COMPARISON OF EFFICACY BETWEEN 128-SLICE MDCT COLONOGRAPHY AND CONVENTIONAL COLONOSCOPY IN DETECTING COLORECTAL POLYPOID LESIONS

BY

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ABBREVIATION

CTC	**Computed Tomography Colonography**
CC	**Conventional Colonoscopy**
CRC	**Colorectal cancer**
HUSM	**Hospital Universiti Sains Malaysia**
ASR	**Age-standardized incidence rate**
DCBE	**Double-contrast barium enema**
BARCO	**Belgian-American Radio Corporation**
PACS	**Picture Archiving and Communication System**
IBD	**Inflammatory bowel disease**
FOBT	**Faecal occult blood test**
MAKNA	**Majlis Kanser Nasional**
HNPCC	**Hereditary non-polyposis colorectal cancer**
CO2	**Carbon dioxide**
MPR	**Multiplanar reformatted**
MAP-EM	**Maximum a Posterior Expectation-Maximization**
SSD	**Shaded Surface Display**
C-RADS	**CT Colonography Reporting and Data System**
ALARA	**As low as reasonably achievable**
CAD	**Computer-aided detection**
FBP	**Filtered back projection**
AIDR3D	**Adaptive iterative dose reduction 3 dimensional reconstruction**

ABSTRAK

Objektif: Untuk menentukan keberkesanan dan persetujuan di antara "128-slice Multidetector Computed Tomography" kolonografi dalam mengesan ciri-ciri ketumbuhan polip kolorectal berdasarkan saiz, kedudukan dan morfologi berbanding dengan kolonoskopi konvensional.

Metodologi: Kajian ini telah dijalankan dari Julai 2013 sehingga Jun 2016 di Jabatan Radiologi dan Unit Endoscopy, Jabatan Pembedahan Hospital Universiti Sains Malaysia (USM). Seramai 75 subjek yang simptomatik dan terbukti secara klinikal telah menjalani CT kolonografi dan kolonoskopi konvensional. Kelulusan etika telah diperolehi dari Jawatankuasa Etika Penyelidikan Manusia USM (JEPeM). Dalam kajian ini, imej CT skan diperolehi menggunakan 128-slice CT dan analisis dilakukan dengan menggunakan PACS and VitreaCore (version 6.7.2020). Subjek adalah berumur dalam lingkungan 22 ke 82 tahun dengan umur purata adalah 56.1±16.0 tahun. Majoriti daripada subjek adalah lelaki (65.3%) dengan nisbah lelaki kepada perempuan adalah 2:1. Kebanyakkannya adalah Melayu (81.4%).

Keputusan: Hanya 46 subjek mempunyai ketumbuhan polip kolorektal dan 29 subjek adalah normal dalam kedua-dua CT kolonografi dan kolonoskopi konvensional. Sebanyak 294 ketumbuhan telah dikenalpasti melalui CT kolonografi, hanya 162 ketumbuhan telah dikesan dalam kedua-dua pemeriksaan. Manakala 132 ketumbuhan tidak dapat dikesan melalui kolonoskopi konvensional sebagai ketumbuhan positif palsu.

Peratusan pengesanan berdasarkan saiz ketumbuhan adalah tinggi bagi CT kolonografi. Untuk ketumbuhan bersaiz di antara 5 ke 9 mm, peratusan pengesanan untuk CT kolonografi dan kolonoskopi konvensional adalah 37.1% dan 2.4%. Peratusan

pengesanan bagi ketumbuhan bersaiz lebih dari 9 mm untuk kedua-dua pemeriksaan adalah 40.8% dan 32.0%. Manakala, peratusan pengesanan bagi ketumbuhan bersaiz kurang dari 5 mm adalah sama di antara kedua-dua pemeriksaan iaitu 22.1% dan 20.7%.

Berdasarkan lokasi ketumbuhan, kolonoskopi konvensional telah mengesan lebih banyak ketumbuhan polip kolorektal pada rectum (10.9%). CT kolonografi mengesan kebanyakkan ketumbuhan pada kolon menaik dan rektum iaitu 17.7% untuk setiap lokasi. Berdasarkan morfologi ketumbuhan, peratusan pengesanan bagi ketumbuhan polip kolorektal adalah tinggi dalam CT kolonografi berbanding kolonoskopi konvensional. Kesemua ketumbuhan polip kolorectal dalam CT kolonografi mempunyai atenuasi "soft tissue" berdasarkan nilai atenuasi dalam unit Hounsfield.

Dalam kajian ini, persetujuan di antara CT kolonografi dan kolonoskopi konvensional telah dibuktikan melalui Cohen's kappa statistik (analisis persetujuan kappa) dalam menentukan saiz, kedudukan dan morfologi ketumbuhan polip kolorektal. Terdapat persetujuan yang sederhana (dengan nilai kappa 0.431) di antara CT kolonografi dan kolonoscopi konvensional dalam menentukan size ketumbuhan. Dalam CT kolonografi, terdapat pertambahan peratusan pengesanan ketumbuhan polip kolorectal yang bersaiz melebihi 9 mm. Terdapat persetujuan yang ketara dan hampir tepat di antara CT kolonografi dan kolonoskopi konvensional dalam menentukan morfologi dan lokasi ketumbuhan dengan nilai kappa 0.990 dan 1.000 (McHugh, 2012).

