EVALUATING THE ADVANCEMENTS AND EFFECTS OF USING NANOTECHNOLOGY IN DIAGNOSIS, TREATMENT AND PREVENTION OF CARDIOVASCULAR DISEASE

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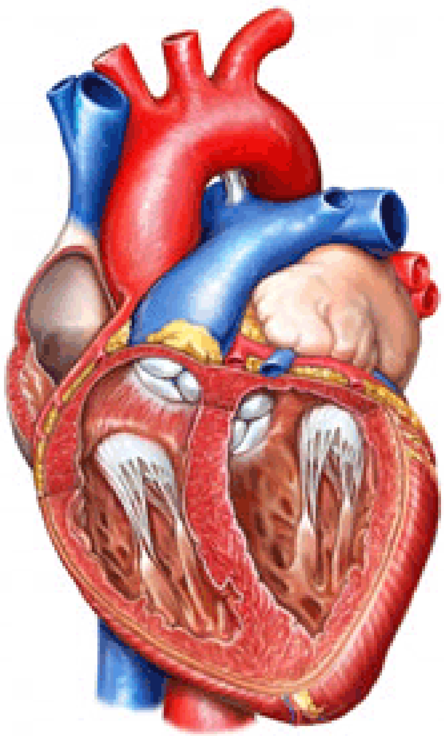
PASS WITH MERIT



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ABSTRACT

Recent data shows that here in the UK, your own body is more of a threat to your life than a cold-blooded killer. You are over 200 times more likely to die due to cardiovascular disease (CVD) than be murdered, and yet there is still no cure.
I predict that the current levels of CVD in the UK alone could be dramatically reduced by the introduction of various applications of nanotechnology (NT).

This paper enforces my ideas and reviews how NT can be harnessed to advance the care given to patients with cardiac conditions and investigates the options that could soon be available from the progression of various aspects of NT. I will also assess the advantages and disadvantages of using this new modernised treatment method, and any ethical implications that arise.

INTRODUCTION – What is nanotechnology?

"Controlling matter on an atomic and molecular scale"

Nanotechnology is the branch of engineering that deals with things smaller than 100 nanometres, with 1 nanometre measuring one millionth of a millimetre.
Nanotechnology all began with the 1959 lecture from Richard Feynman entitled "There's Plenty Of Room At The Bottom". This openly discussed the possibility of science being scaled down to a much smaller size than it was already, and how soon 'molecular machines' would be a reality. In particular, Feynman emphasized the importance of nanotechnology in cardiovascular medicine. There were two main discoveries within nanomedicine to be made over the next 30 years that shaped the medical field as it is today.

Firstly, in 1981, Gerd Binnig and Heinrich Rohrer invented the Scanning Tunnelling Microscope at an IBM laboratory in Zurich, Switzerland and separated out 35 atoms of xenon on nickel. As seen in Figure 1 it allows scientists to individualise atoms and has been described as the most revolutionary achievement in nanotechnology.

Next to be discovered, in 1985, was Buckminsterfullerene or 'Bucky Balls'. This was a new form of carbon and comprised of 60 atoms joined together to form a spherical structure. Due to the hollow centre, it has a very high affinity for carrying drugs, which is what makes it such a vital component of the new drug delivery systems being researched. Figure 2 shows a 'Bucky Ball'.

