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# T O M O G R A P H Y

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## LEARNING OBJECTIVES

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.

## CAD for CT colonography: for what and for whom?

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and Isabelle Mancini**

**S**ince 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.<sup>1</sup> 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.<sup>2,3</sup> 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.<sup>4,5</sup> 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.

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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.<sup>6</sup>

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 gastroin-

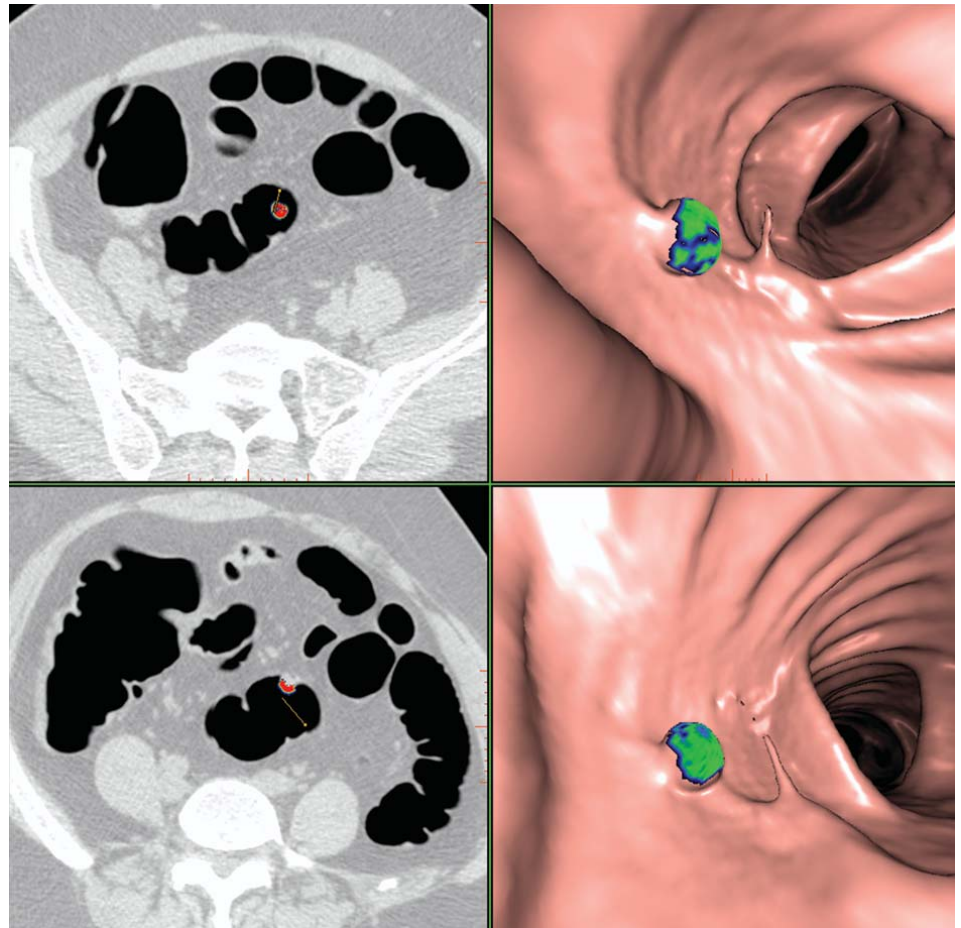


FIGURE 1. Small sessile polyp is highlighted by CAD system in axial slices and endoluminal reconstructions.

testinal societies: the American Gastroenterological Association, American Society for Gastrointestinal Endoscopy, and the American College of Gastroenterology.<sup>7</sup> 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 papillomatous 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.<sup>8,9</sup>

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.<sup>10</sup> 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.<sup>11</sup>

In 2D review, detection is achieved by scrolling up and down through axial slices or multiplanar reformatting 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.<sup>12</sup>

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.<sup>8,13</sup> In fact, 3D review becomes the