Kesimpulan: CT kolonografi berpotensi untuk mengesan ciri-ciri ketumbuhan polip kolorektal berbanding dengan kolonoskopi konvensional berdasarkan saiz, kedudukan dan morfologi ketumbuhan. Walaubagaimanapun, kedua-dua CT kolonografi dan kolonoskopi konvensional adalah merupakan teras dan modaliti utama yang saling melengkapi antara satu sama lain untuk mengesan ketumbuhan polip kolorektal.

ABSTRACT

Objectives: To determine the efficacy and agreement between 128-slice MDCT colonography (CTC) in characterise the colorectal polyp mucosal lesions based on size, location and morphology in comparison with conventional colonoscopy (CC).

Methodology: A cross-sectional study was conducted from July 2013 till June 2016 in Department of Radiology and Endoscopy Unit, Department of Surgery, Hospital Universiti Sains Malaysia (USM). Seventy five subjects who were symptomatic for colorectal carcinoma and clinically indicated for CC were included. Ethical approval obtained from The Human Research Ethics Committee of USM (JEPeM). Image acquisition obtained by using 128-slice CT scan and image analysis performed using PACS and VitreaCore (version 6.7.2020). They ranged in age from 22 to 82 years with mean age of 56.1±16.0 years old**.** Majority of subjects are male (65.3%) with male to female ratio of 2:1 and Malays (81.4%).

Results: Only 46 subjects had positive colorectal polyp lesions and 29 subjects had normal findings on both CTC and CC. A total of 294 lesions were detected on CTC, only 162 lesions detected in both CTC and CC. However, 132 lesions were not detectable on CC as false positive. CTC showed a high percentage of detection based on the size of the colorectal polyp lesions as compared to CC. For lesions with size in between 5 to 9 mm the percentage of detection in CTC and CC were 37.1% and 2.4%. The percentage of detection for lesion size more than 9 mm in both CTC and CC were 40.8% and 32.0%, respectively. However, equal percentage of detection of lesion size less than 5 mm which were 22.1% and 20.7%, respectively. For the segmental localization, CC was detected a

higher number of polyp lesions in the rectum, 10.9%. However, in CTC most of the colonic polyp lesions were detected in the ascending colon and rectum which accounted 17.7% for each segment. The percentage of detection of lesion morphology was higher in CTC as compared to CC. All the detected colorectal polyp lesions in CTC were soft tissue attenuation based on in Hounsfield Units.

In this study, the degree of agreement between CTC and CC examinations were proven by Cohen's kappa statistic (kappa agreement analysis) in determining the size, locations and morphology of colorectal polyp lesions. There was significant moderate agreement (kappa value of 0.431) in determination of the lesion size for CTC and CC. In CTC, increase in percentage of detection for colonic polyp lesions more than 9 mm. There was significant almost perfect agreement between findings by CTC and CC in determination of the lesion's morphology and location with kappa value of 0.990 and 1.000, respectively (McHugh, 2012).

Conclusion: CT colonography has a better performance and is ahead in front of CC in the detection and characterization of the colorectal polyp lesions based on size, location, and morphology. However, both CTC and CC were considered as backbone and prime modality that complementing each other in detection of the colorectal polyp lesions.

CHAPTER 1: INTRODUCTION

1.1 Introduction

The National Cancer Council Malaysia (MAKNA) and National Cancer Registry Report found colorectal cancer (CRC) as the third most common cancer after lung and breast cancer. CRC was an eleventh Malaysia's top fifty causes of death based on the age-standardized death rate per 100,000 populations. According to the age-standardized incidence rate (ASR) of CRC in Malaysia, Chinese ethnicity (ASR 27.35%) was reported as the highest followed by Malays (ASR 18.95%) and Indians (ASR 17.55%). The ASR for CRC was reported higher in males (ASR 24.16%) rather than females (ASR 18.14%) (Muhammmad *et al*. 2016). In 2014, Andrea *et al.* has documented that the CRC is mainly a disease of elderly with incidence of CRC rises sharply after the age of 40 year old and 90% of cases occur over the age of 50 years.

In Malaysia, early prevention of the CRC had been implemented through various interventional programmes such as targeted CRC screening and strategic health education. The pre-malignant polyp and early-stage CRC detection via conventional colonoscopy (CC) and CT colonography (CTC) screening programmes followed by resection can be life saving as majority of the CRC develop from an ever-growing benign adenomatous polyp over the years (Muhammmad *et al*., 2016).

In the past, the most preferable method among clinicians and surgeons in identification of colonic disease or abnormality was by using the CC, also known as optical colonoscopy (OC). It provides a dual purpose to the clinical investigators by a direct visualization of the colonic mucosal surface or lesions combined with biopsy or direct treatment to the lesions in

the same setting. However, lack of acceptance by some patients due to invasiveness, time-consuming and complications from sedative effect (Douglas *et al*., 2006).

Traditionally, double-contrast barium enema (DCBE) were used as a supportive imaging tool for diagnosing CRC with less risk of bowel perforation accounted about 1 in 25,000 cases. Its sensitivity is less than 70% in detecting polyp of size from 5 to 20 mm and about 85% in detecting cancer. At some extent, it shows a degree of difficulty that limits the performance especially in the old-age individuals and less or non-mobilized patients. Other issue of consideration is a study technique due to poor coating of the colonic mucosal lining that may leads to a less accurate finding for colonic lesion detection mainly for the small size polyp (Rockey *et al*., 2006).

