peer reviewed **OPINION ARTICLE**

# In the era of CT colonography, is there any role left for barium enema in the investigation of colonic disorders?

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**Abstract**

Several publications that question the continued use of barium enema are reviewed to determine whether there is merit in their argument that barium enema should be abandoned. This opinion paper includes a comparison of barium enema with colonoscopy, and computed tomographic colonography, in terms of patient preference, sensitivity and radiation dose.

## Introduction

Barium has played an important role in gastrointestinal (GIT) radiology since its first reported safe use in medicine in 1910.[1] Barium sulphate has been used for barium enema (BE) examinations for almost 100 years. Technological advances, such as image intensification, brought about major changes in GIT radiology in the early 1960s.[2] Double contrast barium enema (DCBE) gained in popularity compared with single contrast barium enema over the next few decades.[3,4] In the 1970s there was a decline in the number of BE examinations performed; primarily because fibreoptic colonoscopy had gained ground.[2,5] It was suggested in 1990 that the decline of the DCBE could have been as a result of limitations of technique.[6] A decade later Glick's message, in his review of DCBE and other screening alternatives, was that radiologists should accept the challenge by developing the skills necessary to obtain results.[7]

Since the late 1990s several papers have been published questioning the role of barium enema (BE) in radiology. Of importance is the titles of some of these papers: *The end of barium enemas?*[4] *Is there still a role for double-contrast barium enema examination?*[8] *Colon imaging in radiology departments in 2008: goodbye to the routine double contrast barium enema,*[9] and *Colorectal cancer detection: time to abandon barium enema?*[10]

This opinion paper attempts to unpack the reasons for these papers' titles. This is done so that we can consider whether there is any role left for BE/DCBE in the investigation of colonic disorders when compared with computed tomographic colonography (CTC): also known as virtual colonoscopy. Note that most authors use the term barium enema (BE) for double-contrast barium studies.

## Colorectal cancer

Globally colorectal carcinoma (CRC) is the third most common cancer in men and the second in women.[11] It is the second most common cause of cancer deaths in the United States of America (USA). The latest CRC statistics of new cases in the USA is expected to decrease to 136,830 from a previously estimated number of >143,000 in 2012.[12-14] The number of deaths in 2014 is expected to decrease to 50,310 from a previously recorded number of more than 52,000 deaths per year.[12-14] Most colon cancers, apart from inherited genetic disorders, such as hereditary non-polyposis colorectal cancer, arise from a pre-existing polyp which grows slowly over a period of 10-15 years into a cancer.[15,16] CRC was the fourth leading cancer in South Africa in 2007;[17] more recent CRC statistics are not available.

Screening tests should be available to reduce the incidence of CRC and should be:

i. Accurate
ii. Safe
iii. Inexpensive
iv. Widely available
v. Associated with minimal patient discomfort or disability.[18]

Effective screening tests need to demonstrate early-stage disease, and the benefits should outweigh the costs.[19] The tests should also be supported by patients.[19] Given the high incidence of CRC we need to consider several screening approaches for this disease.

CRC screening tests are divided into two categories: indirect and direct.[20,21] Stool-based tests (fecal occult blood test, fecal immunochemical test and fecal DNA test) involve detecting their by-products (blood, DNA). They are cheap and easy to perform. Approximately 50% may be false positive.[20] Their major limitation is that they detect cancer rather than adenomas. Most CRC progress from small adenomas.[19] Direct tests include sigmoidoscopy, DCBE, colonoscopy, and CTC. According to Glick,[7] Medicare in the USA cover (i) fecal occult blood testing, flexible sigmoidoscopy or DCBE for average risk patients, and (ii) DCBE or optical colonoscopy (OC) for high risk patients. Sigmoidoscopy/flexible sigmoidoscopy performed between the ages of 55 to 64 years has been shown to offer a substantial and long-lasting benefit in terms of CRC incidence (33%) and mortality (43%).[22] OC has been used since the early 1970s in the diagnosis of large polyps and CRC. It has grown exponentially and by 2013 more than 18 million OC studies were performed in the USA. In OC there are inherent risks from sedation and potential bowel perforation.[23] Bleeding following polypectomy may occur and may be severe enough to require blood transfusion. Incomplete cleaning and sterilisation of the colonoscope may cause infection, such as hepatitis B and C, and HIV.[24-27] Another risk of OC is that of anesthetic related problems, such as cardio-respiratory problems, especially in older patients.

