Interview with Dr. Andres Lozano

UTMJ Interview Team (Priya Dhir and Nicholas Scrivens)

Dr. Andres Lozano

Andres Lozano, MD, PhD, FRCSC is the chairman of the Division of Neurosurgery at the University of Toronto, the Dan Family Chair in Neurosurgery, the RR Tasker Chair in Functional Neurosurgery at University Health Network and a Tier 1 Canada Research Chair in Neuroscience. Dr. Lozano received his medical degree from the University of Ottawa, his PhD in neurobiology, and his neurosurgical training from McGill University. He completed his postdoctoral training in movement disorders at Queen Square, London, UK and in cellular and molecular biology at the University of Toronto. In 1999, he became the youngest individual to become appointed as full professor in the Department of Surgery.

Dr. Lozano is best known for electrical recording and stimulation mapping of hitherto unexamined brain areas for the identification and testing of novel therapeutic targets for deep brain stimulation (DBS). He and his team have pioneered the "first in man" applications of DBS in Parkinson's disease, dystonia, Huntington's disease, depression, and anorexia. He is currently leading a large multicenter trial of DBS for Alzheimer's disease. He has the unique distinction of being named the most highly-cited neurosurgeon in the world and has published over 450 manuscripts and 90 chapters and edited 5 books.

UTMJ: Could you tell our readers a little bit about yourself?

AL: My name is Andres Lozano. I went to medical school at the University of Ottawa and then went to McGill for my residency. I did a PhD in neuroscience while I was at McGill. Following this, I did some fellowship training in London, UK and then came to Toronto in 1991 and stayed here ever since. So, I've been here for 26 years. I was always located at Toronto Western Hospital – I've only had 1 job in 26 years, and so far they tolerate me okay.

UTMJ: What triggered your interest in getting into neurosurgery in the first place?

AL: When I was about 15, I decided to be a neurosurgeon. I was inspired by watching Dr. (Wilder) Penfield on television. He was operating on patients with epilepsy and stimulating their brain, and these patients were recalling vivid memories of what they had experienced. I thought to myself, "This is the most interesting thing I can think of, so I'd like to do that too." That's why I went to medical school, and that's why I went to McGill for neurosurgery too, because that's where Dr. Penfield was – I thought that would be the best place to go. Since then, though, I think Toronto is the best place to go!

UTMJ: Being in the field for this many years then, what fascinates you about the brain?

AL: I think what fascinates me the most is that, despite all we have learnt, there is still a huge amount left to be discovered about the brain. I think that that's what really drives me: the curiosity and the interest to try to learn more and explore areas of the brain that are unknown. That's really what we do, in the kind of surgery that I do – I go to new areas of the brain and try to find out what they do and, more so, whether they can somehow be influenced to improve their function.

UTMJ: Speaking of the type of surgery you do, could you maybe provide a brief description for our readers that may not have heard of Deep Brain Stimulation?

AL: Yeah, absolutely. So, it turns out that if you have a psychiatric or neurological disorder, it can most of the time be related to malfunctioning of circuits in your brain. For example, if you have Parkinson's disease, it reflects malfunction within circuits that controls movement. If you have depression, that is malfunction within circuits that control your mood. If you have Alzheimer's disease, it represents malfunction within circuits that control cognition and memory.

Through deep brain stimulation (DBS), we're able to reach these circuits in the brain, intervene within them, and adjust their activity. This can be either turning them up, or down, using electricity. It's very much like having a dimmer switch. When there is excessive activity, for example, something like tremor or seizures, we might want to turn that area of the brain down. However, if the area being targeted is underperforming, as is the case in Alzheimer's disease,

we want to turn it up. So, we're able to basically go anywhere in the brain and adjust the activity of brain areas to see if we can improve function.

UTMJ: What was the timeline of seeing DBS go from being researched as a novel therapy to it being used in clinical practice?

AL: Well, some of this was done in the 1950s and 60s in animals. Then, the idea that this could be done in humans was first thought of in the context of Parkinson's Disease. So, we were involved in using DBS for Parkinson's, but also extracting from those trials – in that, if it could be used to treat a motor dysfunction, it can also be used to treat other parts of the brain for other disorders. It started with doing DBS for other kind of movement disorders, like dystonia. And then we started to experiment with psychiatric illnesses, like depression, obsessive compulsive disorder, Tourette's, and anorexia. The latest foray is into memory and cognitive disorders.

