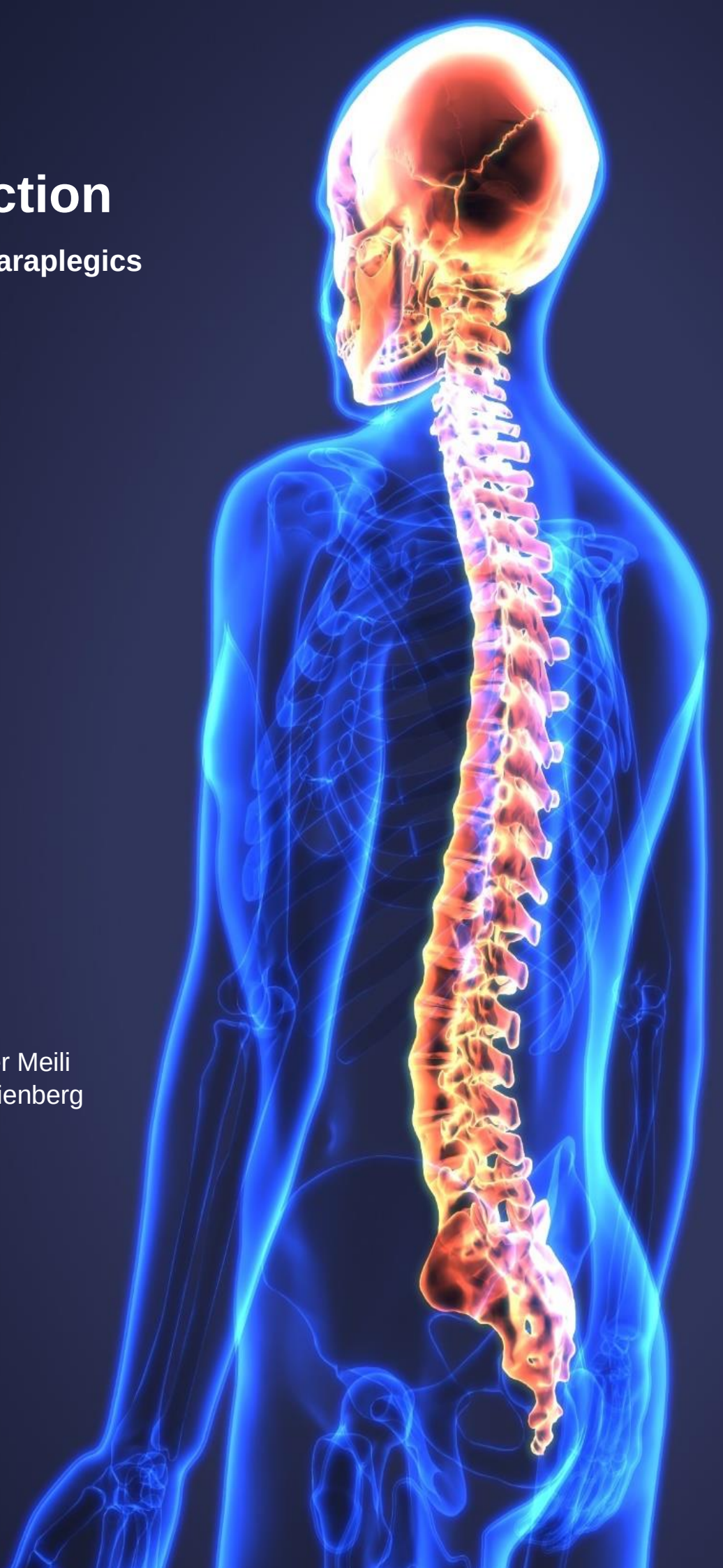
Axon Action

The future for paraplegics



by Alexander Meili
and Timo Meienberg

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1. Preface

As we were looking for a topic to work on, we remembered a documentary on SRF [documentary 1] we saw a couple of years ago. The documentary was about the work of Grégoire Courtine a researcher from the EPFL in Lausanne who, with the help of his technology, was able to make paralyzed people move and walk again. When we rewatched it we both were fascinated by the technology. We thought that this was a ground-breaking achievement and that we wanted to dedicate our work to this topic.

