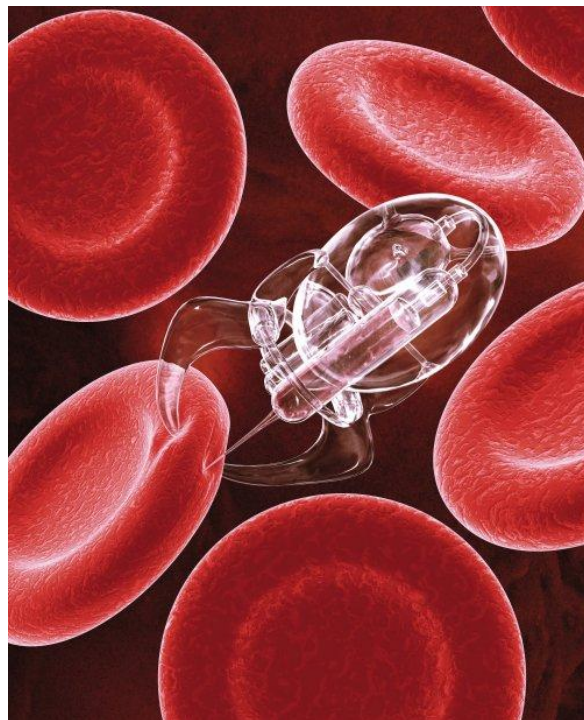


The Use of Nanotechnology in the Treatment of Cancer and the Ethics surrounding Nanotechnology in Medicine

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PASS WITH MERIT



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ABSTRACT

Nanotechnology is one of the most promising ways to treat cancer in the future, because there are so many different angles from which the issue of treating cancer can be approached, some of which are explored below.

This paper looks at possible uses of some aspects of recent nanotechnology research, such as drug delivery and molecular manufacturing. It explores the breakthroughs that could be achieved if the research continues on its upwards path. It also dips into the vast topic that is the ethics of using nanotechnology in medicine.

INTRODUCTION

Nanotechnology has been at the forefront of medical research for the last decade, the reason for this being that there are a range of applications with a variety of nano-particles. Nanotechnology refers to the use of man-made, nano-sized particles for industrial or medical applications specific to their use. It involves the manipulation of properties and structures on the nano scale, which is typically 1-100 billionths of a meter.

The concept of nanotechnology first arose in 1959, physicist Richard Feynman described a process where the ability to manipulate individual atoms and molecules might be developed using one set of precise tools to build and operate another proportionally smaller set, and so on down to the needed scale.

Now, in the modern day we know how to manipulate atoms, molecules, materials and various structures at an atomic scale; we also know the effects and have some understanding of the possible applications. From multiple experiments performed over the years, we have seen that on the nano-scale, the properties of known elements seem to change because of the surface area to volume ratio, for example, nano-sized gold is a semi conductor, whereas bulk gold is a conductor. These changes in physical properties such as colloidal properties, solubility and catalytic capacity have been found very useful in areas of biotechnology, such as bioremediation and drug delivery.

The very different properties of the different types of nano-particles have resulted in novel applications. For example, compounds known to be generally inert materials may become catalysts. The extremely small size of nano-particles allows them to penetrate cells and interact with cellular molecules. Also Nano-particles often have unique electrical properties and make excellent semiconductors and imaging agents. Due to these qualities, the science of nanotechnology has taken off in recent years, with testing and

documentation of a broad spectrum of novel uses for nano-particles, particularly in nano-medicine.

Cancer is a class of diseases in which a group of genetically mutated cells undergo rapid and uncontrolled growth. This growth leads to the development of a tumour which, if not treated, can cause multiple problems: by spreading into neighbouring tissues; causing pressure on body structures, such as the lungs; and the cancer can spread to the rest of the body through the lymphatic system. Cancer is a dreaded, deadly disease (In the UK in 2008, there were 156,723 deaths from cancer); therefore its treatment is paramount in the world of medicine. Most of the modern day treatment involves chemotherapy, radiation therapy, surgery and biological therapies. You may ask why there is such a great need for finding new treatments for cancer when there are already numerous treatments. The reason being is that the current forms of treatment tend to cause side effects that weaken the patient, for example cancer drugs not only destroy cancer cells, but also normal fast growing cells, such as hair cells. As well as the hair and skin, areas of the body that chemotherapy may affect include the mouth and the lining of the digestive system, and the bone marrow, which makes blood cells. The current treatment is also not 100% effective therefore more effective methods are desirable, and many researches think that the answers lie in nanotechnology.