The American Cancer Society[28] includes both DCBE and CTC for CRC screening tests. On the other hand neither DCBE nor CTC was included as options for CRC screening in a recent study in South Africa.[29] This South African study listed

colonoscopy (once every 10 years); sigmoidoscopy (once every 5 years); and faecal occult blood (yearly). The Cancer Association of South Africa (CANSA) includes DCBE in its list of CRC tests. What is significant is that it recently added the option of virtual colonoscopy (CT colonography) based on 3D imaging every 5 years.[30]

## DCBE and optical colonoscopy

In order to consider the reasons for the above cited publications that question the future of BE in the investigation of colonic disorders we need to compare it with OC. BE has played a role in examination of the colon since the early 1920s. Since the 1970s colonoscopy has become an important diagnostic and therapeutic tool for the examination of the colon. It has been shown to be the more effective post-polypectomy surveillance method compared with DCBE.[5] A large prospective clinical trial showed sensitivity of DCBE to be around 50% for significant polyps >10mm. As a result non-radiologist leaders in the colon cancer screening community increasingly dismiss DCBE as an ineffective and obsolete technique.[4,31] A national polyp study[31] showed that the sensitivity of DCBE for polyps >10mm was 44%. Colonoscopy (OC), as the initial diagnostic study for the detection of CRC, was superior to BE. This level of sensitivity was superior in all segments of the bowel.[31] BE performed no better on the left compared with the right colon. Whether BE was performed by gastrointestinal radiologists or general radiologists made no difference in the sensitivity of the BE for CRC. BE was approximately six times more likely to miss a CRC than colonoscopy performed by a gastroenterologist.[31]

A national survey was undertaken in the USA by Klabunde and colleagues in 2002[32] to determine the activities and beliefs about screening effectiveness and future capacity for screening with DCBE. The aim of the survey was to compare radiologists' (n=312) opinions about CRC screening with those of primary care physicians (n=1718). The sample size was selected to provide point estimates of population proportions within ±3% at a 95% confidence interval. The results were that 75% (n=234) of the radiologists said that DCBE was a very effective CRC screening test. Only 33% (n=566) of primary care physicians shared this opinion.

On the other hand, Glick[7] argues that DCBE does have a role in CRC screening, provided radiologists accept the challenge by developing the skills necessary to obtain results. Continued use of DCBE for detecting colorectal polyps has become an area of increasing controversy.

A retrospective study examined the use and yield of DCBE for colorectal polyp detection.[33] The findings of 244 DCBE reports were correlated with OC reports performed within 12 months before or after a DCBE. The main indication to perform a DCBE was to complete a failed, incomplete, or inconclusive colonoscopy (109/244 or 45%). Only 14 of the DCBE reports (14/244 or 5.7%) gave positive reports for polyps. Of the 14 polyps reported, five were shown to be false-positive at a later colonoscopy. DCBE is a low-yield procedure for detecting polyps, with a high false-positive rate, and is not likely to be performed by experienced practitioners in the future. Sensitivity of DCBE for advanced adenoma (i.e >10mm in size) is only 50% hence the examination has been dismissed by leaders in the colon cancer screening community as an inefficient and bygone technique.[33]

Radiology training also has a large part to play in the slow demise of BE. Younger radiologists are less trained with performance and interpretation of DCBE. In a study of colonoscopy and DCBE for surveillance after polypectomy the results showed that the colonoscopic examination was a more effective surveillance method than DCBE.[5]

## CTC

There has been a downward trend of DCBE, as an imaging screening tool, which was hastened by the introduction CTC.[8] There are two critical components to achieve a successful CTC: an adequately cleansed bowel and good distention of the colon with $CO_2$.[16] Tagging agents, such as 250mls of 2.1% w/v Readi-Cat and 60mls diatrizoate (gastrografin), are used. Tagging is an integral part of bowel preparation: barium tags the stool and the gastrografin tags the residual fluid.[16] Barium does not adhere to the colonic wall; it coats the surfaces of polyps making them more conspicuous and easier to diagnose.[34,35] This may reduce the false-positive rate on CTC. Gastrografin has a dual action. It stains the residual fluid white, thus aiding in 2D evaluation of submerged polyps as well as emulsifying the stool adherent to the bowel wall thus causing a secondary catharsis.[34]

