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How Accurate Is CT Colonography?

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Computed tomography (CT) colonography (CTC), also referred to as virtual colonoscopy, has received widespread attention as a new tool for the noninvasive detection of colorectal polyps and cancer. Since the introduction of CTC in 1994, multiple preliminary studies have been performed to evaluate the sensitivity and specificity of CTC in different patient cohorts. During this time, there have been tremendous advances in the image acquisition and display capabilities of this evolving technology. Our purpose will be to first discuss specific parameters that may affect the performance results, followed by a review of studies performed to date.

Study Parameters

Patient Selection

Most of the published studies evaluating the accuracy of CTC have been performed in high-risk patients. These cohorts include patients with a personal or family history of colorectal cancer, patients with symptoms (iron-deficiency anemia, heme-positive stools, or hematochezia), or patients with prior polyps being followed for surveillance. The sensitivity and specificity of CTC for lesion detection in such polyp-rich patient populations may be higher than that in a screening population. Early studies evaluated well-characterized cohorts during the evolution of the technology, but these results cannot be extrapolated to a screening population. Future studies of test performance need to be performed in screening and surveillance populations in which disease prevalence is in general low.

Bowel Cleansing and Distention

Prior to the acquisition of CT data, patients are required to undergo a bowel cleansing regimen. Polyethylene glycol electrolyte lavage solution is the preferred agent by some gastroenterologists for bowel cleansing prior to colonoscopy. Polyethylene glycol is ingested in large volumes and is effective

at cleansing the bowel. However, it often leaves excess residual fluid in the colon; therefore, it is known as a “wet prep.” Residual fluid will obscure colonic lesions and lead to an increase in false negatives. The results from almost all published studies evaluating the performance of CTC for lesion detection are based on patients who have received polyethylene glycol solution as the colonic cleansing agent. Highly osmotic agents such as sodium phosphate (phosphosoda) and magnesium citrate tend to leave the colon relatively dry. However, these “dry preps” tend to leave more solid stool, which can lead to an increased number of false positives and false negatives.

Bowel distention is achieved by retrograde insufflation of the colon with either atmospheric air or carbon dioxide. Carbon dioxide has a steep diffusion gradient across the colonic wall and is resorbed much more rapidly than room air. It is thought to decrease patient discomfort, but it is not clear whether there is any significant effect on colonic distention or polyp detection. Preliminary findings of a prospective randomized study comparing manual insufflation of air vs carbon dioxide revealed similar distention and patient preference for the two gases (McDermott et al. 2001).

The use of glucagon as an antispasmodic agent has been controversial. There is evidence that glucagon does not have any significant effect in improving colonic distention or lesion detection for CTC (Yee et al. 1999; Morrin et al. 1999). Other reasons why glucagon is not likely to be used on a routine basis for CTC include cost issues and the faster acquisition times of multidetector CT scanners. Some of the more recent studies include patients who have not received glucagon.

