	Dual-Source CT
EAR	Excess Absolute Risk
ED	Effective Dose
HUSM	Hospital Universiti Sains Malaysia
HVL	Half Value Layer
ICRP	International Commission on Radiological Protection
LAR	Lifetime Attributable Risk

LET	Linear Energy Transfer
LNT	Linear-no-Threshold
LSS	Life Span Study
MDCT	Multi Detector Computed Tomography
MOH	Ministry of Health
NRPB	National Radiological Protection Board
NCRP	National Council on Radiation Protection and Measurement
PACS	Picture Archiving and Communication System
PMMA	Polymethyl-methacrylate
QA	Quality Assurance
REIC	Risk of Exposure Induced-Cancer
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
XML	Extensible Markup Language

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ANGGARAN DOS EFEKTIF KUMULATIF DAN POTENSI RISIKO PENDEDAHAN SINARAN DARI IMBASAN BERULANG CT KEPALA

ABSTRAK

Di dalam kajian ini, tujuan utamanya adalah untuk menentukan dos organ individu dan dos serapan tisu kumulatif yang diperoleh dari dedahan berulang, serta dituruti oleh analisis dos efektif (ED) kumulatif dan anggaran risiko radiasi yang menyebabkan kanser akibat perulangan dedahan. Sejumlah 323 pesakit (183 lelaki dan 140 perempuan) yang telah menerima pemeriksaan CT kepala berulang (iaitu melebihi 3 kali pendedahan) di Institut Perubatan dan Pergigian Termaju (IPPT) dan Hospital Universiti Sains Malaysia (HUSM) terlibat dalam kajian ini. Kebanyakan pesakit adalah dirujuk daripada Jabatan Trauma dan Neuro di HUSM. Berdasar pada kajian ini , dos organ bagi lensa mata menunjukkan dos tertinggi yang konsisten berbanding semua organ lain kecuali bagi data yang melibatkan 13 kali dedahan: organ tiroid (7.55 mSv) berbanding lensa mata (7.50 mSv). Dos organ paling tinggi adalah lensa mata dengan nilai 8.02 mSv. Berdasarkan perakuan *International Commission on Radiological Protection* (ICRP), nilai tersebut masih rendah iaitu di bawah aras radiasi yang menyebabkan kanser (100 mSv). Disamping itu, dos serapan bagi ≥ 3 kali adalah melebihi aras bagi pembentukan katarak seperti yang dinyatakan oleh ICRP (0.5 Gy hingga 2 Gy untuk satu dedahan dan 5 Gy untuk dedahan berbahagi). Walaubagaimanapun, kedua-dua pengiraan perisian menunjukkan saling hubung yang positif dengan jumlah penambahan dedahan. (*nilai r* =0.98). Selain itu, dedahan CT berulang juga menunjukkan peningkatkan keberangkalian risiko terhadap penyebab kanser. Berdasarkan Risiko Terdedah Sepanjang Hayat (LAR) insidens dan kematian bagi kanser otak, keputusan menunjukkan bahawa populasi perempuan lebih tinggi (53.87 dan 50.17 setiap 100000) berbanding populasi lelaki (21 dan 17.45 setiap

100000) di dalam 10 kali perulangan dedahan. Peningkatan dedahan akan meningkatkan risiko kanser dengan ketara; $X^2(7) = 76.89$, nilai $p = 0.01$ (Otak) dan $X^2(7) = 59.22$, nilai $p = 0.01$ (Kelenjar Air Liur) dengan purata 16.3×10^{-5} untuk otak dan 1.65×10^{-5} untuk kelenjar air liur. Keputusan juga menunjukkan saling hubung yang positif antara LAR insidens dan kematian (*nilai* $r = 0.49$ bagi otak dan 0.42 bagi kelenjar air liur). Maka, perulangan dedahan perlulah diminimumkan untuk mengurangkan dos radiasi yang berlebihan. Justifikasi dos dan pengoptimuman amalan adalah penting berdasarkan konsep pengurangan dos yang munasabah (ALARP).

ESTIMATION OF CUMULATIVE EFFECTIVE DOSE AND POTENTIAL RISKS OF RADIATION EXPOSURE FROM MULTIPLE SCANS OF CT HEAD

ABSTRACT

In this study, the aims are to determine the cumulative individual organ dose and tissue absorbed dose received from multiple CT exposures, to analyse cumulative effective dose (ED) and estimate the risk of radiation induced cancer due to multiple CT exposures. A total of 323 patients (183 males and 140 females) underwent multiple CT head examinations (more than 3 exposures) at Advanced Medical and Dental Institute (AMDI) and Hospital Universiti Sains Malaysia (HUSM) were included in this study. Mostly patients were referred from Trauma and Neuro Departments of HUSM. Based on the study, lens organ dose consistently yields the highest values except for 13 times of multiple exposures; followed by thyroid's dose (7.55 mSv) and lens (7.50 mSv). The highest organ dose was observed at lens (8.02 mSv). Based on International Commission on Radiological Protection (ICRP), the value was still below the level of radiation-induced cancer (100 mSv). However, mean absorbed dose for ≥ 3 times exposureexceeded the level of cataract formation stated by ICRP (0.5 Gy to 2 Gy for single exposure and 5 Gy for fractionated or protracted exposure). Both software calculation showed a positive correlation with number of exposures (*r-value* = 0.98). Besides, multiple CT exposures showed increment of the probability risk to induce cancer. Based on lifetime attributable risk (LAR) of incidence and mortality, the result showed that brain LAR was higher (53.87 and 50.17 per 100000 population) in female population compared to male population (21 and 17.45 per 100000 population) in 10 times multiple exposure. Increased exposures lead to significant increment of cancer risk with $X^2(7) = 76.89$, *p-value* = 0.01(brain), $X^2(7) = 59.22$, *p-*

value = 0.01(salivary), with a mean value of 16.3 x 10^{-5} for LAR brain and 1.65 x 10^{-5} for salivary. The results also showed correlation of LAR incidence with mortality (*r-value* = 0.49 for brain and 0.42 for salivary). Thus, the repeated CT exposures should be minimized as to reduce the unnecessary radiation dose. The dose justification and optimisation of practice is crucial based on the concept of as low as reasonably practicable (ALARP).

CHAPTER 1: INTRODUCTION

Radiology department is the place for patients to seek diagnosis and treatment. In diagnostic imaging, most of imaging modalities use radiation as the source for lesion or disease identification. Multiple patient's exposures to ionising radiation may lead to increasing of unnecessary radiation dose to patients. The long-term goal of this research is to improve and minimise the radiation dose to patient by reducing the number of multiple exposures. The first section of this chapter describes the background of study followed with problem statements, objectives, hypotheses, and clinical significance of the study. Finally, the thesis organisation is provided for the summary of all chapters.