Paraplegia is one of the worst non-fatal injuries imaginable. Worldwide about 2.7 million people are affected with about 130'000 new people every year [link 7]. The treatment [documentaries 1,2 and 3] [see interview] developed by Grégoire Courtine has the potential of changing the lives of all these people and we are convinced that in the future this technology will enable paraplegics to live a normal life in the future.

For our term paper we shall explore to find out how the technology works, and how it's used. Additionally, we shall examine what the limits are today and what the limits of technology will be in the future.

2. Introduction

This technique has gathered quite some media attention. There are articles about it in the largest newspapers across the world like The New York Times, The Guardian, BBC News and National Geographics. This attention can be explained by the fact that paraplegia is one of the biggest unsolved problems in medicine. One can even say that this possibly is the most important innovation in this field of paraplegia since the invention of the wheelchair. For about 400 years no significant progress was made, until Grégoire Courtine came up with the idea to stimulate the nerve cells directly with an electrode array which was previously used to treat chronic pain [see Interview]. This idea led to many new inventions, innovations and studies in the past 15 years which further improved the technique and therapy. In the next couple of years this technology may be implemented and used to treat patients.

This technique is not used as a treatment for patients yet because it is still in the developing phase. But the goal is to use it for paraplegics or tetraplegics to regenerate their spinal cord connections which were damaged so that these patients can use their arms and legs again. This technique of regeneration is only possible due to neuroplasticity. Neuroplasticity allows the nerve cells to reconnect. Thus functions of destroyed nerve cells can be transferred to newly connected nerve cells.

Although there are some alternative treatments for people with SCI (spinal cord injury) like medication [link 5] or therapy to strengthen muscles and nerve cell connections, these only work for patients which already can use their legs and arms. There is also the possibility to use an exoskeleton which executes the movement while containing the patient [documentary 4] [link 4]. Some experiments were conducted with a robotic arm which could be controlled with a brain implant and electrodes attached to the head of the patient [documentary 7].

3. Description of engineering technique

The technique we describe in this term paper was developed by Grégoire Courtine and Co-researchers and currently experiments are conducted with humans to see what can be improved, as the preclinical tests in rodents have succeeded. One of the main facilities where such research is conducted, is the EPFL in Lausanne (Switzerland).

The technique works as follows: A surgeon applies a cut to the back of the patient and to the spine, then an array of electrodes is placed onto the spinal cord, at the exact place where the neurons steering the leg muscles are passing, with the single electrons targeting one specific nerve cell, each. The nerve cells which are targeted can be stimulated with an electrical impulse so that they activate the corresponding muscle, which then contracts. This contraction triggers a movement of the leg [Wagner 2018]. The electrodes get the energy needed from a pulse generator which is also implanted and can receive the information to activate certain electrodes. The pulse generator gets the information on which muscle to activate by a controller in the hand of the patient. The pulse generator is controlled by the patient via a controller, which allows the user to turn on and off the stimulations. When used at home the pulse generator is programmed to activate the electrodes according to a

program [see interview answer no. 4] which simulates the walking movement of an uninjured person. To explore how we move our legs, the researchers analysed the spatiotemporal activation of neurons and their corresponding muscle groups [Wenger 2016]. In the latest experiments the controller was linked with the brain of primates with spinal cord injury, using a semi-invasive brain implant [Capogrosso 2016], allowing it to detect electrical field potentials in the motor cortex [see interview answer no. 10]. These signals can be decoded and then the pulse generator can activate the different muscle groups accordingly. This enabled the primate to move its legs as it wished. The purpose of this device is to enable the patients to train and regain control over paralyzed body parts. This, however, only works because the spinal cord is not destroyed completely in most cases. In most cases are 20 % of the original nerve cell connections left, but these do not suffice to send signals into the region below the paralyzed part of the body. however, since the nerve cells in the paralyzed body part are not dead, this is the reason why they can be reactivated with electrodes. To learn how to walk again and to keep this ability it is important for the nerve cells at the injury to build up new connections (neuroplasticity) [Anderson 2018] as nerve cells cannot reproduce like other cells in the human body. The process of neuroplasticity takes place in the brain and spinal cord and is the process of rewiring neurons and assigning functions of destroyed neurons to neurons which were not destroyed or injured [link 2].