The clinical usefulness of CTC for screening/surveillance of the general population for CRC has been well addressed in the literature.[36,37] CTC has been included in the guidelines for several countries. The Joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology[38] and Korean guidelines.[39] Since 2008 CTC has been able to stand alongside OC as the test most suited to both prevent and detect CRC.[8]

## CTC compared with OC and DCBE

A 2001 study of 300 patients, who underwent CTC, followed by standard colonoscopy for the detection of colorectal neoplasia, showed the overall sensitivity of CTC to be (i) 90% for polyps 10 mm or larger, (ii) 82% for adenomas 5.0-9.9mm, and (iii) 66.9% for adenomas <5mm.[40]

An important advantage of CTC, when comparing it with OC, is its ability to visualise the intra-abdominal and pelvic organs (Figures 1a to d). The majority of findings will ultimately prove to be of little or no clinical significance.[41,42] However, in approximately 10% of cases significant pathology may be identified, such as early cancers of the kidney and ovary as well as abdominal or pelvic lymphadenopathy in underlying lymphoma. Abdominal aortic aneurysms >5cm in transverse diameter may be detected incidentally.[41,42] Visualisation of such pathology is not possible with OC, or a DCBE.[16] CTC is less invasive with minimal complications.[43]

In OC there are inherent risks from sedation and potential bowel perforation.[23] CTC is a much safer study than OC as no sedation is required and the risk of perforation is significantly less with only sporadic cases of perforation being recorded.[19,44] The majority of the reported cases of colonic perforations associated with CTC had underlying colonic lesions including inflammatory and/or obstructive lesions.[45] Certain precautions are recommended to maintain a low perforation rate: (i) the use of a soft rubber catheter as opposed to the large plastic barium enema tube, (ii) constant infusion of $CO_2$ under monitored pressure, and (iii) not performing the study after a recent full thickness biopsy.[44]

