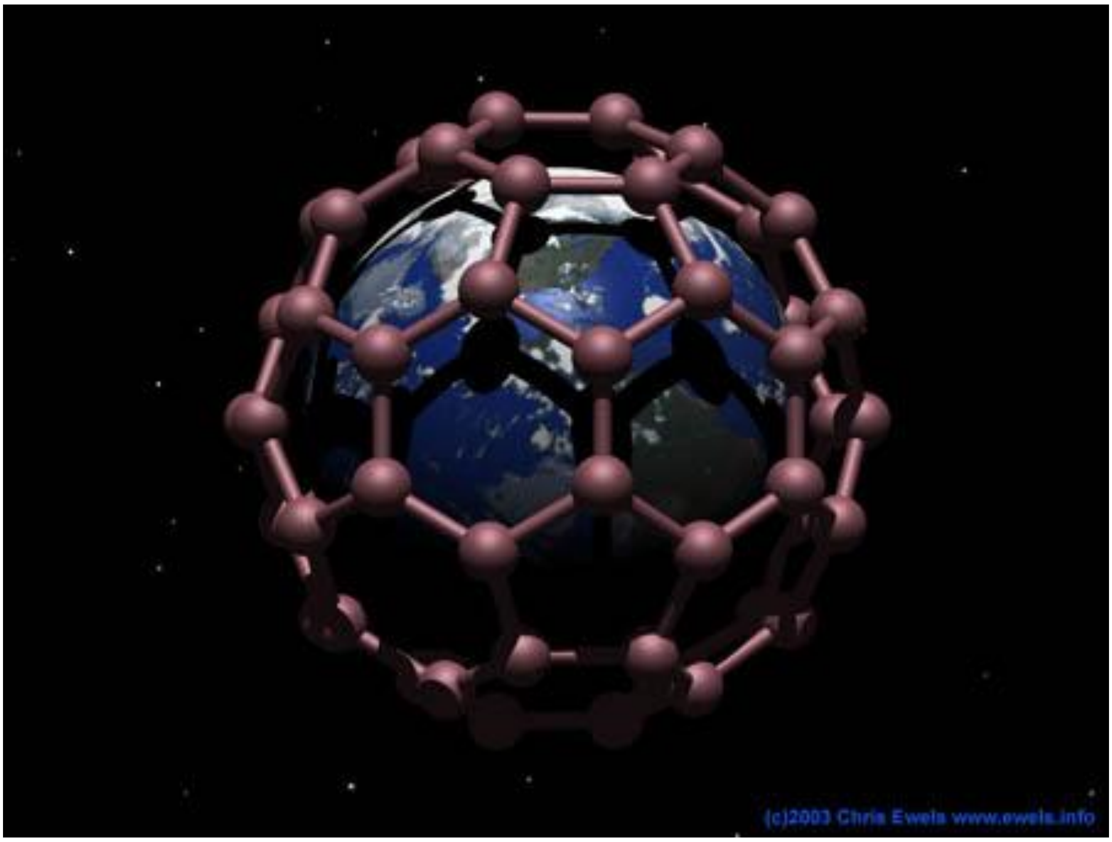
Nanotechnology: Prosthetic grafts for nerves and skin. A way of improving and lengthening lives, a more ethical substitute for stem cells, or a science fiction fantasy?



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PASS WITH MERIT

RESEARCH PAPER
BASED ON
PATHOLOGY LECTURES
AT MEDLINK 2010

Abstract

Since the start of mankind's existen -1- /e been on an endless quest to manipulate matter of ever decrea . Ancient Greek philosophers proposed the concept of atoms and fundamental particles. In 1959 the famous physicist Richard Feynman gave a speech called "there's plenty of room at the bottom". In it he expressed the idea of "manipulating atoms and molecules" to build small but complex objects. This has now driven humans to look at decreasing technology size to the point at which it can replace the function of natural things such as cells. This is known as nanotechnology. It is going to change the way medicine works forever as well as impacting many other aspects of our lives. This paper will consider existing research and my own thoughts on one specific medical application of nanotechnology. This application is synthetic grafts for skin and nerves.

Introduction

In the 18th century John Hunter proposed the idea of grafting damaged tissue by removing other tissue of similar function and composition from a less important area of the body and using it to patch the affected region. This has been common practice for many years but there are issues with it. For one - if an area is lacking in blood supply the graft will not join. This means that trauma surgeons are forced to extend the operation in order to move a muscle to the graft region so that blood is in rich enough supply for the graft to join to existing tissue. This means that the joint moved by that muscle is locked, but more seriously the extension in the operation can prove fatal to many patients. Another massive issue with this practice is that when grafting a nerve the part of the body supplied with sensitivity and movement by the donor nerve becomes dead. The grafting site can only be a maximum of 4cm long before the graft is ineffective.