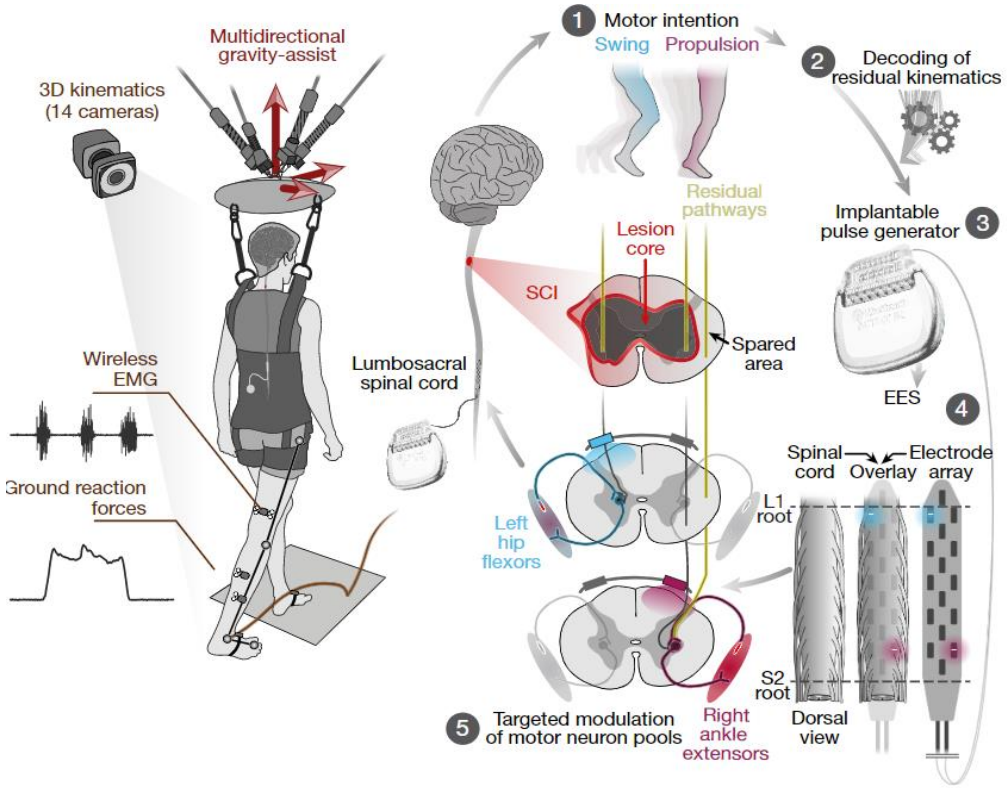

Abb. 1: This picture sums up the complete process of the technique in action.

4. Documentation

Before we started writing the term paper, we made sure that we had an interview partner to answer our questions regarding technical questions but also questions about the future of this technology. When we sent an interview request to Grégoire Courtine his assistant and associate Leonie Asboth kindly agreed, and we had a very informative conversation which is attached in the appendix.

Despite the EPFL being in Lausanne, the Covid situation prevented us from visiting. Thanks to the documentaries on SRF [documentaries 1,2 and 3] we are still able to include some insight from the labs.

Abb. 2: This picture shows the first walking attempt of David Mzee, Mr. Courtine's first patient. The first steps were done with a lot of support from the gravity assist and very hard for David which is not surprising when considering the fact that he didn't move his legs for five years.

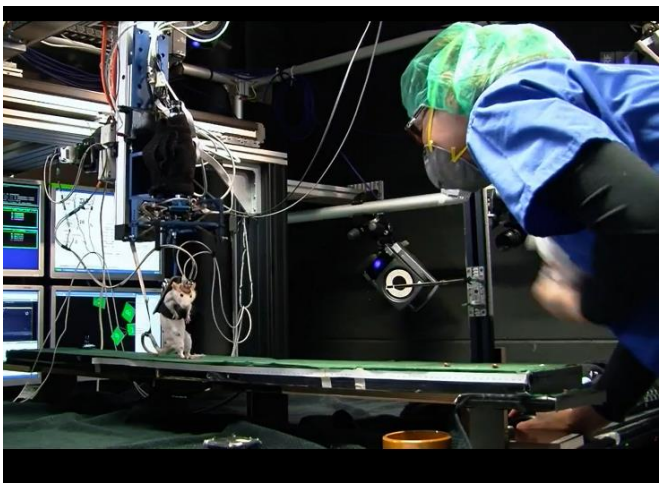

Abb. 3: Before the technique could be used on humans, scientists had to prove its effectiveness on lab rats. On the left we see a paraplegic rat that uses a similar technique as David to walk.

