Spinal Implants - Ref214

with Ben Woodington

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TRANSCRIPT

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Steven Bruce
Good evening, welcome to the academy once again. Great to have you with us. As always, tonight we've got another of our virtual shows, that is to say I don't have my guest in the studio, I've got him on a virtual link, courtesy of Microsoft Teams. Not that that should have any impact whatsoever on the subject matter of our discussion. The subject matter of that discussion sprang out of me reading an article in The Guardian, in which Dr. Damiano Barone, who is a neurosurgeon was interviewed about inflatable spinal implants and it caught my attention. And I thought, this is something which is a fascinating and be relevant to what we all do as osteopaths, chiropractors, physios, and so on. So I thought, let's see if Damiano will come and join us on the show, and he agreed to come on the show. However, as I said, Damiano is a neurosurgeon. And at the last minute he's been otherwise called away. And he has nominated instead, the first author on the paper on this subject, which has Ben Woodington. Now, I'll give you a bit of background on Ben before I actually get him talking. Because it's him we're here to listen to you, obviously. He started life as a medical chemist, moved into pharmaceutical technology after that, where he was doing drug delivery devices, in particular with respiratory conditions such as cystic fibrosis, went back to Cambridge for a master's, and then a PhD in bio engineering, which is neuro technology. But I cocked up that last bit, Ben. But I'm sure you can give us much more detail on exactly what you're doing at Cambridge and about the unit that you work with, and all these fabulous ideas that are coming out of that unit. Welcome to the show, anyway.

Ben Woodington
Thank you. It's a pleasure to be here. I'm sorry, for those of you on the call that were expecting another clinician, I'm not a clinician. I'm kind of an engineer, I'm kind of a scientist, I'm kind of falling between the cracks of both at the moment. But what I am is I guess it's kind of interestingly positioned, because I've been working with doctors, clinicians, for the last eight years of my career now from the engineering side. So I'm hoping that I can cover a lot of bases.

Steven Bruce
You're probably an honorary MD by now, aren't you, I would have thought. I'm feeling more sorry for you because Damiano, having been called away has dropped you in this, not quite at the last minute, but I mean, he couldn't have picked someone better place to discuss spinal implants, neuro technology, could he? So give us a bit of background on the unit that you work with at Cambridge?

Ben Woodington
Yep. So our group is the bio electronics group here at Cambridge, we sit within electrical engineering, but the group is co run by, as you mentioned, Damiano Barone, who works in clinical neurosciences, so the group really has a push pull on the technology. So we, in engineering, we build lots of fun, interesting tools. And then the clinicians tell us often, no, that won't work, you need to design it like this, which is great. We leveraged kind of technologies that have been around in the semiconductor industry for the last 20 or 30 years, which means we can fabricate very, very small, flexible, and biocompatible electronics that we stick in and on the body to do interesting things. The group covers neuro engineering, as you mentioned, that is electronics that we stick on the spinal cord or the peripheral nervous system or on the brain. We have a drug delivery part of the group, that's cancer therapies. And then we also have a cutaneous electronics group. So there's things like EEG or EMG, measuring muscle activity.

Steven Bruce
In terms of, you know, all these wonderful things that you're having fun with at the moment, do you have a good track record of these things, actually making it into the medical market and becoming usable medical devices?

Ben Woodington
Yeah, this is a very good question. It's hard, right. We're developing these technologies that are ahead of what is currently used. And as I'm sure many of your listeners will know, medical device technology moves slow. You're looking at decades, not years. We are working on translatable technologies. So we try not to use crazy materials that are never going to get into a person, that are toxic. We try to develop things that have a track record of being in the medical market. So these are materials like silicones, for example, or parylene which they used to coat pacemakers with, and we're translating those. So in terms of getting to human, yes, we're up to human experiments. Now, though, we're looking at like the next phase is our PI George Malliaras and also Damiano, the co-lead, Damiano Barone, are both very, very enthusiastic. Now in the next few years, okay, we developed this kind of array of technologies. How do we now take them into humans? And you know, into medicine as well, not just first in human but actually on the market?

Steven Bruce
Yeah, and you and I had a bit of a chat about this before we went live. And you were saying that at the moment, most of the funding for the unit is through grants. But for it to become mainstream, it's going to take millions which means there has to be a commercial investor in this. So it's got to be stuff which offers real promise to that investor, isn't it?

Ben Woodington
Absolutely true. You can get so far with grant funding, and you can get up to that, you know, you can do that preclinical animal work that's necessary with grant funding, you can even do this person human testing with grant funding. But in terms of actually launching a product into market, you're looking at 10s of millions of pounds or hundreds of millions of dollars, if you look in the US market, where you get the money from, you get that money from private investors, or you get it from industrial partners, of which there are kind of only a few really in medical devices.

Steven Bruce
Tell me, then, I mean, this might well have come up in questions if I didn't ask it now. But we're very fond of criticising the pharmaceutical industry for skewing the research so that they can get stuff they've invested into on the market, sometimes with questionable medical success, it's probably a polite way of putting it. Is there any of that sort of pressure on you from investors? And I don't know if you've got them yet for what we're going to talk about this evening. But is there any that sort of pressure on you to make sure the research fits what they're investing in?

Ben Woodington
I think my experience is primarily from the UK and European side of things. And there I think is far less pressure in Europe and in the UK. I think there's less pressure in medical devices. However, the route to

market for medical device tends to be easier there. It's still complicated, but it's easier to get in usually than a pharmaceutical product, which, you know, changes the draft strategy slightly.

Steven Bruce
So we're, let's go to these inflatable spinal implants, which was the Guardian headline, I think, could you put a bit more body on that? No pun intended, exactly what it is you're working on?

Ben Woodington
Yeah, no, absolutely. I mean, this is probably if we can, can we see the slides at the same time here?

Steven Bruce
Yes, of course.

Ben Woodington
Okay, so maybe if we go to slide eight to begin with, perfect. So this slide is just showing some of the flexible electronics that have been developed in the lab. So probably most of these kind of technologies will be unfamiliar to people who are used to dealing with sort of bulky silicone devices that if anyone's placed a spinal cord stimulator, I'm sure there'll be lots of them. They'll be familiar with these kinds of semi flexible devices with kind of thick layers of platinum on the inside. They're pretty robust, you do get cable breakages quite regularly, but they're relatively robust. A surgeon can knock on it around on the table, and it tends to be okay. Well, we develop a much, much thinner, like orders of magnitude thinner. So we use thin layers of polymers that are made of, as I mentioned, parts of nickel, parylene C and silicones. But they're in the order of microns, so maybe four to 100 microns.

Steven Bruce
So this thing here is what, human hair width?

Ben Woodington
Even thinner. So human hair is, what, 30 to maybe 80 microns?

Steven Bruce
My hair's a bit thinner than most.

Ben Woodington
Mine's getting that way, unfortunately. The two devices that you can see on the left are four microns in thickness. So you know, they're tiny, a 10th of the hair. The spinal cord devices, the device that you can see on the right of the image, the sort of gold device that's wrapped around a tube, which is kind of simulating the vague size of a spinal cord, that device is about 60 to 80 microns thick.

Steven Bruce
Ah sorry, no, I was misled there. I thought this was the device. This represents the spinal cord. The device is just this little bit of film that's lying over the top.

Ben Woodington
The device is that one sat on top. Yeah, absolutely. Absolutely. So it's just demonstrating there the kind of flexibility of the device and the conformability of the device, which kind of is an intrinsic benefit of using these thin materials, right? So especially when you're looking at the brain, you want to be going over the curvature of the brain, not just a slab of polymer sat on top of the brain, so that those electrical contacts are actually in contact with the tissue. So yes, those spinal cord devices, they're about 80 microns. And I can explain why that is in a second.

Steven Bruce
This is probably getting ahead of ourselves here. But these are electrodes, where's their electronic signal coming from?

Ben Woodington
Yeah. So again, for anyone familiar with this kind of classic spinal cord stimulators, you've got these bulky silicone paddles, and then cables coming off the back of those and then you've got an implantable pulse generator battery that sits sort of further down in the lower back. So our device is exactly the same. We designed this device to interface with conventional implantable pulse generators. It's a part of the surgery, it's not our innovation. It's not part of the surgery that we want to change. People do it very well already. Those big medical device companies do a good job of miniaturising them, improving battery technologies. What we wanted to do was design a device that we plug straight into that, interface directly into that, but offer a better interface with the spinal tissue and also reduce the clinical burden of implanting one of these so I should wind back a little bit. The beauty of this device is that we can roll them up into tiny, tiny dimensions so about 1 to 1.5 millimeters in diameter, which means we can package them into needles and implant them percutaneously, as one would a percutaneous spinal cord stimulator. At that point, then we inflate the thing, and it unfolds, unfurls onto the spinal cord. At that point, a clinician would then plug it into the IPG that they've sat wherever they choose to place that IPG, then it becomes the active device.

