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## LEARNING OBJECTIVES

Upon completion of this activity, participants should be able to:

- Describe the pathophysiology and epidemiology of colorectal cancer (CRC)
- Explain the preparation for CTC and how it is performed
- Compare the performances of CTC with optical colonoscopy and double-contrast barium enema
- Understand indications for the various CRC screening tests

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Drs. Hock, Ouhadi, and Materne have no significant financial arrangement or affiliation with any manufacturer of any pharmaceutical or medical device and are not affiliated in any manner with any provider of any commercial medical or healthcare professional service.

## Advances in CT Colonography

By Dr. Danielle Hock, R. Ouhadi, M.D., and R. Materne, M.D.

**C**olorectal cancer (CRC) is the second leading cause of cancer-related deaths worldwide. Its incidence spikes in industrialized countries and is continuously rising.

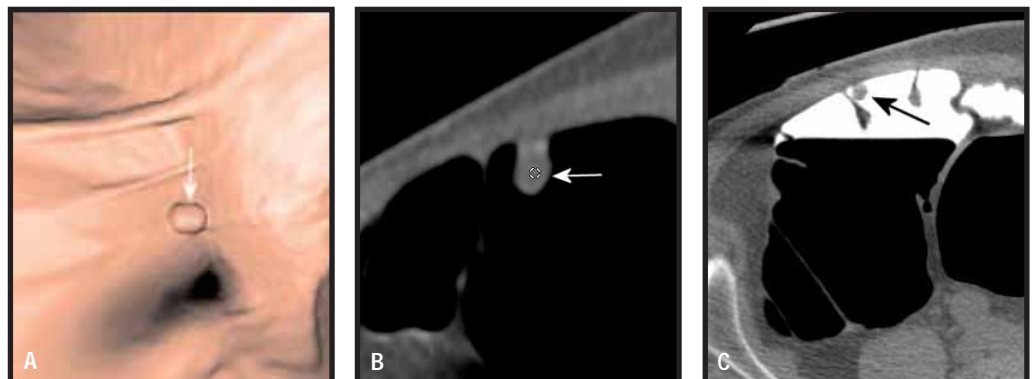
Computed tomography colonography (CTC) was first devised some 12 years ago but remained “experimental” for several years. At about the same time, optical colonoscopy (OC) came to be preferred over double-contrast barium enema (DCBE).

In 2001, Yee et al<sup>1</sup> proved CTC to be highly effective in diagnosing significant lesions. Publication of this study immediately gave rise to great enthusiasm and expectations in the radiological world. CTC became “worth try-

ing” and a favored topic for publication.

Before the end of 2003, Pickhardt et al<sup>2</sup> demonstrated for the first time better performance for CTC than for optical colonoscopy in diagnosing 8 mm and 10 mm adenomatous polyps. Moreover, in his series of 1231 patients, two polyps were malignant, one of them missed by optical colonoscopy.

This was a true revolution and probably the real beginning of widespread use of CTC, coinciding with the large diffusion of multislice CT and dedicated software. Now workshops are organized specifically so that radiologists can gather sufficient theoretical and practical formation to start their own practices.



Sessile polyp. A: Endoluminal view, supine position. B: Axial slice, supine position. C: Axial slice, prone position: the polyp is drowned in the tagged residual fluid, but nevertheless easily visible.

