The Development of Carbon-based Nanotubes and Nanotechnology and their Potential Uses in Medicine, including the Implementation of Nanotube Technology in the Treatment of Damaged Neurons and Nerves

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CONTENTS

ABSTRACT

In recent years, nanotechnology, and its implementation in medicine, has developed rapidly, leading to numerous breakthroughs in the treatment of many conditions previously considered either incurable or too difficult to treat. Spinal injury and nerve damage have long been effectively incurable in the vast majority of cases, but progress in nanotechnology and nanosurgery has provoked the consideration of possibilities of new treatments. This paper will primarily explore the possibilities of carbon-based nanotubes in the treatment of spinal injury, including through the potential implant of such technology. The two methods discussed in this paper are both limited in different ways, but both have the potential to revolutionise the treatment of spinal injury

INTRODUCTION

Since the basic idea behind nanotechnology was first publicly introduced in 1959 during a talk presented by Richard Feynman named, "*There's Plenty of Room at the Bottom"* [1], in which the renowned physicist suggested the possibility being able to precisely manipulate individual atoms and molecules, despite the process being physically impossible at the time, due to the complexity of the tools and procedures required, a huge interest in this intricate process has been sparked throughout the entire science community.

Unfortunately, it took over 15 years before the topic was developed any further, even though the term "nanotechnology" was defined during this period by Norio Taniguchi in 1974 as "production technology to get the extra high accuracy and ultra fine dimensions, i.e. the preciseness and fineness on the order of 1 nm (nanometer), 10^{-9} meter in length" [2], there had been no further advancements in the practical aspect of this undeniably challenging topic. It was not until Dr K. Eric Drexler, an American Engineer, published the paper, *"Molecular Engineering: An approach to the development of general capabilities for molecular manipulation*" in 1981[3] that the possibility of a practical use for this technology was first recommended: the manipulation of biological molecules to create substances such as proteins. This paper was credited by many of the distinguished nanotechnology scientists and researchers at the time, despite the controversy and fears that surrounded it, such as the idea that these enhancements could lead to dangerous technologies if developed by those with wicked intentions.

The probability of further advancements was greatly increased during the 1980's due to the invention of the STM (Scanning Tunneling Microscope), a microscope capable of producing three-dimensional images of a substance at an atomic level. This quickly led to the discovery of fullerenes the first of which being the Buckminsterfullerene, discovered in 1985 by Smalley, Curl, and Kroto [4]. It was not until 1991, however, that the most important discovery as far as this paper is concerned, was finally confirmed: the existence of carbon nanotubes. These cylindrical shapes made entirely of carbon atoms were originally observed by Roger Bacon in the late 1950s, and again by Morinobu Endo in the 1970s, however it was not until 1993 that Sumio Iijima and Donald Bethune at IBM were able to observe a carbon nanotube composed of a rolled up sheet of a single layer of carbon atoms, which later became more commonly referred to as "Buckytubes" [5]. The late '80s saw further progress when Don Eigler manipulated 35 individual Xenon atoms to spell the word "IBM", using a specially designed STM. This was a huge leap forward, as it proved that matter so small could be altered, and nanotechnology was no longer merely a theoretical subject [6].

Since then, there have been numerous advances in nanotechnology, as we have been able to change the shape of more molecules with much greater precision. A plethora of new materials have been created because of this, such as nanofilters, which can filter the smallest of particles and nanocomposites, lightweight, scratch-resistant materials [7]. In recent years, nanotechnology and its applications have moved from strength to strength, and examples of this can be seen in many modern objects. Some sunscreens now incorporate nanoparticles of zinc oxide or titanium oxide, which, due to their reduced size, means that the sunscreen now appears colourless. Self-cleaning glass is another useful development that has come from nanotechnology; the nanoparticles on the glass cause it to be both photocatalytic (UV light stimulates the nanoparticles to break down organic molecules on the surface of the glass), and hydrophilic (water spreads out evenly across the surface of the glass when in contact, aiding the cleaning further) [8].