5. Discussion

With this new technique much progress was made in understanding nerve cells and how they are activated to enable locomotion [Wagner 2018]. But the main progress was made when applying this technical device to humans which were not able to walk before (David Mzee). These paraplegics then were able to learn how to walk again, which reactivated the nerve cells and thus supported the reconnection of nerve cells due to neuroplasticity [Wagner 2018]. This technique will help humans with spinal cord injury to join the healthy people in their everyday live and they eventually will be able to participate in activities which they were excluded from because of their disabilities. At present this technique is not currently available for treatment of patients, but still is in a testing phase, as there are some risks and opportunities which are not yet researched completely. To find a solution which is best for the vast majority of para- and tetraplegics, the scientists need to define and test more parameters and adjust accordingly. Because one mistake could result in severe harm to the patient, as the device is next to the spinal cord (and in the latest projects to the brain). The future research step which is probably the most promising is the so called “Brain to Pulse Generator Interface”. With this, patients would be able to control their legs at will and without using a remote control [Capogrosso 2016].

From an ethical point of view, this technology should be supported, because it can improve the lives of many para- and tetraplegics and could also lead to further improvements in the lives of every human in the form of brain-chips. But on the other hand, the technology has its price: We injure animals on purpose to understand how the technology works and how to improve it. But on balance, we think it is reasonable, as this is compares to testing of new drugs with animals, without this testing, humanity will not make any progress in treating patients more effectively.

The advantages of this technology are (1) that the devices can be implanted in the body, which hides it from the surroundings and protects it from rain and other natural influences, (2) is very light weight and thus does not hinder the person wearing it in any way. The positive points of the battery are its long lifespan (about nine years) and the rather easy surgery to change the battery. The battery is only needed to charge once a day and can support the usage of the device during the day. But it is a battery nonetheless and therefore contains harmful chemicals which are not healthy if the battery should have a leak or is damaged. There is also a benefit to the semi-invasive brain-chip which enables accurate measurement of electron potential and thus can directly read the intentions of the brain to move [see interview answer no. 10]. But the biggest strength of this technology is that it allows to regenerate the ability to walk after a spinal cord injury [Wagner 2018].

The negative aspect of this technology is that it is implanted. This can cause inflammation and other infections [see interview). It also needs a surgery to remove and implant, which constitutes risks on its own, especially if the implant is a brain interface (although the EPFL research group is testing the functions of a semi-invasive brain implant which does not pose as much risks as an invasive brain implant, like the one tested by neuralink [link 3]). Also, the material used to produce the device placed on the spinal cord is harder than the skin and less flexible, which can cause the device to shift, potentially resulting in the device’s malfunction [Schiavone 2018]. Another weakness is the long time it takes the patient to activate the stimulations [see interview answer no. 7]. This may look like a lot of risks, however with further research these risks will be minimized or even completely removed.

The opportunities for this technology are numerous. For example, the EPFL research group wants to test whether the same pulse generator could also help patients to regain control over their arms even though they are tetraplegic. Neuralink [link 3] is trying to research the brain with the usage of a brain chip, which could also lead to helpful insights and innovations to improve the health of mankind. If this technology is accepted by the insurances and healthcare, effected people could get help. Recently, a

study was published in which researchers succeeded to control blood pressure with an electron array. This solves a problem of many patients with SCI as the brain cannot control the bowel, bladder and the heartrate if the connection to the autonomous nervous system is interrupted (autonomic dysreflexia) [link 1] [Squair 2021]. The possibility movement of their legs could address other common problems of paraplegics like obesity and diabetes [link 5].

