Sources of Innovation

Getting an Inside Look: Given Imaging's Camera Pill[a]

Gavriel Iddan was an electro-optical engineer at Israel's Rafael Armament Development Authority, the Israeli authority for development of weapons and military technology. One of Iddan's projects was to develop the "eye" of a guided missile, which leads the missile to its target. In 1981, Iddan traveled to Boston on sabbatical to work for a company that produced X-ray tubes and ultrasonic probes. While there, he befriended a gastroenterologist (a physician who focuses on digestive diseases) named Eitan Scapa. During long conversations in which each would discuss his respective field, Scapa taught Iddan about the technologies used to view the interior lining of the digestive system. Scapa pointed out that the existing technologies had a number of significant limitations, particularly with respect to viewing the small intestine.[b] The small intestine is the locale of a number of serious disorders. In the United States alone, approximately 19 million people suffer from disorders in the small intestine (including bleeding, Crohn's disease, celiac disease, chronic diarrhea, irritable bowel syndrome, and small bowel cancer).[c]

Furthermore, the nature of the small intestine makes it a difficult place to diagnose and treat such disorders. The small intestine (or "small bowel") is about 5 to 6 meters long in a typical person and is full of twists and turns. X-rays do not enable the physician to view the lining of the intestine, and endoscopes (small cameras attached to long, thin, flexible poles) can reach only the first third of the small intestine and can be quite uncomfortable for the patient. The remaining option, surgery, is very invasive and can be impractical if the physician does not know which part of the small intestine is affected. Scapa thus urged Iddan to try to come up with a better way to view the small intestine, but at that time Iddan had no idea how to do it.

Ten years later, Iddan visited the United States again, and his old friend Scapa again inquired whether there was a technological solution that would provide a better solution for viewing the small intestine. By this time, very small image sensors—*charge-coupled devices* (CCDs)—had been developed in the quest to build small video cameras. Iddan wondered if perhaps it would be possible to create a very small missile-like device that could travel through the intestine without a lifeline leading to the outside of the body. Like the missiles Iddan developed at Rafael, this device would have a camera "eye." If the device were designed well, the body's natural peristaltic action would propel the camera through the length of the intestine.

When Iddan returned to Israel he began working on a way to have a very small CCD camera introduced into the digestive system and transmit images wirelessly to a receiver outside of the body. Initially unsure whether images could be transmitted through the body wall, he conducted a very rudimentary experiment with a store-bought chicken: he placed a transmitting antenna inside the chicken and a receiving antenna outside the chicken. The results indicated that it was possible to transmit a clear video image. Encouraged by this, he set about overcoming the battery life problem: the small CCD sensors consumed so much energy that their batteries were often depleted within 10 minutes. Fortunately, advances in semiconductors promised to replace CCD imagers with a new generation of *complementary metal oxide semiconductors* (CMOS) that would consume a fraction of the power of CCD imagers. Iddan began developing a prototype based on CMOS technology and applied for an initial patent on the device in 1994. In 1995, he presented his product idea to Gavriel Meron, the CEO of Applitec Ltd., a company that made small endoscopic cameras. Meron thought the project was a fascinating idea, and founded Given Imaging (**GI** for gastrointestinal, **V** for video, and **EN** for endoscopy) to develop and market the technology.[d]

Unbeknownst to Iddan or Meron, another team of scientists in the United Kingdom was also working on a method for wireless endoscopy. This team included a physician named C. Paul Swain, a bioengineer named Tim Mills, and a doctoral student named Feng Gong. Swain, Mills, and Gong were exploring applications of commercially available miniature video cameras and processors. They scouted out miniature camera technology at "spy shops" in London that supplied small video cameras and transmitters to private detectives and other users.[e] By 1994 they were developing crude devices to see if they could transmit moving images from within the gut using microwave frequencies. By 1996 they had succeeded in their first live animal trial. They surgically inserted their prototype device into a pig's stomach, and demonstrated that they could see the pylorus valve of the stomach open and close. Their next hurdle was to develop a device that could be swallowed instead of surgically inserted.