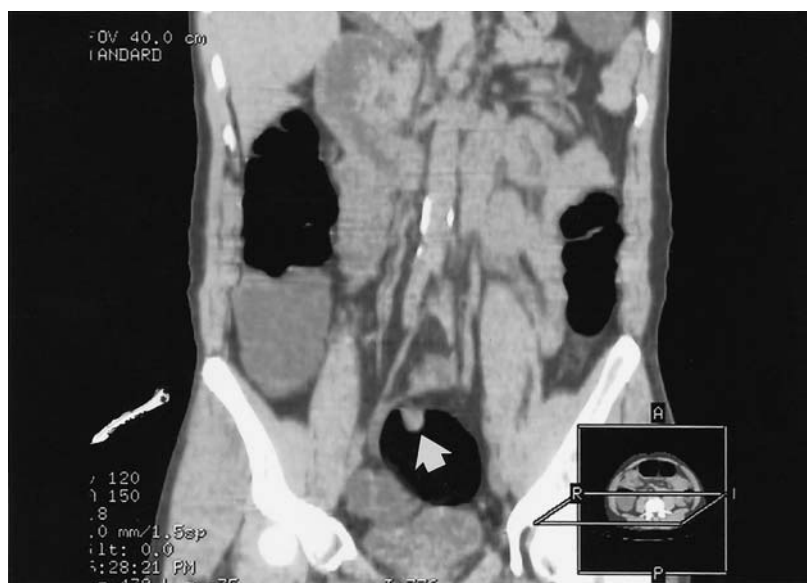
CT Data Acquisition Protocol

Most of the published trials evaluating the diagnostic accuracy of CTC have been performed using a single-detector helical scanner. Single-detector CT protocols that have been studied include various collimations of 3, 5, and >5 mm. Trials are currently in progress exploring the potential for increased sensitivity and specificity using multidetector row CT. Thinner slices of 1- to 2-mm detector width may allow improved spatial resolution and increased sensitivity, in particular for smaller polyps and flat lesions. In addition, narrower collimation may allow easier distinction between polyps and residual stool. However, a higher sensitivity for polyp detection must not be offset by a lower specificity. Limitations of the use of thinner collimation include an increase in image noise that may compromise image quality, an increase in radiation dose to the patient, and larger data management demands.

Essentially all published studies evaluating the ability of CTC to detect polyps have used two-position scanning with supine and prone views. The use of scanning in opposing views has been found to improve colonic distention as well as polyp detection because of shifting of residual material that allows increased surface area visualization (Fletcher et al. 2000; Chen et al. 1999).

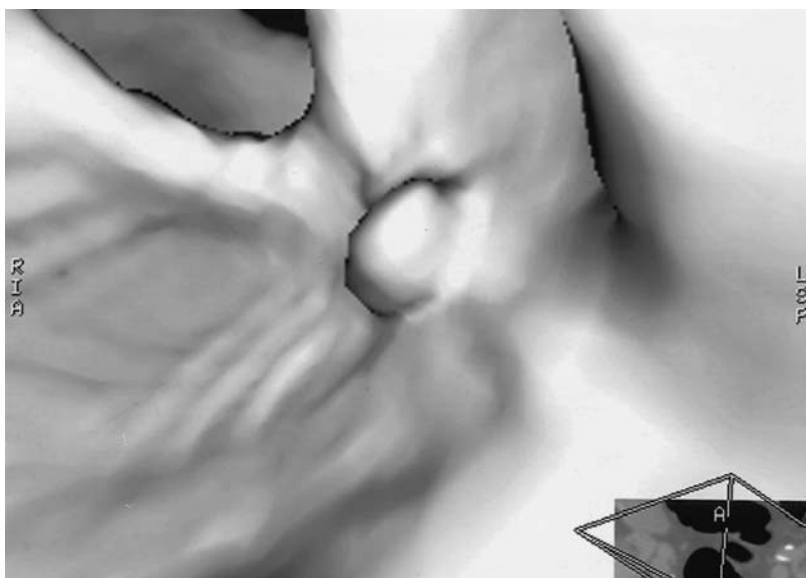
Image Display

The typical image displays used for CTC to date include the 2D multiplanar reformations (2D MPR) and 3D endoluminal views. The 2D MPR allows a seamless interactivity of axial, coronal, and sagittal planes for detection of focal intraluminal lesions in a time-efficient manner (Fig 3.1). Other benefits include improved orientation from the extraluminal point of view and ability to evaluate the source attenuation data for improved characterization. The 3D endoscopic views provide an intraluminal visualization of the colonic mucosal surface (Figs 3.2 and 3.3). The 3D views can exploit different features, such as shaded-surface display or volume-rendered algorithms, color or monochromatic visualization, perspective lighting (to differentiate near field from far field), and manual or automated flight paths for navigation (Rubin et al. 1996; McFarland et al. 1997). Currently, most readers have used the time-efficient protocol of primary interpretation using the 2D MPR images, with selective correlation of focal findings with the 3D endoluminal images (Dachman et al. 1998; Macari et al. 2000). Further evaluations with 3D visualization as a primary method of evaluation need to be investigated as these capabilities evolve.



A

FIGURE 3.1. (A) Coronal reformatted view demonstrates a large sigmoid polyp (arrow). Differentiation from a thickened fold can be made by scrolling through the lesion on the 2D views.



B

FIGURE 3.1. (*Continued*) **(B)** 3D endoscopic view shows the same polyp appearing as a focal protrusion into the lumen of the colon.

