Computed Tomographic Colonography

An Evidence-Based Analysis

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OBJECTIVE

The purpose of this health technology policy assessment was to evaluate the safety and effectiveness of VC as a screening tool in colorectal cancer. This assessment addresses the scientific evidence for CT-based VC.

BACKGROUND

Clinical Need

VC has been proposed as a promising method for colorectal evaluation. The technique is currently under investigation as a potential screening tool for colorectal polyps and cancer. It is believed that colorectal carcinoma could be prevented through early detection and removal of precursor adenomatous polyps in the colon. The evaluation of the colon in an ageing population presents a substantial challenge and is compounded by difficulties in evaluating the caecum (proximal segment of the colon) with standard colonoscopy, which is the gold standard.

Incidence and Prevalence

Colorectal cancer is the most common cause of cancer-related death among non-smokers in Canada (1) and is a major public health concern. In Ontario, there were an estimated 6,600 new cases and 2,300 deaths from the disease in 2002. (1) In the Canadian population, a person's probability of developing colorectal cancer over the next 10 years is shown in Table 1.

Table 1: Probability of Developing Colorectal Cancer in Next 10 Years by Age Group

Age, yr	30-39	40-49	50-59	60-69	70-79	80-89
Men	0.1	0.2	0.8	2.0	3.2	3.1
Women	0.1	0.2	0.7	1.3	2.4	2.7

Source: Surveillance and Risk Assessment Division, Centre for Chronic Disease Prevention and Control, Health Canada

The average lifetime risk of a diagnosis of colorectal cancer in Canada is 6.7% for men and 6.1% for women. The average lifetime risk of dying of colorectal cancer in Canada is 2.9% for men and 2.7% for women. (1)

Adenoma-Dysplasia-Carcinoma Sequence

The development of colorectal cancer appears to be based on the transformation of normal cells to malignant cells due to stepwise genetic alterations. (2) This concept fits with the well-established adenoma-dysplasia-carcinoma sequence. Frequently, colorectal cancers arise in adenomatous polyps; the proportion of colorectal cancers that arises in these fractions is approximately 70%. (3–4)

Approximately 33% to 50% of colorectal polyps are of the adenomatous type, and may be found in about 25% of the population aged 50 years and older. (5) The average time required for a precancerous polyp to progress to a carcinoma is estimated at 10 to 20 years. (6–7)

Distribution of Colorectal Adenoma

Nicholson et al. (8) investigated the distribution of colorectal adenomas in 1,131 asymptomatic individuals who underwent full colonoscopy under the Bowel Cancer Prevention Program in Australia. Most of the patients (80%) had a family history of colorectal cancer. Polyps were found in 270 patients (24%) and were confirmed to be adenomas in 138 (12%). Most (86%) had a single adenoma. Eighty-five of the 138 adenomas (62%) were proximal to the splenic flexure, 34 (25%) were distal, and 19 (14%) were both proximal and distal. The mean age of the patients was 54 (range, 40–78). Another study (9) investigated an older population randomly selected from the population register and found a higher incidence of adenoma. In 193 high-risk individuals (mean age, 67; range, 62–73) who had full colonoscopies, polyps were found in 142 (74%) and adenoma in 83 (43%). Forty-six percent of the adenomas were found in the rectum and sigmoid colon (28% in rectum, 18% in sigmoid colon). Fifty-four percent of the adenomas were located proximal to the sigmoid colon (16% in descending colon, 19% in transverse colon, 13% in ascending colon, and 6% in caecum) Most of the adenomas (93%) detected were smaller than 10 mm.

Colorectal Cancer Screening

It has been shown that most cases of colorectal cancer can be prevented with colonoscopic removal of the precursor adenomatous polyp. The National Polyp Study (3) reported a 76% lower incidence of colorectal cancer in 1,418 individuals who had a complete colonoscopy during which 1 or more adenomas were removed. The reported incidence of colorectal cancer was significantly lower than expected based on the rate in the SEER data (Surveillance, Epidemiology, and End Results), that consists of estimates for the average-risk population.

The aim of screening is to detect and remove precancerous polyps to prevent the development of invasive tumour growth. Currently, diagnostic tests for colorectal cancer screening include fecal occult blood testing (FOBT), barium enema, sigmoidoscopy, and colonoscopy. Each test differs in effectiveness, risk, patient acceptance, and cost. The screening technique for colorectal cancer, as with other screening tests, should be feasible, accurate, acceptable, and cost-effective.

Importance of the Total Examination of the Colon

Colonoscopy is currently considered the gold standard for the detection of colorectal neoplasia in the screening of high-risk, asymptomatic individuals. However, colonoscopy fails to reach the caecum in 5% to 10% of average-risk patients. Right-sided colonic carcinomas are an important subset of colonic carcinoma and account for up to 35% of colonic neoplasms. (10) There has been an increase in the incidence of right-sided colonic carcinoma, particularly in elderly patients. Liberman et al. (11) studied 3,196 individuals who were recruited for screening (including both average-risk and high-risk patients) and observed a trend toward an increased prevalence of advanced proximal neoplasia with age (p<0.001). The prevalence was 2% for patients who were 50 to 59 years old, 4.9% for those 60 to 69 years old, and 5.9% for those 70 to 75 years old.

Obrand & Gordon (12) retrospectively reviewed the charts of 2,169 patients admitted to one institution between 1979 and 1994 with a diagnosis of colorectal carcinoma. They reported that the percentage of right-sided lesions increased from 20.6% to 29.9% (p=0.001), whereas rectal lesions decreased from 22% to 11.3% (p=0.002) from the first to the fourth study interval. The frequency of transverse, left, and sigmoid colon lesions remained relatively unchanged. The authors suggested that any effective screening examination for carcinoma require a complete examination of the colon.

New Technology Being Reviewed

Virtual endoscopy is a non-invasive method that has been used to evaluate the colon, stomach, bronchi, larynx, kidneys, bladder, blood vessels, and paranasal sinuses. Virtual colonoscopy, which was first described in 1994, has been studied at research centres for evaluation of colonic pathologies. Some centres are offering it as a screening method.

Terminology

The term *virtual colonoscopy* is used alongside *CT colonography* (using CT scanning data set) and *MR colonography* (using magnetic resonance imaging [MRI] data set). Various names have been given to different approaches for CT scanning including CT colonography (CT colography) and CT pneumocolon. Computed Tomographic Colonography (CTC) essentially relies on thin collimation and 3-dimensional (3-D) endoluminal computerized reconstructed images. CT pneumocolon, which is a simple extension of abdominal and pelvic CT, uses thicker collimation and intravenous contrast, but does not use 3-D imaging. It does not produce excessive images, and no special software is required. CT pneumocolon is a particularly useful method for staging of colonic carcinoma.

Computed Tomographic Colonography

The technique involves the following steps:

1. Pre-scanning
   - Bowel cleansing
   - Intravenous preparation (optional)
   - Bowel distension (air insufflation)
2. Scanning and Image acquisition
3. Image processing
4. Post processing and navigation

Pre-scanning

Bowel Cleansing

Patient preparation for CTC is more or less identical to preparation for conventional colonoscopy. A meticulous cleansing of the bowel is required for optimal results. Retained fecal matter or fluid can lead to significant perceptual errors. Bowel cleansing is achieved using a mixture of salts and electrolytes.

Intravenous Contrast

Visualization of polyps is possible because of the high contrast between soft tissue and the air-filled colon. Studies show that the use of intravenous contrast material improves the diagnostic accuracy of CTC in the detection of colorectal polyps and cancer. The use of intravenous contrast materials might also help in the detection of local and distant metastases. However, in most centres, CTC is performed without intravenous contrast. Disadvantages of intravenous contrast include patient discomfort, related occasional adverse effects such as nephrotoxicity and anaphylactoid reactions, and added cost.

Spasmolytic Medication

Before CTC scanning, the patient is asked to empty the bowels to ensure that the rectum contains as little fluid as possible. After placing a rectal tube, a spasmolytic agent (such as Buscopan or Glucagon) may be administered.

Air Insufflation

Adequate colonic distension is crucial for high-quality images. Before CT scanning, an enema tip is inserted into the rectum and air or pressure-controlled carbon dioxide is insufflated to the near maximum patient tolerance. The degree of distension can be assessed on the CT pilot view, and the colon can be reinflated and reimaged.

Scanning and Image Acquisition

Spiral CT Scanning Versus Sequential CT Scanning

Conventional sequential CT scanning is a 2-dimensional technique that scans 1 axial slice at a time and then moves the patient to the next longitudinal position before scanning another slice. Even with multiple scans taken during a single breath holding, the rhythm essentially remains discontinuous with repetition of the 2 phases of "planar scan" and 'table motion" in discrete positions, resulting in imaging gaps. Spiral (helical) CT scanning has advantages over conventional sequential CT scanning because it uses 1 period of breath holding to sample the complete information without interruption, eliminating imaging gaps.

Multi-slice Versus Single-slice CT Scanning

Single-slice scanning requires a period of breath holding of about 1 minute during image acquisition. Some imaging protocols require 3 to 4 separate periods of breath holding of about 20 to 22 seconds each. (13) With the development of multi-slice CT scanners, the entire abdomen and pelvis can be scanned within 1 breath hold of as little as 30 seconds. Multi-slice CT scanners are capable of scanning up to 8 times faster than the single-slice CT scanners and of acquiring thinner sections. More centres are using these scanners, as they become more widely available. Since respiratory artefacts have been identified as an important cause of false negative findings, it is expected that the use of a multi-slice CT scanner will improve polyp detection.

Pitch and Slice Thickness

The radiologist has the option of choosing the pitch (p), a parameter defined as the quotient between the table feed per rotation (d) and the slice thickness (s) ($p=d/s$). The higher the pitch, the larger the volume scanned during 1 period of breath holding. The most frequently used range of pitch is 1.25 to 2.0.

Patient Positioning

Patients may be scanned in the supine or prone position. The use of additional prone images improves the sensitivity of CTC for colorectal polyps by approximately 15%, primarily by improving distension in the rectosigmoid colon. (14) Generally, colonic segments that are located posteriorly, including the sigmoid and descending colon, show better distension with prone scanning, whereas the transverse colon, which is located anteriorly, shows better distension with supine scanning.

Image Processing

Two-dimensional and Three-dimensional Images

Two-dimensional (2-D), multiplanar images are oriented in an axial, coronal, sagittal, or oblique direction in relation to the body anatomy. Three-dimensional images can be generated by a variety of computer algorithms. There are 3 main algorithms used to generate 3-D images: surface rendering, maximum intensity projection, and volume rendering. The first 2 techniques use only 10% of available CT data, which limits the accuracy of these images. Surface rendering requires the correct choice of threshold by which tissues of different density can be either included or removed from the final 3-D images. If the threshold value is poorly chosen, the colon may appear to have artificial stenosis or defects in its walls. The third algorithm, 3-D volume rendering, is a newer technique that incorporates the entire data set into a 3-D image and, therefore, provides a more reliable representation of anatomy and pathology. The most important parameter in this technique is the correct choice of an opacity map. Certain tissue types, expressed in CT as density values, are assigned specific levels of opacity. Values between 0% (completely transparent) and 100% (completely opaque) are possible. This parameter is adjusted by the radiologist to indicate which tissue should appear to be opaque or transparent. A 50- to100-fold increase in processing speed is required for volume rendering to become an interactive technique.