**PATHOPHYSIOLOGY OF CRC**

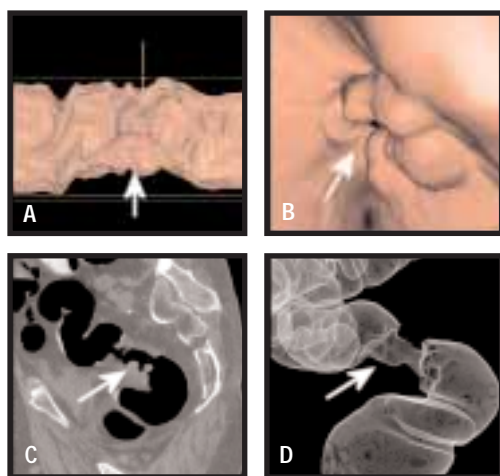
Polyps are common findings in the colon. They are found in 10% to 12.5% of the population and their incidence rises dramatically with age: They become frequent after 50. Seventy percent of the polyps smaller than 5 mm and 50% of those between 5 mm and 9 mm are hyperplastic (always benign). Some polyps are adenomas and a few of them will act as precursors to colorectal carcinoma. It generally takes 10 years for an adenoma to become an adenocarcinoma.

Actually, 3% of all adenomas and 1% of adenomas smaller than 10 mm will become

tous colonic polyps and for their first-degree relatives (immediate family), as well as for patients with inflammatory colitis after 10 years of evolution. This high-risk population represents 15% of all CRCs.

The risk may even rise to 90% for patients who may develop an autosomal dominant hereditary disease such as familial adenomatous polyposis (FAP) or hereditary nonpolyposis colon cancer (HNPCC): this very high risk population represents 4% to 6% of all CRCs.

CRC has a very insidious onset, presenting with change in bowel habit, weight loss, or bleeding.



*Sigmoid colon tumor. A: Auto-dissection: mass disturbing the regular pattern of haustral folds. B: Endoluminal view of the neoplastic stenosis. C: Oblique MPR, displaying the full length of the tumor. D: Air-contrast colic spot-view, demonstrating the tumor aspect and precise location (DCBE-like view).*

malignant. The probability that a given polyp is an adenoma, that when discovered it harbors a cancer, or that it will become a cancer 10 years later, is proportional to its size: Adenomas 10 mm and larger pose a higher risk than do smaller polyps.

The neoplastic process is different in long-standing inflammatory bowel diseases where there is a sequence of inflammation leading to dysplasia leading to carcinoma, making “blind” biopsy surveillance mandatory.

How often carcinomas develop in normal mucosa is unknown (20%?).

**RISK AND SYMPTOMS**

The risk of developing a CRC before age 75 for someone with no personal or family history of the condition is 4%. Eighty percent of all CRCs will occur in this “average risk” population.

This risk rises to 10% for patients with a personal history of cancer or adenoma-

**HOW IS CTC PERFORMED?**

*The principle.* CTC is not a new radiological study of the colon, as it does not allow fine analysis of the colonic mucosa. It is rather a true screening tool for common CRC.

CTC is an outpatient procedure that requires no sedation or analgesia and is faster to perform than optical colonoscopy, as it takes hardly more than 10 minutes. It is, in fact, the study of the colonic lumen to detect nodules and masses of varying sizes corresponding to polyps and protruding tumors.

As with optical colonoscopy or DCBE, the colon has to be freed of its fecal content and inflated to make this possible. A CT scan is then performed and the native thin axial slices will be reprocessed by dedicated software to create an endoluminal reconstruction.

*Colonic cleansing.* The extent to which the colon has to be cleared of fecal residue depends on the size of the target lesion or the radiologist’s reading habits. Means will depend on the patient’s condition.

It is common sense that a good prep facilitates interpretation and helps the radiologist distinguish between the various types of filling defects. Cathartic cleansing with a clear liquid diet such as a sodium phosphate composition (Phospho-soda, Fleet) or a magnesium citrate oral solution (Picolax, Ferring) at 4 p.m., and four bisacodyl tablets (Dulcolax, Boehringer Ingelheim) at 8 p.m. the day prior to the CTC is the most commonly used preparation protocol.

In frail patients or in cases where sodium phosphate is contraindicated, such as congestive heart failure, renal insufficiency, or uncontrolled hypertension, this preparation may be replaced by two days of low-residue diet combined with bi-

sacodyl or even a polyethylene glycol electrolyte solution (Golytely, Braintree Laboratories).