The threats of this technology are that a brain chip could be abused by oppressive states and regimes which seek to control and monitor what their people think. With the charting of the brain and the resulting knowledge this does not seem utopian, as nobody would have thought of handheld computers at the beginning of the computer's history. But not only the monitoring of the population is a threat, also the remote controlling of humans against their will, just like the researchers are controlling the muscles of rodents.

6. Summary

The stimulation of nerve cells with electrodes in people with SCI has the potential to be a solution to a problem with which humanity could not adequately deal for a long time. It may also help in developing new technology and in improving old concepts such as the brain chip [link 6]. As more research is conducted on this topic it becomes more likely that patients finally get access to this treatment as eventually healthcare carriers will accept it as a treatment. Although there is more research needed, we are confident that soon we will see former paraplegics walk. That's why we think that the strengths and opportunities outweigh the threats and weaknesses.

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7. https://www.youtube.com/watch?v=ogBX18maUiM&t=269s

Graphics:

1. Picture on the cover: https://answers.childrenshospital.org/spinal-cord-injury/
2. Abb. 1: Wagner 2018: https://doi.org/10.1038/s41586-018-0649-2
3. Abb. 2: https://www.srf.ch/play/tv/puls/video/der-traum-vom-gehen-neue-hoffnung-fuer-gelaehmte?urn=urn:srf:video:f11a5721-5f27-4c37-8192-7e53ecd96285
4. Abb. 3: https://www.srf.ch/play/tv/puls/video/der-traum-vom-gehen-neue-hoffnung-fuer-gelaehmte?urn=urn:srf:video:f11a5721-5f27-4c37-8192-7e53ecd96285

Interview:

The complete interview is in the appendix.

8. Appendix

The interview with Leonie Asboth (16.12.2021)

This Interview was held oral over teams. The questions were asked by Alexander and Timo, an associate of Grégoire Courtine (Leonie Asboth) from the EPFL answered. The interview text was printed like the pronunciation and grammar used.

1. *Q: So, we would like to know what your motivation is to research on this topic?*

   A: I can also introduce myself because you were interested in Gregoire at first. I did my PhD in the laboratory of Grégoire Courtine, so I started in 2012 and finished in 2017 and I was really working on the preclinical data, so we were first developing all the therapy in rodents so rats and mice and I was really looking at how this therapy of spinal cord stimulation can affect the reorganization of the brain after spinal cord injury and we really found results of the influence of the motor cortex but also the brainstem and that there are changes of the circuitry to regain locomotion after spinal cord injury and at the same time they were developing all these technologies also for humans. The easier part in humans is that there was already a technology for spinal cord stimulation which was accepted for chronic pain so matronic developed this lead that you can implant for chronic pain and we were reusing the same technology but we were adapting it for gates so we were really stimulating it much higher amplitudes and in the region of the spinal cord it was more interesting for us to control the muscles so it all started like this and now we have already nine patients that were implanted with the technology we also scaled up, to have training on daily basis we looked at the effect of training with spinal cord stimulation and now we even have a more studies for brain recordings spinal cord stimulation for blood pressure control and so on. So that's how it started and now we're really scaling up to a lot of different functions.

2. *Q: OK so that's your main field now so you work on that?*

   A: Yes, exactly. Now I'm in a clinical division, so I finished all the experiments with the rats and then worked on the clinical division and we're leaving all the different projects at the clinical division.

3. *Q: Did you still work with the implants into the spinal cord, or was it and I think I saw this on SRF and that's they or Grégoire Courtine said that they had this brain implant, or is it working with this now?*

   A: So, what we did first is that we implanted these nine patients only with the spinal array and once we finish the study we launched this new study for the brain implant, but it's only for patients that were already implanted with the spinal array. So, from these nine patients we now have the first patient that also got a surgery for the cortical implant and we're decoding the intention to stimulate the spinal cord and we already had the first patient that is implanting and trained to use this brain spine interface and eventually in the future we can have maximum three patients so that already have the spinal implant in which we will also add the cortical implant.