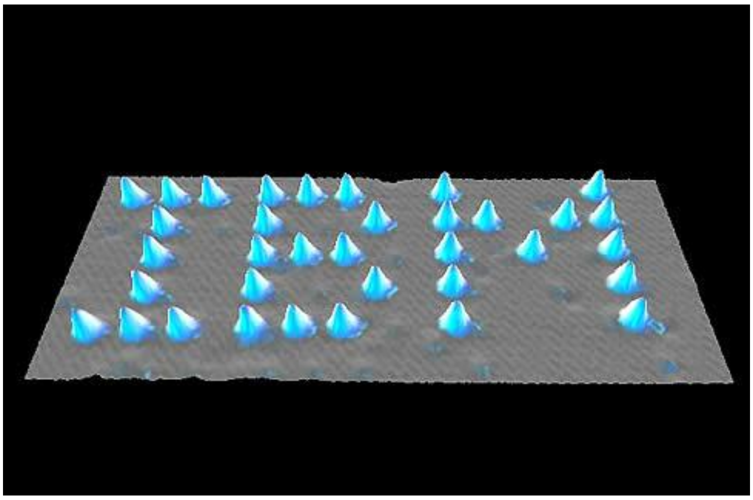

Fig. 1

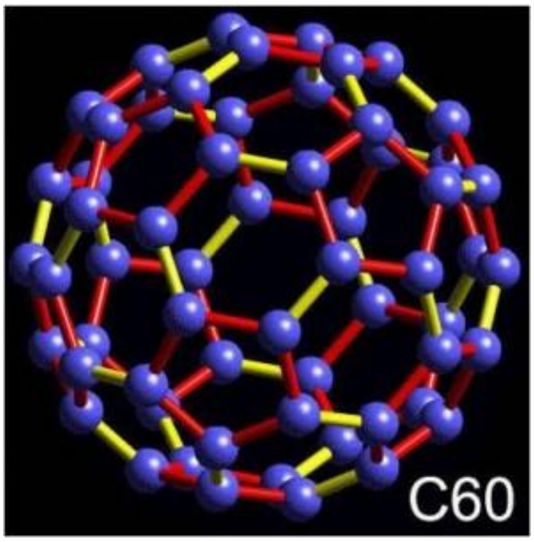

Fig. 2

Not everyone fully realises just how microscopic the ways of treating a patient can get and it is difficult to imagine that 500,000 carbon nanotubes (often used as a stent when regrafting arteries) can fit along the width of a single pinhead. The two mentioned above are amongst a number of great achievements within this field which form the timeline of nanotechnology and each and every one of these milestones has contributed to today's direction of medicine, enabling new areas and ideas to be further constructed which only 60 years ago were unknown and unimaginable.

Uses of nanotechnology within medicine

For such a small-scale field, nanotechnology already has many applications within medicine, and there are regular advancements as to how far this tiny technique can go, and what feats can be achieved next. Drug delivery, DNA analysis, cancer treatment and diagnostic testing are just some of the uses of nanotechnology today.

Undoubtedly the most frequently heard of use for nanotechnology is drug delivery, which mobilises the space within each nanoparticle by implanting disease-fighting and cell-killing drugs that are released at the very core of the problem, for example, inside the tumour in a cancer patient. This technique, once fully mastered by medical professionals, offers a potentially more successful alternative to injections and surgery for patients with a whole range of medical issues, from brain tumours and coronary heart disease to diabetes.

With the case of diabetes, Professor Desai from the University of California, San Francisco, has accomplished the task of inserting millions of healthy and functioning pancreatic cells, capable of secreting insulin, into nanoporous capsules which ideally, once inside the pancreas of a diabetic will remove the requirement for constant pin pricks and insulin injections. Insulin is produced when blood sugar activates the pancreatic cells within the capsules to produce it, and then escapes from the capsules and into the body. Anything that may attack the cells, such as antibodies are prevented from entering the capsules as they are too large to pass through the microscopic pores.

There is also progress with the treatment of brain tumours (and other cancers), where nanoparticles ‘burrow’ inside the tumours and release large doses of destructive and cell-deadly drugs. Harvard Medical School and the Massachusetts Institute of Technology conducted experiments 7 years ago on using nanotechnology to cure human prostate cancer in mice. Here, the nanoparticle in question was a hydrogen and carbon polymer that gradually decomposed leaving only the drug that was woven into it, to target the cancer cells. After 100 days the experimental group of mice were left with no tumour at all, showing just how effective nanotechnology can be, and encouraging the medical profession to research further with a new found hope and expectancy for the performance of nanotechnology.

Cardiovascular disease

In attempting to find a cure, it must first be understood what causes cardiovascular disease in order for it to be prevented or reversed. Cardiovascular diseases are diseases affecting the cardiac muscle or blood vessels. A build up of atheroma within the artery walls (atherosclerosis) narrows blood flow and therefore limits the levels of oxygen that reaches the heart via the blood. A myocardial infarction may then occur if the atheroma forms a clot and fully blocks the artery – leading to death. Collectively, these diseases account for 20% of deaths in men, and around 14.3% of deaths in women in the UK, and although there has been groundbreaking progress in terms of treatment and diagnostics, more is certainly required.

