

The Potential Use of Nanotechnology in the Treatment of Paralysis
Due to Trauma to the Spine

By

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PASS

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Introduction:

Nanotechnology has many uses in medicine both present and future. We are beginning to see the uses of nanotechnology to treat various medical conditions and there is much research into the further uses of nanotechnology. Advances in nanotechnology could be a breakthrough for the treatment of various neurological disorders, including paralysis due to trauma of the spine. In this report I have researched the different uses for nanotechnology and how they can be used to treat paralysis.

Nanotechnology is the engineering of functional systems at the molecular scale. This is engineering within boundaries of 1 to 100nm, manipulating single molecules. K. Eric Drexler was the first man to popularize the word nanotechnology in the 1980's to mean building machines from individual molecule as in his book "Engines of Creation: The Coming Era of Nanotechnology" published in 1986. This was mainly theoretical as the technology was in its infancy at the time; it was only simple molecular structures that it was possible to create on a molecular scale. However, molecular manufacturing, as the building of nanoscale machines is known, may be possible as soon as 2015 to 2020 according to the Centre for Responsible Nanotechnology. This would mean nanomechanical structures consisting of pullys and levers built by molecular robotics. They believe many of the processes used in nanotechnology today could be used to manipulate molecules into these kinetic mechanical structures.

Currently there are mostly passive nanostructures, these are nano sized particles which are not mechanical but are very valuable due to their extremely small size. The use of nanotechnology has already passed into consumer products. According to The Project on Emerging Nanotechnologies, there were 1015 nanotechnology related consumer products as of 2009,

The ability to shape structures on an increasingly smaller scale is also becoming possible, the use of electrons are being used to manipulate structures on a micro scale (see figure 1 which is on a scale of each element being approximately 5000 nm). However manipulation on a nanoscale is also being achieved.

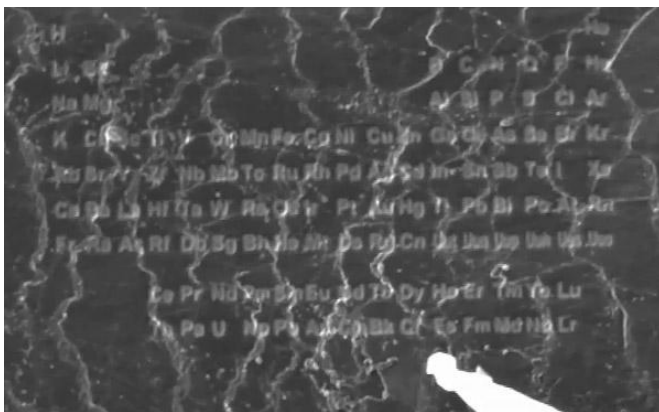


Figure 1, Periodic Table on a single human hair. University of Nottingham's Nanotechnology Department

One advantage of nano sized particles is in the way that they can create a nearly smooth surface, this is almost impossible using standard techniques in engineering as although the material may appear smooth to the naked eye, on a molecular level there is still unevenness. This is already being used in products such as self cleaning windows as dust and other stain causing molecules are washed away due to the superhydrophobicity of the material. This is because droplets of water are repelled by the surface of the material so therefore run off, bringing any other material on the surface with the

droplet. Also, the use of nanoparticles can be used in chemistry and medicine due to their fast reactions caused by their large surface area to volume ratio. This introduces new catalysts and new, potentially faster acting drugs.

Nanotechnology in medicine is growing. A few of the developments are:

Nanoscale Biosensors (Sarah. E. Cross, 2nd December 2007). These allow a cell to be “touched”. It has been proven that cancerous cells have a softer texture to noncancerous cells and that their degree of turgidity relates to the severity of the cancer. This allows a definite diagnosis of cancerous cells as well as opening the possibility of diagnosing other diseases which change the texture of cells. One example may be retroviruses which fill cells, biosensors may be used to diagnose cells infected with the virus.

