



# AMERICAN COLLEGE OF GASTROENTEROLOGY

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September 27, 2007

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Washington State Health Care Authority  
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Submitted via e-mail to: [shatap@hca.wa.gov](mailto:shatap@hca.wa.gov)

Dear Sir or Madame:

On behalf of the American College of Gastroenterology, including some 200 members in Washington State, I would like to provide information for your use in developing a technology assessment for CT colonography/virtual colonoscopy. Currently, colonoscopy is the gold standard for CRC screening; the ACG takes an evidence-based approach to new CRC screening technologies, and supports any colorectal cancer screening technology that is in the best interest of patients. New technologies must have well defined effectiveness, adequate cost-effectiveness, safety and acceptability to patients. It is not yet clear that CT colonography meets this threshold, but it may in the coming years.

The American College of Gastroenterology is a physician organization representing gastroenterologists and other gastrointestinal specialists. Founded in 1932, the College currently numbers more than 10,000 physicians among its membership of health care providers of gastroenterology specialty care. Although the vast majority of these physicians are gastroenterologists, the College's membership also includes surgeons, pathologists, hepatologists, and other specialists involved in various aspects of the overall treatment of digestive diseases and conditions. The College has chosen to focus its activities on clinical gastroenterology – the issues confronting the gastrointestinal specialist in treatment of patients. The primary activities of the College have been, and continue to be, educational efforts directed at promoting and optimizing quality care.

## INTRODUCTION

Our members have been at the forefront of providing colorectal cancer (CRC) screening and the College has taken a leading role in developing clinical guidelines for this screening. Colon cancer is the second most common cancer-related killer in America of both men and women. Yet colon cancer is not only highly detectable, treatable, and curable if found early, it is also preventable with appropriate screening. Indeed, if the cancer is detected early and appropriately treated, the 5-year survival rate is approximately 90%. Not only does appropriate colorectal screening save lives, it has also been demonstrated to be very cost effective. The American College of Gastroenterology was the first and only organization to recommend colonoscopy as the preferred strategy for colorectal cancer screening. We continue to stand by that recommendation.

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## CT COLONOGRAPHY

The ACG believes, based on the current level of evidence, that CT colonography does not yet constitute an acceptable colorectal cancer-screening test. CT colonography requires thorough bowel preparation, insertion of a rectal tube, and distention of the colon with air or carbon dioxide which has been shown to cause patient discomfort. Perhaps most importantly, patients who have polyps must still undergo optical colonoscopy to have them removed. The studies currently in the literature have shown mixed results on the sensitivity of the technology *vis a vis* identifying polyps less than one centimeter in size. While we are aware that other data will be released soon, it is important that independent researchers have an opportunity to analyze the studies and data before any entities rely on the data as a basis for policy decisions. Past experience with this and numerous other medical technologies has shown that policymakers benefit most from rigorous analysis of new data before making policy changes.

Among the key issues in evaluating CT colonography that remain unanswered are the standard that should be used to determine which types and sizes of polyps must be removed and/or reported; surveillance frequency for the test; who will read the intra-luminal and extra-luminal findings; and what are the short and long term radiation risks associated with this test.

The ACG does not support reimbursement for CT colonography until there is validation that the results of the 2003 *New England Journal of Medicine* trial are generalizable. We have seen excellent results before with CT colonography that relied basically on imaging technologies but which could not be reproduced by others. In fact, the range of results with regard to effectiveness in the literature is enormous and much greater than for any other colorectal cancer screening strategy. The software and labeling techniques used in the 3-D studies are not widely available at this time in the United States. Premature approval by technology assessment groups like yours or reimbursement for CT colonography could result in an enormous increase in cost without proven benefits and with associated risks of radiation.

The College also strongly believes that Patients with polyps  $\geq 6$  mm in size detected at CT colonography, who have reasonable life expectancies, should be referred for colonoscopy and polypectomy. If CT colonography is going to compete with other strategies from a cost-effectiveness standpoint and have acceptable radiation risks, it will need to be performed at the same interval that colonoscopy is performed, i.e. 10 years. Although radiologists are currently discussing a 1 cm cutoff size for CT colonography, in which polyps that are detected that are less than that in size would either be ignored or followed up in a few years by repeat CT colonography, there is no evidence to suggest the safety of this approach. Overall, the literature suggests that polyps in the 6-9 mm range have an approximately 1% prevalence of invasive cancer, and it is unlikely that patients or primary care physicians will accept leaving these polyps in place for 10 year intervals. Ignoring polyps  $<1$  cm in size is an approach that has not previously been used in clinical practice and has never been the approach to polyps detected during barium enema.