CTC is a rapidly evolving imaging technique considerably due to rapid advances in CT hardware and software since its discovery in 1994 by Viking et al. It is a noninvasive, attractive alternative and well tolerated by patients with specificity and sensitivity similar to CC. A great amount of researchers are interested for CTC advancement including image visualization, formation and segmentation for the purpose of screening of the entire colon. American Cancer Society, the American College of Radiology and the United State Multi-Society Task Force had recommended CTC as a widely used valuable tool in detecting colorectal polyp lesions and CRC as compared to CC and DCBE.

Over the years, CTC has been endorsed by the national guidelines as a potential CRC screening method in detecting small colonic polyps especially for those who are symptomatic

for the suspicion of malignant colonic pathology or early-stage of CRC. In view of its great advantages of mimicking the endoscopic colonic visualization without the needs of any endoscopic instrumentation, it may displays an accurate cross sectional imaging study that allows intraluminal evaluation combined with transmural and extra-colonic assessment. It provides a better assessment of the entire colonic mucosa including accurate segmental localization, detection of the colonic abnormalities proximal to the obstruction site, complete surgical margin of the colorectal lesions and presence of synchronous lesion in those who has been diagnosed with CRC (Martin e*t al*., 2011).

Many medical institutions and societies have performed reconstructed researches for further updating the advance software algorithm in detection and evaluation of the colonic mucosal lesions (Perry e*t al*., 2011). It is necessary for the radiologists to have the knowledge, skills and experience to identify those colonic lesions. Radiographers are also responsible for CTC protocol and techniques applications. All members of the CTC team need to be able to recognize complications arising before, during or immediately after the procedure and should follow proper recognized protocols to manage any such complications.

To date, the reported constructed research used 16- or 64-slice CT scanners as their test tool and in some studies type of CT machine was not documented. From my literature review, as there was limited previous studies that concentrate on the efficacy of CTC over CC, so this will be the first study use 128-slices CT scan to determine the efficacy of CTC in detecting colorectal mucosal lesions (Emanuele e*t al*., 2010). In our study center, Hospital Universiti Sains Malaysia (HUSM), CTC is considered new but it is a promising tool which involved the

conversion of the digital data into near as good as direct visualization of the colonic mucosa by the gastroenterologist during CC. The main principle is a CT scan with higher slice count can illuminate some of the CT scanner technical capabilities as a higher slice count reduces scan time and produces a high image resolution. Basically, it may provide incredibly sharp 3-dimensional colonic image. However, in our region the implementation of CTC remains less and rather new to both radiologists and surgeons. Therefore, with this study design, it is hope that we can make full use of the more convenient and less invasive procedure which wins both parties, the researchers and the under investigate customers.

CTC is a high technology dependent examination and expected to be ameliorated by the non-stop concrete improvements in the near future. Both CTC and CC should be considered as prime modalities that complementing each other for disease assessment rather than considering them as competing diagnostic tools. These two investigations form the backbone of the imaging protocol in depicting the colorectal pathology that greatly facilitates the appropriate treatment of the disease.

Therefore, this study aims to compare the efficacy and agreement of the CTC in detection and characterization of the colorectal mucosal polyp lesions based on size, location and morphology in correlation with CC. Hope it may gives a betterment in optimization of CTC implementation in Malaysia generally and HUSM particularly.

1.2 Study Objectives

1.2.1 General objective:

To determine the efficacy and agreement of 128-slice MDCT colonography (CTC) in characterise the colorectal polyp mucosal lesions in comparison with conventional colonoscopy (CC).

1.2.2 Specific objective:

i. To determine the efficacy of CTC in characterise the size, morphology and localization of colorectal polypoid mucosal lesions in comparison with CC.

ii. To determine the agreement between CTC and CC in detecting colorectal polypoid mucosal lesions according to size, morphology and site.

CHAPTER 2: LITERATURE REVIEW

2.0 Literature Review

Colorectal cancer (CRC) has become as one of the leading causes of death, particularly in the Western world with 1,000,000 new cases occur per year. The death estimation rate of about 50% people who diagnosed with CRC died of the disease (Parkin *et. al.* 2002). CRC is the third most common cancer in men, which accounted 10.0% of the total cancers, and the second in women accounted about 9.4% of the total cases, worldwide (Charu[DI] et al. 2013).

In 2014, the statistics from the American Cancer Society (ACS) reported CRC as one of the leading cancer in the United State. CRC ranks the third most common cancer and the second leading cause of death with estimated 150,000 newly diagnosed cases and more than 50,000 died at advanced stage of the disease (Siegel *et al*., 2014). A study done by Seong *et al*. (2011) had stated the presence of synchronous lesion or cancerous lesions in 1 to 7% of patient who earlier has been diagnosed with CRC. In Egypt, CRC is one of the most common malignant neoplasms and considered to be the fourth most common cancer which accounted about 6.1%, followed by urinary bladder cancer, breast carcinoma and lymphoma (Ayman *et al.* 2013).

Incidence of CRC was found to be increasing among Asians mainly in Japan, Hong Kong and Singapore from 1983 till 2006 (Tamura *et al*. 1996). Overall, increased incidence of CRC was recorded in Malaysia as the third highest in rank (18.30 per 100,000) among the countries in South East Asia. The highest mortality rate is exhibited by Brunei (12.0 per 100,000). The survival rate depending on the mortality-to-incidence ratio which is greatest in

Singapore, Brunei and Malaysia. In Malaysia, CRC is found to be the second most common cancer analysed by the National Cancer Registry Report of 2007 (Yee *et al*. 2010).