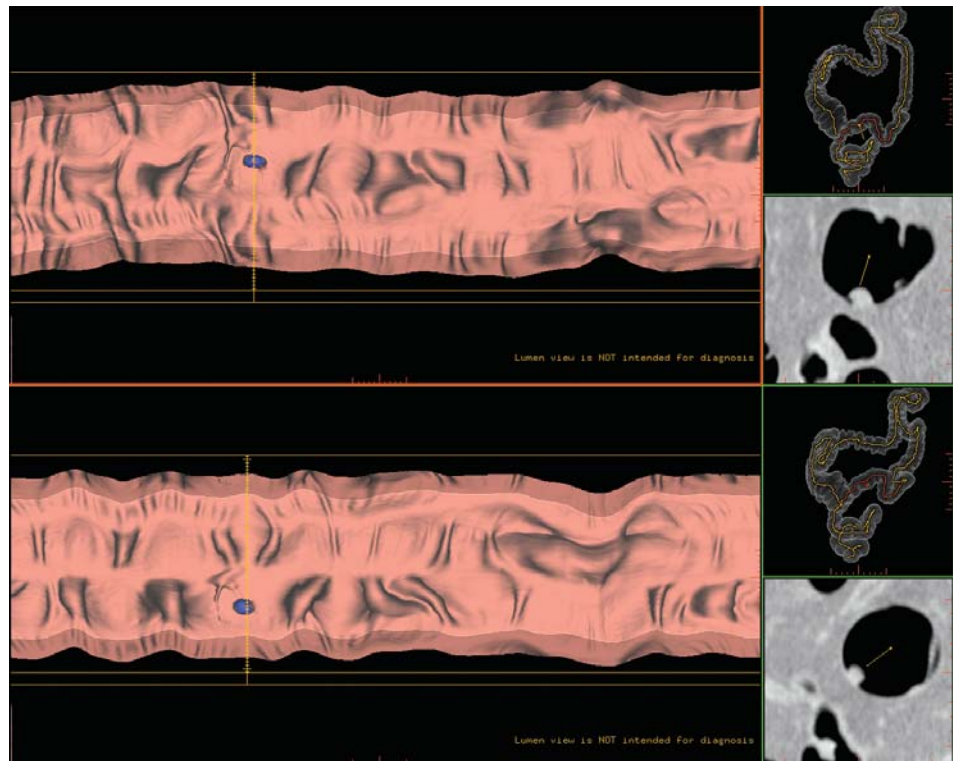


FIGURE 2. Dissection views of same polyp shown in Figure 1.

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



more likely to harbor cancer than polypoid ones. CAD sensitivity thus has to be set for efficient detection of these lesions that both radiologists and gastroenterologists find hard to spot.<sup>22,23</sup>

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.<sup>24</sup> 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.<sup>25-27</sup>

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.<sup>28</sup> 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 polyps 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 al<sup>29</sup> 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.<sup>3,30</sup>

Similar results for per-patient sensitivi-

ty 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.<sup>31</sup>

In a U.K. study, three expert radiologists read 25 CTC studies, which were afterwards analyzed by CAD software.<sup>31</sup> 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 polyps. 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 polyps equal to 10 mm, with their sensitivity improving to 74% with CAD.<sup>32</sup> 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. Halligan et al studied the performances of 10 inexperienced readers using the primary 2D reading technique, in reporting the same 107 cases (142 polyps) first without, then two months later with, CAD assistance.<sup>33</sup> 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 polyps. 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.<sup>34</sup>

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 al<sup>35</sup> compared these two reading techniques and demonstrated a better time efficiency for concurrent-CAD reading, with similar sensitivity for polyps 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 polyps could not have been prompted, this leads to false negatives. Another explanation could be that, consistent with Zheng et al's<sup>36</sup> observation of reduced sensitivity for breast cancer with concurrent-reading CAD, 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 polyp 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 turn anybody into an expert, but it will reduce interobserver variability, allowing more findings to be classified and hopefully limiting the number of missed lesions. ■