4. *Q: Did I understand correctly that with only the spinal implant you need to have a controller separate from the body to stimulate the nerves?*

   A: We have different options one option is what we call the open loop so we just put a program that is automatic so you will have x milli seconds of flexion on the right and at the same time you have extension on the left and then you exchange, and you give this program so it's like a robotic way of walking. That was the very first type of stimulation. Then we did use the closed installation and we added accelerometers on the foot and this is triggering the stimulation so when the patients just starts like leaning forward it's triggering this simulation so in that case it's really dependent when the patient starts doing the movement and for patients that have spinal cord injury like complete spinal cord injury in that case they have the possibility that buttons so it's really a click that they do with their hands and when they click on the button it triggers the simulation and now the brains finding to face it's the level up so it's really the brain that controls the stimulation just by default but at first it was this stereo type stimulation that we have.

5. *Q: In this episode it was mentioned that these nerve cells after the spinal cord breaks or has an interruption is dormant below a certain level. How does this work with the reactivation of the nerve cells and the neural plasticity?*

   A: So, one important point to know is that actually there is no regrowth of the axons that are interrupted but in every patient, even in the most complete paralyzed patients. In the most patients you have spared fibres so you still have a little bit of fibres that cross the injury and these fibres end up with a termination so these are the dendrites and the end of the axons, dendrites that connect to everything that is below the injury and if you train a lot and you reactivate all the local circuitry in the lumbar region you're going to have a growth of these dendrites so you're going to have more connections of the neurons that are spared so it's not an regeneration but it's neuroplasticity meaning the axons are going to go somewhere else neurons are going to connect to other neurons you will have much more connections to different types of neurons but it's not regeneration that's why it's called neuroplasticity.

6. *Q: So that's the effect of training so you do you get new connections?*

   A: yes, exactly and we saw this in the rodents, in humans it's more difficult to look anatomically but in the rats and mice we can do slices of the spinal cord and we can look at these reconnections and that's how we saw that the rehabilitation creates reconnections.

7. *Q: In that SRF episode one patient was portrayed I think it was David and he learned to walk again with this technique, and it was mentioned that there wasn't a ceiling researched for the possible reactivation of the legs and do you think you have now researched the limit for your method or is there still progress to go and possibly to reactivate the legs until they are normal again?*

   A: So yeah, there are several answers several elements to this. The first one is the training so she needs to continue training and probably he did not reach a plateau so if she continues training on a daily basis, you can continue having increase its not the truly accepted therapy gets so, we're not creating any regeneration of the neurons. This is one thing that needs to be developed so on the research part to regeneration of the sectioned axons the second thing is the technology to enable daily rehabilitation so now we have a prototype that we're using so it's we're using it in rehabilitation sessions in the hospital and they have a prototype that they can use at home but the idea is to develop technology to make this even easier so at some point they will have a watch that activates their simulation on the daily basis where they can choose the program and it will be easier and easier to use the simulation every day. When they want to stand up and go to work, when they want to go to the toilet, when they want to transfer in the bed and so on. Currently they need to connect several things plus the watch (so they can use the simulation) (show for night) but it takes a long time for them to use the stimulation, so we are improving the technology so that it gets very quick for them to use. Then they can train more and probably they'll have more neuroplasticity, but at some point, we will still need to develop the regeneration projects to really recreate new connections.

8. *Q: They can't really use it in their everyday lives right now?*

   A: yeah exactly

9. *Q: it was also mentioned that the Tesla founder Elon Musk is working on a very similar project with neuralink but the difference is that the neuralink is invasive into the brain and I think your project is non-invasive could you please explain the difference?*

   A: (Semi-invasive) it's still a surgery it's minimally invasive. But it's still a surgery so it's not into the brain but you replace the part of the of the scalp (Skull) but you still have to do a surgery open up, make two holes and then remove the bone and add this array, but it does not go into the brain.

10. *Q: How can this array still manage to measure the brain signals from the brain when it's not connecting into the brain*

    A: so that's what we call ECOG it's some kind of local field potential. There is e.g., system which are really just electrodes to put on the on the scalp (Skull) these already record the local field potentials, so the local changes of groups of neurons. The one that we have is touching the brain, but it doesn't go into the brain, but you can be more precise on these local field potentials. You don't record neurons individually, but you have impression of the activity of neurons and since you're closer to the brain than this non-invasive technology and you can have a much better resolution of the decoding of the areas that are below this array.