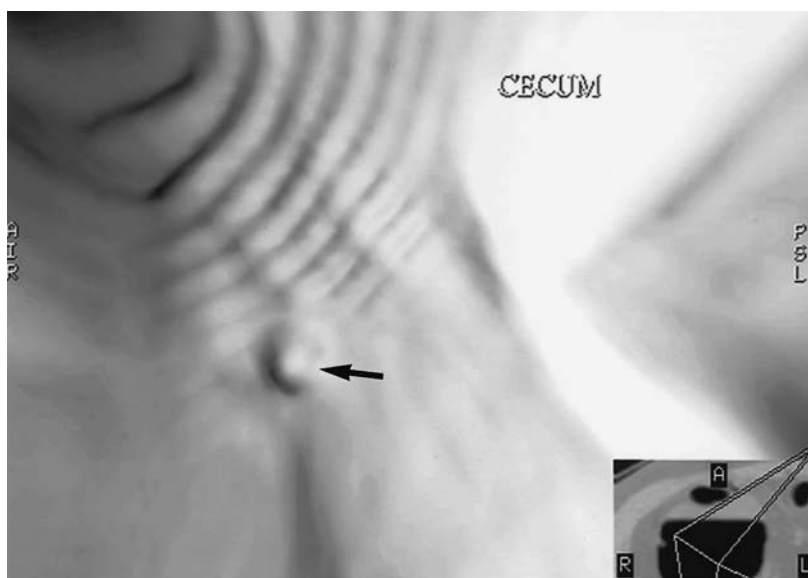


FIGURE 3.2. Excellent distention of the cecum allows detection of a small polyp (arrow) on the 3D endoluminal view.

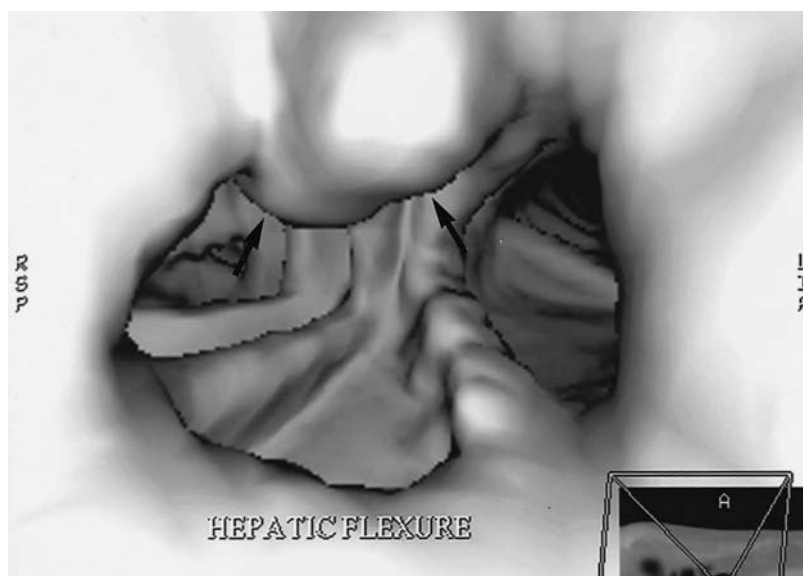


FIGURE 3.3. 3D endoscopic view demonstrates a large mass (arrows) in the hepatic flexure along the nondependent wall. A small amount of fluid is seen layering along the dependent wall.

Readers

To date, experienced abdominal radiologists have predominantly evaluated the early diagnostic performance of CTC. Many of the published studies have utilized single expert readers or consensus readings. Assessment of intra- and interobserver agreement is currently being performed (Pescatore et al. 2000; McFarland et al. 2000, 2002). The work of the American College of Radiology Imaging Network (ACRIN) represents the first large-scale multi-institutional efforts to evaluate newly trained and experienced readers. Future evaluations will require specific training protocols to familiarize new readers with different image display techniques and various sizes and morphologies of colorectal lesions.

Current Results Using 2D and Complete 3D

Yee et al. (2001) performed the largest single-center study to date evaluating CTC performance in 300 patients (Table 3.1). Approximately one-third of these patients were asymptomatic. Single-detector CT was used with 3-mm collimation, 1.5 to 2.0 pitch, 120 to 150 mA, and 1.5-mm reconstructions. Reader protocol consisted of complete interpretation of axial, reformatted, and endoluminal images in supine and prone positions. Interpretation was performed by two readers who evaluated 2D and 3D surface-rendered images in all patients, and a con-

TABLE 3.1. Performance data using complete 2D and 3D interpretation.