## References

1. Taylor SA, Laghi A, Lefere P, et al. European Society of Gastrointestinal and Abdominal Radiology (ESGAR): consensus statement on CT colonography. *Eur Radiol* 2007;17(2):575-579.
2. Pickhardt PJ, Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. *NEJM* 2003;349(23):2191-2200.
3. Cotton PB, Durkalski VL, Pineau BC, et al. Computed tomographic colonography (virtual colonoscopy): a multicenter comparison with standard colonoscopy for detection of colorectal neoplasia. *JAMA* 2004 Apr;291(14):1713-1719.
4. Sosna J, Morrin MM, Kruskal JB, et al. CT colonography of colorectal polyps: a metaanalysis. *AJR* 2003;181:1593-1598.
5. Halligan S, Altman DG, Taylor SA, et al. CT colonography in the detection of colorectal polyps and cancer: systematic review, meta-analysis, and proposed minimum data set for study level reporting. *Radiology* 2005;237:893-904.
6. Kim DH, Pickhardt PJ, Taylor AJ, et al. CT colonography versus colonoscopy for the detection of advanced neoplasia. *NEJM* 2007;357(14):1403-1412.
7. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin* 2008;58(3):130-160.
8. Taylor SA, Halligan S, Burling D, et al. CT colonography: effect of experience and training on reader performance. *Eur Radiol* 2004;14(6):1025-1033.
9. Spinzi G, Belloni G, Martegani A, et al. Computed tomographic colonography and conventional colonoscopy for colon diseases: a prospective, blinded study. *Am J Gastroenterol* 2001;96(2):394-400.
10. Burling D, Halligan S, Atchley J, et al. CT colonography: interpretative performance in a non-academic environment. *Clin Radiol*. 2007;62(5):424-431.
11. Fidler JL, Fletcher JG, Johnson CD, et al. Understanding interpretive errors in radiologists learning computed tomography colonography. *Acad Radiol* 2004 Jul;11(7):750-756.
12. Rottgen R, Fischbach F, Plotkin M, et al. CT colonography using different reconstruction modi. *Clin Imaging* 2005;29(3):195-199.
13. Gluecker T, Meuwly JY, Pescatore P, et al. Effect of investigator experience in CT colonography. *Eur Radiol* 2002;12(6):1405-1409.
14. Lefere PA, Gryspeerdt SS, Dewyspelaere J, et al. Dietary fecal tagging as a cleansing method before CT colonography: initial results polyp detection and patient acceptance. *Radiology* 2002;224(2):393-403.
15. Zalis ME, Perumpillichira JJ, Magee C, et al. Tagging-based, electronically cleansed CT colonography: evaluation of patient comfort and image readability. *Radiology* 2006;239(1):149-159.
16. Liedenaub MH, Gouw CIBF, de Vries AH, et al. Two different doses of iodinated fecal tagging agent for CT colonography: Evaluation of tagging quality, homogeneity, patient acceptance and diagnostic accuracy. Presented at the European Congress of Radiology, Vienna, March 7-11, 2008.
17. Lefere P, Gryspeerdt S, Marrannes J, et al. CT colonography after fecal tagging with a reduced cathartic cleansing and a reduced volume of barium. *AJR* 2005;184(6):1836-1842.
18. Campanella D, Molinar D, Gallo T. Fecal tagging, electronic cleansing and CAD: a new strategy towards mass screening with CT colonography (CTC). Presented at the European Congress of Radiology, Vienna, March 7-11, 2008.
19. Yoshida H, Nappi J. Three-dimensional computer-aided diagnosis scheme for detection of colonic polyps. *IEEE Trans Med Imaging* 2001;20(12):1261-1274.
20. Summers RM, Beaulieu CF, Pusanik LM, et al. Automated polyp detector for CT colonography: feasibility study. *Radiology* 2000;216(1):284-290.
21. Kiss G, Van Cleynenbreugel J, Thomeer M, et al. Computer-aided diagnosis in virtual colonography via combination of surface normal and sphere fitting methods. *Eur Radiol* 2002;12(1):77-81.
22. Soetikno RM, Kaltenbach T, Rouse RV, et al. Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults. *JAMA* 2008;299(9):1027-35.
23. Taylor SA, Robinson C, Boone D, Halligan S. Clinical research in CAD for CTC. Presented at the European Congress of Radiology, Vienna, March 7-11, 2008.
24. Summers RM, Franaszek M, Miller MT, et al. Computer-aided detection of polyps on oral contrast-enhanced CT colonography. *AJR* 2005;184(1):105-108.
25. Luboldt W, Mann C, Tryon CL, et al. Computer-aided diagnosis in contrast-enhanced CT colonography: an approach based on contrast. *Eur Radiol* 2002;12(9):2236-2241.
26. Summers RM, Jerebko AK, Franaszek M, et al. Colonic polyps: complementary role of computer-aided detection in CT colonography. *Radiology* 2002;225(2):391-399.
27. Yoshida H, Masutani Y, MacEneaney P, et al. Computerized detection of colonic polyps at CT colonography on the basis of volumetric features: pilot study. *Radiology* 2002;222(2):327-336.
28. Nappi J, Yoshida H. Feature-guided analysis for reduction of false positives in CAD of polyps for computed tomographic colonography. *Med Phys* 2003;30(7):1592-1601.
29. Summers RM, Yao J, Pickhardt PJ, et al. Computed tomographic virtual colonoscopy computer-aided polyp detection in a screening population. *Gastroenterology* 2005;129(6):1832-1844.
30. Johnson CD, MacCarty RL, Welch TJ, et al. Comparison of the relative sensitivity of CT colonography and double-contrast barium enema for screen detection of colorectal polyps. *Clin Gastroenterol Hepatol* 2004;2(4):314-321.
31. Taylor SA, Halligan S, Burling D, et al. Computer-assisted reader software versus expert reviewers for polyp detection on CT colonography. *AJR* 2006;186(3):696-702.
32. Mani A, Napel S, Paik DS, et al. Computed tomography colonography: feasibility of computer-aided polyp detection in a "first reader" paradigm. *JCAT* 2004;28(3):318-326.
33. Halligan S, Altman DG, Mallett S, et al. Computed tomographic colonography: assessment of radiologist performance with and without computer-aided detection. *Gastroenterology* 2006;131(6):1690-1699.
34. Hock D, Ouhadi R, Materne R et al. Virtual dissection CT colonography: evaluation of learning curves and reading times with and without computer-aided detection. *Radiology* 2008, in press.
35. Taylor SA, Charman SC, Lefere P, et al. CT colonography: investigation of the optimum reader paradigm by using computer-aided detection software. *Radiology* 2008;246(2):463-471.
36. Zheng B, Swenson RG, Golla S, et al. Detection and classification performance levels of mammographic masses under different computer-aided detection cueing environments. *Acad Radiol* 2004;11(4):398-406.