Since its first description in 1989, CT colonography (CTC) has slowly entered radiological practice. 2008 is a turning point for CTC. From a technical point of view, CTC is recognized as an efficient and safe procedure that is acceptable to patients and cost-effective: It could thus qualify as a large-scale screening test for colorectal cancer. Colonic preparation and tagging techniques are easily available, and technical rules have been precisely defined. 1 In practice, a CTC procedure requires only a multislice CT device and dedicated reading software and can be performed in 10 minutes by a technologist. Yet few hospitals provide this screening test.

From a diagnostic point of view, the enthusiasm generated by Pickhardt’s publication in 2003 of the superb results of CTC compared with optical colonoscopy was soon deflated by Cotton’s study, only a few months later, which asserted the contrary. 2,3 Such discrepancies among prominent articles, even if clearly explained by technical, software, and reader differences, led to doubt and reticence. These doubts were strengthened by meta-analyses that confirmed high performance in state-of-the-art conditions but also demonstrated wide ranges of performance among the reported results. 4,5 It thus remained to prove that CTC could indeed be successfully performed in any radiology department, provided state-of-the-art technique was used and experienced readers were in charge. A National CT Colonography Trial (ACRIN 6664) was organized toward this end.

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

- Define the present situation of CTC.
- Identify the difficulties in CTC readings.
- Summarize the different performances of Computer-aided detection (CAD) systems.
- Explain about CAD systems’ usefulness.

Who will benefit:
Physicians, physician assistants, and radiologic technologists will benefit from the information in this educational activity and can receive Continuing Medical Education credit by completing the post test and evaluation provided.

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This trial was carried out in 15 U.S. sites, involving both academic centers and private practices, and recruited 2531 asymptomatic outpatients who underwent CTC followed by same-day optical colonoscopy. The CT studies were performed under state-of-the-art conditions: Patients underwent a cathartic bowel preparation with stool and fluid tagging, insufflations were performed with carbon dioxide, CT scanning devices representing each of the major vendors had at least 16 detector rows and acquired thin and overlapping slices, and reading was performed by CTC-experienced radiologists in either primary 2D or 3D reading techniques. Indeed, readers had to have experience with at least 500 cases or attend a one-and-a-half-day training course. All had to pass a certified exam in which they detected at least 90% of the adenomas 1 cm or larger in a total of 50 cases. More than half of the readers had to undergo additional training in order to succeed at this exam, but all eventually passed.

The preliminary results demonstrated a tight interobserver variability. Seven of the 15 readers detected 100% of the polyps without significant difference in sensitivity between primary 2D and 3D readings. In terms of detection, sensitivity was 90% for adenomatous lesions 1 cm or larger, quite on par with optical colonoscopy performances.

At approximately the same time, Kim and colleagues published similar results in a series of more than 6000 subjects, and two large European multicenter trials (IMPACT from Italy and the Munich Colorectal Cancer Prevention Trial) demonstrated respective sensitivities of 91% and 100% for clinically relevant lesions.6

Finally, in March 2008, the long-expected new recommendations for screening and surveillance for the early detection of colorectal cancer and adenomatous polyps were published, and CTC was officially added to the five-year colon screening guidelines by the American Cancer Society, the American College of Radiology, and the three major gastrointestinal societies: the American Gastroenterological Association, American Society for Gastrointestinal Endoscopy, and the American College of Gastroenterology.7 Today, CTC is ready for widespread use.

CHALLENGE FOR BEGINNERS
The ACRIN trial evaluation involved experienced readers. Beginners have thus to acquire theoretical as well as practical expertise.

• CTC workshops. These dedicated courses deal mainly with the pathophysiology of polyps and cancer; the effectiveness and indications of the various screening tests, as well as their limitations; and the rhythm of follow-up in the event of positive findings. They also illustrate common pitfalls such as adherent compact stools, mucosities, inverted diverticula, spasm versus circumferential carcinoma, or papilomatous ileocecal valves.