Figure 1 shows the Buckminsterfullerene or Buckyball, (first developed by Smalley in 1985) a member of the carbon structures known as fullerenes. New molecules such as these are being developed to carry drugs to specific locations in the body.

Some new findings from the CRN (Centre for Responsible Nanotechnology) state that molecular manufacturing, in which the use of programmable chemistry to build exponential manufacturing systems and high-performance products, will arrive within the next 20 years. The medical applications of molecular manufacturing are numerous; tools of medicine will become cheaper and more powerful. Research and diagnosis will be far more efficient, allowing rapid response to new diseases, including engineered diseases. Small, inexpensive, numerous sensors, computers, and other implantable devices may allow continuous health monitoring and semi-automated treatment. Several new kinds of treatment will become available. As the practice of medicine becomes less expensive and less uncertain, it could become an option for more people.

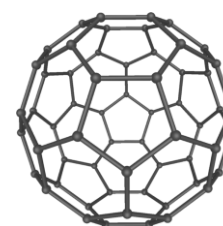


Figure 1

Medical tools today are large and crude at the molecular level, and cause much damage, even a fine scalpel can be considered to be blunt. Nanotechnology should allow us to build a range of complex machines, which will allow us to control molecular tools that have been engineered with precision so that they can enter single cells and carry out accurate procedures, and specific drug delivery.

Despite all of the benefits that could follow from all this research and development, there are ethical issues that arise from the use of nanotechnology in medicine, of which the most important are a changing understanding of human disease and enhancement.

DISCUSSION

Treating cancer is no easy task, there are many complications to consider when deciding which treatment a particular patient is suited to. As explained above, current treatments need to be further developed or new treatments need to be discovered, with the answers potentially lying in nanotechnology.

Drug Delivery

The first concept that I will explore involves the delivery of chemotherapy drugs, and other possible substances directly into the cancerous cells so that the normal cells remain undamaged and a faster treatment of the tumour can be achieved.

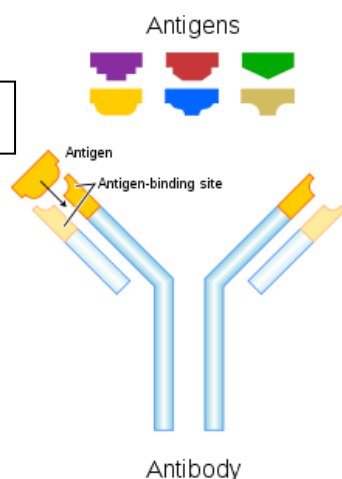


Figure 2

This type of cancer treatment, with specific drug delivery, would be most useful where surgery cannot take place to remove the tumour. Carbon structures such as the fullerene shown in figure 1 were the first to be looked at for drug delivery systems. The physical frame of the carbon structures would allow them to carry a certain drug, which would be protected from contamination by the carbon atoms in their arrangement in the skeleton. The main issue with drug delivery is how to target the drugs specifically to the cancer cells; I believe that the answer could lie in antigens and cell surface receptors. We already know that monoclonal antibodies can specifically adhere to

targeted molecules, because of their specific protein structures that give them a complementary shape (to the desired molecule to be captured) at their binding sites, which can be seen in figure 2. This same principle can be applied to the problem encountered here; the carbon molecule would incorporate many different binding sites, which would specifically bind to the cancer antigens, just like the monoclonal antibodies can bind to proteins, and other molecules because of the complementary shapes. Once a binding site has bound to a receptor on a cancer cell, it would initiate events to take place within the fullerene to release the drugs. Due to the small scale involved, the drug can be injected directly into the cancer cell, which would inhibit the growth of the tumour and destroy the cells just like a chemotherapy drug.

