

# C O N S U L T A T I O N S I N

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## LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Identify the methods of colorectal cancer screening in the U.S. and the potential role of CT colonography.
- Describe the clinical value of CTC for nonscreening applications.
- Respond to patient questions regarding the discomfort involved with performing CTC.
- Answer common patient questions regarding the accuracy of CTC.

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## CT Colonography: Potential Indications and Recent Advances

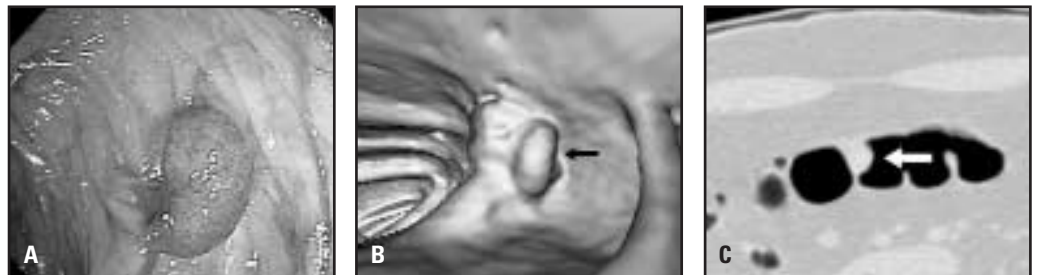
By Abraham H. Dachman, M.D.

**C**olorectal cancer is the most common cause of cancer deaths in nonsmokers. About 135,400 new cases of colorectal cancer and 56,700 deaths per year are expected, based on data from the American Cancer Society. The incidence of and mortality from colorectal cancer declined by 9.1% and 22.6%, respectively, between 1973 and 1996, yet it remains the second leading cause of cancer deaths for men and women.

Screening for colorectal cancer is particularly effective because the goal of screening is the detection not only of early carcinoma, but also of premalignant adenomas.<sup>1</sup> More than 80% of colorectal carcinomas are thought to arise from preexisting benign adenomas. The concept of the “adenoma-carcinoma sequence” became

popular primarily as a result of research from Morson et al,<sup>2</sup> who showed that there is a consistent sequential histologic and morphologic progression from normal mucosa to advanced carcinoma. Two important corollaries to the adenoma-carcinoma sequence are that most colorectal cancers are derived through this pathway and that the time required for such progression is slow, on the order of 10 years or longer. It is this time lag that provides an opportunity for effective screening.

Compliance of the population with current screening strategies is poor;<sup>3</sup> therefore, the development of a new structural examination of the colon has attracted the attention of both patients and physicians. CT colonography (CTC), also called virtual colonoscopy, is now



Sessile polyp in the transverse colon. A: Conventional colonoscopy shows a 15-mm sessile polyp. Endoluminal (B) and prone axial (C) views, as indicated by arrows. The polyp abuts a fold on the ventral wall of the transverse colon. Although relatively dependent in location, it is solid with no internal gas and is thus most consistent with a polyp rather than stool.

considered by some to be a viable alternative for examining the colon for polyps and masses,<sup>4</sup> although there is still some controversy as to its role as a screening examination.

### SCREENING OPTIONS

Among the several screening choices for colorectal cancer are fecal occult blood testing, flexible sigmoidoscopy, a combination of the two, double-contrast barium enema, and colonoscopy.<sup>1</sup> Tests under investigation include CTC and the testing of stool for genetic markers.

The fecal occult blood test, which can be administered in several forms and methods, is inexpensive and readily applied at the mass level. However, it is insensitive to the detection of adenomatous polyps, and a single application has only fair sensitivity for colorectal cancer and requires repeat testing.

Flexible sigmoidoscopy visualizes about one-third of the bowel, but performing colonoscopy after an adenoma is detected improves the sensitivity to approximately

75% for detection of neoplasms. Although flexible sigmoidoscopy is much safer and less expensive than colonoscopy and does not require sedation, a significant portion of lesions will be missed because of their location in the proximal colon.



Alternate and novel views. A: A transparent view indicating the locations of polyps and mass. B: A "virtual dissection" view (GE Medical Systems). A polyp is indicated by an arrow.

