

Exploring Ethical Issues and Advancements in the Latest Research
into Nanotechnology for the Prevention, Detection, Diagnosis and
Treatment of Cancer

BY

MARY WHEELER

NAVID MOGHADDAS

PASS

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ABSTRACT

Cancer has been an untreatable disease for a very long time, but recently, due to the advances in nanotechnology new methods of prevention, detection, diagnosis and treatment are available. This paper will explore these new medical advances, and give our individual views about their application. The background of this paper is taken from sources drawn mainly from the internet, and this paper highlights as much of the current, future and previous research as possible. The central idea was to express how nanotechnology can be applied to the medical implications of cancer. Some of the problems that will be addressed are the issues concerning the treatment of the disease. Some ethical issues will also be discussed.

INTRODUCTION

Nanotechnology has had an increasing role in medical practice in recent years. In the area of cancer research this has led to the development of nanodevices such as the gold nanoparticles are currently being used for the early detection of lung cancers, among other things. Also used are nanoshells (see figure 1), cantilevers and nanowires (see figure 2). For

further reference, one can look at the work of Shuming Nie, PhD, who has written substantial articles about this.

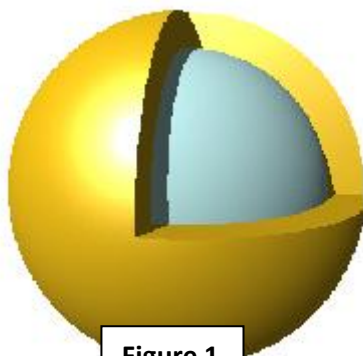


Figure 1

Cancer is a disease where fatalities are less likely, the earlier the disease is detected, diagnosed and treated. Once the cancerous cells have grown to form more easily noticeable tumours and possibly spread around the body, it becomes much more difficult to isolate the cancerous cells and remove them, and a great deal of damage to a body can occur very quickly.

Nanotechnology is the controlling, engineering and development of matter on the atomic scale. One nanometre is equivalent to one billionth of a metre, and therefore these particles are small enough to enter individual cells.

Cancers can occur in any part of the body and can affect any age. On the positive side it is a non-contagious disease. Cancer itself occurs when mutations occur in DNA replication, usually when they are being replicated for growth and repair. These new cells then undergo mitosis uncontrollably which leads to large masses of tissue due to the faster rate of growth. This is called a tumour. There are two types of tumour, benign and malignant. Benign tumours don't spread through the body and are therefore not cancerous. When removed they will not grow back. Malignant tumours, on the other hand, are cancerous and can still reappear in other parts of the body after removal. This is done through the blood vessels. We will be dealing mostly with the second type of tumour in this paper. There are certain

symptoms for cancer which include weight loss, fatigue and fever but these are general. Also can only be seen far too late, when the cancer has developed into an advanced stage.

There are so many things which one could do to significantly reduce your chances of getting cancer. These include more exercise, stop smoking and eating healthily. The sheer number of people who ignore such a message even with the obvious evidence is the main reason we are developing so many cancers and that is why there is so much pressure for new treatments. From 1930 to 2002 there was an increase in deaths due to cancer in the US. In 2003 this number

dropped slightly. We don't think this is due to better treatment of prevention only but another factor could be that people are dying of other diseases while having cancer so it isn't counted statistically as a death due to cancer.

One thing to remember is that not all cancers are caused due the above stated reason. There are cancers that

have a hereditary genetic cause. In such cases prevention is not possible within the field of nanotechnology at this current stage.

Nanoparticle-based delivery systems	Therapeutic and diagnostic uses
Liposomes	Controlled and targeted drug delivery; Targeted gene delivery
Polymeric Micelles	Controlled and targeted drug delivery
Nanosystems	Tumor targeting
Nanoshells	Tumor targeting
Fullerene-based Derivatives	As targeting and imaging agent
Carbon Nanotubes (CNTs)	Drug, gene and DNA delivery; Tumor targeting
Dendrimers	Targeted drug delivery
Quantum Dots (QDs)	As targeting and imaging agent
Gold Nanoparticles (GNPs)	Targeted delivery and imaging agent
Solid Lipid Nanoparticles (SLNs)	Controlled and targeted drug delivery
Nanowires	As targeting and imaging agent
Magnetic nanoparticles	As targeting and imaging agent

Figure 2

DISCUSSION

Before this paper begins to explore the possibilities of the use of nanotechnology in medicine, it is important to consider the ethical issues as well as the practical issues.

