

# Medtech Ventures

This year's EuroMedtech partnering conference, organised by EBD Group, took place in May in Turin, Italy. The two-day event saw over 740 one-to-one meetings take place – up 14% from the previous year – as companies sought investors and partners to help bring their innovation into the market. *Clinica's* Medtech Ventures highlights three very early-stage start-ups which stood out from the crowd

## Hot pick of the month

### ENDOLUMINA

**Specialty area(s):** Real-time assessment of upper GI health

**Based in:** Boston, Massachusetts

**Founded in:** 2010

**No. of employees:** 1

**Total investment received to date:** Seed funding less than \$1m

EndoLumina may have only been up and running for a few months, but CEO Nicholas Barker says that the firm's technology has already attracted a lot of attention from the big medtech players.

The company is developing a swallowable capsule device designed to detect bleeding in the upper gastrointestinal (GI) tract. Spontaneous upper GI bleeding occurs in around 10 million patients worldwide each year, with certain patients – including the elderly and those who are on anti-coagulant drugs and NSAIDs – being more vulnerable than others. Upper GI bleeding is very dangerous and requires urgent clinical attention, says Dr Barker. "The problem is that in most of the suspected cases of upper GI bleeding, you cannot tell if the patient is bleeding or not. The only solution right now is an endoscopy of the upper GI tract, which is carried out under sedation. This is not only traumatic for the patient, but sedation is also contraindicated for some cases, like older, haemodynamically-compromised patients," he tells *Clinica*. Moreover, a full endoscopy procedure costs around \$2,000, which is very expensive to the healthcare system particularly if the patient is found to not be bleeding at all, which accounts for about 40% of suspected cases.

Endolumina is developing a technology which could act as a triage device to

prioritise which patients require urgent treatment. It consists of a capsule embedded with two proprietary sensors. The patient swallows the capsule and as soon as the capsule detects blood – it takes about two minutes to reach the stomach – it differentiates whether it is old or fresh blood and immediately transmits this data wirelessly to an external monitor. Endolumina's system would provide real-time, unambiguous answers that do not require any interpretation, which means the information to support triaging decisions can be generated by a nurse or a paramedic, without the need for a specialist. "The advantage of the technology is that it can be administered in the ambulance, in the ER, in the hospital, in the field," says Dr Barker.

"So if our capsule does not detect any blood, a full endoscopy may not be needed. This accounts for around 40% of patients who present with suspected GI bleeding," he continues. "If it detects only old blood and not new, it means these patients have bled previously but are not bleeding at that time so they would need a non-urgent endoscopy follow-up. That can be scheduled later and doesn't need to be done overnight or weekend. These patients usually account for another 40% of suspected cases." Around 20% of the patients who present are actually actively bleeding and these would then require urgent attention, and Endolumina's technology could classify these patients quickly. "What's key is that the patients who need urgent endoscopic surgery, their outcomes and the overall cost to the healthcare system improve dramatically the quicker the intervention," says Dr Barker. "There is a significant body of literature already to support this fact".

In terms of market competition, there are video capsules – Given Imaging's PillCam, Olympus's Endocapsule, and SmartPill's eponymous device – currently available. However, while these capsule devices do offer a less invasive alternative to conventional endoscopy, they have not been designed as a triage device and have significant limitations which would not allow timely patient triage, based on the information they provide. "These video capsules take around 24 hours to transit, mouth to anus. The video is downloaded and it takes about a couple of hours for a physician to watch the video and interpret what is being seen. So there is a lot of time involved – it's not a triage device at all," says Dr Barker. Another disadvantage is the risk of bleeding lesions being missed by the physician. This could be due to the view being obscured by the presence of old blood in the tract, and to the random passage of the capsule. "Video capsule endoscopy does not offer real-time detection, does not allow immediate surveillance, is not specific for fresh blood and open to interpretation errors – Endolumina's technology solves all of these problems," the CEO tells *Clinica*.

Triaging patients with suspected GI bleeding would be the lead indication, and Endolumina estimates that capturing just over 10% of the US market alone would be worth around \$150m.

However, the total market for the company's technology could expand to as much as \$2bn, taking into account the possible different indications. One of these includes using Endolumina's technology to monitor post-endoscopic surgery patients.

Re-bleeding occurs in around 20% of patients who have previously had upper

GI bleeding. Endolumina's capsule could be sutured to the wall of the GI tract after surgery, and if a re-bleed occurs, the capsule will detect the fresh blood and raise the alarm. "The suture will be biodegradable, so could keep the capsule in place for about 4-5 days post-surgery, before passing out of the body as normal," says Dr Barker.