Study	CT type, collimation, SR vs VR	# Patients and type	By polyp sensitivity ≥10 mm	By polyp sensitivity 5–10 mm	By patient sensitivity ≥10 mm	By patient specificity ≥10 mm
Yee et al. 2001	SD, 3.0, SR	300 (204 high risk)	90.2%	80%	100%	—
Spinzi et al. 2001	SD, 5.0, SR	96 high risk	62%	56%	—	100%
Pescatore et al. 2000	SD, 5.0, SR	50 high risk	—	—	(<10 mm) 38%–63%	74%
Fenlon et al. 1999	SD, 5.0, VR	100 high risk	91%	82%	96%	96%
Royster et al. 1997	SD, 5.0, VR	20 + masses	100%	90%	100%	—

sensus reading was obtained. CTC had a 100% (8/8) sensitivity for the detection of carcinoma. Excellent results were also obtained using two different matching algorithms for larger polyps. Using direct by-polyp matching the sensitivity for polyp detection was 90.2% (74/82) for polyps 10 mm or larger and 80.1% (113/141) for polyps between 5 to 9.9 mm. Using the by-patient comparison, 100% (49/49) of patients with polyps measuring 10 mm or larger were identified and 93% (50/54) of patients with polyps measuring between 5 to 9.9 mm were identified on CTC. The positive-predictive value (PPV) and negative-predictive value (NPV) for clinically significant polyps measuring ≥10 mm was 80.8% and 97.2%, respectively.

Spinzi et al. (2001) obtained lower sensitivity results for the detection of polyps in a study of 96 high-risk or symptomatic patients. CTC was performed using 5-mm collimation, 2 pitch, 230 to 260 mA, and 2.5-mm reconstructions. 2D and complete 3D surface-rendered evaluation was performed by one radiologist. Per-polyp sensitivity for 10-mm or larger lesions was 62% (8/13) with a specificity of 100%. There was also low per-polyp sensitivity of 56% (18/32) for polyps smaller than 10 mm. This study found that CTC had a sensitivity of 88% (7/8) for the detection of cancers.

Fenlon et al. (1999) compared CTC and standard colonoscopy for polyp detection in 100 patients at high risk for colorectal neoplasia. The CT protocol consisted of 5-mm collimation, 1.25 pitch, 110 mA, and 2-mm reconstructions. 2D and complete 3D volume-rendered evaluation was performed by two radiologists who reviewed the CT studies jointly and arrived at a consensus reading. The per-polyp sensitivity of CTC was 91% (20/22) for polyps 10 mm or larger and 82% (33/40) for polyps 6 to 9 mm. Per-patient sensitivity and specificity as well as

PPV and NPV were all 96% for polyps 10 mm or larger. For polyps between 6 to 9 mm, per-patient sensitivity, specificity, PPV, and NPV were 94%, 92%, 92%, and 94%, respectively. Sensitivity results from this study are similar to the study by Yee et al. (2001).

Royster et al. (1997) performed a study evaluating 20 patients with known colonic masses found on fiberoptic colonoscopy. CTC was performed using 5-mm collimation, 1.25 pitch, 110 mA, and 2-mm reconstructions. 2D and complete 3D volume-rendered images were evaluated by two radiologists with a consensus reading obtained. All 20 masses measuring 20 mm or larger were identified. Per-polyp sensitivity for lesions measuring 10 mm or larger and for those between 6 and 10 mm were 100% (2/2) and 90% (9/10), respectively.