Post Processing and Navigation

The large intestine is suitable for real-time navigation because of its long, tubular structure and simple anatomy. Radiologists have the choices of viewing (a) only the non-reformatted axial CT images, (b) only the reformatted 2-D images, (c) only the reformatted 3-D snapshots, (d) 3-D intraluminal images (fly through), and (e) a combination of these aspects.

Unlike endoscopy, CTC cannot provide information about colour or texture, which makes flat adenomas difficult to diagnose. Most software systems allow viewing of the multiplanar reconstruction during navigation to view the external morphology at the same time. Two-dimensional and 3-D images are complementary. Two-dimensional images are particularly useful for accurate assessment of the colonic wall and detection of lesions behind haustral folds. Three-dimensional images are used to confirm lesions and to help to distinguish normal folds from polyps.

LITERATURE REVIEW ON EFFECTIVENESS

Objective

➢ To compare the effectiveness and safety of CTC as a screening method for the detection of colon cancer and precancerous polyps with the reference standard of conventional colonoscopy

Methods

A literature search was conducted using MEDLINE and EMBASE for English language articles from January 1, 2000 to May 31, 2003. For the search, the following medical subject headings were used: virtual colonoscopy, colonography, computed tomographic, x-ray computed.

Inclusion Criteria

Studies were included if they had the following characteristics:
> - 30 or more subjects
> - Used colonoscopy as the gold standard
> - Mentioned diagnosis or screening

Exclusion Criteria

Studies were excluded if they had the following characteristics:
> - Less than 30 patients
> - Investigated areas other than the colon
> - Addressed only technical, educational, or other aspects of CTC

Results of Search

The initial search retrieved 278 articles after duplicates were removed. When the selection criteria listed above were applied and unrelated studies were excluded, 18 published articles were identified and included in the assessment. (13–30) In addition, the result of a large multi-centre clinical trial, (31) which has been submitted to a peer-reviewed journal but has not yet been published, was discussed separately.

Levels of evidence were assigned according to the scale based on the hierarchy by Goodman (1985). An additional designation "g" (grey literature) was added for preliminary reports of studies that have been presented to international scientific meetings (Table 2).

Table 2. Quality of Evidence

Study Design	Level of Evidence	No. Eligible Studies
Large RCT,* systematic reviews of RCT	1	0
Large RCT unpublished but reported to an international scientific meeting	1(g) †	0
Small RCT	2	0
Small RCT unpublished but reported to an international scientific meeting	2(g)	0
Non-RCT with contemporaneous controls	3a	18
Non-RCT with historical controls	3b	0
Non-RCT presented at international conference	3(g)	1
Surveillance (database or register)	4a	0
Case series (multisite)	4b	0
Case series (single site)	4c	0
Retrospective review, modeling	4d	0
Case series presented at international conference	4(g)	0

*RCT refers to randomized controlled trial;†g=grey literature

Assessment of Evidence

Published Clinical Trials of CT Colonography

Eighteen studies compared the diagnostic accuracy of CTC with the reference standard, conventional colonoscopy. A detailed summary of these reports is shown in Table 3.

Table 3: Detailed Summary of Reports of Computed Tomographic Colonography with 30 or More Patients

Authors, Date, Place of Study	No. of patients	Age mean (Range)	Inclusion Criteria	Study Design and Methods	Modality	Positioning
Fletcher 2000 USA	180 consecutive	N/R	Patients with unknown or possible polyps or cancer, family history of colorectal cancer, history of colonic polyps or cancer.	Patients were randomly assigned to undergo either the standard bowel preparation only, or the standard bowel preparation with 120 mL of oral iodinated contrast medium.	Single-slice	Supine/ Supine & Prone
Kay 2000 USA	38	N/R (31-89)	Positive FOBT (9), prior colon polyps (9), altered bowel habit (7), rectal bleeding (5), abdominal pain (3), prior colon cancer (3), family history of colon cancer (1), liver metastases (1)	The earlier version of Voyager software was used.	Single-slice	Prone only
Macari 2000 USA	42	56 (50-82)	Asymptomatic patients (71%), family history of colonic cancer (29%)	Data were examined by 1 of the 2 methods: In method 1, the observer examined the axial 2-D data sets, if findings were suggested an abnormality, focal areas were examined with 3-D. In method 2, the observer examined the data exactly as in method 1, and then data sets were examined with simultaneous review of 3-D CTC, coronal and sagittal reformatted, and axial images (in both antegrade and retrograde fashion)	Single-slice	Supine & Prone
Mendelson 2000 Australia	100	65 (55-80)	Rectal bleeding (36), altered bowel habit (23), family history of bowel cancer (19), abdominal pain (11), and other (11)	The first 10 examinations were undertaken in 2 or 3 separate breath holds, which created artefacts. This problem was obviated by preoxygenation using a face mask and scanning during a 45 second breath hold.	Single-slice	Supine: First 47 patients Supine & Prone: Next 53 patients
Morin 2000 USA	81	N/R	Positive FOBT, anemia, altered bowel habit, weight loss, follow-up of colorectal polyps.	115 patients received contrast material and 85 patients did not. Among 85 patients who had complete colonoscopic and surgical correlation, 48 received IV contrast material and 33 did not.	Single-slice & Multi-slice	Supine & Prone
Pescatore 2000 Switzerland	50 consecutive	68 (50-85)	Patients referred for colonoscopy: abdominal pain (11), IDA (10), history of colon polyp (10), hematochezia or positive FOBT (7), tumour search (7) colorectal cancer with partial colectomy (5)	Polyps were grouped according to size < 10 mm or >=10mm. In case of an incomplete colonoscopy, interpretation of CTC concerned only the segments explored by colonoscopy	Single-slice Surface rendering software	Supine only

Authors, Date, Place of Study	No. of patients	Age mean (Range)	Inclusion Criteria	Study Design and Methods	Modality	Positioning
Hara 2001 USA	237 Single-slice: 77 Multi-slice: 160	Single-slice: 63.3 (46-74) Multi-slice: 63.5 (41-75)	Had history of colon polyps or cancer in a first-degree relative, or had recent onset of IDA.	3 radiologists were instructed to ignore polyps < 5 mm. Results were compared in 2 ways: 1) By requiring only 1 observer to correctly identify the positive examination findings and then by requiring both observers to call the examination findings positive. 2) By randomly choosing 1 of the 2 observers and using his/her results, as well as by using a weighted mean among all the radiologists. The effective dose was equal between the 2 techniques (450-670 mram (4.5-6.7 mSv)	Single-/multi-slice	Supine & Prone
Spinzi 2001 Italy	96 Randomly selected from patients attending an open access endoscopy unit in the large city hospital.	N/R	Follow-up polyps (15.2%), bowel disorders (18.2%), rectal bleeding (25.2%), abdominal pain (26.3%), microcytic anemia (9.1%), positive FOBT (3%), follow-up of ulcerative colitis (3%)	The first 49 patients: colonoscopy first (patients with polyps underwent CTC only if it was decided not to proceed with endoscopic polypectomy because of patient refusal or coagulopathy. The next 50 patients: CTC first	Single-slice	Supine & Prone
Yee 2001 USA	300 Male: 97%	62.6 (25-90)	204 high risk (hematochezia, positive FOBT, IDA, personal/family history of polyp) & 96 asymptomatic screening patients.	The sensitivity for adenoma detection was compared between the screening group and symptomatic group.	Single-slice	Supine & Prone
Wessling 2001 Germany	48	61.5 (N/R)	Low risk, no symptoms; Symptomatic (hematochezia, abdominal pain, weight loss, metastases of unknown primary)	Size and location of polyps were recorded by using a segmental classification scheme (size difference less than 5 mm and same or adjacent segment)	Multi-slice	Prone & supine
Gluecker 2002 Switzerland	50 consecutive	N/R (50-75)	High risk (History of prior polyp or colon cancer, unexplained abdominal pain, IDA)	Data acquisition was achieved with superficial respiration.	Multi-slice	Supine & Prone
Laghi 2002 Italy	165 consecutive	62 (26-84)	High risk (Positive FOBT (31%), altered bowel habits (24%), history of colorectal cancer resection (22%), rectal bleeding, anemia of unknown origin (4%), history of polyps (3%))	Images were analysed by means of a software package with a volume-rendering algorithm.	Single or multi-slice	Prone & supine
Macari 2002 USA	105	58 (49-79)	High risk (Positive FOBT, IDA, hematochezia, history of polyp) No patient was known to have polyp	The weighted CT dose indexes were calculated (the single supine and prone scout images obtained in each patient were not included in the radiation dose calculation)	Low dose multi-slice	Supine & Prone
MacFarland 2002 USA	70	62 (28-82)	Polyp rich study cohort (Patients suspected of having or with a known polyp determined with flexible sigmoidoscopy and scheduled for colonoscopy)	Data were analysed both by patient and by polyp.	Single-slice	Supine & Prone

Authors, Date, Place of Study	No. of patients	Age mean (Range)	Inclusion Criteria	Study Design and Methods	Modality	Positioning
Wong 2002 Hong Kong	71 consecutive	62 (21-82)	Patients referred for diagnostic colonoscopy (abdominal pain (10%), IDA (21%), hematochezia or positive FOBT (11%), tumour search (17%), colonic polyps follow-up (14%), diarrhea/alteration of bowel habit (27%)	All polyps and cancers were proven histologically.	Single-slice	Supine only
Cohnen 2002 Germany	52	60.3 (N/R)	Clinical signs of colonic tumour (19), other symptoms including abdominal pain (33)	In 19 patients with a high suspicion of tumour, tube current was set to 120 mAs, resulting in a CTDI weff of 11.28 mGy. The other 33 patients were examined with 10 mAs, the lowest tube current setting available. Calculated effective doses ranged between 9 and 12 mSv for 120 mAs, and between 0.75 and 1mSv for the low-dose technique.	Multi-slice	Supine only
Thomeer 2003 Belgium	150	58	Primary colorectal screening (14.8%), secondary colorectal screening (42.3%), follow-up of polyposis coli (26.7%) follow-up of colorectal tumour (15.6%), bleeding (16.3%), abdominal pain (11.1%), change in stool habit (4.4%), primary tumour search (4.4%), weight loss (2.2%), anemia (0.7%), other (3.7%)	Patients underwent high resolution CTC. An iodinated contrast agent was added to the preparation to tag the residual colonic fluid and stool. The effective dose per patient measured by WinDose software was 7.03 mSv for men and 10.28 mSv for women.	Multi-slice	Supine & Prone
Yee 2003 USA	182 consecutive: 60% symptomatic 40% asymptomatic	63 (37-88)	High-risk: (60%) (Hematochezia, positive FOBT, IDA, history of colonic polyps) Asymptomatic individuals scheduled for routine colonic screening (40%)	Polyp detection was compared for each position alone and in combination.	Single-slice	Supine & Prone

N/R refers to not reported; FOBT refers to fecal occult blood test; IDA refers to iron deficiency anemia; CTC refers to computed tomographic colonography; mAs refers to milliampere/second, mSv refers to millisievert; mrem refers to milli rem (Roentgen-equivalent-man); mGy refers to milli Gray; VC refers to virtual colonoscopy; IV refers to intravenous; CTDI refers to computed tomography dose index.

Key Considerations in the Evaluation of the Studies Assessed

CTC for Screening the High-risk Population

The published literature reports on 2,017 patients who have been evaluated for screening, of whom 126 (6%) were asymptomatic. Therefore, the results of this assessment would be applicable mainly to individuals with a high risk of developing colorectal cancer.

