Technology Assessment Program
Office of Patient Care Services

Bibliography*: CT Colonography

*Selected, quality filtered, not subject to external review

Policy issue: The VA Deputy Secretary for Health requested guidance from the VA Chief Patient Care Services Officer (CPCSO) on the use of computerized tomographic colonography (CTC), also known as virtual colonoscopy, for the detection of colorectal cancer (CRC) in the VA population. The CPCSO asked that this request be handled by the VA Technology Assessment Advisory Group (TAAG) within the Office of Patient Care Services (OPCS), which was created to deliver evidence-based recommendations for use of new technologies in VA in a timely manner. As part of this process, the VA Technology Assessment Program (VATAP) is charged with providing the best available evidence on a topic within a two-week time period to help support guidance for acquisition and use of CTC in VA.

This bibliography will rely on evidence from the most current systematic reviews supplemented with updated searches to address the following questions:

What is the best available evidence of the safety and effectiveness of CTC for the early identification and management of CRC?

1a. What does the evidence show comparing virtual colonoscopy to optical colonoscopy?

1b. What does the evidence show comparing 2D software (orthogonal planes- grey scale) vs. orthogonal grey scale -3D virtual colonoscopy?

Background[1]**:** In the management of colorectal cancer, endoscopic procedures (primarily colonoscopy) and imaging (double contrast barium enema (DCBE)) are used in early detection strategies to identify and remove polyps in order to reduce the risk of cancer developing or progressing. Computerized tomographic colonography (CTC) is evolving as a noninvasive modality used to generate images of the colon. CTC involves scanning the colon with a helical CT scanner to generate high-resolution, two-dimensional or three-dimensional images of the abdomen and pelvis.

Concerns over the current system capacity to handle the rising volume of colonoscopy procedures have lead to other potential alternatives such as CTC for managing patients with, and at risk for, colorectal cancer. Potential applications for CTC are:

- as a screening test in average risk and above average risk patients for colorectal polyps;
- as a diagnostic test in symptomatic patients or in patients with suspicious findings on a prior screening test; and
- for surveillance of identified polyps or cancer.

To prepare for CTC, patients undergo a standard cathartic bowel preparation, and the colon is distended with air or carbon dioxide while images are taken with the patient in both supine and prone positions without sedation. As with all total colonic examinations, the quality of bowel preparation is essential to being able to distinguish polyps and growths in the colon clearly. The use of fecal tagging, whereby patients ingest oral contrast prior to the study, may facilitate distinguishing stool from mucosal abnormalities, thus enhancing diagnostic performance, and, if

[1] Sleisenger & Fordtran's gastrointestinal and liver disease : pathophysiology, diagnosis, management / [edited by] Mark Feldman, Lawrence S. Friedman, Lawrence J. Brandt.—8th ed. 2006. Saunders, Elsevier: Philadelphia, PA.

administered without a cathartic prep, may conceivably enhance patient compliance. Once detected, lesions that require removal are excised or biopsied by colonoscopy.

Several potential advantages and disadvantages for CTC relative to other CRC screening tests have been reported:

Figure 1.

Main Advantages	Main Disadvantages
• Rapid, safe method of structurally imaging the entire colon • Emerging software and techniques designed to improve the speed, accuracy, and reproducibility of results • No sedation or analgesia needed • Ability to identify extracolonic abnormalities • Ability to identify large-bowel malignancies that cannot be assessed by colonoscopy • Less time consuming and less expensive than colonoscopy • Potential ability to detect abnormalities missed by colonoscopy	• Low sensitivity and specificity • High resource costs—need for rapid high resolution helical CT and radiologist training • Exposure to ionizing radiation (similar to DCBE) • Variation in bowel preparation procedures can affect diagnostic performance • Variation in scanning, image acquisition, image processing and radiologist experience can affect diagnostic performance

Abbreviations:
CT, computerized tomography
DCBE, double contrast barium enema

Systematic reviews

"The complexity of modern technology and its high marginal cost suggest to us that testimonial reviews of new technologies are no longer sufficient." [2]

The complexity and sometimes conflicting nature of available information make it difficult for a reader or decision maker to determine what is best and what is relevant. This is particularly true of costly and rapidly evolving diagnostic technologies.

Synthesis of the available information through systematic review is essential for rational evidence-based policy making. A systematic review applies explicit scientific principles, intended to reduce bias in the review process, to enhance the validity of literature syntheses. Specifically, systematic reviews:

- Ask a focused clinical question;
- Conduct a comprehensive search for relevant studies using an explicit search strategy;
- Uniformly apply criteria for inclusion and exclusion of studies;
- Rigorously and critically appraise included studies;
- Provide detailed analyses of the strengths and limitations of included studies.

Systematic reviews can be quantitative (i.e., meta-analyses) or qualitative. The conclusions and recommendations of a systematic review are based on the quality and content of the evidence, thus allowing medical literature to be used effectively in guiding medical decisions.

[2] Kent DL and Larson EB. Disease, level of impact, and quality of research methods. Three dimensions of clinical efficacy assessment applied to magnetic resonance imaging. Investigative Radiology 1992;27:245-53.

The rigor of this approach is illustrated by the place of systematic reviews in evidence grading schemes where they receive the highest level designation[3,4].

Methods: In August 2007, VATAP used a two-tiered approach to identify the best available evidence for this report.

Search strategies/Inclusion criteria
The first approach was to find the most recent systematic reviews and health technology assessments[5] (HTA) on CTC published in English that would address the questions of safety and effectiveness of CTC. To accomplish this, VATAP conducted preliminary searches in the HTA database (www.inahta.org) and the Cochrane Library databases for completed reports from 2006 to the present and supplemented the searches with a query on August 6, 2007 to the listserv of members of the International Network of Agencies for HTA (INAHTA) for updated work.