11. *Q: what's the advantage from a semi-invasive technology compared to invasive technology?*

    A: the advantage is that you have is that you can remove it whenever you want. I mean the invasive as well, but you don't damage any of the of the neural structures.

12. *Q: OK so it's less risk you take?*

A: The surgery means also less risk of like infections because you don't touch the neurons and so.

13. *Q: You said that the nerve cells or there was still a connection between the brain and the leg even in fully paralyzed patients but why can't they move their legs when there's a connection*

    A: Because it's a reduced to 80%. So they're really is a connection but normally in in you and me we have a full activity like all the regions of the brain they can reconnect and for them there is only a subset of sparing that probably comes from the brainstem but the brain needs to reorganize everything through this pass way so it takes a long time to reconnect and then all the circuitry in the spinal cord in the lumbar region so for the connection of the brain they don't have 80% of the usual connection so it becomes really dormant , that's why we reorganize all of this yeah.

14. *Q: And this dormant nerve cells they also die, or they just keep living*

    A: Yeah, they don't die but they don't have any fuel if you want like neurons, they usually get information from the neurotransmitters like glutamatergic. I don't know if you did a bit of neuroscience also, but all this information come from the brain and here they don't have it anymore so they just become they don't activate so they don't get the fuel to live on, but they don't die neither that's why with the electrical stimulation we can reactivate these neurons we can give the information to these neurons.

15. *Q: Is there a difference between a patient which was paralyzed for five years or patient that was paralyzed like yesterday and then got the implant, or is it the same?*

    A: yeah that's a very good question so we showed also in the in the preclinical so in in rodents we show that it's better if you start training earlier because you don't have this atrophy of the muscles the problem is the longer you wait then more the muscles will become slow because they did not function for a long time and this atrophy is very complicated to regain walking also and also you have more and more what we called demyelinisation so the neurons they have this myelin around the axons and in the region or below like of the of the injury all the neurons become demyelinated, but maybe if we would reactivate them soon enough we would avoid this demyelination. Probably the earlier the better but we did not test it in humans yet.

16. *Q: To come back onto the spinal connection, like the earlier prototype. I would like to know how that works. Could you describe that?*

    A: So first I can describe you this spine connection and then how this simulation works. Maybe I can show you some slides just give me a second … you see the Presentation here?

17. *Q: Yeah, we can see it*

    A: So, this is the spinal cord is really in the lens here and then you have these roots which we called dorsal roots and these dorsal roots they come from the periphery so they come from the muscles and they enter the spinal cord and if you check actually, you can show your another picture … I'm trying to find a good picture that explains this quite a lot here yeah that's how it looks if you take really a slice of the spinal cord you have here from the muscles and from the skin you have all the appearances that enter the spinal cord from the top then from there it connects to interneurons so really neurons everywhere in the spinal cord and here in this region you have the moto neurons and the moto neurons when they get active they send information to the muscles to contract and this is what we call a reflex loop so that's only local in the spinal cords but from the brain you have a lot of information that connects to these neurons or to the moto neurons to activate this circuitry and when we do the spinal cord simulation we can only implant an array on the surface on the top you cannot implant it down there or on the side so it's really a physical limitation so you have to implant it on the top here and the stimulation they're going to activate these large diameter fibres so it's going to activate all these neurons here and then send the information to the moto neuron which will contract the muscles and that's how the spinal cord stimulation works so we activate this which will activate this and then activate the muscles.

18. *Q: OK*

    A: but we have a lot of there are lots of different muscles so here for example this is really a patient you see when you walk basically you have a lot of activation from different muscles so the extension and then the flexion and what we do and all these activations in the spinal cord there are different regions so they're up there but mostly down there so basically what we do is that when we simulate if we want to stimulate for example these muscles we want to stimulate this area of the spinal cord that's why when we implant the technology you're going to choose the electrodes where you want to stimulate so if you want to do the hip flexion we will stimulate with this electrode and with this electrodes if we want to do the extension this area we're going to simulate this election and then you can really choose if you want to have the propulsion we're going to simulate this electrodes that's what we call this spatial temporal stimulation so that's why you need to cover all the this area of the spinal cord, it's not very big, the lead is like this, so if you want to cover the whole area you need to really activate all these different types of electrodes to stimulate is that clear enough.