UTMJ: Is there a specific patient population that would get access to DBS? Or is it currently a treatment modality available to anyone with these disorders?

AL: For Parkinson's Disease, DBS is well-established and we operate on at least 3 patients a week. It's a done deal – very well characterized. Typically, when you're diagnosed with Parkinson's and you are put in medicine, you have a honeymoon period of approximately 2-5 years, where you take the drugs and you can be normal. However, with progression of the illness and ongoing exposure to drugs, you start developing complications. It is at this point that you can consider having a surgical intervention, because it can deliver more than what the drugs can do. Parkinson's is a progressive, neurodegenerative disorder. What we're trying to do is buy time and try to keep people functioning at a higher level for a greater period of time. However, it's not just the motor function that is in trouble; there are also impairments in cognitive function, depression and so on. So, we're merely addressing some of the aspects of the illness for a long time, but we recognize that these are symptomatic treatments and not a cure.

For the other disorders, DBS is still in evolution. They're still investigational and not approved. We're doing research, and typically our patient population for them represents those who have these disorders and have run out of options. They are still disabled, despite the best available medical therapy. In the case of Alzheimer's, it's easy, because the drugs don't do much. In the case of depression, there are at least 30 antidepressant drugs – and we only treat patients who, despite all the available therapy, are still disabled. If patients have tried everything, and still are not able to function in the way they desire, we become involved. I mean, it's a lot to ask for someone to be comfortable with a person drilling holes in their skull and putting electrodes in their brain. So, unless we've tried everything else, it's not going to be something we offer.

UTMJ: How did it feel for you, professionally and personally, to see DBS go from research to the clinic – and more importantly, to see the tremendous impact it had on patients?

AL: I think, for anyone, you want to go to work every day and do things that are exciting and meaningful. So, to take something where we've reached the frontier of knowledge and how much we need to know and say, "This is not acceptable. We want to do more," is making a bold statement. But that's how we move our knowledge forward, especially when it involves surgery of the brain. I think part of it is just saying that we have a bias for getting things done, and not accepting the status quo.

More than that, we rely on the tremendous courage of our patients, who are sometimes the first human beings in the world who are having these procedures. We always have to tell them that we're going to try this but have no idea if it's going to work. So, partnering with our patients is a critical aspect of what I do – and you have to admire their bravery in letting someone operate on their brain when the outcome is uncertain.

UTMJ: It definitely makes you think – if you were in their shoes, how much would you be willing to risk?

AL: Exactly. So, it depends on your outlook and how much you want to fight vs. accept.

UTMJ: Is there a particular patient encounter that has stuck with you over these years, something that may make you see medicine differently?

AL: Yeah, absolutely. Sometimes, we go to areas of the brain where no one has gone before, and when we stimulate those areas, all of a sudden, the brain is revealing itself. It's amazing to discover for the first time what that part of the brain is doing. It's a "eureka!" kind of moment. We've had several patients that that's happened with, because we've gone to areas where nobody has ever gone before. We've stimulated those

areas, and found out that it is where a particular function occurs. That's pretty exciting – there's no other real way of doing that, except via neurosurgery. This is really where neurosurgeons have a huge advantage, because we can actually go in the brain and can probe these areas, allowing it to reveal its secrets to us.

For instance, there was one case where we were treating someone for their obesity. We wanted to regulate their appetite in the hypothalamus. However, when we stimulated that area, we ended up probing very vivid memories. It's on the basis that we're now treating patients with Alzheimer's with DBS, since we have an area in the hypothalamus of the brain, that we can stimulate to drive and enhance memory. And this was totally by accident! However, when you see something novel and exciting, as such, you must grasp the importance of it and take advantage of it.

I think we are always justified by an unmet need in a patient. We see that there is a person who is disabled by an illness, and it's our job to try to help them. If the limits of medical knowledge have been exhausted, it's time to create new knowledge. We are lucky to work in a university and hospital where pushing the frontier of what is known, and what is possible, is encouraged. That, to me, is the excitement of neurosurgery. It really is about learning more, discovering more, and using that knowledge to help people. Ultimately, it's a choice patients and their families make. We don't know if we're going to win or not, and there's a risk because it is surgery. Our job, however, is to say, "This is where we are. This is an idea with pros and cons – are you in?" We hope that patients and families understand that and make an informed decision, and they're active participants. We are more dependent on how they help us, rather than the other way around.

