“Like taking away a part of myself” — life after a neural implant trial

Neural implants can give people with neurological disorders a new lease on life. But it can all be taken all away at the end of the trial.

Liam Drew

By her late 40s, Rita Leggett’s epilepsy had brought her to a dark place. The possibility of a seizure meant she would leave her house only when accompanied by her mother or taken to see her neurologist in Melbourne. When this neurologist suggested she enroll in a trial to test a device that would warn her of impending epileptic activity — an experimental brain implant — she jumped at the opportunity. Three years later, when the device was removed, Rita was heartbroken.
Leggett was diagnosed with epilepsy at 3 years of age. In the tiny Australian town where she grew up in the 1960s, no one knew about this disorder — or cared to understand it. “I was picked on all the time,” she says. “I had no friends.”

When Leggett was 12, her seizures seemed to stop. Gradually, she began to trust that she could have a happier life. She learned to drive. She got a job. But at 18, she was struck by a severe seizure at work. “This was my introduction back into the real world of Rita.”

In late 2010, Leggett was fitted with the experimental device developed by neurotech company NeuroVista. This device detected activity patterns predictive of an upcoming seizure and ‘pinged’ a handheld device that indicated to Leggett that she might experience a seizure within the hour. This allowed her to take a prophylactic dose of clonazepam and take herself out of harm’s way.

“Most people had a reasonable benefit and some people had a spectacular benefit,” says Mark Cook, the University of Melbourne neurologist who led the trial. Of Leggett, he says, “I don’t think anyone could have imagined that anyone could do so well from this device.”

Prior to the trial, Leggett was having around three seizures a month. During the trial, she had none. “I found a new lease on life...” she says, “I could do things that I hadn’t done before. I was happy.” This included feeling well enough to date, and she met the person who became her husband.

As the trial proceeded, Cook and the NeuroVista staff presented potential investors with the first direct evidence that future seizures could be predicted. However, these investors, Cook says, were uneasy about backing such an invasive technology and were worried that patients would not be interested in such a drastic intervention. NeuroVista soon folded.

The implanted devices had a 3-year battery-life. The trial was scheduled for 2 years, with the protocol allowing for an optional extra year of use “as dictated by reasonable medical care.” However, with the company closing shop, there was no option but to explant the participants’ devices.

Leggett’s husband pleaded to buy the device. However, he and Leggett were told this was impossible. The device was built with proprietary components, and without ongoing manufacturing, there was no way to repower it. More pressingly, without the company, there would be no infrastructure to monitor the data and recalibrate the device. Just under 5 months after her wedding, Leggett’s device was removed.
“I didn’t want to let it go,” she says, 7 years on. “The device and I were one. We were successful. It was like taking away that part of myself that made me complete.”

**No trial run**

Implantable brain devices entered mainstream neurology in the 1990s after deep brain stimulation (DBS) was shown to suppress tremors in Parkinson’s disease. The US Food and Drug Administration (FDA) approved DBS for Parkinson’s disease in 1997, for dystonia in 2003 and for epilepsy in 2018, and in 2009, DBS was granted the FDA’s humanitarian device exemption for the treatment of obsessive–compulsive disorder.

Further promising results from several trials using DBS for a range of neuropsychiatric conditions, considerable advances in technology and gains in understanding the functions of various brain regions have driven considerable enthusiasm for implantable brain devices.

However, there is growing concern about post-trial care for these devices. “Our sense as a community is that we could be doing better in post-trial responsibilities for neurodevices,” says Saskia Hendriks, a bioethicist at the US National Institutes of Health (NIH) Clinical Center in Bethesda and lead author of a 2019 review of post-trial responsibilities by an NIH working group. “We currently lack a definitive ethical or regulatory framework and even standard practices regarding post-trials responsibilities in neural device research.”
"I don't want people to suffer like me" says Rita Leggett who took part in a trial testing a neural implant device. Credit: Rita Leggett

One major challenge of this type of work is that animal models only go so far in helping test devices. For researchers to learn if DBS can treat a new indication, people must volunteer to
participate in trials of experimental treatments, and unlike with drugs, there can be no preliminary safety testing for these devices in healthy volunteers. Testing must start in people with serious neurological conditions, most of whom have exhausted other treatment options. If an experimental device improves their situation, it is typically the only known effective intervention for them, and when the device trial terminates, the volunteer still has an implant.

“We consider our operating theatre to be our laboratory,” says Michael Okun, a neurologist at the University of Florida who specializes in movement disorders and developing DBS methods for treating them.

Gabriel Lázaro-Muñoz, an ethicist at Baylor College of Medicine in Texas, says that trial organizers have a responsibility to do what they can to ensure ongoing access to a device if it is successful. Part of that responsibility, he says, stems from reciprocity, given the invaluable contributions to technology development made by trial participants.

These people face the intrinsic dangers of having the device implanted — this is not an extremely high-risk procedure, but it is neurosurgery nonetheless. They risk post-operative infection and adverse effects from the device, and they typically commit to extensive testing and monitoring.

For many trial participants, says Lázaro-Muñoz, their primary motivation is not only their own health but also the betterment of the patient community they are a part of. This was Leggett’s case: “I don’t want people to suffer like me,” she says, “because I know what it’s like to suffer.”