## DETAILED LITERATURE SUMMARY

At this time, CT colonography does not fulfill a common health technology criterion that the scientific evidence must permit conclusions concerning the effectiveness of the technology regarding health outcomes. Thus, the results of clinical trials using CT colonography have been very mixed, with a remarkably wide range of results. For example, the three largest studies of CT colonography have been published since October 2003 (Johnson, *Gastroenterology* 2003;125:311-9; Pickhardt, *N Engl J Med* 2003;349:2191-200; Cotton, *JAMA* 2004;291:1713-9). The study by Johnson et al was a single center study performed at the Mayo Clinic Rochester. Among 703 patients, the reported sensitivity among three experienced examiners for polyps  $>9$  mm was 32%, 35%, and 73%, with a mean sensitivity of 46% (Johnson, *Gastroenterology* 2003;125:311-9). The Cotton study was a nine center study in the United States involving 615 patients, with a primary end point of finding patients with polyps  $\geq 6$  mm in size and reported an overall sensitivity for this end point of 39%, with a sensitivity of 55% for identifying patients with polyps  $\geq 1$  cm in size (Cotton, *JAMA* 2004;291:1713-9). The single largest study (Pickhardt, *N Engl J Med* 2003;349:2191-200) reported a high sensitivity for colon polyps in a screening population. However, this study utilized a three dimensional imaging format that is not widely available as well as oral labeling of retained stool and fluid, followed by electronic subtraction. Patients also had aggressive air distention during the procedure and the study population was a military population that has been speculated to be highly compliant. The relative importance of these components in the improved sensitivity in this study is uncertain. However, we note that the Cotton et al, study also utilized three-dimensional fly-throughs of the colon with only minimal improvement in sensitivity. Thus, while the results of the Pickhardt study are encouraging, we have already seen disparate results with regard to three-dimensional imaging. This situation (disparate results) is very similar to the one that has been seen previously with studies relying primarily on multiplanar two-dimensional imaging. For example, several small studies with highly selected patient populations (high prevalence of patients with polyps  $>1$  cm in size) have demonstrated sensitivities of 90% or higher for  $\geq 1$  cm polyps (Fenlon, *N Engl J Med* 1999;341:1496-503; Yee, *Radiology* 2001;219:685-92; Kay, *Endoscopy* 2000;32:226-32). However, in addition to the poor results obtained with multiplanar 2D imaging noted in the Johnson and Cotton studies above, a study by Miao et al (*Gut* 2000;47:832-7), found a sensitivity for polyps  $>1$  cm of 50%, and five other studies found sensitivities for polyps  $>1$  cm of 45%, 50%, 62%, 67%, and 75% (Pescatore, *Gut* 2000;47:126-30; Rex, *Gastrointest Endosc* 1999;50:309-13; Spinzy, *Am J Gastroenterol* 2001;96:394-400; Mendelson, *MJA* 2000;173:472-5; Fletcher, *Radiology* 2000;216:704-11). The American College of Radiology Imaging Network Study evaluated selected cases from eight medical centers, with a very high prevalence (47%) of cases with polyps  $\geq 1$  cm (Johnson, *Gastroenterology* 2003;688-95). Despite this high prevalence, 18 individual experienced radiologists had a wide range of interobserver variation in both sensitivity and specificity and have an average sensitivity and specificity for large polyps of only 75% and 73%, respectively.

In addition to these concerns about detection of polyps  $\geq 1$  cm in size, there are also issues regarding the sensitivity of smaller colon polyps. Currently, 95% of endoscopically identified colon polyps are  $< 1$  cm in size. (Church, *Dis Colon Rectum* 2004;47:481-5). In some studies, polyps in the 6-9 mm range have a prevalence of cancer of nearly 1% and of high-grade dysplasia of approximately 4% (Morrison, *Proc Roy Soc Med* 1974;67:451-7; Shinya, *Ann Surg* 1979;190:679-83; O'Brien, *Gastroenterology* 1990;98:371-9). Although the natural history of these polyps is uncertain, we expect that in clinical practice they will be considered important by many clinicians and considered a target for detection and removal by colonoscopy. Sensitivities of CT colonography for polyps in the 6-9 mm range have often been quite low and have been 16%, 22%, 43%, 47%, and 39% in five studies (Miao, *Gut* 2000;47:832-7; Mendelson, *MJA* 2000;173:472-5; Rex, *Gastrointest Endosc* 1999;50:309-13; Fletcher, *Radiology* 2000;216:704-11; Kay, *Endoscopy* 2000;32:226-32).