UTMJ: How have you seen the field of neurosurgery change in the last 26 years?

AL: The trends are towards being minimally invasive. Big operations are going away, and we're trying to do smaller and faster surgeries. We are accessing the brain, not only by opening the skull but also by getting through the blood vessels of the brain. We are also using non-invasive methods. One of our new developments is focused ultrasound, which involves using ultrasound beams through the skull to treat people with tremors. So, we are now able to influence and intervene within the brain, without having to open the skull.

The other trend is that neurosurgeons are now taking on disorders that were in the province of neurology and psychiatry, such as Alzheimer's disease and depression. We're interested in an organ called the brain – and anything that has to do with the brain is of interest to us. We should not be pigeonholed into treating only some disorders. And most importantly, these are multidisciplinary efforts. We work with neurologists, psychiatrists, radiologists, and many other fields. It's exciting to work on projects where there's a team, and where you by yourself cannot do very much – but if you combine your efforts, you can do great things.

UTMJ: Do you think the fact that you are able to localize mental illnesses to certain parts of the brain, and treat them via neurosurgical techniques, helps with some of the stigma surrounding mental health?

AL: Yeah, absolutely. When you have these disorders, it's because there's something wrong in your brain. I don't think that depression is any different than diabetes. It's the same stuff: something is not quite working well, and the latter happens to be in a circuit within your brain. We're now learning where those symptoms are generated in the brain. We can reach those areas, intervene within them, and adjust the activity of those brain areas and hopefully that translates into improving our patients. It's absolutely transformative surgery, especially because we're dealing with a killer disease, such as depression. We deal with patients who have a very high suicide rate; it affects young people – and women twice as often as men. We've had several patients who committed suicide while in the process of deciding whether or not they should have surgery. These are very malignant disorders – and we're talking about patients who are very ill and have extinguished all their options. If you can take someone like that and transform their life, that's pretty remarkable.

UTMJ: Could you tell us more about the focused ultrasound techniques you've been working on recently?

AL: We have a new tool in focused ultrasound, and we're trying to figure out what it can be used for. Tremor disorders are kind of the beach head, but we think that it will also have applications across a number of other disorders. For example, we think that we may be able to ablate areas of the brain that are producing epilepsy without opening a head. We might be able to ablate brain tumours without opening a head. In addition, it turns out that we can open up the blood-brain barrier with ultrasound, and so we may be able to clear toxic proteins, such as those in Alzheimer's

disease. We've actually already been able to do this in animal models, and we are now testing if that could be the case in humans with our colleagues at Sunnybrook. It's a very exciting time, because the technology is there to do things that we couldn't do before. We can tackle problems that we previously ignored or gave up on. Now, with these new tools and understanding, we can do things that we've never been able to do before.

UTMJ: Would you have any advice for someone who may be interested in pursuing neurosurgery as a career?

AL: I think most people think that neurosurgery is quite an interesting area, just intrinsically, because it is technical and involves the brain. However, it is a tough training program – physically and mentally demanding. I think, unless you have enough drive and conviction, it's not a good area for people to go into. We tell people to see as much neurosurgery as they can, and rotate or do electives to see whether they feel comfortable with the acuity and illness of the patients, as well as the pace. If the answer to all of the above is yes, there is no field more rewarding or interesting.

UTMJ: What are your interests and hobbies outside of neurosurgery?

AL: Sleeping! If I'm not working, I'd really like to be sleeping! But all jokes aside, I just try my best to stay healthy, eat properly, exercise frequently, and read. I try to study other fields and how they may impact your own. Trying to learn as much as possible from anyone and everyone. I think these are all things that make my life more interesting.

UTMJ: Given how challenging the field of neurosurgery can be, what grounds you and keeps you going everyday?

AL: The sense of purpose. The sense that you're doing something that is interesting, challenging, and have a certain determination to be able to accomplish. And finally, I think it's the impact that we have. When you see what kind of impact you can have on someone and turn someone's tremor off, within a second, or stop someone from seizing, or take someone who was depressed and make them well – that's pretty satisfying.