

## Therapeutic focus - Responsive neurostimulator technology shocks epilepsy market



[Elizabeth Cairns](#)

Devices that send electrical impulses through nerves to the brain as a therapy for epilepsy have been around for more than 15 years. Until recently, the best this technology could do was to reduce the intensity and duration of seizures. Now, though, a technology has reached the US market that can head seizures off before their effects are felt.

NeuroPace gained FDA approval for its responsive neurostimulation (RNS) system late last month, beating companies including Medtronic to the punch. "It's the first responsive closed-loop technology for any neurostimulation indication, and it certainly is for epilepsy," Frank Fischer, NeuroPace's chief executive, tells *EP Vantage*. "We can disrupt and essentially prevent the seizure."

### Closing the loop

Closed-loop stimulation technology is able to detect the minute alterations in the brain's electrical activity that presage an epileptic seizure and automatically deliver precisely calibrated shocks to disrupt it. And it has been sought after by many companies.

In August, Medtronic's deep brain stimulation device Activa PC+S, which can sense electrical disturbances and deliver shocks, was CE marked for four disorders including epilepsy ([Medtronic's first-of-its-kind brain implant could close the loop, August 8, 2013](#)). But the software is not yet sophisticated enough to allow the PC+S's sensor to automatically trigger the stimulator - US trials designed to collect data to allow this have just started - so Medtronic's is not a true closed-loop system. The largest pure-play medtech company has been left in NeuroPace's wake.

Approved for use in patients with uncontrolled partial onset epilepsy, NeuroPace's RNS system consists of electrodes placed near the epileptic focus in the brain, connected to a neurostimulator device which is itself implanted in the skull. "Once implanted, the system continuously monitors the electrical activity from the electrodes and when the patient's unique pattern of abnormal activity that may lead to a seizure is detected by the device, it delivers imperceptible levels of stimulation to disrupt that abnormal activity so it doesn't get picked up by the rest of the brain and thereby result in a seizure," Mr Fischer says.

NeuroPace is also challenging its most direct competitor, Cyberonics, formerly the only company with an FDA-approved device for epilepsy. Cyberonics' vagus nerve stimulation device has been approved in Europe since 1995 and in the US since 1997. The neurostimulator is implanted subcutaneously in the chest with leads to electrodes that wrap around the vagus nerve on the left side of the neck.

"The vagus nerve stimulation (VNS) dampens down those electrical discharges, in some cases stopping them altogether," Greg Browne, chief financial officer at Cyberonics, says. "In almost all cases it will reduce the intensity of seizure and shorten the recovery period from seizure."

### Cost-effectiveness

Unlike NeuroPace's RNS, the VNS sends impulses constantly, Mr Browne says. "The standard settings will be 30 seconds on and five minutes off. It stimulates 24 hours a day until the battery is depleted." The battery lasts around six years on average, compared with just under four years for NeuroPace's system.

The two devices are approved for the same indication in the US - partial onset seizures. Both firms place the market at around 400,000 patients. In Europe, though, Cyberonics' VNS is approved for patients who suffer from any type of seizure.

NeuroPace has not yet sought CE marking in Europe; the company has taken the highly unusual step of pursuing US approval first. "All of our efforts are US-based. We wanted to be able to get through the regulatory process here and then scale up manufacturing and develop the business. Next year we plan to initiate the activity for a CE mark and commercialise in 2015 in selected non-US countries," Mr Fischer says.

"Virtually every part of our system is a custom component: integrated circuits, battery, you name it. The cost

of manufacturing per unit is frankly prohibitive if you try to commercialise in low volume anywhere,” he says.

Cyberonics’ device may not be able to pre-empt seizures before they hit, but it has two distinct advantages over the newer system: it is less invasive, and it is cheaper. Mr Browne says the VNS system sells for around \$20,000 in the US and \$13,000 in Europe, adding that the company has cost-effectiveness data indicating that the device pays for itself in the US in around 18 months by reducing hospital visits.

## Rivals

The company is also working on a new device that matches NeuroPace’s offering more closely. The company has developed a responsive stimulation device which it has submitted for approval in Europe and which it hopes to have on the market within about three to six months, Mr Browne says. “That device attempts to detect when you’re about to have seizure activity or a seizure has just begun and fire off stimulation in response to that.”

While the US remains a two-horse race there are five other companies attempting to contend in the European epilepsy market. Israeli firm Cerebral RX and Neurotech, based in Belgium, both have VNS devices but neither is close to challenging Cyberonics’ dominant position in the market. Neurotech was bought by Sorin a year ago, and it is possible that Sorin intends to devote the technology to an entirely different indication.

There are also two external stimulation devices approved in Europe. NeuroSigma has a device that stimulates the trigeminal nerve which runs across the forehead; its Monarch system consists of a pad placed across the forehead and a generator worn at the waist. German group cerbomed, in which Cyberonics has invested, has developed a device that fits inside the ear and stimulates the auricular branch of the vagus nerve. It is attached to a generator that the patients can carry in their pocket; they must place it in the ear to allow stimulation five times a day.

Mr Fischer says that although its newly-approved technology makes it an attractive takeover target, NeuroPace’s ambition is to go it alone, perhaps going public in a few years’ time. “Our intention is to have the most significant company in the neurostimulation modulation area,” he says.

With over 100,000 devices implanted worldwide, Cyberonics is far and away the market leader, so NeuroPace has a long way to go. But it is bringing something new, and on the technological front, more established companies are playing catch-up.

Neurostimulation devices for epilepsy				
Manufacturer	Device name	Type of technology	EU CE mark	US approval
Cyberonics	VNS Therapy System	Vagus nerve stimulation	1995	1997
NeuroPace	RNS System	Responsive neurostimulation	Expected 2015	2013
cerbomed	t-VNS	External stimulation	2010	-
Cerebral RX	FitNeS	Vagus nerve stimulation	2012	-
Sorin	ADNS-300	Vagus nerve stimulation	2012	-
NeuroSigma	Monarch	External stimulation	2012	-
Medtronic	Activa PC+S	Deep brain stimulation	2013	-

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