Being part of an exploratory trial can also preclude patients from entering later trials of potentially more refined devices, says Frederic Gilbert, a philosopher at The University of Tasmania specializing in neurotechnology.

Gilbert has studied the relationships people form with implanted brain devices, interviewing participants in the NeuroVista trial and other trials. He argues that this technology can have profound effects on a person’s sense of self. In some cases, this leads to what he calls a ‘hybrid identity’, which was pronounced in Leggett’s experience. Such strong effects on personhood, Gilbert says, must form part of the discussion about post-device trial responsibilities.
For Gilbert, removing a device can amount to withdrawing treatment. Discussing Leggett's circumstances, he goes so far as to say that explantation violated her basic human right to have access to available medical care. “You see that she’s still in pain,” he says.

Lázaro-Muñoz says most current protocols do not even include the costs of removing an unwanted device at the end of the trial. He is currently preparing a report on interviews he conducted with 23 neurotechnology researchers. All of them expressed a desire to protect patients after a trial, but, he says, “none of them have a safety net in place where they can ensure access.”

**Funding beyond the trial results**

A typical early-stage clinical trial in the neurotechnology field recruits a small number of patients and lasts, on average, a year or two. It typically costs at least US$1–2 million per patient. Most studies are collaborations of a clinical team and their hospital, the manufacturers of the implanted device, and a research-funding body.

Maintenance of an implanted brain device typically runs in the tens of thousands of dollars per annum, which includes operational maintenance, battery replacement and technical support. Compared with the initial cost of a trial, this is not a large sum of money, but for a patient whose life is often severely restricted by a serious brain disorder, it can be substantial.

A major determinant of whether a participant will receive post-trial maintenance costs is the national healthcare system they fall under. Neurologists Marwan Hariz (Umeå University, Sweden), Jens Volkmann (University of Würzburg, Germany) and Tom Foltynie (UCL Queen Square Institute of Neurology, UK) say that in their respective countries, if post-trial maintenance is deemed clinically beneficial, it is assured either by the national health system or another insurer at the onset of the trial.

However, in the USA, where many companies and researchers are leading the neurotechnology revolution, the situation is much more complicated.

“This is the wild west of innovation,” says Helen Mayberg, a neurologist at the Icahn School of Medicine, New York, who pioneered the use of DBS to treat depression in the early 2000s. She has run small investigational trials and consulted on a major manufacturer-sponsored trial that assessed DBS for depression. In her experience, after a trial, doctors must operate on a case-by-case basis to secure funding for ongoing care for participants.
“You [need to] advocate for your patients”, Mayberg says. Sometimes insurers agree that maintaining effective DBS is the most cost–effective solution. “If there is no insurance, you do whatever you can do to get charity payment, or get the device donated. You horse trade.”

In a 2017 analysis, Okun's team showed that in roughly two thirds of cases at their Florida hospital for which insurers had pre–approved meeting the costs of implanting and maintaining experimental devices, the insurers later reneged on this commitment. “Pre–authorization is worthless,” Okun says. Wrangling with hospitals to write off medical bills or with manufacturers to donate devices has papered over some cracks, but as the sector has expanded, these options have become less tenable.

Okun is involved in discussions with the NIH, the FDA and other stakeholders to try to develop a framework that works for all the involved parties. While some argue that trial organizers should have strict liability for meeting any post–trial maintenance costs that arise, others worry that overburdening neurotechnology developers with insurance and indemnity costs could turn companies away from the sector and stifle innovation.

Cross–compatibility of parts and power sources might be a way to protect people with implants from being left with no recourse when companies fold. Hendriks cites the cardiac pacemaker sector, in which manufacturers have committed to making all devices cross–compatible. Device manufacturers also need to continue to produce the components needed for the maintenance of their own devices. Problems arise if early devices are incompatible with later developments. Navigating a path to such safety nets while still fostering innovation is again the goal.

**Compassion must lead the way**

The responsibility for ensuring that trial participants receive support after a trial lies not only with industry but also with researchers and funders, argues Hendriks. The NIH is exploring the possibility of introducing a section on post–trial care in grant applications for trial funding.

However, even when volunteers are told that treatment will be withdrawn at a trial’s end, there can still be issues. Julia Lawton, a social anthropologist at the University of Edinburgh, UK, has studied the psychological dynamics of participation in clinical trials, including looking at how volunteers with diabetes felt after they completed a trial of an implanted closed–loop device that successfully monitored their blood–sugar levels and released insulin accordingly. Three months later, the device was removed. In post–trial interviews, the
patients expressed anguish and distress at losing a device that had quickly become indispensable. Lawton says that this psychological harm that accompanies the removal of a device must be acknowledged and anticipated by people running trials. Her research has shown that managing trial participants’ expectations and helping them prepare for the trial's end are often overlooked.

As Leggett recalls her experiences, she says she finds it odd how there was no event to mark the end of the trial, and that participants were neither invited to celebrate the trial's scientific success nor offered counseling as they transitioned back to life without an implant — something to “make them all feel like they were...I don’t know, special.”

The day she travelled to the hospital to return the handheld device that had become an essential part of her life, she anticipated a poignant, reflective conversation with the trial coordinator who had accompanied her throughout the process. However, he was not there. Rita had to hand her device over to a stranger, who told her she could leave a note if she wanted.

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