Given the very wide range of results in clinical trials, we believe it is important to see reproduction of the results obtained in the Pickhardt study before accepting the methodology as effective, and we believe that currently the scientific evidence does not allow conclusions regarding the effectiveness of CT colonography regarding health outcomes.

In addition to these concerns regarding sensitivity, we also have significant concerns regarding specificity with CT colonography. The test is an expensive examination, being at least five times more expensive than the current radiographic imaging test for colon polyps, double contrast barium enema. In a recent comparison of CT colonography and double contrast barium enema, there was a significant difference in specificity of DCBE versus CT colonography for polyps  $> 1$  cm (99% versus 96%) (Johnson, *Clin Gastroenterol Hepatol* 2004;2:314-21). The specificity of CT colonography drops off significantly with size. In the best performing study in the literature, the specificity of CT colonography dropped off to 80% for polyps 6 mm and larger in size. The specificity for polyps  $\geq 5$  mm has been as low as 63-78% in some of the largest studies (Hara, *Radiology* 2000;215:353-7; Fletcher, *Radiology* 2000;216:704-11; Kay, *Endoscopy* 2000;32:226-32; Yee, *Radiology* 2001;219:685-92; Johnson, *Gastroenterology* 2003;125:688-95). Thus, 30% or more of patients undergoing CT colonography in many centers might be sent for conventional colonoscopy for false positives. These specificities are indeed lower than what has been traditionally reported for double contrast barium enema. In one large study of CT colonography, 197 of 300 patients had a true or false positive polyp (Yee, *Radiology* 2001;219:685-92). Because of these limitations in effectiveness, we note that no multidisciplinary guideline group (e.g. American Cancer Society, Smith, *Cancer J Clin* 2001;51:38-75) U.S. Multi-Society Task Force (Winawer, *Gastroenterology* 2003;124:544-60), or the U.S. Preventive Services Task Force (Pignone, *Ann Intern Med* 2002;137:129) has endorsed CT colonography as effective. This lack of endorsement also means that there are no guidelines for clinicians in practice to utilize to decide which polyps detected at CT colonography should be referred for colonoscopy. There are also no guidelines for what interval should be used for repeat examinations in patients who have negative CT colonographies, or who have CT colonographies that demonstrate polyps but the polyps are considered to be of a size that does not warrant colonoscopy and polypectomy at present. Further, the cost-effectiveness of CT colonography has not been established. The many uncertainties

regarding the management of small colon polyps and the possibility of repeat CT colonographies at short intervals in clinical practice adds additional concern regarding the possibility of very high costs with uncertain benefits.

Additionally, CT colonography has not been demonstrated to improve the net health outcome. Obviously, there is no long term data to prove that CT colonography improves net health outcomes; however, given the large range of effectiveness reported in the literature, as well as a reduction in specificity compared to double contrast barium enema, there is the possibility that CT colonography will be associated with no improvement in effectiveness and an increase in costs and therefore a reduction in cost-effectiveness. Because of reduced specificity, a large increase in the exposure of patients to costs and risks associated with false positive examinations is possible. Thus, the impact on net health outcomes with CT colonography is very uncertain. This also extends to the identification of extracolonic findings that may have benefits but also have significant costs and risks associated with evaluation of clinically unimportant incidental findings.

CT colonography also does not meet a common HTA criterion that the improvement must be attainable outside the investigational settings. In particular, the very wide range of effectiveness identified in clinical trials, i.e. the investigational setting, raises serious concerns about how the test will perform in clinical practice. In general, we would expect the level of performance to be below that seen in many of the clinical studies thus far performed. The absence of endorsement by professional guideline groups and the absence of any guideline as to proper use of the test in clinical practice would certainly contribute to widely inconsistent use in clinical practice that is frequently ineffective and costly.

Please don't hesitate to contact me if I can answer any questions or clarify any data submitted to you. We appreciate the opportunity to comment on this important technology and look forward to working with you to improve patient satisfaction and the quality of all CRC screening modalities.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "David A. Johnson". The signature is fluid and cursive, with a long horizontal stroke extending to the right.

David A. Johnson, MD, FACP  
President, American College of Gastroenterology