19. *Q: yes really good yeah thank. so, this method would also work on patients that can't move anything from down here like next time so then only with the arms?*

    A: exactly also you have the the injury can be quite high but the region to activate the legs it's everywhere the same so it's quite low actually in the spinal chord I don't know , let me check something else to explain because it's very important to understand. so where do we have this … so you see that's the whole spinal cord right here. so you have the vertebra which is the Bony part and the vertebra in gray and the spinal cord in yellow here and every vertebra you have the roots showing out and everywhere so you have the spinal cord that goes from the brain down there in every route that goes out is activating a different type of muscle so down there it's for the legs there it's for the autonomic function like blood pressure and for the trunk and up there it's for the arms, if you want to stimulate the arms of course you need to stimulate here but if you want to simulate the legs you're always going to stimulate in this area so really in this area here but sometimes the injury can be here or here or here it depends but when we stimulate the legs we always stimulate here. That's where the moto neurons are for the leg activation.

20. *Q: What if this place where the moto neurons are is damaged by this accident, could you still stimulate the legs, or would that be more difficult?*

    A: so normally if the accident is down there the patient still have all these spinal cord that is functional so they can move their arms their trunk they can move like most of the of the legs also but if it's damaged in this area it's going to be very difficult to stimulate this area you can still stimulate but not all the moto neurons are going to respond to this stimulation but also your injury is less affected so if it is really in this area you can still walk a little bit because there is some sparing but it's stimulation you can still do it but in our case we only look at patients that have higher injury so much more complete basically.

21. *Q: So, did you have a question you know that was my question so if you search for patients that have injuries in the higher regions, but under the arms?*

    A: yes, but we also have studies now with the tetraplegic patients they have very high injuries, but they can almost not move their arms anymore.

22. *Q: it was mentioned from Elon Musk that this invasive method would have a much higher infection potential is this also true for the semi-invasive method or spinal connection*

    A: it depends on the on the type of infection. Of course you have always different types of risk you have the risk related to the surgery because you still need to open up and then do a Laminectomy or like remove part of the bone implant the device and all of this is the same so you can have a risk of bleeding you can have a risk of post-surgery infection so if it rejects the foreign body or if something was not sterile enough but normally all the surgeries are extremely sterile so it does not happen very often but this is the same for all types of surgeries. it's just that in the invasive you can have inflammation of the brain so the brain aeras, which you will not have with the semi-invasive technique, but you can still have inflammation around the skin or inflammation around the implant that is still possible but not inflammation of the brain regions.

23. *Q: and one last question for me at least, this spinal connection does it work with a battery and if yes how is this battery charged and could you put this thing be replaced?*

    A: it's like a pacemaker it's called an implantable pulse generator that is not very big (it is like this) which is implanted in the abdominal area below the skin so everything is inside the body it is on the side then cables that go out below the skin to the IPG, the neuro stimulator and this neuro stimulator we connect from the outside through telemetry to charge the stimulator so you can charge it regularly but after nine or ten years so depending how much you use it, it might be that you have to replace the neuro stimulator but it's a very small surgery, local anaesthesia, you open up you put another one and you close again.

24. *Q: The connections stay the same on spinal cord?*

    A: Yes, all the connections stay the same, but we exchange the stimulator.

25. *Q: OK so that means one last question So what is your or what are your goals where you want where do you want to go with your project in the future?*

    A: We have a lot of different goals, but one of the goals is to extend also the functions so now we did a lot of mobility of the legs, now we want to do mobility of the arms, of the trunk. we want to activate different autonomic functions so for example control of the blood pressure, control of the bladder or the bowel so these are extending the mechanisms and stimulations to other functions. The second main aim or objective is to develop the therapy to make it a therapy for everyone so it has to be easy to use and it has to be accepted by the FDA or insurances for example in Switzerland so that everybody can use this therapy and use it also at home and the third one is really to make it like all these other technologies like other people with the thoughts from the brain controls these are the main things for the next years at least.

26. *Q: sounds good*

(End of the interview)