

Computed Tomographic Colonography (Virtual Colonoscopy)

A Multicenter Comparison With Standard Colonoscopy for Detection of Colorectal Neoplasia

Peter B. Cotton, MD, FRCP, FRCS

Valerie L. Durkalski, PhD

Benoit C. Pineau, MD, MSc (Epid)

Yuko Y. Palesch, PhD

Patrick D. Mauldin, PhD

Brenda Hoffman, MD

David J. Vining, MD

William C. Small, MD

John Affronti, MD, MS

Douglas Rex, MD

Kenyon K. Kopecky, MD

Susan Ackerman, MD

J. Steven Burdick, MD

Cecelia Brewington, MD

Mary A. Turner, MD

Alvin Zfass, MD

Andrew R. Wright, MBBS

Revathy B. Iyer, MD

Patrick Lynch, MD

Michael V. Sivak, MD

Harold Butler, MD

COLORECTAL CANCER IS A MAJOR public health issue that has received much attention in recent years. Conventional colonoscopy is widely accepted as the best available method for detection and exclusion of precursor lesions, with the advantage that most can be removed at the same examination.^{1,2} However, there is

See also p 1772.

Context Conventional colonoscopy is the best available method for detection of colorectal cancer; however, it is invasive and not without risk. Computed tomographic colonography (CTC), also known as virtual colonoscopy, has been reported to be reasonably accurate in the diagnosis of colorectal neoplasia in studies performed at expert centers.

Objective To assess the accuracy of CTC in a large number of participants across multiple centers.

Design, Setting, and Participants A nonrandomized, evaluator-blinded, noninferiority study design of 615 participants aged 50 years or older who were referred for routine, clinically indicated colonoscopy in 9 major hospital centers between April 17, 2000, and October 3, 2001. The CTC was performed by using multislice scanners immediately before standard colonoscopy; findings at colonoscopy were reported before and after segmental unblinding to the CTC results.

Main Outcome Measures The sensitivity and specificity of CTC and conventional colonoscopy in detecting participants with lesions sized at least 6 mm. Secondary outcomes included detection of all lesions, detection of advanced lesions, possible technical confounders, participant preferences, and evidence for increasing accuracy with experience.

Results A total of 827 lesions were detected in 308 of 600 participants who underwent both procedures; 104 participants had lesions sized at least 6 mm. The sensitivity of CTC for detecting participants with 1 or more lesions sized at least 6 mm was 39.0% (95% confidence interval [CI], 29.6%-48.4%) and for lesions sized at least 10 mm, it was 55.0% (95% CI, 39.9%-70.0%). These results were significantly lower than those for conventional colonoscopy, with sensitivities of 99.0% (95% CI, 97.1%->99.9%) and 100%, respectively. A total of 496 participants were without any lesion sized at least 6 mm. The specificity of CTC and conventional colonoscopy for detecting participants without any lesion sized at least 6 mm was 90.5% (95% CI, 87.9%-93.1%) and 100%, respectively, and without lesions sized at least 10 mm, 96.0% (95% CI, 94.3%-97.6%) and 100%, respectively. Computed tomographic colonography missed 2 of 8 cancers. The accuracy of CTC varied considerably between centers and did not improve as the study progressed. Participants expressed no clear preference for either technique.

Conclusions Computed tomographic colonography by these methods is not yet ready for widespread clinical application. Techniques and training need to be improved.

JAMA. 2004;291:1713-1719

www.jama.com

consumer resistance to colonoscopy, which may be perceived as invasive and not without risk. There is a need for simpler screening methods that would allow colonoscopy to be used more selec-

Author Affiliations and Financial Disclosures are listed at the end of this article.

Corresponding Author: Peter B. Cotton, MD, FRCP, FRCS, The Digestive Disease Center, Medical University of South Carolina, Suite 210, Clinical Science Bldg, 96 Jonathan Lucas St, PO Box 250327, Charleston, SC 29425 (cottonp@muscc.edu).

tively and efficiently.^{3,4} Computed tomographic colonography (CTC), sometimes called virtual colonoscopy, is a promising candidate.⁵⁻⁹ Computed tomographic colonography involves helical computed tomographic scanning of the colon after cathartic preparation and colonic distension. Several single-center studies have reported sensitivities of more than 90% for detection of lesions sized 10 mm or more,¹⁰⁻¹³ but other studies reported lower data ranging from 61% to 78%.¹⁴⁻¹⁷ The largest recent single-center study reported poor results and considerable variation between readers, with sensitivities of 32%, 34%, and 72%.¹⁸ Although detection (and exclusion) of all lesions is the ultimate goal, the key screening parameter is the ability to detect participants with clinically significant lesions because the detection of any lesion would lead logically to colonoscopy, which should detect nearly all lesions. The definition of a clinically significant lesion is important. Most physicians agree that it is crucial not to miss participants with lesions sized more than 10 mm in diameter and it is desirable to detect all lesions sized more than 6 mm. Studies have reported CTC sensitivities of 85%, 90%, 96%, and 100% for the detection of participants with lesions sized at least 10 mm and sensitivities of 84%, 88%, 93%, and 94% with the threshold at 6 mm.^{11,12,14,15} Most of these studies were initiated by committed radiologists, many of them pioneers in the technique, and were restricted to single centers. To be valuable as a screening tool, CTC must perform well in routine practice. Our goal was to assess the accuracy of CTC in a large number of participants across multiple centers. Since this study was completed, good results have been reported from a study conducted in 3 US Armed Services Hospitals.¹⁹

