



CT Colonography (“Virtual Colonoscopy”) for Colon Cancer Screening

EXECUTIVE SUMMARY

Background: Computed tomographic (CT) colonography, also known as "virtual colonoscopy," is an imaging technique of the colon involving helical computed tomography and computer software to generate high-resolution 2-dimensional and 3-dimensional images of the inner surface of the colon. These images are then interpreted by a radiologist to determine the presence of several types of abnormalities of the colon. CT colonography has been investigated as a technique for colon cancer screening. Although it requires a full bowel cleansing similar to that required for conventional colonoscopy, the procedure requires no sedation or analgesia, and is faster to perform than conventional colonoscopy.

Objective: To determine whether there is adequate evidence to demonstrate that CT colonography screening is effective in reducing mortality from colon cancer.

Search strategy: Studies that examine the diagnostic sensitivity and specificity of CT colonography for the detection of polyps.

Selection criteria: For main evidence review, adequately designed studies which assess the diagnostic sensitivity and specificity of CT colonography. Studies were included if they had the following characteristics:

1. Prospective enrollment of subjects undergoing both CT colonography and optical colonoscopy
2. Valid reference standard (usually colonoscopy, sometimes "unblinded colonoscopy")
3. Valid per-patient analysis of CT colonography allowing calculation of both sensitivity and specificity at a specific polyp size threshold, and adequate data to calculate prevalence rates of polyps and referral rates (test-positive rates)
4. Minimum sample size of 50 patients

Main results: Diagnostic performance of CT colonography is highly dependent on the technology and techniques used. Thus, many of the older studies reviewed may no longer represent currently possible diagnostic performance of the test. A large study published in 2003 showed diagnostic test performance of CT colonography for polyps to be equivalent to that of optical colonoscopy. Other studies published previously and after that study showed variable performance, with 2 large studies showing much lower sensitivity than optical colonoscopy. Results from the largest study of a screening population, the ACRIN trial, were recently published. This study used 16–64 row detector CT scanners, stool tagging techniques, and minimum training standards for interpreters of the test. The results of this study show 90% sensitivity of CT colonography for polyps 10 mm or larger and 86% specificity; positive and negative predictive values were 23% and 99%, respectively.

Translating this diagnostic sensitivity to an inference of effectiveness for preventing colon cancer mortality requires the same chain of logic that supports optical colonoscopy as an effective screening test. Thus a test that approaches the sensitivity of optical colonoscopy for the detection of clinically relevant polyps should logically approach the clinical effectiveness of optical colonoscopy, as optical colonoscopy is considered to be the most effective techniques for cancer screening and prevention.

Several other differences between optical colonoscopy and CT colonography regarding comfort, convenience, screening intervals, other ancillary health outcomes are difficult to quantify, but are probably small in magnitude in

terms of ultimate health outcomes. However, patients should probably be adequately informed of these differences, as these may very well determine which type of screening test the patient chooses to have.

Authors' comments and conclusions: The conclusions of this Assessment rely on the generalizability of the ACRIN trial to general screening populations and community radiologists.* This trial constitutes the most important and substantively new evidence available since the prior TEC Assessment, which was published in July 2004. The prior TEC Assessment concluded that CT colonography did not meet the TEC Criteria. Overall, sensitivity reported in the literature was quite variable among studies. Interpreter experience and technical factors were suggested to be likely explanations for the observed variability in performance. The 2004 Assessment also noted that clear criteria needed to be established for size polyp size threshold for removal and for frequency of screening in order to estimate the effectiveness of CT colonography.

The ACRIN trial addressed many of the gaps identified in the prior Assessment. Important features of the trial include large population (n=2,600), multiple institutions (n=15), minimum 16-slice CT scanner, stool tagging, and comparison of 3 commonly used bowel preparation regimens. As described in the trial protocol (ClinicalTrials.gov Identifier NCT00084929), the primary aim of the trial was to evaluate the sensitivity of CT colonography, compared to optical colonoscopy, for detecting individuals with a clinically significant large lesion, defined as larger than 10 mm. Secondary aims were sensitivity for detecting polyps from 5–10 mm and for detecting signal characteristics (i.e., high-grade dysplasia, invasive carcinoma, and/or villous features) of polyps 5 mm or larger. Of practical importance, the trial evaluated interobserver variability in accuracy of CT colonography examination interpretation. Additional descriptive data that will contribute to assessing effectiveness of CT colonography include patient acceptance, prevalence and distribution of flat lesions, prevalence and clinical significance of extracolonic findings, and differences in interpretation techniques.