The double-contrast barium enema is relatively inexpensive (equivalent to sigmoidoscopy) and is the safest of all the structural screening tests. Similar to colonoscopy, it requires colonic cleansing, which is usually associated with mild to moderate discomfort. Observational studies suggest that this test can detect up to 90% of large adenomas and 85% to 95% of cancers. However, a randomized controlled trial comparing double-contrast barium enema to colonoscopy reported a detection rate of only half of large adenomas. Declining use of the barium

enema is also due to radiologists' waning interest in performing this procedure, low reimbursement, and inadequate training of radiology residents.

Colonoscopy is considered the definitive procedure for evaluating the colon because it directly visualizes the mucosa and can be used for both diagnosis and therapy, since polyps can be removed if they are small or pedunculated and can be biopsied for histologic diagnosis. Although the risks of perforation and hemorrhage are relatively low, they are higher than with any of the screening alternatives. Unlike sigmoidoscopy, colonoscopy also requires more intensive preparation, which many patients find the most difficult aspect of the test. The completion rate for colonoscopy ranges from 75% to 99% and the national average completion rate for the procedure is about 90%.

### COLONOSCOPY VERSUS CTC

The use of colonoscopy to screen for colorectal cancer has been recommended by several gastroenterology organizations.

The widespread application of screening with optical colonoscopy is hindered by an increasing recognition that the waiting time for optical colonoscopy is often many months, and in some locations, more than a year. Also, there is evidence, based on back-to-back colonoscopies, that 6% of polyps 1 cm in diameter may be missed.

The recent CTC multicenter trial reported by Pickhardt et al<sup>4</sup> used a "segmental unblinding" strategy to test the effectiveness of colonoscopy. They found CTC to be superior to optical colonoscopy for detecting polyps of 8 to 10 mm.<sup>4</sup> Another study by Pickhardt et al<sup>5</sup> showed that optical colonoscopy may in fact miss 12% of 1-cm polyps.

CTC has been advocated for:<sup>3,6,7</sup>

- Evaluating the colon proximal to an obstructing colonic mass or stricture.
- Completing the colonic examination after an incomplete optical colonoscopy.
- Searching for polyps or masses in patients who are at above-average risk for colorectal cancer who refuse optical colonoscopy or whose physicians prefer CTC to avoid sedation or the risk of bleeding (e.g., for patients on anticoagulation).

- Screening average-risk patients for colorectal cancer.

The patient who is already prepared and has undergone an incomplete colonoscopy can be accommodated for a same-day, unscheduled CTC examination, thus obviating a return visit and repeat preparation. Morrin et al<sup>8</sup> studied 40 patients with CT within two hours of an incomplete colonoscopy. Their study showed the portion of the colon that was not visualized by endoscopy in more than 90% of patients, and found a probable cause for the obstruction in 74% of them. Fenlon et al<sup>9</sup> showed that CT depicted all occlusive carcinomas in the 29 subjects, and they fully evaluated the proximal colon in 26 of the 29 patients.

In that study, CT also demonstrated two synchronous cancers and 24 polyps in the proximal colon, many of which were subsequently confirmed by endoscopy, although none could be palpated at surgery. Identification of the synchronous cancers in two patients altered the surgical plan. CT was also more accurate than colonoscopy in localizing the cancers, which may be helpful in preoperative planning. Neri et al<sup>10</sup> studied 34 patients with CT, before and after intravenous contrast injection. In 29 patients, surgery showed 30 cancers (including three synchronous cancers). Colonoscopy missed 10 cancers and three synchronous cancers, all of which were detected with CT. The use of intravenous contrast also permitted a definitive search for metastatic disease with a single CT examination.

### ROLE OF CTC IN SCREENING

In discussing diagnostic accuracy it is important to differentiate between by-patient and by-polyp sensitivities.<sup>11</sup> For patient triage to colonoscopy, only the by-patient results are relevant. Likewise, when studying published research, the discerning reader should look at the sensitivity statistics for a particular size threshold and for potentially malignant lesions only, meaning adenomas (excluding hyperplastic polyps and mucosal tags).

Due to the varied inclusion criteria (often combining patients of average and above-average risk) and varied methodology in performing and reading CTC, it is difficult to find a single reliable sensitivity. Also, since the technology is rapidly evolving, radiologists currently performing CTC are likely using state-of-the-art software, better than that used in many published reports. Available figures on the sensitivity of CTC are based on

cohorts with mixed indications and are often weighted toward above-average risk increase in the prevalence of polyps in the cohort. In one meta-analysis of 1324 patients,<sup>12</sup> the pooled per-patient sensitivity was 88% for polyps 10 mm or larger and 84% for polyps 6 to 9 mm. Specificity remained high.