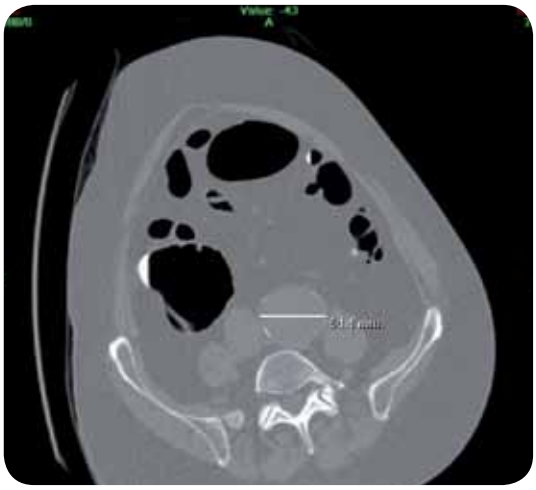

**Figure 1a.** Aneurysm (54.4mm) left iliac artery.

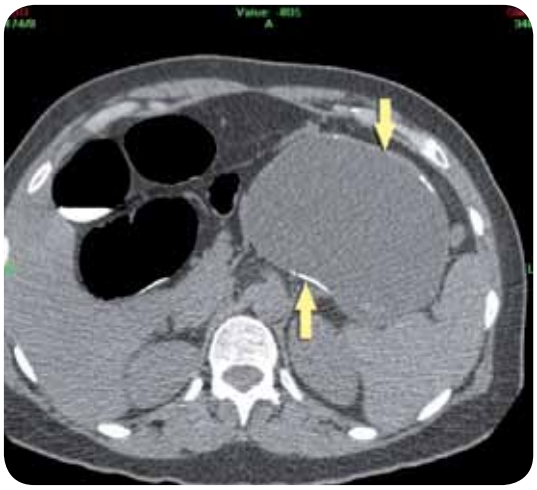

**Figure 1b.** Pancreatic tumour.

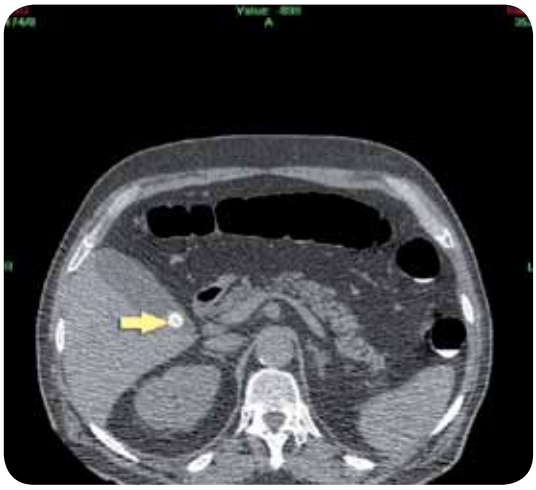

**Figure 1c.** Calcified gall stone.

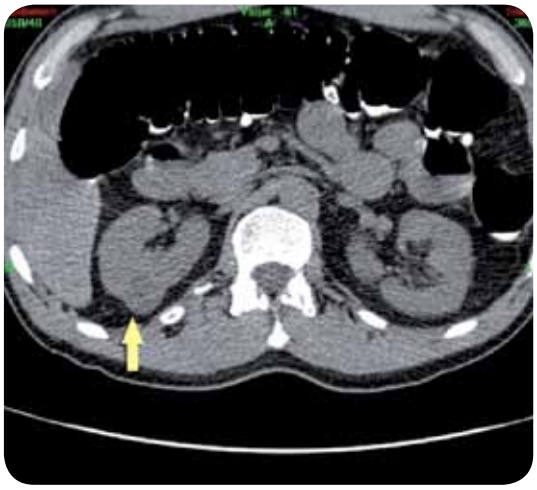

**Figure 1d.** Extracolonic pathology of an early cancer of the right kidney (yellow arrow showing the slight bulge).

A fairly recent study shows the sensitivity of DCBE at around 50% for polyps >10mm[46] whereas for CTC it is 97% for polyps >10mm.[47] According to Yee *et al*[40] the sensitivity of DCBE in retrospective studies for CRC ranged from 71% to 95%. Whereas in prospective studies DCBE sensitivity was reported to be as low as 50%-75% in asymptomatic patients with positive faecal occult blood results.[40]

A comparative study[5] of DCBE and colonoscopy of 973 patients was undertaken as part of the national polyp study in the USA for surveillance of patients with newly diagnosed adenomatous polyps. Although BE was performed first, the endoscopists did not know the results. The study permitted a direct blinded comparison of colonoscopic examination with BE without interfering with complete colonoscopy in each patient. The DCBE findings were positive in 222 (26%) of the paired examinations. The proportion of DCBE examinations, in which adenomatous polyps were detected, was significantly related to polyp size. Nineteen additional polyps, 12 of which were adenomas, were detected on colonoscopy re-examination done in the same location of 139 cases with positive results on DCBE but negative on colonoscopy. The study showed that colonoscopy is a more effective method of surveillance than DCBE. The latter was found to have a poor detection rate of 48% for polyps 10 mm or larger; for adenomas its detection rate was 39%.[5]

A study[48] of 276 DCBE radiology and pathology reports were reviewed to determine the number of patients who had polypoid lesions 10mm or larger, polyps <10mm, or advanced neoplastic lesions of any size. DCBE performed in average-risk adults older than 50 years had a diagnostic yield of 5.1% for neoplastic lesions 10mm or larger and 6.2% for advanced neoplastic lesions, regardless of size.[48]

## CTC: imaging of polyps

Data of the national polyp study in the USA highlight the adenoma-carcinoma sequence.[19] On average it takes 10 to 15 years for most small adenomas <5mm to develop genetic alterations to become cancer. The sequence is: small → large ones >10mm → noninvasive carcinoma → invasive carcinoma.[19] The greatest diameter of sessile or flat polyps is measured (Figure 2).[49] The greatest diameter of the head of a pedunculated polyp is measured: the stalk is not measured (Figure 3).[16]