Only 2 studies included asymptomatic individuals. A study by Macari et al. (16) included asymptomatic patients (71%) and patients with a family history of colon cancer (29%). Another study by Yee et al. (21) included asymptomatic patients referred for conventional colonoscopy for colorectal cancer screening (32%).

Colonoscopic Miss Rate

All studies considered the results of conventional colonoscopy as the gold standard. It cannot be automatically assumed that conventional colonoscopy fulfils the role of the gold standard in screening colorectal cancer and polyp. Rex et al. (32) demonstrated that in 183 patients who were given 2 complete colonoscopies in close succession, 27% of polyps smaller than 5 mm, 13% of polyps 5 to 9 mm, and 6% of polyps larger than 10 mm were missed at the first colonoscopy, for an overall miss rate of 24%.

Postic et al. (33) estimated the miss rate of colonoscopy by comparing the results of colonoscopy with the examination of surgically resected colon as a gold standard. In this retrospective analysis, sensitivity was determined by counting the number of lesions detected by colonoscopy compared with those found in the resected segment. Seventy-three synchronous lesions were present in the resected segments of 156 patients. Colonoscopy detected 56 (77%) of 73 lesions and missed 17 (23%) lesions. Fourteen of the 17 missed lesions were polyps smaller than 10 mm. Of the remaining 3, 1 was a 10-mm adenoma in the ascending colon, and 2 were cancers in the same patient in whom endoscopy detected a sigmoid cancer, but missed synchronous lesions in the caecal and ascending colon. The authors concluded that colonoscopy is associated with a significant miss rate for polyps less than 10 mm.

Hixson et al. (34) prospectively studied the colonoscopic miss rate of large colorectal polyps in a blinded trial featuring tandem colonoscopy, and reported that less than 5% of large colorectal polyps were missed during the index colonoscopic examination in a well-prepared colon. In a separate report of the same study, the miss rate for colorectal neoplastic polyps less than 10 mm in size was reported at about 15%.

In light of the above studies, colonoscopy is an appropriate gold standard for colorectal neoplasia for lesions 10 mm and larger, but for smaller lesions, it may not be a valuable diagnostic tool with which to compare the results of an alternative technology.

Method of Reporting Accuracy Data

Most of the studies analysed the data on a "per-polyp" basis. In per-polyp analysis, the lesion identified on CTC had to have a match according to location and size of the polyp found on conventional colonoscopy. In "per-patient" analysis, the results were considered to be true positive only when at least 1 polyp identified on CTC was matched to a lesion seen on conventional colonoscopy. However, due to the lack of uniform criteria, studies used different criteria concerning the size and location of the polyps. For example, 1 study considered the lesions to be concordant when both methods showed a polyp or lesion of the same size, regardless of the location of the polyp, whereas another study considered both size and the location. In addition, the cut points for size and location were not consistent among the studies.

It should be noted that when selecting patients for a more complete evaluation among asymptomatic patients, it is reasonable to consider the accuracy of the test reported as "per patient" rather than "per polyp." This is more important at the stage of economic evaluation and cost-effectiveness.

Polyp Size

Most investigators reported separately for lesions larger than 10 mm, 6 to 9 mm, and less than 5 mm. It is generally agreed that lesions smaller than 5 mm have a very low likelihood of

malignancy. The clinical significance of 6 to 9 mm polyps has generated debate, not only because sensitivity and specificity are affected, but also because the interval at which the examination should be repeated will change.

Given the above, the analysis of combined data for all sizes would not be meaningful; therefore, this report addresses the accuracy of CTC according to polyp size.

Diagnostic Outcomes

Table 4 shows the sensitivity and specificity of CTC for 2,017 reported patients between 2000 and 2003.

Table 4. Published Reports of Diagnostic Accuracy of CTC (2000-2003)

Study	Sensitivity for cancer % (No. of cases)	Per polyp sensitivity % (No. of cases)			Per patient sensitivity % (No. of cases)	Specificity % (No. of cases)
		>=10 mm	6-9 mm	<=5 mm		
Fletcher 2000	No cancer	Supine: 64 (77/121) Supine & prone: 75 (91/121)	30 (43/142) Supine & prone: 47 (67/142)	Not reported	Not reported	Per polyp Supine: >=10 mm: 93 <=5 mm: 80 Supine & prone: >=10 mm: 93 <= 5 mm: 72
Kay 2000	No cancer	91 (10/11)	38 (5/13)	No polyp by colonoscopy	>= 10 mm: 90 5-9 mm: 66.7	Per patient >= 10 mm: 82.1 6-9 mm: 75
Macari 2000	No cancer	100 (1/1)	60 (3/5)	20 (2/10)	>= 10 mm: 100 (1/1)	Per polyp: 100
Mendelson 2000	67 (4/6)	67 (8/12)	30 (9/30)	10 (7/73)	Not reported	Not reported
Morin 2000	100 (16/16)	90 (18/20)	65 (13/20)	33 (9/27)	Tumor: 100 10 mm: 87 6-9 mm: 73 <=5 mm: 57	Per patient Tumor: 96 10 mm: 100 6-9 mm: 96 < 5 mm: 92
Pescatore 2000	Observer 1: 25 (1/4) Observer 2: 75 (3/4)	Observer 1: 43 (3/7) Observer 2: 57 (4/7)	Polyps < 10 mm Observer 1: 71 Observer 2: 71		Observer 1: 75 Observer 2: 71	Per patient Cancer & >=10 mm: 74 (observer 1 or 2) < 10 mm: 59 (observer 1) 69 (observer 2)
Hara 2001	No cancer	Single-slice: 89 (8/9) Multi-slice: 80 (8/10)	Not reported		Single-slice: 100 (5/5) Multi-slice: 78 (7/9)	Per patient >=10 mm Single-slice: 90 (65/72) Multi-slice: 93 (140/151)
Spinzi 2001	87.5 (7/8)	61.5 (8/13)	Polyps < 10 mm: 56.2 (18/32)		80*	Per patient Overall: 92.6 Tumors: 100 >=10 mm: 100 < 10 mm: 81.8
Yee 2001	100 (8/8)	90 (74/82)	80 (113/141)	59 (178/301)	Overall: 90 (164/182) Cancer: 100 (8/8) >=10 mm: 100 (49/49) 6-9 mm: 93 (50/54) <=5 mm: 82 (65/79)	Per patient Overall: 72 (85/118)

Study	Sensitivity for cancer % (No. of cases)	Per polyp sensitivity % (No. of cases)			Per patient sensitivity % (No. of cases)	Specificity % (No. of cases)
		>=10 mm	6-9 mm	<=5 mm		
Wessling 2001	100 (1/1)	100 (3/3)	86 (6/7)	70 (14/20)	Not reported	Per patient All sizes: 78 Cancer: 100 >=10 mm: 97 6-9 mm: 94 <=5 mm: 85
Gluecker 2002	No cancer	82 (9/11)	33 (5/15)	3 (1/41)	Not reported	Per patient: 90 (19/21)
Laghi 2002	100 (30/30)	92 (11/12)	82 (14/17)	50 (4/8)	Per patient: 93	Per patient: 97 (110/113)
Macari 2002	100 96/6)	88 (7/8)	70 (19/27)	12 (11/91)	Not reported	Polyp-to-polyp 97.7 (515/527)
MacFarland 2002	3 cancers (not reported)	Per polyp: 68 Per patient: 88	Per polyp: 36 Per patient: 71	Per patient: 48	Not reported	Per patient: 60 (Note: patients with polyps 5 mm or smaller were defined as negative)
Wong 2002	100 (5/5)	88	0 (Note: there were only 2 polyps 6-9 mm)	68	Per patient: >=10 mm: 88 6-9 mm: 0 <=5 mm: 53	For polyp of any size: 93
Cohnen 2002	Normal dose: 100 (7/7)	Normal dose: 100 (1/1) Low dose: 100 (3/3)	Normal dose: 86 (6/7) Low dose: 93 (13/14)	Normal dose: 60 (6/10) Low dose: 59 (16/27)	Normal dose: 100 Low dose: 63	Per patient Normal dose: 75 Low dose: 65
Thomeer 2003	86 (6/7)	92 (11/12)	Observer 1: 64 (25/39) Observer 2: 67 (26/39)	Were ignored	Not reported	Per patient Polyps > 5 mm Observer 1: 94.2 Observer 2: 95
Yee 2003	No cancer	Supine: 58.5 (924/41) Prone: 51.2 (21/41) Combined: 92.7 (38/41)	Supine: 47.2 (42/89) Prone: 41.6 (37/89) Combined: 79.8 (71/89)	Supine: 36.3 (65/179) Prone: 30.2 (54/179) Combined: 60.3 (108/179)	All sizes Supine: 64 (73/114) Prone: 59.7 (68/114) Combined: 90.4 (103/114)	Per patient: Supine: 85.3 (58/68) Prone: 97.1 (66/68) Combined: 82.4 (56/68)

*From Dachman 2002

Multiple large studies have demonstrated the ability of CTC to detect cancer and polyps larger than 10 mm in diameter with high sensitivity. The largest study published to date (21) included 300 patients (204 high risk and 96 asymptomatic screening). Results of colonoscopy were normal in 118 (39%) patients. A total of 8 carcinomas and 524 polyps were identified by colonoscopy. CTC demonstrated 100% sensitivity for the detection of carcinoma (8 of 8). With per-polyp matching, the sensitivity of CTC for the detection of polyp was 69.7% for all lesions (90% for large, 80% for medium and 59% for small size polyps). With per-patient comparison, the overall sensitivity, specificity, positive predictive value, and negative predictive value for the detection of polyp were 90%, 72%, 83%, and 82.5% respectively. In this study, 114 (72%) of 159 missed polyps and 142 (77%) of 185 false positive polyps were in poorly distended and/or poorly prepared segments of the colon.

In almost all the studies, colonoscopy was performed a few hours after CTC. Spinzi et al. (20) divided the study patients into 2 groups. The first 49 patients underwent colonoscopy before CTC, and the next 50 patients were examined by CTC first, then by colonoscopy. The 2 groups were comparable for age and sex. In the first group, CTC identified 12 (40%) of the 30 polyps detected by colonoscopy compared with 7 (47%) of 15 in the second group. The difference was not statistically significant.

Discussion of Diagnostic Outcomes

Explaining the Variability of Results

Several factors could explain the variability in results. These include the following:

- Patient characteristics
- Bowel preparation
- Earlier versus recent studies
- Multi-slice versus single-slice scanning
- Dual versus supine positioning
- Radiologist's experience

Patient Characteristics

Eight of the 12 studies that provided the age range included patients younger than 50 years of age. Three studies did not report the age of the patients. (14; 18; 20) Two of the studies provided only the age range (15; 23) and 3 studies provided only the mean age of the patients. (22; 28; 29) The youngest patient in the assessed studies was 21 years old and the oldest patient was 90 years old.

Bowel Preparation

CTC is dependent on proper bowel preparation. Inadequate bowel preparation and poor bowel distension are reported by most of the authors to be the main reasons for false results. Most of the authors argued that inadequate bowel preparation appears to be a major factor for accurate interpretation of data. Spinzi et al. (20) has argued that it may be more important than the size of the polyps. Adherent stool can mimic a polyp or mass and residual fluid may hide a submerged polyp or mass.