Steven Bruce
Sorry, where typically is that IPG, which is the power pack that stimulates the thing that sends a signal to the electrodes?

Ben Woodington
It sits down sort of in the lower back and under the skin as well. That's all implanted as well, but away from the actual, you know, the sensitive neural tissue, the spinal cord.

Steven Bruce
Okay, so it sounds all very well that you can implant this using a hypodermic needle. But somehow, someone's got to connect the wires on the end of this to something which is inches below it in the back.

Ben Woodington
Yeah, usually, maybe 30 centimeters or so are stretched down. But yeah, importantly, it's away from any of the delicate parts of the body. Only the sort of soft interface goes within the spinal column and inflates on spinal cord, what we do have then is obviously a line of wires and a fluidic tube as well, that comes off the back of that device.

Steven Bruce
Right. So those come out through the spinal column and are sitting under the skin rather than along the spinal cord itself.

Ben Woodington
Absolutely. If we go to slide 13, there's a bit more of a clearer image of how that works as well.

Steven Bruce
Okay.

Ben Woodington
So those devices on the left-hand side are the kind of classical spinal cord stimulators that people will be familiar with implanting, I think these are from Boston Scientific, these devices. So you've got those bulky, wide, semi flexible implants that are maybe 15 millimeters wide or so. And then you've got those percutaneous leads that are 1.5 mil. So yeah, about 1.5 mil, 2 mil wide. Our device as you can see in the image on the right-hand side actually goes through, it's a tui needle that you can thread that device through as one would a percutaneous lead. And then the diagram is just showing the device on the spinal cord and then kind of popping open onto the tissue.

Steven Bruce
Right. Okay, you've got, a little bit later on, two slides further on, number 15, you've got a little bit of a video going on there. No, won't play. That's my fault for messing around with your slides. I'm sorry, Ben.

Ben Woodington
It's not a problem. So what we're seeing there is the device rolled up, it's in a kind of simulated environment. So we set the pressure inside this sort of balloon, inside a tube to simulate the epidural space in the spinal column. The device has kind of just been threaded, and then what we're doing in that video is actuating that device and it's kind of unfurling across, filling that space. And then the image to the right of that, what we can see is actually the device before it's been packaged inside any of the kind of percutaneous tubing, we sit this thing inside like a silicone sheath tubing to protect sort of delicate electronics. And you can see the device there just like lying out on the table, the device is about 50 mil, 55 mil in length, and then it kind of matches the dimensions of those. It matches one of the Medtronic devices, the 565 Medtronic device, which is a very common spinal cord device most people are familiar with. Again, we can make much more complicated devices than this. But we're kind of going baby steps, like what are surgeons, what are clinicians familiar with, we can match that device architecture, but using a very, very minimally invasive surgical procedure.

Steven Bruce
It's amazing stuff. I just want a quick word for our viewers. I would normally share the slides with you after the show in the form of a handout. Ben's asked me not to do that, because some of this stuff hasn't been published yet. So we're at the cutting edge of the cutting edge here. Ben, I think if I send them to the unit's website at Cambridge, quite a lot of these images and a lot of the background information is available there, isn't it?

Ben Woodington
Yeah, absolutely. And you know what I, you know, I didn't have time to do it, given Damiano's short notice. But I can take away the information that we just don't want public. And I can send you a slide deck that I'd be happy for you to share.

Steven Bruce
That would be great, thank you. I mean, it's useful for people to have that as a record because, you know, it's hard to keep up with all this stuff that you're putting over to us. And I have had a polite request to say that we are simple osteopaths and chiropractors, could you please speak a bit slower because we don't follow it?

Ben Woodington
I absolutely will. I apologise. I should know that after working with clinicians for the last three years, four years in this field I ask the same thing and a lot of language that I've had to absorb very quickly.

Steven Bruce
Another explanation for you. The system whereby people ask me questions auto generates the names for them on one of the channels that we have. So I'm forced to redress people by very strange titles sometimes. And the first question has come in from someone who is known as Helpful Person who wants to know who typically is going to benefit from this.

Ben Woodington
Yeah. So the device has been designed with pain management in mind. So these conventional spinal cord stimulators, they're used for drug refractory pain. So, a patient often gets put on, you know, increasingly difficult drugs. Usually, they're on a bunch of opioids by the end, for any kind of pain, but usually pain of neuropathic origin. And but they have been used also for sort of angina, and lower limb pain, all this kind of stuff. Pain management is what they're used to for the moment, that's what we're targeting. They're very effective at treating pain in patients for a period of time. But what we're kind of excited about in this group, are the future applications, the blue-sky applications, of which there are many. Not to diminish pain, I have spoken to many people suffering from chronic pain, and it is a completely debilitating issue that completely halts your life. But we're also looking at movement disorders in Parkinson's, and also, interestingly, spinal cord injury. So there's a lot of excitement at the moment in the field of using these types of devices to treat people with spinal cord injury during their rehabilitation phase for movement disorders, of course, but also for bladder function, and for sexual function, for blood pressure. And there are lots of applications here as well.

Steven Bruce
Let's go back to the pain relief aspect for a second. Does this mean that this is just an internal version of TENS?

Ben Woodington
It functions in the same principles; it functions in the same principles. They're far more effective. They're on that tissue, you can target the neuromodulation, where you're directing the power, far better than a

TENS machine. The TENS is sat on two contacts, I think, four contacts, nowhere near as effective, but they work on similar principles.

Steven Bruce
So it's pain gating that's going on, is it?

Ben Woodington
Precisely, yeah. It's very, very contentious, the literature on pain gating is very contentious. Well, I mean, you know, there were these theories of pain gating from I think, 1965, that kind of seminal publications that people can still stand next to, and by, though, I think many aspects of it has kind of been disproven. People come along with high frequency stimulation. So people usually, they stimulate tonically. Between, I think it's like 20 to 100 hertz, usually, then a company called Nevro came along and started simulating in a high frequency regime, at 10 kilohertz, the mechanism seems to be completely different. The way the pain is treated seems completely different. And it seems that no one really knows why, lots of people have theories, and then they trade their theories, but there's no really prevailing mechanism, or, you know, underlying theory as to why these actually work.

Steven Bruce
It's always a bit chastening to realise that there is still so much uncertainty in the medical world, isn't there. And I imagine that your sort of research and any other research is vastly complicated by the fact that the placebo effect will play an important role in this as well as the actual technology.

Ben Woodington
I mean, yeah, you hit the nail on the head there, especially when, you know, running a placebo is difficult when we're running a control group, I should say, it's difficult when someone has to undergo a surgery, right? They're having a device implanted, and you can have a device operating that's not actually stimulating. But there have been studies haven't there, where people have had, I mean, you and your audience will know this way better now, but where people have had knee surgeries, and they've done nothing, they've not tried to fix anything, and they still report pain relief. We are a little bit in the Wild West, I think, we're sort of where pharmaceuticals were some decades ago, where people are running experiments where they do neuromodulation on the spine, or on the vagus nerve or somewhere else, and they get an effect. And they don't really know why or what the underlying mechanism is. But they are getting an effect. So they kind of shrug their shoulders and they say, okay, let's move on to clinical development.

Steven Bruce
Yeah, and frankly, a lot of us would say, well, that's a good approach. As long as there are no adverse effects. I mean, let's just get benefit for the patients.

Ben Woodington
Yeah, of course. Understanding the underlying mechanisms, then you can design better treatment modalities, which is kind of not where we are right now. We're sort of we, the 10 kilohertz treatment seemed to have come out of nowhere, but we tried it and it worked. And so there we are.

Steven Bruce
So in terms of spinal cord injury, which you mentioned a little while ago as well. Are you suggesting that with these devices, we don't have anything to show this on the screen, but we can reconnect across a rupture, or?

Ben Woodington
Reconnecting is difficult. It's something that we're sort of vaguely trying to do. And I can touch on some of our kind of even more cutting-edge research in a second, but recording from above an injury and stimulating below is difficult. Some people say it's impossible for reasons that I'm happy to go into if people are interested.