Residual fluid is unavoidable and problematic as its density is approximately the same as the colonic wall and it will thus obscure possible lesions on the dependent surface.

To reduce fluid quantities, a “dry” colonic prep (Phospho-soda) is preferred over the “wet” one (Golytely) currently used by gastroenterologists. For the same reason, a bisacodyl suppository is usually inserted one to two hours before the CTC as it will trigger an expelling bowel movement, thus helping to evacuate some of the remaining fluid.

To minimize its “masking” effect, the residual fluid is often rendered opaque through ingestion of 100 ml of Gastrografin the evening before a procedure. This solution will not only help visualization of possible polyps through the residual fluid in a 2D reading, but it also has a laxative effect.

Finally, residual feces may also be tagged by ingestion of 250 ml of diluted barium (2.1%) at 6 p.m. the day before the CTC. Since bowel cleansing is the most unpleasant and inconvenient aspect of colonic examination, several attempts to reduce or eliminate the need for cathartic drugs are under way. These preparations allow only 2D reading but have proved to be highly effective in the diagnosis of significant lesions.<sup>3</sup>

*Colonic distension.* The colon may be distended using either air, by manual squeeze-bulb insufflation, or with CO<sub>2</sub>, thanks to an automated device that can achieve a constant and persistent insufflation.

The difference lies not in the quality of colonic distension, which is approximately the same, with a slightly but not significantly better distension for CO<sub>2</sub>,<sup>4</sup> but in patient comfort. CO<sub>2</sub> is absorbed through the colonic mucosa and excreted through the lungs, thereby preventing postexam cramping. Indeed, two minutes after the end of the colon exam, half of the CO<sub>2</sub> has been resorbed. This results in better patient compliance with CO<sub>2</sub><sup>5</sup> as the study is more comfortable with fewer symptoms of abdominal pain and bloating.

*Technical data.* Thin slices are mandatory for accurate detection of small lesions. A review of current practices in virtual colonoscopy found 88% agreement on a maximum tolerated width of 3 mm.<sup>6</sup> Since the wide acceptance of multislice CT, most radiologists use overlapping 1.5 mm axial slices.

Two acquisitions are taken (in prone and supine positions or, for frail patients, in supine and right lateral positions) in order to mobilize the residual fluid and to allow study of the complete colonic circumference. This rotation of the patient will also move any residual feces to the opposite wall, thus helping to differentiate it from polyps.

A major limitation of CTC that prevents it from being used in screening programs for patients at risk for carcinoma is its high radiation exposure. The mandatory double acquisitions,<sup>7</sup> higher radiation dose delivered by multislice CT compared to single-slice,<sup>8</sup> and narrow slice collimation are all factors in this high exposure.<sup>9</sup> In an attempt to reduce the dose, CT manufacturers offer devices for automatic tube-current modulation, which can reduce the dose by 32% to 35% with no statistical difference in image noise.