The ACRIN trial featured a training and operator qualifying examination component. The news item summarizing the preliminary ACRIN results also included comments from the principal investigator of the trial citing the importance of adequate training and credentialing of CT colonography readers for the effectiveness of the technique. This suggests the need to credential providers who perform this procedure, at least in the initial phase of dissemination. The 2008 guideline on colon cancer screening, a joint guideline of the American Cancer Society, the U.S. Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology (ACR) notes that, following the publication of the results of the ACRIN trial, the 2006 ACR Practice Guidelines for Performance of Computed Tomography (CT) Colonography in Adults will be updated. The ACR Guidelines address "the techniques, quality control, clinical uses, training, and communication of results for [CT colonography]." The joint guideline also notes that the ACR is piloting quality metrics for CT colonography, has begun construction of an interactive training facility, and is evaluating "a process for individual certification and proficiency." Standards for training of gastroenterologists performing CT colonography were published by the American Gastroenterological Association in 2007.

Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel made the following judgments about whether CT colonography for colon cancer screening meets the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) criteria.

1. The technology must have final approval from the appropriate government regulatory bodies.

CT colonography may be performed using any CT scanner capable of producing helical (spiral) thin-section images (<5 mm). More recent studies have been conducted using commercially available multidetector-row (multislice) helical CT scanners that facilitate faster image acquisition and thinner sections. The 2-dimensional cross-sectional CT images may be interpreted directly and software algorithms using 3-dimensional reformatting techniques may also be used to facilitate interpretation. Three-dimensional reformatting software may be cleared through the U.S. Food and Drug Administration (FDA) for this specific application. For example, the Viatronix V3D-Colon® virtual colonoscopy system (Viatronix, Inc., Stonybrook, NY) was cleared for marketing by the FDA via the 510(k) process on April 19, 2004, for use as a screening tool in detecting colon cancer.

2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

No direct evidence is available on health outcomes. An inference of effectiveness must be made based on a chain of logic that starts with the diagnostic sensitivity and specificity of CT colonography. The ACRIN study, a large trial of a screening population, using the latest scanners and techniques for bowel preparation and image interpretation, showed a 90% sensitivity of CT colonography for detection of polyps 10 mm or larger and a specificity of 86%; positive and negative predictive values were 23% and 99%, respectively.

- 3. The technology must improve the net health outcome; and**
- 4. The technology must be as beneficial as any established alternatives.**

Given the chain of logic and other underlying evidence which support the practice of accepted colon cancer screening techniques such as optical colonoscopy, a 90% sensitivity of CT colonography for detection of polyps 10 mm or larger is consistent with an improvement in health outcomes due to detection and removal of precancerous lesions. The 86% specificity of CT colonography would result in some false-positive tests, which, in turn, would result in some unnecessary follow-up colonoscopies. However, compared with optical colonoscopy, there are several other types of health outcomes that may differ in terms of convenience, cost, detection of unrelated health problems, and radiation exposure. These are difficult to quantify, and are probably small in magnitude compared to the health benefit of identifying and removing cancer precursors.

5. The improvement must be attainable outside the investigational settings.

The results of the ACRIN trial were dependent on the technical standards required for performance of the test and the training and skill of the interpreters of the test. Each participating radiologist was required to submit confirmation of having interpreted at least 500 CT colonographic examinations or having participated in a specialized 1.5-day CT colonography training session. In addition, all participating radiologists were required to complete a qualifying examination in which they achieved a detection rate of 90% or more for polyps measuring 10 mm or more in diameter in a reference image set. If these practices can be replicated in the community, then it is likely that improved health outcomes can be achieved outside investigational settings. Standards of performance and interpretation of CT colonography consistent with those reported in the ACRIN trial will be necessary for CT colonography to be an effective screening test.

Based on the above, CT colonography for the purpose of colon cancer screening meets the TEC criteria.

*At the time this Assessment went to press, the U.S. Preventive Services Task Force (USPSTF) published its 2008 recommendations for colorectal cancer screening. The evidence for CT colonography was judged to be insufficient to evaluate the benefits and harms. This guideline was based on concerns about potential harms of radiation exposure and potential for harm due to evaluation of extracolonic findings. In contrast, the 2008 edition of cancer screening guidelines released by the American Cancer Society (ACS) in conjunction with the U.S. Multi-Society Task Force on Colorectal Cancer and the American College of Radiology, recognizes two types of screening tests: colon cancer prevention and cancer detection. Colon cancer prevention tests detect both early cancer and adenomatous polyps. The cancer prevention options recommended were flexible sigmoidoscopy every 5 years, colonoscopy every 10 years, double-contrast barium enema every 5 years, or CT colonography every 5 years.

Given that much of the evidence supporting colorectal cancer screening is indirect, it is not so surprising that consensus groups reviewing the same evidence might come to different conclusions, as have the USPSTF and the ACS regarding CT colonography. Although both groups reviewed the same evidence and similar decision models to reach their conclusions, an editorial accompanying the USPSTF publication suggests that subtle differences in emphasis may underlie the differing conclusions. The USPSTF appears to put more emphasis on the potential unknown effects of radiation exposure and workups for extracolonic findings, taking a more longitudinal perspective. The ACS report concentrates on the capability of CT colonography to detect large polyps in a single screening visit as the principal criterion to determine colon cancer prevention. Thus, the ACS report favors screening technologies with superior single screening detection characteristics over less sensitive tests that have demonstrated efficacy with repeated screening.

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