

# The Role of CT Colonography in Screening Colorectal Neoplasia: A Gastroenterologist's Perspective

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## Introduction:

CT colonography, or virtual colonoscopy, has excited the medical world since it was first described in 1994. [1] Patients were attracted to this technology because it offered the hope of a quick, thorough screening test without requiring the invasiveness and distaste of screening tests such as conventional colonoscopy or sigmoidoscopy or the handling of feces, required with fecal occult blood testing. The cancer community viewed virtual colonoscopy with great excitement, hoping that it would offer better public acceptance and result in improved patient adherence to screening guidelines. Many gastroenterologists, however, initially viewed this emerging technology with dread primarily due to concerns about lost income from decreased volume of colonoscopies. As CT colonography has been better studied and defined, the consensus in the gastroenterology community has shifted from one of dread to one of acceptance with skepticism about performance and cost-effectiveness. In this review, I will provide a gastroenterologist's view of the need for better colorectal cancer screening tools, the benefits and limitations of CT colonography, and the remaining challenges to bring CT colonography into the realm of clinical practice.

## Colorectal Cancer: magnitude of the problem

Colorectal cancer is a significant problem throughout the world, most notably in industrialized nations, and associated significantly in countries with particular dietary practices. In the United States, colorectal cancer is the second leading cause of cancer death in men and women.[2] In

Japan, the incidence of and mortality from colorectal cancer are increasing, as is its proportion among all malignancies.[3]

In addition, because colorectal cancer is detectable in its pre-clinical phase, screening and surveillance strategies involve identifying pre-cancerous polyps and removing them.[4, 5] This effective strategy has been shown to reduce the mortality from as well as the incidence of colorectal cancer.[6, 7]

Although there are a number of different types of colon cancer screening tools, there is mounting evidence that colorectal cancer screening should involve some examination and visualization of the entire colon. Fecal occult blood testing is felt to be too insensitive and non-specific. Recent studies have demonstrated that screening colonoscopy was significantly better than flexible sigmoidoscopy for the detection of proximal polyps.[8, 9] In both studies, less than 50% of patients with proximal advanced lesions had associated index adenomas, suggesting that current screening guidelines which utilize sigmoidoscopy are insufficient. Additional data have also suggested that barium enema is inferior to colonoscopy.[10] In response to this data in the United States, the government-sponsored healthcare for the elderly (Medicare) has now approved payment of screening colonoscopy for patients over age 65. It is expected that other third-party payers will follow this precedent.

#### Colonoscopy: the preferred screening test, but it has its limits

Despite the proven effectiveness of screening colonoscopy and polypectomy for detection and prevention of colorectal cancer, this test has its limits. It is estimated that between 2%-10% of colonoscopies are incomplete due to patient discomfort, adhesions, tortuous colon, or hemodynamic instability, and that 12-13% of 5-10 mm polyps and 0-6% of polyps greater than 10 mm may be missed by an experienced colonoscopist due to inadequacy of the preparation or lesions located behind folds.[11, 12] In addition, colonoscopy carries a risk of perforation or serious hemorrhage of 1/2000-1/5000. Finally, patients greatly fear this invasive test, and most of all dislike the noxious cathartic cleansers that are required prior to the exam.

In addition, in both the United States and in Japan, there are now reports of “flat and depressed adenomas,” lesions that are smaller than the typical polypoid adenomas, and therefore more difficult to identify using conventional colonoscopic techniques. Japanese, European, and American descriptions of these lesions suggest that they may have an incidence as high as 20%-30%, and have significantly different biologic features than polypoid lesions. They have been found to have earlier transformation to high-grade dysplasia, and, when cancer is present, more rapid invasion into the submucosa.[13] Conventional colonoscopy may be insufficiently sensitive for these lesions, so gastroenterologists may need to use chromoscopy or magnification endoscopy to identify them.