A known factors that increase the risk of CRC includes those with (1) a first-degree relatives that diagnosed with CRC or a large adenomatous polyp before the age of 60 years, (2) an inflammatory bowel disease, (3) a family history of familial adenomatous polyposis (FAP) or hereditary non-polyposis colorectal cancer (HNPCC) syndromes, and (4) a prior history of adenomatous polyps or colon cancers. However, approximately 75% of all cases of CRC occurrence were without specific risk factors (Micheal *et al*. 2005).

According data analysis from National Polyp Study on the adenoma-carcinoma theory, adenomatous polyps are the precursors of most CRC. A study done on 5066 removed polyps in 2362 patients, 66.5% were adenomatous, 11.2% were hyperplastic, and 22.3% were other types (normal colonic mucosa, inflammatory or juvenile polyps, or other less common entities). Up to 90% of all CRCs are likely to develop through a series of genetic mutations and alterations from a small adenomas which was only 5 mm size, transformed into large adenomas about 10mm in size, then into non-invasive carcinoma and finally into invasive carcinoma. Average estimation of the transformation rate of the large about 10 mm size adenomatous polyp into cancerous lesion is about 5.5 years (Ronald *et al.* 2010).

CRC incidence and mortality have been decreased in the recent decades due to effective screening for and removal of the precancerous polyps or suspicious colonic mucosal lesions. This is really depends on the accurate identification and resection of these relevant lesions

especially precancerous colonic polyps before their transformation into frank malignancy. Besides, there were several cases of premalignant precursor which missed on segmental non-blinded CC study (Joseph *et al.* 2015).

In view of implication for patient care, CTC and CC may be complementary to one another as both studies considered equivalent in term of sensitivity for CRC detection (Pickhardt *et al.* 2011). CTC is a distinct and complementary modality for colonic polyp or advanced colonic neoplasia detection which is equivalent overall to CC. CTC helps in detection of right sided colonic evaluation which can be missed by using CC (Dustin *et al.* 2015). Most colorectal cancers missed at CTC were located in the left-sided colon due to less distension predominantly involving the rectosigmoid colon, rectum and proximal to the splenic flexure. However, most cancers on the right-sided colon were difficult to be assessed by CC due to increase distance in physical endoscopy complicated with colonic tortuous angulations and redundancy. As a result, both studies are complementary to each other (Perry J, *et al.* 2011).

Non-detection of the proximal synchronous lesion especially in incomplete CC study due to impassable obstructing mass was a major dilemma to the gastroenterologists. In the new era of CTC, there is a great solution for the detection of the synchronous lesions proximal to the distal occlusive mass, which provides a paramount pre-operative evaluation of proximal colon, and any synchronous lesions. In post-surgical patient, CTC is an accurate tool for practical surveillance even without clinical or laboratory evidence of recurrence with less-invasiveness to both colon and extra-colonic organs or structures (Kunwarpal *et al.* 2015). In recent conducted study demonstrated the efficacy of the CTC in detection of colorectal polyp lesions and masses.

It showed 83% sensitivity and 95% specificity with positive predictive value (PPV) of 95% and a negative predictive value of 83% according to the size of the colonic mucosal or colorectal polyp lesions (Cigdem *et al*., 2016).

In CTC, several techniques need to be considered for study optimization including (1) proper bowel preparation in colonic cleansing strategy as residual colonic stool or liquid could leads to a false positive and false negative results (Ayman *et al.* 2013), (2) faecal tagging method as residual faecal marking strategy that helps to distinguish fecaloid materials from the actual colonic lesions (Kaan Meric *et al.* 2015), (3) adequate bowel distension with a sufficient colonic insufflation via the silicone tip that placing in the rectum while patient in the left lateral decubitus position either by using the room air or carbon dioxide (CO2) depending on the patient's tolerance. This method to prevent false positive and false negative results due to significant amount of residual fecal matter and colonic fluid or water lakes (Andrea *et al*. 2014), (4) spasmolytic agents such as Hyosine-N-butyl Bromide 20mg (Buscopan) is an optional and given intravenously with the purpose to reduce patient discomfort by minimizing the bowel peristalsis and possible colonic spasm during examination which provides better colon distension. However, it is contraindicated in those with glaucoma, prostatic hypertrophy and heart disease (Kaan Meric *et al.* 2015), (5) intravenous contrast medium administration to facilitates the detection of colorectal polyp lesions especially in the presence of a large amount of residual colonic fluid and to interrogates the extra-colonic organs or structures involvement as part of staging element especially in the cases of distant metastases. Image acquisition performed during portal venous phase in supine and prone positions (Christine et al. 2013).