Steven Bruce
They will be, definitely.

Ben Woodington
But what's more interesting is kind of the rehabilitation. So if you don't have a complete spinal cord injury, and I have to confess this is not the expertise of my group, but the expertise of groups in Switzerland, you can stimulate in a certain pattern at the injury or below the injury. And you can kind of reinforce that movement again, so paired with very, very intense rehabilitative therapy and spinal cord stimulation, they have managed to get people to a point that they would never got just in terms of rehabilitation alone.

Steven Bruce
Right. Okay. Rupert says, does playing around with the connections on the spinal cord alter application of the device, calibrate which nerves are activated below the lesion? I didn't quite flow there, but you get the idea.

Ben Woodington
Is the question sort of, can you can you target... Can you read it again?

Steven Bruce
Does playing around with the connections on the spinal cord after application of the device, calibrate which nerves are activated below the lesion? So it was my poor reading of the question.

Ben Woodington
No, playing around with connections on the spinal cord, I don't quite follow. But I mean, we can definitely...

Steven Bruce
I guess he means, you know, where does this thing actually sit on the spinal cord? I mean, how would you position it precisely to target the part of the spinal cord that you need.

Ben Woodington
It's something that we can do by numerous electrodes, which is kind of, again, the benefit of this device over something where you just have electrodes, once you've got the electrodes on the spinal cord, you can then tune and play with the parameters to direct that electric field, which is something we want to do,

we have tracks on the spinal cord. Usually, with these devices, we're only targeting the dorsal column on the spinal cord. But we can kind of aim that electric field towards one side, towards the other or towards the branches of the spinal cord. A benefit of working with microelectronics, which we can do by making these devices, is we can put if we wanted to hundreds of electrodes on the spinal cord, not be limited by eight or 16, which means we can target then tracks kind of anywhere we like on the spinal cord. And what we're trying to work on now is okay, we built this based on the Medtronic footprint of this sort of like 15 mil wide device, because that's what people do at the moment. But if we go wider, if we wrap around the spinal cord, how much further can we go? And how much more control do we have over those tracks on the spinal cord?

Steven Bruce
And that control is practiced, exercised externally by some sort of remote control of the sensor, which is internal to the patient.

Ben Woodington
Yeah, exactly. So usually, there'd be like a trial phase and a tuning phase where someone would sit with the patient undergoing the surgery, and they would tune and kind of calibrate that device. But once they've set those parameters, the patient is stitched up, patient goes on his way, the device has not been touched until they need to reprogram it, if they do need to reprogram it at some point.

Steven Bruce
Okay. Moving a bit upward from the spinal cord itself. Jos has asked whether this would help stroke patients, potentially.

Ben Woodington
Yeah, people have looked at stroke as well. For sure. The devices we usually use for stroke are sat on the brain not on the spinal cord, but it's definitely not the application that we're exploring.

Steven Bruce
Right. And Alex has asked how it actually works, asking for a bit more precision here on whether it stimulates the spinal cord or nerve axons or something else?

Ben Woodington
Yeah. Again, I think it's a good question. So the are theories that you're stimulating these dorsal tracks, these ascending sensory tracts for pain. For the rehabilitation side of things, again, very contentious. There's some amazing work by Gregoire Courtine, from Switzerland and Marco Capogrosso. These guys do phenomenal work in this exact area, trying to figure out when you're stimulating for rehabilitation for spinal cord injury, what are you actually doing? What the hell are you doing? Like, what are you activating? Are you activating just those dorsal pathways? Probably not, you're probably activating something deeper in the spinal cord, are you activating this kind of afference they're going back into the spinal cord record, and is that having some sort of like, effect on central pattern generators that are also kind of contentious in origin? But it's work that people are really trying to figure out like, what are you actually doing when you're doing these neuromodulation therapies? What are you stimulating? And what

are you triggering? And what are you trying like, what are you hacking in the body's biology to get people out of pain or walking again?

Steven Bruce
And have you actually put any of these inflatable devices into a human yet?

Ben Woodington
Only human cadavers.

Steven Bruce
Right. If we assume that the effect is likely to be similar to those larger paddles and devices that you showed earlier on, have there been, would you expect there to be many adverse side effects from these?

Ben Woodington
No, absolutely not and it's something that we're working very, very closely on. Which has been quite helpful. There's another slide actually, that would support this. Maybe it's the next slide, actually. Next slide. 16 possibly.

Steven Bruce
Okay. This is making devices with the clinician in mind.

Ben Woodington
Yeah, so this is unfortunately it doesn't look like the video is going to run again. But that's okay. It can be used. So will there be adverse effects, we don't want to just be engineers running in with our tools and saying, hey, chuck this in a human body, it'll be fine. I'm sure. This is why we work with clinicians. This is why we work hand in hand with clinicians to be like, how do we design these devices to have therapeutic benefit without causing any damage, because otherwise, these devices are dead in the water. So the original device that we built, was kind of sharp on the front, too sharp on the front, as opposed to the soft silicon devices that they used at the beginning. And as we went in percutaneously, the very, very first cadaver session, the device went straight through the spinal cord, down to the backside, hit the bone, and then you're running on the backside. Okay, that's, you've just, you know, lost the use of someone's legs. So required a redesign, we had to redesign it to make the device softer. And then another aspect we had to do was the way the device inflated at the beginning inflated, as you describe, kind of like a balloon. If a device inflates like a balloon, and you get a kind of anterior posterior expansion, so you're putting pressure on the spinal cord, you're, again, you're going to cause damage, so it's something we had to engineer out. It's why we do these cadaver experiments; it's why we don't even think about moving to preclinical animal work before we actually get out these kind of fundamental engineering problems first. So we did now design the device in a way that it means it can be introduced in a much more effective way reducing the risk of damage to the spinal cord. And then with the way the device unfurls, it's kind of cleverly engineered so that it only unfurls laterally rather than in this dimension, so that it doesn't put pressure on the spinal cord.

Steven Bruce
Oh, I'm glad you practice on cadavers first, that's probably everyone's advantage. Pip has sent in an observation. She says that pain is there for a reason in many cases, it stops people doing things they shouldn't be doing. These devices, are they likely to stop pain completely? Or do they just reduce pain? Are they likely to encourage the patient to do things they shouldn't?

Ben Woodington
No, I mean, again, yeah, it's the beauty of neuromodulation over kind of just being absolutely chock full of opiates, is you don't want to block that acute pain. You're right. You don't want to put your hand on the hub and burn it and not be aware because you're getting, you know, but that's spinal cord stimulation. But these don't.These are intended to block chronic pain. They're intended to block pain of, again, as I say, like neuropathic origin and pain targeted specifically for the particular ailment that person has, whether that's sciatica, angina, or failed back surgery syndrome. You tune for that; you don't tune to make people numb in the legs so that they're going to injure themselves. And it's a very important part of the clinical procedure.

Steven Bruce
Right. Robin sent in a really useful interesting question from our point of view, which is, he's asked about how robust these devices are. Because of course, if we as osteopaths, chiropractors, physiotherapists, start wrestling around with a patient's spine, trying to mobilise things and rebuild their strength and their stability, are we going to damage these things?

Ben Woodington
Yeah, again, a very important point, and something that we had to work with our surgeons on as well. These four micron devices that I described are, we handle them in the lab very delicately, we're fine with them. But as soon as you give them to someone who's not familiar with how, you know, flimsy these things can be, they can start pulling them around, tagging them and they can tear. So this is why another reason this device is a little bit thicker, still thin enough that we can roll it up but thicker than some of our hyper conformable devices that we would stick on the brain, so that they can be tugged around, they also need to be robust enough so that they can be explanted. So it's no good just sticking a device into someone, they maybe have to have that device taken out at some point, they probably will have to have that device taken out at some point. And the device needs to be retrieved. You don't want to make these things flimsy enough that, as the surgeon goes to pull it out, it snaps off and stays inside the patient and that is a lawsuit waiting to happen for the developer or the surgeon or whoever else.

Steven Bruce
So these are not actually stuck to the spinal cord, they're just lying on the surface and staying there by what surface tension.

Ben Woodington
Absolutely. So they sit in the epidural space. So they sit epidurally and they're kind of surrounded by fat and tissue in a kind of like virtual enclosed space. So they're held by surface tension, by capillary forces on the spinal cord but also they're stuck within a space, they're not free floating, which again is one of the benefits actually of these paddle type devices, the linear probes, they move, they migrate quite a lot.