1.1 Background of Study

The advancement of computed tomography (CT) technologies have led to increasing number of CT scans in clinical applications, especially after the introduction of helical CT scan. CT scanner is widely used as imaging modality in patient's diagnosis. Most CT examination on the head, chest, abdomen and pelvis are used for diagnosis and treatment because it provides good quality and detailed image in analysing the human body tissues (Sharma & Aggarwal, 2010). As a result, the advancement of CT has increased concern on radiation dose received from medical exposure amongpublic and health care professionals. The major concern is related to radiation dose received and the potential radiation-related health effects that might be received by the patients due to multiple CT scans exposure and type of CT examination received at certain age (Smith-Bindman et al., 2015). The practitioners in diagnostic imaging are also interested in dose reduction and management. Based on the report by National Council on Radiation Protection and Measurement (NCRP), there was seven times increment in radiation exposures since 1980s until 2006 that mainly arise from the increased utilisation of CT imaging and nuclear medicine (Aw-Zoretic et al. 2014). The concern was also increased since the high-level radiation incidents at Hiroshima and Nagasaki. The population from the incidence are still suffering from the effect of high dose radiation, followed by their next generation. In current state of knowledge, the issues of low-level exposure are still in debate because most of the reported data are focused on high level radiation (Hiroshima and Nagasaki; Chernobyl) and most of previous studies focused on multiple regions exposures of CT scan. There was no previous research focused on the single head scanning because most of the patients underwent multiple regions CT exposures.

Radiation can be divided into high and low LET radiation. Both LET can cause damage to the DNA and wide effects to human. The risk models have been established and developed known as Biological Effects of Ionising Radiation (BEIR) to estimate the risk of single exposure from CT scan examination, and it reported that the range of low radiation dose ranged from near zero up to 100 mSv (Barros, 2012). With the current knowledge, it has been concluded that the current scientific evidence on the low-level radiation is consistently linear with ionising radiation in development of solid cancer.

CT scan is a high-cost modality and used in diagnostic radiology for clinical applications. The advancement of CT applications helps specialist in accurately detecting the lesion in specific area. These applications are used for the cancer diagnosis, trauma, and diseases screening. The CT technique also reduces the invasive or intervention procedure to diagnose the human’s body such as blood vessel study. It also reduces the management time for each patient who undergoes the CT procedure. However, previous researchers have proved that the absorbed dose from CT scan can cause the risk of radiation induced-cancer based on the frequency of the CT scan examination received by patients (Smith-Bindman et al., 2015).

In current clinical practice, the dose length product (DLP) and volume CT dose index ($CTDI_{vol}$) are used to present the radiation dose received by patients during CT examination. Since these dose indices are computed based on the standard-size phantoms, thus they do not provide accurate information regarding absorbed dose based on tissue density of human organs (Russo, 2018). This study aims to assess and estimate the potential risks of radiation associated with multiple CT exposures based on age, sex and gender of the patients. The effective dose has been used because it is known as a single parameter to represent the relative risk from radiation exposure for the whole population (ICRP, 2007b). Effective dose reflects the risk of biological effects from radiation exposure. According to the International Commission on Radiological Protection (ICRP), effective dose is defined as a single dose quantity from any radiation exposure, where the risk is averaged over all ages and both sexes (ICRP, 2007b). It is also useful to compare the risks for reference patient from different imaging techniques and procedures. However, the effective dose is not suitable for single individual exposure. Nonetheless, it is useful in comparing between modalities such as dose from radiography, CT and nuclear medicine.

In this study, the cumulative organ dose and effective dose received by the patient from multiple or repeated CT exposures were assessed. The study sample includes patients who underwent multiple CT examination at Imaging Unit, Advanced Medical and Dental Institutes (AMDI), USM Penang and Radiology Department, Hospital Universiti Sains Malaysia (HUSM), Kelantan.

1.2 Problem Statements

There has been increasing concern on the probability of cancer induction by radiation from CT imaging. It is necessary for the team in diagnostic CT imaging, especially physicians who will communicate with patients during CT scan procedure, to have the basic knowledge on CT radiation dose and its potential adverse effects. In CT head, multiple exposures can increase the stochastic or deterministic effect to the patients. Lens, brain, and bone marrow are among the most sensitive parts within the head area. The deterministic effect is related to the absorbed dose and the effect increases due to increasing of low-level or high-level radiation. It has a range of threshold and it vary from person to person. However, once the threshold has been exceeded, the severity of an effect also increases. The stochastic effect will also increase, if the patients received multiple exposures and particularly in latent risk.

A systematic review of the literatures had been done on the radiation dose, a cancer risk from CT exposure, parameters associated with CT dose, the benefit or limitation of the effective dose and the risk of low-level radiation. In previous studies, there was still no clear evidence related to the risk of cancer induction at low-level exposure (below 100 mSv) compared to the high-level exposure (> 100 mSv) (ICRP, 2007b). The high-level radiation is referred to the victims of Hiroshima atomic bomb who were exposed to high acute radiation and increased risks of cancer mortality (Brenner et al., 2003).

The rising of the number of CT scan exposure has increased the assumption that the cumulative of effective dose will increase proportionally to the number of CT scans. The rationale of this study is to investigate the potential risk of low radiation level on cancer incident and mortality due to the multiple radiation exposures to the patient. Multiple radiation exposures may accrue high accumulation of dose and risk to the exposed body organs. Thus, better understanding and awareness on dose are vital as a dose guideline that will be beneficial to support the dose optimisation and help in manipulating the parameters for patient benefits without reducing the diagnostic value.

1.3 Objectives of Study

General objective:

The study aims to evaluate the effective-organ dose and radiation risk received from multiple CT head scans.

Specific objective:

1. To calculate the individual organ dose and tissue absorbed dose received from multiple exposures of CT head scans.
2. To calculate and compare the cumulative effective dose received from multiple exposures of CT head scans using two methods, manual and software-based calculation.
3. To estimate the risk of radiation induced cancer due to multiple exposures of CT head study.

1.4 Research Hypotheses

The purpose of this work presented in this thesis was to investigate the following hypotheses:

1. *Hypothesis 1*

   The cumulative organ dose of CT scan from AMDI and HUSM does not exceed the baseline of disease induction in specific organ disease.

2. *Hypothesis 2*

   There is a significant difference between manual and software-based calculation method of effective dose.

3. *Hypothesis 3*

   The risk of multiple CT exposures at AMDI and HUSM is considerably low as compared to the previous reported values.