Searches and electronic inquires of INAHTA members identified five systematic reviews or HTAs in various stages of completion (See Table 1), plus one single-site primary study assessing the role of CTC versus colonoscopy within the Australian health system (Roberts-Thompson (in press)). Of these, two are recently completed comprehensive syntheses of systematic reviews of CTC that will serve as the basis for this report:

- Computed Tomographic (CT) Colonography for the Detection of Colorectal Cancer—a Technical Brief. June 2007. New Zealand Health Technology Assessment. (Broadstock 2007)
- Computed Tomography (CT) Colonography. HTA Scoping Report. May 2007. NHS Quality Improvement Scotland (Macpherson 2007)

Each report is a synthesis in final draft form of the highest quality evidence from systematic literature reviews and meta-analyses published through 2007 and in English. Macpherson (2007) also considered evidence-based guidelines and consensus statements that addressed outcomes of CTC versus colonoscopy or DCBE studied in adults with positive results from CRC screening tests or symptoms suggestive of CRC. Collectively, these two syntheses comprise systematic reviews of primary studies that were published through the end of 2005.

VATAP identified one other systematic review of the efficacy and safety and cost-effectiveness of population screening tests for colorectal cancer, including CTC, in average risk populations from the Health Technology Assessment Unit (UETS[6]) in Madrid Spain (see Table 2). The full report, currently in final draft stage, is in Spanish with a structured abstract in English. It included primary research and secondary research published through September 2006 comprising three systematic reviews that were included in Broadstock (2007) and Macpherson

[3] Cook, DJ, Guyatt GH, Laupaucis A, Sackett DL, Goldberg RJ. Clinical recommendations using levels of evidence for antithrombotic agents. *Chest.*1995 Oct;108(4 Suppl):227S-230S.
[4] Guyatt, GH, Sinclair JC, Hayward R, Cook DJ, Cook RJ. Users' guides to the medical literature. IX. A method for grading health care recommendations. *Journal of the American Medical Association.*1995;274(22):1800-4.
[5]Health Technology Assessment (HTA) is a multidisciplinary field of policy analysis that systematically studies the medical, social, ethical, and economic implications of development, diffusion, and use of health technology.
[6] Analysis coste-effectividad del cribado de cancer colorectal in poblacion general: primera parte revision systematica sobre su eficacia y seguiridad. Nieves Calcerrada Diaz-Santos. Unidad de Evaluacion de Tecnologias Sanitarias UETS. Agencia Lain Entralgo. Madrid, Espana. July 2007. [English abstract].

(2007). Based on the evidence, UETS could not recommended CTC for colorectal cancer screening in an average risk population.

In August 2007, multiple searches were then conducted to update previous systematic reviews. The Cochrane Library® via the Wiley web-based system, plus PubMed®, EMBASE®, and Current Contents® via Dialog were searched using an array of controlled vocabulary, MeSH, and free text words and phrases for colonoscopy, coloscopy, virtual colonoscopy, MRI or CT colonography, and computed tomographic colonography. Because each of these databases uniformly add citations at the beginning of their indexing process, it was imperative to use a comprehensive free text strategy in addition to controlled terms to capture citations that may have been missed when relying solely on controlled vocabulary searches. The Dialog search results were filtered for controlled studies, randomized trials, meta-analyses, systematic reviews, guidelines, methods reviews, plus related synonyms. These results were further filtered for human studies, adult ages, English language, and the years 2006 to the present.

VATAP included only primary studies that met the following criteria:
- Comparison of CTC with optical colonoscopy for screening or diagnosis;
- Clear description of methods, study population and technology used;
- The most recent or largest version of a study by the same investigators for the same purpose (to eliminate redundancy).

Meeting abstracts, animal studies and studies already reviewed in included published systematic reviews were excluded.

One author (Adams) selected citations for full-text retrieval, reviewed all articles, and prepared this overview. Abstract information from included articles is presented in the end references.

Results: Searches of additional primary studies uncovered 166 citations, of which ten were retrieved for further appraisal as potentially relevant to this report. All ten met criteria for inclusion (See end references):

- Two feasibility studies evaluating the diagnostic performance of contrast-enhanced CTC in detecting local recurrence of CRC following curative resection (You 2006) and in differentiating colonic adenomas from carcinomas in polyps 1 cm or larger (Summers 2006).
- One feasibility study evaluating CTC as a complement to colonoscopy in the postoperative surveillance of patients who had colon cancer (Leonardou 2006).
- Four diagnostic accuracy studies of CTC versus conventional colonoscopy in high risk or populations (Renkonen-Sinisalo 2007; Reuterskiold 2006; Selcuk 2006; Roberts-Thompson (in press))
- One technical efficacy study comparing primary 2D versus 3D review methods for CTC with regard to polyp detection and perceptive errors (van Gelder 2007)
- Two cost-effectiveness studies of CTC in screening for colorectal neoplasia (Vijan 2007; Arnesen 2007)

Guidelines
Guidelines published from 2006 to the present were identified in the searches and are listed in Table 3. The guidelines were derived from literature reviews of variable comprehensiveness, in which the systematic nature of the review was not always reported, along with expert

consensus. Based on reported methods of guidelines development, The Institute for Clinical Systems Improvement (ICSI) guideline process appears to be the most rigorous with clearly defined information sources, quality appraisal and grading scheme for evidence-based recommendations.

The general consensus among these guidelines supports the use of CTC for colonic evaluation of symptomatic individuals following an incomplete colonoscopy due to obstructive or stenosing colonic lesions. The American College of Radiologists expands use of CTC to all patients who have an incomplete colonoscopy. ICSI expands the use of CTC in anticoagulated patients who cannot safely discontinue anticoagulation therapy and in patients who refuse colonoscopy and understand that their insurance may or may not cover the cost of the CTC. In all cases, availability of CTC and appropriately trained radiologists will need to be considered. All other uses are considered experimental or investigational.