They're just smaller in footprint. And so they slide around. But when you have something that actually opens up and sits on the surface of the spine, kept in that space, it tends to stay relatively still. Obviously, as I've just said, you can spend hours tuning the parameters of this device to treat specific pain of wherever in origin, you don't want the device to then slip out of line and be targeting somewhere else and be ineffective anymore.

Steven Bruce
I think I might have dragged you away rather quickly from this slide here. And I just wonder if you could explain what's going on in it. Because we've got three images on here. And it's not clear to me exactly what they are showing.

Ben Woodington
Yeah, no, absolutely. So if we go to the next slide, actually, that'll be slide 17. Yeah, so what I just wanted to show first on the images on the left is a, don't lacerate the spinal cord with a device, the images below show after we've developed a soft tip device, it means that we can make contact with the tissue, the dura or the spinal cord, and then run up the spinal cord.

Steven Bruce
What is lying within those hashed white rectangles?

Ben Woodington
So that is where the spinal cord is sitting. Yeah. And then beyond that is the spine, the kind of darker areas of the spine.

Steven Bruce
I see. Yes, of course, yes.

Ben Woodington
And then within the kind of yellow hash box is the spine, and then the device is actually sat there on the surface of the spinal cord. And then we can guide the device then, and sort of train the device up the spinal cord then through a percutaneous needle that sits much further down. The image I want to show you on the right is actually another demonstration of designing with the clinician in mind. So we developed this super, super fine device, very thin, using very thin layers of metal that were in the order of hundreds of nanometers. And we said this is going to be great, this is going to work perfectly, look how flexible it is, look how much it rolls up. And then we took it into the surgery working with these human cadavers. And the clinician says, so how do I see it? What do you mean, how do we see it? Well, we usually use fluoroscopy, a kind of type of X ray to image the device and to see where it's gone and how it's been placed. And 100 or 200 nanometers of gold, you cannot see with an X ray and layers of Perylene or layers of silicone, you absolutely cannot see on an x ray. So what you would see is a tui needle sat where it was supposed to be and then nothing. Which makes the minimally invasive procedure completely redundant and useless. Because I'd have to open up the, you know, I'd had to perform a laminectomy, I'd have to open up the spinal column to actually see where the device is. What we actually had to then do is develop X ray of peak markers, something that's still flexible, still conformable, but actually allow us to know where the boundaries of the device are, and whether or not the device is actually unfurled and

deployed where we expect it to be. To then actually a surprising amount of time on an engineering challenge here thinking, you know, being kind of proud, cocky engineers, we're like, ah it's easy, we just make it a bit thicker, and we'll see it on an X ray. It actually took quite a lot of work to get that figured out, how to do that and how to do it safely, and how to also package all of this still inside of that tiny needle.

Steven Bruce
Yeah, and you make it sound as though it's easy and good fun. But I think most of us can recognise if you're working in materials that are nanometers thick, that it's quite sophisticated stuff that you're actually doing here. I mean, cadavers won't be complaining too much. But one day is going to go into somebody real.

Ben Woodington
Exactly, right. And it's important, it's important that we do this right now. And we don't want to go - we don't want to be, as engineers, we don't want to go two years down the line without really, really engaging with clinicians, free the device, and then it just be completely useless because it has to be completely redesigned with as I say, the clinician in mind, with the surgical procedure in mind, because that's what we're doing it for. We're not just doing it to make a pretty paper or be out on the benchtop in the lab and wave it around and show people. We want it to be in clinicians' hands and in patients bodies eventually.

Steven Bruce
Yeah. Now I compared this to TENS earlier on. Bob has actually sent in a very interesting observation. Could this be used for functional electrical stimulation? For example, to treat things like foot drop?

Ben Woodington
Yep. Yep, absolutely. And I mean, it's something that people, again, do with this technology, both cutaniuously on the muscle or wherever else, you can use these types of devices, but also invasively as a kind of cuff somewhere in the body. The beauty of these devices again, is maybe I can touch on it in a second, is we design them using something called a conductive polymer interface. So we use a material called pedot, our lab absolutely loves pedot. It's a marvelous material. It means that you can massively increase the current injection, so you can do things like functional electrical stimulation or spinal cord stimulation, without upping that power to such a point that is going to start causing damage.

Steven Bruce
That's fantastic. So where would the stimulation, let's say we're treating foot drop, where does the stimulation come from to overcome the foot drop? How does it know when to fire the muscle?

Ben Woodington
That is not my expertise. On a call with clinicians, I would not want to start explaining procedures of treating foot job.

Steven Bruce
Okay, well, we will move on from that, it's fine. Simon says, so this is only about pain control, and he's moving on to an area where I think you were going to go, what about lack of nerve innovation such as MS, on those recovering from spinal cord injury? How does it work there? Or can it work there?

Ben Woodington
Yeah, I mean, it's something that many groups, including ours, are looking at as well is not just functional stimulation, but then regeneration as well. So there are groups that have looked at, for example, like killing the nerves and allowing regrowth back into electrodes, or, you know, co treatment with stem cell therapy, for example, or someone in our group actually works on a bio hybrid technology where they implant sort of stem cells on devices, and then look at like, functionally restoring the nerves as well as using electrical stimulation.

Steven Bruce
Thank you. Lawrence, I think rather facetiously, has asked how these things are charged, do they take double A batteries?

Ben Woodington
Yeah, I mean it's an important question. There was a large investment on wireless charging of devices. So these batteries sit inside the body for a surprisingly long time, they can last for five years, for 10 years, depending on the kind of power characteristics of the device, then there was a push to look at kind of inductively charged devices. So you don't want the device to be taken out every five years and replace it with a new battery. So instead, what we'll give you is an inductively charged device that is implanted, but then a belt that one would wear to charge that device seems like a great idea. Turns out patients don't really want that. I think a lot of patients would opt for their five years, you know, change of battery over having to wear this belt all the time and charge. Again, it's an interesting question around like human centered design, like, you think, oh, let's remove the surgery, patients hate surgery. But actually, patients then have to remember to charge their belt and stick it on every day. And if they don't, the device dies and the pain comes back.

Steven Bruce
Yeah, yeah, good thinking. When I was thinking how easy it would be to just stick my iPad charger onto my back of my iPhone charger onto my back and recharge this thing every night. But yeah, I take the point. We're not dealing with people with mild aches and pains here, are we. We're dealing with people who are in severe, severe pain.

Ben Woodington
Absolutely. Yeah.

Steven Bruce
This kind of follows on from what I said earlier on, but somebody who has been named Divine Specimen by the system says, are there any problems that you can get with the devices, any risks in fitting them and clearly it is surgery, although is minimally invasive?

Ben Woodington
Yep. There always are, right. There are always risks with these kinds of devices, with any kind of surgery, as you say. But certainly, when you're introducing a device, there are always risks, there are infection risks, there are risks that you do damage the spinal cord in some way, shape or form, you can cause a hemorrhage if you lacerate something that you're not supposed to. There are always these risks, we try

to reduce them as much as possible, when we're designing these devices, we try to reduce them as possible. In terms of the device engineering, there are both kind of hardware and software controls on the device so that you don't, you know, jack up the power so much that you're causing damage. So the risks really, with our device, when we're at that stage, are supposed to be in line with the kind of existing surgical risks of doing an invasive surgery, which are always going to be there, right.

Steven Bruce
Yeah, one would like to think the risk could be a lot less. I mean, one of the guiding principles of medicine, surely, is that new technologies or new approaches shouldn't be simply as good as the old ones, they should be better.

Ben Woodington
Absolutely. I mean, this is why we're moving to this minimally invasive approach. So rather than going for full laminectomy, where I would presume, please, any of the clinicians on the call call me out, but I presume if you're going for a full laminectomy, the infection risk is higher than a percutaneous lead going straight in. But also the risk of damaging the spinal column, spinal cord is also higher, right, rather than just going between the vertebrae and guiding a device up the spinal cord. So that's kind of the approach we've taken here, like how do we reduce the surgical burden? And then a lot of patients don't qualify for those kinds of invasive surgeries, right? And maybe you don't want a kind of invasive, you know, surgery where they're going to take days to recover. And they do just want that outpatient procedure.

Steven Bruce
Somebody did ask and I've lost the question for the moment, and it sort of follows on from what you were just saying there. What is the threshold for being referred for this sort of surgery and maybe that's outside the scope of operations for an engineer. But where would you imagine that to be?