METHODS

Study Design

The study was a nonrandomized, evaluator-blinded, noninferiority design in which each participant underwent CTC followed up with conventional colonos-

copy within 2 hours. Participants aged 50 years or older who were scheduled for a clinically indicated elective conventional colonoscopy were invited to participate. The study did not include a screening population and excluded participants who had undergone colonoscopy within 3 years. Participants were instructed to consume a clear liquid diet (a minimum of 8 oz of liquids every hour) for 24 hours before the CTC examination, and 45 mL of laxative (C. B. Fleet Company Inc, Lynchburg, Va) in 8 oz of cold water. Another 45 mL of the laxative was consumed on the day of the examinations. The radiologist distended the colon with room air or carbon dioxide (by hand pump or automatic insufflator) and obtained a standard computed tomography (CT) scout film to determine adequate bowel distension. Participants were not given oral or intravenous contrast media or smooth muscle relaxants. Imaging was performed by using 2-section and 4-section CT scanners. A nominal slice width of 2.5 mm and a reconstruction increment of 1.5 mm were used for Picker and Siemens software (Picker International Inc, Cleveland, Ohio, and Siemens Medical Solutions, Iselin, NJ). Sites with General Electric (GE Medical Systems, Waukesha, Wis) equipment used a nominal slice thickness of 5.0 mm and a reconstruction increment of 1.0 mm. Complete scans of the colon were performed in the prone and supine positions, each in a single breath hold. Scans were read in 2-dimensional slices, and when necessary by focal 3-dimensional snapshot reconstructions. The radiologists (D.J.V., W.C.S., K.K.K., S.A., C.B., M.A.T., A.R.W., R.B.I., H.B.) recorded their interpretations in 5 sealed envelopes, 1 each for the following colon segments: the rectum and sigmoid, descending colon and splenic flexure, transverse colon and hepatic flexure, ascending colon, and the cecum. Endoscopists were blinded to the CTC results during insertion of the colonoscope. The colon was examined on withdrawal, with the results recorded for each segment. After each segment was examined and the results recorded, the CTC results for that

segment were revealed to the endoscopist, allowing immediate reexamination for any discrepancy. This technique of "segmental unblinding" has been used in other studies.^{15,19} The radiologists and endoscopists were instructed to record the adequacy of the bowel preparation (presence of fluid or stool) for each colon segment as well as the level of confidence for each detected polyp and each colon segment. Confidence data were recorded as determinate or indeterminate. Full 3-dimensional automated video reconstructions (3-dimensional "fly-throughs") were examined later by the same radiology readers without referring back to their initial 2-dimensional reviews. The 3-dimensional fly-through results were included in the secondary analyses. A preference questionnaire was sent home with each participant with instructions to return the completed form to the clinical center within 48 hours.

The protocol was approved by the institutional review board at each participating center, and all participants provided written informed consent. An independent data and safety monitoring committee was assembled to review participant safety and progress of the study.

Criterion Standard

The criterion standard for the diagnosis of lesions was defined as a combination of the initial findings of conventional colonoscopy, any additional findings on conventional colonoscopy after segmental unblinding to the CTC reports, and the results of additional diagnostic tests performed at a later date when clinically indicated. This means that the positive predictive value for conventional colonoscopy was 100% by definition. Lesion size was defined by measurement of any removed lesion (before fixation) or, if the polyp was not retrieved, by comparison with biopsy forceps during colonoscopy. The data from each participant were reviewed by 2 independent evaluators (V.L.D., Y.Y.P.) by using a matching algorithm, depending on the size and location of each identified lesion. Le-

sions found at CTC and conventional colonoscopy were considered to be the same lesion (ie, true matches) if their sizes agreed within 50% and if they were in the same or adjacent segments.

Setting

Nine clinical centers (8 in the United States and 1 in England) were recruited in which there were gastroenterologists and radiologists who agreed to collaborate in the study. Each center was limited to 3 named endoscopists and 2 radiologists. Radiologists were required to have performed at least 10 CTC procedures. Optical disks of 5 of their examinations performed according to protocol procedures were mailed to a central panel of radiologists for review of image quality, not diagnostic accuracy, before starting the study.

