An **inside view**

There are few medical procedures dreaded more than a colonoscopy. But what if there was a new, less invasive way to diagnose colon cancer? **Laura Hopperton** reports.

Colonoscopies can be an uncomfortable procedure for patients who may already be worried about what the results may find. The process involves probing the large intestine with a tiny fibre optic camera, known as an endoscope, embedded in a 4ft long, flexible tube.

As well as colon cancer, colonoscopies can be used to detect and diagnose a whole host of diseases, including irritable bowel syndrome (IBS) and Crohn’s disease.

The procedure itself is not only uncomfortable and expensive, it can also be ineffective at spotting smaller tumours – leading to misdiagnosis. Around 750,000 incomplete colonoscopies occur each year in the US alone, which means patients often have to undergo an additional procedure, such as an X-ray or CT scan, in order to complete the colorectal examination – incurring extra costs and risks in the process.

While modern endoscopic techniques have revolutionised the diagnosis and treatment of diseases of the small intestine, oesophagus and stomach (ingestible pill cameras have been around for more than a decade now), the last remaining frontier has been the large intestine. The main problem is that the narrow tubes of the colon are cavernous and highly folded, making them hard to get to.

**Footage relayed wirelessly**

Now, an Israeli company called Given Imaging has been given approval from the US Food and Drug Administration (FDA) for a revolutionary capsule camera technology that is capable of imaging the large intestine. PillCam Colon 2 is a pill sized video camera measuring 11.6 x 31.5mm that captures colour video from both of its ends at an adjustable frame rate. A ring of LEDs (between four and six depending on the application) provides the necessary illumination for image capture and, once swallowed by the patient, the device relays footage wirelessly for between eight and 10 hours to a recording device worn by the patient.

“PillCam Colon 2 is the only minimally invasive tool that offers direct visualisation of the colon at low risk and high accuracy,” says Gregory Davault, VP of global market development for capsule endoscopy at Given Imaging. “It doesn’t require sedation, which means patients can carry on with their normal day, and recovery is immediate.”

Inside the capsule is an off the shelf silver oxide battery with 3V DC output, an RF transmitter and antenna, two CMOS image sensors (placed centrally at either end), and two circuit boards with the LEDs. The imagers, developed over a number of years in collaboration with Zarlink Semiconductor (now part of Microsemi), can detect objects as small as 0.07mm. An adjustable frame rate means the devices can take images at 4frame/s when virtually stationary and up to 36frame/s when moving.

**Travelling naturally**

There is no internal memory or internal processing capability within the capsule itself. Instead, data is transmitted in real time via the RF transmitter and on-board antenna to a data recorder worn by the patient either on a shoulder strap or a belt.

As with traditional endoscopies, patients are required to take specific medication beforehand to cleanse the colon. This promotes certain movements in the body, and makes the bowels more active to help move the capsule along.

When the PillCam is closed, two magnetic strips on the lid activate a MEMS switch to keep it in the off state. The device only activates when the lid is opened.

Once this is done and the pill is swallowed, it travels naturally through the gastrointestinal tract and the device can get to work scanning for suspicious polyps, ulcers and lesions. “We use image analysis to determine where we are during the procedure,” Davault explains. “We look at the images being captured and run these through proprietary algorithms to determine what we’re seeing. The level of image processing is quite remarkable.”

The data recorder worn by the patient recognises the location of the capsule and how long it has been there. If after an hour the capsule is still in the stomach, for example, it will notify the patient by sending an alert and/or vibrations to the sensor belt to inform the patient to ingest another laxative.

In order to preserve battery life, the imagers are only switched on once the PillCam has reached a certain point in the body. The LEDs are timed to light in conjunction with these, as earlier studies determined that the images weren’t as clear if they were left on the whole time.

The PillCam usually passes through the body within one or two days. It is designed to be disposable, for ease of use and sanitary purposes. “We always joke that you wouldn’t want to be the second person using it,” Davault
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Say. “For that reason, and because of battery limitations, the PillCam is only designed for single use.”