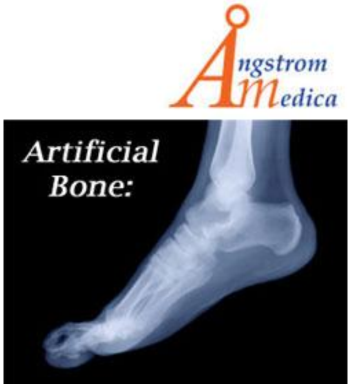

Fig.1Angstrom™ Medica's Artificial Bone

Medicine has also developed methods of utilising this technology in the treatment of patients, and many scientists are still exploring and researching into new applications of nanotechnology. Current uses include more "body friendly" hip replacements, and nano coatings, which can reduce the spread of infections in hospitals [9]. One company in particular has received a lot of publicity due to their development of synthetic bone. Angstrom™ Medica were able to create a material that is structurally identical to human bone by the manipulation of calcium and phosphate at a molecular level, and are the first company to have FDA approval for a nontechnology device. This drug is now sold under the name "NanOss™" and is used as a "scaffold" in natural bone repair [10]. Buckminsterfullerenes have also been found to be useful in medicine, as they are able to trap the free radicals formed in an allergic reaction, and prevent inflammation.

Although the current uses of nanotechnology in medicine are fairly limited due to the impracticality of certain procedures, there is great promise for the future. The possibility of using nanoparticles of iron oxide coated with peptide to improve MRI scans of cancerous tumours is becoming increasingly likely. New dressings, antibiotics and creams are also being tested which contain nanoparticles with nitric oxide gas, and have been shown to significantly reduce infection when applied to mice. Even nanorobots have been adequately designed to fight diseases in a similar way to our natural immune response [11] [12].

DISCUSSION

Before this paper discusses the nature of treatment of spinal injury and nerve damage using nanotechnology, it is important to consider the ethics and limitations of, and the dangers surrounding, the treatment of such injuries, and to take the uncertainty that accompanies nanotechnology into account.

i. Spinal Injury

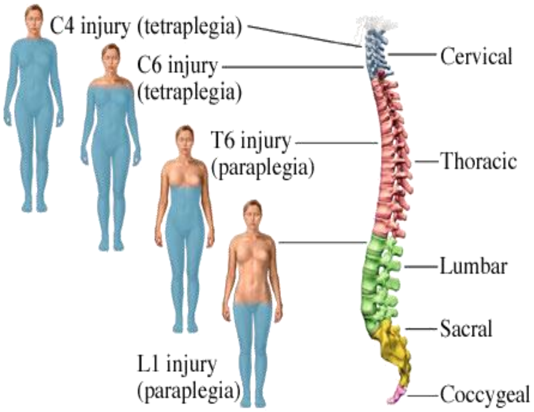

Fig 2. Effect of Major Spinal Injury depending on Location

In the USA alone there are roughly 12,000 incidences of spinal injury a year, and over 250,000 people living with some degree of spinal injury[13]. These range from injuries that have caused only a small loss of sensation, to damage so severe that it results in paraplegia or even full tetraplegia depending on the location of the injury. These more severe injuries are debilitating, often humiliating and were, for many years, considered lost causes.

Spinal injuries can be caused by many different factors, such as trauma, cancers, ischemia and genetic disorders, but almost every spinal injury has a crucial similarity; the damage to and loss of neurons is segmental. Normally, the neurons and spinal cord above and below the injury remain intact, and it is this feature of spinal injuries that provokes so much research into their treatment, as the obvious solution is simply to somehow connect the neurons either side of the injury again. However, this has proven incredibly difficult to implement. In minor injuries, it is not uncommon for neurons to re-grow and reconnect of their own accord, but with major spinal injuries, this repair mechanism is almost always prevented, whether by scarring, debris from the injury or simply the vast extent of the damage.