Outcome Measures

The primary outcome measure was the sensitivity and specificity of CTC (ie, the initial radiologist's report, without any later fly-through data) and conventional colonoscopy in identifying participants with and without lesions sized at least 6 mm.

Secondary outcome measures included the correct detection rate for lesions of any size for CTC and conventional colonoscopy, the detection of advanced lesions, the positive and negative predictive values for CTC and conventional colonoscopy, fly-through data, effect of increasing experience with reading the CTC images, and participant preferences for CTC vs conventional colonoscopy.

Statistical Considerations

The goal of the study was to assess whether the differences between the sensitivity and specificity of CTC and conventional colonoscopy in the detection of colorectal lesions were small enough to use CTC as a tool for the diagnosis of colorectal lesions. Because both CTC and conventional colonoscopy were performed on the same participant, McNemar paired-sample test approach was used for the calculation of the sample size.^{20,21} Assuming the

sensitivity (and specificity) of conventional colonoscopy was 95% (and 98%) for identifying participants with (and without) at least 1 lesion sized at least 6 mm, 248 participants with at least 1 lesion sized at least 6 mm were necessary to assess the sensitivity of the CTC (power=90%). Approximately 160 participants were required to assess the specificity of CTC. Assuming a 6-mm or more lesion prevalence of 25% and a dropout rate of 5%, approximately 1050 participants were required for enrollment.

The data were processed, managed, and analyzed by the Clinical Innovation Group. Statistical analyses were conducted using SAS version 8.2 (SAS Institute, Cary, NC).

RESULTS

Recruitment was slower than expected. For this reason, the study was stopped after 615 participants were enrolled between April 17, 2000, and October 3, 2001. Mean (SD) age of the participants was 61 years (8.34 years); 45% were men, 87% were white, and 13.5% had a history of colon polyps. Reasons for colonoscopy included overt and occult rectal bleeding, change in stool habit, abdominal pain, and surveillance after polypectomy. Six hundred three participants underwent CTC, 602 had conventional colonoscopy, and 600 had both procedures. Recruitment varied widely between centers, from 10 to 188 participants per center.

Lesions

By the criterion standard, a total of 827 true lesions were detected. In order of frequency, these lesions were found in the sigmoid colon (30.7%), rectum (17.2%), ascending colon (17.2%), transverse (10.5%), descending (9.9%), cecum (7.5%), hepatic flexure (5.3%), and splenic flexure (1.7%). The lesions were detected in 308 participants (51%), varying from 1 to 20 lesions per participant. Of the total 827 lesions, 654 (79.1%) were 1 to 5 mm, 119 (14.4%) were 6 to 9 mm, and 54 (6.5%) were at least 10 mm. There were 29 advanced lesions of more than 6 mm

in diameter (19 adenomas with villous features, 2 with high-grade dysplasia, and 8 cancers).

Primary Outcome

One hundred four participants had at least 1 lesion sized at least 6 mm. The CTC identified 41 of these participants (sensitivity, 39.0%; 95% CI, 29.6%-48.4%), whereas conventional colonoscopy identified 103 (sensitivity, 99.0%; 95% CI, 97.1%>99.9%). Four hundred ninety-six participants were without any lesion sized at least 6 mm. The CTC identified 449 of these participants (specificity, 90.5%; 95% CI, 87.9%-93.1%), whereas conventional colonoscopy identified all of them (specificity, 100%).

Secondary Outcomes

The sensitivity and specificity of CTC and conventional colonoscopy for detecting participants with lesions were assessed also for other lesion sizes (TABLE 1). The sensitivity of CTC for detecting participants with lesions sized at least 10 mm was 55.0% (95% CI, 39.9%-70.0%), substantially less than conventional colonoscopy (sensitivity, 100%). For detecting participants without lesions sized at least 10 mm, the specificity for CTC was 96.0% (95% CI, 94.3%-97.6%) and 100% for conventional colonoscopy. The sensitivity of CTC for detecting participants with advanced lesions was 64%; 2 of 8 cancers were missed (a 17-mm lesion in the rectum and a 7-mm lesion in the ascending colon).