1.5 Significance of Study

The results of this study will provide better understanding regarding patient dose received from multiple CT head scans. The calculated effective dose can serve as guideline to help practitioners in minimizing the multiple exposure and determine the best alternative techniques. It should be possible for practitioners to manipulate the CT acquisition parameters without adhere to the default setting from CT manufacturer while maintaining the diagnostic value of CT image. However, the quality of CT images and radiation dose should be balanced to provide the best diagnosis without unnecessary multiple exposures and dose to the patient. Thus, these findings would be a highly significant in clinical imaging application.

1.6 Thesis Outline

A brief description of each chapters in this thesis:

- Chapter 2 is related to the theory and literature reviews. It discussed the historical and basic principle of CT imaging and described the evolution of CT technology. This chapter also focused on fundamental knowledge such as the types of dose unit, radiation risk and correlation between dose-parameters. This chapter also provides literature review of the previous studies related to this work.
- Chapter 3 describes the materials and methodology of this project. It presents the CT machine and accessories at both centres, and briefly explained about CT dose validation, patients dose survey and determination of organ and cumulative effective dose. Furthermore, this chapter also presents the related equations involve in estimation of excess absolute risk (EAR) and lifetime attributable risk (LAR).
- Chapter 4presents the research findings such as the overall demographic of patients' data including related CT parameters. The results from this study were analysed based on multiple CT exposures. It also presents the statistical analysis on the data such as correlation between manual and software-based calculation. Finally, it proved that the risks of radiation dose are depended upon the age and sex of patients in each group of different number of multiple exposures. Finally, the scientific explanation and discussion on the research findings were also elaborated in detail.
- Chapter 5 presents the conclusion of this study and recommendation for the future works.

CHAPTER 2: LITERATURE REVIEW

This chapter focuses on the theory and literature review. It discusses historical, basic principle of X-ray and computed tomography (CT) imaging. It explains on the production of X-ray and evolution of CT technology and basic principles of CT imaging. The effects of radiation are also described in this chapter which includes introduction of radiation effects, level of radiation effects and impact of radiation. Literature review on the previous studies related to this work such as the probability of cancer induction are also elaborated in this chapter.

2.1 X-ray

Wilhelm Conrad Roentgen was discovered X-ray production in 1895 and received numerous honours for his discovery of X-ray, including the first Nobel Prize in 1901 (de Herder, 2014). The process of X-ray had been discovered when he finds electromagnetic radiation that contains both magnetic and electrical fields. In other words, electromagnetic radiation is also known as a stream of photons, with each of them has energy and travels at a level of velocity of light (Russo, 2018).

In physics principles, velocity of light € has strong relationship between frequency (f) and wavelength (λ) as stated in Equation 2.1. In equation, the length of time for 1 cycle based on light travel is described in unit of seconds (s) and frequency is the number of cycles per seconds (s^{-1}) or Hertz (Hz). The velocity of the electromagnetic radiation travels in a vacuum is $c = 3.0 \times 10^{8}$ ms^{-1} (Georgi, 1993). Moreover, wavelength is showed as electromagnetic radiation travel for certain distance in a cycle and described in units of nanometres (10^{-9} m).

$$C = \lambda f \qquad 2.1$$

In Figure 2.1, spectrum for electromagnetic elaborate more specific based on the amount of energy contains in electromagnetic radiation. It contains the specific low energy radiation to a high energy radiation. Based on previous article, electromagnetic radiation is related with photon energy and frequency (Equation 2.2). The photon energy € is proportional to the frequency wave (f), where h is a Planck's constant, $h = 6.62 \times 10^{-34}$ $Js^{-1} = 4.13 \times 10^{-21}$ eVs^{-1}(Duffey, 2012). In Dance et al., (2014), the photon energy influences the frequency of electromagnetic waves, which increase in the frequency will increase the photon energy (Dance et al., 2014).

$$E = hf \qquad 2.2$$

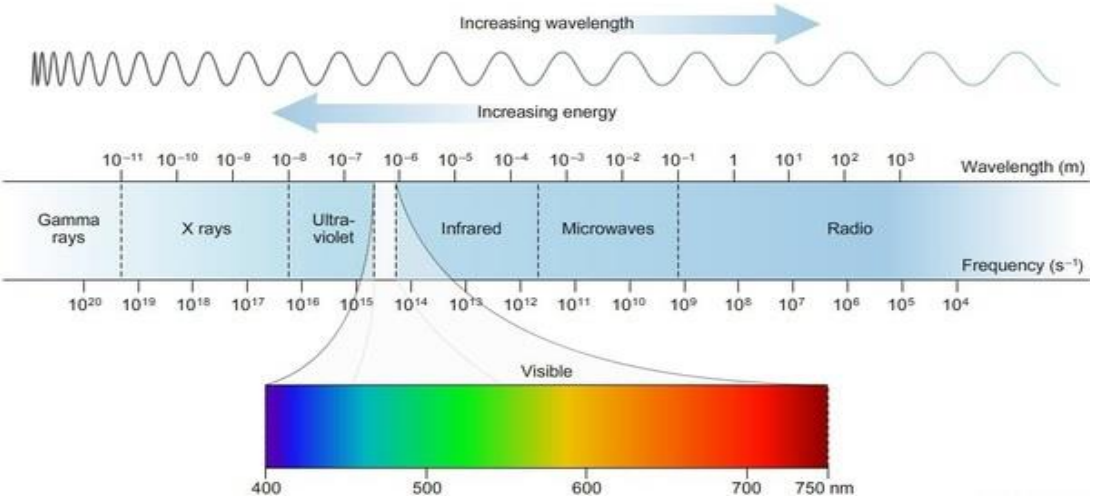
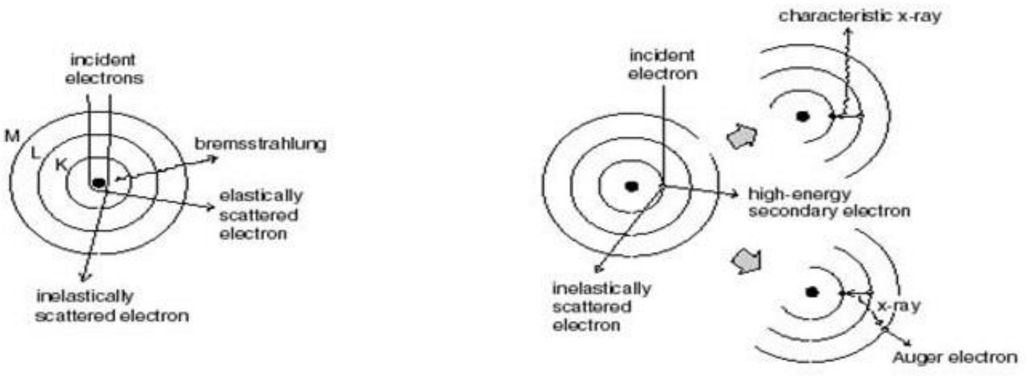


Figure 2.1 The electromagnetic spectrum related to the X-ray wavelength and energy. The short wavelength caused high energy. The high energy uncontrolled can cause damage to living tissue and resulting in radiation burns, cancer, cell damage, radiation sickness human and finally death. (Boutet & Yabashi, 2018)

However, X-ray tube only 1% accelerated electron are converted to X-ray, while 99% of electron is being converted into heat. The X-ray is produced by accelerating the electron in the vacuum environment with high bombard velocity to the target metal. When the voltage is applied to the circuit, it results with large increase in tube current and causes intense heating of the filament due to its electrical resistance.