Conclusions/Discussion:

What is the best available evidence of the safety and effectiveness of CTC for the early identification and management of CRC? The best available evidence from systematic reviews and meta-analyses finds that CTC is a relatively safe procedure compared to DCBE, and at least as safe as, or safer than, diagnostic colonoscopy. There is a low but cumulative risk of ionizing radiation exposure with regular screening and a low risk of colonic perforation. Findings are scant and inconsistent regarding patient preferences for and experiences with CTC versus other procedures, but they trend toward patients favoring CTC over colonoscopy with respect to pain and discomfort. There is no evidence reporting on overall health outcomes of CTC including efficacy in reducing CRC incidence or mortality.

What does the evidence show comparing virtual colonoscopy to optical colonoscopy? With respect to diagnostic performance, evidence is limited to indirect comparisons of CTC using optical colonoscopy as a gold standard. Existing evidence for CTC has been studied in high risk populations, while evidence from average risk populations has been lacking. Per-patient pooled sensitivity and specificity values from the meta-analyses included in the two evidence syntheses are summarized as follows:

	Polyp size Sensitivity % (95% CI)			Polyp size Specificity % (95% CI)		
	≥10 mm	6-9mm	≤5 mm	≥ 10 mm	6-9mm	≤5mm
Halligan 2005[7]	93 (73-98)	86 (75-93)		97 (95-99)	86 (76-93)	
Mulhall 2005[8]	85 (79-91)	70 (55-84)	48 (25-70)	97 (96-97)	93 (91-95)	91 (89-95)
Sosna 2003[9]	88 (84-93)	84 (80-89)	65 (57-73)	95 (94-97)		
Rosman and Korsten 2007[10]	82 (76-88)	63 (52-75) (6-10mm)	56 (42-70) (<6mm)			

[7]Halligan S, Altman D, Taylor S, Mallett S, Deeks J, Bartram C and Atkin W. CT colonography in the detection of colorectal polyps and cancer: systematic review, meta-analysis, and proposed data set for study level reporting. Radiology. 2005;237(3);893-904.
[8]Mulhall B, Veerappan G and Jackson J. Meta-analysis: computed tomographic colonography. Ann Intern Med. 2005;142(8);635-650.
[9] Sosna J, Morrin M, Kruskal J, Lain P, Rosen M and Raptopoulos V. 2003. CT colonography of colorectal polyps: a meta-analysis. *Am J Roentgenol*, **181**, 1593-1598.
[10] Rosman, AS and Korsten MA. Meta-analysis comparing CT colonography, air contrast barium enema, and colonoscopy. Aermican Journal of Medicine. 2007;120:203-210, e204.

CTC generally exhibits a high specificity and sensitivity in larger polyp sizes and lower specificity and sensitivity in smaller polyp sizes. The sensitivity of CTC is quite variable within and across polyp size groups. There is a need to better understand the wide variations in test accuracy found in the literature and the reasons behind them. Factor affecting detection rates may include: prevalence of polyps in the study population; polyp size and morphology (small, flat polyps are less well visualized than large polyps or cancers and may result in false negative results); study design characteristics (referral process, underlying characteristics of the study population, blinding of readers etc.); the experience of the radiologist; and variations in imaging technique. Evidence from recent primary studies would not alter these conclusions.

What does the evidence show comparing 2D software (orthogonal planes- grey scale) vs. orthogonal grey scale -3D virtual colonoscopy?

MacPherson (2007) reports: *"Based upon a small number of studies, there is evidence for the superior efficacy of 3D fly through imaging technology, but the general view is that at present 2D and 3D imaging modalities are complementary"* with 2D images being used to assess the colonic wall and to detect lesions behind folds and with 3D images being used to confirm lesions and helping distinguish folds from polyps. Broadstock (2007) found mixed conclusions from limited studies regarding the superiority of one mode over the other or the optimal combination of 2D and 3D imaging. The mode of imaging may be one of many factors influencing the variability in test accuracy of CTC.

A recent study by van Gelder (2007) found no significant difference in the detection of medium-sized and large polyps between primary 2D and 3D modes. The sensitivity of both modes dropped with decreasing polyp size, and 3D yielded considerably more false positive results, and a correspondingly lower specificity, than 2D potentially triggering more unnecessary colonoscopies. A major cause of false positive findings was the misinterpretation of residual stool. The authors reported a small but statistically significant difference in review times (3D review took approximately two minutes longer than 2D); however, it was unclear whether this difference was clinically significant. The authors concluded that the variation in diagnostic performance found in the literature may be due less to the imaging mode and more likely influenced by reader training, experience, bowel preparation and scan technique. It is clear that further study is needed to more clearly define the optimal mode of CTC in screening populations for CRC.

Vijan (2007) of the VA HSR&D Center for Practice Management and Outcomes Research in Ann Arbor, Michigan examined the cost-effectiveness of 2D and 3D CTC as a screening test for colorectal neoplasia. They used a Markov model of the natural history of CRC and based effectiveness of screening on the diagnostic accuracy of tests in detecting polyps and cancer. They concluded: *"CT colonography is an effective screening test for colorectal neoplasia. However, it is more expensive and generally less effective than optical colonoscopy. CT colonography can be reasonably cost-effective when the diagnostic accuracy of CT colonography is high, as with primary 3-dimensional technology, and if costs are about 60% of those of optical colonoscopy. Overall, CT colonography technology will need to improve its accuracy and reliability to be a cost-effective screening option."*

Arnesen (2007) estimated the cost-effectiveness of CTC in two Danish populations at high risk of colorectal tumors using CTC as the primary examination for detection of colorectal polyps followed by colonoscopy to remove polyps versus colonoscopy alone. CTC images were analyzed as 2D images, using 3D images to confirm or reject findings suggestive of colorectal

neoplasias. The investigators found that cost-effective detection of colorectal polyps ≥ 5 mm by CTC with polypectomy by colonoscopy is possible if carried out by an experienced radiologist in an efficient organization. As with Vijan (2007), the cost-effectiveness mainly depended on the sensitivity of CTC and colonoscopy and on costs associated with equipment depreciation and staffing.