Colonoscopy reached the cecum in 98.5% of participants. The CTC and initial conventional colonoscopy examinations both failed to detect 2 large lesions (2.0 cm in the transverse colon and 4.3 cm in the rectum, which were both found by surgery); both of these patients had other lesions sized at least 10 mm that were detected by conventional colonoscopy. Conventional colonoscopy also missed one 7-mm lesion in the sigmoid colon and 19 lesions of 1 to 5 mm. In 95 participants (16%), immediate endoscopic evaluation was needed after opening the envelope with

Table 1. Detection of Participants With and Without Lesions*

True Lesion Size, mm	Total No. of Participants With Lesions	Initial Conventional Colonoscopy		Computed Tomographic Colonography	
		No. of Participants With Detected Lesions	Sensitivity, % (95% CI)	No. of Participants With Detected Lesions	Sensitivity, % (95% CI)
≥6†	104	103	99.0 (97.1->99.9)	41	39.0 (29.6-48.4)
≥10	42	42	100	23	55.0 (39.9-70.0)
6-9	76	75	98.6 (95.9->99.9)	23	30.0 (19.7-40.3)
1-5	274	265	96.7 (94.6-98.8)	37	13.5 (9.5-17.5)

True Lesion Size, mm	Total No. of Participants Without Lesions	Initial Conventional Colonoscopy		Computed Tomographic Colonography	
		No. of Participants Without Detected Lesions	Specificity, % (95% CI)	No. of Participants Without Detected Lesions	Specificity, % (95% CI)
≥6†	496	496	100	449	90.5 (87.9-93.1)
≥10	558	558	100	535	96.0 (94.3-97.6)
6-9	524	524	100	488	93.1 (90.9-95.2)
1-5	326	326	100	295	90.5 (87.3-93.7)

Abbreviation: CI, confidence interval.

*Participants with multiple lesions are represented in more than 1 size category.

†Primary outcome.

Table 2. Detection of Individual Lesions

True Lesion Size, mm	Criterion Standard (No. of Lesions)	Initial Conventional Colonoscopy		Computed Tomographic Colonography	
		No. of Detected Lesions	Sensitivity, % (95% CI)	No. of Detected Lesions	Sensitivity, % (95% CI)
≥6	173	170	98.0 (95.9->99.9)	55	32.0 (25.0-38.9)
≥10	54	52	96.0 (90.8->99.9)	28	52.0 (38.7-65.3)
6-9	119	118	99.0 (97.2->99.9)	27	22.7 (15.2-30.2)
1-5	654	635	97.0 (95.7-98.3)	50	7.64 (5.60-9.68)

Abbreviation: CI, confidence interval.

the segmental CTC report. This revealed 15 lesions in 13 participants. One was the 7-mm lesion noted and the other remaining lesions were 1 to 5 mm in size. In these 95 participants, 88% of the lesions reported by the CTC were false-positive. The CTC correctly identified 55 of 173 lesions sized at least 6 mm (sensitivity, 32.0%; 95% CI, 25.0%-38.9%), whereas conventional colonoscopy identified 170 lesions (sensitivity, 98.0%; 95% CI, 95.9%->99.9%) (TABLE 2). For lesions sized at least 10 mm, sensitivities were 52.0% (95% CI, 38.7%-65.3%) and 96.0% (95% CI, 90.8%->99.9%) for CTC and conventional colonoscopy, respectively.

Radiologists used 3-dimensional snapshots for trouble-shooting in 60% of the cases in which lesions were suspected. The rate of correct lesion identification was 28% when snapshots were used and 13% when they were not used.

Technical issues that might affect interpretation were analyzed. Several centers reported anecdotally that CTC interpretation was hindered by colon fluid but the data did not confirm this as a major issue. The CTC identified 14% of the lesions when preparation was rated optimal (small amount of fluid) and 10% when suboptimal (large amount of fluid or stool). There were no obvious differences with the type of colon distension (hand-pump or insufflator, air or carbon dioxide), presence or absence of diverticula, or whether the radiologist rated the report as confident.

Fly-through data were analyzed at a later date by the same radiology readers without referring back to their initial 2-dimensional review. The sensitivity and specificity for detecting participants with and without at least 1 lesion sized at least 6 mm were 45.0% (95% CI, 35.4%-54.6%) and 93.0%

(95% CI, 90.8%-95.2%), respectively (TABLE 3). The sensitivity for detection of individual lesions was 15% for any size and 36.4% for those lesions sized at least 6 mm. Incorporating the fly-through data with the initial evaluation increased the sensitivity of CTC for the primary outcome (detection of participants with lesions ≥6 mm) by 17% to 56% but reduced specificity by 5%. For participants with lesions sized at least 10 mm, the fly-through data increased the sensitivity by 12% to 67%, and decreased the specificity by 1%.

The positive predictive values for conventional colonoscopy detection of lesions and participants were both 100% by definition because the conventional colonoscopy result was part of the criterion standard. The positive predictive values for CTC detection of lesions and participants and the negative predictive values for both procedures are shown in TABLE 4. The positive predictive value for CTC detection of participants with lesions sized at least 6 mm was 46.6% (95% CI, 42.9%-50.3%), and for those participants with lesions sized at least 10 mm was 50.0% (95% CI, 35.6%-64.4%). Negative predictive values for participants identified as not having a lesion sized at least 6 mm were 87.7% (95% CI, 84.9%-90.5%) for CTC and 99.8% (95% CI, 99.4%->99.9%) for conventional colonoscopy.