Double Nanoemulsion Droplets (Jarrod A. Hanson, 4th September 2008). Although not on the nanoscale yet, the technology to develop the water droplets within an oil droplet is increasingly becoming closer to that which is capable at a nano scale. Similar to the “Buckyballs” of Smalley (1996), it is believed the water droplet could contain key hormonal drugs or proteins which are then brought straight to the targeted cells. There is also a potential use of these nanoemulsion droplets in cancer treatment. The water would contain a toxin to kill the cancerous cell while the oil droplet surrounding the water would protect noncancerous cells from the toxin whilst also containing another anticancer drug. The two drugs acting simultaneously would lower the risk of the cancerous cells developing a resistance to the drugs.

Nanovalves and nanoimpellers (Jie Lu, 31st March 2008). These are another method of drug transportation, with an opening and closing “vault”. In Figure 2 you can see the 8 “flower petals” which make up the walls of the vault and then the closed vault. The vault would be opened, the drug inserted, closed, ingested then transported in the blood or injected into the cancerous site. The vaults would reduce the amount of non targeted cells that are affected by the drug. Nanoimpellers can capture and store anticancer drugs and then release them as a response to light. This would mean very exact control of drugs as the nanoimpellers can be exposed to light only when they have reached the targeted sites within the body. However, for areas deep within the body, this may not be possible.

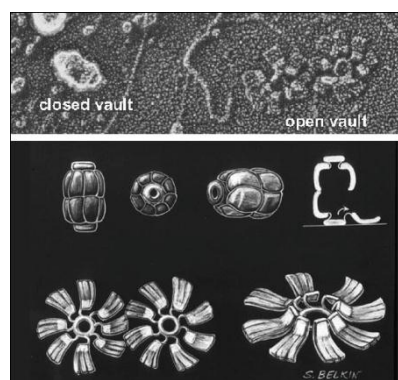


Figure 2, electron microscope image (top) and diagram of nanovalves, California Nanosystems Institute

Main Discussion:

Nanotechnology is further advancing to more complex and mechanical designs. These in medicine could be used for drug transportation, destroying pathogens in the body or even artificial cells. I am focusing on nanotechnology being used as one particular artificial cell, the neurone. Many cells have very complex actions and chemical reactions within them, and act as a tissue to perform a function. Motor neurones are pathways from the brain to the muscle and this is what leads me to artificial bypasses of an injured part of the spine using nanotechnology. Thus curing or easing paralysis.

Neurones pass signals through chemical reactions containing ions, it is the movement of these charged particles which cause a small voltage and current within the cells which then passes through the neuron to the presynaptic ending for ions to be transmitted across the synapse and trigger the next neurone. However, in spinal cord injury, signals to and from the brain are disrupted as the neurone pathway of the signal has been destroyed. However, bioactive signalling molecules may pave the way for creating an artificial bypass of the spinal cord.

Devices which release bioactive signalling molecules are currently limited to uncontrolled delivery of a hormone or other signalling molecules, for example the contraceptive implant. However, nanosized artificial bioactive signalling molecules are being developed that can be triggered by other biological signalling molecules from cells in the body. This paves the way for a simple artificial cell which serves only the function of receiving and sending signals (hormonal or otherwise). These nanosized bioactive signalling molecules, combined with a conducting material to carry the induced current up/down the spine could create the artificial bypass of the injured spinal cord.

Another reason I chose an artificial neurone as a potential use of nanotechnology is the adaptability of the nervous system. The brain is a very complex organ, which can respond to stimulus in adaptable ways. Take, for example, the cochlear implant (Figure 3) where external acoustic sound is converted to an electrical impulse which is sent straight to the area around the auditory nerve, these electrical impulses travel along the auditory nerve to the brain where they are translated into acoustic sound. Although people who had hearing before turning deaf describe the noise from the implant as “mechanical” or “synthetic”, they slowly adapt to the implant and feel the noise as normal, generally over the course of a few weeks. This also shows how we already have the technology for sending electrical impulses to the nerves.