Ben Woodington
This is probably where you would want Damiano on the call, because he probably would be able to answer that question. These devices tend to be reserved for patients who are suffering the most pain. Patients, as I mentioned, who are having drug refractory pain, so they've been on all the treatment options, they're still struggling, or they're on such a cocktail of opiates that they can't really live their life, they can't work, they can drive, whatever else. Those are the patients you're looking for. What we again, we're trying to do with this device is reduce those surgical barriers so that more people can qualify for this device, again, or more people would opt into this device, a simple in out procedure, rather than kind of hectic, invasive surgery, that one would have to go through. But that does mean it's a *audio problems* picture, whether they have this paddle type device or that percutaneous device, that level of pain changes and kind of the threshold that a patient would be accepted for this. And then where you are geographically. So these procedures are carried out far more regularly in the US than they are carried out in Europe. The UK does carry out some of them but not nearly as many.

Steven Bruce
On that note, are other people doing the same thing as you elsewhere probably in the US? Or is this Cambridge's own sort of development?

Ben Woodington
Yeah, as far as we know, this is completely novel and no one's working on it at the moment, we filed a patent to try to protect that. And so raise our money to work on this further. There is an Italian company who work on something vaguely similar, but we have benefits over them that they can only, it's a mechanically sprung device. So they can only go a little bit wider than the percutaneously, we can get really, really wide coverage by kind of active unfurling rather than just passive.

Steven Bruce
Okay. Helpful Person's come back in and said, how long does it need to be in there once it's implanted? And how is it monitored? And to follow on, when and what are you looking for as a success? And how do you work out a prognosis?

Ben Woodington
There's a lot of questions there.

Steven Bruce
There is, isn't there. I didn't realise when I started that one, there were several questions in there.

Ben Woodington
How long it's in there for, unfortunately, this is not a cure, this is a treatment. So you're treating the symptoms of the pain. So these devices stay in as long as they work. And unfortunate problem with spinal cord stimulation for pain is they tend to stop working after a period of years. 5, 10, 15, 20 years, at some point, it has to stop working. Again, there's no clear...

Steven Bruce
Sorry, when you say that the device doesn't stop working. But it ceases to be effective?

Ben Woodington
The patient stops responding to the treatment. You can tune the parameters all you like; the patient stops responding. There's no clear literature or consensus as to why that happens. And we hope with this kind of technology where we're sitting even more comfortably onto the spinal cord that we would not have that effect. But we can't say that, that's speculative until we've done the trials. Understanding that would be huge. And again, maybe introducing more electrodes and being able to tweak exactly where your electrodes are, spinning your electrodes so you're treating the top half and then halfway through the treatment, you go into the lower half of the device. Maybe that would have some better effect. But again, it's entirely speculative and would require lots of research to understand that. There were more parts that question, would you mind repeating them?

Steven Bruce
To ask a bit more on that, how many years before it stops working generally?

Ben Woodington
Variable. I think 10 is around the mean, but I think it's quite variable. These patients are, to be slightly dark, these patients are often older. So 20 years of treatment, may be what you need.

Steven Bruce
Well, that was my next question, is there an age threshold for doing this? And as you said, a lot of people in chronic severe pain are elderly. Being minimally invasive, I presume is more acceptable for the older patient?

Ben Woodington
It's what we're looking for. Yeah, exactly. We don't want to go for these very invasive surgeries for elderly patients or you know, and those are criteria that people get dropped for in these kind of surgeries, but age is definitely one of them as well. Yeah.

Steven Bruce
Yeah. So back to Helpful Person. She, I'm going to assume that Helpful Person is a she, has said, how is it monitored?

Ben Woodington
Monitored in terms of, I assume they mean, once the device is implanted, how do we keep an eye on it?

Steven Bruce
Yeah.

Ben Woodington
The patient would go back to the doctor regularly, and they get checkups. But usually this is self reported.

Steven Bruce
Symptomatic, rather than there being some sort of printout that you get every five minutes from the device.

Ben Woodington
Precisely. Some of these devices now are running kind of, I guess you'd call it telemetry. The devices are collecting certain levels of data on how the treatment is kind of going and being reacted to that. But the patient is not intended to see any of that information. It wouldn't help the patient in any way. So usually if the pain comes back, the patient would go back to their clinician and say, the pain's come back. And then you could reprogram the device or you could explant the device if that was, you know, the necessary route.

Steven Bruce
I might be getting a bit matrix on this at the moment, but I'm just thinking that, presumably, there's the scope that this thing will report its data to a smartphone, and the smartphone will report its data to a central hub. And you'll be able to monitor the activity levels of the patient and relate it to what the device is doing or somebody will, not you necessarily, which is all a little bit Big Brother-ish, but possibly very helpful in development of the devices.

Ben Woodington
Well, that's it and important in treating people. I mean, data is gold, I would say that as, maybe as an engineer, as a scientist, but that data is so important. I mean, knowing where the electrodes are, and how long that pain has been treated for and in what way, in which kind of condition you're treating is incredibly valuable and not data that is gathered at the moment, and maybe if it was or when it is, you'd be able to design better protocols, okay, so a patient is presenting with failed back surgery syndrome, they need this device, we placed this device in this place, we use these particular power parameters. And it worked in this way. I don't think that data is really collected at the moment, if it is, it is very sporadic. And on very few case numbers. It's like, you know, 10s of patients rather than hundreds or 1000s.

Steven Bruce
Bow Man wants to know, how long you've got with this device to treat a severed nerve before it's just not going to respond?

Ben Woodington
I would not know the answer to that I'm afraid. I would not know the answer to that. No, no. There will be some plasticity, right. And it will stop at some point.

Steven Bruce
And I imagine there all sorts of other functions or other factors in the survival of a nerve beyond just the axons in the nerve itself. Lawrence says, as the opiate pathways focus on the posterior of the spinal cord, does pain reduction through this device function in the same way.

Ben Woodington
No, it doesn't function in the same way. They don't function the same as good drugs. They function in a very different way, they function by this gating pathway that opiates absolutely do not. The gating pathway for people who maybe are not familiar with it on here. My mentor, my boss, Damiano, has described it in a very good way for me before I started that when you stub your toe, what's the first thing you do, you rub it. If you burn your finger, you grab it, and you put some pressure on it, and you're trying to send different signals to the ones, quicker signals, in fact, than the slow signals for the acute pain. So the original devices were made basically to initiate paresthesia, where you get a kind of tingling sensation in your back. And that kind of distracts, distracts is a crude way, but distracts from the slower signals of pain. Opioid drugs, again, not my specialty but do not function in that way. Definitely not.

Steven Bruce
Given what you've just said, is a patient who has one of these devices implanted, would they feel anything from the device, as you would from TENS? Would they feel that tingling?

Ben Woodington
Absolutely. So for tonic stimulation, the stimulation I mentioned earlier in the range of kind of 20 to 100 hertz, they feel a tingling sensation. That can be quite irritating, I think. But with high frequency stimulation, this kind of new way of treating, paresthesia free, you don't feel anything at all, which is why many people are saying this is a different pathway. You're not doing the same thing. You're doing something entirely different, different mechanism.

Steven Bruce
Yeah, just not quite sure what it is.

Ben Woodington
Just not quite sure what it is. Yeah.

Steven Bruce
Lawrence's is getting very clever on me here. He says pain gating question mark, does that increase the post synaptic membrane potential, or changes the potentiation of the chronic pain pathways?

Ben Woodington
He sounds like he knows better than me.

Steven Bruce
Lawrence, perhaps you come on the show, sometime in the near future and explain all these things to us. A couple of people asked if the dynamics of the spinal cord allows the device to stay in place, the cauda and cauda equina move quite a lot in flexion and extension within the spinal canal.

Ben Woodington
Yeah, that's absolutely right. And it's testing that we carried out as well. Flexing, twisting, bending. And then also, depending on whether the patient is stood upright or laying down changes the pressure on the device, changes the expansion of the spinal cord. And all of this affects how the device moves. With our device, because it's so thin and flexible, it does it moves with the body rather than reacting to the body.

Steven Bruce
When you say moves with the body, it stays in the same place on the spinal cord as the body moves?

Ben Woodington
As the body moves. Yeah, so we've done studies where we have like a flexing, and we see the device kind of flexing with the spinal cord as well, which is incredibly important because again, you want those electrodes to stay in place, but you also want the electrodes to stay in contact with the tissue. If the patient stands up, the spinal cord expands and device moves kind of further away, there's a increase in CSF thickness and the device moves further away, you're going to change exactly how much power is going into the spinal cord and it changes the treating parameters. This is vaguely important for pain. So you can get away with it. When you're looking at spinal cord injury and trying to fire up motor pathways this becomes incredibly important. Like you don't want to be targeting the completely wrong area of the spinal cord for when you're looking at rehabilitation.