During the course of the procedure, the capsule captures approximately 30,000 images. These are then made into a video for the physician to review before making a diagnosis.

“There are three different types of patients we are aiming this at,” says Davault. “The PillCam can be used for patients who, for whatever reason, refuse to have an endoscopy. It’s also suitable for people who have had an incomplete endoscopy, and those that are at higher risk of complication from the traditional procedure. With the colonoscopy, the field of view is typically only 150 to 170° and you only have one camera head. With PillCam, you have two camera heads with a field of view of 270°, allowing nearly 360° coverage of the colon. We don’t claim that it’s better than a colonoscopy, but some physicians like it because you can look at the colon from both angles.”

Another advantage is PillCam’s comparatively low cost. At the moment, the procedure will set you back around $650 (£385). In comparison, a traditional colonoscopy typically costs about $4500 (£2660). The device is based on the current third generation PillCam platform. The researchers at Given Imaging say they wanted to build it 10 years before it came to fruition, but were limited because the technology to build it didn’t exist.

Smartphone camera brings benefits

“When we first came up with the idea for the colon camera, the components weren’t small enough and battery capacity wasn’t high enough,” says Bill Garner, Given Imaging’s VP of product management for capsule endoscopy. “The technology from which we’ve benefitted the most is the smartphone camera. Chip makers have had to invest a lot of money in the imaging chips used for mobile phones in recent years, and that’s an advance that has allowed us to improve the quality of these very small imagers. Battery technology has also improved greatly in the last decade. Before, it was a challenge getting eight hours for a study. Now we can get 14 hours without great difficulty.”

Given Imaging was founded in 1998 by Dr Gabi Iddan and Dr Gavriel Meron. The company’s first capsule endoscopy product, called M2A, gained CE marking in May 2001. In August 2011, rebranded as PillCam, it was cleared by the FDA for imaging the small intestine. To date, more than 1.5 million people have used the small bowel PillCam and more than 10,000 have used PillCam Colon.

“There were definitely performance problems with the first product,” says Garner. “One of the things we learned from our trial was that the capsule behaves very differently in the colon than it does in the small bowel. The diameter of the colon is about the twice the size and the peristaltic movements are different. In the small bowel, you have steady peristaltic movements that help propel the pill through it steadily, whereas in the colon you may have two or three peristaltic waves per day. This meant that the capsule would literally park in a section of the colon for a period of time and then, after a large peristaltic wave, move and then park again very quickly, meaning it would miss some markers along the way. It was only through the use of specially developed medication and the adjustable frame rate of the imagers that this could be overcome.”

New products in the pipeline

A number of competitors exist on the market today, but thus far Given Imaging’s PillCam Colon 2 is the only one to receive FDA approval for imaging the large intestine in any application.

“We are aware of the competition, but no other company has made this a focus in the way we have. It was our product, our primary purpose,” notes Davault. “The other products that have come along have all been what we would call ‘me too’ products, usually equivalent to our previous generation devices. No other company has been able to be more effective in this space of the market than Given.”

The company is currently in the midst of a major business shift, with Irish device firm Covidien completing its $850 million acquisition of the camera pill maker in February this year. Looking forward, Davault says the two companies will continue to innovate and develop PillCam further, with new products already in the pipeline.

“We have a very active R&D department,” he says. “We’re interested to see if we can combine sensors with imagers to detect different elements in the GI tract. We also want to explore the potential for a sensor that can detect the presence of blood, and a capsule that can identify things like pH levels and temperature, as well as capture images.

With further development, we believe it could be possible to make the PillCam manoeuvrable through the use of magnetics. A lot of science fiction prototypes show smart pills with robotic arms that can take samples and deliver drugs. These are areas we continue to look into to understand all the challenges involved. However, it will be some time yet before this kind of thing is possible.”

Looking at how far the technology has come in just 10 years, it will be interesting to see how it evolves over the next decade and what new vistas of the human body it will open up to our vision and understanding.