Earlier Versus Recent Studies

Studies published more recently reflect greater experience and familiarity with CTC as well as improvement in the technology when compared with those of earlier studies. For these reasons, the ranges of reported sensitivities differ between the studies published between 2000 and 2001 and those published between 2002 and 2003. Figure 1 demonstrates the range of reported sensitivities for identifying cancers and polyps of different size reported by the studies published between 2000 and 2003. Figures 1(a) and 1(b) show earlier and recent studies separately.

Figure 1. Diagnostic Accuracy of CTC: Earlier vs Recent Studies

Figure 1. Diagnostic accuracy of CTC for detection of colonic cancers and polyps of different size (Studies published in 2000-2003)

Figure 1 (a). Diagnostic accuracy of CTC (Studies published in 2002-2003)

Figure 1 (b). Diagnostic accuracy of CTC (Studies published in 2000-2001)
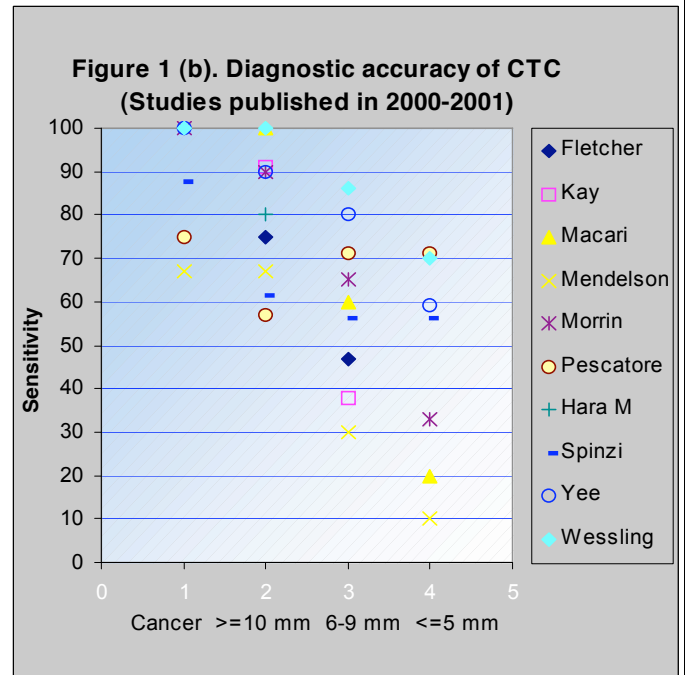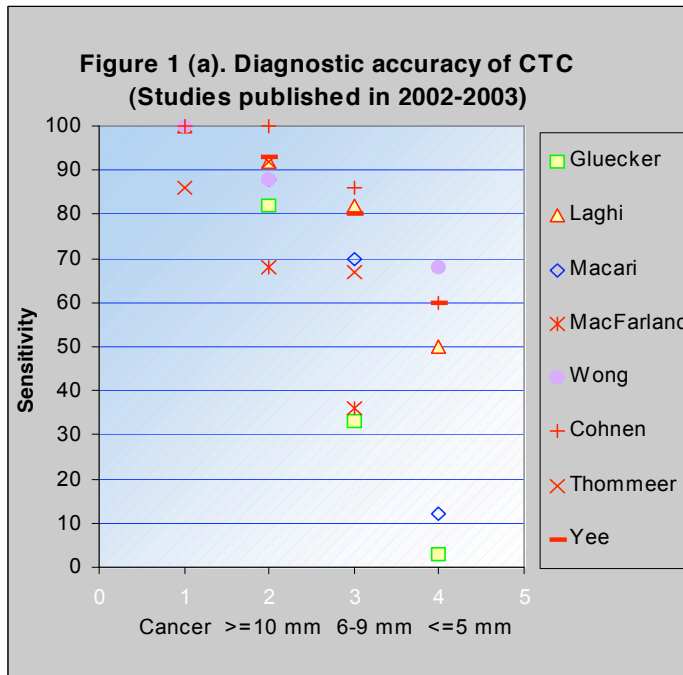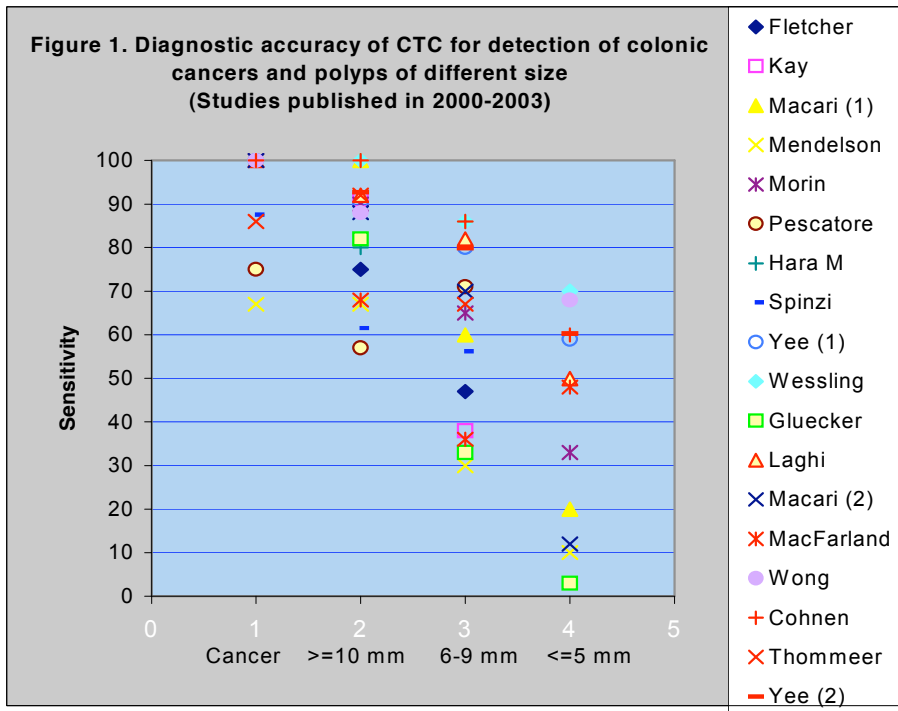
Note: For multiple observers, the highest value was considered.
Sensitivity for medium size polyps reported by Wong was not considered (there were only 2 polyps in this sample)

Dual Versus Supine Positioning

Studies in which scanning were performed in both supine and prone positions demonstrated improved sensitivity (Table 5).

Table 5: Range of Reported Sensitivities of CTC with Supine and Prone Positioning Versus CTC with Supine Positioning Alone

Polyp Size	Supine & Prone Positioning %	Supine Positioning Alone %
>=10 mm	61.5–100	43–100
6-9 mm	22.0– 86	0– 86
<=5 mm	3.0– 70	0– 68

Most authors used dual positioning to improve the distension of the sigmoid colon by compression of the small bowel and transverse colon. Fletcher et al. (14) showed that dual positioning increases the detection of colonic polyps by 11% for large-size and 17% for medium-size polyps. However, due to improvements in CTC technology, higher sensitivities with supine positioning alone have been reported in recent studies. Residual material in the colon (fluid and/or stool) and collapsed segments can be detected with the patient still on the scanner table. It can be decided based on the first scan whether a second scan with the patient in a different position is necessary. In addition, intravenous contrast is helpful for problem solving when residual stool or fluid is present. Wong et al. (27) used an intravenous non-ionic contrast agent and reported a high sensitivity for all sizes of polyp with supine positioning alone. Table 6 shows reported sensitivities for supine positioning for preliminary studies and more recent studies, which shows that sensitivity for CTC for detection of polyps has improved, possibly due to changes in CTC technique and/or technology.

Table 6: Reported Sensitivity of CTC Performed with Supine Positioning

Year	Authors	Sensitivity % >=10 mm	6-9 mm	<=5 mm
2000	Mendelson et al.	57	42	0
	Pescatore et al.	43–57	N/A	N/A
2002	Wong et al.	82	N/A	68
	Cohen et al.	100	86	60

A study by Yee et al. (30) reported significant improvement in the sensitivity of the combined (supine and prone) position scanning as compared with either supine or prone scanning alone for each size category of polyp ($p<0.001$). There was no significant difference in the sensitivity between supine scanning versus prone scanning for each size category. Combined scanning produced a significantly higher sensitivity than that with either supine or prone scanning (90.4%, $p<0.001$). The specificity for detection of patients with polyps was significantly higher with prone scanning (97.1%) compared with supine (85.3%) or dual positioning (82.4%).

Multi-slice versus single-slice scanning

Studies on multi-slice CTC demonstrated high sensitivity and specificity for large- and medium-size polyps. The first study on multi-slice CTC (22) showed high sensitivity and specificity. The results of most studies show improved sensitivity for different sizes of polyps with the exception of a study by Gluecker et al. (23) in which most of the false negative results were related to respiratory artefacts and perceptual errors.

Hara et al. (13) showed that respiratory artefacts were significantly reduced with the multi-slice scanning compared with the single-slice. In this study, 84% of the images by multi-slice had no identifiable respiratory artefacts compared with 39% of the single-slice images. The decrease in respiratory artefacts with multi-slice images was observed because all images were acquired in a single short breath hold (21 seconds) rather than the multiple long breath holds required for the single-slice CT scans. Reducing artefacts is most helpful in reducing evaluation time and diagnostic errors.

The range of reported sensitivities using single-slice or multi-slice scanning are shown in Figure 2(a) and 2(b).

Figure 2. Diagnostic Accuracy of CTC: Multi-slice vs Single-slice Scanning
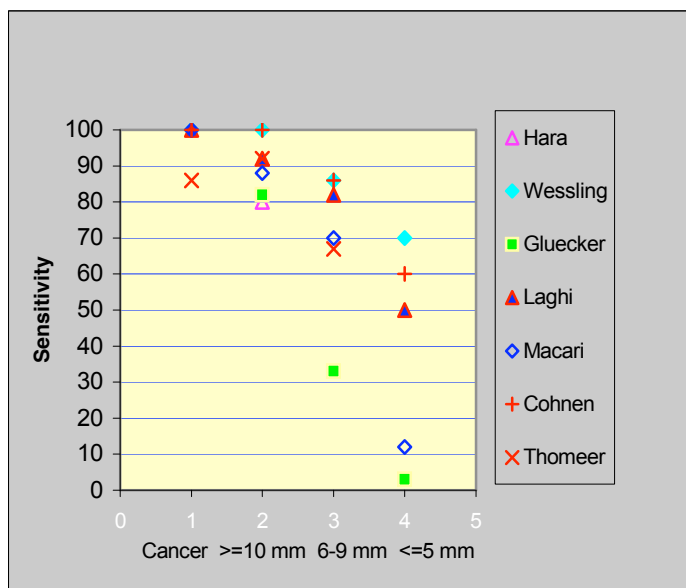
Figure 2 (a). Studies performed with multi-slice scanner
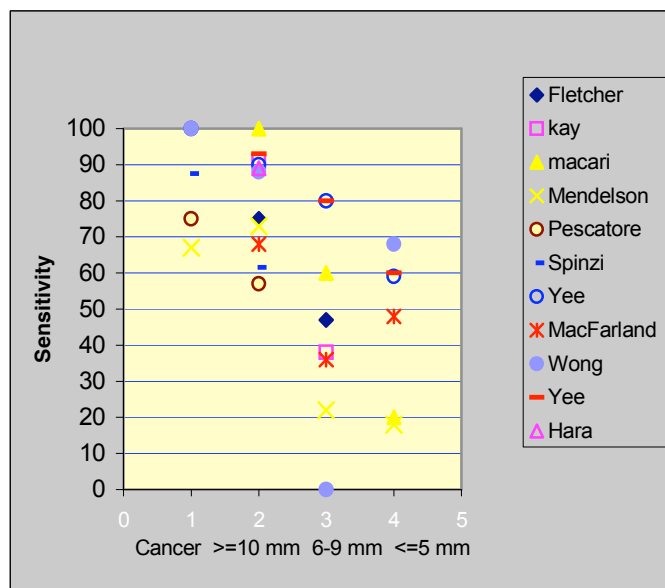
Figure 2 (b). Studies performed with single-slice scanner

A narrower slice collimation generates a superior sensitivity profile. Although an altered scanning technique may increase detection of smaller polyps, this would require increasing the radiation dose. In addition, a very low slice thickness creates a large number of images, and this is very demanding on the storage capacity and viewing station.