This theory does not stop there; my research also led me to discover that different molecules can also be 'wrapped up' by nano-particles, and the treatment has been successful with trials on rats. Scientists wrapped up genes in microscopic nano-particles which were taken up by cancer cells, but not their healthy neighbours. Once inside, the genes stimulated production of a protein which destroys the cancer. The human clinical trials are set to take place later this year.

Radiation Therapy

Now, we turn to radiation therapy. Radiation therapy has one main drawback, which is the destruction and damage to healthy tissue because of the excessive exposure to the radiation used. The problem with it is that the radiation waves cannot be specifically directed to only destroy the cells of the

tumour, and so healthy tissues that obstruct the pathway of the rays often succumb to damage beyond repair.

A possibility is the use of a nano-particle that would enhance the effect of the radiation waves because of some sort of electrical properties. Figure 3 shows the use of 'nanoshells' which will find the tumour and bind to them, probably using the specific antigens on the surface on the cancer cells. Once bound,

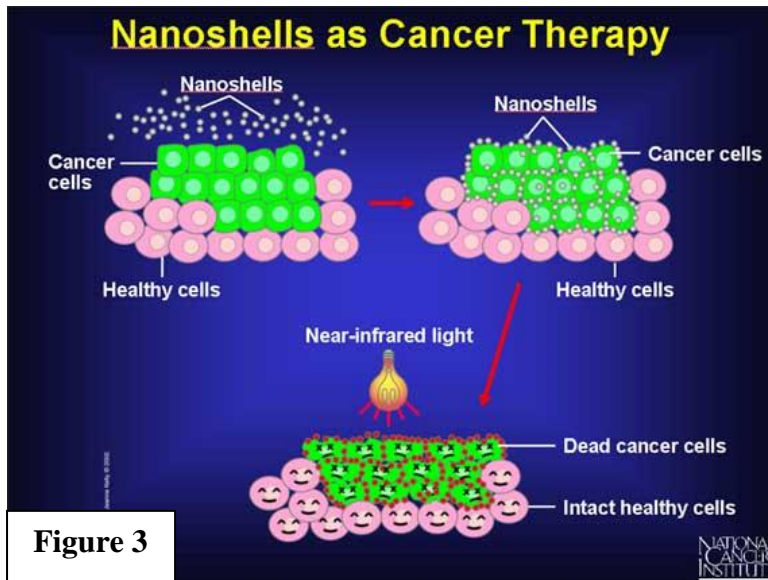


Figure 3

infrared light can be shone towards the area of the tumour; this will activate nanoshells to somehow activate a process that will destroy the cancerous cells, by either releasing a drug or gene to prevent further growth, or enhance the effect of the radiation being shone onto it. This is no 'Star Trek' science; research had been carried out by Nanobiotix, an emerging nano-medicine company, which say "Our

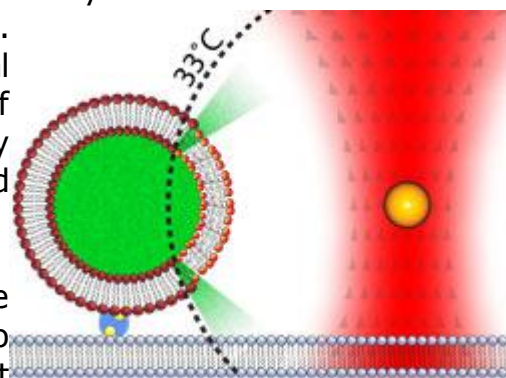
nanotechnology is designed to allow for the precise destruction of cancer cells via the controlled application of an outside-the-body energy source in this case, an x-ray. We are highly encouraged by these latest results, with confirmation of good tolerance and negligible toxicity observed in animals." Laurent Lévy, Ph.D., President and CEO of Nanobiotix and Co-President of the French Technology Platform on Nanotechnology (FTPN) (2010).