Another important, potential indication for Endolumina's device is the monitoring or screening of cardiac patients, who have to take anticoagulant drugs, such as warfarin and Plavix. Such anticoagulant drugs dramatically increase the risk of upper GI bleeding. "There is a role for our device before and after cardiovascular intervention. Prior to the cardiac procedure, patients are usually, given a full upper GI endoscopy to find out they are predisposed to bleeding, have bled at some point, or are bleeding and no one knows about it," explains Dr Barker. Instead of endoscopy, EndoLumina's technology could provide a more convenient and cheaper alternative to assess the patient's risk characteristic. This patient screening could also be done by the cardiology team in the hospital, who then can choose to involve GI specialists based on the risk assessment. Then after the

cardiac intervention, when the patient is on an anticoagulant regime, Endolumina's capsule can be used to monitor the patient for spontaneous GI bleeding.

"The advantage of the cardiac indication is that the patient is already having an expensive cardiac procedure so the EndoLumina pill could be an adjunct to the whole procedure. It may not need to be reimbursed under a separate code, and it can be administered by the cardiologist," says Dr Barker.

As Endolumina's system is mostly made up of off-the-shelf electronic components, the company believes the manufacturing could be easily scaled up and the profit margins could be significant.

For now, the technology is still in the very early stages of development. A small preclinical study assessing its fresh blood sensor on five pigs has been completed, the results should publish shortly. The sensor has so far demonstrated it is able to detect as little as 1ml of blood in gastric contents, according to Dr Barker.

The company is now looking to raise \$3.5m to help complete product development and all the way through to a Phase I clinical trial. This would be the first

financing round for the company, which has so far been operating as a very lean organisation and intends to continue to be as capital efficient as possible. Says Dr Barker: "Like most medtech start-ups today, we subcontract most functions; our goal is to be a virtual company."

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## Did you know?

Endolumina's technology is the result of a collaboration between researchers – three of whom are the company's co-founders – at Harvard University and Brigham & Women's Hospital. Chris Thompson is a gastroenterologist and director of development endoscopy at B&W and an assistant professor at Harvard; Marvin Ryou is a clinical fellow in gastroenterology at B&W; and Bob Westervelt is a Mallinkrodt Professor of Applied Physics and director of the Nanoscale Science and Engineering Center at Harvard.

## ESTIMME

**Specialty area(s):** Electrical stimulation implant for tinnitus

**Based in:** Tel Aviv, Israel

**Founded in:** 2008

**No. of employees:** 5

**Total investment received to date:** Seed funding of under \$1m

An estimated 1% of the world population suffer moderate-to-severe tinnitus, an ear disorder where the affected individual perceives the sensation of sound within the ear, independent of an external source.

Tinnitus stems from damage – caused by various factors ranging from repeated exposure to loud noise to head and neck trauma – to the tiny hair-cell endings of the hearing nerve in the cochlea. These hair cells are responsible for converting vibrations into neural signals, which are sent up the cochlear nerve to the brain and interpreted as sound. When damaged, the hair cells fail to send these signals and the lack of these signals leads to hyperactivity in the central auditory system, which in turn results in sound being perceived, even in the absence of external stimuli.

While there are treatments aimed at tinnitus sufferers, these products are mainly

palliative and do not get to the root of the problem, which is neurological in nature.

"The treatments and devices that are available try to help the patients ignore the tinnitus sensation or mask it," says Michael



ESTimME's neurostimulation implant for tinnitus

Vardi, CEO of ESTimME, an Israeli start-up developing a technology that specifically targets the neuromechanism that causes tinnitus.

ESTimME's technology has its roots in previous research on cochlear implants, devices which electrically stimulate the cochlear nerve to restore hearing in

profoundly deaf patients.

"In recent years, work on cochlear implants have shown that about 70% of deaf patients who also have tinnitus experience a beneficial effect once they have had a cochlear implant fitted," says Mr Vardi. "This is logical, as the electrical stimulation regains the loss of neural activity in the neurons of the damaged hair cells, so this reduces the hyperactivity in the auditory pathway that causes tinnitus."

However, fitting tinnitus patients with cochlear implants is not a viable solution. Not only are the devices very expensive, since it is a hearing-aid implant dedicated to treating profound deafness, during the implantation, the ossicles are removed (the three tiny bones in the ear) and the cochlea irreversibly damaged, resulting in the loss of autonomous hearing, he adds.

"With our technology, we are applying the same principle of action as cochlear implants, but using a very minimally invasive approach which does not require the patient to be put under heavy anaesthesia. In addition, the implantation is completely reversible," Mr Vardi tells *Clinica*.

Another advantage of our system is that the stimulation is non-audible. "Patients

do not hear any masking sounds – they may have a slight tingling sensation of electricity but that dissipates after a couple of minutes,” the CEO says. The EStimME implant consists of a tiny neurostimulator, as small as a grain of rice, which sits in a self-expandable stent-like structure. The implant is delivered through the ear canal, by raising the ear drum, and into the middle ear. The stent then expands to adjust itself to the contours of the middle ear, and the neurostimulator is fixed in the vicinity of the round window membrane. “Stimulating the round window is a bit similar to cochlear stimulation because of the high electrical conductance of the membrane, so we’re influencing the cochlear without having to penetrate it. It’s extracochlear stimulation, we’re keeping the cochlear intact. There’s no drilling no heavy tissue damage,” explains Mr Vardi. Once the implantation is complete, the neurostimulator is then programmed and powered by an external unit, via radiofrequency.