ETHICAL ISSUES AND CONCERNS

Some ethical issues arise when nanomaterials are sold in the form of cosmetics, because consumers are unaware of the nanodevices used, and currently there is no law that states that these products must be reviewed, and so in some instances health and safety is

compromised. To prevent this it is important that consumers are aware, and this would be made possible by the review of products by the Food and Drug Agency (FDA) and other private agencies.

Discussing the ethical issues of nanotechnology in general is not possible, as there are so many different applications of it, and so many different diseases treated by it; therefore each one should be considered separately. It is debateable whether someone who has been enhanced or treated using nanodevices is still the same person, or even human. This is because nanoparticles are foreign to the body, and thus need to be able to conceal this from the body, so that it does not initiate an immune response and the production of antibodies. Does the presence of man-made nanotechnology in the body make the person any less human?

Some Christians are against the use of nanotechnology, as they consider the controlling of atoms to be 'playing God'. They believe that God has a plan for everyone, and by the introduction of nanomaterials this is going against God's plan for humanity. In the United Kingdom 54.1% of people find nanotechnology morally acceptable. To us this number seems low, possibly because in France, in contrast, 72.1% of people find it acceptable. On the other hand, only 29.5% of Americans agree with its use. It is possible that this is related to religious beliefs, as 78.4% of Americans are Christian. In the United Kingdom it is less biased and could change to become more religion-orientated or the opposite in the future.

Ethical concerns include how nanotechnology's incredibly small scale makes it difficult to control and trace the particles. The size of the nanoparticles means that regulating and managing them can be problematic; however, this is likely to be overcome in the near future as research progresses. We believe that in the future it may be possible to detect the number of cancer cells killed by nanotechnology, so that it is possible to gauge their effectiveness. In addition, it may become possible to calculate more precisely the number of nanodevices required in order to overcome the cancerous cells, so that less are wasted, although it would still be necessary to introduce more nanodevices into the body than are exactly required, in case some got lost in transportation or malfunctioned.

This country may seem advantaged in the development of nanotechnology, as it has more money and is able to fund more research into these areas. However, lesser economically developed countries (LEDCs) lack this funding. Money could be saved if fewer nanodevices were lost (if the process was made more efficient and accurate, as discussed above) and this money could be used towards researching and using more nanotechnology in LEDCs to help prevent, diagnose and treat cancer.

16 million new cases of cancer are predicted to develop by 2020, of which 70% will occur in developing countries. This shows that developing countries need new research more

urgently than developed countries, as the use of new research in nanotechnology in developed countries is reducing the number of cancer cases so dramatically. This gap between scientific knowledge in developing countries and LEDCs is commonly known as the 'nanodivide', and needs to be abridged. One third of cancers affecting the developing world are potentially preventable and another third treatable if detected early. Providing them with funding will enable them to reach this potential.

Another ethical concern is the potential of failure of the nanodevices to function properly; for example, leading to healthy cells and damaging them in such a way that an organ or tissue is no longer to function as effectively. This could lead to a decreased lifespan or other serious consequences.

Malignant tumours can just grow back. So are we not just wasting our time and money by "treating" people with this form of tumour when those with benign tumours could be cured easily? We need to make sure the nanodevices we use not only eradicate some of the cancerous cells but all of them.

PREVENTION

"Prevention is better than cure." - Desiderius Erasmus

The prevention of cancer using nanotechnology is possible, and being able to completely prevent cancer in the future is something we should be aiming for. Currently, researchers in the field of nanotechnology are capable of preventing the disease; however, there have been issues regarding the safety of prevention methods, as the person at risk would need to take the chemopreventive agent on a regular basis for a long time, for it to have the desired effect.

A research team in Wisconsin used nanoparticles to load biocompatible polymer nanoparticles with epigallocatechin - 3 - gallate (EGCG), a naturally occurring molecule with chemopreventive properties, to make it almost ten times more effective. This made it possible for it to be used in clinical practices, as it was sufficiently chemopreventively active to negate the effects of the body's rapid degradation of the compound.

Current research has shown that nanoscale devices are able to deliver cancer prevention agents that are able to act within specific cells or organelles at risk of developing the disease. One such nanoscale device is capable of holding tens of thousands of small molecules.

Scientists are working on designing multicomponent anticancer vaccines using nanoscale delivery vehicles, and on developing nanoscale devices that can deliver these cancer preventing agents. Such devices already exist, but they are still limited by a lack of accuracy,

which is significant, as it is important that the molecules are released into only the target cells or organelles where they are required.