The electrons cloud is produced at the cathode regions and then electrons are released towards anode due to the potential difference between cathode and anode (thermionic resistance) (Russo, 2018). The X-ray is produced within the target anode area and will interact with patients or objects directly through radiation exposure.

Bremsstrahlung and characteristic radiation are generated when the electron hit the anode target. Bremsstrahlung is known as a braking radiation. It is generated when the high velocity electron has been suddenly slowed down and given off energy in the form of braking radiation due the electron is attracted to the positively charged nucleus (Russo, 2018). Furthermore, the characteristic radiation is produced after the incident electron has enough energy to eject out an inner layer electron. Ejection of inner electron creates a “hole” in the inner layer orbit of the atom and replacement of electron from the higher states to fill the vacancy will emit as an X-ray photon with a loss of energy (Russo, 2018).



(a) (b)

Figure 2.2 Two X-ray radiation generated known as bremsstrahlung (a) and Characteristic radiation (b). (Russo, 2018)

2.2 Multi-Slice CT scanner (MSCT)

CT refers to the system used many X-ray measurements taken from different angles to produce cross-sectional images of region of interest of a scanned object. The technology of CT scanner is developed rapidly compared to the previous imaging system. The first CT scanner was built in 1971 by Godfrey Hounsfield and commercially introduced in 1972. About two decades later, the era of the helical/spiral CT scanner emerged, in which the patient/table feed into the gantry with fast continuously scanning (Figure 2.3). By using helical or spiral technique, it offers three main advantages, first Spiral or helical scan can develop or produce images without overlapped scans, Second, the technique also minimises blur images reconstruction by complete scanning in single breath hold without patient movement and lastly, the images with uniform density and contrast due to consistent table/patient movement in scanning direction. By introduction of overlapping images, it provide the reconstruction of 3D images (Taubmann et al., 2018). Thus, this helical or spiral has also paved the way for the development of 3D images tool for manipulation and vital component in newer generations of the CT scanners.

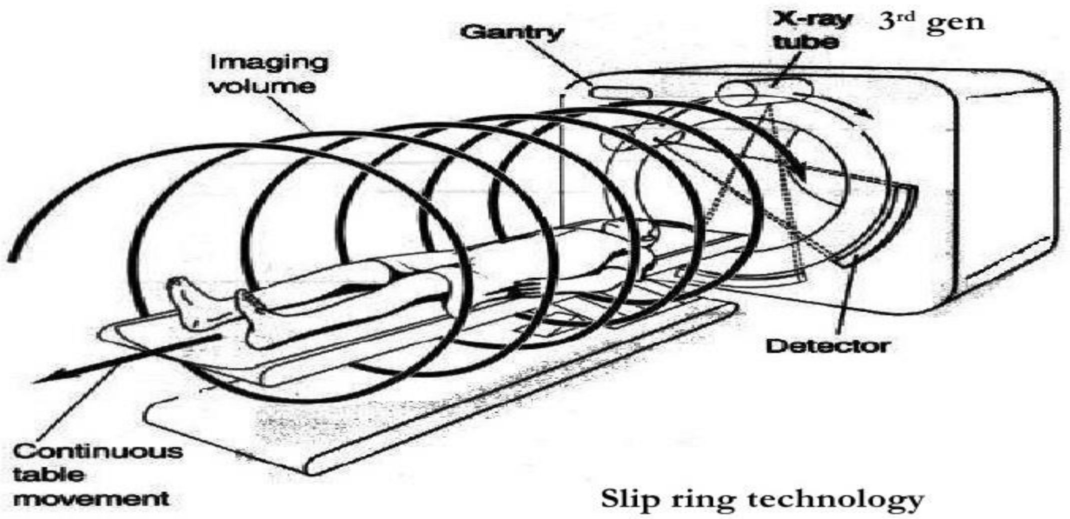


Figure 2.3 The basic principle of helical or spiral. The table or patient is translated at constant speed while the data is required. The tube and detector synchronize and continuously rotated in helical shape. The images can be reconstructed. (Kirova & Hadjidekov, 2005)

In 1998, first four-slice CT system was invented and introduced. The invention of four slice CT has solved two major problems from single-slice CT scanner for helical/spiral technique: First, lack of spatial resolution in longitudinal axis due to wide collimation and second insufficient single scanning within a single breath hold. The four-slice system can reduce time scanning due to large volume coverage and improve longitudinal resolution (Flohr et al., 2005). Hence, four rows of detector have been used instead of single detector and it also can be classified as a multi-detector CT (MDCT) scanner (Figure 2.4).

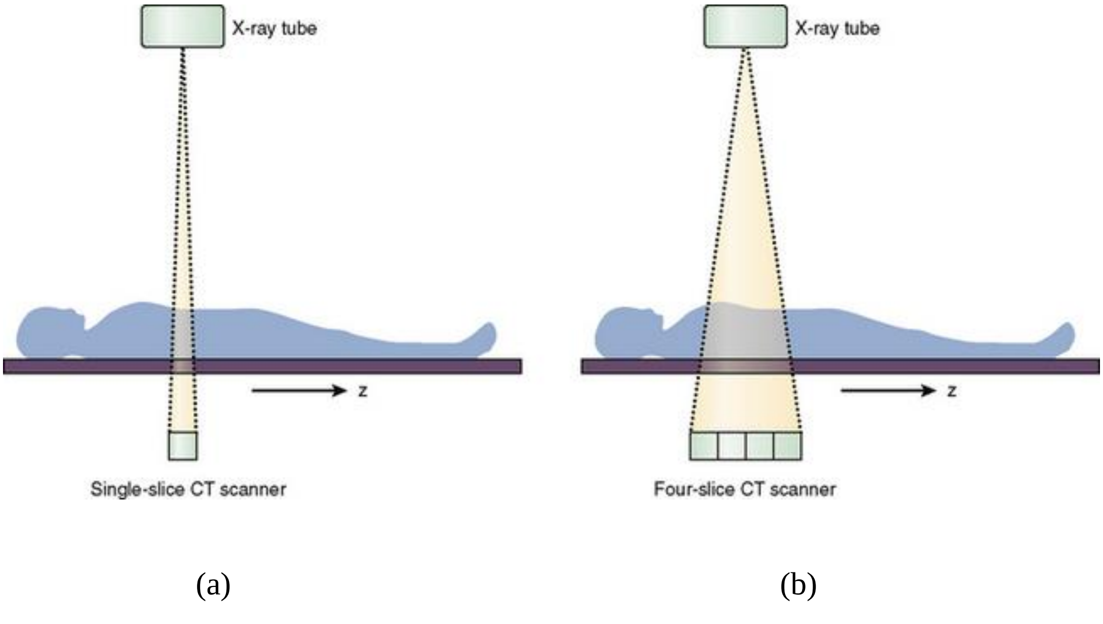


Figure 2.4 Diagrams of a single-slice CT systems with one detector row (a) and four-slice (b) system. (Flohr et al., 2005)