Previously the only way around this issue was to use stem cells as they can differentiate to form any tissue, but this is new research and is not yet tested enough for people to trust it. Also many regard stem cell treatments as unethical due to the fact that they are often taken from embryos, and even if they are taken from bone marrow it is popular belief that stem cell research is playing God. Nanotechnology might overcome all of these obstacles.

Nanotechnology has been used in the engineering of materials considerably more over the past decade. This is because synthesising materials on a molecular or even atomic level allows us to change their properties to our advantage. Carbon nanotubes are a fantastic example of this. They are comprised of many carbon atoms bonded artificially in a planar arrangement. Many of these nanotubes weaved together will form sheets of nanomaterial. Due to the fact that the atoms are bonded in a planar arrangement each carbon atom has free electrons that can be delocalised allowing the material to carry charge and conduct electricity. The fact that the tubes are cylindrical is also a huge advantage. It means that the material is rigid in one direction, because of the tubes' compressive strength, but flexible in the other. These materials are therefore heavily used in industry but they also have applications in medicine as they can be used for special bone braces and casts. But it has now become apparent that similar synthetic materials could be used for the grafting of skin and nerves and in other prosthetics.

But at the moment prosthetic nanotechnological materials can only form the base of skin grafts and research into producing nerve grafts. The base of many skin grafts is now formed from prosthetic nanomaterial. The webbing shown on the arm in the image to the left has been manmade from nano particles. The arrangement and the nature of the particles will allow it to stretch to accommodate muscular contractions and general growth. The gaps seen here will soon be filled with additional tissue harvested from the inner thigh or buttocks.

Image from http://www.virginmedia.com

In 1985 a collection of students from Rice University were awarded a Nobel prize for their discovery of fullerenes. A fullerene is a spherical arrangement of carbon atoms, most commonly of 60. It is an important step forward as it may give the potential for mankind to protect drugs from the body's natural defences. For example insulin is a protein and therefore cannot be taken orally as it would be digested by proteases. But suppose we case the insulin in buckminsterfullerene (spherical C60)? The carbon will not allow the insulin to fit into enzymic active sites and so will prevent the insulin being digested. The reason that this cannot be used at the moment is that once the insulin has passed through the system the casing will not break away. But a newly developing application of buckminsterfullerene is to protect molecular matter that forms the natural substances that make up cells and tissues. Scientists are now looking at how this may apply to strengthening weakened tissues or grafted tissue.

Now, in the 21st century, research is advancing so quickly that more complex concepts are beginning to become reality. At the Cambridge Nanoscience Centre some ground breaking work is going into using prosthetic nanomaterial as more than just the base of a graft. They have begun to suggest that we may be able to get "E skin" to interact with organic tissue in such a way the whole graft could be nanoskin. Their current research shows prosthetic skin in a new light. They propose fabricating the elastic synthetic

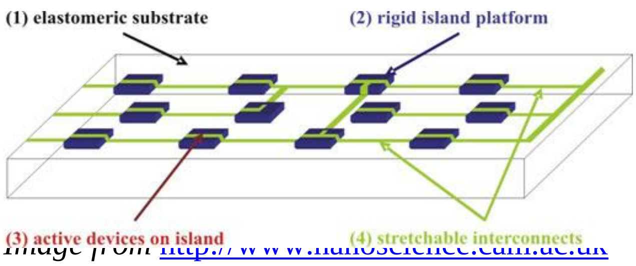

Image from http://www.nanoscience.cam.ac.uk material with transducer circuits as shown in the image below. The circuits they wish to use have to be connected using synthetic wires that are made from the carbon nanotubes I mentioned previously. The “active devices” of the circuits (the components that are used for interactions) have been place on rigid islands to protect them from damage. (more information on this can be found at www.nanoscience.cam.ac.uk). The electronics of the system allow the prosthetic skin to function like organic skin. It is therefore able to interact with nerves giving some sensitivity, however this is not at the same level as organic skin. Similar principles of integrating nano-sized electrical components with organic structures are also beginning to be applied to nerves. But at the moment attempts with nerve grafting have not yet been tested within humans, although prosthetic nerves have been used to move artificial limbs. In an article that can be found at (www.technologyreview.com) Emily Singer speaks about a prosthetic arm that uses “A new technique that capitalizes on remaining nerves allows amputees to intuitively control their prosthetic limb”. This technique uses organic nerves in the body interacting with prosthetic nerves in the false limb. It does not allow much sensitivity but provides movement. But as far as grafts are concerned many institutions at the moment are using tubular synthetic materials that give nerves a site to rejoin. More information can be found at www.ncbi.nlm.nih.gov/pubmed/2443551.