In Pickhardt's recent trial<sup>4</sup> (in which stool tagging and electronic subtraction of stool was employed), the by-patient sensitivity for adenomas 8 mm or larger was 93.9% with 92.2% specificity, and the by-polyp sensitivity for adenomas 8 mm or larger was 92.6%. A large national trial on a screening cohort, the National CT Colonography Trial, sponsored by the American College of Radiology Imaging Network (ACRIN) is now under way. A panel of experts, the Boston CTC Working Group, has also developed standards for reporting and follow-up recommendations for patients undergoing CTC.<sup>13</sup>

#### CTC TECHNIQUE

- **Bowel preparation.** Retained fluid can hide masses on CTC, so a "dry prep" using magnesium citrate or sodium phosphate is preferred over polyethylene glycol.<sup>14</sup> However, most published data comparing CTC and optical colonoscopy have reported on patients undergoing both examinations on the same day after a "wet prep." A bisacodyl suppository on the morning of the examination may help evacuate residual fluid.

- **Stool opacification.** Stool and fluid opacification is often used, but it is still under investigation.<sup>15</sup> Both barium and a water-soluble oral contrast medium can be administered with each meal on the day before or morning of the examination. The resulting images can be read in 2D or 3D.

At the University of Chicago we use a low-fiber diet (NutraPrep) combined with a very small volume of barium (Tagitol V) at breakfast, lunch, and dinner the day before the CT and a small amount of water-soluble contrast (5 cc Gastroview in a cup of water) the evening before and day of the exam. This could potentially eliminate cathartic preparation.<sup>16</sup> Electronic subtraction of stool and fluid is another strategy that may help make the exam easier to interpret and more amenable to a primary 3D read.<sup>4,17</sup>

- **Colonic insufflation and antispasmodics.** Antispasmodics add some expense and probably makes patients more comfortable,<sup>3</sup> but it is not certain that they improve the diagnostic quality of the examination. When used, 1 mg of glucagon

can be administered subcutaneously about 10 minutes prior to the scan.

- **Insufflation and scanning.** The entire CTC exam usually takes about 15 minutes of room time. A rectal examination should be done by the referring physician before proceeding, as lesions in the anal canal or near the anal verge may be missed on CTC. A small, thin, rectal tube with or without a retention cuff is introduced. Insufflation can be accomplished with either room air or carbon dioxide. The latter may have the benefit of rapid absorption, which will make the patient more comfortable after the examination. Manual insufflation with a "blue puffer" or mechanical insufflation with a mechanical pump, or even self-inflation by the patient, have all been successful. A mechanical pump designed specifically for CTC is now available.

When insufflation has caused moderate patient discomfort, a scout view is performed during deep inspiration to judge the adequacy of colonic distension. Once adequate insufflation is seen, the patient should hyperventilate to minimize respiratory movement on the subsequent scan. The supine scan is usually performed first. The patient is then turned to a prone position, and scout scanning repeated before the prone scan is performed.

With the use of fast 16- to 64-slice CT scanners, respiratory motion is rare, but elderly patients could benefit from supplemental nasal oxygen to ensure an adequate breath-hold. These scans commonly require a 10-second breath-hold.

A multidetector scanner should be used with collimation of 3 mm or less and a pitch under 2. Reconstruction should be approximately 1 mm for high-quality 3D endoluminal images. A low-radiation-dose protocol is used. Some researchers are using "ultralow-dose" protocols.

#### RADIOLOGIST INTERPRETATION

Any software package used for the interpretation of CTC must permit both 2D and 3D evaluation of the colon.<sup>18</sup> Ideally, both styles of interpretation should be possible: a "primary 2D read with 3D problem solving"<sup>6</sup> and a "primary 3D read with 2D problem solving." In this context, a 3D view refers to an endoluminal perspective optimized for examining the

colon, using either surface- or volume-rendered imaging. The 2D and 3D views should be seamlessly integrated.

The 3D view should offer both manual navigation and an automated centerline fly-through of the lumen. Two-D imaging should offer simultaneous sagittal and coronal views and ideally should permit simultaneous synchronized paging through the supine and prone views. Novel views now "cut the colon open" and display it like a flat sheet.