In the fall of 1997, Gavriel Meron met Dr. Swain at a conference in Birmingham, England, and they concluded that their progress would be much faster if they joined forces. Swain's team had superior expertise in anatomy and the imaging needs of diagnosing small intestine disorders, while Iddan's CMOS-based sensors enabled the production of a smaller device with lower power requirements. The teams thus had complementary knowledge that each knew would be crucial to producing a successful capsule endoscope.

In 1999, the team got permission from the ethics committee at the Royal London Hospital to conduct their first human trial. Dr. Swain would be the patient, and Dr. Scapa (whose initial urgings had motivated Iddan to develop the wireless endoscope) would be the surgeon who would oversee the procedure. In October of 1999, in Scapa's clinic near Tel Aviv, Israel, Dr. Swain swallowed the prototype capsule. The first images were of poor quality because of the team's inexperience at holding the receiving antenna in an optimal position. The team was not sure how far the capsule had traveled, so they used a radiograph to find the position of the capsule. The radiograph revealed that the device had reached Swain's colon, and

thus had successfully traversed the entire length of the small intestine. The team was thrilled at this victory, and urged Swain to swallow another capsule, which he did the next morning. Now that the team was more practiced at optimizing the receiving antennas, they achieved much better quality images. Swain remarked that he "enjoyed watching the lovely sea view" of his lower intestine. Though the first capsule had transmitted for only about 2 hours before its battery life was depleted, the second capsule transmitted for more than 6 hours, and the team knew they had obtained quality images of a substantial length of small intestine.[f]

Over the next few months the team conducted several animal and human trials, and by April of 2000 they had used the device to find a small intestinal bleeding source in three patients with "obscure recurrent gastrointestinal bleeding" (a difficult problem to diagnose and treat). An article on the device was published that year in *Nature* (a prestigious scientific journal), with a header reading "The discomfort of internal endoscopy may soon be a thing of the past."[g] By August of 2001 the device had received FDA clearance, and by October of 2001 Given Imaging had gone public, raising $60 million in its initial public offering.

Given Imaging marketed its device as a system that included a workstation, proprietary software, wearable video recording packs, and the swallowable capsules (called "PillCams"). After swallowing the $450 PillCam, the patient goes about the day while the PillCam broadcasts images to a video recording pack the patient wears around the waist. When the patient returns the pack to the physician, the physician uploads the images and can both view them directly and utilize Given's computer software, which employs algorithms that examine the pixels in the images to identify possible locations of bleeding. The PillCam exits the patient naturally. By February of 2006, more than 300,000 patients had utilized the system worldwide, and many insurers provided coverage for the treatment.[h]

Until 2005, Given enjoyed the benefits of offering a medical technology with tremendous advantages over existing alternatives, and having no competitors. However, in 2005, Japanese optics giant Olympus introduced its own camera pill—the "Endocapsule"—into the European market, and received FDA approval to market the drug in the United States in 2007. In 2008, Philips Research announced that it too had developed a camera pill called the iPill that incorporated a drug delivery system, permitting the pill to release medicine directly to multiple locations within the intestine. Additionally, several teams of scientists around the world were working on developing capsule endoscopes that would incorporate robotic functions such as small legs and clamps that would enable the capsule to move, attach to the wall of the intestine, or remove a small amount of tissue for a biopsy.[i] Given defended its position in the U.S. market by filing for a thicket of patents on the technology, and by trying to rapidly build its installed base of Given workstations in hospitals and clinics. The more Given workstations that were in use, and the more physicians trained in their use, the greater the switching costs would be for a hospital or clinic to adopt a competing technology. It also began work on versions of the camera pill that would target the esophagus and the colon, respectively.

By 2011, Given had introduced several generations of PillCam technology, and had grown to $178 million in annual sales. Its products were marketed and sold in over 60 countries, and though it still faced formidable competitors such as Olympus, Given Imaging remained the world leader in capsule endoscopy devices.