It seems like a fantasy but these concepts are being applied more and more frequently. Prosthetic grafts are now used as bases for organic grafts as common practice. These new grafts are in early stages of development but have been seen as effective already.

Discussion

It seems clear to me that there is [illegible] y to go with these concepts and in the next few years we will see rapid advances. In my mind it is important to focus on the idea of integrating nano-electronics with synthetic materials to create something that can be used alongside organic tissues.

A lot of work is going into polymeric materials. These materials are again nano structured and can be used to grow and multiply cells in the body. The latest research into these materials has allowed them to be created quickly and in large quantities. The value of these materials is that they can graft nerves and other tissues without the use of tissue from elsewhere in the body. It has been suggested that these materials may be a far more ethical substitute for stem cells and I agree with this view point.

The E skin that Cambridge is working on certainly is not perfect but if we combine it with the synthetic or existing nerves it could become more sensitive. But instead of using an elastic synthetic material and lining it with nano wires and components we could perhaps make the whole thing semi conductive. In order to do this researchers would have to weave together carbon nanotubes or similar fibrous nanostructures that have the ability to conduct electricity. This would allow the whole material to conduct impulses from the nerves. In order to ensure that the nerves join to components, not the main body of the material the base of these components could be lined with a webbing of polymeric material that connects to the main nerve network of that region.

It would now be necessary for researchers to find a way to allow the E skin to transmit a signal that matches the stimuli. This is where complex research is important. We know that the nerve impulse through the body is different for every stimulus. This means that it is theoretically possible to measure the magnitude of a nerve impulse when the stimulus provides pleasure, pain, heat, cold etc. By finding the magnitude of these impulses it might be possible to create nano-sized components that can vary the impulse intensity from the E skin depending on a sensed stimulus. For example if a nanosensor picks up a rise in temperature, it creates an impulse intensity that triggers the brain to respond to the stimulus through sensation of heat.

However, this might not be necessary if we can track existing nerves through E skin. I have mentioned polymeric materials have the ability to grow cells within the body, but this would not be enough to web nerves across the E skin as they require an existing section of nerve that can be used as a base. A possible way around this issue is to use stem cells to create a base for nerves to grow from. This would be done by introducing stem cells to the section of nerve that needs to be lengthened and then using a polymeric material to web the nerve through the E skin. But the ethical issues associated with stem cell research may mean that this possibility does not gain acceptance.

Ethics are an area that should be considered throughout research into nanotechnology. The reason for this is that people have to trust something to allow it to treat them. Replacing organic tissue with synthetic tissue could be seen as unethical as it is could be perceived to rival God's creation. This idea of human arrogance has caused popular anger towards many types of research especially stem cells. Ray Kurzweil made the suggestion that nanotechnology could keep people alive forever, and it is this sort of outrageous idea that could kill the research. This sort of suggestion has been made before and it led to a serious decline in the human genome project. The reason that this sort of idea is so detrimental to newly starting research is that people do not want to live forever as it seems clear that all life has an end. It also contradicts many peoples' religions. New thoughts are seen as dangerous. People have to adjust to every stage of human development. If someone from the Middle Ages was given a car and told they could go 70 miles per hour in a metal shell they would fear that car. It is the same with issues now. If someone tells people nanotechnology could lead to ridiculous ends they fear it because they haven't got used to it. So in my mind it is important not to look so far into the future that people forget the present.

It is also important to consider the views of the patient. It may seem to most people that the grafts will significantly benefit the patient but these benefits are purely medical and not mental. The patient may feel on edge about having part of them replaced by what are effectively very small machines. These feelings could be expected, as even non-religious people can feel as though their body should be natural and not man-made. To ensure that this issue is taken account of psychological help would have to be provided to patients who are trailling new research and, if this becomes a mainstream practice, to those who have had no choice but to have a prosthetic graft.

But something I do think is just around the corner is the beginnings of nanotechnology meeting the brain. I believe that an advance that will be made in the next decade is the ability of being able to link prosthetic material to certain areas of the brain thus bypassing a faulty nerve. This would completely remove the need for complex nerve grafting and allow restoration of function to paralysed areas of the body. The way I envisage this happening is that synthetic nerves would be made from materials with less resistance than existing nanomaterials. This could be done by manipulating fundamental particles such as quarks to give electrons and nucleons more charge. In addition to this scientists could potentially use a less resistive atom as a base for nanotubes, for example gold. This would allow less loss of charge from impulse to muscle and therefore a prosthetic nerve could travel a much further distance. Another potential issue with this idea that researchers would have to overcome is the complexity of connecting something to the brain. But it may be that we do not have to. This is because research has been going on into how the brain functions and scientists have noticed that the brain radiates waves with different characteristics depending on what action it wishes to perform. If a sensor was placed next to the brain (on the outside of the cerebral dura) it could pick up these waves and transmit an impulse down the prosthetic nerve accordingly. This would mean that people with paralysis might be able to regain a missing part of their lives.