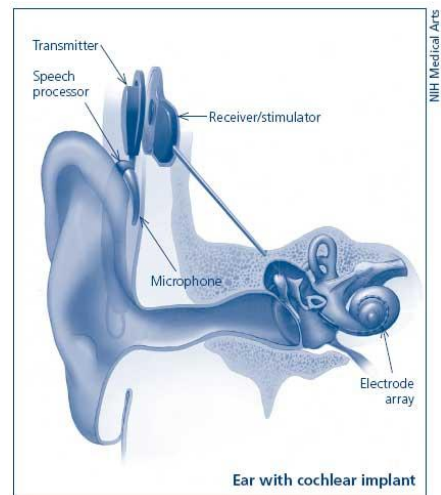


Figure 3, Cochlear Implant Diagram, NIDCD

The nanotechnological side of the bioactive signalling molecules, reacting to the stimulus from other neurones, combined with a mechanical implant similar to the cochlear implant to send the electrical stimulus to neurones higher up/lower down the spine would form one unit to replace the damaged section of the spinal cord. Initially, this may be used as a conventional electrical implant, needing to be charged or replaced after however long. However, using one of the many nanosized transportation techniques covered in the introduction, the ions needed to replenish the implant could be delivered either by a pill or by injection to the area. It may be possible to produce nanovalves mentioned in the introduction which respond to a certain feature of the implant. The nanovalves could be adapted to respond to electrical impulse by the implant or even have an active site similar to enzymes. This may be possible as altering of molecular shape is becoming possible on a more complex basis.

The surgery to insert the implant into the spine would of course be major surgery. It would need specially skilled surgeons as there is the danger of damaging more spinal cord and therefore compromising the use of more limbs in the body. The implant may be small enough to insert within the vertebrae however, this could affect the flexibility of the spine if the implant is too big. The amount of spine which is damaged would alter the size the implant would need to be. Also, accessibility to replace or recharge the implant may be easier if the implant is situated outside the vertebrae. However, a method must be used to connect the implant to the spinal cord in order for the electrical impulse to be sent up and down the spinal cord and for the implant to respond to neurones.

As with any object inserted within the body, there is the chance of rejection. This would be very serious within the delicate region of the spine, as inflammation around the spinal cord is a major factor in causing paralysis, meaning that even more damage could be done to the spinal cord. However, new research is pointing to “stealth nanoparticles”, these are nanoparticle coatings which have been designed to evade the natural immune response. They mean that the foreign drug or object is not recognised as a pathogen by enzymes and therefore the immune response is not “switched on”. Although these “stealth nanoparticles” are being mostly tested in the blood and for use on nanoscale drug delivery, there should be a strong chance of this technology being used for implants as well. This

would of course be largely advantageous to the patients as it reduces the chances of complications. This also increases the likelihood of the implant being successful.

Of course, surgery to restore control of the muscles of the limbs must be carried out fairly swiftly after the trauma to the spine. This reduces muscle wasting and also could be combined with exploratory surgery to discover any further damage to the spine (vertebrae or other). However, the patient will obviously need time to recover from the accident which caused the trauma to be strong enough for major surgery. The implant could be combined with current methods of restoring the control of muscles and occupational therapy.

Ethical/Social Issues Surrounding Artificial Bypass of the Spine:

As with any new medical procedure, many years of research and testing must be done before the method can be used on patients. For example, a general cancer drug may have 6 years research (cell and animal studies) until it reaches clinical trials and then another 8 years before it can be accepted by a regulating body. This will cost money and time. Thought is needed on who or where the funding for the years of research and testing will come from. In Britain, this may partly come from the government to improve the health of the population in future years. The money may also come from various foundations such as Wellcome Trust. Investments from medical companies may mean higher costs of the treatment in the future as the procedure is owned by profit making companies. The high costs of the research may mean that although the resulting procedure is not very costly, the debt from the years of investment is passed onto the patient or National Health Service paying for the procedure. This therefore could exclude many poorer patients or patients in less economically developed countries from receiving the procedure.

