Mayo Clinic researcher details next-era advances in use of scopes for cancer detection

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Just as cameras and televisions have been reinvented in the last decade with improved optics, sharpness and brightness, so have the tiny imaging scopes that physicians use to peer into the body's nooks and crannies -- its organs and digestive system.

And few places in the United States are testing the power of these new endoscopic optics as thoroughly as are researchers at Mayo Clinic. Gastroenterologists at Mayo are pitting multiple high-tech probes against each other to see how well they detect the tiniest precancerous polyp in the colon. They are testing other scopes to search lymph nodes outside of the lung for evidence of micrometastatis -- the spread of cancer cells that can't easily be seen. They are also finding new ways to reduce laborious and painful screening in patients with Barrett's esophagus.

"We can see detail that was unimagined 10 years ago," says Michael Wallace, M.D., a gastroenterologist at Mayo Clinic's campus in Florida. "With the newest systems, we can zoom in on a potential problem spot in the colon or esophagus with 1,000-fold magnification, leading to a day when we can perform virtual biopsies on patients -- meaning that we will be able to tell if a lesion is precancerous by looking at it, and if it isn't, we can leave it alone. Now we have to remove anything that looks even slightly suspicious."

Dr. Wallace leads many clinical trials testing the newest scopes. At the Digestive Disease Week (DDW) 2010, an annual international meeting of physicians and researchers in the fields of gastroenterology, hepatology, endoscopy, and gastrointestinal surgery, he will discuss how these advanced scopes can potentially help prevent or detect early colon cancer, lung cancer metastasis and esophageal cancer.

Probe is most accurate to date in performing virtual biopsy of colon polyps

A Mayo Clinic research team, led by Dr. Wallace, has found that an endoscopic imaging tool only one-sixteenth of an inch in diameter shows the highest accuracy yet in detecting small precancerous polyps inside the colon wall.

In the study, 84 patients were tested with three different technologies while undergoing a colonoscopy. Two of these technologies -- use of regular white light and a blue light that highlights blood circulation -- are a standard feature on most high-definition scopes in use today. They allow a physician to switch between light sources to pick up additional detail in colon tissue. The third technology, the probe-based confocal laser endomicroscopy (pCLE) system, is a state-of-the-art technology that is being tested and used at Mayo and a few centers in the U.S. This is a separate device that can magnify structures by 1,000-fold, to the point that it can detect precancerous changes in a single cell -- a condition that could indicate development of a precancerous polyp.

The researchers found that the pCLE system was the most accurate at determining whether a small (6 millimeter) polyp was precancerous. Its specificity was 100 percent, meaning that polyps it identified as abnormal were, in fact, abnormal. All 145 polyps found in the patients were examined with all three methods and then removed and examined by a pathologist to see if they were benign or precancerous.

Dr. Wallace says that the sensitivity of the pCLE system was 91 percent. "The benign small polyps

were correctly determined to be benign 91 percent of the time by the pCLE system," he says. "Our goal is to bring that figure up to as close to 100 percent as possible."

The researchers are working toward using an endoscopic probe to perform virtual biopsies. As envisioned by Dr. Wallace, the endoscopic probe will be able to determine if a polyp is benign, and if so, that polyp can be left in the colon. Currently, all lesions are removed during a colonoscopy and examined, but about half of all polyps are found to be harmless. This adds time, expense, and a possible risk of side effects to routine colonoscopies, Dr. Wallace says.

Use of three imaging techniques together identifies suspicious lesions in patients with Barrett's esophagus

At Mayo Clinic, Dr. Wallace's research has also shown that the pCLE system can reduce the number of biopsies necessary in Barrett's esophagus, a condition where the tissue lining the esophagus is replaced by tissue that is similar to the lining of the intestine —which can then morph into cancer.

To rule out cancer development, physicians normally biopsy every four inches of the esophagus in Barrett's esophagus patients to detect the same kind of precancerous changes that occur in the colon. Usually only one out of 100 biopsied samples of the esophagus has a lesion that is precancerous when examined by a pathologist, Dr. Wallace says.