Any sort of surgery on the spine carries huge dangers. The risk of causing additional damage to the spinal cord is ever-present, and a great number of arteries supply the spinal cord with nutrients, adding the risk of severe blood loss, and thus death, to any operation. And, until recently, effective treatments for segmental neuron loss have simply not existed.

ii. Ethics of Spinal Surgery

It is due to the considerable risks of surgery on the spine that ethical concerns are raised. Should any corrective surgery be attempted on a severed spinal cord, the risks of making a serious problem worse are substantial, to the extent that it is almost always questionable whether any surgery should take place, despite possible beneficial effects. Not only is there the serious risk of major blood loss, but damage to healthy neurons around the injury is also a very real possibility; not only is there the risk of damage caused to neurons by the surgeon himself, but any blood vessel which is not sutured leaves a risk of causing blood to pool in the spinal cord, which can easily lead to pressure on neurons, damaging them, and, of course, as with any surgical procedure, the risk of infection is a serious concern, especially as an infection can demolish large numbers of neurons in only a small amount of time.

Patients with severe spinal injuries are also prone to desperation for treatment, arguably making them less able, mentally, to make informed or well-judged decisions on whether they want to undergo dangerous and even experimental treatments, as they are willing to try almost anything to change their deplorable situation. Because of this, healthcare professionals need to contemplate whether the patient is agreeing to a method of treatment whilst fully comprehending the risks involved, or if they are willing to go under the knife without really considering the potential harm such a treatment could result in.

iii. The Uncertain Nature of Nanotechnology

Nanotechnology is, unfortunately, a relatively new area of science, and, as such, much is still unknown. For instance, with carbon nanotubes, the potential uses of which will be discussed later in the paper, many properties are still being researched, including toxicity, which is obviously a major concern when contemplating the use of a substance in medicine. For this reason, it is important that, while research goes ahead, large scale human testing of any treatment using nanotechnology should be considered carefully until key questions about nanomolecules are answered.

iv. Nanotechnology and Spinal Cord Treatment

The amount of research into this area is quickly growing and has already yielded stunning results. This paper will discuss two methods of treatment involving nanotechnology, one which is already in development, the other of which is still restricted by the technology of today.

v. Nanotube Scaffold Treatment

The combined work of Dr Kessler, of the National Institute of Neurological Disorders and Stroke, and Samuel Stupp, Ph.D, of Northwestern, led to the key discoveries which made this method not only plausible, but positively tangible. The method fundamentally revolves around the idea of creating a scaffold within the area of damage to support the growth of neurons across the gap, and their subsequent reconnection. The method was tested on mice by injecting the scaffold into the spine at the site of damage, and was attempted using numerous different substances, but these yielded disappointment, with little sustained re-growth.

However, a type of carbon-based nanotube has produced encouraging results. A nanogel, formed by the nanotubes and a growth-stimulating protein called laminin, provoked substantial re-growth and reconnection of neurons in the damaged area very quickly in the mice, with 35% of descending neurons of treated mice having re-grown and bridged the gap within 11 weeks. This enabled the mice, which had been given the treatment 24 hours after a spinal cord injury causing hindlimb paralysis, to use their once useless limbs again to take weight-bearing steps[14]. This type of recovery would be life-changing for a paraplegic human, and, due to the nature of the treatment, it is extremely likely that it could be used to aid recovery from almost any spinal cord injury, regardless of location.

The nanogel deals with two key problems in recovery: re-growth and scarring. While the scaffold produces a stable environment for the neurons to grow into, the laminin encourages neuron growth, and the nanotubes of the nanogel reduce the amount of scarring by preventing the production of astrocytes, which cause the scarring in the spinal cord. The scaffold only forms once within the body, meaning that the nanogel can be injected in liquid form without pre-formation of the structure, reducing the risks of using this method of treatment by negating the need to actually perform surgery.

