

As Published In:

# START-UP

Windhover Information Inc. | windhover.com | Vol. 14 No. 7 | JULY/AUGUST 2009

**GASTROENTEROLOGY  
DEVICES**

## invendo medical GMBH

*Potentially painless, sedationless  
colonoscopy*

Apparently, most people would rather have a root canal than undergo a colonoscopy. Colorectal cancer makes for the ideal screening paradigm; it's deadly—in the US, more than 50,000 people die from the disease each year; it afflicts people with no identifiable risk factors other than advanced age, and perhaps 90% of the cases would be curable if caught early. Nevertheless, compliance with colorectal screening recommendations is low, only around 50% for colonoscopy, the gold standard for detecting precancerous polyps.

The disconnect is startling: colonoscopies prevent deaths from cancer, but the majority of the patients aged 50 and above who should be having the procedures at regular intervals just don't, because colonoscopy is more invasive than people think a screening procedure ought to be. As conducted with conventional semi-rigid endoscopes, colonoscopies can be painful, so in the US, the majority of patients undergo the screening procedures in a state of sedation, and, in the largest proportion of cases, even deep sedation.

Many patients avoid the procedures because of logistics—a colonoscopy procedure involving deep sedation requires them to take a full day off from work, and, since they're recovering from the effects of anesthesia, they will not be discharged until about an hour after the procedure and unless someone else can drive them home. Indeed, under the current state of affairs, screening

colonoscopies present difficulties not only for patients, but for all three health care constituents: the patients, the providers and the payors.

From the provider side, working with anesthesia or even conscious sedation creates the need for patient management above and beyond the scoping procedure, including infrastructure and staff to manage patients recovering from sedation. Payors, too, don't like the additional risk of anesthesia, or having to pay an extra fee for the anesthesiologist required to administer the drug propofol for deep sedation.

Aware of these drawbacks, in 1992 two German physicians, Konstantin Bob, MD, and Alexander Bob, MD, founded a new endoscope company that would eventually become **invendo medical GMBH**, with the goal of enabling sedationless colonoscopy. The company's early funding of DM 5 million (approximately \$3 million) came from an angel investor, who, as a survivor of pancreatic cancer, had first-hand knowledge of the burden of numerous colonoscopic examinations. The company plodded along, and it wasn't until 2001 that it began raising its first venture capital money in earnest, convincing Heidelberg Innovation to invest €1.5 million. By 2007, the company had hit a rough patch—in need of funding and having failed to deliver on its milestones, it was close to closing its doors. Two venture partners at Heidelberg Innovation intimate with the company crossed over into its operations to completely revamp the company—Berthold Hackl as CEO, and Timo

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**Contact:** Berthold Hackl, CEO  
**Business:** Single-use endoscope  
**Founded:** 2001  
**Founders:** Konstantin Bob, MD; Alexander Bob, MD; Manfred Lautenschlaeger  
**Employees:** 23  
**Financing to Date:** \$40 million  
**Investors:** Heidelberg Innovation; TVM Capital; Wellington Partners; 360° Capital Partners; Mannheim Holdings LLC  
**Board of Directors:** Dr. Gerald Moeller, Chairman (formerly Boehringer Mannheim); Prof. Dr. Ulrich Abshagen (Heidelberg Innovation); Sidney Braginsky (formerly Olympus North America); Jürgen Dernbach (Lautenschlaeger); Dr. Rainer Strohmer (Wellington Partners); Dr. Axel Polack (TVM Capital); Diana Saraceni (360° Capital Partners)  
**Medical Advisory Board:** Lawrence B. Cohen, MD (Mt. Sinai Hospital, NY); Piet de Groen, MD (Mayo Clinic College of Medicine); Nicolas Hoepffner, MD (Centrum Gastroenterologie, Bethanien, Frankfurt); Felix W. Leung, MD (David Geffen School of Medicine, University of California, Los Angeles); Douglas K. Rex, MD (Indiana University School of Medicine); Thomas Roesch, MD (University Hospital Hamburg-Eppendorf)

Hercegi as CFO. Hackl had previously been on the industry side for 16 years, as a member of the management teams at Pharmacia Biotech and Biacore (both now part of GE Healthcare), and at orthopedics company Stratec Medical (now Synthes Inc.), among others.