Currently the methods of diagnosing CVD include MRI scans, blood tests and ECGs. These use magnetic fields, analysis of blood composition and electrical impulses respectively in order to detect irregularities with the heart so treatment can be identified and administered. However this range of options could be further varied by the involvement of nanotechnology developments. MRI images of cancer tumours, for example, can be enhanced by using iron oxide nanoparticles coated by a peptide which binds to the tumour, and because the iron is magnetic, the scanner can pick up traces much more effectively.

DISCUSSION

There has been an outstanding progression on the frontline of battling CVD with this technology, by many institutes and universities worldwide, proving how important these discoveries are and that so many people regard nanotechnology as holding the key to curing conditions in the future.

Rutgers University in New Jersey has developed further the concept of combining nanotechnology with the treatment of cardiovascular disease and the prevention of myocardial infarction. Their research aimed to combat the process where oxidized, low-density lipoproteins (LDLs) attach to, and are attacked by, macrophages. These are the antigen-presenting white blood cells, which are heavily involved in the body's immune response by stimulating phagocytosis and therefore regularly preventing the body being under attack by foreign pathogens. The macrophages commence the secretion of chemicals, destroying nearby tissue which is then converted into 'fatty foam cells'.

'Nanolipoblockers' are the nanoengineered molecules being used, and they work in groups to prevent the oxidized LDLs fusing to macrophages by targeting specific receptor molecules on cell membranes. The research team found that this process cuts the build-up of oxidized LDLs by up to 75%, and are now continuing their research on living organisms. This method, if harnessed successfully, could be incorporated into pills (such as the ones using drug delivery) to locate and target the LDLs, and could be distributed to those suffering from high cholesterol, so that build up of atheroma in the cardiac arteries is dramatically reduced.

Another new development is from the University of Santa Barbara, where atherosclerosis is being cured by micelles, spheres formed by lipid-based molecules which present a peptide on their surface that attacks the build up of plaque, by binding to its' surface. The micelles are nanoparticles and their creation brings society one step closer to treating aspects of CVD. Once again this research was carried out on mice by maintaining them on a high-fat diet, followed by an injection of the micelles into their bloodstream. As atherosclerosis is a major cause of myocardial infarction, if the use of this plaque-annihilating treatment could be further developed and approved for humans, rates of CVD could also decline rapidly.

At the Department of Internal Medicine and Research Center of Regenerative Medicine, Ural State Medical Academy in Yekaterinburg, Russia, a combination of nanotechnology and adult stem cells were used in an effort to remove atherosclerotic plaque and also regenerate the arteries. The current methods to treat an atheroma are:-

a. Angioplasty, whereby a balloon is inflated within the artery and then removed, leaving only a stent and,

b. Thrombolysis, which involves the use of clot-dissolving drugs.

In experiments on pigs, nanoparticles with adult stem cells were implanted into the pigs' hearts where biophotonics (light therapy) was used to heat the nanoparticles in order for them to burn away the plaque. An average reduction in plaque of 56.8% was recorded six months later on the experimental group of pigs, which had received both nanoparticles and stem cells. The control group that only received saline showed a 4.3% average increase in plaque. Alexandr Kharlamov M.D., lead author and research manager, said "This unique approach holds promise for use in humans for acute care and urgent restoration of blood flow. Biophotonics (light therapy), plasmonics (plasma therapy), stem cell therapy and nanotechnology might someday offer a completely novel treatment to reduce artery plaque build-up." From this a conclusion could be drawn that human atherosclerosis could be helped with not only nanoparticles but stem cells too, and the perfection of this combination could prove very beneficial to those wishing to avoid angioplasty that could potentially need repeating if it fails.

Some hard-to-reach parts of the body may be made more accessible now, if researchers at the Nanophysics laboratory of Monash University, Australia can improve their nanobots which are powered by piezoelectric motors where electricity is generated through vibrations. They measure just a quarter of a millimetre and could be the key to the beginning of treatment to fragile and critical locations like the cranial or cardiovascular arteries. While these nanobots have yet to be trialled on animals, it is likely that one day, once a means of controlling their movement has been mastered, this treatment can take over from catheters, much like catheters took over from cut and sew operations.