In summary, the evidence does not support the use of CTC in generalized screening protocols for colorectal cancer. There is a growing acceptance for using CTC as a diagnostic tool in symptomatic patients who are unable to undergo complete colonoscopy. Several key issues need to be addressed before incorporating CTC into routine screening protocols, including:

- Defining what constitutes a clinically important polyp regarding size and morphology detected by CTC that will require a follow-up colonoscopy;
- Determining the diagnostic characteristics of CTC in an average risk screening population;
- Determining the appropriate frequency of CTC in a healthy screening population;
- Improving bowel preparation techniques that may increase patient compliance and detection rates;
- Estimating the number of colonoscopies that could be avoided by using CTC;
- Estimating cost-effectiveness.

Evaluations of CTC must be made in the context of a rapidly evolving field in which improvements in colon evaluation are being made. It is likely that the organization of service delivery of CTC in relation to colonoscopy or DCBE for screening polyps will require the greatest consideration.

Ongoing Research: The evidence reviews and results from INAHTA queries cited in this report identified two large trials that should provide valuable information regarding the use of CTC in detecting colorectal polyps and cancer in populations of varying risk. In both cases, recruitment has closed and data analysis has begun.

ACRIN Protocol 6664 The National CT Colonography Trial Main Objective: To clinically validate widespread use of computerized tomographic colongraphy (CTC) in a screening population for the detection of colorectal neoplasia. Study Design Summary: The study addresses aspects of central importance to the clinical application of CTC in several inter-related but independent parts that will be conducted in parallel. In Part I, the clinical performance of the CTC examination will be prospectively compared in a blinded fashion to colonoscopy. In Part II Optimization of the CT Technique will be performed in view of new technological advances in CT technology. In Part III, lesion detection will be optimized by studying the morphologic features of critical lesion types and in the development of a database for computer-assisted diagnosis. In Part IV, patient preferences and cost-effectiveness implications of observed performance outcomes will be evaluated using a predictive model. Participants: Male and female outpatients, aged 50 years or older, scheduled for screening colonoscopy, who have not had a colonoscopy in the past five years. Source: http://www.acrin.org/6664_protocol.html

NHS R and D National Coordinating Centre for Health Technology Assessmemt (NCCHTA). (UK) ISRCTN95152621. Computed tomography (CT) colonography, colonoscopy, or barium enema for diagnosis of colorectal cancer in older symptomatic patients. This trial compares CTC with colonoscopy and barium enema in two parallel, prospective multicentre randomized trials (randomized two to one in favor of the standard test),

with choice of the standard test depending on local factors such as availability and expertise. The detection or exclusion of significant large bowel cancer/polyps will be determined for each of the three tests, including the number and nature of any additional tests required to confidently exclude bowel cancer and the incidence, nature, and significance of incidental disease outside the large bowel detected by CTC. The frequency and nature of procedure-related adverse events will be recorded and psychological effects of each test will be measured using validated questionnaires. Patient specific records of costs and outcomes including influence of having follow-up tests and multiple investigations will be obtained and models developed to compare management plans with outcome cost. We will also use the data collected to populate models that summarize the health effects and costs of these alternative diagnostic approaches in patients of differing ages, risks, and preferences. Source: http://www.controlled-trials.com/ISRCTN95152621/colonography

Table 1. Syntheses of Systematic Reviews of CT Colonography for Detection of Colorectal Cancer Published in 2007

Citation	Inclusion criteria	Selected evidence	Main results
NHSQIS (Macpherson 2007)	• Adult population with positive results from CRC screening test or symptoms suggestive of CRC • Intervention=CTC • Comparator=colono-scopy or DCBE • Outcomes=test performance for detecting polyps, morbidity, mortality, adverse events, acceptability to patients, incremental cost • No language or date restrictions	• 18 HTAs or systematic reviews identified and retrieved;14 met inclusion criteria and quality assessed against a validated checklist • One ACR guideline and two consensus statements included for review	Diagnostic performance for detecting polyps: • The sensitivities with CTC vary greatly within and across polyp size ranges—CTC sensitivity tends to be higher with larger polyps. • Further research on the technique and its standardization, including consensus on diagnostic thresholds, is required. Size of polyp and its clinical significance is still unclear. • Limited evidence suggests a valuable role for CTC in patients where bowel obstructions prevent complete colonoscopic exam. Role for CTC in patients who are elderly, on anticoagulation therapy or where sedation is contraindicated is not supported by evidence. • Limited evidence suggests superior efficacy of 3D fly through imaging technology, but at present 2D and 3D imaging modalities are viewed as complementary. Safety of CTC: • CTC has fewer procedure risks but rare occurrences of bowel perforation have been reported. Radiation exposure is similar to that of DCBE. • CTC requires no sedation and therefore allows quicker return to normal activities. However if a suspicious mass is discovered, a subsequent colonoscopy is then necessary. Patient preferences compared to colonoscopy: • Limited evidence suggests that patients are more accepting of CTC than colonoscopy, and stronger evidence that CTC is more acceptable to patients than DCBE. • Given variation in individual preferences, and the major impact on acceptance of embarrassment relating to the nature of the examination, which is common to all techniques, it is not possible however to clearly differentiate between the approaches. Other findings: • CTC, in contrast to colonoscopy allows the identification of abnormalities outside the colon, however there is insufficient evidence to determine the impact of this aspect of the technique on overall effectiveness. • While a number of economic evaluations of CTC have been undertaken, no information on the cost effectiveness of CTC in a Scottish setting was available from the literature considered. **Conclusions:** "*The review concluded that despite the fairly extensive body of literature on this topic, there is as yet insufficient evidence to inform recommendations on the routine use of CT Colonography as a diagnostic tool in Scotland. The technique does appear to be useful as an alternative approach in particular patient groups in certain circumstances, however consideration would need to be given as to how such use would operate in practice. The manner in which services need to be organized to deliver CTC, in comparison to colonoscopy of DCBE is likely to be at least as significant, if not more so, as diagnostic performance, in making choices between the techniques. Evidence gathering needs to continue in a structured manner. A large RCT currently in progress will contribute UK clinical and cost effectiveness*