Most experts would agree that large polyps (>10mm) detected at CTC screening warrant polypectomy. Diminutive polyps (5mm or less in size) do not appear to be a compelling reason for colonoscopy and polypectomy (Figure 4).[50] Ransohoff[51]

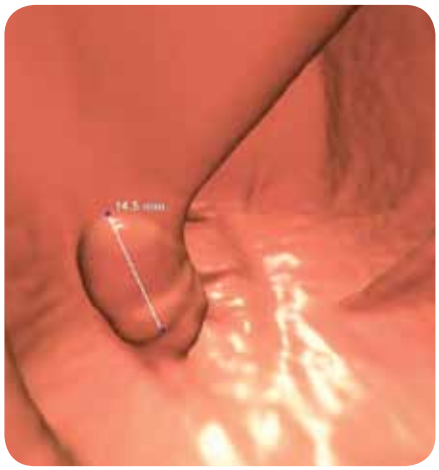


**Figure 2.** Sessile polyp (14.5mm) on the anterior colon fold (>10mm = advanced adenoma).

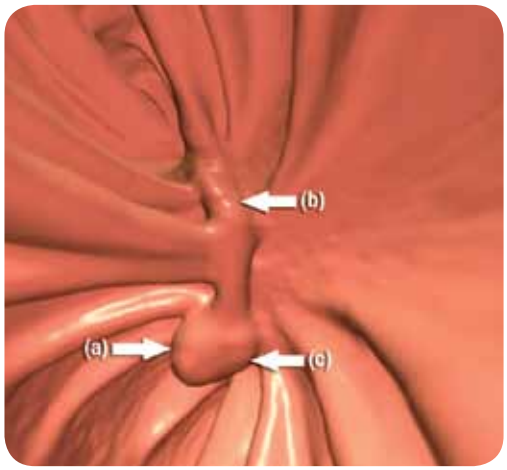


**Figure 3.** Pendunculated polyp on a long stalk, (a & c) head and (b) stalk.

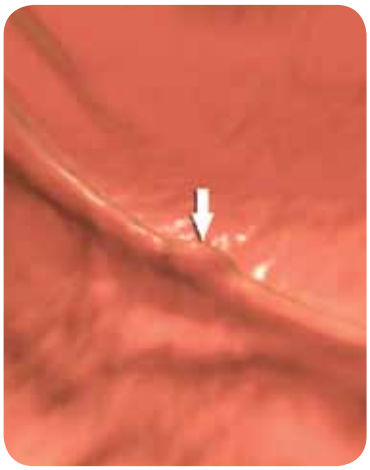

**Figure 4.** Diminutive polyp on haustral fold.

added that a near-term death threat does not apply for the overwhelming majority of diminutive lesions. Most gastroenterologists are of the opinion that 6-9mm polyps should be removed at the time of colonoscopy. Other studies have shown the benign indolent nature of sub-centimeter colorectal polyps. No study to date has shown that leaving 6-9mm polyps is a harmful practice.[52,53] Hofstad and colleagues[54] performed serial colonoscopy on unresected sub-centimeter polyps. After three year follow-up, most polyps remained stable or regressed in size. Their findings underscore the safe practice of leaving unresected 5-9mm polyps for this time span.

According to Bond[55] in view of a large volume of scientific data, clinicians should move their approach, from simply finding and harvesting all diminutive colorectal adenomas, toward strategies that allow reliable detection of much less common, but dangerous advanced ones.

Classification of polyp sizes: diminutive (≤5mm), small (6-9mm), and advanced adenomas (≥10mm). One third of diminutive polyps are adenomas; the rest are non-adenomas (e.g. muscle tags and hyperplastic polyps). One third of small polyps are non-adenomas; the balance are adenomas. Advanced adenomas, regardless of size, harbor (i) a significant villous component >25%, and (ii) high grade dysplasia. As a polyp increases in size the ratio of adenomas to non-adenomas reverses. Lesion size is widely accepted as the single most important determinant of clinical significance.[49,55] Larger lesions are usually more glandular and more often show advanced histology: they represent the vast majority of life-threatening cancers.[52,53] Figures 5a and 5b depict colon cancer.