Looking at those who already have or have had cardiovascular disease, where diagnosis or prevention may be too late, progression in treatment may prove to be a worthwhile invention. Today, one can find a mechanical heart, a heart grown from stem cells and now even a damaged and diseased heart could be rejuvenated in situ thanks to the work carried out at the London Royal Free hospital. Here, a team has used nanotechnology to create an artificial artery, which could be used not only in the heart but also all round the body where plaques, clots and implications would once mean amputation (or death). The new artery is made from a polymer embedded with special molecules, offering a multitude of different functions from aiding circulation to stimulating the coverage of its walls with stem cells, which is vital for allowing the man-made tissue to bond better with the body's natural tissue. In addition, what many see as the greatest benefit is that it is resistant to clotting and can also carry a pulse, extremely important for cardiac arteries.

In 2005, the Program of Excellence in Nanotechnology (PEN) was also established, publishing over 80 research papers, another indication of the growing awareness and focus on nanotechnology- related advancements by the scientific and medical communities.

Overall, an effort is being made globally to attack the burden that is cardiovascular disease. Whether it be the nanobots or micelles, designed to treat and cure, or the biosensors created to detect and diagnose, billions of pounds are being invested world wide in an attempt to be rid of this debilitating and life threatening disease forever, sometime in the future.

ETHICS

As with all revolutionary concepts, there are certain ethical dilemmas, which must be taken into account as investment and invention progresses. Primarily, a fear held by many with knowledge of nanotechnology is the potential for it to be mastered in weaponry and become a main path of attack or defence for both countries and extremists. This could lead to the destruction of buildings and people on a molecular level, and result in the opposite to what was intended, for advantageous developments in medicine.

Another leading cause for concern within nanotechnology is the scenario already put forward by a researcher named Eric Drexler, in 1986, when he imagined “The Gray Goo Scenario”. Here, nanoparticles and nanobots with an intentional use of breaking down molecules to benefit the Human Race, could ‘escape’ and begin to take apart every molecule they came across in an apocalyptic way.

Finally, one issue within the medical community is the opportunity for people to customise their appearance and characteristics to suit them. If the chance arose for someone to increase their IQ or strength, or even gain superhero-like powers, most would embrace it. Price, however, would become an issue, as these kinds of procedures would inevitably cost a small fortune, leaving only the wealthy on a high enough pedestal to reach up and take the option. Potentially two sub-races could be left with one not rich enough to genetically enhance themselves. This follows closely on from the ‘designer baby’ trend, where embryos could be genetically altered to give them sought after traits like specific hair colour, eye colour and skin colour.

A variety of health-related concerns must also be evaluated as a number of discoveries have led to an air of caution around the safety of nanotechnology and its impact upon the human body. The titanium nanoparticles used in sunscreen have been found to destroy DNA by creating free radicals, whilst gold nanoparticles, used for drug and gene delivery, may be able to move through the placenta from mother to foetus, as brought to light by British scientist Vyvyan Howard. This could potentially lead to poisoning of the foetus. Cadmium selenide nanoparticles were identified as potentially dangerous, when research from the University of California showed that they can cause cadmium poisoning within the body. Due to their minute size, there is also a fear that nanoparticles could cross membranes, imperative for life, into the skin, lungs and brain as shown in Figure 3.