Citation	Inclusion criteria	Selected evidence	Main results
			data to the evidence base. Survey work relating to the usage of CT colonography in Scotland, and an economic evaluation based upon Scottish costs and practice could be usefully undertaken."
NZHTA (Broadstock 2007)	• CTC used for screening average risk or high risk patients or for diagnosing disease in symptomatic populations as surveillance or management • Intervention=CTC • Comparator=colonoscopy or DCBE with a valid reference standard • Outcomes=health outcomes, test performance for detecting polyps or CRC, benefits, harms, preferences and patient acceptability • Published from July 2004 to 2007 in English	8 systematic reviews and HTAs included in report as best evidence on topic	Diagnostic performance for detecting polyps: • CTC has reasonable test sensitivity and specificity in the detection of large and medium polyps, but is poorly accurate for small lesions. • Specificity has been consistently high, but sensitivities have varied and pooled statistics should be viewed with caution. • Limited evidence suggests that CTC is highly accurate in the detection of symptomatic cancer. • Limited evidence suggests that CTC is more accurate than air-contrast barium enema for detection polyps and cancers in increased risk or symptomatic patients. • Colonoscopy appears to be more accurate than CTC for both large polyps and smaller polyps, as well as smaller, flat polyps. Safety of CTC: • Relatively safe compared to DCBE and at least as safe as, or safer than, diagnostic colonoscopy. • Relatively low ionizing radiation exposure but a cumulative risk for regular screening. • Very small risk of colonic perforation. Patient preferences compared to colonoscopy: • Findings are inconsistent regarding preferences for and experiences from CTC • Findings from one meta-analysis of CTC in increased risk or symptomatic patients suggest that CTC may be preferred over colonoscopy and preponderance of results favor CTC over colonoscopy regarding pain and discomfort. Other findings: • No studies reporting on overall health outcomes of CTC including efficacy in reducing CRC incidence or mortality. **Conclusions**: *"Limitations of the current evidence base include a lack of evidence about the accuracy of CTC for primary screening in average risk populations. There is also a need for greater investigation of the reasons for such wide variations in test accuracy in different trials with respect to patient and scanner characteristics…the definition of what constitutes a clinically important polyp in size and morphology also requires evidence-based elucidation….Based on the evidence and conclusions considered in this review, CTC is not currently recommended for generalized screening."*

CTC, CT colonography
DCBE, double contrast barium enema

Table 2. Responses from Members of the International Network of Agencies for HTA (INAHTA) for Recent Systematic Reviews and HTAs (as of August 14, 2007)

Agency	Response	Contact
AETMIS (Quebec, Canada)	No	
CADTH (Canada)	We have been asked to look at screening strategies that incorporate CT colonoscopy as a strategy, in anticipation of the results of the American College of Radiologists Imagining Network (ACRIN) randomized trial at the end of the calendar year. Two brief unpublished scoping reports conducted Health Technology Update (May 2007), we also had an article on virtual colonography using magnetic resonance imaging, available: http://www.cadth.ca/index.php/en/hta/reports-publications/health-technology-update/health-tech-update-issue6/magnetic-resonance Virtual colonoscopy was shortlisted for a full assessment by the CADTH Devices & Systems Advisory Committee. Topic refinement has just taken place and the report is expected to be completed by Spring 2008.	Don Husereau [DonH@cadth.ca] Leigh-Ann Topfer [LEIGH-ANNT@CADTH.CA]
CVZ (The Netherlands)	No.	
DACEHTA (Denmark)	DACEHTA published an HTA-report on virtual colonoscopy in 2005 (in Danish with Summary in English at page 9, please find the link.) Nothing new on the topic in 2006 or 2007. http://www.sst.dk/publ/publ2005/CEMTV/CT_kolo_rapport/CTkolo_rapport.pdf	Helga Sigmund [HSI@SST.DK]
DAHTA @ DIMDI	HTA is in progress. Publication slated for fall.	Rüther, Alric, Dr. [Ruether@dimdi.de]
IAHS (Aberdeen, Scotland)	No, but UK HTA Programme commissioned a trial a few years back.	
MSAC (Australia)	Single-centre study available comparing CT colonography vs. colonoscopy in the Australian system (accepted for publication but not yet published)	Brendon Kearney brendon.kearney@imvs.sa.gov.au
NHSQIS (Glasgow, Scotland)	Final draft available. Official release pending as of August 2007.	Karen Macpherson [KAREN.MACPHERSON@NHS.NET]
NZHTA (New Zealand)	Final draft available. Official release pending as of August 2007	Susan Bidwell [susan.bidwell@otago.ac.nz]
UETS (Madrid, Spain)	Final draft available. Official release pending as of August 2007. (In Spanish with English Abstract)	Juan Antonio Blasco Amaro [juan.blascoa@salud.madrid.org]

Table 3. Guidelines and Policy Statements on the Role of CT Colonography in Colorectal Cancer Screening

Note: limited to recommendations published since 2006, in the public domain and in English