Radiologist's Experience

Table 7 summarizes the number of radiologists in each study, their levels of experience, and their average review times.

Table 7: Review of Radiologist's Experience, Level of Experience, and Average Review Time in CTC

Author, Year	No., specialty	Study Conditions	Level of Experience	Review Time Mean† (Range) min	
Kay, 2000	1 radiologist	Blinded to the results of colonoscopy and prior imaging	Radiologist interested in abdominal radiology Endoscopist experienced	First 20 patients Next 18 patients	60 35
Macari, 2000	2 radiologists	Blinded to the results of colonoscopy Independently examined CTC data sets with Method 1 or 2 Method 1: Observer examined the axial and prone 2-D data sets in a cine mode and 3-D was used only as a problem solver. Method 2: Method 1 plus data was then completely examined using navigator software for simultaneous review of 3-D fly-through, coronal, sagital multiplanar reformatted, axial images.	Radiologists had training and experience in the interpretation of CTC	Method 1 3-D rendering was used in 62% of patients Method 2	16 (10–23) 40 (28–62)
Spinzi, 2001	1 radiologist 1 endoscopist	Both were blinded to the results of the other test	Radiologist, inexperienced Endoscopist, skilled, experienced (> 400 pancolonoscopies per yr for >= 5 yrs	25 (9–45)	
Yee, 2001	2 radiologists	Both blinded to the patient's history and colonoscopy results	Not reported	Radiologist 1 Radiologist 2	Median 31 27
Wessling, 2001	2 radiologists	Blinded	Not reported	Data transfer, interpretation	45
Gluecker, 2002	1 radiologist 1gastroenterologist	Blinded	Radiologist, limited experience (60 CTCs) Gastroenterologist with vast experience in colonoscopy	13	
Laghi, 2002	2 radiologists	Blinded	Experienced	25	

Author, Year	No., specialty	Study Conditions	Level of Experience	Review Time Mean† (Range) min
Macari, 2002	1 radiologist	Blinded to the patient history and demographic data	4 yrs interpreting CT colonographic studies	11
MacFarland, 2002	4 radiologists	Each radiologist independently evaluated the 70 patient data sets	Mean 12.3 yrs prior experience with CTC	20 (15–23)
Wong, 2002	1 radiologist	Blinded to the clinical information and colonoscopic findings	Experience in the interpretation of sectional images	10–15 60 min for 3-D reconstruction
Cohnen, 2002	1 radiologist 1 gastroenterologist	Blinded to the results of colonoscopy	Radiologist, experienced	40–50
Yee 2003	2 radiologists	Blinded to patient history and colonoscopic findings	Not reported	15–45

Note: Only those studies in which the average review time was reported, † except where specified

Explaining False Results

The following reasons have been discussed as the main reasons for false negative results:

➢ Poor patient preparation (poor bowel preparation, inadequate bowel distension, and collapsed segments)
➢ Perceptual errors (inadequate analysis of 2-D images and learning curve)
➢ Flat polyps

The following reasons have been discussed as the main reasons for false positive results:

➢ Poorly prepared bowel
➢ Incomplete bowel distension
➢ Residual stool and fecal debris
➢ Perceptual errors (misinterpretation of stool or haustral folds)
➢ Appendiceal stump
➢ Motion (respiratory) artefacts

Collapsed colonic segments may mimic a tumour. Retained fecal residue may mimic colonic polyp. Fecal debris often contains bubbles of gas and may shift in position between supine and prone. However, small particles of adherent fecal debris may not contain gas and may not move with changes in patient position. Diverticular disease is also a common cause of false positives.

Careful choice of window settings is important in reducing false results. For example, analysis with soft tissue windows reduces the risk of false negatives for larger lesions. Furthermore, diagnostic pitfalls will be reduced in experienced hands.

Table 8 shows the number and details of false negative and false positive results of each study.

Table 8: Reasons and Details for False Negatives and False Positive Results in CTC

Study	False Negatives		Reasons/Details	False Positives		Reasons/Details
	No. of Polyps or Cases			No. of Polyps or Cases		
Kay 2000	>=10 mm 6–9 mm	1 8	2 due to the collapsed rectum 2 due to retained stool 5 unknown		6	1 was reported as ileocaecal valve 1 due to misinterpretation of stool and/or mucosal folds 1 was spasm 3 not reported
Macari 2000	6–9 mm <=5 mm	2 8	2 in caecum 4 in ascending 1 in transverse 3 in sigmoid	Method 1 Method 2	0 3	3 in 1 patient due to residual stool
Pescatore 2000	Cancer Team 1 Team 2 >=10 mm Team 1 Team 2	 3 1 4 3	Perceptive errors and inadequate analysis of 2-D images	Not reported		
Hara 2001	Single-slice Multi-slice	1 2	Perceptive error 1 polyp > 10 mm missed by both observers 4 other polyps were missed by 1 observer 2 polyps > 10 mm were missed by both observers: 1 due to colonic collapse, 1 unknown 5 other polyps were missed by at least 1 observer.	Single-slice Multi-slice	7 11	5 due to retained stool 1 attributed to a haustral fold 1 unknown 6 due to retained stool 2 attributed to the haustral fold 1 due to the appendiceal stump 1 due to incomplete distension 1 unknown
Spinzi 2001	Cancer >=10 mm <10 mm Mean size, 9.3 mm (Range, 4–25)	1 4 15	Polyps: 1 in rectum 7 in sigmoid 4 in descending 3 in transverse 4 in ascending 68.4% not identified because of poor bowel preparation and insufficient distension 31.6% attributed to the learning curve, 5 of those were among the first 25 patients.	By polyp	4	All < 10 mm, and due to inadequate bowel preparation

Study	False Negatives			False Positives		
	No. of Polyps or Cases		Reasons/Details	No. of Polyps or Cases		Reasons/Details
Yee 2001	By polyp	159	159/524	By polyp	185	185/524
	>=10 mm 5–9 mm <=5 mm	8 28 123	72% (63% of polyps >=10 mm) were in poorly distended and/or poorly prepared segments 72% of 159 missed polyps (63% of >=10 mm or larger) were in poorly distended and/or poorly prepared segments.	>=10 mm 5–9 mm <=5 mm	24 97 64	77% (88% of >=10 mm) were in poorly distended and/or poorly prepared bowel
	By patient	18		By patient	33	
	5–9 mm <=5 mm	4 14		>=10 mm 5–9 mm <=5 mm	2 23 8	
Wessling 2001	By polyp	7	Collapse or inadequate bowel preparation was the most common cause for false negative results	By polyp	13	10 polyps were < 6 mm in 5 patients
				By patient	8	
Gluecker 2002	Per polyp	52	52 lesions were missed at the first review (location not reported) 27 of the missed polyps were found in retrospective review of the images (2 >=10 mm; 7 6-9 mm; 18 <=5 mm) 22 lesions were missed at the retrospective review (12 in rectosigmoid, 1 in descending, 2 in transverse, 7 in ascending and caecum)	Per polyp	1	In spastic region of the sigmoid in a patient with insufficient bowel preparation
Laghi 2002	Per polyp	8	4 due to perceptual errors 3 misinterpreted as residual stool 1 due to collapsed bowel segment	Per polyp	6	3 misinterpretation as fecal debris 2 hypertrophic pilae; 1 perceptual error
	Per patient	4		Per patient	3	

Study	False Negatives			False Positives		
	No. of Polyps or Cases		Reasons/Details	No. of Polyps or Cases		Reasons/Details
Macari 2002	Per polyp	89	9 were >=10 mm 4 of these 9 polyps were identified retrospectively From the 5 polyps > 5 mm in diameter that could not be detected retrospectively, 1 was located in rectum, 1 in hepatic flexure, and 3 in transverse colon	Per polyp	12	1 was believed to probably represent a fold 3 was related to adherent stool 8 were filling defects
				Per patient	9	
MacFarland 2002	Per polyp	36		Per polyp	21	1 in rectum 7 in rectosigmoid 4 in descending 7 in transverse 2 in ascending colon
	>=10 mm	10	5 in rectosigmoid 4 in the transverse colon 1 in the descending colon			
	6–9 mm	26	14 in rectosigmoid 7 in the transverse colon 3 in the descending colon 2 in the ascending colon			
				Per patient	15	
Yee 2003	>=10 mm Supine Prone Combined >=5 mm Supine Prone Combined	17 19 3 16 23 3	Poor preparation, poor distension, and motion artefact	>=10 mm Supine Prone Combined	3 5 6	Poor preparation, poor distension, and motion artefact

Note: The above table demonstrates only those studies in which the details of false results are provided.

Flat Polyps/Cancers

A topic that continues to be debated in the literature is that flat or depressed adenomas may have the potential to degenerate into flat cancers. Flat lesions have often been reported as CTC false negatives. No studies of flat lesions have yet been performed.

Though flat and depressed adenomas appear to be common in Japan (35), some reports indicate that their malignant potential may be lower in Western countries. (36) However, Wolber and Owen (37) from the University of British Columbia reported a high incidence of high-grade epithelial dysplasia (41%) in flat adenoma that had a radial diameter of 10 mm or less, whereas they found only 4% of the polypoid adenoma 10 mm or smaller contained high-grade epithelial dysplasia. They suggested that flat polyps might be precursors of flat ulcerated colonic carcinomas and

recommended a heightened colonoscopic surveillance of patients in whom flat adenomas have been identified.

Apparently, the rate of severe dysplasia of flat adenomas increases with increasing size. Adachi et al. (38) found that flat adenomas more than 5 to 6 mm may change shape or progress to higher atypia. Furthermore, they found that flat adenomas with central depression were larger and demonstrated a significantly higher incidence of malignancy compared to those without central depression.

The percentage of flat adenomas in all adenomatous lesions detected by colonoscopy has been reported as 6.7%. (38) Detection of flat adenoma is difficult and substantially increases the duration of colonoscopy.

Since flat lesions are difficult to detect by CTC, the use of CTC in identifying polyps in patients who may be prone to the development of flat cancers such as ulcerative colitis should be discouraged.

Patient Outcomes

Ease of Use

CTC requires meticulous bowel preparation and air insufflation. The colon is distended with air or carbon dioxide with a rectal tube. Carbon dioxide produces less discomfort than air insufflation but is more expensive. An antispasmodic agent may be administered before scanning. There are no reported short-term complications from CTC.