The company used a group of nano-particles they call NBTXR3; it is a suspension of inert crystalline nano-particles of hafnium oxide, which is the therapeutic source. However, only when its electrons are excited by the application of an external beam of x-ray, will the source be activated. NBTXR3 works according to an "on-off" activity status. When the nano-particles are not activated, they do not have any effect because they are inert. Under standard external beam x-ray activation, x-rays are absorbed by NBTXR3 nano-particles exactly as ionizing radiations are absorbed by water molecules, leading to emission of electrons losing energy and the subsequent creation of free radicals.

Gold Nano-particles

Due to their attractive electronic, optical, catalytic and thermal properties; gold nano-particles have emerged with great interest. In particular, the thermal properties exhibited by gold nano-particles under certain conditions, could be used to destroy a tumour in the body. The gold particles are excellent conductors of heat, and because of their size, they can be used for creating localised heating in cancer cells which would destroy them.

This technique may be a possible use in the future; German researchers at the Niels Bohr Institute have measured the temperature of nano-sized gold particles with extreme precision and have examined their ability to melt the lipid membranes surrounding cells, as shown in figure 4. The particles were heated with infrared light from optical tweezers, and by tuning the light up or down, the heat of the particles can be controlled. From this experiment, they found that gold nano-particles can reach several hundred degrees at a light intensity of just 1 watt.



This means that we can use the gold particles as tiny little heat sources, that can melt the lipid membrane of a cell so that it is killed. This technique can be so precise, that just one particular cell can be killed at a time. The question here is whether or not the heat will affect other neighbouring, healthy cells; the answer is no. The temperature decreases rapidly as the distance from the surface of the particle increases, so much so that at a typical cell length away, the temperature will have decreased so much that it is harmless.

Figure 4:

Tiny gold particles are heated using infrared light from an optical tweezers and the hot gold particle is brought closer and closer towards an artificial cell membrane.

Another way of utilizing the heat properties of these particles to destroy cells has been discovered by scientists at Rice University. They used lasers to make 'nano-bubbles' inside cells by heating the gold nano-particles; in tests on cancer cells, they found they could tune the lasers to create either small, bright bubbles that were visible but harmless or large bubbles that burst the cells.

Molecular Manufacturing

There is a sound level of enthusiasm amongst researchers about Molecular Manufacturing (MM); it's potential to build complex manufacturing systems and high performance products sparks off many ideas. The medical benefits of such systems are numerous, and some could well be used to treat cancer either directly or indirectly in the future.

The CRN have spotted many medical benefits of MM, but the most relevant to the problem here, is the possibility to manufacture and implement nano-robots into the body which can perform a number of procedures. These devices could be used in the future to aid the surgery of removing a tumour, or propel itself into the tumour and destroy it with heat.

This is not a far fetched idea; there have been multiple experiments to develop such contraptions. In 2002, Ishiyama et al. at Tohoku University developed tiny magnetically driven spinning screws intended to swim along veins and carry drugs to infected tissues or even to burrow into tumours and kill them with heat. Brad Nelson's team at the Swiss Federal Institute of

Technology in Zurich reported the fabrication of a microscopic robot small enough (w200 nm) to be injected into the body through a syringe and this simple micro robot has successfully manoeuvred through a watery maze using external energy from magnetic fields, with different frequencies that are able to vibrate different mechanical parts on the device to maintain selective control of different functions.

The greatest benefit of these nano-robots will emerge in the 2020's, when we will be able to design and construct them using diamondoid molecular gears (figure 5.) and bearings. In the future, these robots will incorporate numerous sensors, tools, computers, motors and manipulators so that they can find their way round the body. However getting all of these complicated systems to self assemble will become increasingly complex as machine structures become more complex. They need to be assembled using a technique called positional assembly, which involves placing the molecular parts one by one such as the robotic arms manufacture cars.