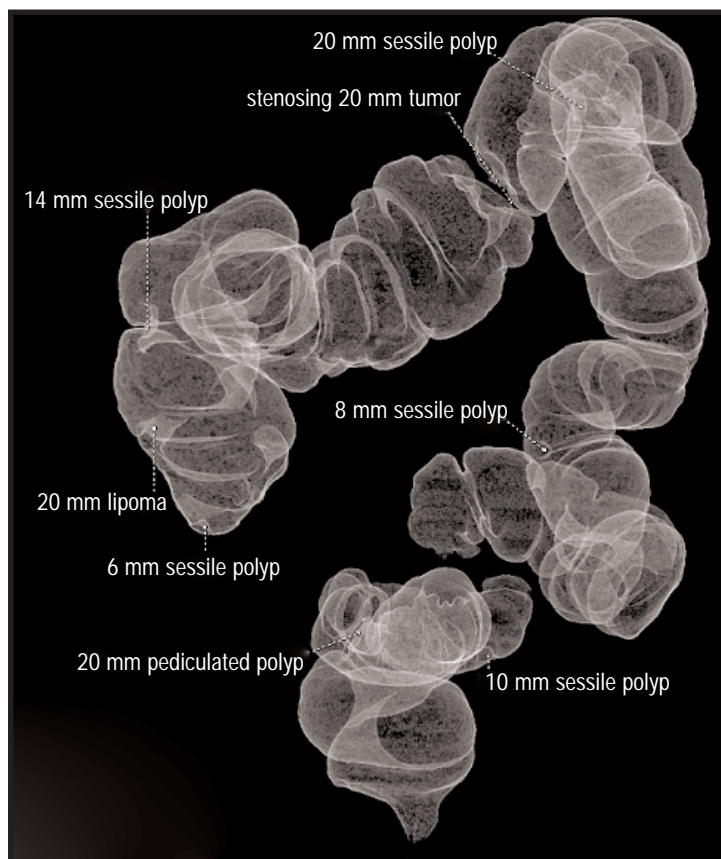
There is also a trend toward using ultralow-dose protocols, which do not interfere with the diagnosis of tumors and polyps, even small ones, but provide a poor assessment of low-contrast structures so that extra-colonic findings become illusory. Also, imaging of obese patients might be unfeasible.

**IV contrast.** No IV contrast agent is needed for the detection of polyps or tumors as there is a spontaneous contrast between gas and colonic wall. Even small polyps, which could be drowned in residual fluid, will be recognized thanks to the Gastrografin fluid tagging and the dual patient positioning.

IV contrast is indicated only for patients with an obstructing carcinoma, for detection of eventual synchronous lesions, and in surveillance of patients who have had previous CRC surgery.

**Postprocessing.** Dedicated software reconstructs endoluminal views, which will be used for “fly-through” (visual inspection of the colonic lumen, both forward and backward) and for better understanding of complicated folds.

Some radiologists are 2D readers: they scroll through the axial slices to detect potential lesions and use 3D images for problem-solving. Others are 3D readers, using



DCBE-like view, displaying size and location of the numerous polyps and transverse colon tumor: helpful for planning the endoscopic and surgical resections.

endoluminal views to spot lesions, but making a diagnosis by axial slice analysis.

#### WHAT ABOUT CTC PERFORMANCE?

CTC can be compared only with optical colonoscopy and DCBE, as these are the only screening tests providing a full study of the colon.

Available research offers widely varying results. The best results were achieved by a study conducted by Pickhardt et al,<sup>2</sup> under state-of-the-art conditions, comparing CTC and OC with segmental unblinding. For CTC this study demonstrated a sensitivity per polyp of 92.2%, a sensitivity per patient of 93.8%, and a specificity per patient of 96%. These results were superior to those achieved by OC.

One of the worst results was obtained by Cotton,<sup>10</sup> who found a CTC sensitivity per patient of 39% and 55% respectively for polyps greater than 6 mm and greater than 10 mm, while OC reached a sensitivity of 99% and 100%, respectively. These disappointing results can be explained by an outdated technology (5 mm collimation), the poor performance of the reading

software, inadequate quality control, and the inexperience of the readers.

A more objective approach is offered by several meta-analyses<sup>11-13</sup> based on strict scientific criteria and taking into account only studies in fully eligible publications.

They showed a high sensitivity (70% to 92.5%) for clinically significant polyps (larger than 6 mm), poor results (48% to 65%) for small lesions (less than 5 mm), and high specificity (86% to 97.4%) even for small polyps and variability of results due to differences in reader experience.

In 2004, Johnson et al<sup>14</sup> compared the relative performances of DCBE and CTC for the diagnosis of polyps between 5 mm and 9 mm and larger than 10 mm and demonstrated sensitivities of 45% and 44%, respectively, for DCBE, and of 81% and 72%, respectively, for CTC. In 2005, Rockey et al<sup>15</sup> published another study also

concluding that CTC was superior to DCBE.