However, this treatment is limited to immediate response to spinal injuries. It relies on being injected swiftly enough to prevent the scarring which hinders the neuron growth through the damaged area, and is thus effectively useless if administered too late. This means that, while this treatment could potentially prevent debilitation for many future victims of spinal injury, it does not offer a solution to those who have already sustained spinal injuries, nor those who sustain them but cannot reach a hospital with the necessary resources to administer the treatment before scarring takes place.

vi. Nanotube Implant Treatment

A treatment for those sufferers from spinal injuries for whom the scaffold treatment is ineffective is unlikely in the immediate future, but one potential is the production and subsequent implant of artificial neurons into the spinal cord.

Nanotechnology is advancing extremely quickly, sparking progress in both nanotube technology and the miniaturisation of computing devices. Carbon nanotubes are in constant improvement, with nanotubes as long as 18.5 cm being produced[15], and the price of nanotubes is dropping rapidly as manufacture becomes easier, meaning that carbon nanotubes are quickly becoming far more viable for practical use, even at greater lengths.

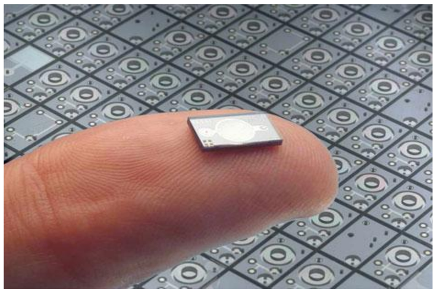

Fig. 3 Debiotech's new insulin Nanopump™

Advances in the miniaturisation of computing devices are also taking place at a surprising rate, with devices which were once large and cumbersome become incredibly small and convenient, for example, Debiotech's new insulin Nanopump™, which is miniscule compared to previously existing insulin pumps, and yet amazingly controls flow electronically through a tiny computer in the pump itself. This is just one example of the exponential rate at which normal technology is being reproduced on a far smaller scale using nanotechnology, and also how chemical detection circuitry is becoming smaller [16].

The production of afore-mentioned artificial neurons would be reliant on continuing progress in nanotechnology, requiring microscopic computers to enable them to function, and incredibly intricate nanosurgery to implant, on a scale not possible with modern technology.

The artificial neuron would comprise of three main parts; the axon would be constructed from a long carbon nanotube, insulated either using a synthetic polymer or a protein, such as myelin, a chemical detecting computer at one end to detect the secretion of neurotransmitter molecules from the transmitting cell, and another mechanism at the other end to secrete neurotransmitter molecules on receiving an electrical signal along the nanotube. It would not replicate the natural mechanism of depolarisation to transmit an impulse, but would instead generate an electrical signal and send it along the nanotube to the other, secreting mechanism as a signal for neurotransmitter molecules to be released.

It would be essential for the nanotube used for the axon to be an armchair nanotube with (n=m) dimensions in order for it to have the metallic electrical conduction required for the mechanism to work. A nanotube would be the logical choice of material for use in the artificial neuron due to its small diameter, allowing it to easily fit within the space that a normal live neuron would occupy, and, importantly, its immense tensile strength, allowing it to easily withstand the pressures exerted during implantation and movement once within the body, whereas using conventional metal wiring of the same diameter would be far weaker and more prone to damage. Due to the use of an electrical current rather than the depolarisation mechanism of natural neurons, it would be necessary to insulate the nanotube to prevent the potential loss of such a signal to the surroundings.

The receiving end of the neuron would feature a simple computing system, releasing an electrical current upon detecting neurotransmitter molecules. The neurotransmitter molecules would then be relayed to the connection with the nanotube, which they would then diffuse down due to the concentration gradient. This mechanism would allow the neurons to be implanted without needing to be linked to a source of neurotransmitters, a feature which would render the concept impractical if not impossible, as the nanotube can be used to move neurotransmitter molecules to the secreting end of the neuron. This function of the nanotube is another example of why an ordinary metal wire couldn't be used for the axon.