Steven Bruce
I can understand that. Dave has asked in terms of nerve blocking; would this treatment be used on nerves tethered by scar tissue post-surgery? He says he's come across this more than once and patients end up on massive doses of medication.

Ben Woodington
Okay, where these, sorry, repeat the beginning?

Steven Bruce
That when nerves are tethered by scar tissue after surgery.

Ben Woodington
Again, it sounds like a question that ought to be asked to a clinician rather than an engineer working with clinicians. But I mean, it sounds like we would have similar kind of procedures there.

Steven Bruce
Technical question then, Stuart says, do the control boxes currently exist into which these probes plug? And if yes, how do they work? If it's not a pain gate theory, how are they perceived to function? I think we've dealt with the last part. And in terms of control boxes, obviously, you've mentioned the power pack. Presumably that is adjustable for send different signals to different parts of the device.

Ben Woodington
Yeah, absolutely. So you have an external programmer, which is a larger machine, you plug this into this implantable pulse generator that you then are programming and the device has a what's called like a pigtail connector that goes into that. So at some point, the patient is very wired up, they have a device sat on the spinal cord, usually they have a trial stimulator first placed in that's run with the external programmer. If it works, they then have the real device put in. But it's quite a procedure.

Steven Bruce
Right. Okay. Which I suppose leads into this next question, again, from Helpful Person who says, how is the process being used today? And is it available on the NHS? And clearly the stuff that you've been developing is not yet available in humans? But in terms of the receding devices? Is that an NHS service?

Ben Woodington
Yeah, as far as I'm aware, it is. NICE recommended some, the 10 kilohertz I think as their treatment, relatively recently within the last few years. So yes, it's just, I think expensive. The economics are interesting, actually. I mean, it's a whole different discussion. People think these devices are expensive, and they are expensive. They cost between 10 and 20,000 pounds, usually to the NHS plus then the surgery, obviously, the surgical burden as well. But the cost of keeping a patient on opioid drugs for 10 years, 20 years, you know, can far exceed that, especially in the US, perhaps not in the UK. I don't know the cost of opiate drugs in the UK, but a sustained treatment for many, many years is less economically viable than a device you place once and can be forgotten about in many cases.

Steven Bruce
There's the intangible benefit as well, isn't there of having a patient who is not on opiate drugs, which, they have all sorts of potential side effects.

Ben Woodington
Well, absolutely. And they become, you know, they're treated with the spinal cord prosthesis, and they can become often like a functional member of society. Again, they can go back to work, they can live their lives rather than stuck doing nothing.

Steven Bruce
Yes, possibly criteria, which the NHS is less keen to look at, they tend to look at the budget more than anything else. Simon wants to know, if there's a chance that this will be developed into a purely subcutaneous technology where you can just plug it in externally.

Ben Woodington
So then the, sort of the IPG would be sat externally and the device would be internally?

Steven Bruce
I think that's what he means, yes.

Ben Woodington
I mean, usually you want to go one or the other. So usually, you don't want to leave ports in the skin, you know, it leads to infection. We do this for clinical research, any kind of preclinical animal work, but in a human you don't want to be doing this. You don't want to be leaving things externally or going through the skin cutaniuously. These devices can be placed subcutaneously, and they are placed subcutaneously for other applications. And again, if you're looking at like muscle activation, you look at it subcutaneously, some recording devices that go on the brain or on a spinal cord can also go subcutaneously, but usually you want to be as close to the target as possible being the brain, spinal cord, the peripheral nerve.

Steven Bruce
Right. Peripheral nerves, you did mention those earlier on. Somebody who hasn't given their name says that some patients who've had chemotherapy can then have peripheral neuropathy. And are these devices able to help out with that?

Ben Woodington
I guess if the neuropathy is leading to pain, they can be. There are also cuff devices that function in the peripheral, so maybe in the arms and vagus nerve or in the leg or wherever else they do that as well. We don't use them for pain, generally.

Steven Bruce
When you say cuff devices, what do you mean?

Ben Woodington
So these are devices that wrap around the nerve.

Steven Bruce
Right, yes.

Ben Woodington
So it's hard to do in the spinal cord, though it's exactly what we're trying to do on the spinal cord, we're trying to completely circumferentially wrap the device around the spinal cord to do very interesting things to it. But on a peripheral nerve, it's just easier, it's far more accessible. So you can wrap devices all the way around the nerve. There is quite a lot work, both academically and also in industry looking at this, so Galvani, the company that was set up jointly by alphabet, I guess they're called now Google verily, and GlaxoSmithKline are looking at peripheral nerve stimulation. So splenic nerve stimulation. There are several other companies that are looking at vagal nerve stimulation for migraines, and for heart control and lung control asthma, all kinds of things. It's not generally what we do, we do a little bit of vagal nerve work, vagus nerve work, but it's possible as well to do that.

Steven Bruce
When you say those companies are doing it, presumably they're doing it through a research organisation such as yours, but it's just not your organisation.

Ben Woodington
Absolutely. I mean, they work collaboratively with these universities, including ours. But certainly Galvani and some of the others now are looking to commercialise it, I think they're probably leaning away now from the academic space. And looking more at what is the actual indication, how we're getting into that right now.

Steven Bruce
And you mentioned heart disease earlier on, how can these be used in connection with heart disease?

Ben Woodington
People are looking at replacing kind of beta blockers or the whatever is used instead of beta blockers now, but instead looking at vagus nerve stimulation, so from the vagus nerve, you can record the signals coming from the heart and from the lungs, and from other parts of the body as well, you can kind of probe that information to figure out, so you can look at, for example, you can look at the vagus nerve glucose levels, you can also look at breathing rate, or kind of whether the lungs are tensing or not, then you can go backwards and you can stimulate to try and override those things. So you can try to speed up the heart, you can try to slow down the heart, you can try to speed up breathing, you can try to relax the soft tissue in the lungs. Very, very early research, again, not my research, but they're using these similar technologies.

Steven Bruce
I was going to say, I might have missed something there. Because you're saying that devices like the one that you've talked about, they not only stimulate, they can also measure, record what's going on.

Ben Woodington
Yeah, absolutely. And I mean, it would probably be a good chance if we go to slide 11.

Steven Bruce
11.

Ben Woodington
Yeah. So it's kind of, this is some older work from a related group to ours, a collaborator. But it's kind of where these technologies originally came from. So taking these very, very fine, thin electronics. And what you can see the image on the left is actually like a lotus flower with the device lying on it. The image on the right is a device lying on the brain, what you can do is make hundreds if you want 1000s, if you really want tiny, tiny electrodes, and you record the electrical signals from the brain, you're not recording the electrical signals from a lotus flower that's just aesthetically pleasing. But it means that you've got these very hyper conformable devices, they can sit on the brain, spinal cord, peripheral, wherever you would like to. And if you go to the next slide, actually, slide 12. And this is just a demonstration of the kind of data that you can get. So the black and blue lines at the bottom there are signals that you'd be recording with conventional metal based electrodes. And then the signals that we're getting, the upper is looking at polymer-based transistor technologies that are developed. So these are the sensors that are very, very close to the tissue and kind of amplified at site, which means you get much, much higher signal to noise ratio. And you can do much more clever things by probing the brain or whatever, the vagus nerve, the spinal cord, and actually trying to extract that information from the neural tissue.

Steven Bruce
Kate's asked an interesting question about sort of the stimulation that we're talking about here. Does the electrical conduction over five to 10 years that this device might be working, does that itself cause damage to the nerves? Or does the heat from the battery cause any damage if the battery generates heat?

Ben Woodington
Yeah, so heat is not an issue. These batteries are designed in such a way and the electrodes have been designed in such a way that you're not getting heating effects or if you are, you're getting very, very mild heating effects that are not going to cause damage to the tissue. The body is not happy with anything you put in it, that isn't itself. So though these devices are more biocompatible, they're softer, they're more flexible, the body still recognises it as a foreign object, and will attack it as such. So it's less that you're doing damage to the body over a long period of time, it's more that the body's natural defenses are coming up and trying to attack the device, you're getting foreign body reaction and you know, tissue is building up to try to explant that advice from the inside out. We can do things to fix that, we can do things to change that. But it's a problem in terms of stimulation because you're getting these layers of tissue buildup, which means you have to up the power of the device to kind of overcome that barrier that's built up around it. In stimulation we can do that. In stimulation, we can jack up the power and if we're using especially these conductive polymers, that's not a problem. For recording devices, it can actually can become quite a severe problem, because the signal integrity is going to degrade over time. So once upon a time, you've had a beautiful array of sensors that are placed on the brain and the brain is happy. After months or years, the body is building up barriers, there's the tissue and that signal integrity is degrading. And maybe the application has gone where it once was.