The new management team did a major overhaul, brought in new investors Wellington Partners, TVM Capital, and 360° Capital Partners, bringing its total funding to date, as of April 2009, to \$40 million, and added John Cifarelli as EVP, global markets, to a management team that also includes the new chief technology officer Christoph Schnurer-Patschan, PhD, who holds a PhD in physics and has more than 15 years of experience in technology-driven start-ups. Cifarelli brought additional market development and endoscopy experience to the team; joining *Invendo* from start-up **PEAK Surgical Inc.**, Cifarelli had also been with endoscopy market leader **Olympus Corp.** for 18 years as VP of sales and most recently as general manager/VP of surgical endoscopy.

The newly revamped *Invendo* medical crystallized its mission around solving not just the single issue of sedationless colonoscopy, but all three of what the company characterizes as the major drawbacks of colonoscopy. Cifarelli lists them as 1) patient discomfort (triggering the costs and complications of sedation); 2) the ease-of-use issue, or rather, the challenging learning curve of conventional endoscopes; and 3) the reusability that leads to cumbersome cleaning routines and residual infection risk. The latter issue has bubbled to the top in the past six months in light of an ongoing investigation at certain VA Medical Centers, which sent letters to thousands of patients recommending that they seek testing for HIV, hepatitis B and hepatitis C after undergoing procedures with contaminated endoscopes. Some of those patients were actually infected, including with hepatitis C.

“We will play to our strengths—the sedationless component and the improved efficiency. There will be those patients drawn by the absence of sedation, and physicians excited about being able to differentiate themselves and attract new patients, run a less complex practice and increase procedure volumes.”

—John Cifarelli

*Invendo* has a platform that addresses all three issues with a new technology that demonstrates the potential to be less burdensome and less painful than conventional scopes on unsedated patients, also addresses the ease-of-use and fatigue issue for physicians, and finally, obviates the issue of hygiene and the cleaning infrastructure, with a single-use model.

Hackl explains that the pain and discomfort that calls for sedation stems from the fact that conventional scopes are semi-rigid. They need to be, because they are advanced by pushing through a long and winding organ. Flexibility is necessary to negotiate the bends and curves of the digestive tract but so also is rigidity, because physicians otherwise can't push conventional scopes forward. In effect, a conventional scope requires the anatomy to conform to the medical device, and Hackl points out that if you push something semi-rigid against a soft tissue like the bowel, the soft part gives way. That's what causes patients pain. *Invendo*'s endoscopy system contours to the anatomy rather than *vice versa*, says Hackl.

*Invendo* has developed a non-push scope that drives itself under the operator's control. The physician doesn't actually touch it during the procedure, says Hackl; remotely controlled, it only increases its length at the tip, like a rolled-up carpet as it unfurls. Hackl says “Think of the floor as the colon wall and the carpet as the instrument. When you roll it out, it only moves at the tip. The rest of it lies still so there is no shear force.” Of course it's not in the form of a rolled-out carpet, Hackl explains, but an inverted sleeve where one polymer hose is pulled over itself to create a double-

walled hose. “You move the inner wall of that double-walled hose ahead, and it moves inside until it reaches the tip, where it inverts inside-out and grows.” The device has an instrument channel, and a novel electrohydraulic deflecting tip. The doctor steers the endoscope exclusively with a simple handheld device that has a joystick for deflecting and buttons for rinsing, suction, and insufflation. The system is propelled by an external motorized drive unit.

*Invendo*'s system gained the CE mark at the end of 2007 and has already been used in more than 360 cases in Europe during clinical development. The newest member of the management team, Cifarelli, says that when he joined he was struck by just how vast the accumulated clinical experience already was and how easy the procedure was for patients. “The patients walk in, they lie down, they get scoped, and afterwards, without any recovery room time, they get up, walk out, and drive home. For an asymptomatic and healthy 50-year-old getting screened, that's how it should be,” he says.

Preeminent gastroenterologist Douglas Rex, MD (of the Indiana University School of Medicine), was in Germany for investigator training recently, says Hackl, and it took him just two cases to become comfortable and proficient with the procedure using the *Invendo* colonoscope. He was doing some difficult cases in which the rate of reaching the cecum (at the end of the large intestine) was historically low, and according to Hackl, “it worked out beautifully.” Rex came away from the experience saying, “I thought the image quality was quite good and very adequate for screening. I do think that the device is pretty operator-independent with regard to passage and I will likely train my nurse practitioner to do it—at least the driving to the cecum.”

