Virtual Colonoscopy Poised To Gain Wide Acceptance

BY KATE JOHNSON
Montreal Bureau

BOSTON — The debut of virtual colonoscopy as a mainstream option for colorectal cancer screening may be just months away, experts said at an international symposium on virtual colonoscopy sponsored by Boston University.

The much-anticipated results of the American College of Radiology Imaging Network's (ACRIN) national trial, are expected to be announced by late March 2007. The results are expected to show virtual colonoscopy (VC), also known as CT colonography, in a favorable light in comparison with conventional optical colonoscopy (OC), said one of the investigators, Dr. Judy Yee of the University of California, San Francisco.

The American Cancer Society expects to announce its updated colorectal cancer screening guidelines at about the same time, said Robert Smith, Ph.D., the society's director of cancer screening.

To date, the ACRIN trial has enrolled 2,468 of the 2,607 subjects needed to complete its comparison of both screening modalities, and the trial is scheduled to conclude in late November, said Dr. Yee.

"Where will the results fall?" she asked. In terms of the three most important multicenter trials comparing VC and OC, the excellent performance of VC in the landmark Pickhardt trial (New Engl. J. Med. 2003;349:2191-2200) was not replicated in the two more recent trials (JAMA 2004; 291:1713-19, and Lancet 2005; 365:305-11), Dr. Yee said.

"I don't think I am going out on a limb by saying the ACRIN results will fall right between," she said. "I don't think the ACRIN trial will be able to achieve the 92% sensitivity [for VC] seen in the Pickhardt trial, but taking an educated guess I would say that sensitivity will fall maybe somewhere between 80% and 90%."

Results like that would launch VC into the mainstream, predicted Dr. Joseph Ferrucci of Boston University. "We hope they will be the data that will be the final tipping point for the American Cancer Society to amend its guidelines to include VC," he said in an interview.

Dr. Smith agreed that the ACRIN trial results will be important, but he would not comment on how they would influence the American Cancer Society's guidelines.

"I can't tell you whether we are going to wait [for the ACRIN results] or not," he said in an interview. "We know the ACRIN timetable, and we are working on our guidelines now. If we are not done by the time the ACRIN results are out, we will most certainly want to see them at the earliest opportunity. We live in an electronic age, which means our guidelines process is always active. The potential is always there to adjust the guidelines in very short order if necessary."

Recognition by the American Cancer Society of VC's strength as a colorectal cancer screening tool would likely carry it over the threshold toward full public and medical acceptance, said Dr. Perry Pickhardt of the University of Wisconsin, Madison, principal investigator of the 2003 landmark trial.

The end result will hopefully be better patient compliance with screening. 'Currently, more than 40 million adults over the age of 50 are not being screened.'

"This is an exciting time for VC as we move from validation into implementation," said Dr. Pickhardt, adding that the next step needs to be acceptance by third-party payers. "We are treading water now waiting for widespread reimbursement."

Dr. Smith agreed that the reaction of the American Cancer Society to the ACRIN results will be important. If VC is added to the society's guidelines, it is reasonable to expect a resulting improvement in competence among those who perform the test, greater overall investment in the approach, and greater public awareness, he said.

The end result will hopefully be better patient compliance with screening, Dr. Pickhardt said. "Currently, more than 40 million adults over the age of 50 are not being screened," he said. ■

Virtual Screening May Reduce Polypectomies

BY KATE JOHNSON
Montreal Bureau

BOSTON — With virtual colonoscopy expected to soon take center stage along with other colorectal screening tools, the management of colorectal polyps is poised for a major shift, according to several experts.

Virtual colonoscopy's main attraction—its minimally invasive quality—is also its main weakness. A problematic lesion that is found on virtual colonoscopy (VC) cannot be immediately removed, as it can during conventional optical colonoscopy (OC), although same-day OC with polypectomy following VC is often an option.

"The central issue is whether some of these polyps can be left," said Dr. Joseph Ferrucci of Boston University. "Optical colonoscopy with polypectomy for all visualized polyps may be therapeutic overkill," he said in an interview at an international symposium on virtual colonoscopy that was sponsored by the university.

Most physicians agree that small polyps (under 5 mm) can be safely left in place, and large polyps (more than 9 mm) should be removed immediately. The debate lies with medium-sized polyps measuring 6-9 mm, Dr. Ferrucci said. During OC, such polyps are normally removed because the opportunity is there, but there is no strong evidence to support this practice, and there is a growing body of evidence against it.