Patient Perceptions and Preferences

Several investigators have studied patients' preferences. A large prospective study by Gluecker et al. (39) investigated the factors that influence a patient's decision to participate in colorectal screening. The survey questionnaires, which were completed by patients after screening examinations (CTC, colonoscopy, barium enema), measured overall preferences, preferred method to repeat the examination, examination discomfort, and bowel preparation. Most patients directly expressed their overall preference for CTC over colonoscopy or barium enema. Most of them indicated that they would prefer to be re-examined by CTC with bowel preparation (36.9% vs. 26.5%) or CTC without bowel preparation (79.2% vs. 63%) if the period between examinations was a 1-year interval. Preferences for a 3-year interval period depended on the bowel preparation. At this time period, patients were equally willing to undergo either CTC or colonoscopy with bowel preparation (50.6% vs. 51.2%) whereas omitting bowel preparation significantly improved patients' willingness to undergo colonoscopy (16.8% vs. 29.4%). For an interval of 5 years, more patients were willing to undergo colonoscopy with bowel preparation (10.7% vs. 18.9%) or without bowel preparation (3.6% vs. 6.6%).

Patient Safety

CTC exposes patients to high doses of ionizing radiation. Radiation dose is an important issue, particularly if the method is eventually aimed at colorectal cancer screening in which repeated investigations are required in a large number of individuals.

Radiation Exposure

The International Commission on Radiological Protection and the National Council Radiation Protection and Measurements have made recommendations on dose limits for ionizing radiation for workers and for the public. According to these organizations, the risk of radiation-induced cancer is now 3 times greater than a decade ago. They specify that a dose limit for occupational exposure is 100 milli sievert (mSv) in 5 years with the condition that there will be no more than 50 mSv in any 1 year. (40) Estimating radiation dose to the patient became mandatory in Europe in 1997.

It is evident that radiation exposure in CTC procedure is not negligible, especially if images are obtained with the use of multi-slice scanners and in both supine and prone positions. Any long-term negative outcome, which can turn in to a population health hazard, should be considered in the safety profile of any new technology before it can be considered for a widespread use.

Relatively little data is available with which to assess the long-term effects of the cumulative radiation dose from medical diagnostic exposures. It is necessary to review the radiation characteristics of CTC in greater detail for reassurance of the safety of this procedure.

Scan Parameters

The radiation dose to the patient is a function of scan parameters such as tube current and beam quality. Currently, various professional organizations have differing image acquisition protocols. The median effective dose for CTC at institutions that perform CTC research is currently 8.8 mSv. (41)
Typical CT scanning techniques use 30 mAs for lung cancer screening, 75 mAs for coronary calcification scoring, and 100 mAs for screening the abdomen and pelvis. The studies included in this assessment used an x-ray tube current of 50 to 300 mAs and a beam quality in the range of 110 to 130 peak kilovoltage (kVp). Tube current is a parameter that can affect image quality and examination efficiency. Increasing kVp increases both radiation dose and penetration. For example, with all other scan parameters kept constant, an increase from 120 to 140 kVp generally increases the patient radiation dose by 30% to 40%. (42)

The radiation doses from CTC are about 50% greater with multi-slice compared to the single-slice scanner. (43) Scanning in both supine and prone position increases the radiation dose to the patient. The time required for the scanning is also an important determinant of radiation dose.

The Entrance Skin Dose (ESD) in diagnostic radiography is proportional to the tube current, the length of exposure, and the square of kVp. A fourth factor that applies to all of the modalities is the *inverse square law*. The dose at any location is inversely proportional to the square of the distance to the source. (44)

The 2 main variables used to describe doses received from CT scanning are the *computed tomography dose index* (CTDI) and the *multiple scan average dose* (MSAD). The United States Food and Drug Administration requires manufacturers to report CTDI delivered from phantoms for head and body scanning. In general, the MSAD ranges from 4 to 6 rad (40–60 mGy) for head scans and from 1 to 4 rad (10–40 mGy) for body scans. (44)

Neoplastic Transformation

Neoplastic transformation due to x-ray exposure has been demonstrated (45) in human hybrid cell lines. Although, it is not known if and how the mutation risk measured in vitro in cultured cell lines translates into cancer risk in the CTC procedure, there might be a theoretical possibility for high-risk individuals with premalignant polyps.

A similar concern has been raised in the context of mammography. Frankenberg et al. (45), have suggested that women with an inherited increased breast cancer risk should avoid the frequent and early mammography screening. For these women, alternative screening methods such as MRI or sonographic techniques have been suggested.

Organ Doses

Radiation absorbed dose delivered to the organs during an x-ray examination is an important issue. Specific organs of interest include, but are not limited to, active bone marrow, thyroid, breasts, gonads, colon, and the lens of the eye. (44)

Risk of Radiation in Women

The radiation dose during CTC procedure is about 50% higher for woman than for men. The calculated effective doses to the patient during CT procedure are 5.507 mSv for men and 8.29 mSv for women. Macari et al. (25) calculated the effective dose for their study as 5.0 mSv for men and 7.8 mSv for women using WinDose software. In Thomeer's study (29), the effective dose per patient was 7.03 mSv for men and 10.28 mSv for women.

The potential biological damage from CT radiation is greater in women than in men. It should be noted that with the patient in the supine position, the skin of the back would have the greatest exposure, whereas in the prone position, the breast would be closer to the surface of the table. Considering the "*inverse square law*" described above, scanning in prone position will expose the breasts to high amount of radiation.

The ovary, a radiosensitive organ, is also exposed to x-ray radiation during the CTC procedure. The estimated dose to the uterus from barium enema study is 10 mGy, whereas it is 30 mGy from abdominal CT scanning (Table 12).

Table 12: Estimated Radiation Doses to the Uterus from Diagnostic Procedures

Examination		Absorbed Dose	
		mrad	mGy
Upper gastrointestinal series		100	1.00
Cholecystography		100	1.00
Lumbar spine radiography		400	4.00
Pelvic radiography		200	2.00
Hip and femur radiography		300	3.00
Retrograde pyelography		600	6.00
Barium enema study		1,000	10.00
Abdominal (KUB) radiography		250	2.50
Hysterosalpingography		1,000	10.0
	Head	~0	~0.0
CT	Chest	16	0.16
	Abdomen	3,000	30.00

Adopted from Parry et al. 1999 (44)

mrad refers to milli rad; mGy refers to milli Gray.

Extensive information on the risk of radiation-induced cancer has been gained from long-term follow-up of several populations with radiation exposure. For example, ionizing radiation as a causative agent for breast cancer has been reported in women treated with radiation for various medical conditions in adult life, such as multiple fluoroscopic examinations of the chest for the treatment of pulmonary tuberculosis (46–49), women who received x-ray examinations in the treatment of scoliosis, (50) the treatment of acute post-partum mastitis, (51) and the treatment of ankylosing spondylitis.

A significantly increased incidence of breast cancer in women who received irradiation for treatment of Hodgkin's disease has been reported. (52) Hancock et al. (53) reported a relative risk of 136 for women treated before 15 years of age (95% CI=34–371). The relative risk declined with age, but remained significantly elevated in groups under 30 years old at the time of irradiation (age range, 15–24, RR=19, 95% CI=4.7–51.1, p=0.0003; age range, 24–29, RR=7, 95% CI=3.2–14.4, p=0.0004).

The radiation dose to specific organs is associated with patient orientation with respect to the x-ray tube. Delarue et al. (46) estimated the radiation dose to the breast in patients who had multiple fluoroscopy of the chest. The total radiation dose to the breast in supine position was 17 rad. The investigators indicated that had these patients been examined in the prone position (estimating the mid breast to be 1.5 in from the surface of the table) the same number of fluoroscopies would have produced an exposure of 308 rads.

Overall, in women, the risk due to radiation exposure from CTC procedure may exceed the benefit of colorectal cancer screening for the following reasons:

➤ According to the current scanning protocols, the exposure rate in the CTC procedure is higher for women than for men.
➤ Breasts and ovaries are radiosensitive organs and are exposed to considerable amount of radiation during the CTC procedure.

- High sensitivity for CTC is achieved by supine and prone positioning, but prone positioning increases radiation exposure and the risk of developing breast cancer.
- Time is an important determinant of radiation dose. Typical mammography requires 5 seconds, whereas CTC requires 30 to 60 seconds for each position.
- The prevalence of colorectal cancer is lower in women than in men (Table 1).
- Life expectancy is longer for women; therefore, it may exceed the latent period for the carcinogenic effect of radiation.

Considering the above discussion, patients can be managed more effectively by colonoscopy, which does not have the risk of radiation, is more sensitive in detecting small and flat lesions, and offers the opportunity for performing biopsy or removal of the lesions.

CTC for Screening the Average-Risk Population

The results of the studies of high-risk populations cannot be extrapolated to the screening of an asymptomatic population in which the prevalence of disease is low. A higher prevalence of disease may bias the radiologist to search more thoroughly (suspicious bias), thus increasing the examination sensitivity. Patients in whom there is low suspicion of abnormality may have tests performed or interpreted in a manner that is not as careful as in patients with higher clinical suspicion.

Of the 18 studies, 8 included patients under the age of 50 years and 6 did not report the age range of the patients. Therefore, patients in most of these studies are not representative of the population eligible for screening, normally over 50 years of age.

Since the inception of CTC, only 3 studies included asymptomatic patients in their study population, 2 with a small number of patients. Before the year 2000, there was only 1 study that included individuals over the age of 50. Rex et al. (54) studied 46 asymptomatic individuals, mostly men all 60 years or older. This study was conducted during the earliest phase in the development of the technology (1995–1996) and, since CTC failed to identify a significant number of large benign polyps and most small adenoma, the investigators did not recommend CTC as a colorectal cancer screening test. Per-patient analysis showed sensitivity of 50% for detection of polyps 10 mm or larger, 43% for polyps 6 to 9 mm, and 11% for polyps 5 mm or smaller. Specificity for patients with lesions 10 mm and larger was 89%. Low sensitivity was a particular problem for broad, flat adenoma in the right colon.

Macari et al. (16) studied 42 asymptomatic individuals in which 12 (29%) had a family history of colorectal cancer. They found an overall sensitivity of 38% and a specificity of 96% to 100%. The low sensitivity in their study was mostly due to the polyps measuring less than 5 mm. CTC detected the only 10-mm polyp (sensitivity 100%), 3 of 5 polyps 6 to 9 mm (sensitivity 60%), and 2 of 10 polyps 5 mm or smaller (sensitivity 20%).

The study by Yee et al. (21) included 96 asymptomatic individuals (32%) and 204 symptomatic patients (68%). No statistically significant differences in the performance characteristics of CTC were identified between the 2 groups. With per-polyp comparison, the overall sensitivity for polyp detection was 69% in the screening group and 69.7% in the symptomatic group (p=0.25). With per-patient analysis, the sensitivity and specificity of CTC for the asymptomatic group was 88% and 82% respectively, versus 90.9% and 67% for the symptomatic group (p=0.59 and 0.12 respectively).