Currently, modern detectors for CT scan are made from high sensitivity radiation materials. These detectors convert the attenuated X-rays into visible light, which automatically will be detected by photodiodes. The photodiodes device used to convert visible lights into electrical currents, and then they are amplified into digital signals. Moreover, tube for MDCT requires large heat storage capacity in the area on anode plate (Ulzheimer et al., 2019). This characteristic can be achieved by thick graphite layers attached to the rotate envelope or anode plate X-ray tube. Based on X-ray tube design, anode plate is located at outer wall of the X-ray tube and direct contact with cooling oil. Thus, it helped in excellent heat dissipation. An example of rotating envelope tube X-ray is shown in Figure 2.5.

Figure 2.5 A rotating envelope X-ray tube. The blue arrow showed direct contact between X-ray tube and cooling oil in the tube housing. This design allows for better heat dissipation via thermal conduction. It has no moving parts and no bearing in the vacuum.(Ulzheimer et al., 2019)

By modern technology systems, it has changed CT imaging development rapidly accordingly to the health needs. In 2005, the first scanner with dual-source CT (DSCT) system was developed. This system has two X-ray tubes and detectors that are mounted onto the rotating tube with an angular offset of 90 degree, as shown in Figure 2.6. The DSCT also can use different kVp in simultaneously tube rotation (Ulzheimer et al., 2019). It can provide additional information regarding to the morphology of disease based on X-ray attenuation coefficients. Hence, DSCT has led to the introduction of MDCT with 320 slices in 2007.

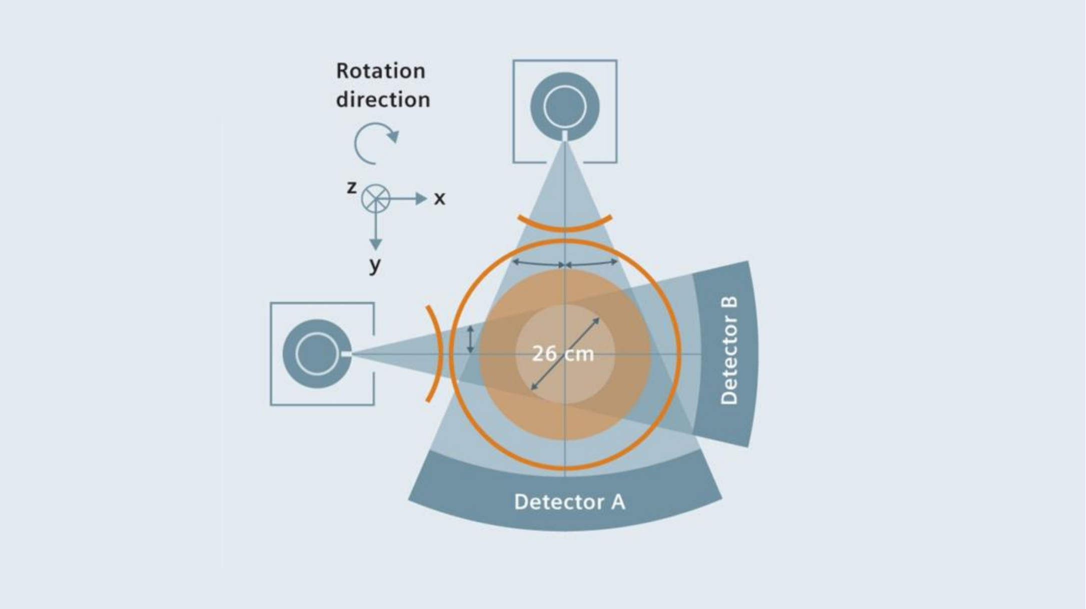
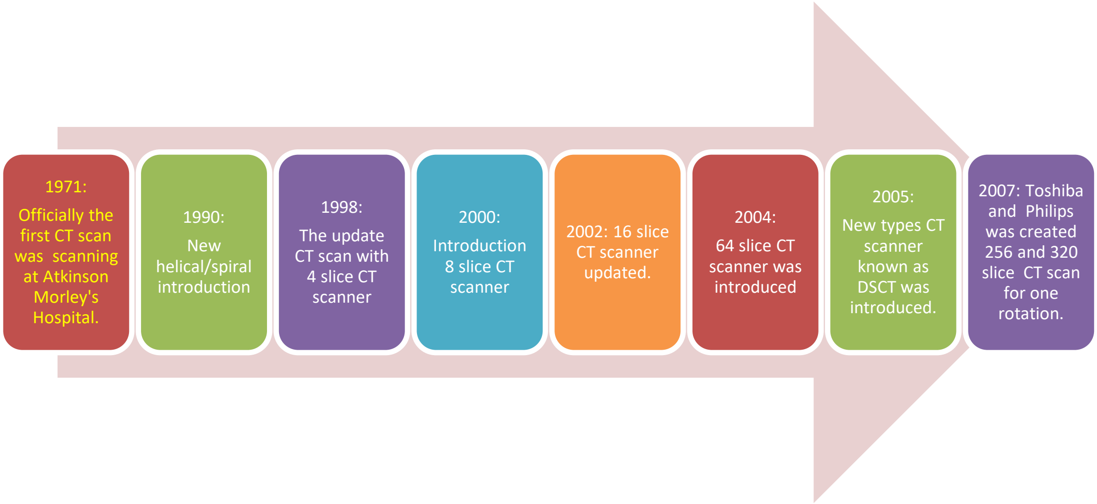


Figure 2.6 Schematic illustration of dual source CT scan which used two tubes with two corresponding detectors offset 90 degrees.(Ulzheimer et al., 2019)



1971: Officially the first CT scan was scanning at Atkinson Morley's Hospital.

1990: New helical/spiral introduction

1998: The update CT scan with 4 slice CT scanner

2000: Introduction 8 slice CT scanner

2002: 16 slice CT scanner updated.