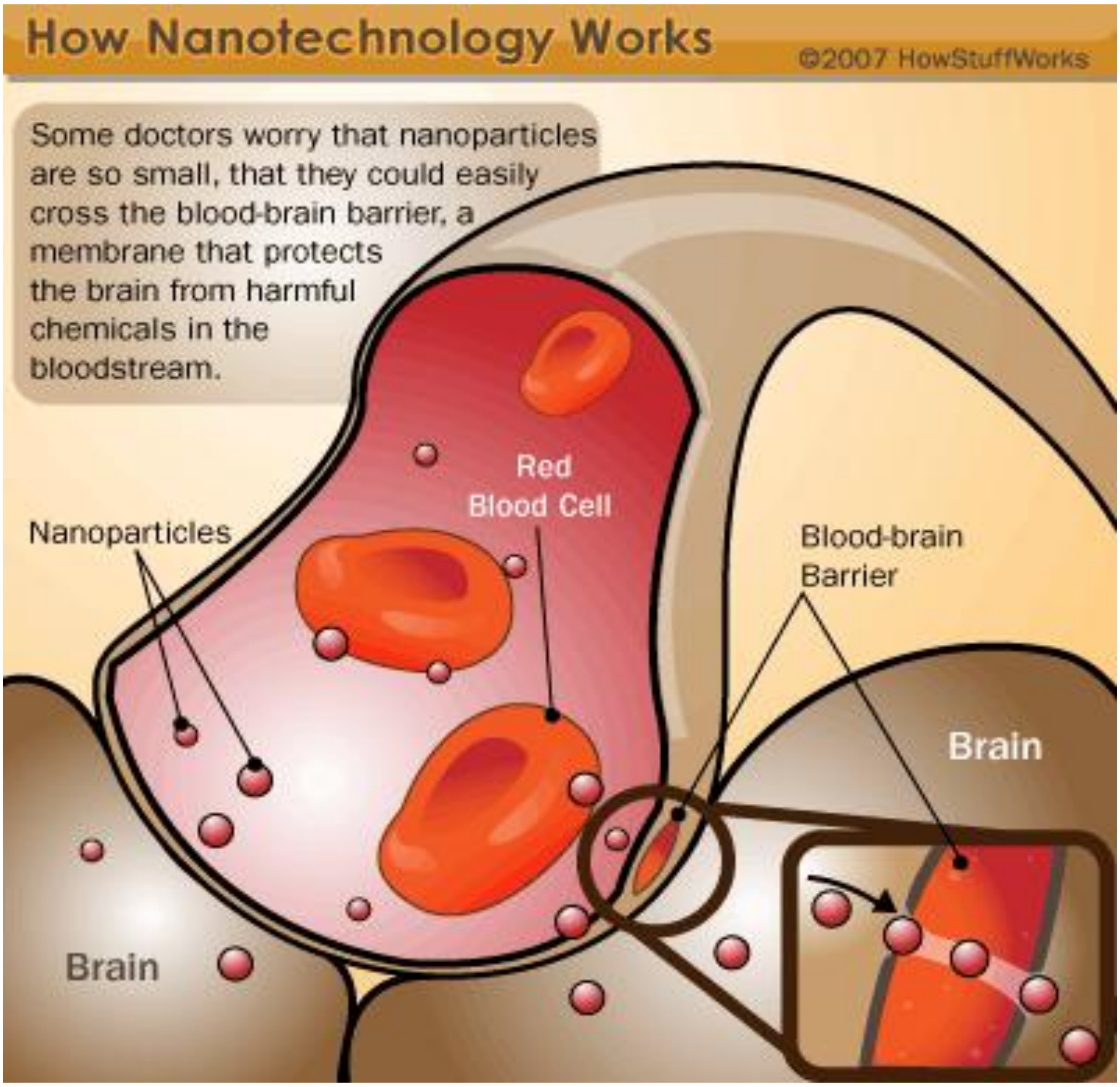

Figure 3

All these possible implications must be examined before nanotechnology is prescribed on a mass scale, as peoples' lives are at risk from a danger so tiny that we may not be able to stop it. The idea of miniature robots and particles literally taking over the world may seem far-fetched and absurd, but a string of mutations and mistakes could lead to them being found 'in the wild', and potentially wreaking havoc upon society.

CONCLUSION

In the world today, some may argue that constantly improving and perfecting processes – like the treatment of the heart with nanotechnology – will only eventually lead to a negative outcome. However, already in trials many patients have found their health benefited from some form of treatment involving nanotechnology, particularly those unlucky enough to have cancer. In various trials it was found that nanoparticles could penetrate the tumours, and the drug delivery feature meant healthy cells could be left unharmed as the tumours were attacked. Certainly these people and those who in the future will find themselves in similar situations, would agree that developing nanotechnology is definitely the way forward, and why not if there could be millions of lives eventually saved by this groundbreaking therapy.