Examination of the grey literature for the average-risk population revealed a large multicentre clinical trial (31) on CTC. The abstract only is published at the Digestive Disease Centre, Medical University of South Carolina Web site, but more information was obtained through the principal investigator. (55) The full results have been submitted for publication in a peer- reviewed journal. The clinical study design was a non-inferiority trial using a matched-pair design to test whether the differences between the 2 procedures were minimal enough to accept CTC as an alternative standard screening tool. This multicentre study included 615 individual aged 50 years or older who were at low-to-average risk for colorectal cancer. CTC performed poorly in this study. Sensitivity and specificity for polyp detection was 55% and 96% for polyps 10 mm and larger, 39% and 90.5% for polyps 6 mm and larger. Two of the 8 cancers were missed (sensitivity 75%). Patients reported pain during procedures as discomfort, distressing, or horrible significantly more often with CTC than with colonoscopy (27% vs. 15%), presumably related to receiving sedation or analgesia during colonoscopy.

One difference between this study and the other clinical trials is that the fly-through reconstruction of the CT images were reviewed separately at a later time. The level of experience with CTC was lower than that in the other small clinical trials. A few centres had many years of experience, but most had experience of performing about 10 CTCs. Measuring the radiation dose was not incorporated into the study design. Analysis by centre showed a considerable variation in accuracy of the CTC among the centres. The highest per-patient sensitivity rate was 80% and the lowest was 0% (due to the small number of polyps in 1 centre).

Incomplete Colonoscopy

Twelve studies reported that all colonoscopies were completed, and 6 studies reported incomplete colonoscopy (Table 9). The rate of incomplete colonoscopy among 18 studies varied from 0% to 10%. The main reason for incomplete colonoscopy was obstruction or stenosis due to the presence of a tumour.

Table 9: Number of and Reasons for Incomplete Colonoscopy

Study	No. (%) of Incomplete Colonoscopies
Fletcher 2000	All completed
Kay 2000	All completed
Macari 2000	All completed
Mendelson 2000	All completed
Morin 2000	All completed full colonoscopy or surgical correlation
Pescatore 2000	2 (4) Both due to stenosing masses
Hara 2001	All completed
Spinzi 2001	2 (2%) 2 patients had incomplete colonoscopy and these patients in addition to another patient in which colon could not be distended properly were excluded from the analysis.
Yee 2001	All completed
Wessling 2001	All completed
Gluecker 2002	All completed
Laghi 2002	9 (6) All due to presence of colonic neoplasm. CTC was able to visualize the entire colon in these cases, but no additional lesions were found.
Macari 2002	2 (2) 1 due to the residual fecal material; 1 due to an obstructive neoplasm
MacFarland 2002	All completed
Wong 2002	7 (10) 4 due to tumour obstruction, 1 due to previous surgery, and 1 due to poor bowel preparation
Cohnen 2002	All completed
Thomeer 2003	5 (3) All due to obstructing tumours; CTC was able to visualize the entire colon in all 5 cases but no additional lesions were found.
Yee 2003	All completed

The above finding prompted a search for reports of the usefulness of CTC for patients after an incomplete colonoscopy. A separate literature search identified studies on the subpopulation of patients who had incomplete colonoscopies, as well as patients with obstructive/stenosing colonic lesions in which colonoscopy cannot be performed in a routine fashion.

Utility and Effectiveness of CTC for Patients with Incomplete Colonoscopy

Table 10 shows the performance of CTC following an incomplete colonoscopy.

Table 10. CTC Versus Other Tests After an Incomplete Colonoscopy

Study/ Comparison	Patients/indications/ mean age	Colonic distension and visualization	Identification of the causes for incomplete colonoscopy	Visualization of cancer/polyps	Extra-colonic information
Morrin 1999 **CTC vs BE**	40 patients in whom caecum could not be reached. Indication for colonoscopy: pasage of blood via the rectum (17), family history of colon cancer (7), positive FOBT (7), history of colonic polyps (5), and altered bowel habits (4). Mean age: 62 ± 17 (22-96)	CTC: adequately revealed 96% of all colonic segments. (almost all patients in whom colonoscopy did not progress beyond hepatic flexure, had adequate distension of the non-visualized segments before air insufflation) BE: adequately revealed 91% of all segments (p<0.05)	CTC: the causes for incomplete colonoscopy were identified in 74% of the patients. BE: the causes for incomplete colonoscopy were identified in 65% of the patients. Not statistically significant	CTC: identified 9 polypoid lesions in 7 patients (7 were measured 5 mm, one measured 6 mm, one measured 8 mm) BE: identified only 2 lesions (6 and 8 mm) (None of the 5 mm polypoid lesions (n=7) were visualized on BE)	CTC: clinically significant extra-colonic abnormalities were identified in 13% of the patients. This included a 60 mm aortic aneurysm, a mesenteric and pericolic lymphadenopathy, a complex ovarian cyst, an obstructing ventral hernia and a large fibroid tumor with bowel compression.
Macari 1999 CTC vs BE	10 patients who underwent incomplete colonoscopy. Indications for olonoscopy: screening (8), and bleeding (2). Mean age: 65 (50-80)	Not reported	CTC fully evaluated the proximal colon	CTC: found 8 normal colon, two polypoid lesions [one 10 mm in ascending colon and one 7 mm in transverse colon]. BE: confirmed 8 normal colon, two polypoid lesions [one in ascending colon and one in transverse colon].	Not reported
Neri 2002 **CTC vs colonoscopy**	34 patients who underwent incomplete colonoscopy. Indications for colonoscopy: bright red blood per rectum, positive FOBT, altered bowel habits, anemia of unknown cause and pain in the right lower quadrant. Mean age: 63 (35-76)	Total colonic distension with both supine and prone scanning was achieved in all patients. (Supine images: the sigmoid lumen was totally collapsed in 46% of the patients Prone images: inadequate distension of the transverse colon was observed in 11% of the patients)	Group A: 19 patients in whom the distal occlusive tumor was found by colonoscopy Group B: 15 patients in whom the causes of incomplete colonoscopy were patient intolerance, stricture, due to diverticulitis, residual fibres after surgery All group A and 67% of group B underwent surgery	Gold standard of surgery or colonoscopy **Sensitivity for cancer:** Group A: CTC: 100%, colonoscopy 90% (P=0.42) Group B: CTC: 100%, colonoscopy: 0% (P<0.01) **Sensitivity of CTC for polyps:** >=10 mm:100% 6-9 mm: 100% <=5 mm: 86%	For hepatic lesions: Sensitivity of enhanced CTC: 100% (11/11) Sensitivity for non-enhanced CTC: 64% (7/11)

BE=Barium enema

The completion rate for colonoscopy based on an internal audit (56) of 5,000 patients in Hamilton Ontario is 91%. In a study (56) conducted at McMaster University, the reasons for failure to complete the colonoscopy were redundancy or tortuosity of the colon, pain or spasm, fixed bowel loops, diverticula, and colonic obstruction/stenosis. Eighty percent of those patients in whom fixed bowel loops contributed to the failure of colonoscopy had undergone previous surgery. Several studies indicate that completion of colonoscopy is inherently more difficult in women than in men, most likely due to pelvic anatomy. (56)

Neri et al. (57) compared the sensitivity of CTC with that of conventional colonoscopy in 2 groups of patients. Group A consisted of patients with a distal occlusive tumour found by colonoscopy. Group B consisted of those in which the causes of incomplete colonoscopy were patient intolerance, stricture, diverticulitis, and residual fibres after surgery. All the patients in Group A, and 67% of the patients in Group B underwent surgery, and the results were confirmed with surgery or colonoscopy. In Group A, CTC identified more cancers than colonoscopy (sensitivity 100% vs. 90%). In Group B CTC found all the cancers, but colonoscopy identified none (sensitivity 100% vs. 0%).

Two studies compared the performance of CTC after incomplete colonoscopy with that of the barium enema. In a study by Morrin et al., (58) CTC identified more lesions than did the barium enema in endoscopically unseen regions of the colon. CTC identified 9 polypoid lesions in which 7 measured 5 mm, and 2 were 6 and 8 mm. The barium enema identified the larger lesions, but none of the 5-mm lesions could be identified with this method. A study by Macari et al. (59) showed equivalence between the 2 techniques. However, due to the lack of a gold standard in such comparisons, it is difficult to compare the sensitivity of the 2 techniques following incomplete colonoscopy.

In contrast to the barium enema, CTC has the potential to identify clinically significant extracolonic lesions. In Morrin's study (18), extracolonic abnormalities were identified in 13% of the patients including a 60-mm aortic aneurysm, a mesenteric and pericolic lymphadenopathy, a complex ovarian cyst, an obstructing ventral hernia, and a large fibroid tumour causing bowel compression.

The barium enema may be contraindicated on the same day if a polypectomy has been performed. There is also a concern that there may be serious risk attached to performing a barium enema shortly after a failed colonoscopy. There are reports of perforation of the large bowel and extravasation of the contrast material after a barium enema performed the same day as colonoscopy.

Utility and Effectiveness of CTC for Patients with Obstructive/Stenosing Lesions

For patients with suspected colonic obstruction, a non-invasive method of diagnosis with the ability to distinguish between obstruction and non-obstruction is ideal. Colonoscopy is currently the examination of choice for evaluating patients with colonic obstruction. Evidence shows that CTC has higher sensitivity than colonoscopy in evaluating colonic obstruction.

Table 11 shows the performance of CTC in patients with obstructive/stenosing lesions.

Table 11. Performance of CTC in Occlusive/Stenosing Lesions

Study	Patients	Indications for colonoscopy	Colonic distension and visualization	Visualization of cancer/polyps	Extra-colonic information
Frager 1998 **CTC vs colonoscopy**	75 patients with possible colonic obstruction suggested by colonic dilatation on abdominal radiographs. 25 patients underwent surgery Age range (39-91)	Dilatation of transverse colon on abdominal radiograph (55); dilated small bowel on abdominal radiograph (12); clinically obstructed (8)	Not reported	Gold standard: surgery and/or endoscopy Diagnosis of obstruction: **Sensitivity:** CTC: 96% (45/47) Colonoscopy: 80% (20/25) (p=0.045) **Specificity:** CTC: 93% Colonoscopy: 100% Not significant **NPV:** CTC: 93% Colonoscopy: 16.7% p=0.0004].	Not reported
Fenlon 1999	29 patients with distal occlusive colorectal carcinoma identified at colonoscopy. Mean age: 65 (46-83)	Not reported Colonoscopists were unable to visualize the proximal colon in any of the 29 patients.	CTC enabled a complete evaluation of the colon in 26 of the 29 patients. 72 segments of colon were proximal to occlusive carcinoma and were not seen by colonoscopy. 86% of the 72 segments was clearly seen by CTC.	CTC: identified all 29 occlusive carcinomas and demonstrated 2 synchronous cancers (surgical findings confirmed the correct prediction of the location of all 29 occlusive cancers) CTC identified 24 polyps in the proximal colon (4 to13 mm). None of these lesions were identified by means of intra-operative palpation. 16 of the polyps detected by CTC were confirmed by follow-up colonoscopy and removed. False positive: 1 False negative: 2 (these polyps (4 and 5 mm) were identified at postoperative colonoscopy	Not reported