Prevalence of polyps: large (≥10mm) 6%; small (6-9mm) 8%. Approximately 50% of adults older than 50 years may harbor at least one colorectal polyp.[56] More recent studies show a prevalence range of 14% as an approximate average of polyps ≥6mm.[52,53]

## Radiation dose: CTC and DCBE

Early studies of single-section CT scanner indicated an effective dose of 18mSv from a high mAs protocol. The effective dose of CTC in a 2002[56] study that compared it with colonoscopy was reported to be 5.0 mSv for men, and 7.8mSv for women in a two view examination. The detection of 10mm or > polyps was >90% when an effective value of 50mAs was used. Studies using a 4 slice CT scanner, 10mAs, and 140kVp showed 100% sensitivity for polpys >10mm. The resultant effective dose was 1.8mSv for men, and 2.4mSv for women.[57]

CT manufacturers have taken heed of increasing concerns about radiation dose. They have developed radiation reduction tools, such as automated tube current modulation, automated tube potential, and iterative reconstruction, in the latest generation scanners.[58] With the introduction of tube current modulation, protocols can now concentrate on setting an appropriate noise level to minimise dose. A tube current modulation system is used (Smart mA, GE Healthcare) whereby the noise level is set at 30 for the supine study and 50 for the prone study and the tube current range at 30 to 300mA[16]. This has yielded a 40% reduction of dose in the prone position with minimal degradation of 3D and 2D images. For MDCT scanners not equipped with a tube current modulation system, a technique with a tube current-time product in the range of 50-75mAs usually suffices.[59] A tube current-time is set between 50-75mAs for those machines that are not equipped with a tube current modulation system. These protocols result in a median effective dose of 4.5mSv for both supine and prone studies: CTC is a low dose examination.[60]

The results of a recent evaluation of barium enema and CTC were as follows.[61] Maximum local skin doses in DCBE were less than 100mGy despite relatively long average fluoroscopy times of 8 minutes; organ doses ranged from 9-26mGy in the abdomen. The effective dose of 10.7mSv for analogue radiography decreased by 12% when digital radiography was used, even though more than 80% of the dose was due to fluoroscopy. Organ doses, within the primary X-ray beam, were between 30mGy and 44mGy for paired scans in routine CTC: a relatively high mean effective mAs of 119 was used for the accurate detection of colorectal cancer and extra colonic lesions. In a low-dose set-up with an effective mAs of 27, the doses were approximately 10mGy. The comparative effective doses were: routine CT colonography (23mSv), low-dose CT colonography (5.7mSv), and analogue DCBE (10.7mSv).[61] In other words CTC performed with a low dose technique has a lower radiation dose compared with that of DCBE.

## CTC options

CTC plays a role in examination of the colon of patients who are clinically unsuited to undergo colonoscopy: severe

cardiac or pulmonary disease, amongst others. For example, a 68-year old male patient recently underwent a low-dose CTC because of his comorbidities of hypertension, ischaemic heart disease, diabetes and chronic obstructive airways disease. OC was thus contraindicated.[62] A Spigelian hernia was demonstrated on 2D and 3D CTC images ( Figures 6a &b).

CTC is indicated after an incomplete colonoscopy examination or evaluation of the colon proximal to an obstructing neoplasm.[19]

CTC has been proven to be a safe, minimally invasive procedure for CRC screening of asymptomatic patients.[36,63]

## Patient preferences

Gluecker *et al*[64] undertook two studies of 696 asymptomatic patients to determine their preferences in terms of CTC, colonoscopy, and DCBE. Group 1 underwent both CT colonography and colonoscopy. Group 2 underwent both CTC and DCBE. Overall, patients preferred CT colonography to colonoscopy (group 1, 72.3% vs 5.1%; $P < .001$) or to DCBE (group 2, 97.0% vs 0.4%; $P < .001$). Patients undergoing CRC screening preferred CT colonography to both colonoscopy and DCBE. The majority of patients experienced discomfort and inconvenience with cathartic bowel preparation.