Current Results Using 2D with 3D for Problem Solving

Hara et al. (2001) compared single-detector vs multirow-detector CT for lesion detection in 237 patients. Seventy-seven patients underwent single-detector CTC with 5-mm collimation, 1.3 pitch, 70 mA, and 3-mm reconstructions. Using this protocol, three to four CT volumes were obtained with 3-cm overlap. The majority of patients (160) underwent multidetector CT scanning with 5-mm collimation, 0.75 pitch, 50 mA, and 3-mm reconstructions performed in one breath hold. Two of three radiologists who interpreted each of the studies used magnified axial images for the primary interpretation with 3D volume-rendered views for problem solving. CT results were considered positive if either of the two radiologists reported a finding. Per-polyp sensitivity for lesions larger than 10 mm was 89% (8/9) for single-detector CT vs 80% (8/10) for multidetector CT, with differences not found to be statistically significant. Per-patient sensitivity and specificity were 100% (5/5) and 90% (65/72) for single-detector CT vs 78% (7/9) and 93% (140/151) for multidetector CT, respectively, with differences also not found to be statistically significant. Although performance of CTC for polyp detection was similar for both single- and multidetector CT, it was found that colonic distention was better using multidetector CT with fewer respiratory artifacts.

In a study of 44 high-risk patients by Dachman et al. (1998), 2D images were used for primary interpretation and surface-rendered endoluminal views were reviewed only when needed to differentiate polyps from folds. Two radiologists interpreted each CT study independently. The CTC protocol consisted of 5-mm collimation, 1.5 pitch, 100 mA, and 2.5-mm reconstructions. A per-polyp sensitivity of 83% (5/6) was obtained for both readers for lesions 8 mm or larger with a specificity of 100%. The sensitivity for 5- to 8-mm polyps was 33% (1/3) for both readers. The endoluminal view was used for problem solving in 52% (23/44) of patients by both observers and did not significantly impact on interpretation times.

Morrin et al. (2000) evaluated 33 high-risk patients who did not receive intravenous contrast material and used a similar interpretation method in which surface-rendered endoluminal views were generated only in questionable areas found on the 2D views. CTC was performed using single- and multidetector scanners. Single-detector CT was performed on the majority of patients, and the pro-

tocol consisted of 3.0-mm collimation, 2 pitch, 120 mA, and 1.5-mm reconstructions. Multidetector CT protocol consisted of 2.5- to 5.0-mm slice thickness, 11.25- to 15-mm/s table speed, 200 mA in high-speed mode. Per-polyp sensitivity for 10- to 19-mm polyps and 5- to 9-mm polyps was 91% (11/12) and 58% (7/12), respectively. Per-patient sensitivity and specificity for the 10- to 19-mm polyps was 86% and 100%, respectively.

Fletcher et al. (2000) evaluated 180 patients with polyps or risk factors for colorectal cancer. Single-detector CT scanning was performed using 5-mm collimation, 70 mA, 1.3 pitch, and a 3-mm reconstruction interval. Three or four 20-second breath holds were required to cover the abdomen and pelvis with 3-cm overlap used to cover gaps. In addition, 89 patients were randomly assigned to receive oral iodinated contrast with a bowel-cleansing regimen the day before the CT. One reader interpreted the supine images alone and another reader evaluated both supine and prone data sets. Per-polyp sensitivity for lesions 10 mm or larger and for polyps between 5 and 9 mm were 75.2% (91/121) and 47.2% (67/142) respectively. Per-patient sensitivity and specificity for 10-mm or larger polyps were 85.4% and 93% respectively. It was found that the use of both supine and prone data sets significantly improved the ability to detect patients with polyps 5 mm or larger. The use of oral iodinated contrast in this study did not appear to improve polyp detection.

Macari et al. (2002) published a low-dose multidetector CT study in 105 high-risk patients. Images were acquired at 1-mm detector width, effective mAs of 50, and variable pitch to cover the abdomen and pelvis in 30 seconds. One reader evaluated the images with primary use of axial 2D as the major image display, with a mean interpretation time of 12 minutes. Sensitivity was 70% (19/27) for 6- to 9-mm lesions and 93% (13/14) for 10-mm and greater lesions. Overall specificity was found to be 98% (see Table 3.2).

TABLE 3.2. Performance data using 2D and 3D interpretation for problem solving.