Analysis of all cases across all sites by sequential accrual blocks of 10 participants showed no evidence for increased accuracy of CTC later in the study for participants with or without a lesion sized at least 6 mm ($P = .08$) or for lesions sized at least 10 mm ($P = .72$).

Of the 518 preference questionnaires that were returned to the clinical centers, 46% of the participants preferred CTC, 41% preferred conventional colonoscopy, and 13% had no preference. Participants were also asked to rate their experience compared with what they expected. For CTC, 62% stated that the procedure was better or much better than anticipated, 23% stated it was as anticipated, and 14% stated worse or much worse than anticipated. The respective data for conventional colonoscopy were 71%, 23%, and 6%. The respective ratings for the bowel preparation were 50%, 32%, and 18%.

Minor adverse events were experienced by 14 participants (2.3%). These included 1 episode of mild bleeding after polypectomy and 8 cases in which lesions of possible clinical relevance were observed outside of the colon on the CT scans.

COMMENT

The main result of this study was surprising and disappointing. The primary outcome measure, the sensitivity of CTC for the detection of participants with lesions sized at least 6 mm, was only 39% and was not much higher (55%) with a threshold of 10 mm. These data contrast remarkably with many other studies, almost all of which come from single-center studies in which the lead author was a radiologist. An obvious question is whether the radiologists in our study were sufficiently experienced. All were

well trained and experienced in CT abdominal imaging. They had to have performed at least 10 CTC cases and have 5 recorded procedures reviewed centrally for quality, but not accuracy, before starting the study. Only 1 of the centers had substantial prior involvement with the technique. It contributed the most participants ($n = 184$) and had the best results, with a primary outcome sensitivity of 82%. These data were very similar to previous data published from the same center.¹⁵ The sensitivity for all other centers combined was only 24%, with no correlation between increasing experience and accuracy. Analysis of all the data in sequential blocks of 10 did not show any progressive improvement in accuracy as the number of cases increased (ie, no evidence of a “learning curve”). However, because there was no formal feedback to the participating radiologists

Table 3. Results of Fly-Through Interpretations

Lesion Size, mm	Criterion Standard (No. of Participants)		Per Participant Sensitivity		Per Participant Specificity		Per Lesion Sensitivity		
	True Positive	True Negative	No. of Participants With Detected Lesions	Sensitivity, % (95% CI)	No. of Participants Without Detected Lesions	Specificity, % (95% CI)	Total No. of Lesions	No. of Detected Lesions	Sensitivity, % (95% CI)
≥6	104	496	47	45.0 (35.4-54.6)	462	93.0 (90.8-95.2)	173	63	36.4 (29.2-43.6)
≥10	42	558	25	59.5 (44.7-74.3)	547	98.0 (96.8-99.2)	54	30	55.6 (42.3-68.9)
6-9	76	524	27	35.5 (24.7-46.3)	495	94.5 (92.5-96.5)	119	33	27.7 (19.7-35.7)
1-5	274	326	48	17.5 (13.1-21.9)	295	90.5 (87.3-93.7)	561	39	6.95 (4.85-9.05)

Abbreviation: CI, confidence interval.

Table 4. Positive and Negative Predictive Values for Computed Tomographic Colonography and Conventional Colonoscopy

True Lesion Size, mm	Computed Tomographic Colonography per Participant			Computed Tomographic Colonography per Lesion		
	Total No. of Participants With a Positive Test Result	No. of Participants With Lesions	Positive Predictive Value, % (95% CI)	Total No. of Lesions With a Positive Test Result	No. of Lesions	Positive Predictive Value, % (95% CI)
≥6	88	41	46.6 (42.9-50.3)	135	55	41.0 (32.7-49.3)
≥10	46	23	50.0 (35.6-64.4)	58	28	48.0 (35.1-60.9)
6-9	59	23	39.0 (26.6-51.4)	77	27	35.0 (24.3-45.7)
1-5	68	37	55.0 (43.2-66.8)	123	50	41.0 (32.3-49.7)

True Lesion Size, mm	Computed Tomographic Colonography per Participant			Initial Conventional Colonoscopy per Participant		
	Total No. of Participants With a Negative Test Result	No. of Participants Without Lesions	Negative Predictive Value, % (95% CI)	Total No. of Participants With a Negative Test Result	No. of Participants Without Lesions	Negative Predictive Value, % (95% CI)
≥6	512	449	87.7 (84.9-90.5)	497	496	99.8 (99.4->99.9)
≥10	554	535	96.5 (95.0-98.0)	558	558	100
6-9	541	488	90.2 (87.7-92.7)	525	524	99.8 (99.4->99.9)
1-5	532	295	55.5 (51.3-59.7)	335	326	97.3 (95.6-99.0)

Abbreviation: CI, confidence interval.