The results of a multicenter randomised trial of CTC versus BE for diagnosis of CRC or large polyps were: patients experienced more physical discomfort with BE, as well as post-test cramps, soreness, nausea, soiling, and wind.[65,66]

## Concluding remarks

CTC in CRC has two roles: present and potential[66]. Its present role is to be integrated into screening programmes as a replacement of BE in the case of incomplete colonoscopy. Its potential role is to be used as a first-line screening method, together with indirect tests and the direct test of colonoscopy.[67] There are several papers that question the continued used of BE in the investigation of colonic disorders.[4,9,10,19]

In screening tests, cancer is not the prime target: it is the detection and removal of advanced adenomas.[9] BE does not compete with 90% sensitivity for significant adenomas of both OC and CTC. Advanced adenomas are the key targets in cancer prevention. It is hard to justify continuing with routine DCBE in hospital (clinical) practice. CTC is more accurate, preferred by patients, has fewer complications, shorter room time, lower radiation exposure, and shows significant extracolonic lesions in 5-10% of cases.[16,41,61,62,68]

It is beginning to seem rather irresponsible to continue to offer routine DCBE examinations.[9] The performance of DCBE is inadequate for the exclusion of CRC.

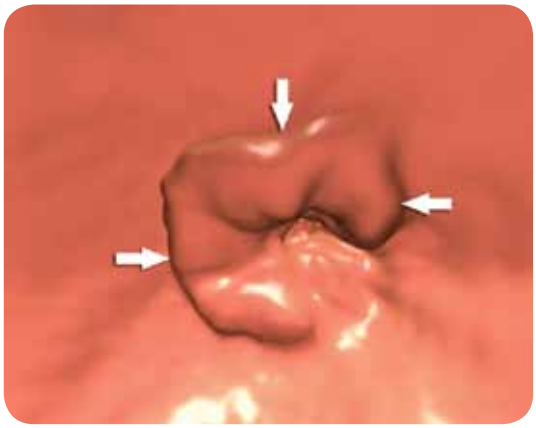

**Figure 5a.** Sigmoid colon cancer.

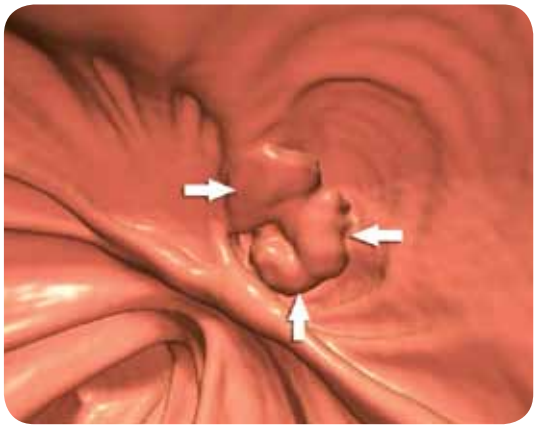

**Figure 5b.** Large fungating cecal pole mass.

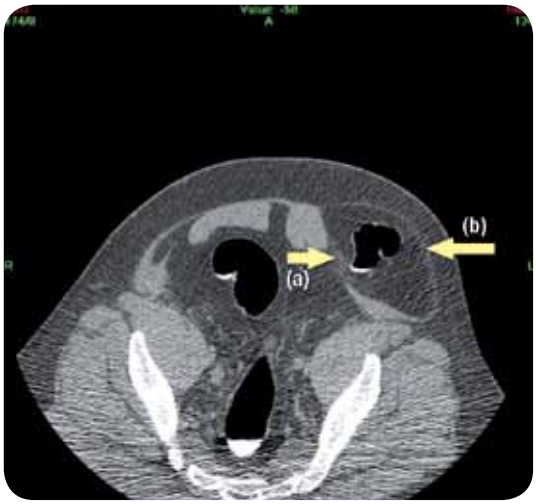


**Figure 6a.** Spigelian hernia; (a) site of muscular defect; (b) the rim of the external oblique muscle.

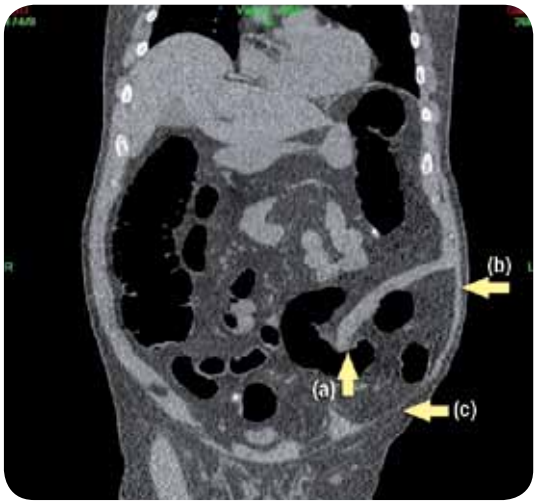


**Figure 6b.** Coronal 2D of Spigelian hernia through the muscular defect; (a) site of muscular defect; (b) external oblique muscle; (c) marked thinning of external oblique muscle.