Organization /Citation	Recommendation	Comment
Heiken JP, Bree RL, Foley WD, Gay SB, Glick SN, Huprich JE, Levine MS, Ros PR, Rosen MP, Shuman WP, Greene FL, Rockey DC, Expert Panel on Gastrointestinal Imaging. Colorectal cancer screening. [online publication]. Reston (VA): American College of Radiology (ACR); 2006. 7 p. http://www.acr.org/SecondaryMainMenuCategories/quality_safety/app_criteria/pdf/ExpertPanelonGastrointestinalImaging/ColorectalScreeningCa ncerDoc4.aspx	• In average risk and moderate risk populations, "The role of CTC in colorectal cancer screening is still being investigated." • In high risk populations, colonoscopy is preferred. • CTC deemed appropriate following an incomplete colonoscopy regardless of risk level. "Currently, most third-party payers are providing reimbursement for screening CTC only after a failed colonoscopy or in some cases for individuals who have a contraindication to colonoscopy (e.g., those on chronic anticoagulation or with severe chronic lung disease who are at risk for undergoing sedation). Several studies have demonstrated the usefulness of CTC in individuals who have undergone an incomplete colonoscopy or in patients with an occlusive colon carcinoma."	Based on literature review (??systematic) and expert consensus Appropriateness rating scale—proprietary
Institute for Clinical Systems Improvement (ICSI). Colorectal cancer screening. Bloomington (MN): Institute for Clinical Systems Improvement (ICSI); 2006 Jun. 50 p. http://www.icsi.org/colorectal_cancer_screening/colorectal_cancer_screening_5.html	"Currently, CT colonography seems to be a reasonable colonic imaging examination in the following clinical situations: 1) after incomplete screening or diagnostic colonoscopy; 2) in anticoagulated patients who cannot safely discontinue anticoagulation therapy; 3) patients who refuse colonoscopy and understand that their insurance may or may not cover the cost of the CT. If polyps or other pathology is seen on CT colonography this may require further evaluation with colonoscopy. Only some of these indications are reimbursed by Medicare. In many locations, CT colonography is not available and barium enema can be performed in the situations described above."	Based on systematic review, HTA, explicit methods, and expert consensus
National Guideline Clearinghouse (NGC). Guideline synthesis: Screening for colorectal cancer. In: National Guideline Clearinghouse (NGC) [website]. Rockville (MD): 1998 Jun 7 (updated 2007 May). [cited August 15, 2007]. Available: http://www.guideline.gov.http://www.guidelines.gov/Compare/pdf.aspx?file=CRCSCREEN11.inc&out=1	CTC considered but not recommended as a screening option.	Synthesis of multiple guidelines published through 2005. This Synthesis was updated again on May 15, 2007 to withdraw ACS (Amer. Cancer Soc) guidelines following their removal from the NGC Web site.
AETNA Clinical Policy bulletin: Virtual colonoscopy http://www.aetna.com/cpb/medical/data/500_599/0535.html Last review: 11/03/2006	"Aetna considers virtual colonoscopy (also known as three-dimensional computed tomographic (CT) colography, CT colonography) medically necessary for colonic evaluation of symptomatic members with a known colonic obstruction or an incomplete colonoscopy due to obstructive or stenosing colonic lesions. Aetna considers virtual CT colonoscopy experimental and investigational for all other indications, including the screening or diagnosis of colorectal cancer or inflammatory bowel disease in persons without an obstruction or incomplete colonoscopy."	Based on literature review (??systematic), guidelines of other organizations, and expert opinion Next Review: 08/09/2007

END REFERENCES

Systematic reviews included in report

Broadstock M. Computed Tomographic (CT) Colonography for the Detection of Colorectal Cancer—a Technical Brief. June 2007. New Zealand Health Technology Assessment. NZHTA Technical Brief Vol 6 No 6. *Final Draft*

Macpherson K. Computed Tomography (CT) Colonography. HTA Scoping Report. May 2007. NHS Quality Improvement Scotland. *Final Draft*

Primary studies included in report

Arnesen, R. B., B. Ginnerup-Pedersen, et al. (2007). "Cost-effectiveness of computed tomographic colonography: a prospective comparison with colonoscopy." Acta radiological. 48(3): 259-66. PURPOSE: To estimate the cost-effectiveness of detecting colorectal polyps with computed tomographic colonography (CTC) and subsequent polypectomy with primary colonoscopy (CC), using CC as the alternative strategy. MATERIAL AND METHODS: A marginal analysis was performed regarding 103 patients who had had CTC prior to same-day CC at two hospitals, H-I (n = 53) and H-II (n = 50). The patients were randomly chosen from surveillance and symptomatic study populations (148 at H-I and 231 at H-II). Populations, organizations, and procedures were compared. Cost data on time consumption, medication, and minor equipment were collected prospectively, while data on salaries and major equipment were collected retrospectively. The effect was the (previously published) sensitivities of CTC and CC for detection of colorectal polyps > or = 6 mm (H-I, n = 148) or > or = 5 mm (H-II, n = 231). RESULTS: Thirteen patients at each center had at least one colorectal polyp > or = 6 mm or > or = 5 mm. CTC was the cost-effective alternative at H-I (euro187 vs. euro211), while CC was the cost-effective alternative at H-II (euro239 vs. euro192). The cost-effectiveness (costs per finding) mainly depended on the sensitivity of CTC and CC, but the depreciation of equipment and the staff's use of time were highly influential as well. CONCLUSION: Detection of colorectal polyps > or = 6 mm or > or = 5 mm with CTC, followed by polypectomy by CC, can be performed cost-effectively at some institutions with the appropriate hardware and organization.