Although a previous study examining cost-effective colorectal cancer screening in Japan suggested that immunological fecal occult blood testing was the most cost effective screening strategy,[14] more recent work in the United States has shown that colonoscopy may be a more cost-effective approach to screening, because it reduces mortality at relatively low incremental

costs given the insensitivity, screening intervals, and poor compliance involved with other screening strategies.[15]

### Why gastroenterologists need help

Despite our knowledge that colorectal cancer is preventable with adequate screening, patients and physicians are not following established guidelines. The United States Centers for Disease Control used a 1999 Behavioral Risk Factor Surveillance System survey of >50,000 Americans to show that only 44% of respondents had undergone appropriate colorectal cancer screening within the recommended time period.[16] It is estimated that screening compliance may be similar in Japan. One study showed 55% compliance rate with annual fecal occult blood testing.[17]

Poor colorectal cancer screening adherence is thought to be due to a number of important factors. Patients do not want to discuss their colons or bowel movements, are afraid or in denial about colorectal cancer, and are afraid and embarrassed by the available screening tests. Because colorectal cancer is asymptomatic in its early stages, physicians may not remember to screen for this disease when patients present with other complaints. In addition, the variety of available screening tools and different guidelines are confusing for physicians and for patients. Misunderstanding is a likely explanation for some non-compliance.

In addition, although the American government and other insurance companies will be sponsoring screening colonoscopy, even if patients and physicians were more compliant with recommendations, there is a vast undersupply of colonoscopists to meet the anticipated demand.[18, 19]

### Need for a Better Screening Tool: is CT colonography the answer?

An ideal screening tool for colorectal cancer would be highly sensitive and specific, widely available, cost-effective, and acceptable to patients and physicians. CT colonography may meet some of these criteria, by offering mass appeal, quick examinations, and theoretically (and still unproven) safer, more thorough examinations.

### Performance of CT Colonography: polyp detection

A number of large studies using modern equipment to examine CT colonography have now been completed.[20-23] They all were performed on high-risk patients with known polyps or masses, and therefore, their performance results are biased. Nonetheless, CT colonography performed impressively well. When trained and experienced radiologists read these exams, they identified 1 cm polyps approximately 90% of the time. False positive results occurred when stool, folds, or collapsed loops of bowel were misinterpreted, and specificity therefore was approximately 80-85%. In addition, there has been a trend toward improved sensitivity over time, probably due to increased experience of these radiologists. Some of the trials have attempted to look at “clinically significant” findings, analyzing their results “by adenoma” or “by patient” rather than simply “by polyp,” and doing so improves sensitivity, but does not necessarily answer the concern about a single patient with a single lesion. Controversy remains as to whether the

threshold of detection should be lowered to include 5-9 mm lesions, which would increase the screening interval and further decrease the number of missed lesions of clinical significance. However, given current performance, lowering the detection threshold would greatly decrease sensitivity and specificity.

An additional concern remains the distal rectal lesion, which might be obscured by the insufflation rectal tube. Finally, although CT colonography is excellent at determining a mucosal-based lesion from a lipoma or extrinsic lesion, major limitations of CT colonography remain its inability to biopsy lesions or perform polypectomy.

### Performance of CT Colonography: incomplete colonoscopy

Despite the limitations of CT colonography for screening polyp detection, an area that seems to be well suited for CT colonography is the incomplete colonoscopy. A number of recent studies have demonstrated that CT colonography is superior to barium enema for incomplete colonoscopy, and may even offer additional information of clinical utility (such as cancer staging).[24-26] In our practice, we find a CT colonography performed the same day as the incomplete conventional colonoscopy is of great satisfaction to the patient and to the primary physician.

### Do patients prefer CT colonoscopy to conventional colonoscopy?

Patients appear to prefer the concept of CT colonography as a minimally invasive exam over barium enema or conventional colonoscopy.[27, 28] However, preliminary results of small survey studies suggest that after both CT colonography and conventional colonoscopy are completed, patients' preferences may be neutralized, primarily because their perceptions of conventional colonoscopy change after an adequately sedated exam.[29] In our experience, patients are attracted by the name "virtual" colonoscopy, but they are rarely as enthusiastic once they understand that 1) they still require a bowel cleansing, and 2) the test requires insertion of a rectal catheter and insufflation without sedation. Although CT colonography is extremely well-tolerated, we have encountered several patients who experienced abdominal bloating and discomfort after their CT colonography, exacerbated further when undergoing the scheduled same-day conventional colonoscopy.

