

DIAGNOSTIC DEVICES

Crospon Ltd.

Balloon catheter for imaging of GERD

New imaging technology employed through a therapeutic endoscope provides the most relevant information to diagnose gastroesophageal reflux disease (GERD), according to its manufacturer, **Crospon Ltd.** Furthermore, the Irish start-up says its novel *EndoFLIP* (endoscopic functional lumen imaging probe) technology can be used to assist in GERD surgeries and to assess the results.

Chronic GERD is a prevalent disease, affecting between 10 and 20% of people in the US. It manifests itself as severe heartburn caused by stomach acid backing up into the esophagus (the tube that carries food and liquid from the mouth to the stomach). This occurs when the valve separating the esophagus and stomach—the lower esophageal sphincter (LES)—fails to close properly. If GERD symptoms can't be controlled with drugs, patients may pursue minimally invasive surgical techniques to fix the faulty junction between the stomach and esophagus.

Current methods for diagnosing GERD are far from perfect. "Any gastrosurgeon will tell you that it is very difficult to make the decision to put the patient forward for GERD surgery. Part of the reason is that the arsenal of diagnostic tools at their disposal is less than complete," says John O'Dea, Crospon's founder and CEO.

That arsenal includes endoscopic imaging to identify severe esophagitis; pH monitoring to determine acid backup, done either with a transnasal catheter inserted into the esophagus for a 24-hour period, or with a deployed capsule that attaches to the wall of the esophagus and transmits pH levels to a wearable receiver over a 48-hour or longer period; impedance testing that measures changes in electrical current as substances pass through the esophagus; or esophageal manometry, which is used for swallow studies and to measure LES pressure to assess the degree of closure of the lower esophageal sphincter.

"The problem with pH monitoring and impedance is that they only tell you if you have GERD or nonerosive reflux disease, not why you have it," O'Dea says. Likewise, manometry has come under criticism. "The American Gastroenterological Association recently issued a position statement that manometry is not a reliable diagnostic test for GERD," O'Dea says. In contrast, he continues, Crospon's *EndoFLIP* offers a more physiologically relevant way of assessing the sphincter compared with manometry. "Our technology allows you to tell if the sphincter is the cause of the GERD."

The *EndoFLIP* system consists of a series of electrodes that sit within a balloon catheter that is attached to a data recorder with a screen. These electrodes are able to measure resistance

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Business: Medical devices for the gastroenterology and drug delivery markets

Founded: November 2006

Founder: John O'Dea

Employees: 16

Financing to Date: \$7.6 million

Investors: Individual angel investors; Western Development Commission; Enterprise Ireland

Board of Directors: John O'Shaughnessy (formerly with MedNova Ltd.); Michael Quinn (Bank of Scotland); John O'Dea; Caroline Sherlock (formerly with Respironics Ireland); Conor McNamara (Western Development Commission)

Scientific Advisory Board: John Pandolfino, MD (Northwestern University); Hans Gregersen, MD (Aarhus University, Aalborg University); Barry McMahon, PhD (Adelaide and Meath Hospital, Dublin); Blair Jobe, MD, FACS (University of Pittsburgh Medical Center)

or impedance to calculate cross-sectional areas at different points along the balloon. The balloon stimulates the sphincter and acts as a challenge test to determine its functionality—a normally functioning sphincter will keep food in the stomach rather than coming back up into the esophagus.

In the procedure, the deflated balloon catheter is attached to a prefilled syringe, which is inserted into the syringe pump on the front of the *EndoFLIP* system. The deflated balloon is then passed through the working channel of a therapeutic endoscope and introduced across the lower esophageal junction under direct visualization. Once the balloon has been correctly

located, it is inflated with specially formulated conductive fluid to a specific volume. Inflation may be performed a number of times to precondition the tissue.

But the backbone of the technology is impedance planimetry, which is a technique that can convert an impedance measurement into an area measurement. The 16 electrodes in the balloon send data to the *EndoFLIP* system, allowing the generation of an image of the LES in real time. "You are creating a 16-slice image of the lower esophageal junction," O'Dea says. The display shows the changes in the estimated diameters as the balloon challenges the gastroesophageal junction. The entire test takes five to 10 minutes.