To see if there is a better way to analyze the esophagus, Mayo Clinic contributed the largest number of patients with Barrett's esophagus to an international study testing pCLE imaging. The results are being presented at DDW. Dr. Wallace is the senior author. The study findings will be presented by the principal investigator, Prateek Sharma, M.D., from Kansas University Medical Center.

The 97 patients enrolled in the study were examined with a standard endoscope that had both white and blue light, and then by pCLE. A total of 718 random locations were biopsied and 138 suspicious lesions were found. Researchers found that the three different technologies, when used independently, detected 85 percent of precancerous changes, and that a combination of white and blue lights identified 92 percent of these lesions. When pCLE was added, 100 percent of precancerous lesions were identified.

"We have now shown that adding pCLE to standard endoscopes gives us the ability to identify all suspicious lesions in these patients," Dr. Wallace says. "It is a simple matter to use them all in clinical practice. The white and blue lights are part of one endoscope, and pCLE device can be added to the scope. Our hope is that, in the future, we will not need to remove so many samples from patients, and focus only on those that have potential to become cancers. Our combination scope can do that, and our hope is that this changes the kind of surveillance that patients with Barrett's esophagus have to undergo."

Minimally invasive scope and molecular test can check lung cancer patients for evidence of cancer spread to lymph nodes

Lung cancer is the most common cause of cancer death in the United States. A patient's best hope is that the cancer is detected and treated before it spreads from the lungs. Determining whether patients diagnosed with lung cancer have malignant lymph nodes near their lungs -- the first site the cancer usually spreads -- has always been difficult. Even after these mediastinal lymph nodes have been removed, examined, and determined to be cancer-free, cancer still returns in 30? percent of patients. Whether the cancer has spread makes a difference in a patient's treatment.

Researchers at Mayo Clinic, working with scientists at the Medical University of South Carolina, had earlier found a panel of five markers -- molecules only expressed in lung cancer cells -- that could identify micrometastasis in these lymph nodes. Micrometastasis is the spread of cancer that is too small to see with any current imaging or pathology technology. They found in one of their first studies that ultrasound-guided endoscopy used in a biopsy of the lymph nodes, combined with real-time

analysis of the markers in the nodes, detected evidence of micrometastasis in about 20 percent of lymph nodes that had been deemed to be cancer-free by pathological examination.

The examination is minimally invasive and is done before surgery, says Dr. Wallace, who has led this research. The scope is threaded down the esophagus and, with the assistance of ultrasound, guided to the mediastinal nodes. There, a fine needle removes a tiny sample of the tissue node.

Dr. Wallace and a team of physicians and researchers have shown that patients whose lymph nodes showed molecular evidence of micrometastasis had significantly worse survival rates than patients whose nodes did not express these molecules. The findings suggest that this technology, dubbed EUS-FNA (endoscopic ultrasound-fine needle aspiration), can help physicians decide which therapy to offer patients whose lymph nodes show cancer spread.

"It may be better to give these patients chemotherapy and radiation before surgery," says Dr. Wallace. "That will be our next study."

Short training session is enough to teach physicians how to interpret pCLE images -- suggesting it could be widely used

No matter how accurate the pCLE probe (described above) is in mining the colon for precancerous polyps, if most gastroenterologists find it too difficult to use, the probe will sit on the shelf and not benefit patients, according to Dr. Wallace. That is why he and his research team decided to see what kind of learning curve physicians who have never worked with the pCLE system need to undergo before they can use it.

In a small experiment, they taught a group of 11 physicians how to interpret 20 video sequences taken by pCLE of benign and precancerous polyps. "Since the pCLE is a high-definition imaging tool, we had to know if these physicians could accurately interpret the images they were given," Dr. Wallace says.

The physicians were then tested on 76 new video sequences, taken from 54 patients. After seeing 50 images, the group, on average, had an accuracy level of 86 percent, which is similar to highly experienced users, Dr. Wallace says. "The ability to interpret these images is rapidly learned, and the technology could be fairly easily adopted into a general practice," he says.

Provided by Mayo Clinic