during the trial, aspects of learning were missing. Only another study after intensive and specific training would clarify this issue. It is worrisome that a recent large study from the Mayo Clinic showed substantial variation in reporting among 3 radiologists, despite the fact that each had experience of more than 150 CTC examinations, with colonoscopy correlation.¹⁸ Conversely, the Armed Services study had excellent results despite relatively little prior experience.¹⁹

The use of colonoscopy as the criterion standard in this study may be criticized, because colonoscopy cannot claim complete accuracy, even in the hands of experts.^{22,23} Indeed, 2 large lesions were missed by colonoscopy in patients who had other identified lesions. However, this design, including segmental unblinding, has been used in other major studies and it is difficult to conceive of a realistic alternative.^{15,19,20,24,25} The CTC reported numerous lesions that were not observed at the initial colonoscopy evaluation but 88% of these were judged to be false-positives when the endoscopist reexamined the suspect area.

The fly-through data were not included in the primary outcome because all centers could not guarantee to complete the readings within the 2-hour time frame before colonoscopy. Later analysis of the fly-through data did increase the sensitivity of CTC in our study and improved software now makes these elements easier and quicker to report.

Patient preference is an important issue, with discrepant results in the literature. Our participants did not indicate a strong participant preference for CTC over conventional colonoscopy but the use of sedation for most colonoscopies may be relevant. However, the preference question is complex and the answer may depend on how it is framed.^{26,27} Participants might opt for CTC as seeming to be less invasive. However, the bowel preparation (now needed for both examinations) is the worst part. Many participants may opt to go directly to colonoscopy if they know that there is approximately a 20% chance that colo-

noscopy will be needed also for treatment, with a second bowel preparation.

The study recently reported from the Armed Services medical centers had remarkably different results.¹⁹ In a screening population of 1233 adults, the CTC detected 93.8% of polyps sized more than 10 mm in diameter and 88.7% of participants with lesions sized more than 6 mm. The possible reasons for these results are being debated. The study differed from other studies in using 4-section and 8-section scanners, the 3-dimensional fly-through as the primary diagnostic tool, and intensive bowel preparation, including oral contrast and barium. It is not stated how the barium may have affected the accuracy of colonoscopy.

Even if the results of CTC continue to be good in the hands of experts, it has yet to be proven that this expertise can be taught and disseminated reliably into daily practice. There is an analogy with the barium enema examination. Published data mostly showed good accuracy but everyday experience was less satisfactory.²⁸

Currently, CTC may have application in patients with obstructing tumors,^{29,30} and in patients where colonoscopy is incomplete for other reasons.³¹ The fact that the technique may detect extracolonic lesions can be observed as an advantage or a disadvantage.³²

The CTC technology is evolving. Scanners are becoming more sophisticated and faster. Prepress CTC using electronically subtractable fecal markers is a tantalizing possibility.^{33,34} The combination of electronic cleansing and faster 3-dimensional reconstruction appears promising.³⁵ Radiation exposure can be eliminated by using magnetic resonance scanning.³⁶ There is even the possibility of automating lesion recognition, which could greatly reduce the burden of reporting (now in excess of 1000 images per patient).^{18,37,38}

Our results indicate that CTC using these techniques is not ready for routine use at this time, as many others have concluded.^{4,7,39-41} There is an obvious need for continuing collabora-

tion between radiologists and gastroenterologists in further evaluation of this exciting new technology. If and when results do justify widespread introduction, similar multidisciplinary collaboration will be needed to ensure its efficient application.

Author Affiliations: Department of Gastroenterology (Drs Cotton and Hoffman) and Radiology (Dr Ackerman), The Digestive Disease Center, and Department of Pharmacy and Clinical Sciences (Dr Mauldin), and The Clinical Innovation Group (Drs Durkalski and Palesch), Medical University of South Carolina, Charleston; Departments of Gastroenterology (Dr Pineau) and Radiology (Dr Vining), Wake Forest University School of Medicine, Winston-Salem, NC; Departments of Radiology (Dr Small) and Gastroenterology (Dr Affronti), Emory University Hospital, Atlanta, Ga; Departments of Gastroenterology (Dr Rex) and Radiology (Dr Kopecky), Indiana University Hospital, Indianapolis; Departments of Gastroenterology (Dr Burdick) and Radiology (Dr Brewington), University of Texas Southwestern, Dallas; Departments of Radiology (Dr Turner) and Gastroenterology (Dr Zfass), Virginia Commonwealth University Medical Center, Medical College of Virginia, Richmond; Department of Radiology, St Mary's Hospital, London, England (Dr Wright); Departments of Radiology (Dr Iyer) and Gastroenterology (Dr Lynch), M. D. Anderson Cancer Center, Houston, Tex; Departments of Gastroenterology (Dr Sivak) and Radiology (Dr Butler), University Hospitals of Cleveland, Cleveland, Ohio.