Hands-on training should be performed with the software that will later be used in day-to-day practice. As there are diverging opinions regarding reading techniques, a first choice has to be made between 2D or 3D review, using either fly-through or dissection views. Each method will be needed to solve the problems posed by the other.

There is no consensus regarding the number of cases to be read to acquire minimal expertise. Directed training on 50 cases with endoscopic correlation has generally been considered sufficient, but competence cannot be assumed; some individuals require longer training.8,9

In a U.K. study, 13 subspecialty radiologists, whose experience in CTC ranged from five to 350 cases, were asked to read 15 cases selected from the
European Society of Gastrointestinal and Abdominal Radiology (ESGAR) training data set.10 Taken together, they performed with accuracy comparable to that of radiologists recruited in the ESGAR pan-European study, who trained on 50 cases. But individual sensitivities ranged from 53% to 93%, with U.K. subjects’ performances correlating strongly with the number of cases they had read in the past. The time-to-plateau of the learning curve may indeed be long.

- Reading techniques. CTC learning is a complicated process involving two difficulties: detection of a possible lesion, which is the major challenge for beginners, then its classification as a polyp or a nonpolyp.11

In 2D review, detection is achieved by scrolling up and down through axial slices or multiplanar reformating reconstructions, following the tortuous path of the colonic lumen and mentally reconstructing the folds into 3D images while looking for a protrusion that is not a fold. In the 3D fly-through reading technique, “polyp-candidates” are spotted by flying from the rectum to the caecum and then in the opposite direction. In both acquisitions, special attention is paid to the sides, between and behind prominent haustral folds where possible findings could be hidden.

In the 3D virtual dissection review mode, the full circumference of the lumen is displayed as flat, rectangular segments allowing them to be read “from above,” so providing unimpaired observation of the colonic mucosa. But these views are a distorted representation of anatomy, so require specific reading skills.12

It might be assumed that detection would be easier with the 2D method to which radiologists are accustomed than with 3D review that makes reference to endoluminal images with which they are less familiar. However, studies involving readers who had never before been exposed to CTC found slightly better performances by 3D than by 2D readers.8,13 In fact, 3D review becomes the favorite method for many experienced readers.

Once detected, a finding has to be classified as polyp or nonpolyp. Classification calls on common radiologists’ skills such as analysis of texture, contours, and densities as well as comparison of shape and location between the two data sets. Nevertheless, this process is difficult, as it is often complicated by untagged residual fluid; the tortuous disposition of the colon, whose total length varies according to distention; the mobility of some segments; and possible spasms or insufficient distention, which results in partial or complete lumen collapse.

- Colonic preparation. Which colonic preparation method will be most convenient will depend on the chosen reading method and the capabilities of the reading software. Full bowel purgation, leaving as few liquids and as little fecal residue as possible, facilitates the reading, for both primary 2D and primary 3D readers. This purgation may be achieved through different ways, according to patient’s condition or preference. Liquid diet, Fleet-Phospho-Soda, and four tablets of bisacodyl allow a one-day preparation, but they are contraindicated in cases of renal insufficiency, congestive heart failure, or severe hypertension. In those cases, the same full cleansing can be achieved by a two-day low-residue diet combined with 8 g of magnesium phosphate and four tablets of bisacodyl or Go-Lytely.

Residual fluid, being of identical density as the bowel wall, may hide possible polyps in pools, especially when using the Go-Lytely preparation. This problem is solved by dual acquisitions, moving fluid from the posterior to the anterior aspect of the colon, as well as by Gastrografin oral fluid tagging, which allows the radiologist to recognize protruding lesions even in submerged sections of the colon. A bisacodyl suppository, inserted one hour before the patient leaves home, activates colonic motility, thus helping to reduce excessive amounts of fluid.

That the cathartic bowel preparation required for both virtual and optical colonoscopy is unpleasant has been shown...
in several published studies and is thought to be the major inhibiting factor for screening compliance; less than half of all screening-age individuals are ever tested. Since unprepped optical colonoscopies are unfacile, patient-friendly minimum-preparation CTC techniques are being investigated. These may make patients’ lives easier, but they complicate the radiologist’s job.