Steven Bruce
Claire says, does this device constantly stimulate? Or is the patient able to control it, modulate it in the way that you might say with a TENS device?

Ben Woodington
So the patient, no, the patient does not have control over that with most of these technologies. Whether the treatment is on all the time or not depends on the treatment, depends on what you're treating. So some of them work in a manner where they're on for a period of minutes or hours or however long and then they switch off. But many of them are on all the time that they're stimulating.

Steven Bruce
Yeah. And in terms of treating something like muscular sclerosis, how is the divine essentially working there? If you've got damage all the way along various neural pathways, how does one of these devices affect the patient?

Ben Woodington
I'm not familiar with these devices being used to treat MS.

Steven Bruce
It was on one of the press releases. That was one of the hopes for it, that it will be able to treat MS. Maybe that was the hope of the journalist not of the researchers and the technicians.

Ben Woodington
Maybe. I'm not familiar with that application.

Steven Bruce
Okay. Lisa says, is the wrapping of these devices around the nerves, is that effectively similar to remyelination?

Ben Woodington
No, unfortunately, not. Not quite as functional as remyelination, different applications for sure. But no, unfortunately not. You'd need to be looking I think for a, you know, a biotech application.

Steven Bruce
This is taking us back to something we did touch on a few minutes ago. James has asked whether manual treatments such as mobilisation, the sort of thing that we do, is that going to be contra indicated in patients who have these implants.

Ben Woodington
As far as I'm aware, again, this is a question that a clinician should answer better than I can, but as far as I'm aware, these treatments are used in parallel with kind of existing mobility, as well as standard rehabilitation. The same goes for spinal cord injury as well. You don't want to remove the rehabilitative therapy; you want to use a device in tandem to kind of improve the outcome.

Steven Bruce
Okay. Helpful Person says, me again, and she says, how do patients get a referral them? Where do they go? And actually, I was thinking this earlier, and I was thinking, I'm sorry to admit that when I read that

press release, this is I think the first time I'd heard of this, so would you expect most spinal consultants to be fully au fait with this technology and to know how to get it for their patients?

Ben Woodington
The spinal consultants that I've spoken to here in Cambridge are, very, but as far as I'm aware from Damiano, there are only a few centers in the UK who will regularly carry out these kind of surgeries. Probably if you're in one of those, I think Liverpool is one, Addenbrooke's is another one, then you'll probably will be very au fait. In terms of how you get a referral, Steven, that's probably more, as I see, as an experienced surgeon, that's probably more your experience than mine.

Steven Bruce
I'd love to say I was an experienced surgeon, but I'm not. Yeah, I guess my suggestion would be, now that we know about these things, we tell patients to ask. And if they ask if they're referred to a spinal consultant, orthopedic consultant, and they ask about this technology, maybe there's a chance that they will be pointed in the right direction. I don't know.

Ben Woodington
Yeah, I mean, I think you're right. And I think that's what we want as well, right. We want more patients to be going out there and more clinicians to be demanding these technologies, if they are as effective as we believe they are, then we want those just being treated with them. And the only way to do that is through demand.

Steven Bruce
Yeah. And I think we would all love to say, oh, we'll fix everybody with our hands. But we're not stupid enough to think that we can do that. And what we would like to do is to stop people having to use drugs of any sort, opiates in particular, and maybe something like this is a much more attractive option for them. Neeve has asked how you actually remove the devices, once you achieved what you regard a success with your rehabilitation. And you said earlier on, actually, these things are there for good because they're not going to fix people. But actually, sometimes pain relief gives the body a chance to develop the stability and the strength in the right areas in order to overcome the problem, doesn't it? So maybe there's a point where you say, well, I'm going to take this thing out, is it a simple process?

Ben Woodington
Absolutely. And it is a simple process, simpler than putting it in. And it's something that many pain surgeons or neurosurgeons are familiar with doing, because sometimes these devices are not compatible with MRI, if the patient has to have an MRI, that's one of the most common reasons to remove the device. So well characterised how you exactly go about that. For our device, it's exactly the same, you take the IPG out, and you pull the device out the back. It's nothing more complicated than that.

Steven Bruce
When you put it in, it was all nicely rolled up, though. Now you're pulling it out, it's not rolled up any longer. So does that make it more difficult?

Ben Woodington
It doesn't, because these devices are so thin, they collapse in on themselves. If you had something like a semi rigid device, maybe with like a mechanical actuator or a passive actuator, yes, you're not going to be able to pull that back through the same tiny percutaneous hole that you inserted it in. But for our device, we've run these experiments as well, you absolutely can, you can just pull the thing back through a fine hole, through your one to two mil hole and the device just crumbles back in on itself.

Steven Bruce
From what you said, though, your device is perfectly compatible with MRIs.

Ben Woodington
It is yeah, yeah.

Steven Bruce
So there are fewer reasons to have to remove it until it stops working or stops being effective.

Ben Woodington
Yeah, absolutely. I mean, that's the goal. I mean, it's something that we're working on at the moment, especially using these markers. We're adding kind of metals then to the device, more metals device. And we have been looking at like, does that change the MRI compatibility as well? Do you get heating effects on the device? Or do you get artifacts in the MRI and is something, again, like with the clinician in mind, you really have to think about, you can't just throw these devices out there and hope for the best. Some of the implantable pulse generators are also not MRI compatible through heating effects. But it's something, again, that the industry has been working on to make sure that new devices are.

Steven Bruce
Okay. Lawrence, again says this all sounds great. Paracetamol was discovered in 1893 and is used widely. They have theories but still don't know how it works. All they know is that it works centrally, chronic pain can be distracting and disabling. But if the devices work, then go for it. So, he's just supporting what you say that there's no reason not to do something just because we don't know why it works properly.

Ben Woodington
I've used the exact same anecdote about paracetamol. So that's why I say we're kind of in a similar neuromodulation therapy. Like, we're in this place now where people have so many, so many indications, so many things, and no one quite knows how they're all working. Maybe that's okay.

Steven Bruce
Well, I don't know how often in your particular position you come across patients in chronic pain, because clearly yours is a research and development organisation rather than a clinical environment. But I mean, Lawrence is putting it mildly to say that chronic pain can be distracting. You know, chronic pain stops people sleeping. And sleep deprivation is one of the first tactics when you're interrogating people because it's really, really unpleasant and makes life miserable. And of course, chronic pain just makes people's lives completely miserable, doesn't it? Carrie says, would it be possible still to use an epidural with these in place?

Ben Woodington
Safe to use an epidural. I would believe so. I wouldn't want to be that call. Again, probably a pain surgeon should advise on that. But I can't see why not, as long as you're going below the device you should be fine, right. You don't want to be having a needle placed on the device. You are going through similar, but I think epidurals will be placed, probably often an epidural will be placed lower than this device, but please consult a pain clinician.

Steven Bruce
Well, we don't administer epidurals either. So I mean, somebody else can think about that when we come across these. DJB says in my knowledge of spinal issues in neurology, my explanation to patients or animal owners is that typical structures involved are the disc joint, facet joint, sacroiliac joint etc. While the spinal cord may not necessarily be compromised, are the devices you've been describing able to be used within those structures to modulate the nociceptive and mechano-receptive activity.

Ben Woodington
Yes, but I mean, again, it's a very important point again, like what is the root cause of the pain and you know, is this the right therapy to treat it? Because if the pain is not of neuropathic origin, then you're already at a place where you're sort of like, is this necessary? Or should there be some sort of corrective surgery first? And probably many would say, first, you try to cure, right? Not just treat the symptoms. And it's something we're actually exploring, again, with a, as mentioned, and dogs as well, with a veterinary surgeon to look at, you know, many of these dogs suffer from back problems way more than people and they're usually through skeletal issues, bone issues. We're looking at these devices in companion animals as well in dogs and saying like, does this makes sense in those places as well or not?

Steven Bruce
So you're looking at them in dogs and asking that question, what answers are you getting so far?