Financial Disclosures: Dr Pineau is a minor stockholder and Dr Vining is a major stockholder in PointDX, a radiology structured reporting company.

Author Contributions: Dr Cotton had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Cotton, Durkalski, Pineau, Palesch, Mauldin, Vining, Small, Rex, Kopecky, Butler.

Acquisition of data: Cotton, Durkalski, Pineau, Mauldin, Hoffman, Vining, Small, Affronti, Kopecky, Ackerman, Burdick, Brewington, Turner, Zfass, Wright, Iyer, Lynch, Sivak, Butler.

Analysis and interpretation of data: Cotton, Durkalski, Pineau, Palesch, Mauldin, Small, Ackerman, Brewington, Iyer, Lynch.

Drafting of the manuscript: Cotton, Durkalski, Mauldin, Turner.

Critical revision of the manuscript for important intellectual content: Cotton, Durkalski, Pineau, Palesch, Hoffman, Vining, Small, Affronti, Rex, Kopecky, Ackerman, Burdick, Brewington, Zfass, Wright, Iyer, Lynch, Sivak, Butler.

Statistical expertise: Durkalski, Palesch, Mauldin.

Obtained funding: Cotton, Mauldin.

Administrative, technical, or material support: Hoffman, Affronti, Ackerman, Burdick, Turner.

Supervision: Cotton, Pineau, Mauldin, Vining, Kopecky, Brewington.

Funding/Support: This study was supported by grant N00014-99-1-0784 from the Office of Naval Research of the US Department of Defense.

Role of Sponsor: The US Department of Defense did not participate in the design and conduct of the study, in the collection, analysis, and interpretation of the data, or in the preparation, review, or approval of the manuscript.

Previous Presentation: Presented in part at the Annual Meetings of the American Society for Gastrointestinal Endoscopy in May 22, 2002, San Francisco, Calif, and May 20, 2003, Orlando, Fla, with publications in abstract form (*Gastrointest Endosc.* 2002;55:AB98 and *Gastrointest Endosc.* 2003;57:AB174).