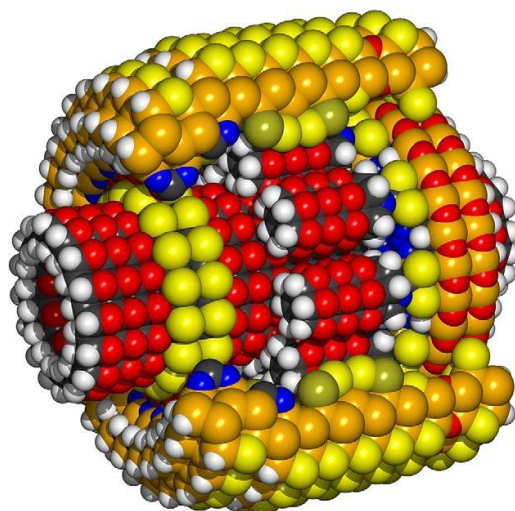


Figure 5:

A molecular planetary gear is a mechanical component that might be found inside a medical nano-robot. The gear converts shaft power from one angular frequency to another. The casing is a strained silicon shell with predominantly sulfur termination, with each of the nine planet gears attached to the planet carrier by a carbon-carbon single bond. The planetary gear shown here has not been built experimentally but has been modelled computationally. Copyright 1995 Institute for Molecular Manufacturing (IMM).

The Ethics of Using Nanotechnology in Medicine

There are so many other possible future treatments of cancer using nanotechnology; however we must consider the ethical issues that arise around the use of such technology in the world of medicine. Ethics plays a major role when deciding what is right and what is wrong; therefore in the future, ethics will influence whether using nanotechnology in correspondence with the body is either right or wrong and ethics will set the boundaries that we must not cross.

The first path that I will explore looks at what effect nanotechnology will have on our understanding of human disease. The advancing technology means that sensors will give more detailed diagnosis, and eventually even the slightest abnormality in the body could be detected. This produces the question as to what relevance these minute abnormalities actually have. Diagnostic technologies will be able to detect the slightest change in DNA or blood chemistry; these changes will cause a doctor to wonder whether they are of any significance. They will then wonder if they could escalate into a deadly disease or if it will simply cause no harm at all. A doctor's perception of a healthy person may change all together once they have access to all of the information that can be gathered using nanotechnology. The diagnosis of

a disease such as cancer will have to be carefully thought about, is a genetic mutation in a few cells that has been known to cause cancer a diagnosis? In a small number of cells, say 5 are cancerous; can we tell the patient that they have cancer?

This change in perception has already started to take place; nano-medicine pioneer Robert Freitas Jr. proposes a new view of disease, which he terms the "volitional normative" model. In his model, normal or healthy is considered to be when a person is at optimum functioning according to their own genetic programming opposed to the 'healthy' of the wider population base, and the patient's own wishes are crucial as to define a state of good health.

Recognitions of disease and health will have to be re-modelled, such as the model described above, once our diagnostic technologies have reached a stage where every detail is monitored.

Nanotechnology has the potential to replace organs, tissues and various other parts of the body; if this comes into practice in the future then it is inevitable that human enhancement will be possible. This idea of enhancement involves lengthening the human life span, enhancing human senses such as sight, enhancing muscles to make us stronger and many more possibilities.

In the last few thousand years, the human life expectancy has been tripled because of advances in technology and our social developments. Evolution has not played much part in this, whereas improvements in such things like: sanitation, medicine, education and nutrition have all had a very positive effect on life expectancy. Curing disease would not increase life expectancy as much as you would think. For example, in the USA if you were to cure all types of cancer, then the life expectancy would only gain about 3 years. This is because as we get older we become more susceptible to disease, so if not cancer then it could be pneumonia or heart disease.

This then leads us to think about technologies that are specifically designed to help us live longer. Some people are in favour of such technologies, as they feel that with a longer life, they could achieve and learn so much more and make more of an impact on the world. Others however, are against increasing the human life span; they believe that the meaning of life would be deprived.

If people begin to live longer, and people begin to take advantage of the nanotechnology in the future, then many problems are more than likely to branch out. If the replacement of body organs using nanotechnology becomes a reality in the future, then people would begin to take more risks in life; they would have less fear as they know that the world of medicine would make them better. This would be an imposing problem on the whole world, and it is a huge topic to be considered.