Another issue with the research needed for the artificial bypass of the spine is the potential use of animals in testing. The testing cannot be purely on cell samples as it involves a whole working body system, this makes it more likely the procedure will need to be tested on animals to check the safety for use on humans. Many animal rights groups are against animal testing and would be concerned over the conditions of the animals. The animal testing may have to include forcibly inducing trauma to the spine of the animals to cause paralysis, so as the technology can be effectively tested. This causes many concerns over the animal experiencing undue pain and distress. However, the use of effective pain killers and other control measures about the conditions of the animals whilst testing can reduce the pain and distress. Also, the thought that in the future, these measures mean many people can live a higher quality of life may persuade the public that animal testing is needed.

Another issue of the use of nanotechnology in treatment of paralysis is the future need. Currently, an estimated 250, 000 to 400,000 people in America alone have a spinal cord injury. 45.7% of people with paralysis have complete quadriplegia or paraplegia worldwide. This shows there is an obvious need for a treatment of paralysis as not only is it affecting many people worldwide, the consequences of paralysis on their quality of life is significant. Also, the average American medical bill for a spinal cord injury patient is around \$99, 553, being able to treat and cure paralysis would save the patient money they may not have otherwise been able to afford. However, as I have discussed, the cost of the surgery may be highly expensive. The figure for an American medical bill sheds light on the cost for the NHS also, as the surgery may be vastly cheaper than the continual care for a paralysis patient. Also, car accidents are the cause of spinal cord injury in 44% of cases followed by acts of violence at 24%. Future advances in car safety may reduce the number of paralysis cases and therefore reduce the need for a treatment of paralysis. However, acts of violence are unlikely to reduce worldwide so there will still be a significant number of cases of spinal cord injury.

The procedure itself could cause many concerns as the patient may be worried other parts of their body could be affected if the procedure goes wrong. The spinal cord is very delicate, and the effects on the body from damaging it in surgery could cause catastrophic consequences including, potentially, full body paralysis. However, in patients with full body paralysis the procedure could be life

changing, even if only the sensory nervous system is restored in their body. This also brings another potential ethical issue, the results of the surgery could be unexpected such as causing the patient much pain due to the brain reacting to the stimulus as pain. This, of course, would reduce their quality of life rather than raise it. However, the bypass could be removed and the symptoms may be reversed.

The use of nanotechnology is sometimes distrusted in society. There are theories such as nanotechnology being toxic due to its high reactivity and potential ability to fit through cell membranes. Patients and the public may worry that as the nanotechnology in the bypass is so small, it could fit through pores in membranes and cause unthought-of havoc within the body. There is, of course, some reason behind this theory however methods could be used to keep the technology close or attached to the bypass. The toxicity of the nanotechnology must be considered as the release of ions or sending electrical impulses into cells other than the neurones could have many adverse effects such as changing the pH of cells and denaturing enzymes. In studies on rat liver cells, cells which were exposed to higher doses of nanoparticles (100-250µg/ml) became irregular and abnormal in shape and size. On the very small scale that the nanotechnology could “leak” into cells, this may not have too much effect on the whole body. However, on a large scale this could be quite serious to the health of the patient.

The results of sending electrical impulses to the brain could be unexpected. I have already mentioned the possibility of the bypass causing pain but there is also a risk of the nervous system not responding properly to the signals. The cochlear implant only shows that the brain can adapt to artificial stimulation, the muscles may not. It is obvious that muscles spasm when given an electric shock, however the control over the muscles could be limited due to the signal being artificial. There is also the complex problem of many different nerves carrying different signals, for example motor neurones or sensory neurones, and these signals could become confused due to the bypass meaning the brain/muscle cannot interpret them.