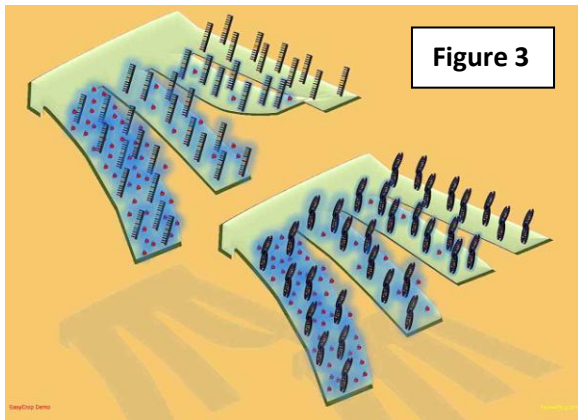
Nanoparticles made from solid lipids are also currently undergoing research; these are called SLN particles. They may have potential in both cancer prevention and therapeutics.

DIAGNOSIS AND DETECTION

Firstly, when cancer cells multiply by mitosis they lead to a tumour forming. When this primary tumour has grown, cells start breaking off it and circulate in the blood stream. Hence the name circulating tumour cell (CTC). These CTCs have the potential to start tumours in other parts of the body by a process called metastasis.

The detection of these CTCs was initially by antibodies with a complementary shape to the antigen on the CTCs. The problem was that white blood cells had a similar shape and therefore were falsely identified as CTCs. Therefore the polymer-coated and dye studded nanoparticles were linked to an epithelial growth factor peptide (EGP) rather than an antibody. Then the epithelial growth factor receptors (EGFR) on the tumour cells can bind to this causing due to the vast numbers of these on the cell surface membranes. This is particularly for head and neck cancer.

Cantilevers can be used to detect cancer. They are flat platforms which antibodies can attach to and can detect single molecules of DNA and therefore be able to recognise the



gene (as shown in figure 3). This can occur as the cancer cell releases proteins which are complementary to the antibodies. These nanoscale cantilevers are very useful as they can produce immediate results.

Currently, the imaging methods used widely in hospitals are only able to detect cancers once they have made a fairly significant change to a tissue. By the time the cancer has been detected by these methods, enough damage has been done – thousands of cells will have been mutated and affected. In addition, once the change to the cells has been identified, a biopsy must be performed to obtain a sample of the affected tissue, in order for the disease to be confirmed. This means that a large number of cells must be removed, and invasive surgery is required.

Replacing all of the imaging machines in hospitals would take a long time and be extremely

expensive – instead, it would be more effective to use nanoparticles, injected into the body, which could correlate with the scanning equipment already readily available in hospitals.

This has already been thoroughly investigated, and it is thought that nanoparticles which produce a high contrast signal on Magnetic Resonance Images or Computed Tomography scans would be particularly useful, as they could be used combined with specific antibodies that attach to antigens found more commonly in cancerous cells. When the antibodies and nanoparticles bound to cancerous cells they would light them up for the scanner, and make it easy and quick to spot any cancerous cells in the body.

We believe that using this method to diagnose cancer would be extremely effective, and could save lives, as it would allow the diagnosis to take place before any significant effects of cancer could otherwise be seen. By the time that cancer can usually be diagnosed, too many cells have been proliferated for the cancer to be easily treated, and some cancerous cells may have metastasized, making the cancer even more serious. Through the use of nanotechnology, cancerous cells will be highlighted, which doctors would be unable to detect through the use of conventional scanning methods.

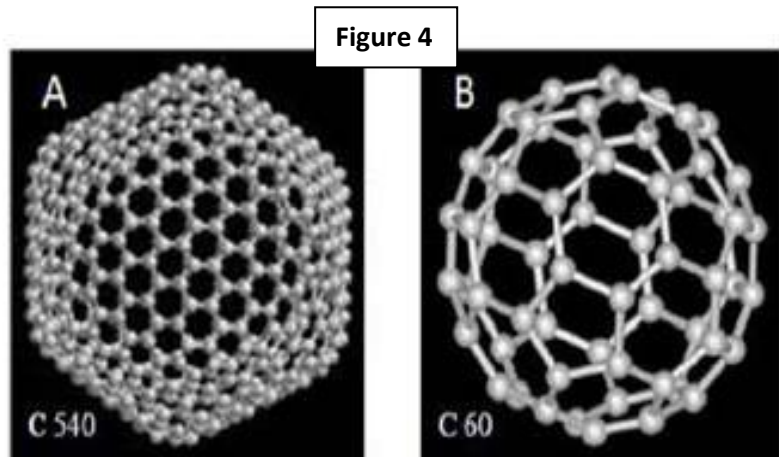
However, while the usage of nanotechnology for the enhancement of cancer screening seems flawless at first, it is not a simple solution. There are many different types of cancer, and so many different biomarkers may need to be detected simultaneously in order to identify a cancer able to be treated. Antibody-coated quantum dots could be used to screen for different types of cancer; these would allow specialists to be able to identify individual cancers depending upon the range of colours shown in the spectrum when scanned. Unfortunately however, under some conditions quantum dots can become cytotoxic, which would make them unsafe. Scientists are currently working to extend their potential, and this paper suggests the modification of quantum dots by PEG glycation and encapsulation, as this may be capable of limiting their cytotoxicity.