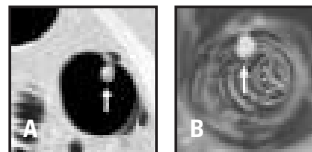
Sufficient training and experience in reading colonoscopically proven cases is critical. We suggest that 20 to 50 proven cases be read under supervision, with the reader achieving a reasonable sensitivity for polyps 10 mm or larger, before he or she offers the test to the public

for a fee. Several publications deal with methods and pitfalls of interpretation.<sup>7,18</sup>

In a 3D approach, each view (supine and prone) is read twice, once with a forward and once with a backward fly-through. Lesions are characterized as stool, polyps, or lipomas using 2D images. Wide soft-tissue windows can be used to search the 2D images for flat lesions. In a primary 2D read, magnified axial images are used to page through the scan and meticulously evaluate each loop. Three-D images can be used to help differentiate normal folds from polyps. Generally, polyps greater than 5 mm are reported. Foci 5 mm or smaller usually represent stool or hyperplastic polyps.

As stool is characterized by mottle seen on lung or soft tissue window setting, active adjustment of window/level settings during the interpretation is necessary. For stool lacking a mottled pattern, comparing supine and prone views will help to show the mobility characteristic of stool. Stool opacification with oral contrast agents such as barium might help identify residual stool, though the mobility of a polyp on a long stalk—or of the colon itself—could be a pitfall.<sup>7</sup>

If CTC is performed with a sufficient radiation dose, it will be able to detect and characterize incidental lesions in the kidney as solid (possible renal cell carcinoma) or cystic. Other significant abnormalities such as an abdominal aortic aneurysm, ovarian masses, lung lesions, and adenopathy can be detected. A meta-analysis found a 12% incidence of significant extracolonic findings on CTC.<sup>19</sup>



A 10-mm pedunculated polyp in the splenic flexure detected by CAD. Axial CT image (A) showing a polyp (arrow) and the 3D endoscopic view (B) of the polyp.

## COMPUTER-AIDED DETECTION

Computer-aided detection software for CTC is expected to become commercially available this year and offers the possibility of a double reading of CTC images by a radiologist and a computer.<sup>20</sup>

A CAD system automatically detects polyps and masses from CTC data and provides the locations of suspicious polyps to radiologists. If CAD is sufficiently sensitive and specific, the "second opinion" it offers has the potential to increase radiologists' diagnostic performance in the detection of polyps and masses and to solve the problem of the steep learning curve for reading CTC. Several prototype CAD schemes have been proposed for CTC.<sup>21,22</sup> It appears that the best performance can reach by-patient sensitivity up to 100% with 1.3 false positives per patient for polyps greater than 5 mm,<sup>22</sup> and the performance of many CAD schemes ranges between 80% and 100% sensitivity with one to 10 false positives per patient. When they are compared, especially in

terms of sensitivity, it appears that CAD performance approaches that of a human reader.

One of the arguments for the use of CTC is the limited availability of optical colonoscopy, suggesting that gastroenterologists' resources should be reserved for a prescreened cohort with a high prevalence of disease. Because every positive CTC must be referred to optical colonoscopy, this may be a more cost-effective use of resources. The cost-effectiveness of CTC will depend on how much is charged and on the interval at which a normal exam needs to be repeated.

The complication rate for CTC is extremely low and reports of colonic perforation are rare. CTC should not be performed on anyone with an increased risk of perforation, such as patients with peritoneal signs.

### SUMMARY POINTS:

- CTC, or virtual colonoscopy, is a new, minimally invasive technique to detect

colorectal polyps and masses that avoids the need for sedation and can be done in an outpatient setting.

- CTC is the best test for patients who have an incomplete optical colonoscopy or who cannot or refuse to undergo optical colonoscopy.

- CTC for colorectal cancer screening is still controversial, but is offered in many locations.

- CTC can be performed after colon cleansing, but is adaptable to less vigorous cleansing strategies than optical colonoscopy because oral contrast can be used to "tag" stool and residual fluid.

- CTC interpretation requires significant training and experience.

- Specialized software for 2D multiplanar and 3D image generation is commercially available, ideally with an automated 3D fly-through of the colon.

- Rapid advances in CAD software that automatically finds polyps and masses will help radiologists achieve accurate and confident interpretations.

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