O'Dea, who earned a PhD in electronics engineering from University College Dublin, has considerable device experience, most of it in the respiratory arena. For most of the 1990s, he held R&D management positions with Nellcor Puritan Bennett, a market leader in life support and ventilation. Then, in 1998, he co-founded Caradyne, an Irish respiratory medical device company that was acquired by Respironics Inc. in 2004. Two years later, the Irish facility was closed down to consolidate sites. "We had a strong R&D team in Galway," O'Dea says. "I felt it would be a shame to have that facility scattered to the winds."

Fortunately, in early 2007 O'Dea and his colleagues came across the *EndoFLIP* technology, which had been developed by Barry McMahon and Hans Gregersen. McMahon, chief physicist and head of the department of medical physics and clinical engineering at the Adelaide and Meath Hospital in Dublin, has a strong background in endoscopic instrumentation and imaging. Gregersen, who resides in Denmark, has authored a textbook on the biomechanics of the gastrointestinal tract, and has published nearly 300 scientific papers.

"At that time, The *EndoFLIP* needed some good design engineering, rather than good research since there had already been a reasonable number of preclinical studies," O'Dea relates. He initially hired eight R&D employees from Respironics. The company has a licensing agreement with the two developers of the technology. "Royalties are within industry norms," O'Dea says.

A number of clinical papers have been published on the technique that demonstrate proof-of-principal. Most of the 30 to 50 patients were treated in Aalborg, Denmark. "You could see the effect of GERD surgery," O'Dea says. "Up until now, there has not been a good tool available to assess the degree of surgical tightening of the top of the stomach. Difficulty in swallowing after surgery is a common problem caused by overtightening. The *EndoFLIP* allows surgeons to determine during surgery if they have overtightened that particular sphincter."

The Irish company is initially focused on the US market, where approximately 700,000 diagnostic endoscopies for GERD are performed annually. Of that number, about 200,000 patients are considered for surgery, followed by nearly 35,000 patients who actually undergo surgery.

In March, Crospon submitted a 510(k) application to the FDA for *EndoFLIP* clearance. "We expect approval sometime this summer," O'Dea says. He expects that the product will hit market in the first quarter of 2009.

The purchase price of the *EndoFLIP* system will likely be in the \$13,000 to \$14,000 range, which is 10 to 20% less than manometry, according to O'Dea. There will also be a disposable catheter fee of \$250 to \$350 for each imaging session, which compares favorably to pH testing. Reimbursement scenarios are still being evaluated. "We are not in a position to make a definitive comment," O'Dea says. "However, there are a number of existing reimbursement codes for gastrodiagnostics that we believe may be usable."

The company's greatest hurdle to growth "will probably be building the clinical evidence for the *EndoFLIP*'s diagnostic capability as distinct from its imaging capability," O'Dea says. The company envisions a strategic partnership, either with one of the current diagnostic players or an entity looking to move into the space. "We hope to have something

agreed by summer," O'Dea says. "That strategic partner would probably be the distributor of the product."

The three major gastrodiagnostic players currently in the market are **Sierra Scientific Instruments Inc.** (*ManoScan*), **Sandhill Scientific Inc.** (*Insight, ZepHr*), and **Medical Measurement Systems BV** (*Solar GI, Ohmega*). All three firms offer a product for manometry (measurement of pressure in the sphincter), whereas Sandhill and Medical Measurement Systems also provide for ambulatory pH monitoring and impedance testing. **Medtronic Inc.** (*Bravo*) is the leader in capsule pH measurement.

Enterprise Ireland, the Western Development Commission, and individual angel investors seeded Crospon with €2.3 million (\$3.1 million) in June 2007. In April 2008, Crospon completed a Series A venture round of \$4.5 million from existing investors for completion of design, manufacturing start-up, and early clinical work. It expects to raise an additional \$4.5 million in the third quarter of 2009.

Crospon plans to launch the first of a series of other balloon catheters for different parts of the gastrointestinal tract, including for bariatric surgery, the esophagus, and the anorectal region in late 2009. The company also plans to deploy a nonendoscopic version (transorally or transnasally) of the *EndoFLIP* sometime next year.

Separately, Crospon entered a licensing agreement with **Hewlett-Packard Co.** last September for a drug delivery platform that enables painless, controlled release of one or more drugs in a single patch applied to the skin. Unlike transdermal patches for nicotine delivery (which rely on absorption through the skin), the HP-developed skin patch uses microneedles that barely penetrate the skin. As a result, O'Dea says that patient discomfort is significantly reduced and the patch can be used with a much wider variety of drugs and biopharmaceuticals.

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—BOB KRONEMYER

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