Physical enhancement has always been a desire; it is shown in the media such as films, and to an extent in some people taking steroids for bigger muscles. However is physical enhancement right?

There are many ways that nanotechnology could help us improve what we might call bodily capacities, which include stamina, strength, dexterity, flexibility, coordination, agility, and conditioning. Physical enhancement is especially desirable for those who take part in sport. The spirit of sport is the celebration of the human spirit, the body and the mind according to the World Anti-Doping Agency (WADA). So to keep the 'spirit of sport' physical enhancement cannot take place; which is rightly so because the competition is not then between individuals physical or mental abilities. However sports men and women prepare for competitions in ways that dogs or horses cannot, and so the competition is not simply between the biological potential.

Physical enhancement also applies when someone is recovering from an illness or injury; improving bodily capacities can be a difficult and painful feat after a major illness or injury. If the person does not have the capacity to recover, because of age for example, then the results could be fatal. Therefore would it be okay if a recovering patient was to receive physical enhancement?

Religion also has a part to play in this matter, many religious people would argue that enhancement would be interfering with the natural world and that it is totally wrong to use such technologies to enhance the bodies. The religious matters open up a whole new world of issues regarding the use of nanotechnology in medicine.

CONCLUSION

My investigation has shown that there are many possible future treatments for cancer using nanotechnology. Sophisticated drug delivery systems are more than likely to be developed, using nano-structures such as the fullerenes to carry the drugs or other substances, such as proteins, directly to the cancerous cells. They would incorporate a technique used by monoclonal antibodies to bind to the specific cell surface receptors on the cells of the tumour.

Nano-particles in the future could also be used in coalition with radiation therapy. They would also, like the fullerenes, adopt the method of binding to the cell receptors of the cancer cells, the specific properties of these particles would then be utilized when they are exposed to some form of radiation. The tumour could then be destroyed in a few different ways: the nano-particles could enhance the effect of the radiation onto the tumour, or the particles could release a drug or possible other substances such as a protein designed to kill the cells.

The gold particles have great potential in the search for new cancer treatments as they exhibit such attractive thermal properties. These properties have been shown to melt a lipid membrane such as those on a cell. This shows that these particles have the potential to be used in a therapy to

treat cancer. Some institutes such as Rice University have already begun experiments to find how gold particles could be utilized in the body to destroy cells using heat.

Nano-robots used to be a farfetched idea; however molecular manufacturing makes them an exciting prospect for future generations. If the technology evolves, they could be used to aid the surgical removal of a tumour and they could also burrow into a tumour and destroy it using heat. The possibilities are quite remarkable, and medicine will develop in various ways with such molecular machines.

There is however, a question to be asked, how will the body respond to the nano-particles? We do not yet know how exactly our immune systems will respond to such foreign materials that are proposed here. Our bodies may choose to attack the nano-particles and structures, which could itself create a whole new dimension of problems as the particles would not be easily destroyed. Such complications may be conquered by possibly incorporating some sort of signal or DNA into the nano-particles, which would tell the body that they are not harmful.

Despite all of the multiple benefits nanotechnology will undoubtedly bring to medicine, there are ethical issues that arise. The technology of the future may well be able to detect the simplest and minute changes in the body; these will make the doctors pause and think about what these changes could mean. Ultimately we will have to reconsider what it means to be healthy and what is classed as disease.

Physical enhancements could obviously be achieved with nanotechnology; however there are many points to consider as to whether it is right or wrong. It will be desired mostly in the realm of sport, where physical capacities such as strength, stamina, coordination etc. can be boosted. The argument here is that physical enhancement does not comply with the 'spirit of sport'. These enhancements however, could be used when a patient is recovering from a serious illness or injury, but some people and some religions deem it wrong for us to meddle in the mechanics and composition of the body.

Nevertheless, nanotechnology is an increasing area of research and development that will ultimately lead to many benefits to the medical world, and in particular to the treatment of cancer.

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