Even advancements outside of the medical field may help in people avoiding the need for medical treatment in the future. As seen in The Sunday Times' 'Style' magazine, published 30th January 2011, they claim that "Soon, chocolate, mayonnaise and cakes oozing cream could be made up with half the fat, but without losing the taste." And "wonder junk food is not too far away". These statements are backed up by an explanation that, as scientists use nanotechnology more and more, the calorie content in food can be manipulated and you can eat 'junk food' without the extra strain on your heart and body. In terms of health benefit, the risk of obesity and therefore all the factors of CVD that accumulate along the way, such as high blood pressure, atherosclerosis and blood clots, can be reduced or even avoided completely. This means fewer cases of CVD, which means fewer people needing the costly treatment for it.

Overall, the idea that a particle could save your life is a very appealing one indeed, cutting out routes of life-threatening surgery and expensive alternatives. More research needs to be done into nanotechnology, obviously, before it can begin domination of medical treatments, but scientists do believe that every achievement is one step closer.

To conclude, I believe that nanotechnology has taken the cardiac unit of the medical profession by storm, and as levels of CVD are continually increasing, so are the efforts of those trying to cure it. Once experiments have been carried out to assess any lurking dangers to the body of this new technology, the general public can really start to feel the benefits such as possibly curing CVD. Only then will society show its gratitude for the scientists' unacknowledged work from the past few decades, and it really will come from the heart!

REFERENCES - websites

http://www.nhs.uk/conditions/coronary-heart-disease/Pages/Introduction.aspx

www.thewellingtoncardiacservices.com

http://www.bhf.org.uk/heart-health/conditions/cardiovascular-disease.aspx

http://webarchive.nationalarchives.gov.uk/+/www.dh.gov.uk/en/Healthcare/Longtermconditions/Vascular/Coronaryheartdisease/index.htm

http://news.bbc.co.uk/1/hi/uk/8153392.stm

http://www.bhf.org.uk/plugins/PublicationsSearchResults/DownloadFile.aspx?docid=07a5d384-ac93-4d2b-a84d-918620d7a9f0&version=-

1&title=G30+UK+CHD+statistics+factsheet+2009-10&resource=G30U%2F0210

http://www.nanofolio.org/win/nanotechnology01.php

http://www.nanoforum.org/educationtree/othersections/nanotimeline.htm

http://www.3rd1000.com/bucky/bucky.htm

http://www.nanotech-now.com/nanotube-buckyball-sites.htm

http://www.patient.co.uk/health/Preventing-Cardiovascular-Diseases.htm

http://www.understandingnano.com/medicine.html

http://science.howstuffworks.com/nanotechnology.htm

http://www.smartplanet.com/people/video/nanotechnology-to-end-insulin-injections-for-diabetics/370926/

http://www.msnbc.msn.com/id/9885176/ns/health-cancer/

http://www.emaxhealth.com/92/5839.html

http://www.touchcardiology.com/articles/benefits-nanotechnology-cardiovascular-surgery-a-review-potential-applications?page=0%2C1

http://www.dailytech.com/Scientists+Ready+New+Nanobots+to+Swim+in+Human+Blood+Stream/article14018.htm

http://www.scientistlive.com/European-Science-News/Nanotechnology/Treating_cardiovascular_disease_with_nanotechnology/22563/

http://www.understandingnano.com/heart-disease-nanotechnology.html

http://www.healthjockey.com/2010/07/24/nanotechnology-allegedly-helpful-in-treating-heart-disease/

http://www.nanowerk.com/spotlight/spotid=6883.php

http://singularityhub.com/2010/01/05/nanotechnology-creates-artificial-artery-for-clinical-trials/

http://www.nanowerk.com/news/newsid=18329.php http://www.actionbioscience.org/newfrontiers/chen.html

http://science.howstuffworks.com/nanotechnology5.htm

http://www.scu.edu/ethics/publications/submitted/chen/nanotechnology.html

http://www.nanotech-now.com/ethics-of-nanotechnology.htm

http://www.wisegeek.com/what-are-the-possible-dangers-of-nanotechnology.htm

http://thechart.blogs.cnn.com/2010/03/22/nanotech-cancer-treatment-shown-to-work-in-humans/

REFERENCES – Paper

Brave New World (30th January 2011) The Sunday Times 'Style' Page 53