This last ethical issue is rather futuristic; however technology involving the nervous system could potentially evolve to be used inside the brain. Although this would be a large jump in technology as the neurones of the brain vary in complexity from the motor neurones running up the spine. Creating artificial neurones by manipulating molecules to the exact shapes of various neurones to replace damaged parts of the brain would be vastly controversial. Many people would consider this as changing the patient’s personality and devaluing human life. The potential future military use of this technology would be a major ethical issue, as although it could be used to repair damaged tissue the same technology could be used to disrupt brain activity, such as the use of electrolysis to treat severe depression can produce a lasting change from disrupting brain activity. There is no way of knowing how complex and advanced nanotechnology in the nervous system could be in the future, however these issues will need to be dealt with as new technology arises.

Conclusion:

In conclusion, I believe that nanotechnology could be used to treat paralysis in the near future. However, my theories are based on research that is not fully developed so how near in the future we cannot tell. New methods to treat paralysis may lead to my own theory being redundant or the technology may not advance enough for my theory to work. However, the latter is unlikely as nanotechnology is advancing rapidly and I have based my theories in known areas of research and advances in nanotechnology. I have also included the ethical and social issues surrounding my theory as these will be very influential in the future of nanotechnology. The public will see nanotechnology on a more day to day basis as the technology enters more consumer products, therefore public trust and opinion on nanotechnology may change. Government legislation and the worldwide acceptance of new nanotechnological breakthroughs will be another factor in how nanotechnology will be used in medicine in the future. However, nanotechnology is already being accepted in medicine so we are likely to see an increase in nanotechnology in medicine in the future, including in the treatment of neurological disorders such as paralysis.

References:

(Notes from)

“All of the Nerve” lecture, Brighton Science Festival 2011

Boisseau P., Kiparissides C. (2005) Vision Paper and Basis for a Strategic Research Agenda for NanoMedicine. In the European Technology Platform on Nanomedicine

British Cochlear Implant Group. Frequently Asked Questions

<http://www.bcig.org.uk/site/professional/allprofs/faqs.htm>

California Nanosystems Institute. Health and Medicine

<http://www.cnsi.ucla.edu/research/healthmed#nano>

Center for Responsible Nanotechnology. What is Nanotechnology? <http://www.crnano.org/whatis.htm>

Emedicine. Spinal Cord Trauma and Related Diseases

<http://emedicine.medscape.com/article/1149070-overview>

The Engineer, Nanoparticles Deliver Drugs Under Immune System Radar.

<http://www.theengineer.co.uk/sectors/medical-and-healthcare/news/nanoparticles-deliver-drugs-under-immune-system-radar/1007661.article?cmpid=TE01P&cmptype=newsletter&cmpdate=040311&email=true>

In vitro toxicity of nanoparticles in BRL 3A rat liver cell

<http://nanotoxcore.mit.edu/tox%20core/nano%20toxicity%20papers/Hussain,%20et%20al,%2006-17-2005.pdf>

Nanotechnology Now. Current Uses

<http://www.nanotech-now.com/current-uses.htm>

Neural Transmission Explained. How Neurones “Talk” to Each Other

<http://www.yorku.ca/eye/neuron2.htm>

The Project on Emerging Nanotechnologies. Inventory of Consumer Products

http://www.nanotechproject.org/inventories/consumer/analysis_draft/

Wellcome Trust, Funding Technology-Transfer

<http://www.wellcome.ac.uk/Funding/Technology-transfer/index.htm>

Wikipedia, Clinical Trial

http://en.wikipedia.org/wiki/Clinical_trial#Length

Disabled World, Spinal Cord Injury

<http://www.disabled-world.com/disability/types/spinal/>

Spinal Cord Information Network, Paralysis

<http://www.tjhsst.edu/~jleaf/disability/elequipo/index.html#Stats>