2004: 64 slice CT scanner was introduced

2005: New types CT scanner known as DSCT was introduced.

2007: Toshiba and Philips was created 256 and 320 slice CT scan for one rotation.

Figure 2.7 Summary of the evolution of CT scan from the first introduction of officially use of CT scanner and follow by the development of multi-slice CT scanner.

Concern has increased regarding radiation exposure received from medical procedures, especially in CT imaging which involves greater radiation dose compared to other radiography techniques. The most contribution of man-made ionising radiation exposure to the human being is from medical diagnosis. CT procedures contribute to approximately half of the cumulative dose from medical radiation exposures even though it represents only 16% of medical imaging procedure as reported in the USA (Sodickson et al., 2009). For the last 7 to 10 years, the use of CT scan has increased at a rate of 8% to 15% per year (Brenner 2007). In Malaysia (2011 -2013), Clinical Research Centre (CRC) of Ministry of Health (MOH) Malaysia was summarized 552836 of CT scan had been done in Malaysia. This number showed the CT scan examination was important in diagnostic or treatment side (Malaysia, 2021b).

Increased CT use has resulted in growing rates of multiple and repeated exposures in different population of patients over a period. Based on study done by Griffey & Sodickson, (2009), more than half of the population received more than 10 exposures with high cumulative dose. They reported that 5% of the studied population received between 22 and 132 CT scans. Recurrent or repeated CT imaging has resulted in high cumulative doses to patients (Sodickson et al., 2009). In order to control the radiation exposures, the American College of Radiology (ACR) recommended the identification of population with high cumulative radiation dose due to repeat CT imaging (Jones et al., 2012).

Patients with chronic disease are always undergoing multiple imaging studies and therefore, the multiple dose accumulation may increase the probability of higher accumulated lifetime radiation doses. Higher dose associated with CT imaging also led to increased risk of carcinogenesis (Brenner & Hall, 2007). Patients who undergo repeated or multiple CT examinations have developed substantial underlying disease and greater risks than typical patient (Griffey & Sodickson, 2009).

The rapid evolution of CT technology in advanced clinical application with the significance of increased CT dose levels have created a compelling need to understand detailed information regarding CT dose. In standard clinical practice, the radiation dose can be quantified by several methods and parameters. The CT Dose Index Volume ($CTDI_{vol}$) and Dose Length-Product (DLP) are typically used as reference indices for CT dose. However, both $CTDI_{vol}$ and DLP do not represent the actual patient dose as they only estimate the patient dose based on radiation output and not specific patient’s characteristic (McCollough et al., 2011). These descriptors are also generated based on standard phantom measurement. Therefore, the best choice of dose descriptors is important to determine the effect and radiation risks associated with multiple exposures of low energy radiation.

2.3 $CTDI_{vol}$

X-ray has been used to examine normal and abnormal conditions of human body. However, increase use of X-ray might affect the human body. The radiation can be deposited into human body and specification of the amount of radiation in CT examination is according to unique dose metric known as the CT Dose Index (CTDI). CTDI is measured in unit milliGray (mGy) and calculated based on the data from 100 mm long pencil shaped ion chamber inserted in cylindrical acrylic phantom placed at the scanner isocentre (McCollough et al., 2011; Taubmann et al., 2018). In the past $CTDI_{100}$ and $CTDI_W$ were used to estimate the dose for CT scanner. Nowadays, helical scanner uses $CTDI_{vol}$ as dose descriptor to measure the dose. The unique dose metric of $CTDI_{vol}$ has also been used by the American College of Radiology (ACR) for CT practice accreditation. Based on previous studies, variation of CTDI still happen in default kVp and mAs due to different filters and tube X-ray design. Some scanners also provided the different CTDI_{vol}. Thus, the CTDI_{vol} cannot be used as a patient dose but indicates as radiation intensity. Table 2.1 shows the overview of CTDI metrics.

2.4 Dose-Length Product (DLP)

Newer CT scanner provides the information for DLP dose value. The DLP refers to the total amount of radiation incident that is indicated by CTDI_{vol} and scan length (in centimeters) and measured in milligray-centimetres. However, DLP still cannot be categorised as specific patient dose because it is independent to the size of patient. It can be specified as total radiation intensity (Christner et al., 2010; McCollough et al., 2011).

There are several factors that contribute to radiation dose manipulation. The factors can be divided into inherent, incontrollable and controllable. Generally, the higher tube potential (kVp) and current-time (mAs) will result in lower noise image, but impart a higher radiation dose and consequently lead to the higher cancer induction risk (Huang et al., 2009). It is known that the radiation dose is the primary factor that affects the magnitude of radiation risk, but other factors such as sex, age at exposure, attained age, and tumor site are also contributing to the risks (Ivanov 2014).

Table 2. 1 Summary of CTDI metrics used in CT dosimentry.

Metric	Unit of Measure	Comments
CTDI_{100}	mGy	In one rotation CT X-ray tube, the average air kerma in 100 mm ion chamber divided by X-ray beam width
CTDI_{air}	mGy	The dose measured at the CT scanner isocentre in the absence phantom or human.
CTDI_{p}	mGy	The measured dose at periphery of an acrylic phantom.
CTDI_{c}	mGy	The measured dose at centre of an acrylic phantom.
CTDI_{w}	mGy	Equal to $1/3(\text{CTDI}_{\text{c}}) + 2/3(\text{CTDI}_{\text{p}})$. The CTDI_{p} is averages from 4 periphery dose.

CTDI$_{vol}$	mGy	The value is related to the CTDI$_{w}$ devided by pitch.
DLP	mGy-cm	The total of CTDI$_{vol}$ for one scan length.

2.5 Kilovoltage Peak (kVp)

Tube potential is known as the electrical difference between anode and cathode of the X-ray tube. Kinetic energy of electron is determined by the amount of voltage applied. The accelerated electron in the CT X-ray tube is manipulated by kilovoltage peak (kVp) parameter. The previous researchers stated changes in the kVp vary the energy of the incoming electron prior to maximum energy of X-ray photons in Bremsstrahlung. Then, more electrons will strike the target if the kVp increases. Moreover, exposure to the patient will increase due to exposure is approximately proportional to the square of tube voltage, kVp in the diagnostic energy range. For example, 80 kVp will increase 78% of exposure compared to 60 kVp. It does not have a linear effect on the dose. In other words, reducing the kVp from 100 to 80 kVp results in 1.5 times reduction in radiation dose (McCollough et al., 2011). In conclusion, kVp can manipulate the dose to patient in CT scan and change the quantity and quality of the X-ray beam.