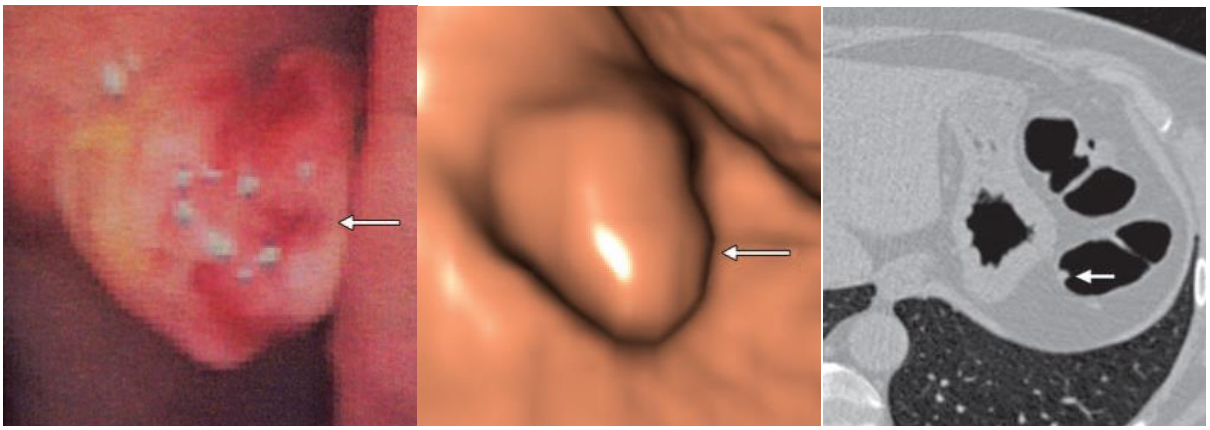
Some researchers implemented several type of post-processing software application such as (1) basic 2-dimensional incorporates with multiplanar reformatted (MPR) images, (2) 3-dimensional visualizations displays which supplemented with an endoluminal reconstruction image that allows time-efficient navigational fly through of the colonic lumen in two directional pathways which are antegrade and retrograde pathways that responsible in visualization of the blind spots that may exist behind a prominent haustras (Martinez et al. 2013), (3) segmentation algorithms with a proper colonic wall extraction supported by both geometric and textural information analysis gives potential image accuracy for a proper detection of early sign of colonic abnormality. Examples of segmentation algorithms are maximum a posterior expectation-maximization (MAP-EM) (Zhengrong *et al*. 2010) and electronic colon cleansing (ECC) (Shmuel *et al.* 2009), and (4) shaded surface display (SSD) is one of the image reconstruction software system for trimming off the unnecessary part with Scalpel program, together with magnification and rotation methods.

In some centres, the most recommended application software systems were automated system (Vitrea 2, and V3D-Colon) or semi-automated system (Navigator) which flight from rectum till caecum or vice versa with continuous colonic air column based on 2-dimensional and 3-dimensional images. Of the three application software systems, the navigational success rate of the V3D-Colon system was significantly higher than the other two systems with p value less than 0.001 (Martinez et al. 2013). The excellence foundations of the V3D-Colon software system includes "electronic cleansing" or digital subtraction of an opacified luminal fluid or water, ability to flip back and forth between supine and prone scans without exiting the viewer, a “centerline path” which skips over collapsed segments, display an overview colon "road map"

that can be used for placing bookmarks or arrows at point of interest, displays a real-time position indicator, shows percentage estimation of colonic mucosal surface that visualized during 3-dimensional evaluation, provides translucency rendering image that allows internal density evaluation of a colorectal polyp lesion. However, the features were not seen in the other two systems. In the Navigator and V3D Colon software systems, a truer automated centerline path allows improvement in surface visualization with smooth endoluminal flight. In Vitrea 2 software system, the automated flight path appeared “discontinuous” and close to the sidewall, resulting in poor colonic surface visualization. Besides, for the Vitrea 2 application software system, the colon CT "3D lit fly-through" was used with "direct light-shiny" rendering and "CT fat–muscle–bone" coloring (Perry *et al.* 2003).

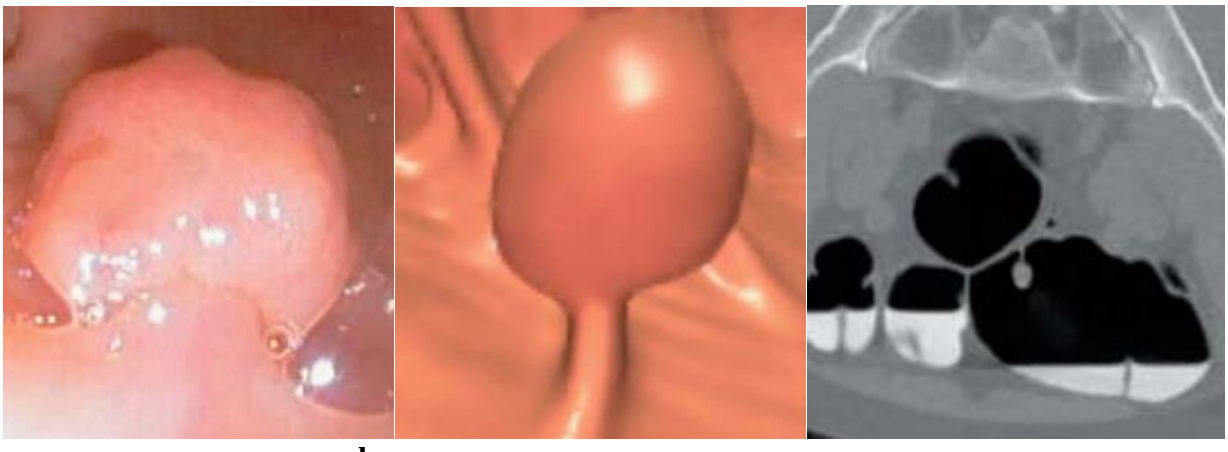
A term “polyp” is defined as any colonic lesion that bulges into the colonic mucosal surface or projecting intraluminally with smooth contour, homogeneous soft tissue attenuation and fixed point of attachment to the colonic wall. A “mass” is defined as any colonic lesion with soft tissue attenuation and size is greater than 3 cm in its largest dimension (Joseph *et al.* 2015). The characterization of the colorectal polyp includes lesion size in millimetres, segmental location, and morphology features such as sessile, pedunculated or flat. A sessile polyp is the most frequent detected morphological appearance with a broad base of implantation and width greater than vertical height which attached to the colonic wall and do not move with changes in patient’s position (**Figure 2.1**). A pedunculated polyp is characterized by presence of stalk or pedicle with a well-defined head that moves to the dependent portion when change in position. The length of the stalk determines the degree of mobility of polyp’s head. In certain extent, it can simulate feaces (**Figure 2.2**). A flat polyp is more difficult to be detected but with