It may thus be concluded that CTC is a reliable screening tool in experienced hands and is certainly at least the second best test after OC.

#### EXTRA-COLONIC FINDINGS

An important issue for CTC, except when using ultralow-dose protocols (10 mAs), is the possibility of detecting extra-colonic abnormalities. This is, of course, impossible for OC. These findings may be minor (of little or no importance), moderate (needing verification of patient history or clinical, radiological, or other follow-up), or major (of vital significance, such as an aortic aneurysm; renal, ovarian, or pancreatic tumor; ascites, etc.). Major findings involved 10% to 23% of cases, increase with patient's age, and will be more numerous in patients with malignancy (up to 70%).<sup>16</sup>

For medicolegal and ethical reasons, these findings must be reported. Their added-cost per examination is low (\$28 to \$34),<sup>17</sup> but their precise impact on patient outcome is unknown.

**WHICH SCREENING TEST FOR WHICH RISK?**

**Mass screening.** Today, CTC is defined as “an emerging, promising screening tool.” But it is still not on the list of official diagnostic options for the major oncological and gastroenterological societies.

Currently, the American College of Radiology recommends a DCBE every five years. It is probable that CTC will soon follow the same recommendation. In the “average risk” population, screening should begin at age 50 with FOBT, sigmoidoscopy, DCBE, or OC. CTC could be considered.

In the high-risk population, in cases of personal or family history of CRC, OC is the recommended screening test, but CTC could be an option for patients unwilling or unable to undergo this test. In case of inflammatory pancolitis after 15 years of evolution, optical colonoscopy with biopsies every two years should be the only tests performed.

In very high risk cases, screening will include oncogenetic consultation, frequent endoscopic colonoscopies or prophylactic colectomy.

**Individual screening.** As it takes 10 years for an adenoma to become an adenocarcinoma, if a screening test is performed during this time, the adenoma can be resected and the cancer prevented.

Thus, personal and family history must be investigated, as screening should have begun five years before the onset of cancer in a first-degree relative.

Fifty-year-old patients at average risk should be informed of their risk and about the various possible screening tests. Indeed, any abdominal symptom could be the opportunity to run one of these tests, which will have to be repeated every seven to 10 years.

Optical colonoscopy is the gold standard, although it is an operator-dependent procedure that sometimes fails to explore the whole colon and seldom explores the whole surface of the colonic mucosa. In addition, this procedure requires hospitalization and anesthesia, is expensive, and is not 100% safe. These are probably the reasons why healthy patients facing a 4% risk of CRC are often unwilling to undergo the test. For these patients, CTC is indicated, being an outpatient and absolutely safe procedure, well tolerated, and less costly than OC.

Moreover, with the fast image reconstruction and transfer times now available, and thanks to the performance of dedicated software programs, immediate reading is possible. While the patient is still fasting it is possible to proceed directly to the resection of possible adenomatous polyps without the need to repeat the bowel-cleansing process.

CTC is also the procedure of choice in case of incomplete OC, contraindication to anesthesia, and bleeding factors. Similarly, old and frail patients, in whom anesthesia should be avoided as much as possible, could benefit from CTC, particularly since the bowel preparation can be adapted to their condition. Indeed, they often have a fragile, adherent and redundant colon, rendering OC difficult and delicate, thus frequently resulting in incomplete studies.

**CONCLUSION**

CTC is a safe, outpatient procedure that offers a full study of the colon and may be directly followed by optical colonoscopy for polyp resection. Although it has not yet been included among the traditional methods of colorectal cancer screening, CTC has been shown to be equivalent to optical colonoscopy and more accurate than DCBE in diagnosing lesions of significant size. Since the generalization of multislice CT and of highly efficient dedicated software, this procedure is no longer experimental and is part of the daily practice of many radiologists.

As CTC involves minimal discomfort and is well accepted, it will certainly prove useful in convincing patients to undergo CRC screening and, hopefully, will help decrease still too-frequent and often avoidable cancer-related deaths.

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