2.6 milliampere Per Second (mAs)

Tube current-time is referred as milliampere per second (mAs), which determines primarily the rate of electron striking the anode and influence the number of emitted X-ray photons. Increasing the number of X-ray photon led to variation of both Bremsstrahlung and Characteristic X-ray portion of X-ray spectrum. On patient dose, tube current has a direct linear on radiation dose compared to tube potential.

Double mAs will also double the radiation dose to the patient and mA does not produce energy shift in either portion of spectrum (McCollough et al., 2011).

2.7 Organ Dose

Organ dose is suggested to be used for estimation of individual radiation risks from multiple CT exposures (Ivanov et al., 2014b). Thus, in this study, organ dose is used to estimate the potential risks to personal. Few methods have been developed to estimate the specific organ dose such as using computational software and specific patient size-based method (Gao et al., 2018; Papadakis et al., 2016). Based on previous studies, the highest organ dose value was noted at the eye lens during CT head examination among all CT procedures (Barros, 2012; Karim et al., 2016). Theoretically, biological sensitivity of the tissue or organ would not have the same potential biological effect (Medicine, 2008). For example, the effect of 100 mGy dose to the pelvis is not same with 100 mGy effect on extremity. Body habitus and age also play a role in the biological effects (Hall & Brenner, 2008). However, biological effects of low dose X-ray are still debatable, and the biological effects associated with low dose exposure have been investigated for more than a century. Moreover, there is still no clear answer regarding low level radiation can induce cancer mortality. Then, the progressively larger epidemiologic studies are needed to investigate the risks of low doses of radiation (Brenner & Georgsson, 2005).

2.8 Effective Dose (ED)

Other studies suggested that cumulative effective dose is the best descriptor that reflects to the risk of radiation exposure in terms of an equivalent whole-body exposure associated with CT examinations (Aw-Zoretic et al., 2014; ICRP, 2007a; Smith-Bindman et al., 2015). The effective dose is derived from the weighted sum of tissues doses that sensitive to radiation and provide dose quantity related to probability of health detriment due to stochastic effects associated with low dose radiation exposure (Martin, 2007). Effective dose is one of the most frequently reported measurements used to facilitate the comparison of biological effect between different types of diagnostic examination.

Previous studies reported that CT imaging resulted in higher average effective doses which ranged between 2 – 20 mSv (Cohnen et al., 2003; Griffey & Sodickson, 2009). Recent study showed that the highest effective dose is received during CT trunk imaging with mean value of 12.2 ± 3.3 mSv among other types of CT examination (Vilar-Palop et al., 2016). However, effective dose cannot be used to estimate the dose and radiation risk to specific individual. Li et al., (2011) suggested the term risk index to accurately estimate individual patient risks (Li et al., 2011). Effective dose is usually used to cover general population and its calculation involves many assumptions, including a mathematical model of a standard human that does not accurately reflect to one individual (Ivanov et al., 2014a; Medicine, 2008). Effective dose can be used to optimise the examination and compare the risks between proposed exams.

Theoretically, the effective dose is age dependent. Thus, for the same absorbed organ doses, the calculated effective dose would vary in patients of different ages due to differences in radiation sensitivities of the tissues (Griffey & Sodickson, 2009). The younger age of patient received the radiation exposure, the higher the risk of cancer induction. Theoretically, the paediatric population is more sensitive and susceptible to radiation dose compared to the adult. This is due to the proportion of dividing cells in an organ that is more sensitive to radiation, which will decreases with increasing age (Barros, 2012; Brenner & Georgsson, 2005). The statement was also supported by previous researchers, they identified that the neonates are at four times higher risk of lifetime cancer compared to adults (Huda & Vance, 2007).

Table 2. 2 Summary of radiation dose quantities commonly encountered in medical imaging.

Quantity	Unit	Comments
Air kerma	mGy	The kinectic energy transferred to electrons in air, measure in joules per kilogram and measured based on X-ray beam intensity.
Absorbed Dose	mGy	Radiation dose deposited into the organ and measured per unit mass of a substance.
Equivalent Dose	mSv	Indicates effects on specific individual organ and tissues
ED	mSv	Total effects of equivalent dose

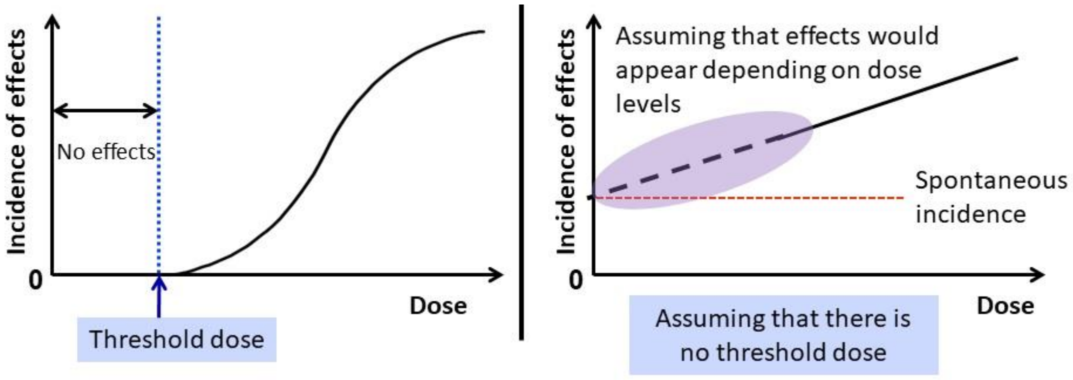
In the previous studies, the increased of cancer in victims of Hiroshima bomb and thyroid cancer in the survivor of the nuclear plant incident in Chernobyl in 1986 increased the concern of people regarding the risk of radiation. Risk projection methods allow the researchers to assess the potential magnitude of radiation-related cancer risks based on low-level radiation exposure. Generally, large study and long-term follow-up are needed to achieve accurate and effective statistical outcome. In this study, the risk models will be used to calculate the risk of late stochastic effects and cancer induction associated with medical exposure.

2.9 Nonstochastic Effects (Deterministic Effects)

The severity of radiation dose towards the patient varies in different exposure setting. The nonstochastic effects are characterised based on the existence threshold dose and generally result from high dose exposure in a short time period. The exposure is linearly proportional relationship with the effects of radiation. It might appear within hours or days. Based on ICRP, 2007b, they assumed people who were exposed to the same dose of radiation and certain symptoms appeared in 1% of them, said dose is considered as threshold dose (ICRP, 2007b). On other word, radiation above the threshold dose can cause death and degeneration of many cells in one time and automatically increase the rate of incidence sharply (Barros, 2012; Hamada & Fujimichi, 2014). Examples of the nonstochastic effects are erythema (skin reddening), tissue skin burns, sterility, cataract formation and death. The effects are different at each dose exposure.