TREATMENT

Nanoshells (see figure 1) can be injected into the blood stream and have the potential to kill cells. But you don't want to damage all the cells, just the malignant ones! Therefore they need to be able to detect the difference between the two. They do this by enhanced permeation retention (EPR) and covering the nanoshells with certain antigens. Once they bind with the cancer cells the next step can happen which is to provide energy. This can be in many forms including mechanical, radio frequency or optical. The nanoshells absorb this heat which in turn heats the cancer cells which are killed as any proteins are denatured – therefore the DNA is affected and the cell cannot control anything!

This same idea can be used with different particles. For example one of the tumour killing agents is called tumour necrosis factor alpha (TNF) and there is a Thiol-derivatized polyethylene glycol (PEG-THIOL) both of which attach to a golden nanoparticle. The latter of these hides the molecule from the immune system so it isn't recognised as foreign. One of the heating methods is using a nanoparticle called Auroshell. Also a nanoparticle called nbtxr3 is activated by X-rays which cause it to release electrons which attach to the cancer cells.

Another method is sending coded information to the cancer cells in the form of ribonucleic acid (RNA) which contains information to halt the progression of the cancer. These particles are small enough to be able to pass straight through the plasma membrane yet big enough to carry strands of RNA within them. Scientists in Purdue University have developed such a nanoparticles and performed positive experiments on mice. They also formed their own bacteria-killing virus (phi29) from strands of RNA which mimic its function.



'Bucky Balls', or fullerenes, are also undergoing

Fullerene-based derivatives; (A: fullerene C540, B: fullerene C60).

research, as their cage-like structure is ideal for attaching anticancer agents, and they have a high stability, which makes them both unique and ideal for safely delivering the toxic substances required to kill tumours to the areas required. (as shown in figure 4).

CONCLUSION

To summarise this paper, it has included specific information about the disease cancer, and it shows the research we have done into the previous, current and future developments concerning the use of nanotechnology and methods available to prevent, detect and treat it. We have discussed the use of nanodevices, and the potential medical research and advances in their use have for medicine. In addition, this paper has considered the ethical issues and concerns involved, as these are so vital in the advancements of new technology.

In the future, we believe that nanotechnology will revolutionise medicine. However, there are a number of problems that have yet to be overcome; for example, scientists still struggle

to be accurate enough while working at the atomic scale. We believe that these problems will not be overly significant, as every year individual countries alone spend millions of pounds on cancer research, a large proportion of which has recently been focused on the use nanotechnology. In the United States, in 2009, the National Cancer Institute (NCI) alone spent in excess of \$311 on cancer research.

As scientific knowledge concerning the practice and the use of nanotechnology in the treatment of cancer becomes more common, it is likely that in the future it will be less opposed by religions and other organisations, as it becomes clear how significant it could be in the saving of lives. For example, this paper suggests the use of epigallocatechin - 3 - gallate (EGCG) for the prevention of the disease; if those particularly at risk of contracting the disease were able to gurantee it's prevention, millions of lives could be saved, and less money and fewer resources would be required to treat cancer, as fewer people would develop the disease in the first place. Scientists are currently using nanoparticles to make these chemicals stay in the body for longer before they are degraded; once this research is complete, it will be possible to completely prevent the mutation of cancerous cells.

In this paper, we have also discussed the use of quantum dots, as a method of detecting cancerous cells before they have grown significantly, and explained the problems involved with this. We have suggested that these quantum dots are modified using glycation and capsules to limit their possible toxicity. In addition, the different types of nanodevices have been explained, along with their individual potentials, in relation to medicine.

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