### Is virtual colonoscopy a cost-effective screening option?

Cost effectiveness remains a crucial concern for this screening tool, but models currently are limited by many assumptions and rapidly changing technology. Sonnenberg, et. al. used a Markov model to examine the cost effectiveness of CT colonography.[30] He concluded that in order for CT colonography to be cost effective in the United States, it had to be 54% less expensive than the cost of a colonoscopy (including radiologists' fees), and be performed at 10-year intervals with compliance rates 15%-20% higher (even with 100% sensitivity). However, if sensitivity is increased to include smaller lesions and thereby decrease the interval between exams, current performance dictates that sensitivity and specificity are simultaneously decreased, and therefore more colonoscopies and more people require therapy for missed colorectal cancers.

Improved technology and computer-aided diagnosis may bring the cost for this test into the affordable and effective range.[31, 32]

In addition, identification of incidental extra-colonic findings during CT colonography has been touted as an advantage by some experts and a disadvantage by others. The cost-effectiveness of workup of these “incidentalomas” remains unclear, but it is likely to cost more from both monetary and psychological perspectives as patients await workup of lesions of uncertain significance.

### Which patients would not benefit from CT colonography?

CT colonography for colon cancer screening operates on the principle of identifying raised lesions in the colon. It is therefore unsuitable for surveillance of flat dysplasia or dysplasia-associated lesions or masses (DALMs) in patients with chronic inflammatory bowel disease. The flat or depressed adenoma also would likely fall under the current threshold of CT colonography, a matter of great concern if the associated higher rate of dysplastic transformation and invasiveness is confirmed.

### Practical matters

In order for CT colonography to become an acceptable screening tool for colorectal cancer, a number of issues will need to be resolved.

1. Population studies need to be performed in average risk patients. Currently, one such multi-center trial is occurring in the United States.(Peter Cotton, Principal Investigator, Medical University of South Carolina.)
2. The sensitivity and specificity of the test needs to be improved to greater than 90% for lesions 6-9 mm in size. This would correspond to the performance characteristics of colonoscopists, and would identify the adenomas which, although small, have a 0.1%-1% risk of containing carcinoma[33] (possibly higher if the data about flat or depressed lesions is confirmed). Identifying lesions this size will enable CT colonography to be performed at 10-year intervals, and will likely improve compliance and cost-effectiveness.
3. Digital rectal exams should be performed by radiologists prior to inserting the rectal tube in order to identify distal rectal lesions.
4. Computer-aided diagnostic schemes should be developed in order to increase sensitivity and specificity while simultaneously decreasing reading times.
5. More work should be done to eliminate the much-disliked colonic cleansing preparation.
6. CT colonography needs to be coordinated with gastroenterologists, so that a positive finding on a CT colonogram can be referred to a gastroenterologist for a same-day colonoscopy and biopsy/polypectomy. It is more likely that this arrangement would be most acceptable to patients, would eliminate the need for patients to undergo repeat bowel catharsis, and would reduce the chance of patients being lost to follow-up or being non-compliant with recommendations. There are a number of logistical challenges to making this proposal a reality:
  - a. Radiologists and gastroenterologists would need to coordinate their schedules.
  - b. We need to define a standard method to report results in a way that the gastroenterologist can find the lesion(s).

- c. There must be a protocol when the gastroenterologist is unable to find the lesion described by the radiologist. Should the patient undergo repeat colonoscopy? Repeat CT colonography? Barium enema?
  - d. Patients must be accompanied by a friend or family member who can drive them home after their sedated colonoscopy. This would need to be coordinated prior to the screening CT colonography as well.
7. An approach to extracolonic findings needs to be identified. This would involve altering the consent form for CT colonography to include the possibility of extra-colonic findings, as well as incorporating work-up of these lesions into the overall cost of this exam.

### Conclusions

We desperately need better colorectal cancer screening tools, and CT colonography may be one possible solution. It appears to offer public appeal, safety, and tolerability. However, its performance as a screening tool has not been adequately tested, and its threshold of detection may be set at a level which is not cost effective, even more so given the growing understanding of flat and depressed adenomas. CT colonography already plays an important role for the incomplete colonoscopy, and it is likely to continue to gain usefulness in other areas as technology, experience, and acceptance grow. Gastroenterologists should embrace this tool as a supplement to our armamentarium, and not as a threat to our survival.

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