That ease of use will be a key differentiator that will have an impact on workflow and throughput in the endoscopy suite. Today, gastroenterologists schedule endoscopy days, and may do ten to 16 cases in one day. They start in the morning and do cases until the end of the day, scheduling perhaps 40 minutes for each one. A difficult case can throw off the entire schedule, which is a common source of frustration, says Cifarelli. But

there is also the issue of fatigue. “The manipulations the physician has to do are almost like doing a dance. They have to manipulate the scope quite a bit as the colon works around the scope. At the end of the day they are fatigued.” With the invendo system the gastroenterologist can do the procedure sitting down or standing up with just the control device in his or her hand.

Because the scope does most of the work, says Cifarelli, it potentially reduces the dependency on skill, which could be beneficial for more widespread use in colorectal cancer screening. The company’s experience so far in investigator training points in that direction, Cifarelli says.

There is one additional drawback that invendo addresses—the need to clean and disinfect conventional endoscopes after each procedure and the delays that sometimes ensue when a disinfected scope is not ready. Invendo addresses this issue with a disposable model that appears to match up evenly with the price of capital-equipment-based products today, according to Cifarelli. “The cost of ownership of scopes is quite high today. In today’s market list prices for video colonoscopes are between \$30,000-\$38,000 for the scope alone. Each scope, on average, requires a major overhaul about once a year, which is another \$8,000-\$9,000, and each practice requires many multiples of scopes to get the cases done. The cost of ownership of our single-use product will be advantageous to providers.”

Invendo is now getting ready to conduct its pivotal trial for FDA approval, which the

company will begin later in the year. The company expects to file for FDA clearance in the US early next year.

Of course, when it gets there, it will have to face off against Olympus, the dominant player by far with more than 70% of the GI endoscopy market and more than 30 years of development behind it, and other large players. Part of Cifarelli’s job is to create a direct sales force in the US. Beyond that, he says, “We will play to our strengths—the sedationless component and the improved efficiency. There will be those patients drawn by the absence of sedation, and physicians excited about being able to differentiate themselves and attract new patients, run a less complex practice, and increase procedure volumes.”

It has taken a long time for invendo to get to this point because with new and improved technology, breaking into a market dominated by a large player like Olympus isn’t as easy as it sounds. Newcomers have to beat standards in an established marketplace. Invendo looks like it has a great shot at the market, but others haven’t made it. NeoGuide Systems Inc. was developing a robotic endoscope that would simplify insertion, but the product was overly complex for the marketplace and didn’t bring sufficient benefits. Having closed up shop, its assets, which have applications in the NOTES (natural orifice transluminal endoscopic surgery) space, were recently acquired by **Intuitive Surgical Inc.** **Boston Scientific Corp.** has successfully created a large market for single-use instruments for GI endoscopy that it dominates, but it still doesn’t have its own

endoscope, since it ceased development of its in-house project. The *PillCam*, the swallowable capsule endoscopy camera of **Given Imaging Ltd.**, while great for imaging the small bowel, hasn’t been able to match the sensitivity and specificity of colonoscopy in colorectal cancer screening, and hasn’t been approved by the FDA for colonoscopy.

Other companies are working their way around some of the problems inherent in colonoscopy; **Johnson & Johnson’s Ethicon Endo-Surgery Inc.** division just got the nod of an FDA advisory panel on its *SEDASYS* computer-assisted personalized sedation system, which will allow physicians and nurse practitioners to administer the anesthetic propofol for colonoscopy without an anesthesiologist.

Invendo feels like it can succeed where others have failed with one system that addresses all of the major shortcomings of conventional colonoscopes. Hackl says, “This is one of the largest diagnostic markets of all in terms of numbers of cases and dollar volume and there seems to be endless growth, because the population of age 50 and older is increasing for the next 10-20 years. In the US, there are potentially more than 14 million and a large part of the eligible population remains unscreened. There is increasing awareness that screening is a good thing. If, with a single-use, painless device we can help popularize screening and pick up even a single-digit market share in this arena, that’s a big chunk of money.”

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—MARY STUART