Study	Patients	Indications for colonoscopy	Colonic distension and visualization	Visualization of cancer/polyps	Extra-colonic information
Morrin 2000	34 patients who underwent colonoscopy (20 colorectal masses, 7 benign obstructive stricture, 7 prior colorectal resection) In 15 patients colonoscopy was incomplete because of obstructing lesions. Mean age: 64.2 (19-91)	Rectal bleeding (12), positive FOBT (9), altered bowel habits (8), anemia or weight loss of unknown cause (5)	There was adequate distension of all colonic segments with CTC 97% of all colonic segments were adequately visualized by CTC In 9 patients who underwent BE, 60% of all colonic segments were adequately visualized (p<0.01)	Gold standard: surgical findings or colonoscopy CTC Sensitivity for colorectal masses: 100% (20/20) Specificity for colorectal masses: 95% False positive: 2 Sensitivity for synchronous polyps: 93% (16/17) CTC correctly staged 81% (13/16) of all colorectal cancers	Both patients with liver metastases were correctly identified. CTC correctly identified 80% of patients with significant pericolic lymphadenopathy.
Laghi 2002 **CTC vs colonoscopy**	33 patients with known colorectal carcinoma diagnosed by colonoscopy (stenosing lesions) and 9 incomplete colonoscopy due to stenosing lesions	Patients affected by colorectal carcinoma	CTC allowed for adequate visualization of the entire colon in all cases.	Gold standard: histologic examination or colonoscopy CTC identified all 33 primary cancers, 2 synchronous cancers (20-150 mm) and 10 polyps (6-10 mm) Colonoscopy identified 33 carcinomas and 4 polyps (missed 2 synchronous tumors and 6 polyps located proximal to the stenosis) CTC correctly staged 26 of 33 carcinomas (accuracy 78.7%.	CTC detected 23 hepatic metastases in 6 patients (3 in 3 patients were confirmed by histologic examination, 20 in 3 patients were confirmed by intraoperative ultrasonography)

NPV=Negative predictive value

In Frager's study (60), colonoscopy could not establish the diagnosis of obstruction in 20% of the patients (sensitivity 80%), whereas CTC diagnosed the obstruction in 45 of the 47 patients (sensitivity 96%). CTC was statistically more sensitive (p=0.045), more accurate (p=. 047), and had a better negative predictive value (p=0.0004) compared with colonoscopy. In a study by Laghi et al., (61) CTC identified all 33 primary cancers, 2 synchronous cancers, and 6 polyps, whereas colonoscopy missed 2 synchronous cancers and 10 polyps proximal to the stenosis. In addition, in studies by Fenlon et al. and Morrin et al., (62; 63) CTC identified all occlusive carcinomas.

In conclusion, the above studies show that CTC can be the examination of choice for those patients who had obstructive/stenosing colonic lesions. The advantages of CTC in these patients include the following:

- CTC investigates the entire colon in most patients with occlusive tumours or stenosing lesions.
- CTC has demonstrated a high sensitivity in detecting cancers and obstructive tumours.
- CTC has the ability to detect synchronous colorectal carcinomas, tumour metastases, and extracolonic lesions. Therefore, the technique can provide additional information before surgery, which may influence surgical conduct such as the extent of resection.
- CTC provides useful information for tumour staging.
- CTC may be preferable to barium enema in terms of the extent of the proximal colon that can be visualized and the detection of extracolonic lesions.

Evidence-Based Summary

CTC is a novel imaging modality for the detection of colonic cancers and polyps. Currently CT and MRI are the primary imaging sources for VC. MRI has the advantage of not using ionizing radiation and of providing better soft-tissue contrast resolution, whereas its disadvantages include higher costs and limited availability. The existing literature on MRI colonography with appropriate sample sizes is scarce. Hence, it is too early to conduct a full assessment of this imaging technique.

Diagnostic Performance of CTC

➢ Performance of CTC depends on the size of the lesions:

- Sensitivity for cancer detection ranges from 67% to 100% for single-slice and 86% to 100% for multi-slice scanning.
- Sensitivity for detection of polyps 10 mm and larger ranges from 80% to 100% for multi-slice and 57% to 100% for single-slice scanning.
- Sensitivity for detection polyps 6 to 9 mm ranges from 33% to 86% for multi-slice and 0% to 80% for single-slice scanning.
- Sensitivity for polyps 5 mm or smaller ranges from 3% to 70% for multi-slice and 18% to 68% for single-slice scanning.
- The clinical significance of small size polyps is controversial.
- Small flat lesions are often reported as CTC false negatives.
- Flat or depressed adenomas have about a 40% chance to degenerate into flat cancers.

➢ The diagnostic performance of CTC depends on technical and technological factors including the following:

Scanning techniques

- The diagnostic accuracy of CTC increases with multi-slice scanning.
- Multi-slice CT scanning allows for thin slice examination of the entire abdomen in one single breath hod. Therefore, it reduces respiratory artefacts by reducing the scanning time.
- Thin slices improve polyp detection but require a higher tube current to maintain image quality.
- Dual positioning increases the accuracy of CTC technique. Errors due to retained fluid and collapsed segments can be reduced with additional scanning in prone position.

Methods of bowel preparation

- CTC requires the same bowel cleansing preparation as conventional colonoscopy.
- Poorly prepared colon makes it difficult to distinguish between stool and lesions and a fluid-filled colon may hide submerged polyps.

Adequate bowel distension

- Failure to adequately distend the colon may obscure the lesions or produce false positive findings.
- Moving the patient from the supine to the prone position allows for a redistribution of insufflated air that often results in a distension of collapsed segments.

Radiologist's experience

- CTC is subject to interpreter variability.
- The radiologist's accuracy in interpretation improves with experience.
- Endoluminal 3D images are useful in problem solving situations.

Evidence for the Use of CTC

CTC for colonic evaluation in the presence of obstructive/stenosing tumours

CTC is a useful diagnostic modality in colonic evaluation of patients with incomplete colonoscopy due to obstructive/stenosing colonic lesions. The following reasons support this statement:

- CTC was able to visualize the entire colon in most patients with occlusive tumours or stenosing lesions.
- CTC has demonstrated a high sensitivity in detecting cancers and obstructive tumours.
- CTC has the ability to detect synchronous colorectal carcinomas, tumour metastases, and extracolonic lesions. Therefore, the technique can provide additional information before surgery, which may influence surgical conduct such as the extent of resection.
- CTC may be preferable to barium enema in terms of the extent of the proximal colon that can be visualized and detection of extracolonic lesions.
- CTC can provide useful information for tumour staging.

CTC following incomplete colonoscopy in non-occlusive lesions

For patients with incomplete colonoscopy (due to non-occlusive lesions), 2 studies that evaluated the clinical usefulness of CTC compared with barium enema showed them to be equivalent for identifying lesions larger than 5 mm.

CTC for colorectal screening

The most important characteristic of a screening test is an optimal sensitivity with acceptable specificity. Although CTC offers the potential advantage of being less invasive than colonoscopy and has the ability to image the entire colon, it lacks the necessary sensitivity required for screening. In addition, CTC offers no therapy that can be applied once an abnormality is detected.

Safety of CTC

- Protecting individuals from the biological effects of ionizing radiation should be taken into account when performing the CTC procedure. Exposure to ionizing radiation is a potential disadvantage of CTC.
- Concerning patient protection, VC based on MRI data sets may be a more reasonable alternative since this technique does not use x-ray radiation.
- Inherent in the design of multi-slice scanners are elements or parameters that have the potential to increase radiation exposure.
  - The radiation doses to patients are about 50% greater with multi-slice compared to the single-slice scanner.
  - The thinner the slice, the better the spatial resolution, which increases the likelihood that a small polyp will be detected. On the other hand, the thinner section mode increases radiation dose.
- Scanning in both supine and prone position increases the radiation dose to the patient.

- Radiation exposure from CTC procedure is about 50% higher for woman than for men.
- In women, the risk due to radiation exposure from CTC procedure may exceed the benefit of colorectal cancer screening.
- Currently, there is no consensus for an image acquisition scanning protocol. Although research is now in progress and holds promise for further dose reductions, this will probably not be in general use for a few years.
- A safe image acquisition protocol needs to be developed by scientific communities to estimate radiation dose.
- The question of whether the CTC procedure confers a cancer risk or accelerates neoplastic transformation has not yet been investigated. If there is a risk of cancer promotion, then the latent period may not exceed the life expectancy in many patients and may result in an increased incidence of cancer in exposed organs years after the exposure.

Professional Aspects

- CTC interpretation requires a long training period.
- CTC performed in centres with professional and technical expertise can be a highly accurate method for evaluation of colon in a high-risk population.
- The high rate of false positives in centres with limited experience will result in unnecessary additional testing, increased cost, and increased anxiety for patients.
- Further improvement in CTC techniques may become possible with the development of computer-aided diagnostic techniques that have the potential to identify polyps with high sensitivity and an acceptable false positive rate.

Advantages

- The advantages of CTC from the patient's perspective are as follows:

- Short examination time
- Less invasive
- Does not require sedation
- Creates no immediate complications

- The advantages of CTC from a technical perspective are as follows:

- Less dependent on the skill of the operator
- Needs no barium, therefore does not interfere with subsequent endoscopy
- More accurate in spatial location of lesions
- Provides information on pericolonic structures
- Possibility of retrograde/antegrade visualization provides the opportunity to detect polyps that are hidden behind mucosal folds

Disadvantages

- The major limitation of CTC is that the patients must undergo a colonoscopy whenever an abnormality is found.
- Patients are exposed to ionizing radiation.
- Polyps smaller than 6 mm diameter are difficult to detect because of current imaging protocol.
- Interpretation is time-intensive.
- Patients must undergo bowel cleansing and air insufflation.

CONCLUSION

With the limited sensitivity and specificity of CTC relative to colonoscopy, together with the lack of therapeutic intervention, this method of screening may result in inconvenience, cost, and complications of both tests.

Based on the current evidence, CTC cannot be proposed for population-based colorectal cancer screening.

Patients with colonic symptoms or a personal/family history of polyps will benefit more in several ways if they undergo colonoscopy including excision of premalignant polyps.

Considering the possibility of assessing the entire colon, extracolonic structures, and tumour staging, CTC can be the examination of choice for preoperative evaluation of patients with colorectal carcinomas.

CTC can be considered for diagnostic purposes in patients in whom performing colonoscopy is clinically contraindicated or for those patients who had incomplete colonoscopy because of stenosis or obstruction of the colon.

Exposure to ionizing radiation is a potential disadvantage of CTC.

Radiation dose associated with CTC is higher with the use of multi-slice scanner and increases with dual positioning.

Radiation exposure is higher for female than the male.

MRI-based VC that excludes the risk of ionizing radiation could become more attractive than CTC in the future.

GLOSSARY/ABBREVIATIONS

Ampere   Unit for measuring electric current
CT   Computerized Tomography
CTC   Computerized Tomographic Colonography
CTDI   Computed tomography dose index
$CTDI_w$ Weighted CT dose index
ESD   Entrance skin dose
FOBT   Fecal occult blood test
Gy   Gray, a measure of absorbed x-ray dose.
                     One Gray is equivalent to an energy deposition of 1 joule per kilogram (J/kg) of tissue
                     [mGy (milli Gray)]
IDA   Iron deficiency anemia
kVp   Peak kilovoltage
mAs   Milliampere/second
rad   Outdated unit of *radiation absorbed dose* which equals to 0.01 Gy
RCT   Randomized Controlled Trial
rem   [*Roentgen-equivalent – man*] The quantity of any ionizing radiation which has the same biological effect as 1 rad of x-ray.
                     [1 rem=1 rad* RBF (relative biological effectiveness); 1 rem = 10^{-2} joule/kgr or 10^{-2} Sv]
Sv   Sievert *[1 sievert = 1 joule/kgr = 100 rem];* mSv (milli sievert)

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