The secreting mechanism at the other end of the artificial neuron would gradually accumulate neurotransmitter molecules for an initial period, before having a fairly constant supply due to diffusion down the nanotube. The simple computer at this end would be engineered to release neurotransmitter molecules from a reservoir on receiving an electrical current sent down the nanotube. This would allow the signal to be transmitted to the next live neuron in the normal chemical fashion.

With segmental neuron loss, this method could even be used to produce not only individual neurons for implantation but entire nerve bundles. This would make the repair of an entire missing section of spinal cord using this method far more practical, as the entire damaged section could be artificially constructed outside the body and implanted whole or in large segments. If successful, a transplant could theoretically return full control and sensation of previously paralysed areas of the body, completely reversing the effect of a spinal injury and leaving the patient only requiring rehabilitation and physiotherapy. And this method would not be restricted to treating spinal injury, but could be implemented on nerve damage anywhere in the body, excluding the brain.

However, the surgery required to implant such artificial neurons or nerves would be extremely complicated. It would require extremely high resolution and magnification imaging equipment, and particularly delicate tools with which to manipulate the microscopic artificial neurons. The ends of each neuron would have to be individually positioned close enough to the live neurons in both directions to replicate the dimensions of a synapse, requiring exact construction of the neurons prior to implantation. This extremely exact surgery would be inefficient, slow and incredibly difficult using current techniques and equipment, and advances would be required to make such a procedure practical.

Nanotube technology is already at the level which would be required to produce the axon for the artificial neuron, although research would be required to decide which material would be most appropriate for the electrical insulation and protection around the nanotube, although research would first have to be carried out as to whether carbon-based nanotubes are harmful or toxic to human cells, and as to how well and long the nanotubes would remain unaltered within the body. Also, the size of the computers required is far smaller than modern technology allows, and thus significant development in nano-scale computing would be required for the method. The current rate of progress in the area, however, is promising, so the computers required may not be as distant as they seem.

The ethics of such implants are also questionable. Although artificial replacements are not uncommon in medicine, for instance, hip replacements, there is the possibility that certain groups would oppose the treatment on the grounds that implanting machines into the nervous system specifically is too close for comfort to the science-fiction prospect of the part-man, part-robot. This treatment, unlike the scaffold treatment, would also require open spinal surgery, the ethical implications of which have been considered earlier in this paper (in Discussion part ii. Ethics of Spinal Surgery), potentially rendering the prospect of the implementation of such a method less probable.

CONCLUSION

This paper has looked at the origins of nanotechnology, noted its advancement from strength to strength and acknowledged its potential for the improvement of medicine and medical procedure. Our focus has been on nanotechnology's potential to help those suffering in a debilitated lifestyle due to spinal injury and future treatments which could give them the fullness of life which all people should be entitled to. Despite the limitations of both the treatment methods discussed, whether they be due to technological restraint or restrictions of the methods effectiveness itself, this paper strongly endorses the work by Dr Kessler and Dr Stupp into the development nanogel treatment that has shown such promise and encourages research into other means of rectifying spinal damage.

Due to the limitations of modern technology the research into the idea of artificial cells for implant has been restricted from further progression. However with the rapid rate of progress in nanotechnology the resources required for such intricate, yet potentially life-changing, machines may well become available within the foreseeable future. The concept of an artificial neuron is ambitious, but not farfetched; in a world where medical science advances faster than almost any other area, technology with potential such as this may soon be within mankind's grasp.

However it is too soon to say that there will be a cure for those suffering from paraplegia and tetraplegia and full-body paralysis. While the work into the nanogel treatment has been encouraging, and trials on mice have yielded remarkable results, it cannot be assumed that the effect in humans will be comparable in its magnitude, and, as previously stated the technology required for the implant method is still reliant on future developments; these could come within years, or decades. Nevertheless, it is possible to see a beacon of hope for sufferers, and it seems almost certain now that whatever the eventual cure is, nanotechnology will be at its heart.

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