Ben Woodington
We have not answered that question yet.

Steven Bruce
All right. Okay. Jane's going back to the removal of these things and says, doesn't the buildup of scar tissue make it difficult, more difficult to remove them?

Ben Woodington
Yes, it can. But it tends to be okay. Obviously, we've not tested these particular devices yet on living patients. So we'll have to assess that. The percutaneous and the pelvic devices tend to be fine. They can be taken out with relative ease; we expect ours will be the same. You wouldn't expect scar tissue to be kind of completely encapsulating the device. There's no perforations in device, there will be no tissue growing through the device. But it's something of course, we'd have to try. And we'll be trying in the coming years.

Steven Bruce
Okay, well, we've got a few minutes left, Ben. You teased me earlier on before we came on that there was lots of other stuff going on around you. So what's coming up next? What am I next going to read in The Guardian that's going to pique my interest?

Ben Woodington
Yeah, I mean, so we're about to submit a paper actually, which I will speak only slightly about, where we're looking at devices that once we've covered the dorsal part of the spinal cord, how much further can we go around, and what utility is there in going all the way around, and we've got some really, really cool data where we've wrapped this device all the way around the spinal cord, covering, you know, fully the ventral side of the spinal cord. And we started recording studies. So this is kind of never been done before, like placing a device circumferentially is only possible by using these particular soft materials.

Steven Bruce
Have you done this in a living creature?

Ben Woodington
Yes, yes.

Steven Bruce
Well. Are they still alive?

Ben Woodington
They are not alive at the moment. No, but that was because they got to the end of their study. But we're looking at actually probing that information. So, can you understand like which pain pathways are activated, and also which motor pathways are activated when the person's living their life, or an animal is living its life. So moving around, and you know, stubbing a toe or like pinching a finger, like, what is lighting up in the spinal cord, and which reflex pathways are lighting up in the spinal cord. It's not something that's ever been able to have been done before without penetrating probes, without actually sticking wires into the spinal tissue, which causes damage and ends up being completely useless. It's okay for understanding fundamental neuroscience questions. But it's completely useless for any kind of like, how does this behave in the real world, what's going on in the real world? So what we've done is a very interesting work where we've wrapped the devices round, we've looked at motor effects, sensory effects, we've looked at spinal cord injury and which pathways are still alive when there's an injury in place. We've looked at stimulating above and below that injury, and kind of really, really trying to probe the spinal cord like, what is going on and when and where. We're going to be setting up lots of collaborations at the moment with that device that we've developed now. We're going to go first in human interpretively and look at like how exactly these tracks, these pathways in the spinal cord are working.

Steven Bruce
And I'm just being dragged back to the earlier bit of the discussion by some of these questions. Jen says that she's confused and thought this was only being used on cadavers. And now we're talking about patient referrals. Am I right in saying that it's not the inflatable devices being used currently in patients. It's the older pedal devices. So you can get referrals for those.

Ben Woodington
Precisely. Yeah, yeah. So spinal cord stimulation exists, it's been out in the market for, you know, 50, 60 years now, I think. People can get these devices currently, our device if we check all the right boxes, and we get the right funding, you know, we're still looking at some years before we ever market.

Steven Bruce
How many years would you speculate, assuming all goes well and getting funding.

Ben Woodington
Medical devices take a long time to develop. We've got a pretty healthy grant that we've just been awarded, which will take us up to preclinical work in the next, maybe first inhuman in the next sort of couple of years. It will then take another three to four years probably to actually get to market. You're looking at five years minimum really to get a medical device, if you do very well. We're talking about highly invasive, class three medical devices. Really, needs to be jumped through a lot of hoops to get them out onto the market, anywhere in the world, but especially in the UK and the US.

Steven Bruce
You need some sort of massive virus to affect the spinal cord, which will prompt people to get these things through more quickly, perhaps.

Ben Woodington
Maybe that's what we need to accelerate.

Steven Bruce
George has asked if this is what Elon Musk's neural link is based on?

Ben Woodington
Yeah, we get asked that question a lot in our lab. Musk's technology is built on pedot:pss, which is the conducting polymer that we use in our lab as well and have used for the last decade or so. They're looking very similar, underlying technologies with different application. They've got some profound innovations on the way they placed the electrodes using these kinds of surgical robots. But ultimately, yes, we're looking at similar technologies.

Steven Bruce
I'm not familiar with a neural link, is it aimed to achieve the same patient symptomatic relief?

Ben Woodington
So they're looking at brain treatment, brain probes for people suffering from paraplegic, tetraplegic to begin with, they have grander plans than that. Elon Musk always does have grander plans than that. For their first effect they're looking at they're looking at people who've lost the use of some part of their body. It's an interesting application, of course.

Steven Bruce
Ben, this has been, this is really good. I mean, we've had lots and lots of fantastic comments about the discussion this evening, and I'm sure we'll get more coming in any second now, but just that you're aware, one viewer has called you the Ben Fogle of the PhD world. I'm not personally familiar with Ben Fogle, but I gather that's a really, really nice compliment to you. Simon has said that you really should be an osteopath. It's probably chiropractors saying, you should have been a chiropractor as well, because in Simon's case, you remind him of his father-in-law, who was an engineer before he was an osteopath, and who will soon celebrate his 100th birthday. So my own view is that if you were an osteopath, we'd need somebody still doing your sort of work, because otherwise, patients would go without.

Ben Woodington
100 years, that's amazing, isn't it?

Steven Bruce
There's still time for you to have yet another career, isn't there. Medical chemistry and pharmaceutical devices, you could move on to osteopathy. Craig says, if we can treat people with devices in place, they could help with osteopathic research to see exactly which pathways are being affected with treatment. Yeah, I guess that's one for the osteopathic and chiropractic worlds that perhaps we could if we could monitor what's going on using devices like this. And Joe has asked about the cadaver work, should we be worried about the Frankenstein effect? I think there's a certain amount of tongue in cheek in that question.

Ben Woodington
On your osteopath question, please, anyone reach out, if they do think these applications, our group are very keen to collaborate with these kinds of applications. So please do reach out to us as well.

Steven Bruce
Well, I mean, it won't have come across your radar, I'm sure. But physical therapy suffers from a lack of evidence because nobody's putting money into physical therapy for evidence. You know, if you're trying to develop a drug or something which will sell for millions, then you can easily do the research. And I suspect that will still be the case with these, but I will feed that question back to you about how we might incorporate it into osteopathic or chiropractic research. We've had lots and lots of lovely comments, I'm told. And I speculated before we started that we get somewhere between four and 600 people and I was pretty much right, we've got 550 according to my team here. So yeah, that's a pretty damn good audience for a Tuesday evening. And they could be out enjoying the pub or whatever else it is people do on Tuesday evenings. Before we close, anything else you'd like to tell us about what's coming out of your department?

Ben Woodington
There's so much coming up out of this department. I'm not sure what my PI would like me to talk about and what not to talk about.

Steven Bruce
Tell us what PI is.

Ben Woodington
My principal investigator is Professor George Malliaras, he runs the lab here, he is a phenomenal mentor and a brilliant scientist. He is not in this room. He's not telling me to say that. Though I am in his office at the moment. We're working on so many exciting technologies. We really do. Many of us in this group, the clinicians we work with, and also George, we really, really do believe this is the future of medicine. We believe it's the future of measuring what the hell is going on in the body. And then how to treat it downstream as well. I think there are a lot of people getting involved in the space now, academically, it's been going for 10 to 20, 40 years, probably. There are a lot of companies now jumping on this. And I think finally we're starting to get translation because we're getting monitorisation of these technologies because the kind of safety questions are being answered we're going to start doing that translation into the medical world and I think we'll start so these technologies actually, people will be more familiar with them, doctors will be more familiar with them.

Steven Bruce
And it's just fantastic. It really is. We like to think that we try to treat the causes rather than the symptoms. But there comes a point when you've got to treat the symptoms. Maybe because there is no other resolution for a problem, but also maybe because treating the symptoms gives you that opportunity to help the body recover, you know, all these things. So I think we're extraordinarily grateful for the work that you're doing. And I'm looking forward to seeing these things on the market and seeing some benefit for our patients. Ben, it's been great. Thank you very much for giving up your time. Again, I'm sorry that you were bounced into this by Dr. Barone. And you can tell him that he missed out on the clinical questions which you were unable to answer, but that's not your fault at all. We've had so many wonderful comments about all this information that you shared this evening that yeah, he should be jolly pleased that he put you in the spot.