Leonardou, P., K. Striggaris, et al. (2006). "Screening of patients after colectomy: virtual colonography." Abdominal imaging 31(5): 521-8. BACKGROUND: Virtual colonography is a powerful new method of imaging the entire colon and is useful to assess polyps and diagnose colon cancer. We evaluated virtual colonography in the postoperative screening of patients who had colon cancer. METHODS: Fifty-three patients were examined with virtual colonography 12 to 48 months postoperatively. Forty-four patients had received segmental colectomy with restoration of the gastrointestinal tract, and nine patients underwent abdominoperineal resection and permanent colostomy. After proper cleaning of the colon and distention with air, spiral computed tomographic examination of the abdomen with a slice thickness of 5 mm (table speed [TS] 10 mm, reconstruction interval [RI] 2.5 mm) was performed in the supine and prone positions (including intravenous contrast medium infusion). Images were transferred to a separate workstation (Philips Easy Vision) for postprocessing, three-dimensional rendering, and endoluminal viewing. RESULTS: Eleven recurrences (16.41%) were identified in 10 patients by virtual colonography, but one recurrence was missed. Conventional colonoscopy was incomplete in six cases, and two patients with colostomy refused colonoscopy. In these eight cases (15%), virtual colonoscopy was completed without problems. A second tumor in one patient who had received abdominoperineal resection was demonstrated by virtual colonography, but conventional colonoscopy failed to demonstrate the lesion. Liver metastases were identified in only one patient. CONCLUSIONS: Virtual colonography seems to provide a good alternative in the follow-up of patients after colectomy. The technique is effective in the diagnosis of locoregional recurrences and distant metastases and is well accepted by patients, and results are equal to those of the conventional colonoscopy.

Renkonen-Sinisalo, L., A. Kivisaari, et al. (2007). "Utility of computed tomographic colonography in surveillance for hereditary nonpolyposis colorectal cancer syndrome." Familial Cancer **6**(1): 135-140. Computed tomographic colonography (CTC) is suggested to be an alternative to colonoscopy as a

surveillance tool in subjects with a high risk for colorectal cancer (CRC). To evaluate the utility of CTC we successively examined 78 subjects, all with a DNA mismatch repair gene mutation, by CTC and colonoscopy. We detected altogether 37 polyps or tumors in 28 subjects (prevalence 35.9%), adenomas in 13 subjects (16.7%), CRC in two (2.6%), and hyperplastic polyps in 13 (16.7%). A great majority of the polyps were diminutive. The per-patient sensitivity for detecting all lesions with CTC was 0.25 an d 0.29 by two radiologists and the specificities 0.82 and 0.76. For lesions of 10 mm or larger the sensitivities were 0.6 and 1.0 and the specificities 0.96 by each examiner. Each diagnosed the two cancers correctly. We concluded that CTC has an acceptable accuracy for large lesions in the colon but the detection rate for small polyps is not comparable to that in colonoscopy. Therefore CTC remains a second choice in surveillance for use when colonoscopy for some reason is incomplete or unsuitable.

Reuterskiold, M. H., A. Lasson, et al. (2006). "Diagnostic performance of computed tomography colonography in symptomatic patients and in patients with increased risk for colorectal disease." Acta radiologica 47(9): 888-98. PURPOSE: To evaluate the diagnostic performance (colorectal lesions) of computed tomography (CT) colonography in 111 patients, a majority of whom were at high risk for colorectal neoplasia. MATERIAL AND METHODS: After bowel preparation, CT colonography was performed, immediately followed by conventional colonoscopy. The diagnostic performance of CT colonography was analyzed relative to lesion size, histological diagnosis, and diagnostic certainty. RESULTS: The sensitivity of CT colonography increased with lesion size (P<0.001), and was 91% (21/23) for lesions > or = 10 mm. All 10 carcinomas and 86% (19/22) of adenomas > or = 5 mm were detected. Unconfirmed or false-positive CT findings were generally small and/or reported with low diagnostic certainty. The specificity of CT colonography would be 45% (30/66; 95% CI 34% to 57%) if patients with findings of any size and any diagnostic certainty were selected for follow-up, and 92% (85/92; 95% CI 85% to 96%) if only patients with CT findings > or = 10 mm classified as certain were selected. CONCLUSION: CT colonography had a high sensitivity for lesions > or = 5 mm. The diagnostic performance increased with lesion size and degree of diagnostic certainty, and was higher for adenomas.

Roberts-Thompson, I. C., G. R. Tucker, et al. (2007). "Single-centre study comparing computed tomography (CT) colonography with conventional colonoscopy." in press.

Selcuk, D., K. Demirel, et al. (2006). "Comparison of virtual colonoscopy with conventional colonoscopy in detection of colorectal polyps." The Turkish journal of gastroenterology : the official journal of Turkish Society of Gastroenterology 17(4): 288-93. BACKGROUND/AIMS: To determine the sensitivity and specificity of multidetector computed tomography-based virtual colonoscopy for colorectal polyp detection by using conventional colonoscopy as the reference standard. METHODS: 48 patients with high risk for colorectal cancer underwent virtual colonoscopy followed by conventional colonoscopy. Examination results were compared with conventional colonoscopy, which served as the gold standard. RESULTS: Virtual colonoscopy correctly depicted 19 of 22 polyps (sensitivity, 86%) that were detected in conventional colonoscopy. All 4 polyps that were greater than 10 mm in size (100%), 6 of 7 polyps 6-9 mm in size (85%), and 9 of 11 polyps 5 mm in size or smaller (81%) were correctly depicted with virtual colonoscopy. Virtual colonoscopy had an overall sensitivity of 86% and specificity of 98%. CONCLUSION: Multidetector computed tomography-based virtual colonoscopy has excellent sensitivity for the detection of clinically important colorectal polyps.