high sensitivity on CTC. It was defined as plaque-like colonic lesion with broad based. The commonest documented diameter is about 6 to 29mm and height of 3mm or less (**Figure 2.3**) (Paola *et al.* 2015).



a. **b.** **c.**

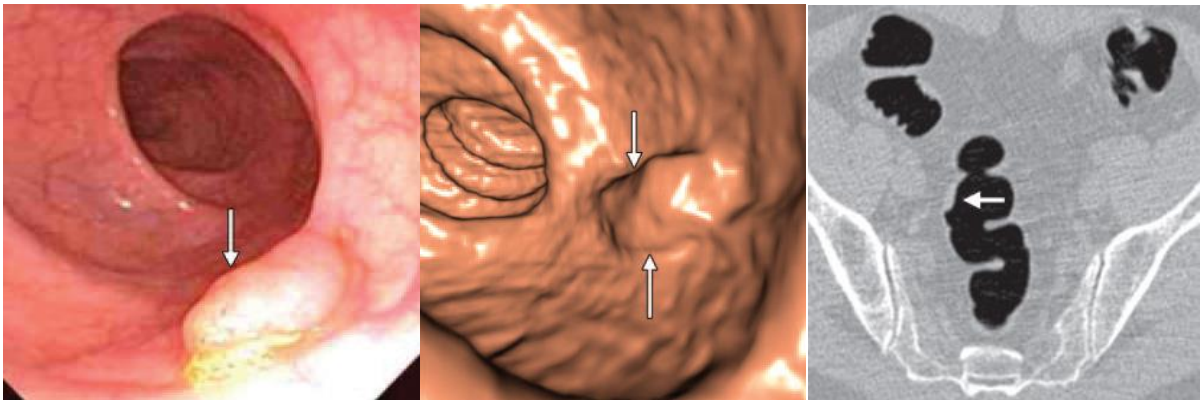
Figure 2.1. A 5.0 mm splenic flexure sessile polyp in a 53-year-old man. **(a)** Conventional colonoscopy image shows identical sessile polyp (arrow), **(b)** 3-Dimensional endoluminal CT colonographic image shows sessile polyp, **(c)** Axial CT image obtained in supine position shows small colonic polypoid lesion (arrow) in the splenic flexure.



a. **b.** **c.**

Figure 2.2. Solitary 16 mm pedunculated caecal polyp in a 55 year old man. **(a)** conventional colonoscopy shows pedunculated polyp in caecum, **(b)** a 3-dimensional endoluminal "fly-

through" view shows the caecal polyp, **(c)** axial two-dimensional CT image (in prone) shows the polyp with a stalk within the air-filled cecum.



a. **b.** **c.**

Figure 2.3. A flat polypoid morphology in the sigmoid colon in a 64-year-old man, **(a)** Conventional colonoscopic view shows flat polypoid morphology (arrow) in the sigmoid colon, **(b)** 3-Dimensional endoluminal CT colonographic view shows flat polyp (arrows), measured 2 mm in height and 12 mm in width, **(c)** Axial CT image shows barely perceptible raised lesion (arrow) in sigmoid colon.

The study done by Charu *et al.* (2013), [D2]patients were divided into three groups according to the size of the lesions; 10mm and above, between 6mm and 9mm, and 5mm and below. Basically, the targeted lesion in CTC is the advanced colorectal adenoma with the size of more than 1 cm and presence of villous component which may shows high grade dysplasia with a greatest risk of progression to the cancerous lesion. Other lesions that can simulate colorectal polyps such as neoplasms, submucosal lesions, non-tagged faeces, pseudopolyps, impacted diverticula or postsurgical changes need to be evaluated properly and thoroughly (Martinez et al. 2013).

Based on CT Colonography Reporting and Data System (C-RADS), the polyp size was directly correlated with the risk of malignancy which may determine and influence the clinical

managements. In this system, category C2 is recommended for surveillance or CC and category C3 for CC. However, a consensus from multiple national medical institutions and societies recommend an immediate polypectomy for all polyp size of 6mm or larger **(Table 2.1)**. In the meantime, the most preferable display on CTC for an accurate polyp assessment and diameter measurement is in 3-dimensional view due to its resemblance to CC (Ronald *et al.* 2010).

Table 2.1. CT Colonography Reporting and Data System (C-RADS) categories

Category	Diagnosis	Follow-up Recommendation
C0	Inadequate study/awaiting comparisons	Obtain comparisons
C1	Normal colon or benign lesion; no polyp ≥ 6 mm	Routine screening every 5–10 years
C2	One or two 6–9-mm polyps or indeterminate finding	CT colonography surveillance or colonoscopy
C3	Polyp ≥ 10 mm or three or more 6–9-mm polyps	Colonoscopy
C4	Colonic mass, likely malignant	Surgical consultation

Source: Radiology Society of North America 2005:236:3-9.