EStimME has already developed a fully functional prototype of the system, although it has not yet done a clinical study on the

system itself. For now, the company is running a clinical trial assessing the safety and efficacy of applying electrical stimulation to suppress tinnitus, using an off-the-shelf system which allows different parameters of neurostimulation to be controlled.

“What we’re doing now is very similar to the screening process in other neurostimulation therapies (ie spinal cord stimulation, deep brain stimulation). In our screening process, we are able to tell which individual would be a good candidate for electrical stimulation therapy. So far, about 50% of our patients have responded very well. Patients who have had some kind of cochlear damage that resulted in tinnitus have reported moderate to significant suppression of tinnitus.” The length of time which this suppression is sustained varies from patient to patient and can range from hours to days – some, even weeks – following the stimulation, says Mr Vardi, adding that the treatment protocol could be different for each patient, depending on how they respond to the therapy. “There is strong evidence of residual inhibition. The stimulation could be carried out twice a day – once in the morning, once at night – for an

hour, and the patient would then experience residual inhibition throughout the day.” The advantage of having an external control unit is that the patient would be able to fully control the stimulation themselves and change their regime accordingly.

The company has so far been financed by funds from the RAD BioMed Accelerator in Israel, where the firm is also based. It has also received grants from Israel’s Office of the Chief Scientist. EStimME is now looking to raise \$1.5m in its first round of financing. The funds would enable completion of EStimME’s R&D activity – running a study with the implantation of the device in large animals, and production of the clinical batch to be implanted in humans – and take it to the verge of running a pilot study. “By that stage, we hope to have very good strategic partners,” says Mr Vardi. If all goes to plan and the pilot study runs successfully, the company could CE mark its device as early as 2014.

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## SIRIUS IMPLANTABLE SYSTEMS

**Specialty area(s):** Cardiac rhythm management devices

**Based in:** Granot, Israel

**Founded in:** 2004

**No. of employees:** 3

**Total investment received to date:** Seed funding under \$1m

“Every decade has seen a new innovation in the field of pacemakers. In the 1990s, it was the decade of pacing diagnostics. In the 2000s, it was remote monitoring. In this decade, we’re moving towards leadless pacemakers,” says Dan Gelvan, who is confident his company Sirius Implantable Systems would be at the vanguard of this technological trend.

There are two key issues which must be resolved in the development of a successful leadless pacemaker. The first is the routes of communication between the external and internal source and the second is a power source for the pacemaker. “The first issue is not a big problem; there are many solutions available for wireless communication,” says Dr Gelvan. The issue of finding a viable power source, however, is trickier, as the pacing lead plays an integral role as a conduit for the delivery of energy pulses to stimulate the heart.

Sirius is developing a technology that generates electrical energy originating from the movement of the heart itself. “Our generator can be designed as a pacing device in itself – for example, like a small button on the heart – or it can act as a leadless electrode that is subordinate to another device,” Dr Gelvan tells *Clinica*.

It is this latter application – a leadless electrode for cardiac resynchronisation therapy (CRT) – which the company would most likely go for first, before targeting the bradycardia pacing application. “up to 40% of CRT implants fail, and this is partly because the electrode lead cannot be implanted at a location that is optimal for the therapy. That’s equivalent to \$1bn of therapy wasted – our technology can eliminate the problem of lead positioning and save money. There is an acute need to improve the current CRT technologies but no good solutions yet” says the CEO.

Leadless bradycardia devices also have a clinical advantage over their wired cousins. “Leadless pacemakers/electrodes can go on the left side of the heart, which reduces the risk of atrial fibrillation. Conventional pacemakers only go on the right side of the heart,” explains Dr Gelvan. The company has

already done animal trials on its technology and has demonstrated that the generator is able to harness enough energy to power a pacemaker. It is currently refining the design of the generator and is looking to raise €1.8m (\$2.6m) to complete generator development. “The technology is conceptually at a late-stage; it would take us about two more years to have a full prototype,” says Dr Gelvan. If the company is able to raise more money, it should be able to begin clinical trials “about three years from now”.

Sirius is far from alone in the leadless pacing field. In May, St Jude invested in Nanostim, which is developing a miniaturised leadless pacemaker, and the deal included an option for the multinational to buy the Milpitas, California-based start-up. EBR Systems, another California company, is developing the WiCS wireless cardiac stimulation system, which uses ultrasound to transfer energy from the parent device to the electrode.

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