Summers, R. M., A. Huang, et al. (2006). "Assessment of polyp and mass histopathology by intravenous contrast-enhanced CT colonography." Academic radiology 13(12): 1490-5. RATIONALE AND OBJECTIVES: We sought to demonstrate that intravenous contrast-enhanced CT colonography (CTC) can distinguish colonic adenomas from carcinomas. METHODS: Supine intravenous contrast-enhanced CTC with colonoscopic and/or surgical correlation was performed on 25 patients with colonic adenomas or carcinomas. Standard deviation of mean polyp CT attenuation was computed and assessed using ANOVA and receiver-operating characteristic analyses. RESULTS: Colonoscopy confirmed 32 polyps or masses 1 to 8 cm in size. The standard deviations of CT attenuation were carcinomas (n = 13; 36 +/- 6 HU; range 28-48 HU) and adenomas (n = 19; 49 +/- 14 HU; range 31-100 HU) (P = 0.005). At a standard deviation threshold of 42 HU, the sensitivity and specificity for classifying a polyp or mass as a carcinoma were 92% and 79%, respectively. The area under the receiver-operating characteristic curve was 0.89 +/- 0.06 (95% confidence interval 0.73-0.96). CONCLUSIONS: Measurement of the standard deviation of CT attenuation on intravenous contrast-enhanced CTC permits histopathologic classification of polyps 1 cm or larger as carcinomas versus adenomas. The presence of ulceration or absence of muscular invasion in carcinomas creates overlap with adenomas, reducing the specificity of carcinoma classification.

Vijan, S., I. Hwang, et al. (2007). "The cost-effectiveness of CT colonography in screening for colorectal neoplasia." The American journal of gastroenterology 102(2): 380-90. BACKGROUND: We examined the cost-effectiveness of 2- and 3-dimensional computerized tomography (CT) colonography as a screening test for colorectal neoplasia. METHODS: We created a Markov model of the natural history of colorectal cancer. Effectiveness of screening was based upon the diagnostic accuracy of tests in detecting polyps and cancer. RESULTS: CT colonography every 5 or 10 yr was effective and cost-effective relative to no screening. Optical colonoscopy dominates 2-dimensional CT colonography done every 5 or 10 yr. Optical colonoscopy is weakly dominant over 3-dimensional CT colonography done every 10 yr. 3-D CT colonography done every 5 yr is more effective than optical colonoscopy every 10 yr, but costs an incremental 156,000 dollars per life-year gained. Sensitivity analyses show that test costs, accuracy, and adherence are critical determinants of incremental cost-effectiveness. 3-D CT colonography every 5 yr is a dominant strategy if optical colonoscopy costs 1.6 times more than CT colonography. However, optical colonoscopy is a dominant strategy if the sensitivity of CT colonography for 1 cm adenomas is 83% or lower. CONCLUSIONS: CT colonography is an effective screening test for colorectal neoplasia. However, it is more expensive and generally less effective than optical colonoscopy. CT colonography can be reasonably cost-effective when the diagnostic accuracy of CT colonography is high, as with primary 3-dimensional technology, and if costs are about 60% of those of optical colonoscopy. Overall, CT colonography technology will need to improve its accuracy and reliability to be a cost-effective screening option.

Van Gelder RE, Florie J, Nio CY, Jensch S, de Jager SW, et al. (2007). "A comparison of primary two- and three-dimensional methods to review CT colonography." European Radiology 17(5): 1181-1192. The aim of our study was to compare primary three-dimensional (3D) and primary two-dimensional (2D) review methods for CT colonography with regard to polyp detection and perceptive errors. CT colonography studies of 77 patients were read twice by three reviewers, first with a primary 3D method and then with a primary 2D method. Mean numbers of true and false positives, patient sensitivity and specificity and perceptive errors were calculated with colonoscopy as a reference standard. A perceptive error was made if a polyp was not detected by all reviewers. Mean sensitivity for large (>=10 mm) polyps for primary 3D and 2D review was 81% (14.7/18) and 70%(12.7/18), respectively (p-values >=0.25). Mean numbers of large false positives for primary 3D and 2D were 8.3 and 5.3, respectively. With primary 3D and 2D review 1 and 6 perceptive errors, respectively, were made in 18 large polyps (p=0.06). For medium-sized (6-9 mm) polyps these values were for primary 3D and 2D, respectively: mean sensitivity: 67%(11.3/17) and 61%(10.3/17; p-values >= 0.45), number of false positives: 33.3 and 15.6, and perceptive errors: 4 and 6 (p=0.53). No significant differences were found in the detection of large and medium-sized polyps between primary 3D and 2D review.

You, Y. T., C. R. Chang Chien, et al. (2006). "Evaluation of contrast-enhanced computed tomographic colonography in detection of local recurrent colorectal cancer." World J Gastroenterol **12**(1): 123-6. AIM: To evaluate the diagnostic accuracy, sensitivity, specificity of contrast-enhanced computed tomographic colonography in detecting local recurrence of colorectal cancer. METHODS: From January 2000 to December 2004, 434 patients after potentially curative resection for invasive colorectal cancer were followed up for a period ranging from 20 to 55 mo. Eighty of the four hundred and thirty-four patients showing strong clinical evidence for recurring colorectal cancer during the last follow-up were enrolled in this study. Each patient underwent contrast-enhanced computed tomographic colonography and colonoscopy on the same day. Any lesions, biopsies, identified during the colonoscopic examination, immediate complications and the duration of the procedure were recorded. The results of contrast-enhanced computed tomographic colonography were evaluated by comparing to those of colonoscopy, surgical finding, and clinical follow-up. RESULTS: Contrast-enhanced computed tomographic colonography had a sensitivity of 100%, a specificity of 83% and an overall accuracy of 94% in detecting local recurrent colorectal cancer. CONCLUSION: Conventional colonoscopy and contrast-enhanced tomographic colonography can complement each other in detecting local recurrence of colorectal cancer.

Bibliography*:
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