Several factors that may influence the polyp size measurements either due to acquisition factors, display factors or measurement factors. Acquisition factors include spatial resolution and partial volume averaging, motion, and image noise. Display factors include the use of 2-dimensional multiplanar versus three-dimensional endoluminal images, the choice of rendering thresholds and window settings, the quality of the colon segmentation, and the effects of high-attenuation endoluminal contrast agents. Measurement factors include observer variability and choice of measurement tools (Damian *et al*. 2007). In spatial resolution, partial volume effects due to a collimation or thicker reconstruction interval may cause inaccurate measurement especially for a smaller size colonic polyp. An effective depiction of colonic polyp morphology

is directly correlated with the section thickness as compared to polyp size. Thus, the recommended options are less than 2.5 mm collimations and 1.25 mm or less for reconstruction intervals for better polyp size measurement. Difficulty in colonic polyp detectability due to motion artefacts produce by bowel peristalsis and bulk patient motion that may adversely affecting polyp size measurement. These problematic matters can be overcome by using a single breath hold technique as the bowels peristalsis is sufficiently intermittent or low amplitude on the time of scan duration (Ronald *et al.* 2010).

A rendering threshold technique that applied in the 3-dimensional endoluminal surface reconstruction of CTC can affect the colorectal polyp size measurement. The variation of the threshold setting is highly sensitive to the shape and size of polyp as in complicated condition it may cause disappearance of the polyp especially the smaller size. The recommended rendering threshold for accurate polyp size measurement was approximately -500HU (midway between air and water attenuation). Similarly, the window width and window level values on a 2-dimensional CTC images need to be adjusted accordingly for an accurate polyp size measurements (Pickhardt et al. 2003).

In a study done by Thomas et al. (2004) stated the presence of intrinsic and extrinsic factors on 2-dimensional and 3-dimensional images that influence colonic polyp visualization. Intrinsic factors affecting polyp conspicuity are size, shape morphology, and surface contour. The extrinsic factors includes the relationship of polyp to folds or flexures of the colon, distension or collapse of a colonic segment and quality of preparation based on the amount of residual fluid or stool post-colonic cleansing.

For the image interpretation and analysis, the colorectal polyp lesion and colonic segmental localization were evaluated by dividing the colon into six segments which are caecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, sigmoid colon, and rectum (Rogier *et al*. 2004). On CTC, majority of the CRC involvement is highly detected in the rectosigmoid colon accounted 66.4% followed by the right side of the colon about 26.3% and transverse colon in 2.6% of patients. Increased occurrence of colorectal pathology in the rectosigmoid region was found to be statistically significant with p value less than 0.05 on applying non-parametric Chi Square test (Emanuele *et al*. 2010)[D3]. An extracolonic findings on CTC were evident in 92.1% of patients with the most common finding was regional lymphadenopathy accounted about 50% of patients. Other findings included visceral or peritoneal involvement by tumoural spread or metastases (Urszula *et al.* 2014).

As CTC is increasingly used as a screening procedure for patients at average risk of CRC, the radiation dose minimization needs to be considered to maintain the appropriate benefit to risk ratio. Fortunately, a low radiation dose for CTC together with advanced application software may give a relatively high contrast between the colonic wall and the intraluminal bowel gas or content and leads to optimum image quality. The CTC feasibility mainly needs an effective mAs (milliAmpere seconds) of only 10 to 50, enabling a complete supine and prone examination to be done with a total radiation dose of approximately 1.0 to 6.0 milliSieverts (mSv) (Jay P Helken *et al*. 2005).

The concern of using a multi–detector row scanner with thin collimation is increase the exposure dose due to a penumbra effect of radiation which does not contribute to the image quality. To reduce the hazardous effect of radiation by increasing pitch and collimation or decreasing the peak voltage or milliAmpere seconds level (mAs). The mAs is in direct proportion to the absorbed dose with inverse proportion to the image noise. It can be substantially reduce due to extremely high tissue contrast between insufflated gas and the colonic wall without sacrificing polyp detectability. The reduction of the radiation exposure for a proper effective dose can be further applied with recent advancement of the dose-reduction techniques via the automatic tube current exposure and dose modulation (Micheal *et al*. 2005).

For the radiation exposure risk, the efficiency of the CTC for detection of the colorectal lesions combined with low radiation dose is highly recommended as a better screening tool which includes the modern CT hardware optimization, statistical image reconstruction and low-dose raw data acquired by low-mAs protocol. The hazardous effect of ionizing radiation is a major concern to the public. Thus, CTC should follow the principle of maintaining radiation dose as low as reasonably achievable (ALARA) by decreasing radiation dose to the minimum level without compromising the image quality (Zhengrong *et al*. 2010).

In a study by Hesong et al. (2015), the absolute lifetime risk for cancer induction from a normal dose of CTC is 0.14% in a 50-year-old patient and about 0.07% in a 70-year-old patient. Overall, the 6% mortality risk from CRC outweighs the small cancer risk from CTC radiation exposure. Therefore very low dose scanning protocols are emphasized which include optimization of reducing the radiation exposure with preserved an excellent image quality. Even

with the usage of multi-slice scanner, radiation dose is maintains at the minimum risk by reducing the tube current or mAs.