Study	CT type, collimation, SR vs VR	# Patients and type	By polyp sensitivity ≥10 mm	By polyp sensitivity 5–10 mm	By patient sensitivity ≥10 mm	By patient specificity ≥10 mm
Macari et al. 2002	MD, 1.0, VR	105 high risk	92.9%	70.4%	—	97.7%
Hara et al. 2001	SD + MD 5.0, VR	237 high risk	80%–89%	—	78%–100%	90%–93%
Dachman et al. 1998	SD 5.0, SR	44 high risk	83% (>8 mm)	33%	83%	100%
Morrin et al. 2000	SD + MD 3.0, SR	33 high risk	91%	58%	86%	100%
Fletcher et al. 2000	SD 5.0, VR	180 high risk	75.2%	47.2%	85.4%	93%

Interobserver Agreement

Pescatore et al. (2000) performed a prospective study of 50 high-risk patients. CTC was performed in the supine position using 5-mm collimation, 1.5 pitch, 200 mA, and 2.5-mm reconstructions. 2D and complete 3D surface-rendered evaluation was performed by two investigator teams consisting of a radiologist and a gastroenterologist. Each team read out the first 24 patients, followed by evaluation of results. Then, each team read out the remaining patients. Per-patient sensitivity for 10-mm or larger polyps was 38% and 63% for teams 1 and 2, respectively, and specificity was 74% for both teams. The lower sensitivity results could be explained by many patients with poor preparation, scanning in only the supine position, sub-optimal resolution of the software employed, and reader inexperience.

McFarland et al. (2000) initially evaluated inter- and intraobserver agreement in a retrospective library of 30 colonic segments containing 22 lesions using three different image display techniques. Images were acquired using single-detector CT, at 5-mm collimation, 8-mm table increment, and 2-mm reconstruction interval. Three experienced abdominal radiologists, who were recently trained with a teaching set of CTC cases, independently evaluated each case at two different testing periods. Results were similar between 2D MPR, thick-slab 3D MPR, and 3D perspective volume-rendered image display techniques. Sensitivity ranged from 77% to 86% for all polyps and 91% to 100% for polyps ≥ 10 mm ($n = 11$). Overall, intraobserver agreement was good for the three display techniques ($\kappa = 0.6$ to 1.0); however, interobserver agreement of 2D MPR was lower ($\kappa = 0.53$ to 0.80).

McFarland et al. (2002) also evaluated prospectively a polyp-rich cohort of 70 patients, using single detector CT (5-mm collimation, 8-mm table increment, 2-mm reconstruction interval). Four experienced abdominal radiologists independently evaluated each case using 2D MPR as the primary image display, with 3D volume rendered views to further characterize each finding. Analysis by polyp demonstrated a pooled sensitivity of 68% (range 60% to 78%) to detect 10 mm polyps ($n = 40$ polyps). Analysis by patient demonstrated a pooled sensitivity of 88% (range 82% to 89%) to detect patients with 10 mm and greater polyps ($n = 28$ patients). When sensitivity and area under the curve were analyzed by polyp size threshold, results among readers peaked at polyp diameters of approximately 10 mm. Interobserver agreement was 79% for all patients, 72% for patients with 6–9 mm polyps ($n = 20$) and 94% for patients with 10 mm and greater polyps ($n = 28$). When sensitivity and area under the curve were analyzed by polyp size threshold, results among readers peaked at polyp diameters of approximately 10 mm. Interobserver agreement was 79% for all patients, 72% for patients with 6- to 9-mm polyps ($n = 20$) and 94% for patients with 10-mm or greater polyps ($n = 28$).

Future Areas of Validation

Future efforts to validate CTC will be challenged by the continued advances in CT acquisition and image processing capabilities. Optimization and standardization of

the CT protocol will be necessary before further dissemination. Further evaluation of computed-aided diagnosis (Summers 2002), novel 3D image display techniques (Beaulieu et al. 1999; Reed and Johnson 1998), and stool tagging and subtraction (Zalis and Hahn 2001; Callstrom et al. 2001) will be needed. The diagnostic performance of CTC using a broader range of cases in community environments with less expert readers following a training period must be evaluated. Determination of what size lesion is considered “clinically significant” will be important (Glick 2000; Read et al. 1997; Rex and Cummings 1993). Multidisciplinary collaboration will be necessary for establishing screening and surveillance algorithms that account for important covariables, such as age, risk, and comorbidity. Comparison of the diagnostic performance of CTC to existing modalities such as flexible sigmoidoscopy, barium enema, and colonoscopy is also needed. In this way, the role of CTC as a part of the imaging armamentarium for colorectal cancer can be determined.

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