The first issue is fecal tagging, which uses positive oral contrast to augment or replace cathartic agents, giving residual stool a distinctive hyperdense appearance at cross-sectional imaging: Folds or polyps keep their soft-tissue attenuation in contrast to the raised attenuation of any ingested food in the colon. The two most common agents are barium sulfate and iodinated contrast agents such as Gastrografin. Barium is added to the low-fiber diet one or two days before the study. But it is relatively insoluble in enteric fluid, which often leads to heterogeneous tagging. Most investigators use it in conjunction with iodinated contrast agents. Gastrografin is the most commonly used tagging agent in any colonic preparation for CTC. Not only does it have a welcome mild laxative effect, but its transparency allows a same-day optical colonoscopy. Small amounts, such as four doses of 5 mL given over the two days preceding the study, are as effective and better tolerated than larger quantities.

Such reduced preparation regimens include two days of a low-fiber diet combined with either 50 mL of barium the day before the study or 2 mL/kg of Gastrografin or three packets of Movicol (dipolyethylene glycol, manufactured by Norgine, Harefield, U.K.) plus 50 mL of Gastrografin in 1L of water two hours before examination.

These reduced preparations allow 2D reading but impede 3D endoluminal study of a suspected positive finding, as the lumen will be at least partially obstructed by fecal residue. To preserve 3D visualization, software programs that perform electronic cleansing (EC) are being developed. This application uses advanced image processing techniques to remove tagged items from the images, all without altering polyps or other important structures. EC in noncathartic preparations is much more difficult, as the process “eats” at the electronic mucosa; subsequent artifacts complicate the endoluminal reading. EC under these conditions is still in progress.

**BENEFICIAL FOR BEGINNERS?**

Detection being the major challenge for beginners, an acknowledgement of wide variations in reader performance, as well as the need to be fast and accurate in CTC screening in a low-prevalence population, has generated interest in computer-aided detection.

As CTC yields more than 1500 slices from the two acquisitions, a CAD system for polyp detection would certainly be of great help, as it might allow easier identification of possible polyp candidates.

CTC CAD systems are being investigated in both academic and commercial circles and several software programs are already or soon will be available. Most of these programs analyze the surface of the colon to identify and mark any round shapes protruding into the colonic lumen, settings are adjustable to aim at findings with more or less perfect sphericity.

Polyps and masslike nodular cancers will thus be detected, of course, but so will the rectal tube, the ileocecal valve, redundant folds, mucosities, and any fecal residue, which accounts for most of the false positives. As the filter settings are adjustable, depending upon size and shape of the target, the number of false positives will obviously increase with small target settings. As CTC target lesions are advanced adenomas, and as diminutive polyps less than 6 mm should not to be reported (70% of them being simply hyperplastic, so always benign), the CAD settings could be adjusted to point only to potential lesions of a significant size and thereby demonstrate fewer false positives. Unfortunately, such settings would be inefficient in the diagnosis of flat lesions, which are frequent and
more likely to harbor cancer than polyloid ones. CAD sensitivity thus has to be set for efficient detection of these lesions that both radiologists and gastroenterologists find hard to spot.22,23

False negatives consist of small sessile polyps, collapsed or insufficiently distended segments, and flat lesions or those under residual fluid. Consequently, the best results will be obtained with perfect insufflations of a clean, dry colon.

Though electronic cleansing can eliminate tagged fluid, it carries a risk for false diagnosis at the air-fluid boundaries.24 Some investigators either use enhancement characteristics after IV contrast perfusion or analyze the internal attenuation, looking for the presence of heterogeneity or air bubbles in the polyp candidate, in order to reduce the number of false positives linked to fecal residue.25-27

The performances of several CAD systems have been assessed in small series of optical colonoscopy-proven cases with very promising results. For instance, in a series of 72 cases, a CAD scheme from the University of Chicago achieved a sensitivity of 95% for polyps ranging from 5 to 25 mm.28 We tested the work-in-progress GE CAD system, applied to 81 proven-positive cases, and achieved a sensitivity of 98.8% [95% CI: 98.5% to 99%] for 9-mm polyphs and of 95.4% [95% confidence interval (CI): 95% to 95.8%] for polyps between 5 mm and 9 mm, with a total of false positives per series of 5.1% [95% CI: 4.6% to 5.6%] for virtual dissection views and 6% [95% CI: 5.6% to 6.3%] for axial review. Obviously, each CAD system has its own sensitivity in terms of polyp candidate detection and number of false positives.