Basically, an optimum radiation dose with good image quality was crucial in CT colonographic image reconstruction by using filtered back projection (FBP) and a newly introduced adaptive iterative dose reduction three-dimensional (AIDR3D) reconstruction. The former methods to decreasing the radiation dose includes reducing tube current dose (mAs) and tube voltage, increasing gantry rotation and table speed and applying automatic tube current modulation. With AIDR3D reconstruction that balancing the noise suppression and quality details via establishment of a noise model, together with FBP image as original building blocks and utilizing statistical and algebraic iterative algorithm for X-ray noise and electronic noise filtering. Radiation dose was calculated as equal to (dose-length product) × (conversion factor), a conversion factor is refers to conversion factor of different body parts, as for the abdomen is 0.015 mSv × mGy × cm^{-1} (Hesong *et al*. 2015).

Another study done in Japan on the effective doses for routine CTC of 23.4 mSv and low-dose CTC of 5.7 mSv were compared to effective doses for barium enemas with a combination usage of analog radiography and digital radiography (Y Hirofuji et al. 2009) **(Figure 2.4**).

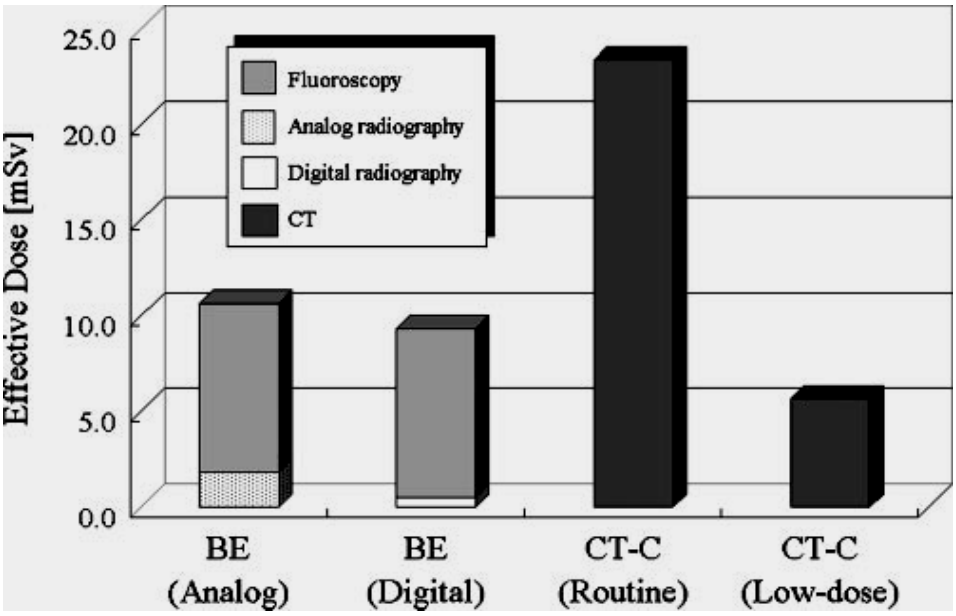


Figure 2.4. Evaluation of patient dose for barium enemas and CTC in Japan, British Journal of Radiology, 82 (2009), 219–227.

The relation between CTC and DCBE based on the effective dose to individuals were considerably lower for those who undergoing screening CTC than DCBE, about 53%. This finding proved that CTC is a radiological imaging technique of the large bowel with the lowest risk of stochastic radiation effects. These findings, together with the high diagnostic confidence of CTC as comparable to CC, support the performance of CTC as an appropriate and effective tool for CRC screening, definitively alternative and substitutive of DCBE.

CHAPTER 3: METHODOLOGY

3.1 Study Design

The study was a cross sectional study conducted from July 2013 till June 2016 in Department of Radiology and Endoscopy Unit, Department of Surgery, Hospital Universiti Sains Malaysia (USM).

3.2 Sample Population

The sample population was all patients who are symptomatic and clinically suspected of colorectal cancer (CRC) that were referred for CTC. The referral patients to endoscopy unit were from surgical outpatient department (SOPD), wards, medical specialist clinic, oncology unit, accidents and emergency department and hospital's private clinic. The reference population of this study is patients with or suspected colorectal cancer.

3.3 Sampling Method

The sampling method of this study was a purposive non-probability. Patients that had found to have a positive result, incomplete CC study or for assess of extracolonic extension and willing to undergo CTC examination were included in this study.

3.4 Sample Size

a) For objective (i):

(Fenlon, McAneny et al. 1999)

Sensitivity, SN = 75%

Z = 1.96 for CI of 95%

Prevalence of disease amongst test population, P = (57.7%), Level of accuracy, W = 0.05

$$TP+FN = z^2 \times \frac{SN(1-SN)}{W^2}$$

$$= 1.96^2 \times \frac{0.75(1-0.75)}{0.05^2}$$

$$= 3.482 \times \frac{0.0475}{0.0025}$$

$$= 3.482 \times 75$$

$$= 261.15$$

$$\text{Therefore : } n(sN) = \frac{TP+FN}{P} = \frac{261.15}{57.7\%} = 450$$

b) For objective (ii):

Expected kappa: 0.75

Rater 1 (sensitivity of CTC based on location) = 0.83 (Filippone et al, 2004)

Rater 2 (expected sensitivity of CC) = 0.75