"The data [show] that an overaggressive approach to polypectomy has consequences. People are asking [if it's] sensible," said Robert Smith, Ph.D., director of cancer screening for the American Cancer Society. Therapeutic colonoscopy is also much more expensive than a screening OC, he said in an interview.

Dr. Perry Pickhardt of the University of Wisconsin, Madison, said VC can act as a filter for determining the need for polypectomy. The medical school at the University of Wisconsin, one of the few to secure third-party coverage for VC, has used the tool to significantly reduce the number of polypectomies.

In a comparison of 2,202 patients receiving primary VC screening and 2,210 patients receiving primary OC screening, 7% of the VC group went on to receive an OC because of detection of a medium-sized polyp, with a resulting 325 polypectomies. The primary OC group ended up with 1,696 polypectomies. Despite that difference, the percentage of polyps identified as advanced adenomas was 3% in both groups, Dr. Pickhardt said. "VC is an effective filter for selective therapeutic OC, resulting in a more efficient use of costly and invasive resources.

Low-Tech Options for Inflammatory Bowel Disease Promising

BY SHERRY BOSCHERT
San Francisco Bureau

MONTEREY, CALIF. — Development of new treatments for Crohn's disease or ulcerative colitis has generally focused on immunomodulators, cytokine therapy, and other biotechnology, but lower-technology options are being tried as well, Dr. Joshua R. Korzenik said.

Probiotics, parasites, and fecal transplants each have shown some positive results, although none are ready for prime time, Dr. Korzenik said at an update in gastroenterology and hepatology sponsored by the University of California, Davis.

► **Probiotics.** Most study findings on the use of beneficial bacteria to treat inflammatory bowel disease have not supported this strategy, but one study of treating pouchitis produced positive results.

The study included 40 patients who were treated for ulcerative colitis with colectomy and an ileoanal anastomosis (or J-pouch) operation and who subsequently developed a chronic inflammatory process, a problem occuring in about 15% of J-pouches. Antibiotics can control the pouchitis, but long term they are not ideal.

The researchers brought the patients' pouchitis into remission with antibiotics, then discontinued the antibiotic therapy and randomized 20 patients to a potent probiotic called VSL#3 and assigned another 20 patients to placebo. The pouchitis returned in all of the patients on placebo by 5 months later, but 17 patients in the probiotic group remained in remission 9 months after starting therapy (Gastroenterology 2000;119:305).

Typical probiotics found in health food stores contain between 1 and 20 billion bacteria per gram. VSL#3, which is sold over the Internet, contains about 1.6 trillion bacteria per gram, and patients in the study took three capsules a day. "You're still talking about relatively small potatoes," compared with the 100 billion to 1 trillion bacteria in each gram of stool, said Dr. Korzenik, codirector of the Crohn's and Colitis Center at Massachusetts General Hospital, Boston, noted.

The VSL#3 treatment regimen costs about $12-$15 per day and is not covered by insurance.

► **Parasites.** Some researchers have speculated that the modern zeal for cleanliness eliminated helminth ova (infectious parasite eggs) from humans, and that this contributes to the development of Crohn's disease and ulcerative colitis. Reintroducing these to the body might help treat these diseases, Dr. Korzenik.

In one open-label study, 29 patients with active Crohn's disease took 2,500 *Trichuris suis* (pig whipworm) ova every 3 weeks for 24 weeks (Gut 2005;54:87-90). The disease responded to the treatment in 79% of the patients, and 72% of them achieved remission. "The results are almost too good to be true, but it's promising," he said.

A separate placebo-controlled trial in patients with ulcerative colitis showed marginal benefit.

The ova are sold from Europe over the Internet as an expensive product called TSO. "I suggested it be called Ova the Counter," he joked. The Food and Drug Administration is considering whether sales should be regulated.

► **Fecal transplants.** This treatment, also called "human probiotics" because the implanted bacteria come from donor stool, is modeled after fecal enemas used to treat some patients with refractory *Clostridium difficile* infection to reestablish normal flora.

In an open-label study of six patients with long-standing ulcerative colitis who received daily infusions for 1 week, all had improvement in symptoms (J. Clin. Gastroenterol. 2003;37:42-7). ■