As such it should now be abandoned as a first line test in patients at risk of CRC: its place to be taken by CTC.[10] The British Society of Gastrointestinal and Abdominal Radiology (BSGAR) and The Royal College of Radiologists (RCR) state in their September 2014 publication that the number of CTC examinations in England has increased, having now replaced BE as the alternative imaging of choice when an OC is incomplete or the patient is considered unsuitable for OC.[69] DCBE has been entirely abandoned in some institutions in the UK: OC or CTC are used instead[69]. An example being the Addenbrooke Hospital in Cambridge.[10] In August 2014 the author personally ascertained that the Royal Free Hospital in London no longer performs DCBE examinations.

We need to question the ethics of performing BE in the investigation of colonic disorders in terms of its low sensitivity and effective radiation dose using fluoroscopy and radiography. CTC of twenty asymptomatic individuals (M:F = 10:10) participating in a CRC screening programme and DCBE of fifteen patients (M:F = 6:9) were evaluated.[70] Effective dose at CTC was 2.17 ± 0.12mSv, with good and excellent image quality in 14/20 (70%) and 6/20 cases (30%), respectively. With DCBE, effective patient dose was 4.12 ± 0.17mSv: 1.9 times greater than CTC ($P < 0.0001$).

The International Commission of Radiological Protection's system of radiation protection is based on three fundamental principles: justification, optimisation and dose limitation.[71] We need to critically consider the role of BE in the investigation of colon disorders in terms of these three principles.

Hong and Park[45] recommend CTC should be used to evaluate the colon proximal to an occlusive cancer either before or after surgical intervention of metallic stent placement. They state that in view of their findings, and despite BE's historical use to evaluate such cancers, it has low sensitivity even in the absence of an occlusive cancer. Barium is also associated with a risk of barium desiccation in the colon proximal to an obstructing cancer.[45]

In a multicenter randomised study, undertaken in England, on symptomatic patients for diagnosis of polyps and CRC the findings were that CTC detected more polyps and cancer than DCBE.[65] This led the researchers to recommend that CTC should replace DCBE as the preferred radiological test for patients with symptoms suggestive of CRC. In light of the evidence of the multicenter studies[65,66], BSGAR and the RCR state in their document that BE can no longer be supported as a suitable radiological investigation for patients with symptoms suspicious for CRC.[69] They concede that performing a CTC adds to an already burdened radiology workload. Hence, in many UK centers, radiographers are responsible for patient pre-assessment, informed consent, and performing CTC examinations; those who have received training make a preliminary reading of the images.[69]

In some countries in Europe radiographers are interpreting CTC images.[72,73]

Mensah *et al*,[74] in their retrospective Ghanaian study, conclude that in poorly resourced countries, where access to OC and CT services is limited or non-existent, BE can play a role in evaluation of patients with colorectal symptoms. They are of the opinion that BE is useful in demonstrating diverticular disease and malignant lesions, especially when CT services are not available. They support the literature that BE does not have a role to play in screening for polyps.

We need to critique BE in terms of screening test criteria: demonstration of early-stage disease; the benefits should outweigh the costs; the tests should also be supported by patients.[19] Accuracy of tests is vital. BE fails to meet these criteria in terms of the literature published over the past 14 years. According to Halligan *et al*[65] the results of their multicenter trial underscore that CTC should now replace DCBE as the preferred radiological test for patient with symptoms suggestive of CRC.

Finally, Stevenson[9] maintains it is hard to justify offering routine DCBE in clinical practice. Training residents (registrars) in DCBE should be phased out. More importantly CTC should be the required component in training programmes.[9]

It is time to heed the clarion call: abandon barium enema as it is an obsolete technique for investigations of colonic disorders.

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