A further thing that grafts have to accommodate for is growth. This is especially important if the graft is on a child. If an organic graft fuses to existing tissue it will divide normally to allow free growth. Prosthetic grafts from nanomaterial will not do this and will therefore loosen as the infant grows. This means that, at the moment, the graft would either have to be too thick so that when it stretches from growth it begins to become an acceptable thickness or the graft would have to be replaced every few years which would cost the NHS more money and be stressful for the patient. This means that researchers have to find a way of getting prosthetic nerves and skin to replicate. I think that research should take place looking at compressing the atoms that make up the grafts into smaller sizes so that they can be stored on the edges of the graft easily. This would mean that as growth occurred, these atoms could be decompressed to fill gaps that formed in the surface of the skin. A further application of this is that the skin could then heal if cut or grazed which is another issue fore the prosthetic skin graft. A possibility for healing E skin can be seen from how nature heals the skin. Normally platelets from the blood form a scab and then the skin heals underneath. But suppose that we introduced nanomaterial into the blood stream? This material would activate when it came into contact with the surface of the E skin and harden, forming a crust over the E skin that patches the wound. Some nano industrial smart materials have already been made to do this. Araldite is an adhesive that will not activate until it comes into contact with a hardener. In the case of the E skin the surface material is the hardener and the adhesive flows through the bloodstream.

The reason that many researchers have chosen not to research into healing prosthetic skin grafts is that the blood carries platelets that will seal the wound long enough that the elasticity of the skin can re-seal it. It is not just E skin that needs to accommodate growth, though. Nano-nerve grafts would break as the spine and other bones elongate. Again, self-replication could be the answer to this but for the moment it might be easier to graft nerves with slightly more material than is needed so that the graft will not snap during growth.

One thing that has not yet been considered is how these prosthetic grafts could benefit doctors and patients even after they have fulfilled their primary function of grafting a wound. It could do this by allowing easy injections. It could do this by acting in a similar way to our own cell membranes. With human cell membranes substances that are lipid soluble may diffuse across the membrane without the use of a pore. We could now apply this to the E skin. If researchers were able to produce nanomaterials that allow anything encased in a bucky ball to diffuse across the skin then drug treatments would be able to be done at home as there would be no need for subcutaneous injection. This would save time and money. In addition to this the E skin could act as a treatment itself. If the skin was made up of two layers (top and bottom) then the space in between could be filled with a drug when required. The bottom layer could then slowly release the drug into the blood stream, treating the disease without the person needing to take the drug at scheduled times. This would also mean that while the patient is asleep their treatment is still occurring. This would reduce NHS costs as they would not have to keep people in hospital for intravenous treatment.

But these grafts could be a problem for doctors as well as a help. On X rays a nerve will not show up. But it is likely that a prosthetic one will. The same problem is likely to occur with E skin as well. Research will have to go into finding a way of getting X rays to pass through prosthetic grafts so they do not obscure X ray images and scans. Most of these nanomaterials are carbon-based and therefore can be scanned by a magnetic resonance imaging machine (MRI machine), however they will block X rays and so CT and X ray scans will show these grafts as different from organic tissue. In many cases this may not be a problem but when looking at bones this may become an inconvenience. A way I envisage science fixing this issue is by separating out fibres of grafts to a point where they will not absorb enough X rays to form a significant image.

Conclusions

I believe that prosthetic skin and nerve grafts will greatly assist peoples' lives. This is due to the fact that they are made on a nano-sized level. These grafts will mean that people who cannot be grafted because of lack of blood supply will be able to be grafted without losing a muscle from elsewhere. The grafts could also mean that those who have sustained large nerve damage will not have to be paralysed or make the choice to lose function of one part of their body to restore function to another. But these grafts would mean more than that - they could provide easier treatment for illness and reduce the cost the NHS spends on IV treatment.

I conclude that the most important area to focus research on now is understanding how nanotechnology can interact with organic tissues. Ultimately it is this that is going to determine whether the thoughts portrayed in this paper become reality or not. This is because prosthetic grafts have a major flaw. They are not organic. It seems obvious but it is a huge problem. Organic tissues grow and die but exploit all the systems of the body. Prosthetic material cannot do this - instead it acts as a puncture repair patch. In other words it is the weak link in the chain. In order to overcome this the material has to behave as much like an organic tissue as possible. But is the height of arrogance to try to produce something so close to what God has made himself? Ethical questions like this are ones that researchers will also have to overcome if they are going to be successful.

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