2.10 Stochastic Effects

This can happen to people who are exposed or non-exposed to the radiation. The effects can occur by chance and consist primarily of genetic and cancer induction effects. The effects do not have threshold and can cause in any dose level. The severity of effect is independent of the dose received. The high and low dose might induce the cancer, but the severity is unknown. The possibility radiation exposure at extremely low doses may exert some effects that can never be eliminated. Based on ICRP 2007, they assumed the effects would appear depending on dose levels and the developing of cancer might take years (ICRP, 2007b). However, the stochastic effects are very difficult to detect due to low radiation dose (below range 100 to 200 mSv). While the effects cannot determine conclusively, then the probability to estimate the risk is still possible. NDT resource centre, they showed US people risk rise from 20% for non-radiation workers to 21% for person who involved in radiation site (Linet et al., 2012). Furthermore, the effect of radiation in animals also provides the data on the reproductive changes in ovaries and testes and it will lead to hereditary effects. The stochastic effects can cause cancer, leukaemia and genetic disorder in the latent time. The higher radiation dose can shorter the latent effects.



(a) (b)

Figure 2.8 The graph of non-stochastic and stochastic effects or radiation. Deterministic or non-stochastic effect appear after a radiation dose exceeded threshold limit (a) while Stochastic can cause in the very low dose and no threshold (b). (Division, 2016)

The risk models have been provided by Biological Effects of Ionising Radiation (BEIR VII) committee for estimating the health effects and lifetime risk associated to low linear energy transfer (low-LET) radiation (National Research Council, 2006). In BEIR VII report, low radiation dose is defined as low-LET radiation ranged from almost zero up to 100 mSv (0.1 Sv) (National Research 2006).

In BEIR VII report, the risk models were developed to estimate the risk that an exposed individual will develop cancer. The risk models are based on the epidemiologic studies on survivors of the atomic bombs in Hiroshima and Nagasaki, as well as from follow-up studies after medical and occupational exposures. The cohort research from atomic bomb incidence has created a “gold standard” in determine the cancer risk due to low dose. The study focused on large population who were exposed to the radiation from the atomic bomb. The survivor from the accident were exposed to the low dose in range of 5 to 100 mSv, which approximately same with the dose from single or multiple exposure of CT scans (National Research Council, 2006).

Managing the risk of radiation typically involves establishing regulation that refers to the limit of radiation exposure to human. According to BEIR VII report, the response and risk of patient to develop cancer are associated linearly with the dose. There is a threshold for cancer induction, but the risk of radiation-induced cancer is small at low doses. Based on NCRP, low-LET radiation can affect all spectrum of tissue types where it will contribute to the overall cancer risk (NCRP 2009). Besides, low doses of radiation also contribute to non-cancer health effects such as heart disease and stroke and occur at certain dose threshold.

At doses of 100 mSv or less, it is difficult to evaluate cancer risk in humans due to statistical limitations. The linear-no-threshold (LNT) model is used to estimate the risks by extrapolation applied on the LNT model (National Research Council, 2006). Based on the atomic bomb study, Brenner (2007) found the risk of all solid cancers is consistent with a linear increase in radiation (Figure 2.9) and the children are much more radiosensitive compared to adult, which continuous decline in radio sensitivity based on age for most cancer. NCRP concluded that males have lower risk compared to female, largely due to the anatomical difference and risks to the ovary and breast. However, lung cancer is much higher in the male than female (NCRP, 2009). However, it should be noted, various countries with difference lifestyle and habitus might show larger risk compared to others.

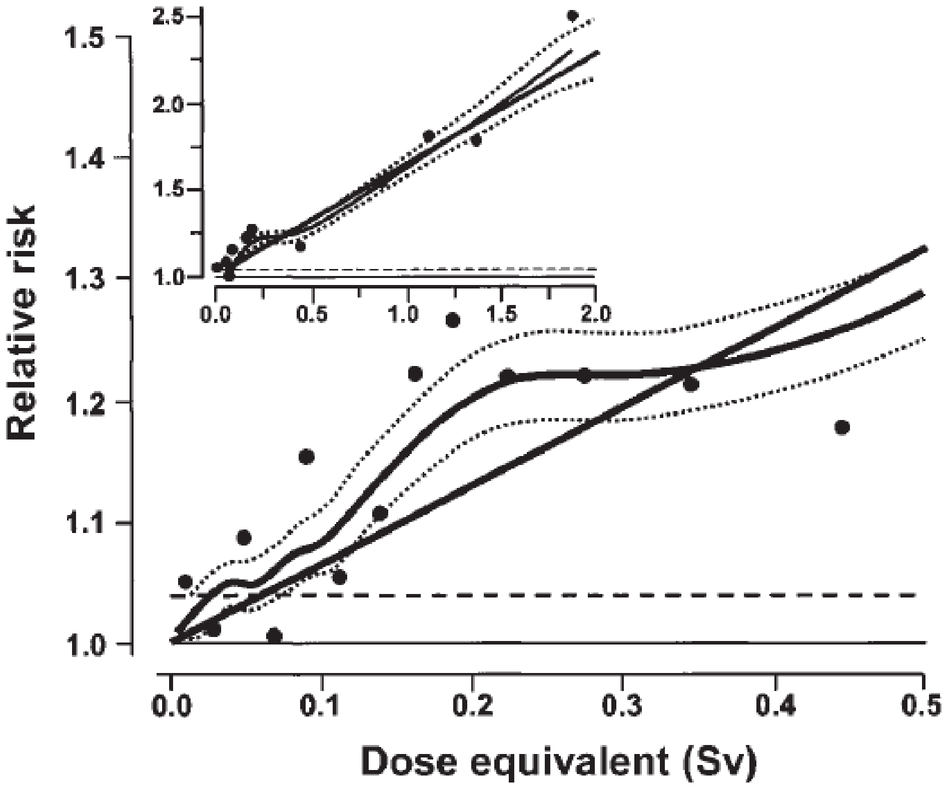


Figure 2.9 Estimated relative risk for cancer incidence in atomic bomb survivor. The graph showed the relative risk was increase directly proportionally with dose receive by radiation when expose. (Brenner et al., 2003)

In preventing the unnecessarily high dose to the patient, the excess absolute risk (EAR) and lifetime attributable risk (LAR) of organ dose will be used as the reference for establishing the minimum multiple CT scan examination scanning for the patients in single year. Based on BEIR VII report, LAR is calculated using the survival function for a population unexposed to radiation and is a close approximation of the more general risk of exposure -induced cancer (REIC). The LAR and REIC are virtually identical to estimate the survival within the dose received by the patients. LAR can also be converted to the percentage of the total expected cancer incidence (Griffey & Sodickson, 2009).