Summers et al29 studied CAD performance in a large population of average-risk patients and compared its per-adenoma sensitivity with first-look optical colonoscopy and expert radiologists. CAD’s sensitivity was equivalent or better at the 10-mm size threshold and significantly better than the results reported by Cotton et al and Johnson et al.3,30

Similar results for per-patient sensitivity at the 10-mm and 8-mm size thresholds suggest that CAD may be similar to or even better than expert readers in the detection of clinically relevant lesions.31

In a U.K. study, three expert radiologists read 25 CTC studies, which were afterwards analyzed by CAD software.31 Then, in consensus and compared with endoscopic results, they classified the prompts as either true or false positives. Compared with the readers, the automated report yielded higher overall sensitivity (81% versus 70%), with both groups detecting 11 of the 12 large polyphs. But most important, the CAD software saw most of the polyps that had been missed by the readers. Similarly, Mani et al compared the performances of three radiologists reading 41 studies with and without CAD: Readers without CAD detected 63% of polyphs equal to 10 mm, with their sensitivity improving to 74% with CAD.32 He also demonstrated that CAD significantly decreased interobserver variability among the three radiologists.

Concurrent CAD reading, if all possible protruding lesions are detected, could be of significant help for beginners. Haggan et al studied the performances of 10 inexperienced readers using the primary 2D reading technique, in reporting the same 107 cases (142 polyphs) first without, then two months later with, CAD assistance.33 According to the readers, per-patient sensitivity was between 23% and 73%; CAD assistance allowed an improvement ranging from 0% to 22% that was significant for seven readers out of 10, especially for the detection of small- and medium-sized polyphs. But mean performance remained as low as 51%.

The same conclusions may be inferred for beginners using the 3D reading technique. We studied the performances of four inexperienced radiologists, after a minimal two-hour teaching session, using 3D virtual dissection, which was supplemented for two of them by concurrent CAD assistance. At the end of a single-day session of 20 cases, the CAD group achieved better sensitivity (83%) than the non-CAD group (54%). After three days (60 cases), the four readers reached 90% sensitivity.34

CAD may be directly incorporated in the reading software (concurrent-reading CAD) or applied only after full unaided observation of the study (second-reading CAD). Taylor et al35 compared these two reading techniques and demonstrated a better time efficiency for concurrent-CAD reading, with similar sensitivity for polyphs 6 mm or larger, although sensitivity is maximized for smaller lesions when CAD is used as a second read. Indeed, compared with unaided reading, concurrent-reading CAD incites faster review of unprompted segments; as some small polyphs could not have been prompted, this leads to false negatives. Another explanation could be that, consistent with Zheng et al’s36 observation of reduced sensitivity for breast cancer with concurrent-CAD reading, which was worst when the CAD false-positive rate was highest, too many CAD prompts can lead to readers placing less weight on correct prompts, especially beginners who are still not used to quick classification.

CONCLUSION
Interpretation of CTC studies is both time-consuming and fatiguing because of the large volume of imaging data. Computer-aided detection software is becoming increasingly available. Its efficiency in revealing clinically significant findings at least equals the standard of experts and, whatever the reader’s experience, tends to raise the level of sensitivity. This is especially true for beginners, for whom detection of polyph candidates is the major challenge.

It could thus be advised that radiologists at the beginning of their practice use the CAD as a second reader, letting it act as a “teacher” pointing at true or false findings possibly missed during the unaided reading session.

As prompting possible flat lesions requires low-sphericity settings, CAD systems still generate many false positives. But most of them can easily be rejected
with training and experience. As with any radiological procedure, and probably especially with CTC, capability is a matter of experience. CAD will not reduce the number of missed lesions.

References