REFERENCES

1. Lieberman DA, Weiss DG, Bone JH, et al. Use of colonoscopy to screen asymptomatic adults for colorectal cancer. *N Engl J Med*. 2000;343:162-168.
2. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy: the National Polyp Study Workgroup. *N Engl J Med*. 1993;329:1977-1981.
3. Walsh JME, Terdiman JP. Colorectal cancer screening: clinical applications. *JAMA*. 2003;289:1297-1302.
4. Rex DK. Current colorectal cancer screening strategies: overview and obstacles to implementation. *Rev Gastroenterol Disord*. 2002;2(suppl 1):S2-S11.
5. Vining DJ. Virtual endoscopy: is it reality? *Radiology*. 1996;200:30-31.
6. Ferrucci JT. Colon cancer screening with virtual colonoscopy. *AJR Am J Roentgenol*. 2001;177:975-988.
7. Bond JH. Virtual colonoscopy—promising, but not ready for widespread use. *N Engl J Med*. 1999;341:1540-1542.
8. Johnson CD. CT colonography: an overview. *Abdom Imaging*. 2002;27:232-234.
9. Gluecker TM, Fletcher JG. CT colonography (virtual colonoscopy) for the detection of colorectal polyps and neoplasms, current status and future developments. *Eur J Cancer*. 2002;38:2070-2078.
10. Macari M, Bini EJ, Xue X, et al. Colorectal neoplasms: prospective comparison of thin-section low-dose multi-detector row CT colonography and conventional colonoscopy for detection. *Radiology*. 2002;224:383-392.
11. Fenlon HM, Nunes DP, Schroy PC, et al. A comparison of virtual and conventional colonoscopy for the detection of colorectal polyps. *N Engl J Med*. 1999;341:1496-1503.
12. Yee J, Akerkar GA, Hung RK, et al. Colorectal neoplasia: performance characteristics of CT colonography for detection in 300 patients. *Radiology*. 2001;219:685-692.
13. Laghi A, Iannaccone R, Carbone I, et al. Detection of colorectal lesions with virtual computed tomography colonography. *Am J Surg*. 2002;183:124-131.
14. Fletcher JG, Johnson CD, Welch TJ, et al. Optimization of CT colonography technique: prospective trial in 1980 patients. *Radiology*. 2000;216:704-711.
15. Pineau BC, Paskett ED, Chen J, et al. Virtual colonoscopy using oral contrast compared to colonoscopy for the detection of patients with colorectal polyps. *Gastroenterology*. 2003;125:304-310.
16. Mendelson RM, Foster NM, Edwards JT, et al. Virtual colonoscopy compared with conventional colonoscopy: a developing technology. *Med J Aust*. 2000;173:472-475.
17. Spinzi G, Belloni G, Martegani A, et al. Computed tomographic colonoscopy and conventional colonoscopy for colon diseases: a prospective, blinded study. *Am J Gastroenterol*. 2001;96:394-400.
18. Johnson CD, Harmsen WS, Wilson LA, et al. Prospective blinded evaluation of computed tomographic colonography for screen detection of colorectal polyps. *Gastroenterology*. 2003;125:311-319.
19. Pickhardt PJ, Choi R, Hwang I, et al. Computed tomography virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *N Engl J Med*. 2003;349:2191-2200.
20. Durkalski VL, Palesch YY, Pineau BC, et al. The virtual colonoscopy study: a large multicenter clinical trial designed to compare two diagnostic screening procedures. *Control Clin Trials*. 2002;23:570-583.
21. Lu Y, Bean JA. On the sample size for one-sided equivalence of sensitivities based upon McNemar's test. *Stat Med*. 1995;14:1831-1839.
22. Postic G, Lewin D, Bickerstaff C, Wallace MB. Colonoscopic miss rates determined by direct comparison of colonoscopy with colon resection specimens. *Am J Gastroenterol*. 2002;97:3182-3185.
23. Rex DK, Cutler CS, Lemmel GT, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies. *Gastroenterology*. 1997;112:24-28.
24. Pineau BC, Paskett ED, Chen GJ, et al. Validation of virtual colonoscopy in the detection of colorectal polyps and masses: rationale for proper study design. *Int J Gastrointest Cancer*. 2001;30:133-140.
25. Cash BD, Schoenfeld P, Rex D. An evidence-based medicine approach to studies of diagnostic tests: assessing the validity of virtual colonoscopy. *Clin Gastroenterol Hepatol*. 2003;1:136-144.
26. Akerkar GA, Yee J, Hung R, McQuaid K. Patient experience and preferences toward colon cancer screening: a comparison of virtual colonoscopy and conventional colonoscopy. *Gastrointest Endosc*. 2001;54:310-315.
27. Ristvedt SL, McFarland EG, Weinstock LB, Thyssen EP. Patient preferences for CT colonography, conventional colonoscopy, and bowel preparation. *Am J Gastroenterol*. 2003;98:578-585.
28. Schrock TR. Colonoscopy versus barium enema in the diagnosis of colorectal cancers and polyps. *Gastrointest Endosc Clin North Am*. 1993;3:585-610.
29. Morrin MM, Farrell RJ, Raptopoulos V, et al. Role of virtual computed tomographic colonography in patients with colorectal cancers and obstructing colorectal lesions. *Dis Colon Rectum*. 2000;43:303-311.
30. Fenlon HM, McAneeny DB, Nunes DP, et al. Occlusive colon carcinoma: virtual colonoscopy in the preoperative evaluation of the proximal colon. *Radiology*. 1999;210:423-428.
31. Neri E, Giusti P, Battolla L, et al. Colorectal cancer: role of CT colonography in preoperative evaluation after incomplete colonoscopy. *Radiology*. 2002;223:615-619.
32. Edwards JT, Wood CJ, Mendelson RM, Forbes GM. Extracolonic findings at virtual colonoscopy: implications for screening programs. *Am J Gastroenterol*. 2001;96:3009-3012.
33. Zalis ME, Hahn PF. Digital subtraction bowel cleansing in CT colonography. *AJR Am J Roentgenol*. 2001;176:646-648.
34. Callstrom MR, Johnson CD, Fletcher JG, et al. CT colonography without cathartic preparation: feasibility study. *Radiology*. 2001;219:693-698.
35. Pickhardt PJ, Choi JH. Electronic cleansing and stool tagging in CT colonography: advantages and pitfalls with primary three-dimensional evaluation. *AJR Am J Roentgenol*. 2003;181:799-805.
36. Lauenstein TC, Goehde SC, Ruehm SG, et al. MR colonography with barium-based fecal tagging: initial clinical experience. *Radiology*. 2002;223:248-254.
37. Masutani Y, Yoshida H, MacEneaney PM, Dachman AH. Automated segmentation of colonic walls for computerized detection of polyps in CT colonography. *J Comput Assist Tomogr*. 2001;25:629-638.
38. Summers RM, Johnson CD, Pusanik LM, et al. Automated polyps detection at CT colonography: feasibility assessment in a human population. *Radiology*. 2001;219:51-59.
39. Hawes RH. Does virtual colonoscopy have a major role in population-based screening? *Gastrointest Endosc Clin North Am*. 2002;12:85-91.
40. Rex DK. Is virtual colonoscopy ready for widespread application? *Gastroenterology*. 2003;125:608-614.
41. Sonnenberg A, Delco F, Bauerfiend P. Is virtual colonoscopy a cost-effective option to screen for colorectal cancer? *Am J Gastroenterol*. 1999;94:2268-2274.